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HOW TO SAMPLE ORDERED PARAMETERS IN PROBABILISTIC SENSITIVITY ANALYSIS

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Background

In health economic models, uncertain ordered parameters are common, for example, a patient's utility in a healthy state should be higher than in a diseased state. All probabilistic sensitivity analysis samples should exhibit the logical order of the given parameters. Typical sampling approaches lack either statistical or clinical validity. We have developed a new method, the Difference Method (DM) approach, which solves this type of problem more effectively than existing approaches.

Methods

The DM approach samples the parameters of interest via a difference parameter Δ. If the parameters are bounded, it involves transforming the variables so that they are unbounded and then sampling via the difference parameter on the transformed scale.

Notation: Two variables X and Y with $Y > X$. Mean of X, Y and Δ are μ_X, μ_Y and $\mu = \mu_Y - \mu_X$. Variance of these parameters are σ_X^2, σ_Y^2 and $\sigma^2 = |\sigma_Y^2 - \sigma_X^2|$.

Unbounded parameters: it samples from either X and Δ or Y and Δ depending on the magnitude of the variances of X and Y.

- If $\sigma_Y^2 > \sigma_X^2$, then define $Y = X + \Delta$. Sample X from Normal(μ_X,σ_X^2) and Δ from Gamma(s,r), where $s = \frac{\mu^2}{\sigma^2}$ and $r = \frac{\mu}{\sigma^2}$. Sampled values of Y are derived from sampled values of X and Δ.
- If $\sigma_Y^2 < \sigma_X^2$, then define $X = Y - \Delta$. Sample Y from Normal(μ_Y , σ_Y^2) and Δ from a Gamma(s,r). Sampled values of X are derived from sampled values of Y and Δ.

Bounded parameters: a four-step sampling procedure is listed in Table 1.

Example

Generate 5000 samples of health related quality of life (HRQoL) and cost from an active (worse) and remission (better) state for a particular condition.

Table 2: Mean and variance of 5000 sampled realisations using four sampling approaches

Variable	Health state	Given mean (Variance)	Generated mean (Variance)			
			DM	Ind sampling	Mod ind sampling	Common RN
Mean HRQoL	Remission	0.70 (0.016)	0.70 (0.016)	0.70 (0.016)	0.73 (0.012)	0.70 (0.016)
	Active	0.54 (0.019)	0.54 (0.019)	0.54 (0.019)	0.51 (0.016)	0.54 (0.020)
Mean cost	Remission	100 (10)	100.02 (9.94)	100.02 (9.94)	99.9 (9.54)	100.02 (9.95)
	Active	110 (15)	109.98 (15.29)	109.98 (15.10)	110.15 (13.87)	110.03 (14.93)

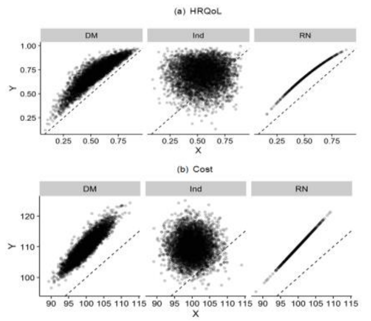

Figure 1: Scatterplots of pairs of samples generated by the three methods: DM (the DM approach), Ind (independent sampling) and RN (sampling use a common random number)

Results

Difference Method approach
- Similar summary statistics
- Maintain the logical order
- Positive correlation

Independent sampling
- Similar summary statistics
- Potential for pairs to have incorrect ordering
- No correlation

Modified independent sampling
- Biased samples
- Maintain the logical order

Sampling from a common random number
- Similar summary statistics
- Potential for pairs to have incorrect ordering
- Extreme dependence

Table 1: The four-step sampling procedure for generating the input parameter mean health related quality of life and mean cost

Sampling procedure	HRQoL	Cost
Step 1: Sample Y and X	Sample 5000 values of Y_u from $Beta(6.52, 5.55)$ and 5000 values of X_u from $Beta(8.49, 3.64)$.	Sample 5000 values of Y_c from $Gamma(1000, 0.100)$ and 5000 values of X_c from $Gamma(806.67, 0.136)$.
Step 2: Transform sampled Y and X from Step 1 to unbounded range	Transform sampled Y_u and X_u from Step 1 to unbounded range using logit function: $Y_u' = logit(Y_u)$ and $X_u' = logit(X_u)$. The mean and variance for the transformed variables are $\mu_{Y_u}' = 0.928$, $\sigma_{Y_u}'^2 = 0.436$, $\mu_{X_u}' = 0.186$ and $\sigma_{X_u}'^2 = 0.364$.	Transform sampled Y_c and X_c from Step 1 to unbounded range, using log function: $Y_c' = log(Y_c)$ and $X_c' = log(X_c)$. The mean and variance for the transformed variables are $\mu_{Y_c}' = 4.60$, $\sigma_{Y_c}'^2 = 0.00101$, $\mu_{X_c}' = 4.70$ and $\sigma_{X_c}'^2 = 0.00124$.
Step 3: Sample the difference between transformed Y and X	Since $\sigma_{Y_u}'^2 > \sigma_{X_u}'^2$, we define $Y_u' = X_u' + \Delta_u'$, where the mean and variance of Δ_u' is 0.742 and 0.072, respectively. Sample Δ_u' from $Gamma(7.64, 0.10)$. Compute sampled values of Y_u' by adding sampled Δ_u' and sampled X_u' from Step 2.	Since $\sigma_{Y_c}'^2 < \sigma_{X_c}'^2$, we define $X_c' = Y_c' + \Delta_c'$, where the mean and variance of Δ_c' is 0.10 and 0.0002, respectively. Sample Δ_c' from $Gamma(41.07, 0.002)$. Compute sampled values of X_c' by subtracting sampled Δ_c' from sampled Y_c' from Step 2.
Step 4: Back transform for X' and Y' to obtain sampled values for X and Y	Back transform sampled Y_u' and X_u' to Y_u and X_u using $Y_u = \frac{e^{Y_u'}}{1+e^{Y_u'}}$ and $X_u = \frac{e^{X_u'}}{1+e^{X_u'}}$.	Back transform sampled X_c' and Y_c' to X_c and Y_c using $X_c = e^{X_c'}$ and $Y_c = e^{Y_c'}$.

Discussion

When performing a PSA, often only the summary statistics of the sampled realisations are compared with their given values to check the statistical validity. It is also important to consider the clinical validity of the induced correlations between the sampled values if they are ordered. The DM approach should be considered as a solution to potential problems in generating PSA samples for ordered parameters.

Publication and software

The manuscript "A new approach for sampling ordered parameters in probabilistic sensitivity analysis" is accepted for publication in PharmacoEconomics. An Excel workbook to implement the method can be download from https://www.sheffield.ac.uk/scharr/sections/heds/staff/ren_k

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