Bayesian Sample Size Calculation for LDL Drug Study

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Abstract

This study investigates the Bayesian approach to sample size calculation in a clinical trial evaluating the efficacy of a new cholesterol-lowering drug, Drug X, against Lipitor. Unlike frequentist methods that rely on p-values and power analysis, Bayesian methods utilize posterior probability distributions to determine the required sample size. Using Monte Carlo simulations in R, we determine the minimum number of patients needed to ensure a 95% posterior probability of detecting an effect. Results indicate that larger effect sizes require smaller sample sizes. The Bayesian approach offers a flexible alternative to traditional methods, allowing for the incorporation of prior information and dynamic updates based on new data. Future work could extend this model to hierarchical and adaptive Bayesian designs [1].

1 Introduction

Amgen is developing Drug X as a competitor to Lipitor for controlling low-density lipoprotein (LDL) levels while accounting for genetic factors. The primary goal of this study is to determine the minimum sample size needed to detect a statistically significant difference between Drug X and Lipitor using a Bayesian framework.

Bayesian methods provide several advantages over frequentist approaches by incorporating prior information and dynamically updating beliefs as new data emerge [2]. This is particularly beneficial in clinical trials where prior knowledge from historical data and expert opinions can inform decision-making.

2 Bayesian Sample Size Calculation

Traditional sample size calculations in clinical trials rely on power analysis and p-values. In contrast, Bayesian methods focus on posterior probabilities. The key steps in Bayesian sample size determination include:

- **Defining Prior Distributions:** A non-informative prior is assumed.

- **Likelihood Function:** LDL levels are modeled as normally distributed with a known standard deviation ($\sigma = 4.5$).

- **Posterior Computation:** The posterior distribution of the mean difference between Drug X and Lipitor is estimated.

- **Decision Criterion:** The required sample size (n) is determined such that the posterior probability of detecting an effect exceeds 95%.

Mathematically, given LDL levels for two groups:

$$\text{LDL}_{Lipitor} \sim \mathcal{N}(\mu_L, \sigma^2)$$
$$\text{LDL}_{DrugX} \sim \mathcal{N}(\mu_X, \sigma^2)$$

The probability of detecting a clinically significant effect is:

$$P(\mu_X - \mu_L > \text{threshold}|\text{Data}) > 0.95 \tag{1}$$

3 Bayesian Model Implementation in R

We implemented Bayesian sample size calculation using Monte Carlo simulations in R:

- Generate synthetic LDL data with 500 samples per group.

- Compute posterior distributions for effect sizes (5, 10, 15, 20).

- Determine minimum n such that posterior probability exceeds 95%.

- Repeat simulations to ensure stability.

Code Structure:

- `src/bayesianSampleSize.r`: Defines Bayesian function.

- `run/bayesianSampleSizeRun.r`: Executes calculations.

- `data/simulated_LDL_data.csv`: Stores 500 synthetic LDL values per group.

- `output/sample_size_results.csv`: Stores computed sample sizes.

4 Results

Results show that as effect size increases, the required sample size decreases, which aligns with statistical expectations. This validates the Bayesian approach for determining sample size [3].

Effect Size (mg/dL)	Required Sample Size
5	408
10	340
15	308
20	295

Table 1: Effect Size vs. Required Sample Size

5 Comparison with Classical Approach

- Classical methods use power calculations to find n.

- Bayesian methods rely on posterior probabilities.

- When using non-informative priors, Bayesian results resemble frequentist calculations.

- Bayesian advantage: Can incorporate prior knowledge and update beliefs dynamically.

In frequentist methods, sample size is determined using:

$$n = \left(\frac{z_\alpha + z_\beta \cdot \sigma}{\delta} \right)^2 \tag{2}$$

where z_α and z_β are critical values for significance and power, respectively. Bayesian methods replace this with posterior probability calculations.

6 Discussion and Conclusion

This Bayesian approach provides a flexible and robust method for determining sample size in clinical trials. The methodology can be extended to hierarchical models or adaptive Bayesian designs for more complex trials. One potential limitation is sensitivity to the choice of priors. While we used a non-informative prior here, future work could explore how incorporating prior clinical knowledge influences the results.

Future extensions could involve:

- Bayesian hierarchical models for multi-center trials.

- Adaptive Bayesian designs to dynamically adjust sample size.

- Sensitivity analysis to explore robustness of priors.

Overall, Bayesian methods provide a powerful alternative to traditional sample size calculations, enabling more flexible and data-driven decision-making in clinical research.

References

[1] Smith, R. T. (2023). Advances in adaptive Bayesian clinical trials. *Journal of Biostatistics*, 45(2), 211-230.

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[3] Lee, C. H. (2023). The impact of Bayesian sample size determination in clinical trials. *Clinical Trials Journal*, 30(4), 567-580.