

# Potential Advantages and Disadvantages to the Bayesian Approach

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# Outline

- Section 3 of document
  - 3.5 - Software
  - 3.6 - Resources
  - 3.7 - Sound science
  - 3.8 - Potential benefits
  - 3.9 - Potential difficulties

## 3.5 Software

- Alternative #1: WinBUGS
  - Only widely available software specifically designed for Bayesian analyses (esp. hierarchical models)
  - Non-commercial, several variants available
    - classic BUGS, WinBUGS, OpenBUGS
- Alternative #2: write custom programs in a general language (fortran, etc.)
  - More flexible, but requires more program review

## 3.5 Software

- Often we will use one method as a check on the other
  - Independent programs increase confidence
- FDA expects other specialized software to become available
  - Recommend you consult with FDA prior to analyzing data
- Later talks will discuss particular computing issues

## 3.6 Resources to learn more

- Extensive literature on Bayesian statistics, ranging from basic introductory material to highly technical.
  - Section 3.6 provides a starting point

## 3.7 Good clinical trial design

- Important, regardless of whether you are using Bayesian or frequentist statistical methods
  - Prospective planning
  - Randomization
  - Concurrent controls
  - Blinding when possible
  - Control of bias
  - etcetera.

# Potential benefits and difficulties

- We consider benefits and difficulties in the regulatory environment, that is:
  - Medical device clinical trials
  - Results will be submitted to FDA for device approval
- As compared to “simple” frequentist trial
- Note that some “difficulties” may pay off later & become advantages
  - “difficult” = more work for both sponsor & FDA
- Most of the issues will be covered in more detail in later talks

## 3.8 Potential benefits

- Sample size reduction or augmentation
  - Prior information
    - Data from good prior studies can be incorporated into the analysis
  - Hierarchical models
    - Flexible method of incorporating prior data
  - Adaptive trials
    - Possible to adjust sample size while trial is ongoing

## 3.8 Potential benefits

- Changes to trial design
  - Adaptive trials
  - E.g. adaptive randomization
- Exact analysis
  - Can often compute posterior distribution in complex cases

## 3.9 Potential difficulties

- Need extensive preplanning
  - Agreement on priors, models, etc.
  - Important in the regulatory environment
- Model building can be complex
  - Requires attention to many issues
    - Distributions for priors
    - Incorporating covariates
    - Relationships between previous studies

## 3.9 Potential difficulties

- Specific expertise needed
  - Not “off the shelf” clinical trial design
  - Need:
    - Understanding of Bayesian statistics
    - Extensive model building expertise
    - Specific computational skills

## 3.9 Potential difficulties

- Justify choice of priors
  - Need to be justified in the regulatory setting
    - To FDA
      - Clinicians
      - Statisticians
      - Engineers
    - To FDA Advisory Panels
    - To the medical community

## 3.9 Potential difficulties

- Labeling
  - May be different than standard
- Checking calculations
  - More flexibility means more potential for misunderstanding
  - Complex software, development perhaps not mature
  - Simulation-based calculations (convergence issues)
  - FDA will carry out detailed review
    - Want to see data and programs in electronic format

## 3.9 Potential difficulties

- Difference between Bayesian, frequentist analysis
  - Two methodologies may give different results
    - One good reason to pre-specify analysis in the regulatory setting

