Historical controls in clinical trials: the meta-analytic predictive approach applied to over-dispersed count data

Sandro Gsteiger, Beat Neuenschwander, and Heinz Schmidli
Novartis Pharma AG, CH-4002 Basel, Switzerland

The formal inclusion of historical controls in the analysis of clinical trials has gained increasing interest in recent years (Berry et al. , 2010). Traditionally, historical information was used informally in various ways for example to support the selection of endpoints, to inform decisions on design, to calculate sample size and so on. The subsequent analysis of the new trial, however, did not make any formal use of the available historical data. Over about the last decade, several authors have discussed formal ways to include data from historical control patients in the analysis of a new trial by specifying informative priors based on the historical data. These authors have either proposed new approaches or refined ideas from existing literature. The most popular ones found in the current discussions are the use of power priors (Ibrahim and Chen , 2000), the commensurate priors (Hobbs et al. , 2011), and the meta-analytic-predictive (MAP) approach (Pocock , 1976; Neuenschwander et al. , 2010).
In the MAP approach, a Bayesian meta-analysis of the historical control data is performed to derive the predictive distribution for the parameter of interest in the control group of the new study. This distribution summarizes the available knowledge about the control arm in the new study and provides an informative prior to be used in the analysis of the new study.
The MAP approach was introduced for (approximate) normal endpoints and summary level data. In this presentation, we study the generalization of these ideas to over-dispersed count data and to the combination of both summary level and individual level data. Summary data may be available from various sources such as trial results published in the scientific literature, or clinical trial registries. Individual level data may be available from in-house trials performed earlier in the same indication. Enrichment strategies to increase the comparability of historical and new trial data are also discussed. With enrichment the amount of historical information may be reduced. The increased homogeneity of the remaining trials, however, may counteract the decrease of information in the resulting prior. We will illustrate these extensions using an example from multiple sclerosis.

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