

# Use of Copula for Correlated Sampling of Cost and Utility Parameters During Probabilistic Sensitivity Analysis Of A Cost-Effectiveness Model

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## Key points of this study

- ✓ During probabilistic sensitivity analysis, cost and utility parameters of cost-effectiveness models can be sampled jointly to account for dependency between parameters.
- ✓ Correlated sampling of key cost and utility parameters may lead to a small change in Kendall tau correlations of incremental costs and QALYs.

## INTRODUCTION

- For probabilistic sensitivity analysis (PSA) of cost-effectiveness model (CEM), cost and utility parameters are typically assigned separate probability distributions and sampled independently.
- In real-world data, correlation could exist between cost and utility, induced by unmeasured confounding variables such as patient socio-economic status that influence both cost and utility.
- Cost and utility may also follow different forms of probability distributions, which more conventional models such as multivariate normal distribution do not adequately address.
- Joint sampling of cost and utility parameters in simulation program of PSA to account for dependency through Copula modeling used in insurance or finance may shed additional insight.

## OBJECTIVE

- To explore potential impact on PSA of joint sampling of cost and utility parameters through use of a copula model.

## METHODS

- The Markov model of the total hip replacement (THR) surgery comparing a standard procedure (SP) group and a new procedure (NP) group in R by Naylor et al. [1] was utilized as the framework.
- Within the model, the re-revision risk after a successful revision for the SP group was modified to be larger than that for the NP group, by the magnitude of the risk parameter within the Weibull regression model for the risk of failure of the primary THR.
- Joint sampling via Clayton copula was conducted with R package *copula* for the parameters of the revision surgery cost based on Gamma (12.67, 417.67) and the revision state utility based on Beta (69.7, 162.63), with different Kendall tau correlations (-0.5 to 0.5) assumed for copulas.
- 10,000 simulations per cohort of incremental costs, QALYs, ICERs, estimated tau between incremental costs and QALYs.

## RESULTS

### 1. Simulated costs, QALY, and ICERs under different Kendall tau values for Clayton Copula

- Means, medians, IQR of costs, QALYs, ICERs were similar, and Kruskal-Wallis tests were not statistically significant (Table 1).
- Cost-effectiveness (CE) planes of simulated costs and QALYs also appear similar between different sampling scenarios (Figure 1, 2).

### 2. Estimates of Kendall tau between simulated results of incremental costs and QALYs

- There was a slight monotonic trend of estimated tau between simulated overall incremental cost and QALYs (Table 2).

Characteristic	Kendall's Tau for Revision Cost and Utility, Simulation Runs			p-value <sup>†</sup>
	-0.5, N = 10,000	Independent, N = 10,000	0.5, N = 10,000	
<b>Incremental Cost</b>				0.72
Mean (SD)	38 (63)	38 (64)	38 (64)	
Median (IQR)	49 (5, 83)	49 (5, 83)	49 (5, 84)	
<b>Incremental QALY</b>				0.55
Mean (SD)	0.060 (0.020)	0.060 (0.020)	0.060 (0.021)	
Median (IQR)	0.058 (0.046, 0.072)	0.058 (0.045, 0.073)	0.057 (0.045, 0.072)	
<b>ICER</b>				0.98
Mean (SD)	954 (1,438)	942 (1,397)	902 (5,594)	
Median (IQR)	823 (68, 1,676)	825 (75, 1,666)	830 (76, 1,676)	

