Probabilistic Sensitivity Analysis

Dispelling the myths…

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Some common myths surrounding PSA…

- But Claxton tells us 'inference is irrelevant' which means that we don't have to worry about uncertainty? Right?
- But PSA is complicated, we can handle uncertainty using standard sensitivity analysis methods? Right?
- But there are so many potential distributions, PSA is just an arbitrary exercise? Right?
- PSA is all very well for simple models, but for my all-singing all-dancing discrete-event micro-simulation Markov-decision-process with policy relevant individual patient prediction module PSA is computationally expensive? Right?

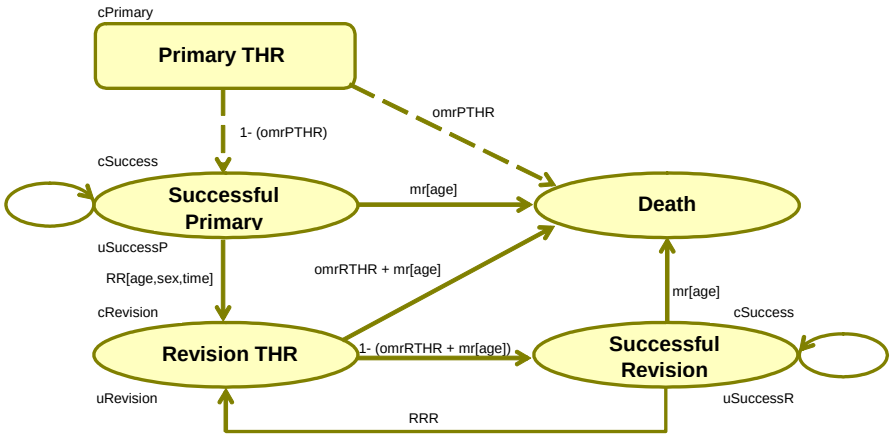
x Wrong

x Wrong

x Wrong

…okay, you got me

A new prosthesis for total hip replacement



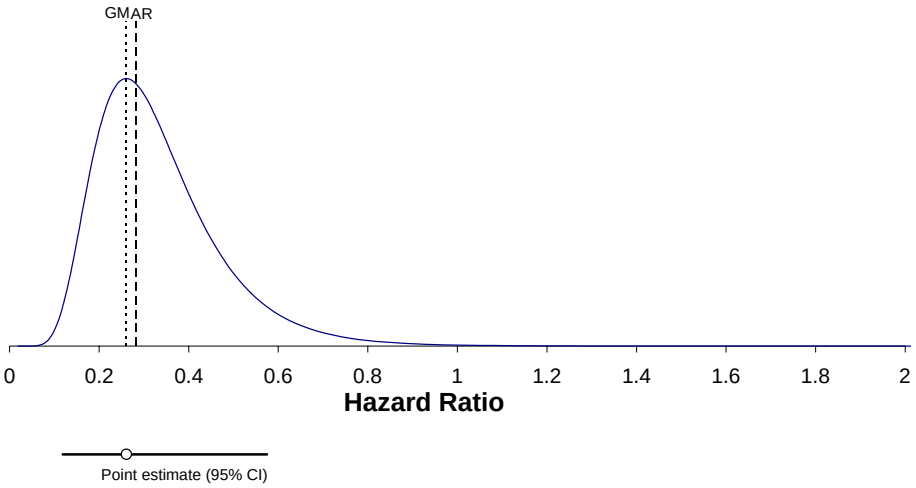
But Claxton tells us 'inference is irrelevant' which means that we don't have to worry about uncertainty?

