

“Time-to-event analysis with competing risks considering cluster structures
- Comparison of methods based on a simulation study”

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In clinical research studies, there is often great interest in demonstrating treatment efficacy. Time-to-event analysis models are usually used for assessment, whereby the time until an event of primary interest occurs is considered. In practice, however, an additional competing event may occur beforehand, which should be considered in the analysis. In addition, clinical trials are often conducted at more than one clinic (cluster) simultaneously. There is an assumption that this cluster structure arising here leads to a potential dependency between the event times.

While the cluster structure addressed is already applied in many other fields, such as mixed linear models, it has been mostly neglected in the evaluation of clinical trials with competing risks.

Now it is of interest how such cluster structures can be taken into account in time-to-event analyses with competing events. Different methods have already been described in the literature, but not yet systematically compared.

Therefore, the aim of this work was to compare these methods by performing a Monte Carlo simulation study and to derive recommendations for future analysis of event times considering competing events and existing cluster structures. The methods considered were based on the Cox proportional hazards model (e.g. Cox model with frailty [1]) or methods modeling subdistribution hazards (Fine and Gray [2] and extensions thereof: Katsahian et al. [3] and Zhou et al. [4]).

In summary, there were only marginal differences between the models considered in terms of bias, mean square error and empirical power. However, the approach of Katsahian et al. showed the best performance in most scenarios based on these values.

References:

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- [3] Katsahian, S., Boudreau, C. (2011). Estimating and testing for center effects in competing risks, *Statistics in Medicine*, 30(13):1608-1617.
- [4] Zhou, B., Fine, J., Latouche, A., Laboin, M. (2011). *Competing risks regression for clustered data*, Oxford University Press, 13(3):371–383.