Sample size estimation in a planned paediatric clinical trial utilising external information of historical trials in adults and children

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Paediatric clinical trials are challenging in that though patient numbers are often limited a high performance of applied statistical methods is requested in order to provide valid scientific results. In order to meet these conflicting conditions and requirements in a planned paediatric trial, in the design and analysis of the future trial existing data of historical trials in adults and children may be utilised. This leads to an increased power of the future trial, so that fewer patients are required to be recruited.

In order to merge historical and future data of several clinical trials a Bayesian meta-analytic-predictive approach is developed. The effect of interest is the efficacy response difference between two treatment groups. In the established model two important features of study-specific effects are accounted for, i.e. random variation of study-specific effects (between-trial variation) as well as a possible difference in mean pooled effects between adults and children. These two features (including the inherent uncertainty in quantifying the corresponding terms) form the basis to determine the amount of evidence that the historical data contributes in a future trial. The determined evidential weight can be translated to an estimated “prior effective sample size”. Thus a certain number of “virtual subjects” is contributed by the historical information and correspondingly fewer patients are required to be recruited in the future trial.

The developed method is applied, utilising historical data of 8198 patients from 18 adult and 1 paediatric clinical trial in order to plan a future paediatric trial. The evidential weight of historical information is quantified by a corresponding number of 116 “virtual subjects”. I.e., if the historical information is utilised in the future trial, the required sample size may be reduced from 580 to 464 patients by 20%.