Illustration of Bayesian Methodology as a Tool for Evidence Synthesis in Veterinary Medicine

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To start with...

"In theory, theory and practice are the same. In practice, they are not."

– Albert Einstein

Real World Problems

Clinical Research Question

Do the oral supplementation glucosamine sulphate (GS) and chondroitin sulphate (CS) have an effect on stiffness in veteran horses?

Higler et al. (2013) The effects of three-month oral supplementation with a nutraceutical and exercise on the locomotor pattern of veteran horses. Equine Veterinary Journal, doi 10.1111/evj.12182

Real World Problems

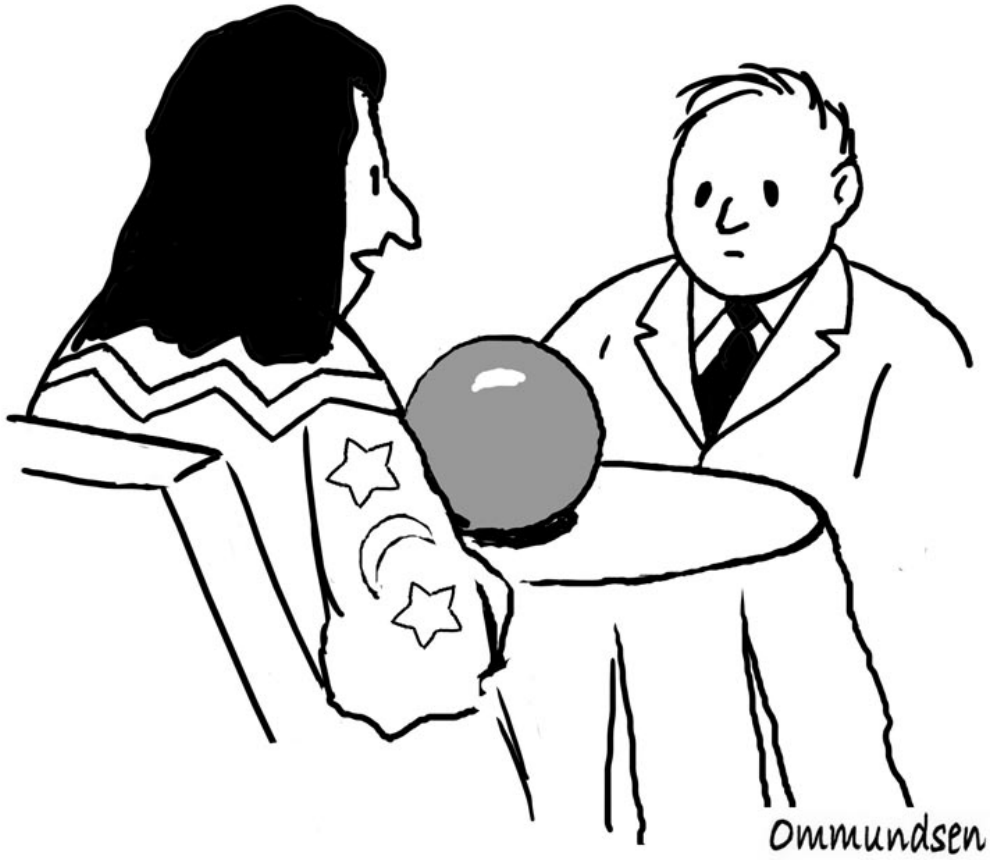
- a Dutch clinical trial
- 24 veteran horses
- 12 in the treatment group, 12 in the control group
- 3 months treatment
- parameters of interest measured before and after treatment, e.g., stride length

Real World Problems

- Conclusion from one trial reliable?
- Do we know more?
  - meta analysis?

What we have...

- Not enough clinical trials done on the same research question
- Enough studies with lower levels of evidence, e.g., observational
- Enough studies from across animal species on approximately the same research question



“Is this needed for a Bayesian analysis?”

