Survival Models with a Cured Fraction: A Zero-Inflated Gamma Frailty–Copula Approach

Masaki Hino[1,2], Takeshi Emura[3,4], Shogo Kato[1]

[1]*The Institute of Statistical Mathematics*

[2]*The Graduate University for Advanced Studies, SOKENDAI*

[3]*School of Informatics and Data Science, Hiroshima University*

[4]*Biostatistics Center, Kurume University*

ABSTRACT

We introduce a zero-inflated gamma frailty copula model to analyze dependent survival times in the presence of long-term survivors. Existing cure frailty copula approaches typically model frailty as a discrete random variable with a mass at zero, so that survivors are naturally represented by zero frailty. While this captures the cured fraction, it offers limited flexibility for modeling continuous heterogeneity among susceptible individuals. By combining a point mass at zero with a continuous gamma component, our construction simultaneously represents long-term survivors and heterogeneous frailty within a copula framework.

The proposed bivariate survival function can be represented as a mixture distribution that depends on whether each subject is cured or not. To estimate the parameters under this mixture structure, we employed both an expectation–maximization (EM) algorithm and a Newton-type algorithm within the zero-inflated gamma frailty copula framework. Numerical experiments indicate that these approaches yield maximum likelihood estimators that provide reasonable estimates of the model parameters. Finally, application to a real clinical dataset demonstrates how the proposed model can effectively capture both the cured fraction and the dependence structure of paired survival times.

Keywords: cure model; zero-inflated-gamma distribution; frailty-copula model; EM algorithm

Mean Residual Life Based Illness-Death Model for Semicompeting Risks Data

Huang Rui, **Liming Xiang**

School of Physical and Mathematical Sciences, Nanyang Technological University

ABSTRACT

Semicompeting risks data are available in many studies, where a nonterminal event (e.g., disease progression) is of interest and may be censored by the occurrence of a terminal event (e.g., death). The illness-death model has been developed as a common approach for regression analysis of such data by modelling transitions between three states using the proportional hazards or accelerated failure time model. In this work, we propose an illness-death model formulated using the mean residual life function, offering a straightforward and interpretable modelling framework for state transitions in the semicompeting risks setting. We facilitate estimation through novel estimating equations derived from a penalized quasi-likelihood approach incorporating inverse probability weighting. Unlike the conventional illness-death model assuming a shared gamma frailty, our method requires no distributional assumption on the latent frailty term, thereby reducing the risk of model misspecification. Simulation studies demonstrate its promising performance in across a range of realistic scenarios and an application to a myeloma progression study illustrates its practical utility.

Keywords: Buckley-James estimate; Conditional inference; Dependent censoring; Inverse probability of censoring weight; Quasi-likelihood function

H-Likelihood Approach on the Joint Frailty Model for Clustered Bivariate Survival Data

Jihoon Kwon[1], Jia-Han Shih[2], Takeshi Emura[3], **Il Do Ha[1]**

[1]*Department of Statistics & Data Science, Pukyong National University, Busan, South Korea*

[2]*Department of Applied Mathematics, National Sun Yat-sen University, Kaohsiung, Taiwan*

[3]*School of Informatics and Data Science, Hiroshima University, Hiroshima, Japan*

ABSTRACT

Recently, clustered survival data have been extensively studied using various correlated modelling approaches, such as frailty models and copula models. These data can take several forms, including bivariate censored data, semi-competing risks data, and competing risks data. Traditionally, each type has been analyzed using a separate model. In this talk, we propose a unified joint frailty modelling approach which is capable of handling all three types of clustered survival data within a single model-based likelihood framework. Here, the unknown baseline hazards in the joint frailty models are modeled based on a cubic M-spline basis function that does not require a specific parametric form. Inference for the model parameters is performed via the hierarchical likelihood (h-likelihood; Lee and Nelder, 1996) method, which avoids the intractable integration over frailty required in marginal likelihood approaches and effectively captures heterogeneity across clusters. Unlike the classical likelihood for fixed parameters only, the h-likelihood is constructed for both fixed parameters and unobserved frailties at the same time. The performance of the proposed approach is evaluated through simulation studies, which demonstrate that the estimated regression coefficients appear reasonable for all three types of survival data. The proposed method is further illustrated using three real-world datasets.

Keywords: Clustered bivariate survival data; Competing-risks data; Joint frailty models; H-likelihood

Inferring Median Survival under Dependent Censoring

Takeshi Emura

School of Informatics and Data Science, Hiroshima University, Japan

ABSTRACT

The key difficulty in survival analysis is the proper handling of censoring. So far, existing inference methods for median survival have been developed under the independent censoring assumption, which is too strong for many applications. As a solution, we develop new methods for dependent censoring regimes. This is accomplished by the median estimator from copula-graphic estimators developed for survival copula models. The proposed method is a median version of our previously proposed method for the Mann-Whitney effect [1]. We present this methodology with simulations and data examples. This is the joint work with Dennis Dobler.

Reference:
[1] Emura, T., Ditzhaus, M., Dobler, D., & Murotani, K. (2024). Factorial survival analysis for treatment effects under dependent censoring. Statistical Methods in Medical Research, 33(1), 61-79.

Keywords: Archimedean copula; Copula; Copula-graphic estimator; Survival analysis; Treatment effect