Chapter 6
Future Developments

Abstract This final chapter introduces two open problems for future research. This might help find research topics for students and researchers.

Keywords Copula-graphic estimator · Dependent truncation · Left-truncation Log-rank test

6.1 Log-Rank Test Under Dependent Censoring

The three most important statistical methods in survival analysis would be the Kaplan–Meier estimator, the log-rank test, and Cox regression. These three methods adopt simple ways to deal with censoring. However, these methods critically rely on the validity of the independent censoring assumption (Chap. 2).

The copula-graphic estimator (Zheng and Klein 1995; Rivest and Wells 2001) is a natural generalization of the Kaplan–Meier estimator in the presence of dependent censoring. Also, the semi-parametric maximum likelihood estimator of Chen (2010) is a natural generalization of Cox regression (Chap. 4). These methods for dependent censoring utilize copulas to adjust for the effect of dependent censoring, and they reduce to the original methods under the independence copula. However, the copula-based generalization of the log-rank test under dependent censoring has not been considered in the literature.

Researchers often wish to separate patients between good and poor prognosis groups and then use the log-rank test to see how well the Kaplan–Meier survival curves are separated between the good and poor groups. This strategy may give biased results if dependent censoring exists in the samples (Emura and Chen 2016; Moradian et al. 2017). In Chap. 5, we apply a permutation test based on the difference between the two survival curves calculated by the copula-graphic estimator. While this approach can account for the effect of dependent censoring, it is not regarded as the log-rank test. The log-rank test should compare the hazard rates between two groups rather than the survival curves.

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Hence, it is interesting to develop an alternative two-sample test, similar to the log-rank test, under dependent censoring. In general, two copulas are necessary for two groups (e.g., good and poor prognosis groups). A starting point may be the assumption that the copula is the same in the two groups, as we have assumed in Chap. 5. While deriving a generalized log-rank test under an assumed copula, it is relevant to study the robustness or sensitivity of the test against copula misspecification as in Rivest and Wells (2001). Based on the sensitivity analysis of Chap. 3, we conjecture that the log-rank test is robust against the effect of dependent censoring modeled via the Gumbel copula.

6.2 Dependent Left-Truncation

Left-truncation often occurs if survival time is measured from birth. In this case, survival analysis may be based on the age-specific hazard function and left-truncation time corresponds to entry age (should not be treated as covariates). This book does not discuss the problem of left-truncation since the theme is focused on censoring. Meanwhile, it is of great interest to design aging research under left-truncation (e.g., Rodríguez-Girondo et al. 2016), where the issue of *dependent* left-truncation may arise in addition to the issue of dependent censoring.

Traditional analyses for left-truncated survival data rely on the *independent truncation* assumption (p.126 of Klein and Moeschberger 2003). For instance, in survival analysis of elderly residents, the age at entry to a retirement center is assumed to be independent of age at death (Hyde 1980). Several different tests for checking the assumption of independent truncation were developed (Emura and Wang 2010). The effect of dependent truncation in competing risks analysis was studied by Bakoyannis and Touloumi (2017). To fit survival data with dependent left-truncation, a copula model between event time and left-truncation time has been considered (Chaieb et al. 2006; Emura and Wang 2012; Emura and Murotani 2015; Emura and Pan 2017). However, these methods cannot be directly applied to the case where event time is subject to both dependent censoring and dependent truncation. In this case, one may consider two copulas, one for dependent truncation and the other for dependent censoring. One may also consider a copula for dependence between truncation time and censoring time.

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