The Formula's

Bayes' Theorem

Suppose we have event A and event B, and the probability of event A $\neq 0$,

$$p(B|A) = \frac{p(A|B) \times p(B)}{p(A)}$$

$$p(B|A) \propto p(A|B) \times p(B)$$

Posterior probability B $\propto$ Likelihood of Event A $\times$ Initial probability B

Parameters of Interest

$$\pi(\theta|D) \propto L(D|\theta) \times \pi(\theta)$$

$L(D|\theta)$ refers to the information in data about θ.

The Formula's

Bayesian Updating

Non-informative prior: $\pi(\theta) = c$

Data 1: $\pi(\theta|D_1) \propto L(D_1|\theta) \times \pi(\theta)$ with $\pi(\theta) = c$

Data 2: $\pi(\theta|D_2) \propto L(D_2|\theta) \times \pi(\theta)$ with $\pi(\theta) = \pi(\theta|D_1)$

Data 3: $\pi(\theta|D_3) \propto L(D_3|\theta) \times \pi(\theta)$ with $\pi(\theta) = \pi(\theta|D_2)$

Data 4: ...

The Formula's

Focus on the current study:

The power prior approach (Ibrahim, J.G. & Chen, M.-H., 2000)

The Power Prior(s)

For a single historical study:

$$\pi(\theta|D_0, a_0) \propto L(\theta|D_0)^{a_0} \times \pi_0(\theta)$$

For multiple historical studies:

$$\pi(\theta|D_{0k}, a_{0k}) \propto \prod_{k=1}^{L_0} [L(\theta|D_{0k})^{a_{0k}}] \times \pi_0(\theta)$$

D_0 and D_{0k} denote the historical study; a_0 and a_{0k} denote the weight.

Parameter Estimates

Posterior $\propto$ Likelihood of the current study $\times$ the power prior(s)

What we have done...

- The Higler et al. (2013) clinical trial as the current study
- Treatment effect is of interest: change in stride length for horses
- Seven historical studies included, they vary in:
  - animal species: horses, dogs, human
  - study designs: such as
    - clinical trials, observational;
    - different treatment duration

The Weight a_0

- $0 \leq a_0 \leq 1$: $a_0 = 0$: data not included; $a_0 = 1$: data fully included
- based on degree of overlap between current and historical study characteristics
- allows the researcher to control the informativeness of the historical studies for the research question of the current study
- experts decide the weights
- expert elicitation
- sensitivity analyses

The Weight a_0

- Two weights were specified with respect to:
  - clinical relevance
  - methodological qualities
- Both experts get 100 points that can be assigned to the seven studies
- $\sum a_{0k} = ?$

The Weight a_0

ID	Clinical expert		Methodologist	
	Score	Motivation	Score	Motivation
1	10	n=35; dog; no negative control	2	control group not optimal; lacked sufficient power
2	26	n=8; horse; small sample size	5	small sample size; results unclear
3	38	n=20; horse; small control group	15	treatment duration short; lacked a direct comparison
4	8	n=222; human; subjective scoring	30	properly executed
5	8	n=572; human/veterans; subjective scoring	30	properly executed
6	6	n=98; human; subjective scoring; only GS	10	treatment duration short; study design not optimal
7	4	n=30; horses; IM product is nonsense	8	lacked a predetermined non-inferiority margin

Discussion: A Bayesian approach is...

- more ethical
- more flexible
- more efficient
- more useful
- more transparant
- more objective

Spiegelhalter et al. (2003) Bayesian Approaches to Clinical Trials and Health-Care Evaluation. John Wiley & Sons, UK.

Discussion: Challenges

Some challenges as an example, there are definitely a lot more out there!

- Sample size from the historical studies:
  - should it be considered in the weighing process?
  - how to assign weights to studies with a large sample size (e.g., observational)?
- Should the current study be weighted by experts as well?

Discussion: Challenges

- Meta analysis in the prior?
- Should weights elicited by different criteria be combined? How?
- Alternative expert elicitation methods?

Conclusion

Transparancy!