

Title: Application of Bayesian borrowing methods in clinical trials for children with type II diabetes mellitus using simulation and case studies

Authors: Roberto Crackel *, Yoonhee Kim - FDA

*presenting author

Abstract:

Clinical trials for children with type II diabetes mellitus (T2DM) pose challenges often due to recruitment issues. Also, the variability in the treatment effect for pediatrics with T2DM tends to be much larger than that for adults. Therefore, a larger pediatric study is needed to independently detect a similar treatment effect than in an adult study. Bayesian borrowing method could aid for reducing the number of patients needed for a pediatric study and therefore increase feasibility and efficiency.

We introduce Bayesian borrowing methods to obtain scientifically sound and conclusive results with adequate study power in anti-diabetic products development for children with T2DM. To apply Bayesian borrowing methods, it is important to 1) identify the external data that can be leveraged, 2) pre-specify model parameters, 3) assess operating characteristics, and 4) pre-specify weights and the maximum amount of borrowing needed to achieve a study win.

We perform simulation studies to explore operating characteristics such as the trial power, posterior probability of success, bias, mean squared error, length of the half-width credible intervals, and effective sample size (ESS) using a mixture prior. An advantage of using mixture priors is that it adapts to the degree of borrowing based on the similarity between the external and pediatric results. Further, we applied Bayesian borrowing methods to two anti-diabetic products using labeling information and explored different variances for the vague component of the mixed prior. It should be considered that a large variance strongly discounts the effect of the vague component, thus making it less robust to departures from the assumptions underlying the borrowing.

In conclusion, the outcomes of our step-by-step demonstration of the application of Bayesian borrowing methods using simulation studies and case studies provides a guide on how to pre-specify parameters and considerations that should be made when planning to implement said methods. One such consideration is when prior-data conflict is a concern, to ensure robustness at the inference stage, the unit variance (i.e., the variance based on 1 patient per arm under equal randomization) or smaller should be highly considered to be used for the variance of the vague component.