Poster # MSR104

Applications of Bayesian borrowing for assessing treatment effects in clinical trials

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Background

- Randomized clinical trials (RCTs) serve as the gold standard for evaluating the safety and efficacy of new treatments, providing robust evidence that drives regulatory approvals and healthcare decisions.
- However, traditional RCTs often face challenges such as the need for large sample sizes, time constraints, and ethical considerations, particularly when it comes to control groups.
- Bayesian borrowing (BB) leverages external data sources—such as historical data, real-world evidence, or previous studies—to improve the statistical power of within-trial comparisons. It allows researchers to make more informed inferences and potentially achieve results with fewer participants.
- The acceptability of BB approaches from a regulatory and HTA perspective is evolving. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA), are increasingly considering Bayesian methods as a viable option in trial design, reflecting a shift towards more flexible and adaptive approaches in clinical research. Anticipatedly, the FDA will release draft guidance on employing Bayesian methods in clinical trials for drugs and biologics by the end of 2025.

Objective

This targeted literature review provides an overview and examples of the implementation of BB in clinical trials, highlighting its potential benefits, methodological advancements, and challenges.

Methods

- The review searched MEDLINE and Embase. The review also searched industry case study reports, as well as Health Technology Assessment (HTA) guidelines including FDA.
- Search terms included ‘Bayesian’, ‘Bayesian borrowing’, ‘Bayesian inference’, or ‘Bayesian methods’. The review restricted to the studies that focused on clinical trials.
- The review included studies in the past five years.

Conclusions

- By allowing researchers to integrate external data sources and real-world evidence, BB methods can reduce reliance on large sample sizes and increase the efficiency of trials.
- While the benefits of BB are clear, several limitations remain, such as the need for careful selection and validation of external data, as well as concerns about potential biases when historical data are not entirely comparable to current trial populations.
- This review underscores the necessity for continued research in Bayesian methodologies to address existing limitations and expand their applicability in health research.

Results

Characteristics of included studies:

- The review included 10 studies. 6 were case studies issued by FDA to promote innovative methodology. 1 study was a case study of the successful implementation of BB to support the approval of a new medicine with the Center for Drug Evaluation in China.
- The other 3 studies compared BB with the traditional frequentist or Bayesian models in existing clinical trials. These studies found that while reducing the sample size, BB provides comparable treatment-effect estimates with generally improved precision.
- BB has been mostly implemented in pediatric trials (3 studies) or rare disease (2 studies) research where patient populations are limited.
- Other research areas included one study that borrowed information in a global study to a regional study in China; one study that borrowed information from historical studies to the ongoing study in pain research; one study that borrowed information to build external control arms; two studies that borrowed external information due to the difficulty to enroll patients in cancer and heart failure device studies.
- Therapeutic areas where BB has been implemented included replacement heart valves, epilepsy, multiple sclerosis, chronic pain, lymphoma, metastatic colorectal cancer, and asthma.

Figure 1. Geographic locations of the 10 included studies.

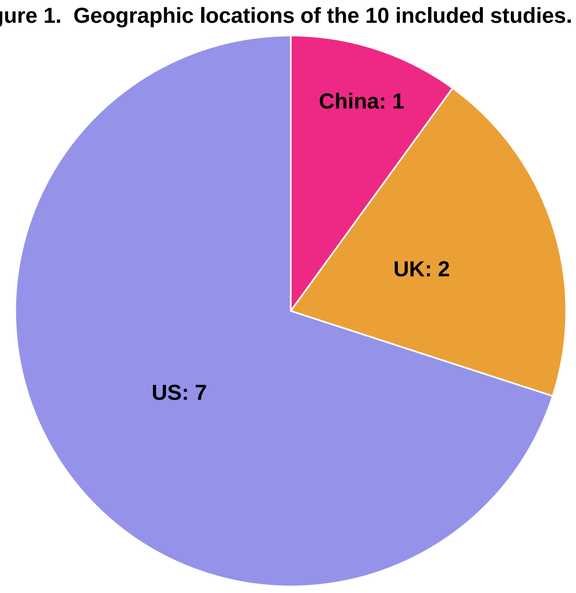
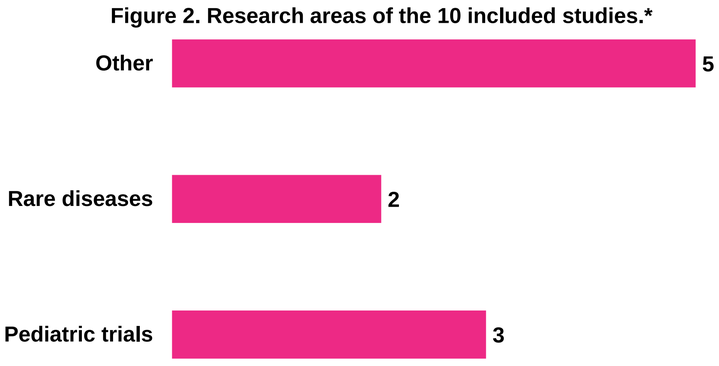


