Quantification of prior impact in terms of prior effective historical and current sample size

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Introduction

- Bayesian trials can take advantage of prior information
- Desire to avoid domination of the prior information on posterior inference
- Assessment and communication of the impact of a prior crucial
- 2 aspects of impact of a prior:
  - Strength of information (dispersion)
  - Commensurability with current data (prior-data conflict)
- Equating the information contained in the prior to a certain sample size gives rise to the **prior effective sample size (ESS)**

Prior Effective Sample Size: Samples from what?

ESS quantified in terms of ...

- ... ***historical* samples / *EHSS***:
  Prior considered as posterior given historical data under a baseline prior.
  ESS quantifies number of samples in this historical data set.

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- ... ***current* samples / *ECSS***:
  Prior information equated to samples from the current data model.
  ESS quantifies number of current samples to be added or subtracted to the likelihood in order to obtain a posterior inference equivalent to that of a baseline prior model (e.g. in terms of MSE).

Prior Effective Sample Size: Samples from what?

Picture a paediatric trial where prior comes from preceding adult trial:

- ***EHSS***: How many (hypothetical) patients with *adult characteristics* are added to the data set of children?
- ***ECSS***: How many (hypothetical) patients with *child characteristics* are added to the data set of children?

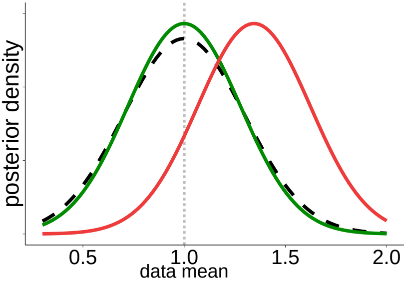
→ Introduce ***ECSS*** and its possible merits

Prior informativeness versus prior impact

EHSS quantifies the amount of prior information,
ECSS intends to additionally quantify its impact on posterior.

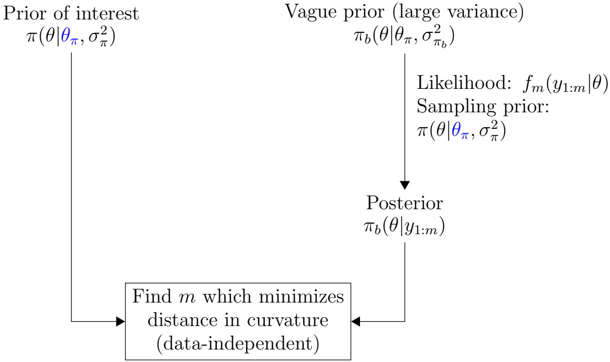
Example: Data $y \sim N(1, 3^2)$, n=100

Baseline prior $N(0, 10^2)$
Prior $N(1, 0.75)$, prior mean=data mean
Prior $N(3.5, 0.75)$, prior mean≠data mean



ESS as samples from *historical* data model: *EHSS*

- Known results for exponential families with conjugate priors, e.g. *EHSS* $= \sigma_y^2/\sigma_\pi^2$ in $y \sim N(\mu, \sigma_y^2)$, $\mu \sim N(\mu_\pi, \sigma_\pi^2)$
- Example: *EHSS*=16 for both priors
- Generalization by Morita, Thall & Müller (2008)



ESS as samples from *current* data model: *ECSS*

Prior of interest
$\pi(\theta|\theta_\pi, \sigma^2_\pi)$

Likelihood:
$f_{k-m}(y_{1:(k-m)}|\theta_0)$

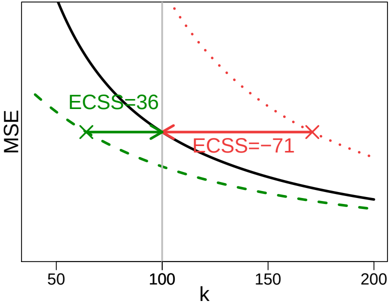
Posterior
$\pi(\theta|y_{1:(k-m)})$

Objective/reference prior
$\pi_b(\theta|\theta_{\pi_b}, \sigma^2_{\pi_b})$

Likelihood:
$f_k(y_{1:k}|\theta_0)$

Posterior
$\pi_b(\theta|y_{1:k})$

Find m which minimizes distance in MSE



In practice: replace θ_0 by the poserior mean under π_b

- Builds on Reimherr, Meng & Nicolae (2014)
- Negative in case of prior-data conflict

When is *ECSS* of potential interest?

The *EHSS* is valuable for prior elicitation when no information about the future trial is yet available.

