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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

Andrew P. Grieve. How to test hypotheses if you must. *Pharmaceutical Statistics*, 14(2):139-150, 2015.

Luis Pericchi and Carlos Pereira. Adaptive significance levels using optimal decision rules: Balancing by weighting the error probabilities. *Brazilian Journal of Probability and Statistics*, 30(1):70-90, 02 2016.

Integrated risk

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

Interest lies in minimizing the integrated risk

$$r(\pi, d) = \int_\Theta \{c_1 \overbrace{I(\theta \leq \theta_0) P^f[d_{c_0,c_1}(y) = 1|\theta]}^{\text{type I error}} + c_0 \overbrace{I(\theta > \theta_0) P^f[d_{c_0,c_1}(y) = 0|\theta]}^{\text{type II error}}\} \pi(\theta) d\theta$$
$$+ \int_\Theta c_q E^f[\theta - d_q(y)]^2 \pi(\theta) d\theta + c_n n$$

Optimal decisions:

- for testing,

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

- 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* π_s: generates the observed data and represents the 'truth'; induces **optimal decisions** d^{π_s}
  - *Analysis (or fitting) prior* π_a: used to obtain the posterior distribution on which the **actual trial decisions** d^{π_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")

S.K. Sahu and T.M.F. Smith. A bayesian method of sample size determination with practical applications. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, 169(2):235-253, 2006.