

Exploring the world of crossing hazards - One method to rule them all?

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Abstract

Comparison of survival in two-armed designs is common in clinical studies with time-to-event outcome and usually done by means of the log-rank test. Unfortunately, the key assumption of proportional hazards is often not checked. If this assumption is violated the log-rank test loses power. Although, several approaches have been developed to solve this problem, most of them are not applied at all. Thus, it is important to identify the most appropriate methods and draw attention to their existence. A particular goal is to simplify the choice of tests for detecting crossing survival differences. To this end, we followed different lines of research:

1. We reviewed 1,400 recent oncological studies, where we applied pre-defined selection criteria to objectively chose data sets. To reconstruct this data, we used a state-of-the-art reconstruction algorithm which requires a Kaplan-Meier curve, the number at risk at multiple times and the total number of events.
2. We performed an extensive simulation study, where we considered different settings covering proportional, crossing and non-proportional hazards without crossing. This allows for a broader impression of the methods' performance under various alternatives.
3. Furthermore we verified our observations on data collected by other researchers to minimize a possible selection bias.