Meeting1

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1 Chapter 1 Statistical approaches for clinicla trials

1.1 Bayesian versus frequentist appraoches in clincial research

- Key differences
  - parameters
  - inference input data and prior
  - **flexibility**, sequential learning
  - probability statements, predictive probabilities
  - decision theoretic
  - comment on role of randomization

Additional reading - Beyond subjective and objective in statistics by Andrew Gelman and Christian Henning - Bayesian is no more subjective than frequentist - Prior can be used meaningfully both computationally and biologically

1.2 Adaptivity

Bayesian is more commonly used for Phase I and Phase II trials. Some appealing adoption including non-fixed sample-size, early stopping and adoptive randomization.

1.2.1 The book argue "full bayesian" with utility function is awkward.

- the expected utility function given poster distribution of the parameter
- an example utility gain (or loss): Y(Z=1, treated)-Y(Z=0, control)

$$\int u(\theta, x)p(\theta|x)d\theta$$

1.2.2 Bayes as a frequentist tool

- flexibility, sequential learning
- posterior predictive probability
- use of prior, borrow info from other studies
- adaptive randomization
- seamless phase II and III design

2 Chapter 2 Basics of Bayesian

Additional reading on choice of prior - https://github.com/stan-dev/stan/wiki/Prior-Choice-Recommendations - http://www.stat.columbia.edu/~gelman/research/unpublished/prior_context_2.pdf

Additional reading on model selection (AIC, DIC, WAIC etc): - Understanding predictive information criteria for Bayesian models, Gelman, Hwang & Vehtari

2.1 Principles of Bayesian clincial trial design

Methods which can be used for clinical decision making

1. Posterior predictive methods
2. Bayesian indifference zone methods

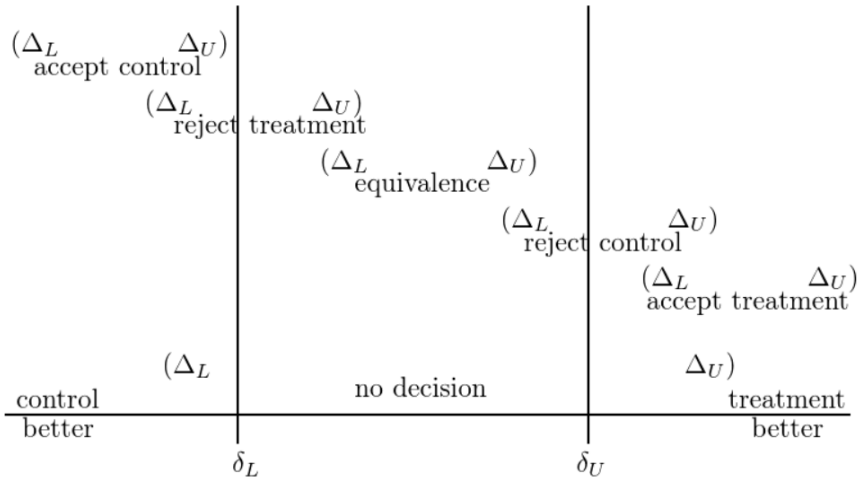

Figure 2.10 *Indifference zone* (δ_L, δ_U) *and corresponding conclusions for a clinical trial based on the location of the 95% posterior credible interval for* Δ.

might terminate the trial when

$$P(\Delta > \delta_U|\text{data}) \tag{2.27}$$

is sufficiently small (deciding in favor of the control), *or* when

$$P(\Delta < \delta_L|\text{data}) \tag{2.28}$$

is sufficiently small (deciding in favor of the treatment). Another rule would

3. Use of priors
4. Operating characteristics - Bayesian trial sample size

Additional reading on Bayesian trial sample size

- Bayesian techniques for sample size determination in clinical trials: a short review
- Using historical data for Bayesian sample size determination
- Clinical Trials and Sample Size Considerations: Another Perspective

Some thing interesting to read: Bayesian and type I error, https://www.fharrell.com/post/pvalprobs/

5. Online Bayesian Phase I and II design apps, https://trialdesign.org/#newsSection

3 Discussions

1. Example Bayesian trial, Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial, https://doi.org/10.1016/S0140-6736(20)32338-2

- The use of potentially optimistic treatment effect target belief
- Cost of using ECMO versus control

2. P-value versus Bayes factor, confidence interval versus credible region. (http://www.utstat.toronto.edu/mikevans/jeffrosenthal/chap7.pdf)