Bayesian Meta-Analysis of Single Arm Clinical Trials

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Motivation

- Arthritic ankles often undergo surgery to fuse or replace the ankle, in order to relieve pain
- How is post-surgical complication or failure rate related to surgery type?
  - Total Ankle Arthroplasty
  - Ankle Arthrodesis - Open
  - Ankle Arthrodesis - Arthroscopic

The Data

- N=38 studies, each with n_i observations
- Continuous covariates (age)
- Indicator covariates (treatment type)
- Count covariates/responses (diagnosis type, complication types, etc.)
- y_i = Response: per-study failure or complication rate

Definitions

- **Meta-analysis:** The combination of the results of multiple similar independent studies to determine an "actual" overall result
- **Effect Size:** The magnitude of the effect that a treatment has on the results of an experiment, compared to a different treatment or control (often standard difference of means, odds ratio, or relative risk ratio)
- **Outcome Measure:** The quantitative result of interest
- **Single-arm Study:** A study designed without a control group, whether for practical, moral, or other reasons

Model 1: Beta-Binomial

Likelihood of observing y_i ankle failures:

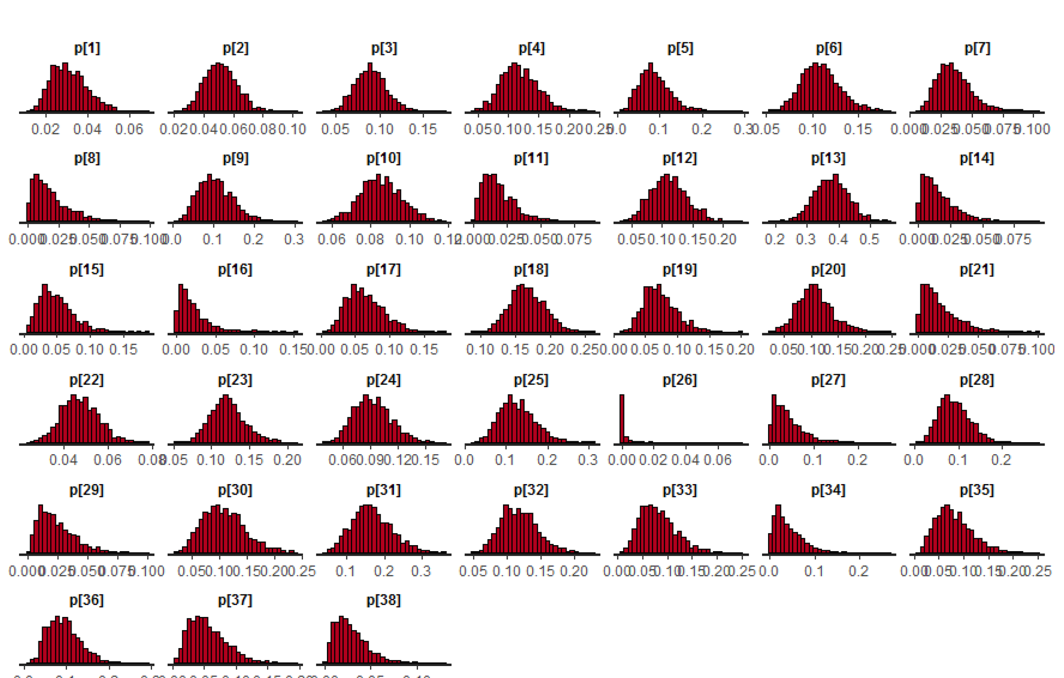
$$f(y_i \mid p_i, n_i) = \left\{ \binom{n_i}{y_i} p_i^{y_i}(1-p_i)^{n_i-y_i}, \quad y_i = 1, 2, \ldots, n_i \right.$$

Prior distribution for p_i:

$$f(p_i) = \left\{ \frac{\Gamma(\alpha+\beta)}{\Gamma(\alpha)\Gamma(\beta)} p_i^{\alpha-1}(1-p_i)^{\beta-1}, \quad 0 < p_i < 1 \right.$$

where

$$f(\alpha) = f(\beta) = \frac{1}{\Gamma(0.01) \times 0.01^{0.01}} (.)^{0.01-1} e^{-(.)/0.01}$$



