

Instructions to users:

1. For a proper use we recommend the use the R version R1.9.1 (you can download it from <http://cran.at.r-project.org/>) or in our Web page. In this way you can avoid problems with changes in R. You can also use previous releases of R such as R1.6.2, R1.7.1 or R1.8.1. Note that you can have more than one R version installed in your computer.

2. Download the msm compressed ZIP file (msm.zip) from our Web page. Select (You must have the msm.zip file in your computer to do this):

```
Package(s)<-Install packages from local zip files...<- msm.zip
```

3. Download the ZIP file “The R library” which contains the Workspace file (tdc.msmLast.RData) from our Web page (which contains the tdc.msm code). Unzip this file and save in your computer.

4. Open the R (version R1.9.1) and load the workspace tdc.msmLast.RData:

```
File<-Load Workspace...<- tdc.msmLast
```

5. In order to make an accurate test of the software you can download the well-known Stanford dataset (stanford.txt). You can read more about these datasets below. To introduce these datasets in R you can use the read.table function.

For the following sessions you only need to execute 4.

Please be careful with missing data. You can avoid the missing data using:

```
myowndata<-na.omit(myowndata).
```

Comments on the Stanford dataset:

This data set, available in Crowley and Hu’s article¹, covers the period from October 1967 until April 1, 1974. Some patients die before an appropriate heart is found. Of the 103 patients, 69 received a heart transplant. The number of deaths was 75; the other 28 patients contribute with censored survival times.

The input data file ‘stanford’ contains the available information about these patients. For each individual, an indicator of its final vital status (censored or not), the survival times from the entry of the patient in the study (in days), and a vector of covariates including age at acceptance, year of acceptance, previous surgery (coded as 1= yes; 0 = no), and transplant (coded as 1= yes; 0 = no) were recorded. The covariate transplant is the only time-dependent covariate, while the other covariates included are fixed.

In the context of multi-state modelling², we may consider the covariate ‘transplant’ as an associated state of risk, and then use the progressive illness-death model of Figure 2. In this model, ‘own heart’ corresponds to having his/her own heart, whereas ‘new heart’ represents having had a transplant. With this multi-state formulation of the Stanford data, main goals of this study include: (a) to assess whether or not a beneficial effect of heart transplant on survival exists. This can be carried out by comparing the transition intensities $\alpha_{13}(\cdot)$ and $\alpha_{23}(\cdot)$; and also (b) to explore the potential fixed covariate effects in each of the transitions.

Although the Stanford dataset requires a multi-state model with only two transient states (see Figure 2), the software we offer can be used in more general situations, which can be formulated by the model represented in Figure 1.

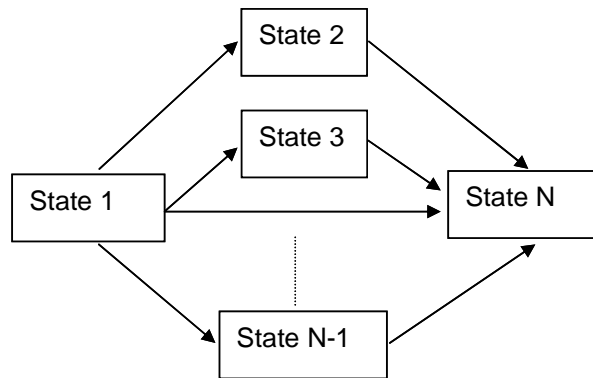


Figure 1. Extended illness-death model.

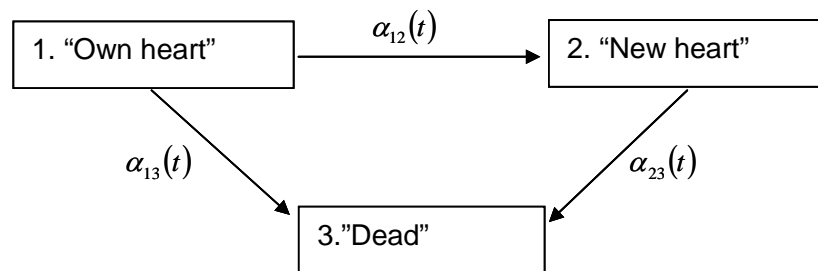


Figure 2. Illness-death model for Transplant Heart Data.

Examples of commands using the above dataset:

```
tdc.msm(stanford, formula=c(6,7,8), models= "ALL", cut=60)
tdc.msm(stanford, formula=c(6,7,8), models= "ALL", graphcov=2, cut=60)
tdc.msm(stanford, formula=c(6,7,8), models= "CMM", graphcov=1)
tdc.msm(stanford, formula=c(6,7,8), models= "HMM", surv.plot=T)
tdc.msm(stanford, formula=c(6,7,8), models= "NHM", cut=60)
tdc.msm(stanford, formula=c(6,7,8), models= "CSMM")
tdc.msm(stanford, formula=c(6,7,8), models= "NPM", plot.trans=T, surv.plot=T)
tdc.msm(stanford, formula=c(6,7), models= "TDCM", surv.plot=T, graphcov=2)
```

Best regards,
Luís Machado

References:

1. J. Crowley, M. Hu, Covariance Analysis of Heart Transplant Survival Data, *Journal of the American Statistical Association* 72 (1977) 27-36.
2. P.K. Andersen, O. Borgan, R.D. Gill, N. Keiding, *Statistical Models Based on Counting Processes*, Springer, New York, 1993.
3. C.H. Jackson, L.D. Sharples, Hidden Markov models for the onset and progression of bronchiolitis obliterans syndrome in lung transplant recipients, *Statistics in Medicine* 21 (2002) 113-128.