Robust Meta-analytic-predictive Priors in Clinical Trials with Historical Control Information

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Historical information is always relevant when designing a clinical trial. Additionally, if incorporated in the analysis of a new trial, historical data allow for smaller number of subjects. This decreases costs and trial duration, facilitates recruitment, and may be more ethical. Yet, under prior-data conflict, a too optimistic use of historical data may be inappropriate. We address this challenge by deriving a Bayesian meta-analytic-predictive prior from historical data, which is then combined with the new data. This prospective approach is equivalent to a meta-analytic-combined analysis of historical and new data if parameters are exchangeable across trials. However, the prospective Bayesian version requires a good approximation of the meta-analytic-predictive prior, which is usually not available analytically. We propose two- or three-component mixtures of standard priors, which allow for good approximations and, for the one-parameter exponential family, straightforward posterior calculations. Moreover, since one of the mixture components is usually vague, mixture priors will often be heavy-tailed and therefore more robust than standard conjugate priors. Further robustness and a more rapid adaptation to prior-data conflicts can be achieved by adding an extra weakly-informative mixture component. We illustrate the methodology for a phase II proof-of-concept trial, and historical control information from four studies. Both frequentist operating characteristics and posterior summaries for various data scenarios show good robustness. Meta-analytic-predictive priors alleviate prior-data conflicts - they should encourage better and more frequent use of historical data in clinical trials.