Sensitivity of heterogeneity priors in meta-analysis

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Bayesian approaches to incorporating historical information in clinical trials

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STAT-Net/COMBACTE

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Synthesis of historical evidence

- Power-prior approach:
  
  Chen et al. (2006), Neuenschwander et al. (2009)

- Meta-analytical approach:
  
  Neuenschwander et al. (2010), Schmidli et al. (2014)
Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia

All-Cause Mortality with Linezolid/Aztreonam:

Rubinstein et al. (2001): $36/203 = 18\%$

$y_1 = \log(\text{odds}_1) = -1.534, \sigma_1 = \text{SE}(\log(\text{odds}_1)) = 0.184$

Wunderink et al. (2003): $64/321 = 20\%$

$y_2 = \log(\text{odds}_2) = -1.390, \sigma_2 = \text{SE}(\log(\text{odds}_2)) = 0.140$
Meta-Analysis

Normal-normal hierarchical model for $i = 1, \ldots, I$:

Sampling model: $Y_i \mid \theta_i \sim N(\theta_i, \sigma_i^2)$

Parameter model: $\theta_i \sim N(\mu, \tau^2)$

Priors for hyperparameters:

$\mu \sim$ flat distribution

$\tau \sim \pi_{a_0}$ scaled distribution
**Scaled distribution**

\[ \tau \sim \pi a_0 = a_0 X \]

Neuenschwander et al. (2010), **half-normal (HN)** prior:

\[ X \sim |N(0, 1)| \]

Simpson et al. (2014), **penalised complexity (PC)** prior:

\[ X \sim \text{Exp}(1) \]

\[ \Rightarrow \frac{1}{\tau^2} \sim \text{Type-2 Gumbel} \]
Sensitivity

How sensitive is the output to the input

\[ \pi_{a_0}(\tau | y) \propto f(y | \tau) \pi_{a_0}(\tau) \]

with a fixed base prior parameter specification \( a_0 \)

for Bayesian hierarchical models?
Epsilon-local sensitivity

Roos, Martins, Held and Rue (2015):

- A formal approach
- Applicable to complex hierarchical models
- Invariant to any one-to-one transformation
- Reacts correctly to an increased number of observations
Epsilon-local sensitivity measure

Roos, Martins, Held and Rue (2015):

Discrepancy measure: Hellinger distance

\[ H(\pi_a(\tau), \pi_{a_0}(\tau)) = \sqrt{1 - \int \sqrt{\pi_a(\tau)\pi_{a_0}(\tau)} \, d\tau} \]

Epsilon-grid:

\[ G_{a_0} = \{ a : H(\pi_a(\tau), \pi_{a_0}(\tau)) = \epsilon \} \]

\[ = \{ a_l, a_u \} \]

for a small, fixed \( \epsilon \)
Epsilon-local sensitivity measure (continued)

Roos, Martins, Held and Rue (2015):

Worst-case sensitivity:

\[ S_{a_0} = \max \left\{ \frac{H(\pi_{a_1}(\tau | y), \pi_{a_0}(\tau | y))}{\epsilon}, \frac{H(\pi_{a_u}(\tau | y), \pi_{a_0}(\tau | y))}{\epsilon} \right\} \]

Marginal posterior densities: R-INLA (Rue et al. (2009))
Results
Discussion

Pros:

– Sensitivity analysis can guide priorities in eliciting priors

– Scaled prior distributions lead to easy epsilon-grids

– Epsilon-local sensitivity can compare different prior assumptions given the data at hand

– Co-parameter sensitivity can be quantified

Further work needed:

– Extend the sensitivity approach to distributions defined by MCMC samples


