Quantifying the Between-Group Difference with Multiple Time-to-Event Endpoints

In a longitudinal study with the time to a specific event as the primary end point, standard methods of summarizing the treatment difference are based on Kaplan-Meier curves, the logrank test and the point and interval estimates via Cox’s proportional hazards model. However, when the proportional hazards assumption is violated, the logrank test may not have sufficient power to detect the difference between two event time distributions, and the resulting hazard ratio estimate is difficult, if not impossible, to interpret as a treatment contrast. On the other hand, the restricted mean survival time (RMST) is an easily interpretable, clinically meaningful summary of the survival function in the presence of censoring. The RMST is the mean survival time of all subjects in the study population followed up to a time point $t$ and can be estimated consistently by the area under the Kaplan-Meier curve over $[0, t]$. In this research, we discuss the extension of RMST in the more general setting of multiple time-to-event endpoints, which includes classical competing risks and semi-competing risks. The methods are illustrated with the data from two clinical studies.