



MRC
Biostatistics
Unit



UNIVERSITY OF
CAMBRIDGE

Bayesian Methods for Clinical Trials

Lecture 3: Prior specification

Libby Daniells & Pavel Mozgunov & Thomas Jaki

MRC Biostatistics Unit

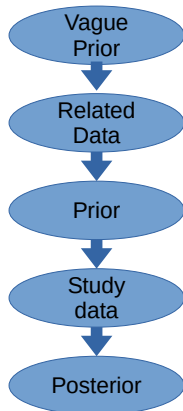
February 24, 2025

Constructing prior distributions

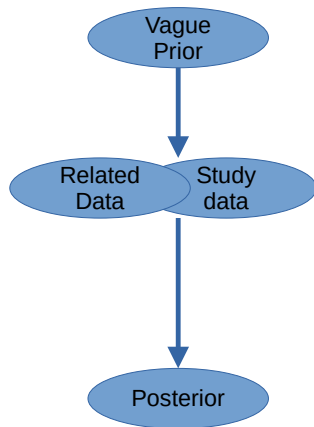
- Use relevant data to construct prior
- Use subjective opinion(s)

A simple idea

- Use vague prior
- Update prior with relevant data
- Use resulting posterior as the prior for the data analysis

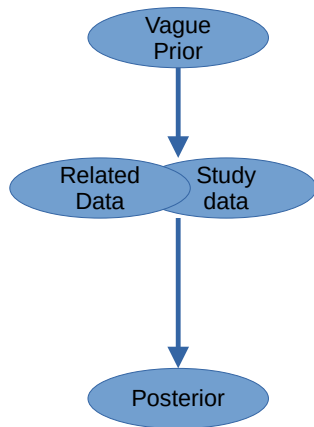


- Use vague prior
- Update prior with relevant data
- Use resulting posterior as the prior for the data analysis



- Use vague prior
- Update prior with relevant data
- Use resulting posterior as the prior for the data analysis

⇒ Identical to the simple idea



Discounts the 'effective prior sample size' by a factor κ . e.g.,

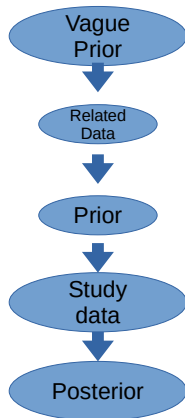
- a fitted $Beta(a, b)$ would become a $Beta(\kappa a, \kappa b)$
- a $Gamma(a, b)$ would become a $Gamma(\kappa a, \kappa b), 2)$
- a $Normal(\mu, \sigma^2)$ would become a $Normal(\mu, (\kappa\sigma)^2)$
- only increases variability

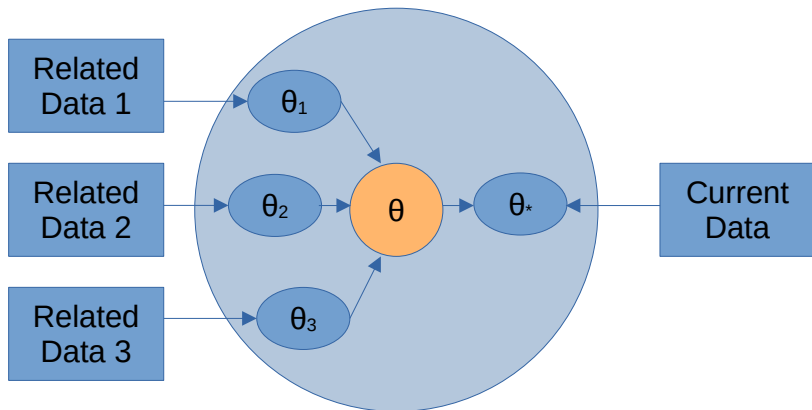
More formally for relevant data \mathbf{x}_0 , initial prior $\pi_0(\theta)$ and discount factor α_0 , the prior is

$$\pi(\theta|\mathbf{x}_0, \alpha_0) \propto f(\mathbf{x}_0|\theta)^{\alpha_0} \pi_0(\theta)$$

and the posterior is

$$\pi(\theta|\mathbf{x}, \mathbf{x}_0, \alpha_0) \propto f(\mathbf{x}|\theta)f(\mathbf{x}_0|\theta)^{\alpha_0} \pi_0(\theta)$$



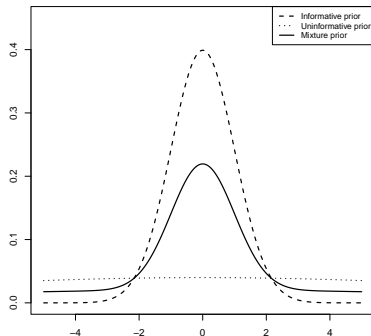


- Typically heavy-tailed, hence naturally robust
- Typically not available analytically, but can be approximated by mixture of conjugate priors
 - ⇒ Easier communication
 - ⇒ Analytical posterior calculation

Mixture (robustified) prior

$$w * \pi_0^I(\theta) + (1 - w) * \pi_0^{NI}(\theta)$$

- $\pi_0^I(\theta)$ is informative
- $\pi_0^{NI}(\theta)$ is vague
- w is the weight of each component
- w will have a prior and hence is also updated



IDEA: Use expert opinion to construct a prior

PROBLEM: Translate opinion into statistical distributions

Identifying experts

Pre-specified criteria should used to identify experts:

- Wish to elicit as many opinions as possible subject to time and cost constraints.
- Invite opinion leaders or use purposeful sampling to capture extremes of opinion.

