An analysis of the recurrence–progression process in bladder carcinoma by means of joint frailty models

C. Santamaría, B. García-Mora, G. Rubio, S. Luján

1. Introduction

In recent years, there has been a growing interest in studying processes which generate events repeatedly over time such as recurrent infections in AIDS patients [1] and the process recurrence–progression in bladder carcinoma [2] among others. In this regard, several modeling approaches have been proposed to analyze this type of data [3] where the interest centers on the effect of covariates on the failure risk.

The general framework is the survival analysis area. Survival analysis is a set of statistical tools to analyze data related to times from an origin time until the occurrence of some or other event. The period of time from the start point to the event is the survival time, represented by a nonnegative random variable \( T \) for each individual. Generally two functions are of central interest: the survival function and the hazard function. The survival function \( S(t) \) is the probability that survival time \( T \) be greater than \( t \), \( S(t) = P(T > t) \), and the hazard function is the instantaneous probability of event at time \( t \) per unit time, given survival up to time \( t \). On the other hand, if the event of interest is not observed during the follow-up period the survival time is censored. It is usually required that survival time be independent of the censoring mechanism, that is to say, the follow-up of the individual is interrupted by causes independent of the event. Otherwise, the censoring is named informative.

When the event of interest occurs repeatedly in the same subject, a correlation between the recurrent relapse times may exist due to either heterogeneity among individuals or event dependence. Heterogeneity is produced because some subjects have a higher (or lower) event rate than the other ones, due to unknown or unmeasurable effects such as, for example...