Estimating the similarity between adult and pediatric dose-toxicity curves to inform pediatric dose-finding.

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We consider Bayesian model-based approaches to dose-escalation trials in pediatric patients, for which information from a trial in adults with the same compound is supposed to be borrowed in form of an informative prior. The adult data from the same compound can be borrowed by applying robust priors as shown previously (Takeda and Morita, 2018, and Zocholl et al. 2022). The degree of borrowing, however, should ideally be controlled by the similarity between adult and pediatric dose-toxicity profiles. Estimating this similarity to enable dynamic borrowing can be difficult due to the small sample sizes. Instead, we propose to estimate a similarity parameter from other compounds to control the degree of borrowing. Prerequisites are that these compounds have previously been tested in adult and pediatric patients and that they are like the compound under investigation with regard to their molecular structure and mode of action. We propose two methods (a hierarchical model and an EXNEX-approach) to estimate such a similarity parameter and investigate the operating characteristics of a pediatric trial design under application of these methods in a simulation study.

References

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