A spline-based nonparametric analysis for interval-censored bivariate survival data

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Abstract: In this manuscript we propose a spline-based sieve nonparametric maximum likelihood estimation method for joint distribution function with bivariate interval-censored data. We study the asymptotic behavior of the proposed estimator by proving the consistency and deriving the rate of convergence. Based on the sieve estimate of the joint distribution, we also develop an efficient nonparametric test for making inference about the dependence between two interval-censored event times and establish its asymptotic normality. We conduct simulation studies to examine the finite sample performance of the proposed methodology. Finally we apply the method to assess the association between two subtypes of mild cognitive impairment (MCI): amnestic MCI and non-amnestic MCI, for Huntington disease (HD) using data from a 12-year observational cohort study on premanifest HD individuals, PREDICT-HD.