However,

1. *EHSS* describes amount of information but not impact of a prior
2. In some situations no consensus on how to compute *EHSS* and a data-dependent measure is desirable $\rightarrow$ e.g. mixture priors
3. In some situations we are rather interested in the current rather than historical prior sample size $\rightarrow$ e.g. adaptive trial

Robust mixture priors

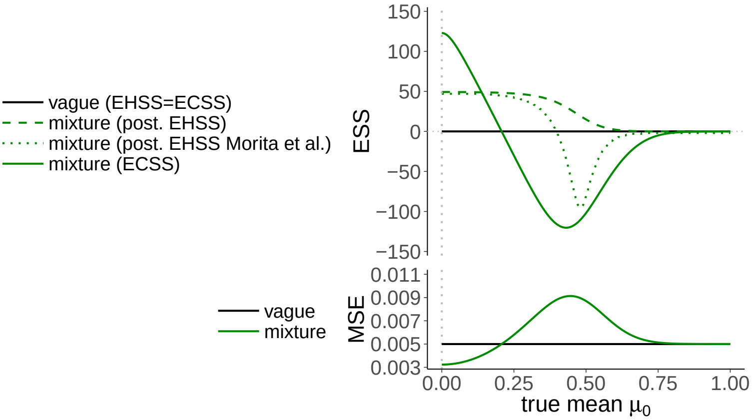
Robust mixture prior: $\pi(\mu) = (1 - \rho)\pi_{informative}(\mu) + \rho\pi_{baseline}(\mu)$

- Mixture of informative and baseline prior
  Heavy-tailed $\Rightarrow$ information discarded for clear prior-data conflict
- No consensus on how to compute *EHSS* for mixture priors
  - Proposals for *data-independent EHSS*:
    - Apply Morita et al's algorithm to prior (1), approximate mixture (2) or take weighted average of *EHSS*s of mixture components (3)
    - May give different results,
      (1) and (2) not significantly influenced by the baseline component
    - Do not describe how much information the prior introduces for given data
  - Proposals for *data-dependent EHSS*:
    - Apply approaches above to posterior and subtract data sample size
    - Problematic if posterior has multiple peaks or is skewed

$\rightarrow$ Data-dependent *EHSS* come with strong assumptions,
ECSS a natural alternative

Robust mixture priors: Example

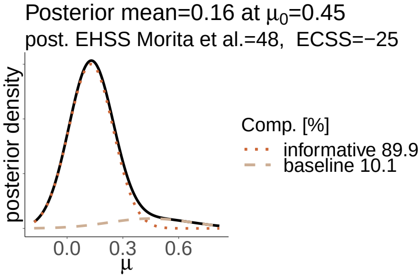
- $y \sim N(\mu, 1)$ for varying μ, $n = 100$
  Prior: $\mu \sim 0.5N(0, 1/50) + 0.5N(0, 10^2)$
- Prior *EHSS* based on weighted avg. of the mixture component *EHSS* = 25, algorithm of Morita et al. provides a prior *EHSS* of 49

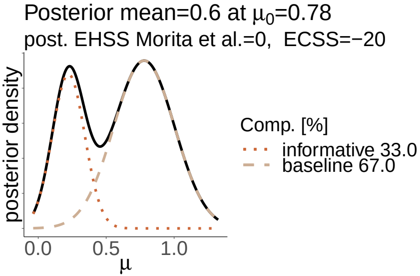


- MSE increased for moderate conflict which is captured by *ECSS*

Robust mixture priors: Bimodality

Examples with $n = 20$ to show effects of bimodality in the posterior





- Prior has strong impact on posterior means in both cases
- *"posterior EHSS Morita et al."* not meaningful
- *ECSS* quantifies samples from homogeneous current population (described by likelihood),
  EHSS approaches try to quantify samples from heterogeneous historical population (described by mixture)

Example: Adjusting the control sample size in adaptive trial

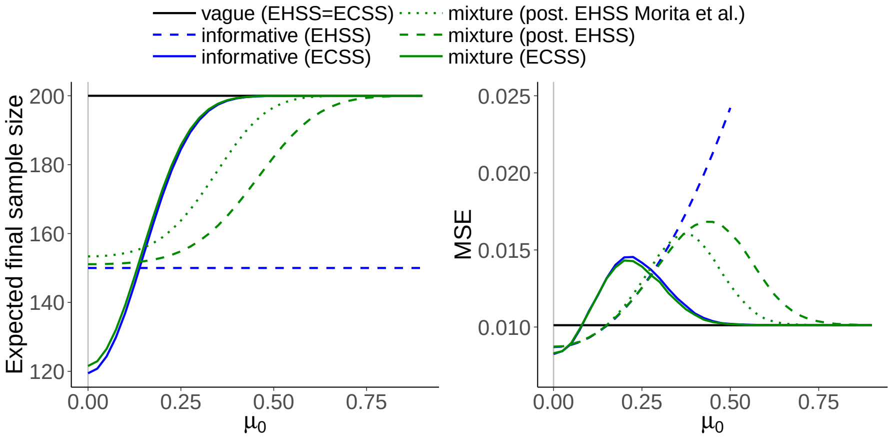
- Two arm trial with $y_{control} \sim N(\mu_0, 1),\ y_{treat} \sim N(\mu_0 + \tau, 1)$;