Even if this were true…

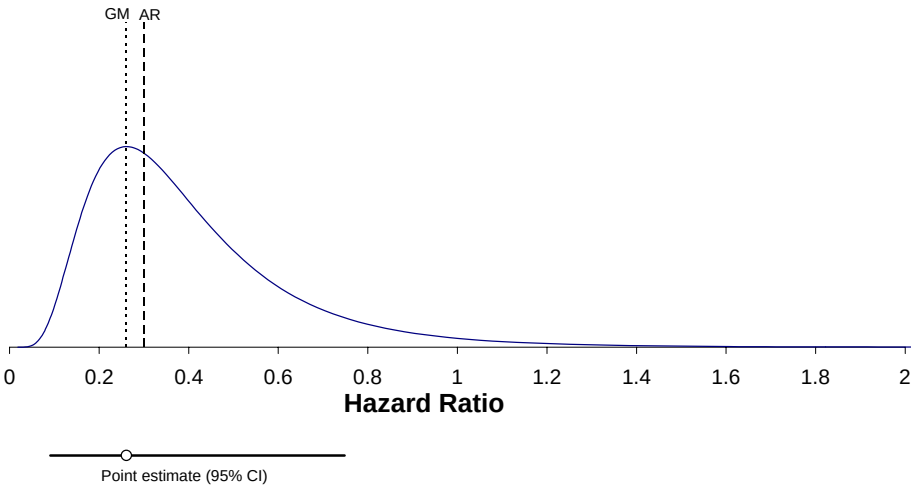
- Input parameters may be skewed and standard reporting may not focus on mean
- Most decision models are not linear
- Uncertainty in input parameters affects the Expectation of the output parameters of interest