For the MYPAN trial (Hampson et al, 2015), defined an expert as a paediatric consultant

- Specialising in rheumatology, nephrology or immunology;
- With experience of treating children with PAN (on average 1 case every 2 years).

A simple clinical study

40 patients are to be treated with an experimental drug

We will observe whether they respond or not (binary outcome)

Let p denote the probability of a patient responding

We assume this probability is the same for all patients

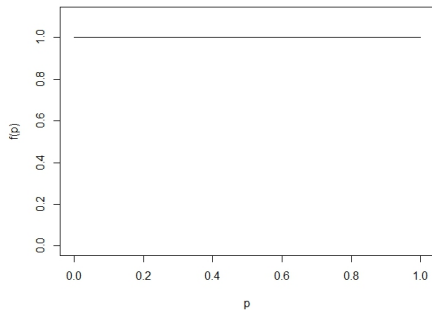
Before any patients are administered treatment, we can consider our prior beliefs about the value of p and characterise it

Prior Beliefs

Let p be the probability of a patient responding

We know that p lies between 0 and 1 but can our belief be described like this?

Every value between 0 and 1 is equally likely

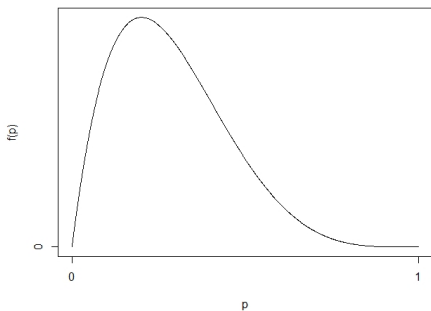


Prior Beliefs

No, our belief is not uniform

We believe p is more likely to be around 0.2

In this case, a Beta(2,5) model has been shown.



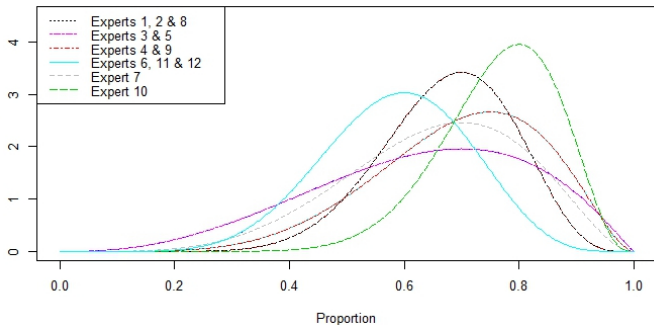
PROBLEM: Ask 5 experts, get 6 answers

SOLUTION: Elicit individually and then aggregate

Structure of an elicitation meeting

- Provide experts with summary of knowledge about disease and treatments
- Discussion of endpoint
- Provide experts with an overview of Bayesian methods
- Perform a toy elicitation exercise to ensure understanding of the questions
- Elicit expert opinion
- Combine expert opinion

Combining elicited priors



- Mathematical aggregation
- Behavioural aggregation

Linear opinion pool (Stone, 1961):

$$\pi_0(\theta) = \sum_{i=1}^n w_i \pi_0^{(i)}(\theta)$$

Logarithmic opinion pool (Genest, 1984):

$$\pi_0(\theta) = k \prod_{i=1}^n \pi_0^{(i)}(\theta)^{w_i}$$

where k is a normalizing constant, w_i is the weight for each prior and $\pi_0^{(i)}(\theta)$ is the prior for expert i . Note that for the logarithmic opinion pool w_i needs to be chosen such that $\pi_0(\theta)$ is a density.

We know that different experts will have different opinions about the parameter of interest

We need a single probability distribution for each parameter of interest to synthesise your knowledge

But what kind of consensus can we hope for?

We do not expect complete agreement!

Hope to obtain a distribution representing the reasonable opinions of an external observer

Opinion of the external observer

RIO is the Rational Impartial Observer






He/she has listened to the discussions and understands the arguments

RIO does not have identical views to any expert

We ask experts to consider judgements that RIO might make

Experts should acknowledge that the RIO may find some merit in all of the differing arguments and opinions

References

-  Genest C. (1984) A characterization theorem for externally Bayesian groups. The Annals of Statistics. 12:1100-5.
-  Hampson LV, Whitehead J, Eleftheriou D, Tudur-Smith C, Jones R, Jayne D, Hickey H, Beresford MW, Bracaglia C, Caldas A, Cimaz R. (2015) Elicitation of expert prior opinion: application to the MYPAN trial in childhood polyarteritis nodosa. PLoS One. 10:e0120981.
-  Ibrahim JG, Chen MH (2000). Power prior distributions for regression models. Statistical Science. 1:46-60.
-  Schmidli H, Gsteiger S, Roychoudhury S, O'Hagan A, Spiegelhalter D, Neuenschwander B (2014). Robust meta-analytic-predictive priors in clinical trials with historical control information. Biometrics. 70:1023-1032.
-  Stone M. (1961). The opinion pool. Annals of Mathematical Statistics, 32:1339-1342.