$$H_0 : \tau \leq 0 \text{ vs } H_1 : \tau > 0$$

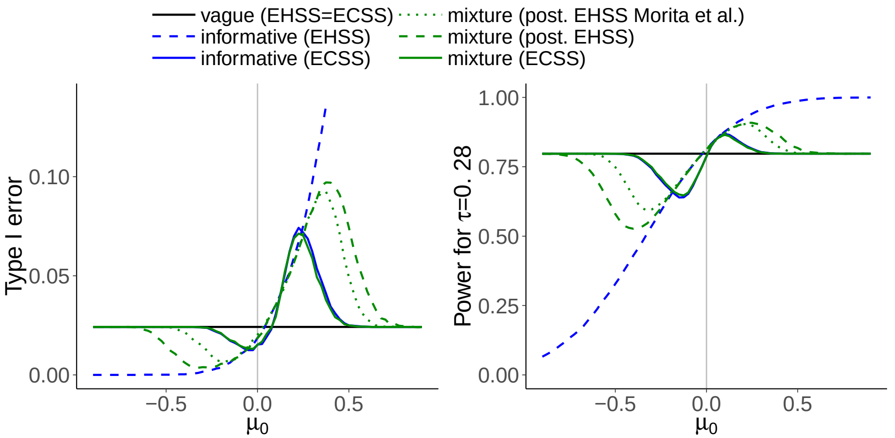
- Final control sample size adapted according to ESS at interim
  - Compute ESS after 100 patients in control group
  - Final sample sizes in test treatment 200, in control group $200 - ESS$
- E.g. Hobbs et al (2013), Schmidli et al (2014), Kim et al (2018); all use *EHSS* with priors adapting to prior-data conflict
- However, *ECSS* intuitively more appropriate: *"How many control samples are offset by prior at final analysis?"*

Adaptive design cont'd (1)

- Informative prior $\mu \sim N(0, 1/50)$,
  mixture prior $\mu \sim 0.5N(0, 1/50) + 0.5N(0, 10^2)$
- If $ESS < 0$, replace mixture by baseline prior ($ESS = 0$)

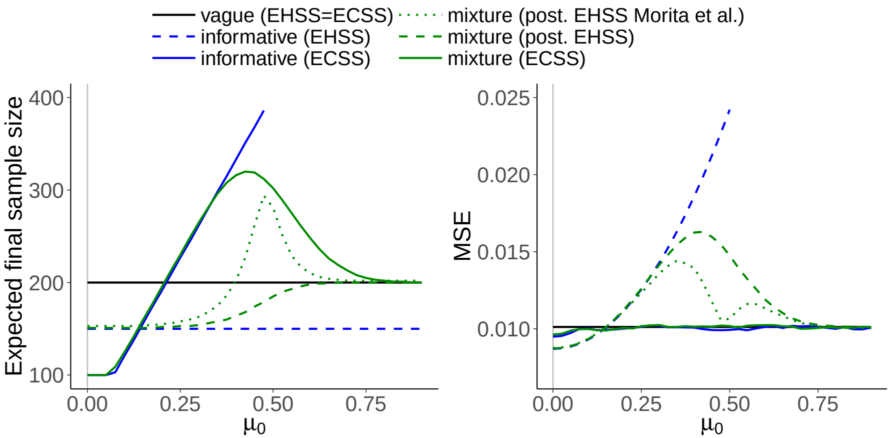


Adaptive design cont'd (2)



→Use of *ECSS* improves all operating characteristics

Adaptive design cont'd (3): Results under known μ_0



Asserts that using *ECSS* equal MSEs under reduced samples sizes for all priors would be obtained if μ_0 would be known.

R package “ESS”

Extends package RBesT for binary and normal outcomes

```
library(ESS)
info <-mixnorm(informative=c(1, 0, .14), sigma=1)
mix <-robustify(info, weight=.2, mean=0, sigma=1)
data=...

ehss(mix, method="mix.moment")
ecss(mix, data=data, n.target=100, min.ecss=-100)
```

Also supports empirical Bayes power priors (Gravestock & Held, 2017)

```
pp=as.powerprior(info)
# Full RBesT functionality can be applied to pp object
ehss(pp, data=data)
ecss(pp, data=data, n.target=100, min.ecss=-100)
```

Conclusions & Outlook

The prior can often only be understood in the context of the likelihood
– Gelman, Simpson & Betancourt (2017)

- 2 frameworks of prior effective sample sizes
  - *EHSS* quantifies historical observations used to elicit prior
  - *ECSS* quantifies number of (virtual) samples from the current data model
- *ECSS* more appropriate than *EHSS* if data dependent measure desired
- *ECSS* provides framework applicable to any likelihood/prior setting
- Alternative measures to MSE may be more appropriate depending on targeted characteristics and data distributions
- Potential for quantifying ESS in hierarchical models
- R package for binary and normal outcomes available on `https://github.com/wiesenfa/ESS`

Thank you!

References

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