Example: Hazard ratio of risk of revision in hip model

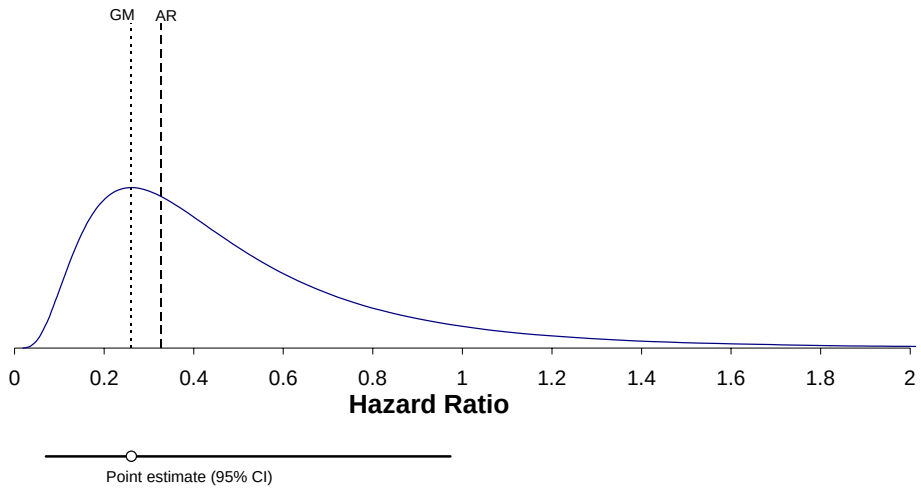
Hazard ratio: CoV=0.3



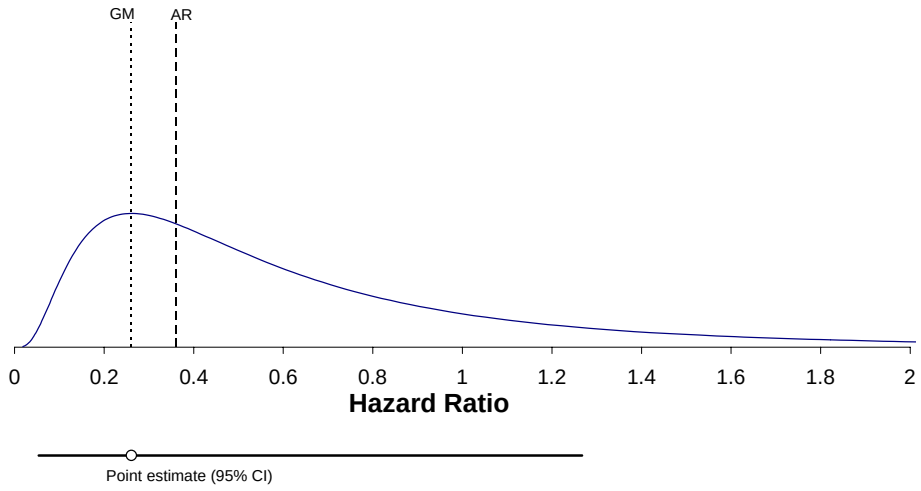
Hazard ratio: CoV=0.4



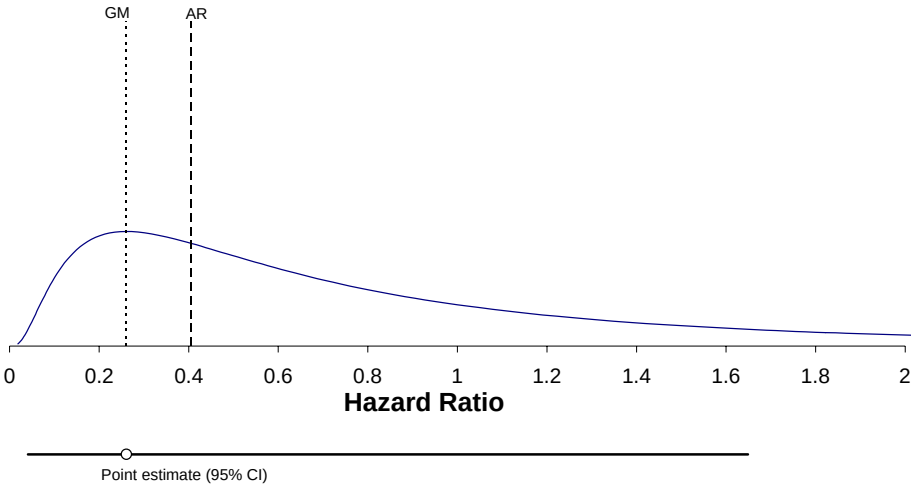
Hazard ratio: CoV=0.5



