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Nonparametric tests for cause specific hazard rates with censored data for competing risks among several groups

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Abstract

For the competing risk setting where the lifetime data are due to one of several distinct and exclusive causes, comparison of cause-specific hazard rates is of interest to researchers. In this paper we survey existing methods for related tests and provide a new test for a common overall rate for all causes and groups. Tests given in the literature for checking for a common rate for causes and a common rate for the groups are shown to be in the same framework as the proposed test for common overall rate. Asymptotics are shown to follow a common theme for each test. An extensive numerical and graphical investigation and an example are presented to substantiate the proposed methods.

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1. Introduction

In many medical and engineering studies, lifetimes of individuals or items are measured. In these applications there can be more than one failure mechanism, commonly called as

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competing risks. In addition, individuals or items can be grouped according to some criteria. It is then important to recognize whether the life distributions have significant differences due to different risks and/or groups. For example, a medical researcher may be interested in survival times of patients with multiple diseases who belong to different ethnic backgrounds (white, black and Asian). Here the 'death' can occur due to several possible causes (stroke, diabetes, heart failure, etc.) where the causes are not necessarily independent. This type of data can be represented in the following general form.

Let X_{ik}^0 be the continuous failure time of the ith subject in the kth group where $i=1,\ldots,n_k$ and $k=1,\ldots,K$. The cause of failure is denoted as δ_{ik}^0, where $\delta_{ik}^0 \in \{1,\ldots,J\}$. We assume that the pairs $(X_{ik}^0, \delta_{ik}^0)$, for each i and k, are independent. The underlying failure mechanisms leading to different causes can be dependent for each subject. It is further assumed that each X_{ik}^0 can be right censored by a random variable U_{ik}, where U_{ik} are assumed to be independent and identically distributed (iid) and independent of $(X_{ik}^0, \delta_{ik}^0)$ for each i,k. Thus, in general, one observes $X_{ik}=\min(X_{ik}^0, U_{ik})$ and $\delta_{ik}=\delta_{ik}^0 I[X_{ik}^0 \leqslant U_{ik}]$, $i=1,\ldots,n_k$, $k=1,\ldots,K$, where $I[A]$ is the indicator function of an event A.

The cause-specific hazard rate (CSHR) for cause j in group k is defined as

$$\alpha_{jk}(t)=\lim_{h\to 0}\frac{\mathrm{P}[t\leqslant X_{ik}^0<t+h,\,\delta_{ik}^0=j\,|\,X_{ik}^0\geqslant t]}{h}.$$

The cumulative incidence function (CIF) for failure corresponding to cause j in kth group is given by

$$F_{jk}(t)=\mathrm{P}[X_{ik}^0\leqslant t,\,\delta_{ik}^0=j]$$

(Kalbfleisch and Prentice, 1980). In cases where X_{ik}^0 and δ_{ik}^0 are independent for $i=1,\ldots,n_k$, F_{jk} are the marginal cdf's of X_{ik}^0, and α_{jk} are the corresponding failure rate functions. We assume that the F_{jk} are continuous and have derivatives f_{jk} with respect to canonical measure so that

$$\alpha_{jk}(t)=\frac{f_{jk}(t)}{S_k(t)},$$

where $S_k(t)=1-\sum_{j=1}^{J}F_{jk}(t)$ denotes the survival function for subjects in group k. We will assume that ties occur with zero probability.

In survival studies where the observed datasets are above type, scientists face the following natural questions:

(a) Are there differences in the CSHR between cause and group pairs? (i.e., are all α_{jk} the same?)
(b) Are there differences between groups?
(c) Are there differences between causes?

The latter two questions have been discussed by several authors under various circumstances. There is no literature that addresses the first question. Our goal in this paper is to survey the methods that are available for questions (b) and (c) above and develop a direct test for the first. Alternatively, one may examine the equality of all CSHR's by way of