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Appendix A: Technical Appendix: Probabilistic Sensitivity Analysis

Probabilistic sensitivity analysis (PSA) was conducted to characterize the impact of second-order uncertainty of all parameters included in the model on results. A parametric Monte Carlo simulation with 10,000 iterations was conducted to populate cost-effectiveness scatterplots and generate cost-effectiveness acceptability curves (CEACs). In each simulation iteration, all model parameters varied using their respective probability distributions (provided in below).

Numerical parameters for each probability distribution were calculated using prespecified quantiles (±15% of the mean), due to limited availability of published numerical parameters. The list below details each function used to calculate these parameters based on the probabilistic distribution:

- Gamma distribution: R function `gamma.parms.from.quantiles()` to calculate gamma parameters and `rgamma()` function to calculate random number
- Beta distribution: R function `find_beta()` to calculate beta parameters and `rbeta()` to calculate random number
- Multinomial distribution: `rmultinom()` to calculate random number. In PSA for probabilities of different outcomes in the decision tree model, this function generated the probabilities of each outcome (revision surgery, successful surgery, and death) for each iteration, based on the base-case values.
- Triangular distribution: `rtri()` to calculate random number

Variable	Value	Reference/ source	Distribution and parameters for PSA
Population characteristics			
Cohort size	1,000	[1]	-
Mean age at the first surgery, years	85	[1]	-
Male sex, %	17.0%	[1]	-
Decision tree model (1st year after index surgery)			
Probabilities			
Revision surgery, fixation without augmentation	4.4%	[1]	Multinomial (.104,.044,.852)
Successful surgery*, fixation without augmentation	85.2%		
Death (without augmentation)#	10.4%		
Revision surgery, fixation with augmentation	0%	[1]	Multinomial (.104,0,.896)
Successful surgery, fixation with augmentation	89.6%		
Death (with augmentation)#	10.4%		
Utilities			
Successful surgery after fixation	0.73	[1]	Beta (α=44.6, β=15.9)

Variable	Value	Reference/ source	Distribution and parameters for PSA
Disutility (multiplier) of revision surgery	0.85	[1]	Beta (α=19.6, β=2.6)
Markov model (2nd year after index surgery to lifetime)			
Probabilities of revision surgery			
1st revision surgery given a successful index surgery	Time dependent	Survival analyses†	Triangular
1 year after successful index surgery	**0.43%**		(0.0036,0.0049,0.0043)
2 years after successful index surgery	**0.30%**		(0.0025,0.0034,0.0030)
≥3 years after successful index surgery	**0.40%**		(0.0034,0.0046,0.0040)
2nd revision surgery	2.4%	**Survival analyses†**	Beta (α=164.9, β=6862.4)
Probability of death			
Mortality given a successful index surgery, year 2 (relative risk)#	**1.57**	**Survival analyses†**	**Log normal (μ=0.44, σ=0.077)**
Mortality given a successful index surgery**, year ≥3#**	Background mortality	[2]	-
Mortality after revision, year 1 (relative risk)	2.13	**Survival analyses†**	Log normal (μ=0.75, σ=0.077)
Mortality after revision, year 2 (relative risk)	1.57	**Survival analyses†**	Log normal (μ=0.44, σ=0.077)
Background mortality	-	[2]	-
Utilities			
Successful surgery (SE)	0.735 (0.028)	[3]	Beta (α=43.7, β=15.1)
Disutility (multiplier) of revision surgery	0.85	[1]	Beta (α=19.6, β=2.6)
Costs and use of healthcare resources			
Total cement augmentation costs	€ 550.8		Gamma (α=168.7, β=0.31)
Cement augmentation material costs	€ 475.8	List price	
Increased OR time (5 minutes, € 15/minute)	€ 75	[1, 4]	
Leakage test costs	€ 12.0	List price	Gamma (α=168.7, β=14.1)
Revision surgery costs‡	€ 10,033.0	[5]	Gamma (α=168.7, β=0.02)

Variable	Value	Reference/ source	Distribution and parameters for PSA
Number of outpatient visits following revision	2.0	[6], expert opinion	-
Costs per outpatient visit following revision	€ 65.1	[7]	Gamma (α=168.7, β=2.6)
Number of days of rehabilitation	21.0	[6], expert opinion	-
Costs per day of rehabilitation[§]	€ 128.4	[8]	Gamma (α=168.7, β=1.3)