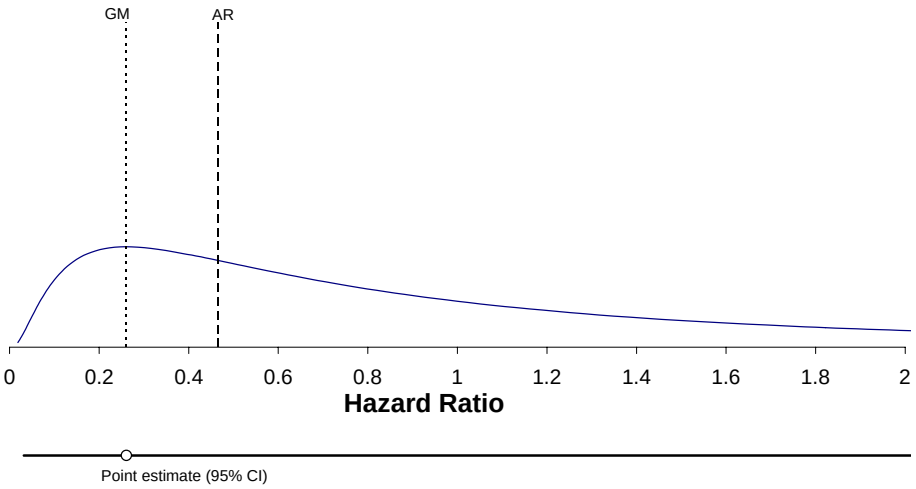
Hazard ratio: CoV=0.6



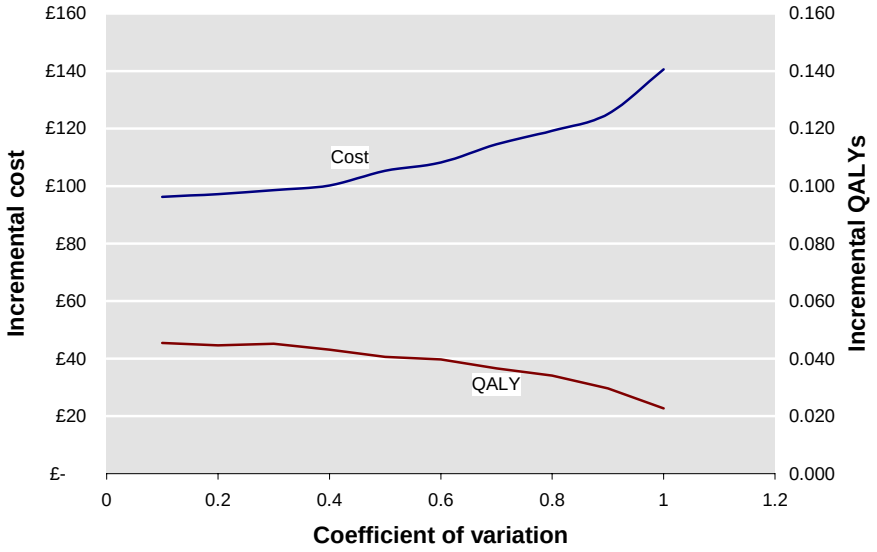
Hazard ratio: CoV=0.7



Hazard ratio: CoV=0.8



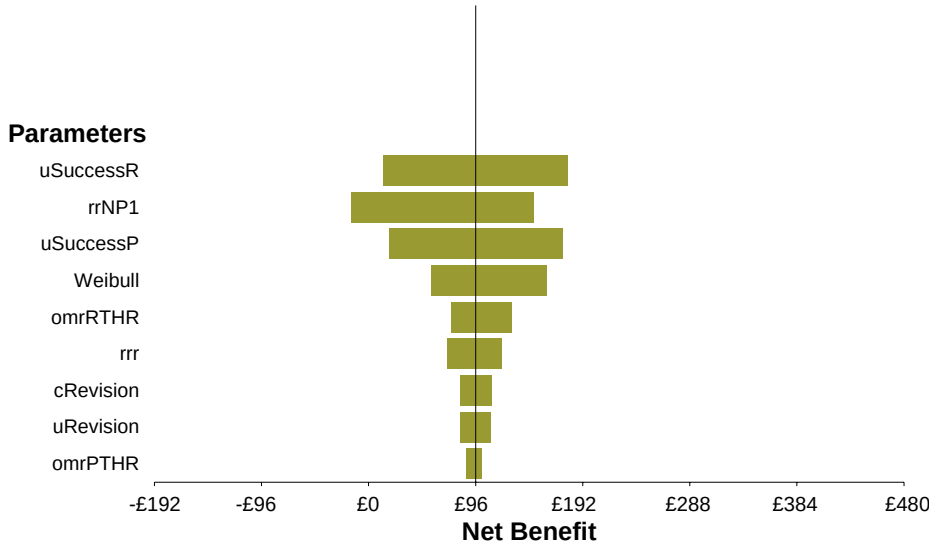
Effect of CoV of HR/ nonlinearity of the model on output parameters



