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. Un-
fortunately, 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 dif-
f erent 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 un-
der various alternatives.
3. Furthermore we verified our observations on data collected by other re-
searchers to minimize a possible selection bias.