* Successful surgery refers to successful index surgery with no revision surgeries needed.
[#] **Increased mortality was included post successful index surgery for two years. The mortality parameter from trial data (for year 1 post index surgery) was used in the decision tree. Relative risk calculated based on survival analyses was used in the Markov model (for year 2 post index surgery). We assumed baseline background mortality in year 3 onwards.**
[†] Survival analyses using the US Medicare Standard Analytical File database
[‡] German Diagnosis-Related Groups (DRGs) reimbursement (€ 8,474.2) plus nursing cost (€ 1,558.8). Nursing cost was calculated as the nursing intensity weights (0.8169) multiplied by nursing compensation factor (€ 163.09) and average length of stay of 11.7 days for DRG I47A.
[§] DRG reimbursement.
PSA: probabilistic sensitivity analysis; SD: standard deviation; SE: standard error; OR: operating room.

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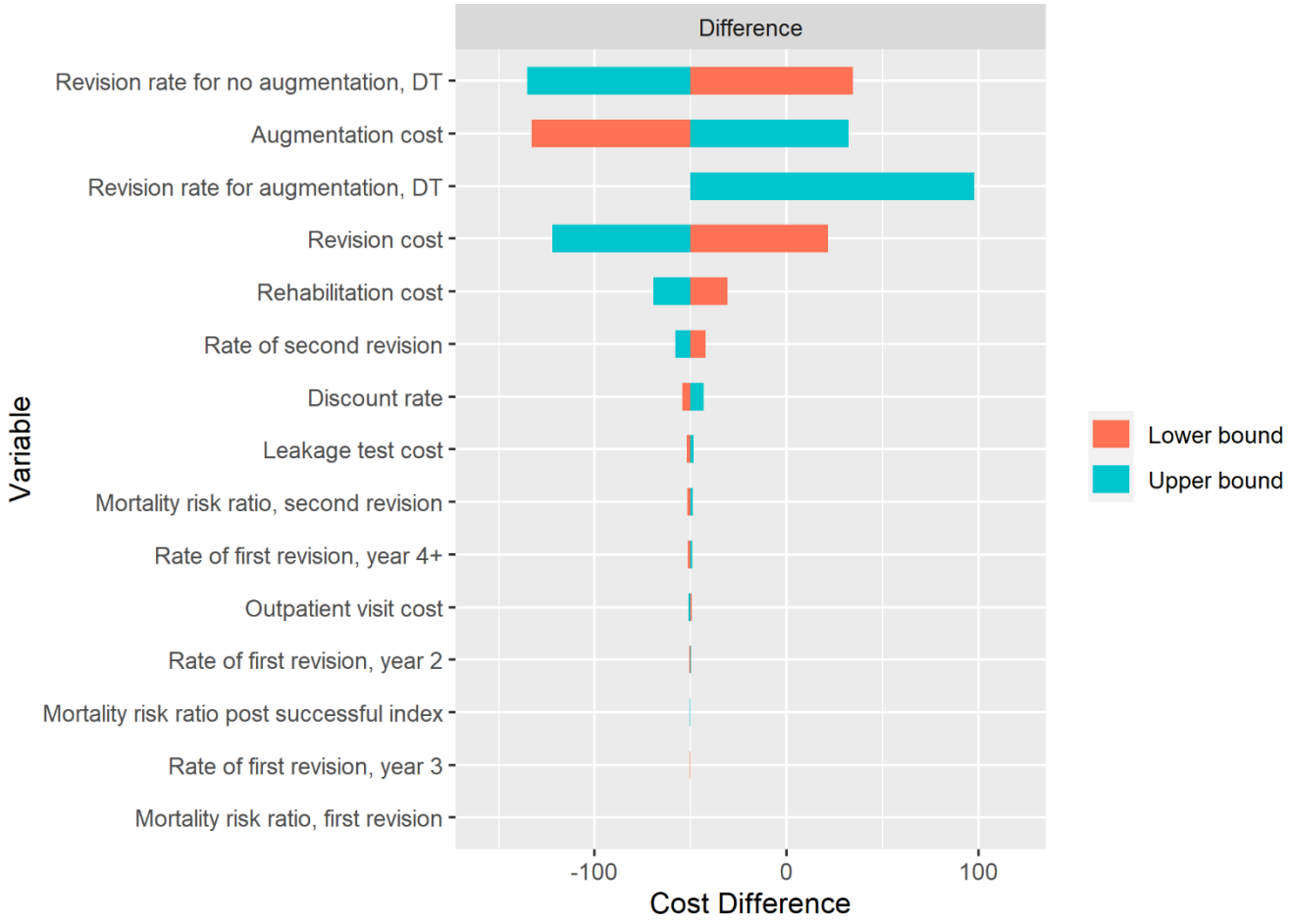
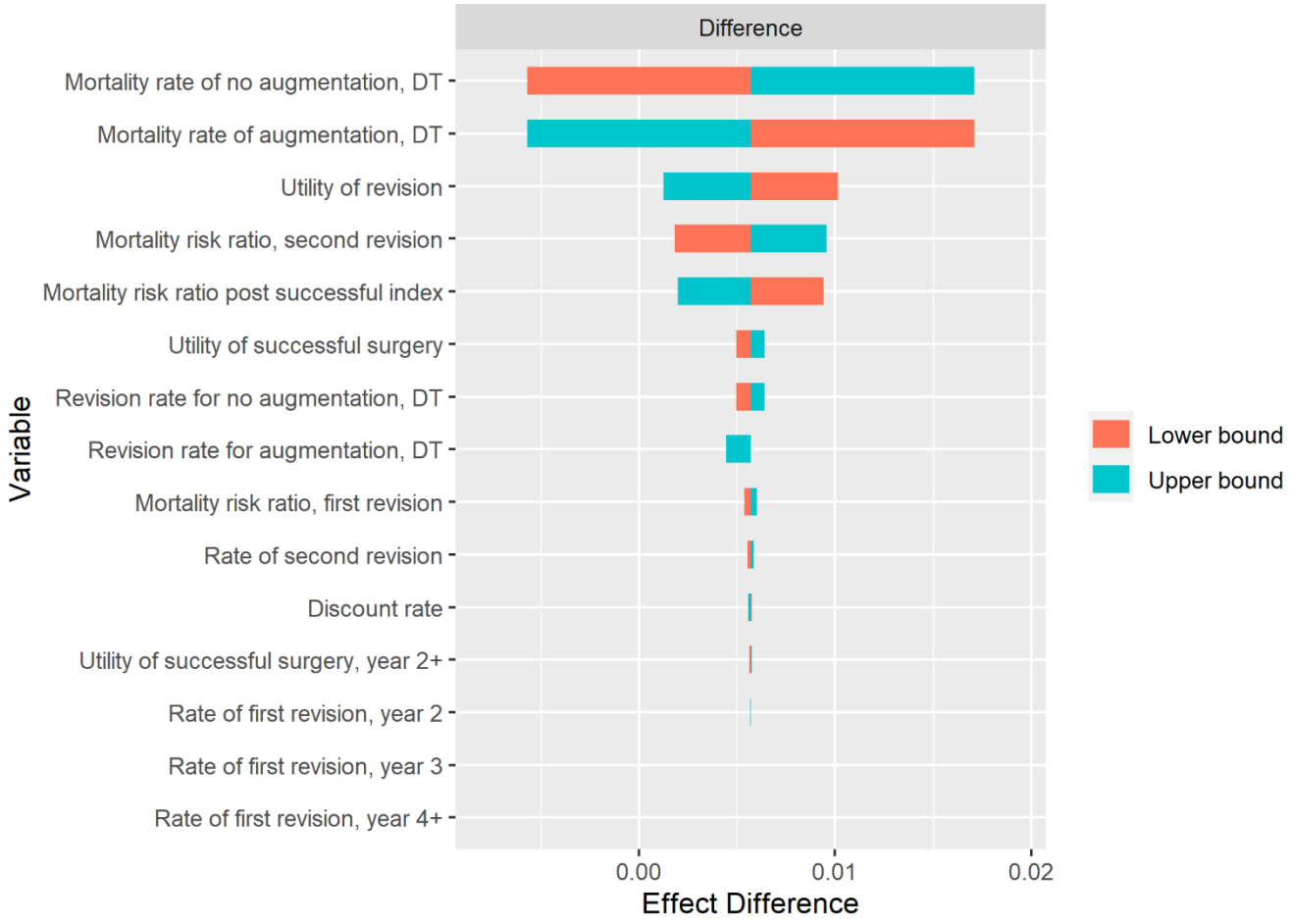


Appendix B: Figure S1

Tornado diagram showing the influence of model parameters on the incremental costs. DT: decision tree.



Appendix C: Figure S2

Tornado diagram showing the influence of model parameters on the incremental quality-adjusted life years. DT: decision tree.