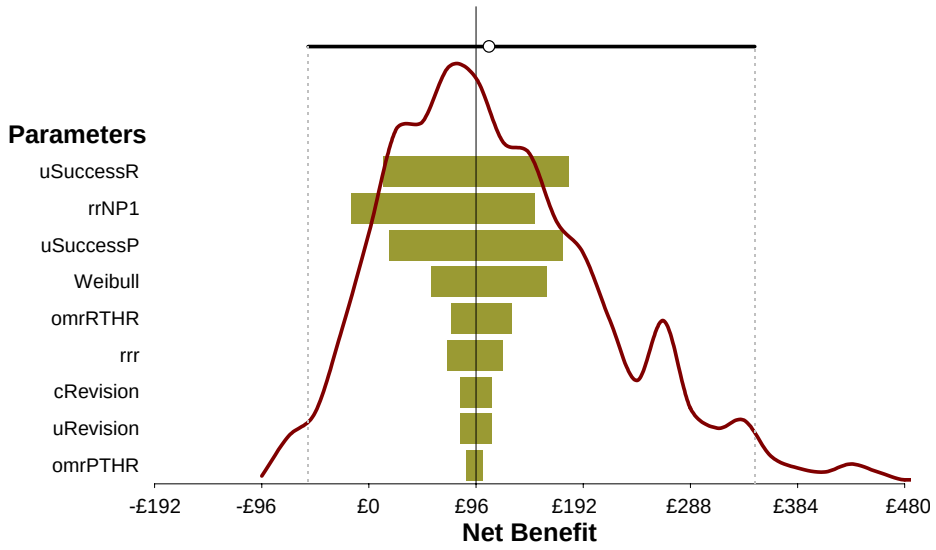
But PSA is complicated, we can handle uncertainty using standard sensitivity analysis methods?

- One-way sensitivity analysis can under-represent decision uncertainty
- Multi-way analysis is cumbersome and doesn't say anything sensible about how likely different combinations of parameters are
- Both effectively ignore correlation