(1-23: TAA; 24-32: AAO; 33:38: AAA)

Technique: Metropolis-Hastings MCMC

1. **Set initial parameter value** (eg $\theta^{(0)}$)
2. **Acceptance/rejection sequence;** for each iteration i,
   a) Draw candidate θ^* from possible posterior distribution, $J(\theta \mid \theta^{(t-1)})$
   b) Compute Metropolis ratio, $R = \frac{f(\theta^* \mid \mathbf{y})}{f(\theta^{(t-1)} \mid \mathbf{y})} \times \frac{J(\theta^{(t-1)} \mid \theta^*)}{J(\theta^* \mid \theta^{(t-1)})}$
   c) Set

$$\theta^{(t)} = \begin{cases} \theta^* & \text{with acceptance probability } min(R,1) \\ \theta^{(t-1)}, & \text{otherwise} \end{cases}$$

Model 2: Normal-Binomial

Likelihood of observing y_i ankle failures:

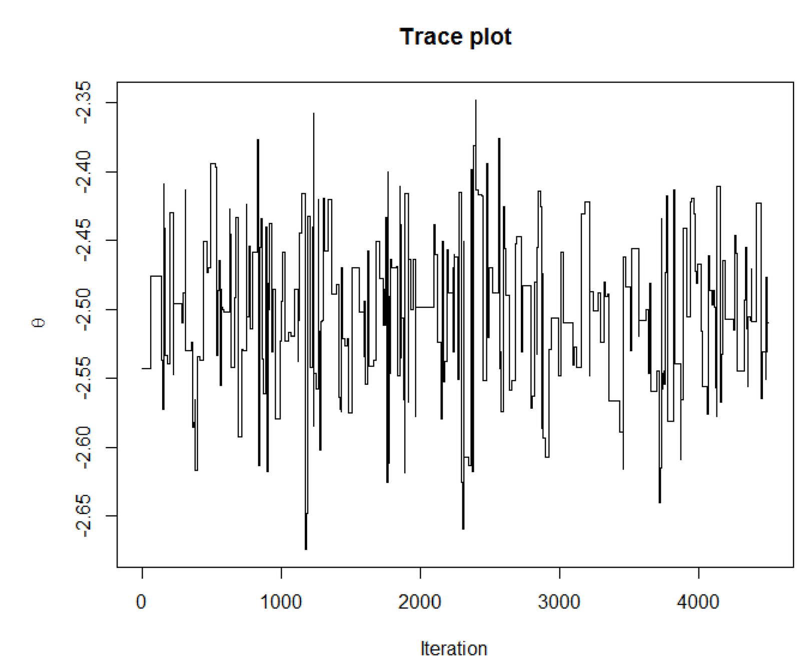
$$f(y_i \mid p_i, n_i) = \left\{ \binom{n_i}{y_i} p_i^{y_i}(1-p_i)^{n_i-y_i}, \quad y_i = 1, 2, \ldots, n_i \right.$$

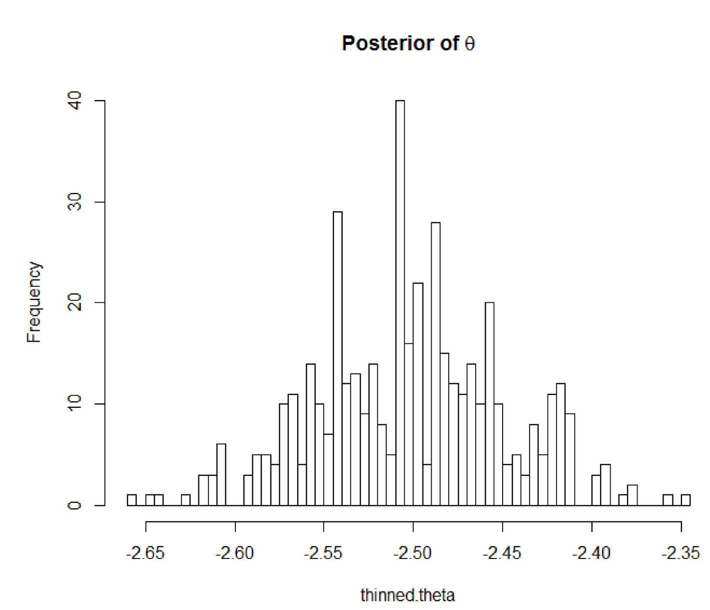
Prior distribution for p_i:

