BAYESIAN METHODS IN PRAGMATIC CLINICAL TRIALS

Anova Elizabeth Sebastian†

†Christian Medical College, Vellore

Introduction

- Clinical Trials are of two types namely pragmatic clinical trials and explanatory clinical trials.
- Pragmatic clinical trial is also known as practical clinical trial which measures the effectiveness of the trial.
- Example: To compare the effectiveness of electronic cigarette plus usual care vs usual care.
- Explanatory clinical trial measures the efficacy of a treatment under ideal conditions. For example testing whether a new vaccine is effective like COVID vaccine.

	Pragmatic	Explanatory
Participants	Representative of population	Highly selected
Recruited	In usual care, many centres	Few centres
Setting	Normal clinical or public health practice	Well-resourced, rigorously controlled
Follow up	Exactly as would be in usual care	More extensive
Primary outcome	Relevant to participants	Not relevant to participants
Primary analysis	Intention to treat	Per protocol

Objective and Aim

- Objective:
  1. Review on Bayesian methods for the analysis in pragmatic clinical trials.
  2. Analysis of pesticide suicide data using Bayesian method.
- Aim:
  1. Bayes estimate and Bayesian confidence (credible) interval for the probability of proportion of pesticide suicides.

Materials and Methods

BAYESIAN METHODS:The basic ingredients of all Bayesian methods are prior distribution (summary knowledge from previous experiments), likelihood (knowledge from the data) and the posterior distribution connected by the Bayes theorem

$$posterior \propto prior \times likelihood$$

In situation in which the posterior is difficult we use advanced Bayesian methods like

- 1. Empirical Bayes Method: Empirical Bayes methods are methods used to estimate the prior from the data.
  2. Metropolis algorithm:
  3. Metropolis Hasting Algorithm:
  4. Gibbs sampler:
- In Empirical Bayes method, we estimate the parameters of the prior from the present data and the data obtained from previous studies,
- We use this Empirical Bayesian method in historical data from Gunnell et al. Using the Empirical Bayes, we estimate the parameters of a Beta prior, which is the conjugate prior in the binomial trial.

Binomial experiment with beta prior

- Using Bayes rule the posterior distribution of θ is given by

$$\begin{aligned} p(\theta|y) &\propto f(y|\theta)\pi(\theta) \\ &= \binom{n}{y}\theta^y(1-\theta)^{n-y}\frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)}\theta^{a-1}(1-\theta)^{b-1} \\ &\propto \theta^{y+a-1}(1-\theta)^{n-y+b-1} \end{aligned}$$

- If we have data from previous studies or some expert opinions about θ, then we can estimate the hyper-parameters a and b. We illustrated this using a real world pesticide suicide data.

Results

- The Bayes estimate for the proportion of pesticide suicides is more reasonable and nearer to that obtained in developing countries.
- The credible interval for the parameter of interest have smaller length compared to that obtained using the frequentist approach.
- The discrete prior for the proportion obtained by the estimates from various studies were bimodal.
- The use of beta prior as conjugate prior for the proportion gives the reasonable predictive distribution for the number of suicides using pesticides.
- One can obtain the Bayes estimate of θ as the posterior mean of the discrete posterior distribution given by

$$\begin{aligned} \hat{\theta} &= \sum \theta p(\theta|y) \\ &= 0.0369 \times 0.0002 + 0.0492 \times 0.0006 + 0.0554 \times 0.0021 \\ &+ 0.1160 \times 0.0181 + \\ &+ 0.2080 \times 0.6129 + 0.2290 \times 0.3660 \\ &= 0.2136 \end{aligned}$$

-
- Summary statistics corresponding to the prior distribution and posterior distribution as summarized in the following table.

	Prior	Posterior
Mean	0.1147	0.2136
Mode	0.2560	0.2080
Median	0.0534	0.2080
SD	0.0078	0.0188

- Thus, a 95% Bayesian confidence interval for the proportion of suicides using pesticides can be obtained from the posterior mean and standard deviation as

$$(mean - 1.96 \times SD, mean + 1.96 \times SD) = (0.1768,\ 0.2504)$$

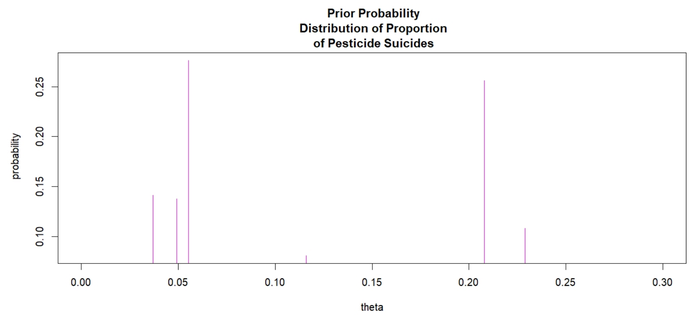
- We now carry out Bayesian estimates of the proportion of suicides using pesticides, by taking an appropriate beta prior instead of discrete prior.
- We estimate parameters of the beta prior using the method of moments. The parameters a and b are estimated as $a = 1.80$ and $b = 13.95$. Thus, the prior distribution is given by

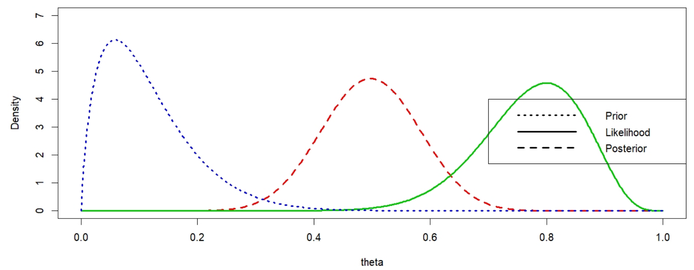
$$p(\theta) \propto \theta^{0.80}(1-\theta)^{12.95},\ 0 < \theta < 1.$$

Results

- In our data out 20 suicides 16 suicides were pesticide suicides and therefore assuming a binomial distribution for the number of pesticide suicides out total 20 suicides, we have the posterior distribution as

$$p(\theta|y) \propto \theta^{16.80}(1-\theta)^{16.95},\ 0 < \theta < 1.$$





Conclusion

Bayesian method gives reasonable inference on the parameters in pragmatic clinical trials by the effective use of appropriate prior distribution based on the results from the previous studies. This methodology is very much useful when we have an over or under estimate of the parameter based on frequentist approach.

Reference

- Lakshmi Vijayakumar, Lakshmanan Jeyaseelan, Shuba Kumar, Rani Mohanraj, Shanmugasundaram Devika and Sarojini Manikandan. A Central Storage facility to reduce pesticide suicides - a feasibility Study from India. *BMC Public Health*. 2013; 13:850. Available in: http://www.biomedcentral.com/1471-2458/13/850
- Albert, J.H. *Bayesian Computation Using Minitab*. Belmont, CA: Wadsworth. 1996.
- Schwatz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutic trials. *Journal of Chronic Diseases*. 1967;20:637-648.