Bayesian clinical trials design and evaluation: a decision-theoretic view

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Why a decision-theoretic approach

A Bayesian decision-theoretic framework to clinical trial design and evaluation allows...

• providing a rationale for type I error inflation
  • by exploiting the relationship between error costs and prior probabilities on test decisions
  • by controlling a weighted sum of errors (see Grieve, 2015; Pericchi and Pereira, 2016)

• incorporating estimation and sampling costs

Integrated risk

Test of $H_0 : \theta \leq \theta_0$ versus $H_1 : \theta > \theta_0$

Interest lies in minimizing the integrated risk

$$r(\pi, d) = \int_{\Theta} \left\{ c_1 l(\theta \leq \theta_0) P^f[d_{c_0, c_1}(y) = 1|\theta] + c_0 l(\theta > \theta_0) P^f[d_{c_0, c_1}(y) = 0|\theta] \right\} \pi(\theta) d\theta$$

$$+ \int_{\Theta} c_q E^f[\theta - d_q(y)]^2 \pi(\theta) d\theta + c_n n$$

Optimal decisions:

- for testing,

$$d^\pi_{c_0, c_1}(y) = \begin{cases} 1 & \text{if } P^\pi[\theta \leq \theta_0|y] < c_0/(c_0 + c_1) \quad \text{(reject } H_0) \\ 0 & \text{otherwise} \quad \text{(keep } H_0), \end{cases}$$

- for estimation, $d^\pi_q(y) = E^\pi[\theta|y]$

- for the sample size $n$, generally requires numerical procedures
How can we exploit this machinery?

- Sensitivity analyses can be performed in the spirit of e.g. Sahu and Smith (2006) through the dichotomy between
  - *Sampling (or design) prior* $\pi_s$: generates the observed data and represents the ‘truth’; induces optimal decisions $d^{\pi_s}$
  - *Analysis (or fitting) prior* $\pi_a$: used to obtain the posterior distribution on which the actual trial decisions $d^{\pi_a}$ are taken
- Such analyses can provide further insights into “robust” priors
- Sample size elicitation can be performed
  - through full risk optimization
  - to reach specific goals in testing and estimation (“goal sampling”)

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