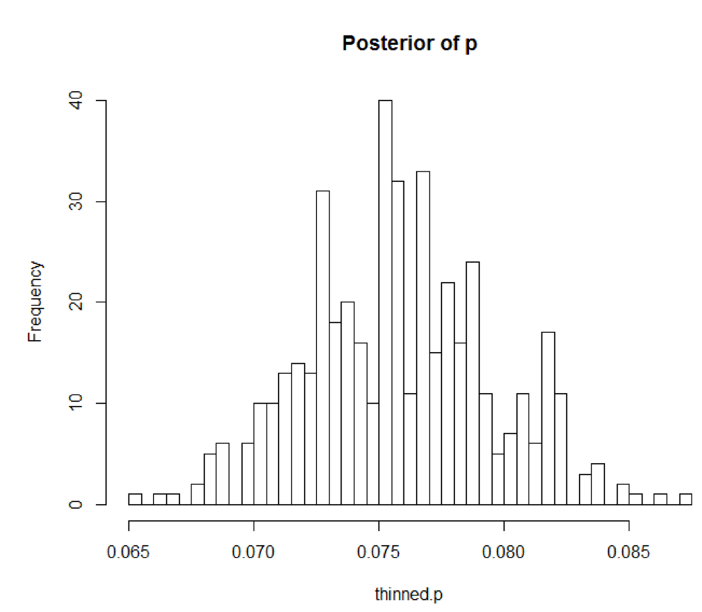
$$f(\theta) = \left\{ \frac{1}{\sigma\sqrt{2\pi}} e^{-\left(\frac{(\theta_i-\theta_0)^2}{2\sigma^2}\right)}, \quad -\infty < \theta < \infty \right.$$

where $\sigma^2 = 100^2$, and

$$\theta_i = logit(p_i) = \left(\frac{p_i}{1-p_i}\right)$$







$$\theta_0 = -2.502, \sigma_\theta = 0.053 \rightarrow p_0 = 0.075, \sigma_p = 0.003$$

Model Advantages:

- **Beta-Binomial:** No transformation necesssary=no division by zero, no log(0), & no log(∞)
- **Normal-Binomial:** Simpler for regressing on additional covariates, & adding random effects (see next panel)