<sup>†</sup> Kruskal-Wallis rank sum test

Table 1 Summary of simulated costs, QALY, ICER

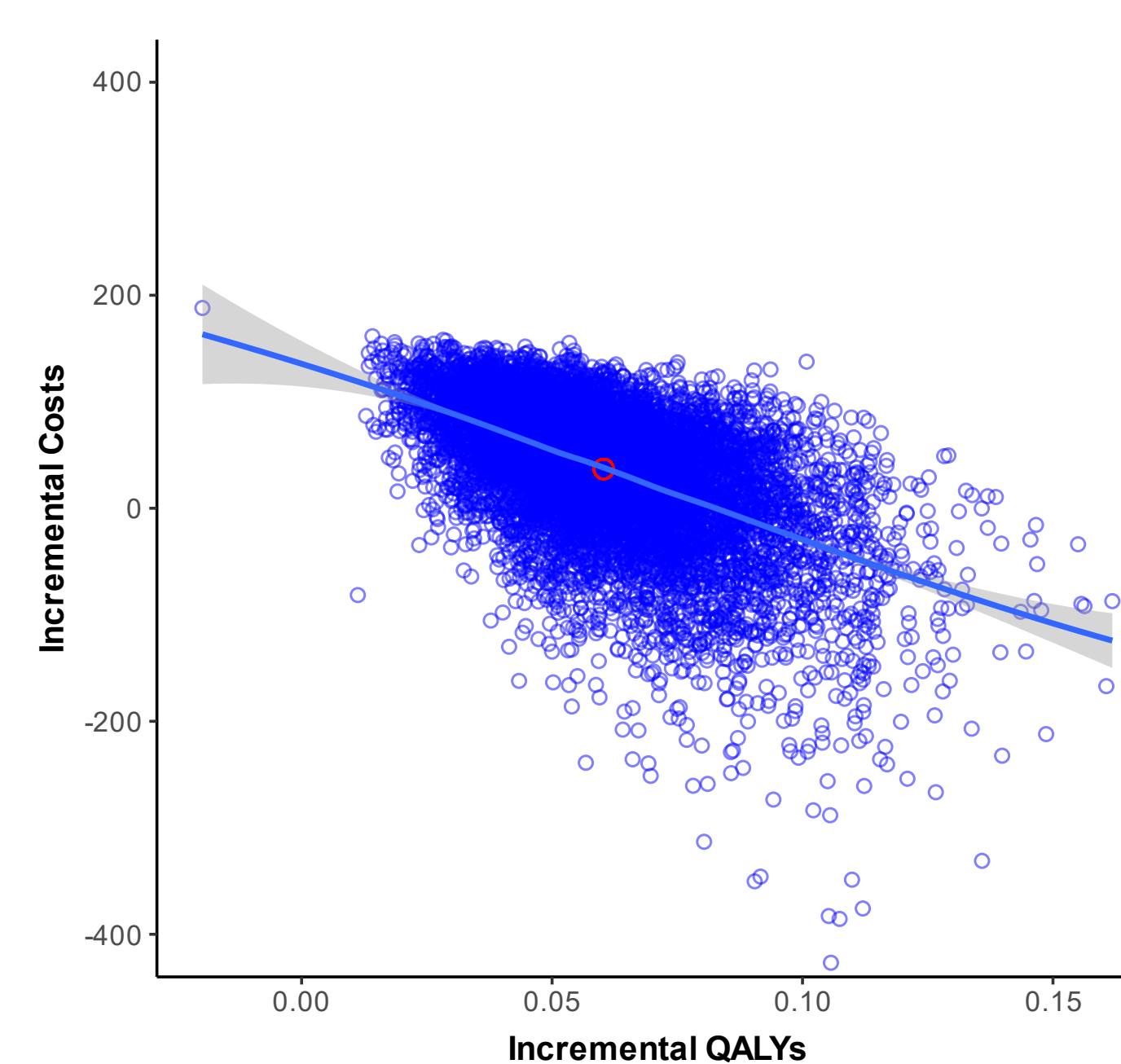


Figure 1 CE plane for independent sampling of cost and utility parameters

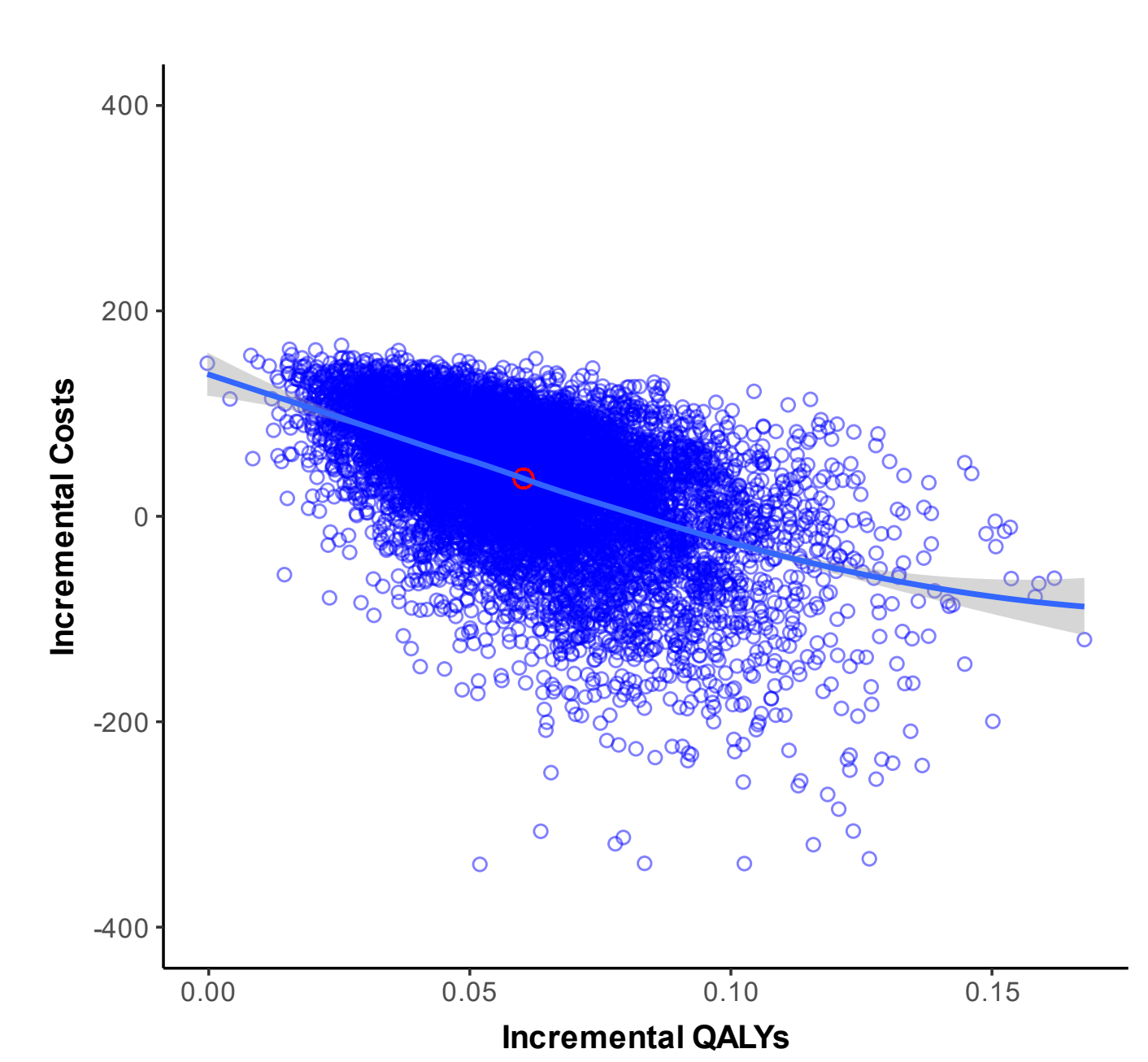


Figure 2 CE plane for copula sampling of cost and utility parameters (tau=0.5)

Kendall Tau (Copula Modeling of Revision Cost and Utility)	Kendall Tau (Simulated Overall Cost and QALYs)	95% CI
-0.5	-0.411	(-0.422, -0.400)
Independent	-0.379	(-0.390, -0.368)
0.5	-0.359	(-0.371, -0.348)

Table 2 Summary of estimated Kendall Tau between overall costs and QALYs

## CONCLUSIONS

- For the current study, correlated sampling of key cost and utility parameters via Clayton copula had relatively little impact on simulated values of overall incremental costs, QALYs, and ICERs.
- This implies that for PSA scenarios with relatively low degree of dependency between cost and utility parameters, independent sampling of cost and utility parameters may still be adequate.
- A small yet consistent trend in estimated Kendall tau correlations of overall incremental costs and QALYs was observed.
- Further research needs to determine when correlated sampling of cost and utility parameters via copula may bring additional insight in evaluation of cost-effectiveness of health technology.

## REFERENCES

- Naylor NR et al. Extensions of Health Economic Evaluations in R for Microsoft Excel Users: A Tutorial for Incorporating Heterogeneity and Conducting Value of Information Analyses. *Pharmacoeconomics*. 2023 Jan; 41(1):21-32.



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