



## Special Issue about Competing Risks and Multi-State Models

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### Abstract

There is a clear growing interest, at least in the statistical literature, in competing risks and multi-state models. With the rising interest in competing risks and multi-state models a number of software packages have been developed for the analysis of such models. The present special issue of the Journal of Statistical Software introduces a selection of R packages devoted to competing risks and multi-state models. This introduction to the special issue contains some background and highlights the contents of the contributions.

*Keywords:* competing risks, multi-state models, R.

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### 1. Introduction

Survival analysis deals with the statistical analysis of the time to the occurrence of an event like death, relapse, or graft failure. Often, in the disease or recovery process of a patient, multiple types of events can occur. These different events may be mutually exclusive or may occur sequentially. The first instance is called competing risks, the second a multi-state model. Significant improvements in information technology, culminating in the Electronic Patient File, have made it common standard to record detailed information on a variety of clinical events on large numbers of patients. The resulting increase in information on different types of clinical events has caused a clear growing interest in competing risks and multi-state models. However, with a few happy exceptions, theoretical study and application of multi-state models in the medical literature has been limited to statistical journals. Correct application of competing risks models in the medical literature is slowly growing more common, although one still frequently sees the misuse of one minus Kaplan-Meier estimates where cumulative incidences should be reported.

There are at least two reasons for the disappointing dissemination of competing risks and multi-state models in the applied literature. The first is that these methods are considerably

more advanced than standard survival analysis, which can be an obstacle both for the applied researcher and for the target journal. (It could even be true that researchers are not actually aware they can or perhaps should pose questions that ask for a multi-state model approach.) The second reason is the idea that there is a lack of good software for the analysis of competing risks and multi-state models. This might have been the case until say three years ago, but with the rising interest in competing risks and multi-state models a number of software packages have recently been developed for the analysis of such models. It is the aim of this special issue of the Journal of Statistical Software to bring these packages to the attention of both statisticians and applied researchers.

Both the introduction and the contributions to this special issue are biased towards medical applications. I am entirely to blame for this bias. Nevertheless I am confident that readers from other fields like demography, geology, and econometrics will be able to judge the usefulness of the methods and the software introduced and discussed in this special issue.

## 2. This issue of the Journal of Statistical Software

The special issue contains seven papers, all of them dealing with R packages (or objects within R packages). The first contribution by [Scheike and Zhang \(2011\)](#) is the only one specifically devoted to competing risks models. It illustrates how the **timereg** package can be used to perform a wide range of direct regression methods of [Scheike, Zhang, and Gerds \(2008\)](#) among others, with possibly time-varying covariate effects on the cumulative incidence function.

The remainder of the papers are devoted to multi-state models, although many of the packages consider a general class of multi-state models which contain competing risks as a special case. The contribution by [Meira-Machado and Roca Pardiñas \(2011\)](#) illustrates the **p3state.msm** package. The software can be used for forward-going multi-state models with a single starting and end state. It implements the methods of [Meira-Machado, de Uña Álvarez, and Cadarso-Suárez \(2006\)](#) that do not rely on the Markov assumption. The contribution by [Allignol, Schumacher, and Beyersmann \(2011\)](#) illustrates the **etm** package. It can be used for non-parametric estimation of transition probabilities in general Markov multi-state models. Next are two companion contributions by [Plummer and Carstensen \(2011\)](#) and [Carstensen and Plummer \(2011\)](#). The first of these illustrates **Lexis** objects, part of the **Epi** package, and shows how these objects can be used to study data with multiple time scales. The second paper shows how **Lexis** objects can be used in multi-state models. It shows how the analyses in the tutorial of [Putter, Fiocco, and Geskus \(2007\)](#) can be performed using **Lexis** objects and enhanced using Poisson modeling. The contribution by [de Wreede, Fiocco, and Putter \(2011\)](#) is a sequel to [de Wreede, Fiocco, and Putter \(2010\)](#). The latter paper lays down the theoretical basis of the methods implemented in **mstate**, including estimation with standard errors of transition probabilities in both non- and semi-parametric Cox models. The contribution in this issue illustrates the use of **mstate** in a concrete elaborate example. The **msm** package features in the last contribution by [Jackson \(2011\)](#). It is the oldest R package for multi-state models. It differs from the other packages featuring in this special issue in that it is based on parametric models (exponential and piecewise exponential) rather than the non- and semi-parametric models underlying the other packages. These parametric assumptions make it possible to analyze panel data, where the multi-state model is not observed continuously, but where the multi-state model is observed at a discrete set of time points. The possibility of state misclassification can also be incorporated in **msm**.

Let me close with expressing the hope that with the publication of this special issue we will see many more successful applications of competing risks and multi-state models, in the medical literature and beyond.

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