Model 3: N-B with Regression & Meta-Analysis

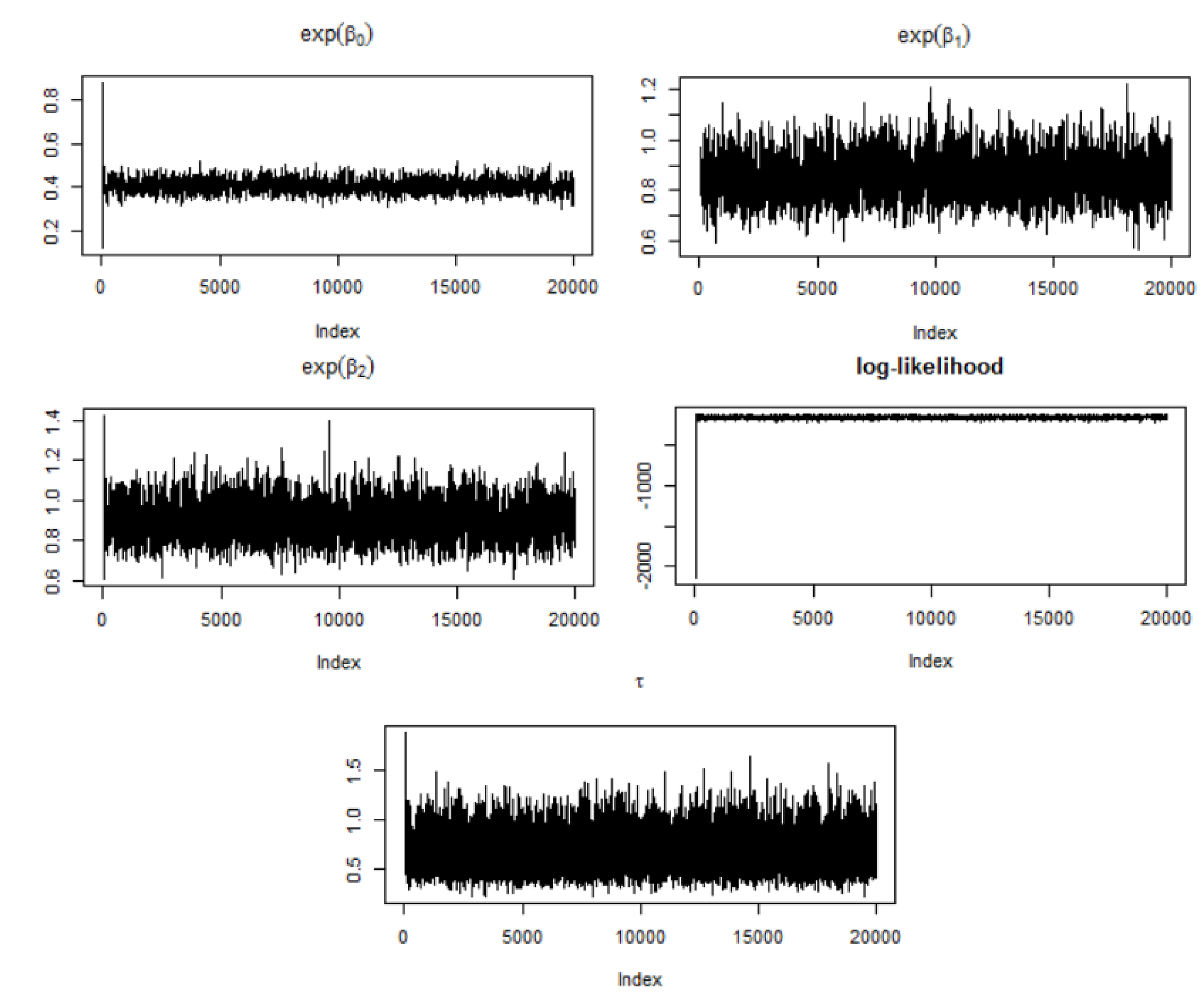
- Add covariates to the model
  - Indicator variables for surgery type
- Include "weights" for meta-analysis (inverse variance)
- Include random effects for $\theta_i = logit(p_i)$
- Same Likelihood for y_i as previous model

Regression:

$$logit(p_i) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + RE$$

- x_1, x_2 are indicators for AAO and AAA, respectively
- $\beta_0, \beta_1, \& \beta_2$ are coefficients ($\sim N(0, 0.1)$)
- Prior for $\theta = logit(p) \sim N(\mathbf{X} \times \boldsymbol{\beta}, \frac{1}{y_i} + \frac{1}{n_i - y_i})$
- RE are random effects $\sim N(0, \tau^2)$, where

$$f(\tau) = \frac{1}{5} e^{-\frac{\tau}{5}}$$



	Mean	Odds Ratio	5%	95%	Odds
β_0	-0.9103	N/A	0.3563	0.4558	0.4024
β_1	-0.1656	0.8474	0.7399	0.9914	0.3410
β_2	-0.1129	0.8932	0.7594	1.0469	0.3594

Future Directions

- Incorporate additional covariates of different types
- Improve techniques to accommodate missing data
- Expand to make descriptive modeling techniques into predictive techniques as well

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