Investigating Input Correlation in Probabilistic Sensitivity Analysis

Taylor M[1], Barker E[1], Fewster H[1], Watts K[1], Gregg E[1]

[1] York Health Economics Consortium, University of York, York, YO10 5NQ

INTRODUCTION

- Probabilistic sensitivity analysis (PSA) is used to characterise uncertainty in cost-effectiveness models.
- Inputs in PSA are often varied independently even when they may be correlated. A partial cause of this is that correlations are poorly reported in source materials. As a result, PSA results could be misestimating uncertainty.
- Decision-making bodies, such as the National Institute for Health and Care Excellence (NICE), explicitly state that the characterisation of uncertainty is a key factor when determining whether to approve a medical intervention for reimbursement.[1]

Objective:

- This study investigated the effects of input correlation on the level of certainty associated with a decision.

METHODS

- A cost-effectiveness model was developed using R with a user interface created using Shiny where setup parameters and inputs can be amended by the user (available online via QR code).
- In a hypothetical case study, an eight-state Markov model was used to estimated the lifetime costs and quality-adjusted life years (QALYs) for a hypothetical 'treatment' and 'comparator'.
- Each health state was assigned one utility value and five costs.
- To explore the impact of parameter correlation, three approaches were built into the model (Table 1).
- In the latter two approaches, inputs that improved the incremental cost-effectiveness ratio (ICER) were positively correlated with each other and negatively correlated with inputs that worsened the ICER, and vice versa.
- The treatment cost, number of health states, and health state costs were varied in scenario analyses to determine the circumstances in which correlation had the largest impact.

Table 1: Correlation options

No correlation	▪ Inputs varied independently to simulate a typical PSA ▪ Costs were generated as independent observations from the gamma distribution, while utility values and transition probabilities were generated as independent observations from the beta distribution.
Part correlation	▪ Correlation within but not between costs. ▪ The effectiveness inputs for each treatment were varied using a single multiplier, based on a lognormal distribution. Similarly, all costs were varied using a single multiplier, and all utilities were varied using a (separate) single multiplier.
Full correlation	▪ Correlation between all inputs. ▪ A similar approach was used to the part correlation scenario, except that one single multiplier was used to estimate all parameters in the model.

RESULTS

- While the ICER was comparable across all correlation options, the likelihood of cost effectiveness differed substantially from 61% to 93% (Table 2).
- The distribution of PSA results on the cost-effectiveness plane varied depending on the correlation option (Figure 1a).
- In all scenarios, the 'no correlation' option displayed the most certain likelihood (closest to either 0 or 1) of cost effectiveness, while the least certain was produced by the full correlation option.