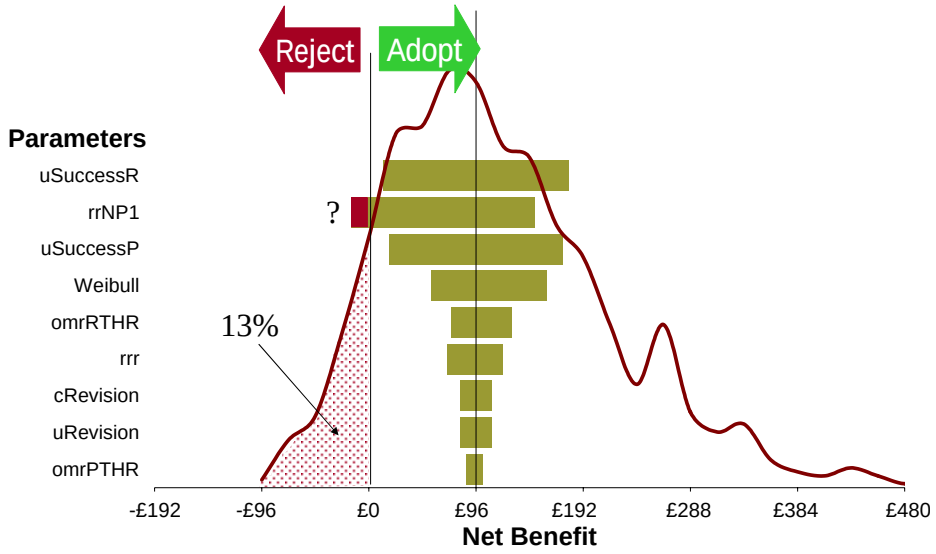
One-way SA – Tornado diagram



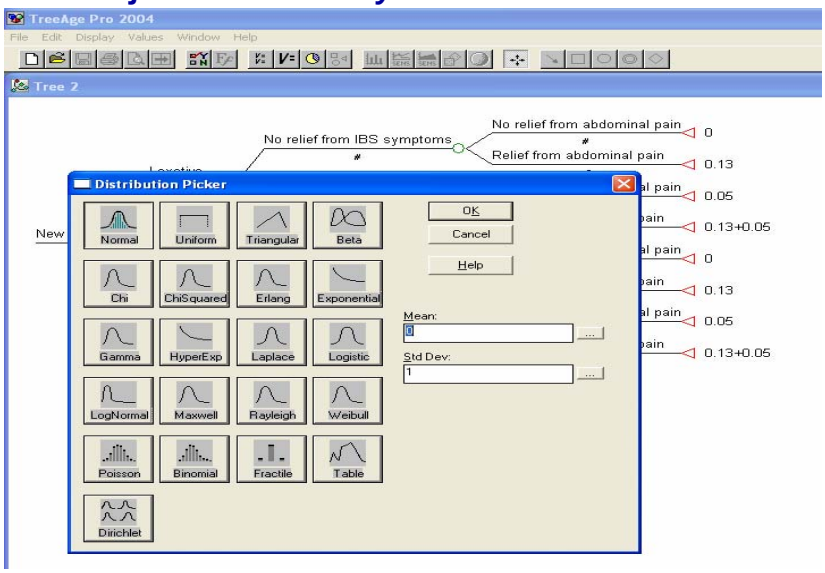
PSA frequency distribution



Probability of incorrect decision making



But there are so many potential distributions, PSA is just an arbitrary exercise?



Choice of distribution is not arbitrary…

- A normal distribution is always a candidate
  - *Central Limit Theorem*
- Otherwise small number of candidates:
  - *Type of parameter (logical restrictions)*
  - *Data being used to inform parameter estimation*
  - *Method of estimation*

For example: Probability parameters
Logical restriction: zero-one interval

- Type of data: binomial
  Estimation: univariate proportion
  - *Use Beta distribution*
- Type of data: binomial
  Estimation: multivariate logistic regression
  - *Use multivariate normality on log odds scale*
- Type of data: time to event
  Estimation: survival analysis
  - *Use multivariate normality on log hazards scale*

PSA is all very well for simple models, but for my all-singing all-dancing discrete-event micro-simulation Markov-decision-process with policy relevant individual patient prediction module, PSA is computationally expensive?

True, but…

- The ends justify the means
- Uncertainty is important, therefore PSA is necessary

So…

- Buy a faster computer
- Leave it running over the weekend/semester/until 2006
  (haven't you heard of Occam's Razor?)

Nevertheless, some important caveats…

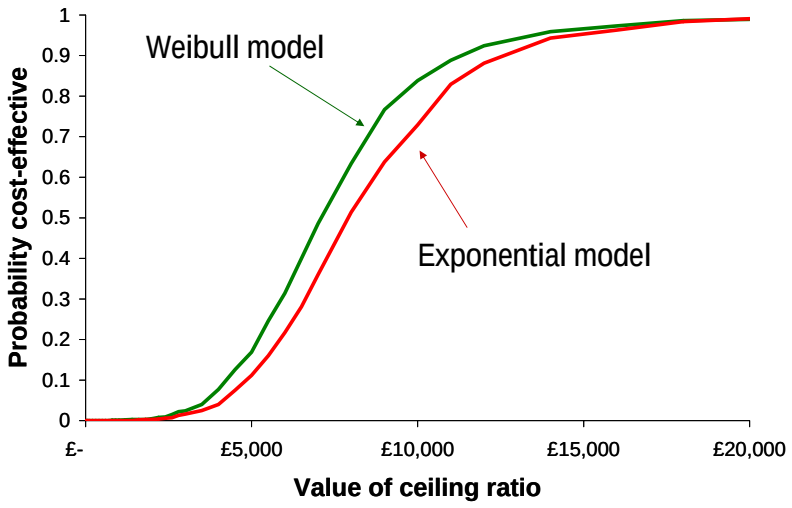
Garbage in / Garbage out

- If we want to make statistical statements about outcomes, we had better be careful how we characterise our inputs
- Your VOI analysis is only as good as the PSA on which it is based!

Parameter uncertainty is not the only uncertainty!

- Structural uncertainty may be just as important
- Continuing role for traditional sensitivity analysis
- Need to see PSA for all scenarios?

Acceptability curves and structural uncertainty



Concluding comments

- Decision uncertainty is important
- PSA can characterise parameter uncertainty to inform decision uncertainty
  - Less arbitrary than traditional SA
  - Process of choosing distributions should encourage more careful consideration of parameter uncertainty
- Continuing role for traditional SA for structural uncertainty
  - In addition to PSA