Figure 2. Research areas of the 10 included studies.*



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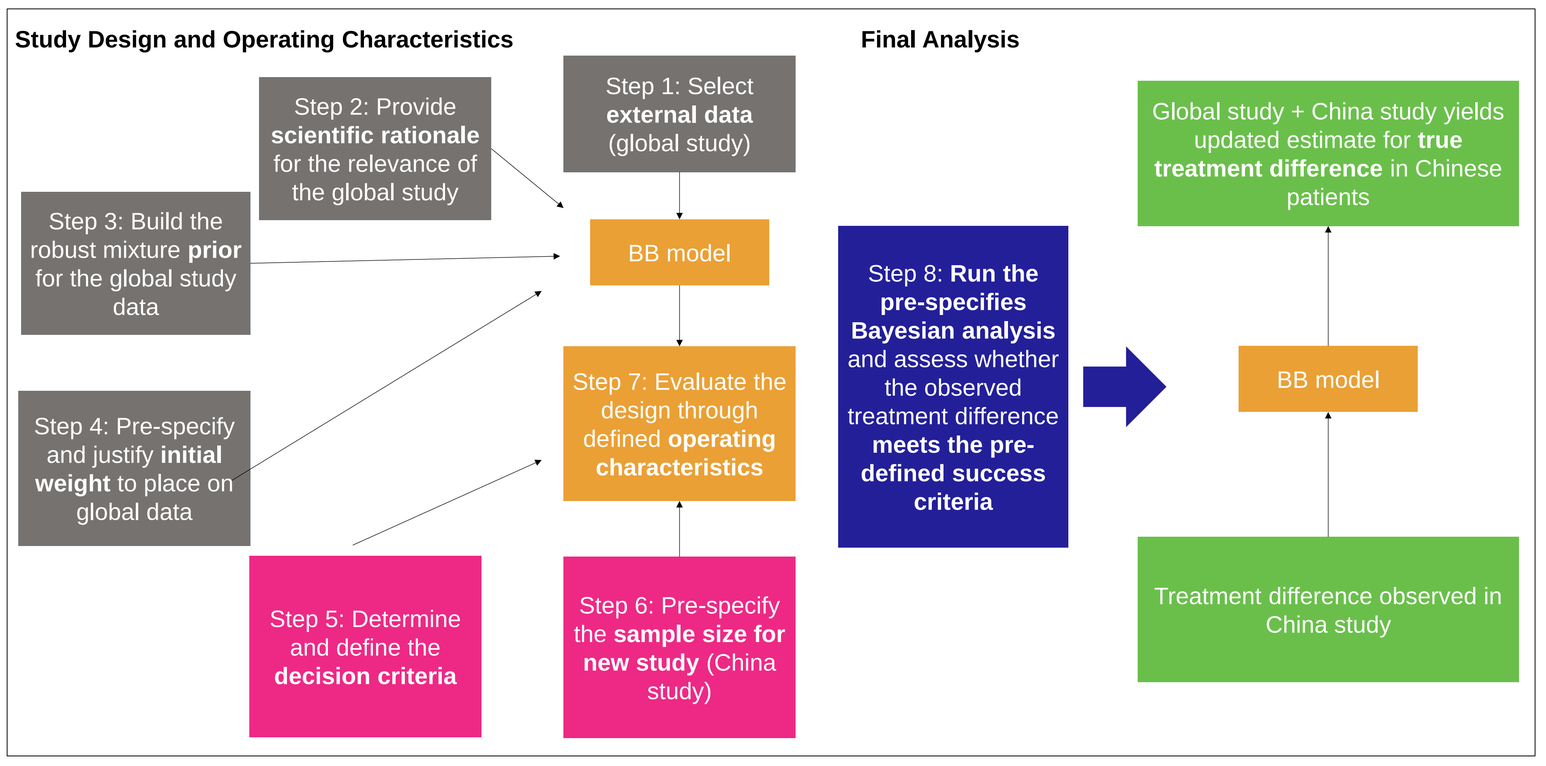
Rationale for conducting BB:

- Global studies were available, and evidence in subpopulations, e.g., certain racial/ethnic group, is needed, and race/ethnicity doesn’t affect the biological mechanism the drug is in play.
- There were no pediatric trials, or the study was underpowered, and adult data are considered relevant.
- The difficulty of enrollment in rare population, e.g., cancer, and the treatment effect is consistent across related indications.
- One study conducted BB to utilize the evidence already available from the global study to provide evidence to Chinese patients, and support registration with the Center for Drug Evaluation (CDE) in China.



Case study:

A global study had been conducted to support the approval of the drug globally; however, Chinese patients were not included and therefore a separate study was required to support registration with the Center for Drug Evaluation (CDE). The BB approach was chosen as it utilizes the evidence already available from the global study [treatment difference 86 units (95% CI: 46, 125)] and was more likely to provide robust evidence than an unpowered standalone study.

1. At the design stage, the external data to borrow from (the “prior” information) needed to be selected. In this case it was the global study.
2. Scientific rationale for relevance of the global data were provided to support the assumption of exchangeability of the treatment effect between the global and new China studies.
3. Choose and construct a prior distribution for the treatment difference in the Chinese population using the global data.
4. Pre-specify and justify the initial weight to place on the “informative” component of the mixture prior.
5. Define the decision criteria of the posterior probability.
6. Pre-specify the sample size for the new China study. A range of sample sizes were explored, and a sample size of 75 patients per arm was selected based on an acceptable balance of operating characteristics (OCs).
7. Evaluate the design through defined OCs such as power (probability of success for a given fixed value of the true treatment difference) and type I error rate, as well as assessing the impact of different choices of initial weight on the global data as well as the impact of different sample sizes.

Figure 3. Steps to implement Bayesian borrowing. The figure is adapted from Edwards D, Best N, Crawford J, Zi L, Shelton C, Fowler A. Using Bayesian Dynamic Borrowing to Maximize the Use of Existing Data: A Case-Study. Ther Innov Regul Sci. 2024;58(1):1-10. doi:10.1007/s43441-023-00585-3.

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