Table 2: Cost-effectiveness analysis results

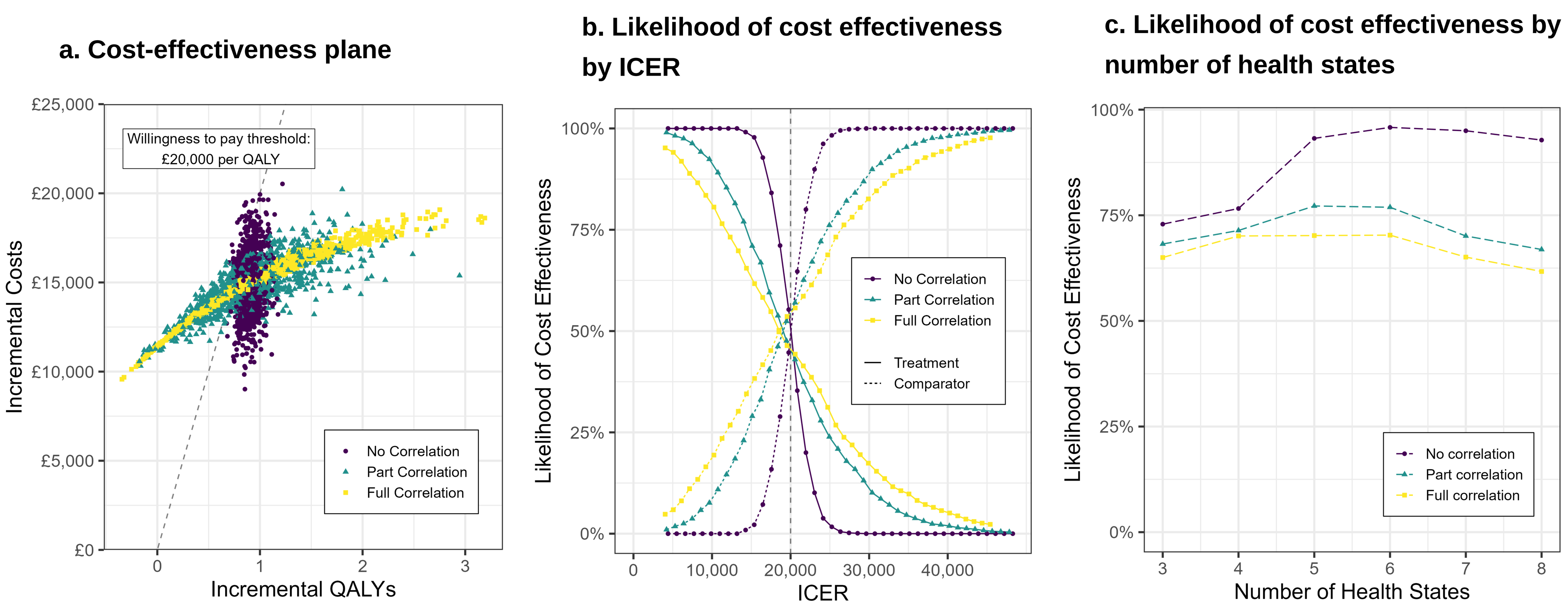
Correlation option	Treatment cost (SD)	Comparator cost (SD)	Treatment QALY (SD)	Comparator QALY (SD)	Incremental cost (SD)	Incremental QALYs (SD)	ICER	Likelihood of being cost effective
No correlation	29,561 (1,495)	14,548 (1,190)	2.5 (0.07)	1.6 (0.05)	15,012 (1,745)	0.9 (0.08)	16,467	92.8%
Part correlation	29,345 (1,081)	14,488 (1,407)	2.5 (0.40)	1.6 (0.21)	14,857 (1,396)	0.9 (0.43)	16,207	66.9%
Full correlation	29,354 (1,026)	14,452 (1,431)	2.6 (0.53)	1.6 (0.09)	14,902 (1,816)	1.0 (0.62)	15,415	61.7%

Abbreviations: CE – cost effectiveness, ICER – incremental cost-effectiveness ratio, QALY – quality-adjusted life year, SD – standard deviation.

Scenario analysis results:

- The difference in the likelihood of cost effectiveness between different correlation options is most pronounced when the ICER is moderately close to the willingness-to-pay threshold (Figure 1b).
- The greater the complexity of the model (i.e. the greater the number of health states), the more pronounced the difference between correlating or not correlating inputs (Figure 1c).

Figure 1: Cost-effectiveness analysis and scenario analysis



Abbreviations: ICER – incremental cost-effectiveness ratio, QALY – quality-adjusted life year.

CONCLUSION

- This analysis demonstrates that input correlation can have a substantial impact on the level of certainty in model outputs and, by ignoring this, the model may be over- or under-stating the true level of confidence.
- Developing a simple guide to critiquing approaches to parameter correlation is difficult as the direction and magnitude of bias will depend on many factors, meaning any 'rules of thumb' could differ in each circumstance.
- For example, where inputs are not correlated, increasing the number of inputs can decrease uncertainty because it introduces a greater likelihood of a type of central limit theorem for the joint distribution of all parameters.
- As such, the '% likelihood of being cost effective' estimates reported in HTA assessments should, in most cases, be treated with a large degree of caution, especially where correlation has been largely neglected.

REFERENCES

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CONTACT US

matthew.taylor@york.ac.uk

+44 1904 323620

www.yhec.co.uk

York Health Economics Consortium

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