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Computational Statistics & Data Analysis 50 (2006) 3165–3178
COMPUTATIONAL STATISTICS & DATA ANALYSIS
www.elsevier.com/locate/csda

Logrank-type tests for comparing survival curves with interval-censored data

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Received 22 July 2004; received in revised form 22 June 2005; accepted 23 June 2005
Available online 19 July 2005

Abstract

We propose logrank-type tests for comparing several survival functions from interval-censored data. The proposed tests do not require use of the so-called EM algorithm because we introduce uniform weights that depend only on the size of the risk set at each observed time instead of the weights involving estimated survivals. This technique reduces computation time. As alternatives for the estimated asymptotic variance of a proposed test statistic, we introduce estimates that mimic the logrank test and the multiple imputation method. Results from simulation studies show that our proposed tests are very satisfactory in terms of size and powers. We illustrate the proposed tests with breast cosmesis data from Finkelstein and Wolfe [1985. Biometrics 41, 933–945] and lung cancer post-operative data from the Yonsei Cancer Center in Korea.

Keywords: EM algorithm; Lung cancer post-operative study; Multiple imputation; Score test

1. Introduction

One complication that arises in the analysis of failure time data is that the event of interest may not be observed in all subjects. In a longitudinal study or clinical trial with periodic follow-up, a subject may be monitored weekly for the occurrence of an event defined by

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doi:10.1016/j.csda.2005.06.014

a clinically observed change of status. If the participant misses a scheduled visit for a few weeks and returns in a changed status, then the event time is considered interval-censored; we only know that the event occurred within the interval of time between clinic visits.

We provide two examples of interval-censored observations. The first is from a retrospective study of 96 early breast cancer patients designed to compare radiation therapy alone versus radiation therapy followed by chemotherapy with respect to time to the appearance of breast retraction. This data set has been used by several authors, e.g., Finkelstein and Wolfe (1985). The second example compares two post-operative treatments for lung cancer with respect to time until an onset of relapse. Fifty-eight patients who underwent partial or total lung cancer resection from September 1990 to September 1994 in the Yonsei Cancer Center were randomly assigned to radiation therapy or to a combination of radiation and chemotherapy. Some patients missed their scheduled visits and returned after having a relapse of lung cancer. For those patients, it is known only that the onset of relapse has occurred between the last two visits.

Turnbull (1976) proposed a generalization of the Kaplan–Meier estimator (Kaplan and Meier, 1958) using a self-consistent algorithm for the interval-censored data. This estimator can also be constructed using an EM algorithm (see Dempster et al. (1977)). Sun (1995, 1997a) extended Turnbull's algorithm to doubly interval-censored data. In addition, the tests for comparing survival functions from interval-censored data have been developed. Finkelstein (1986) discussed the fitting of the proportional hazards regression model to interval-censored data, and derived a score test for the comparison of several survival curves. Sun (1996, 2001) and Zhao and Sun (2004) proposed nonparametric tests for discrete interval-censored failure time data, which is a generalization of the logrank test for right-censored data. Sun (1997b) proposed a score method based on a discrete logistic model for the regression analysis of interval-censored data with a focus on the comparison of different treatments. Regarding Finkelstein's and Sun's score tests, if there are many time intervals, the observed Fisher information matrix of an estimate for the asymptotic variance of the test statistic may often have a high dimension. Consequently, we should use a generalized inverse rather than an ordinary inverse. However, this could result in unstable variance estimates. As indicated in Zhao and Sun (2004), Sun's nonparametric tests cannot be reduced to the ordinary logrank test for right-censored data and could overestimate the size of the risk set and the number of deaths at a specified time.

In Section 2, we propose a new test procedure that can test survival functions in the presence of interval-censored data. Our tests are computationally simpler and faster than those reviewed because the tests do not need an estimation of survival function using an EM algorithm. Moreover, the proposed tests can be reduced to the logrank test with no bias on risk and death sets for right-censored data. In Section 3, we perform simulation studies to investigate the properties of our proposed tests in terms of size and powers. Finally, we illustrate the proposed tests with the examples mentioned above.

2. Logrank-type tests

Let $T_{il} > 0, i = 1, \ldots, n_l, l = 1, \ldots, p(> 2)$, denote the failure time for the ith subject in the lth population. We assume that the failure times T_{il} are interval-censored. That is, for the