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Cost-effectiveness of 3D-guided corrective osteotomy compared with 2D-planned corrective osteotomy for patients with malunion of the distal radius from a Dutch societal perspective: an early economic evaluation

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Abstract

Background: Malunion is the most common complication of distal radius fractures, leading to wrist pain, functional impairment, and cosmetic deformity. Conventional treatment involves corrective osteotomy using two-dimensional (2D) preoperative planning. However, planning a corrective osteotomy using 2D images can be challenging, making it hard to achieve optimal outcomes. The use of three-dimensional (3D) planning and patient-specific guides shows promising effects on patient outcomes. However, 3D planning leads to additional costs. It is crucial to investigate the cost-effectiveness of 3D planning versus 2D planning to determine if the potential benefits of 3D-guided corrective osteotomy justify the higher expenses.

Objective: The aim of this study was to conduct an early cost-effectiveness analysis comparing 3D-guided corrective osteotomy to 2D-planned corrective osteotomy in patients with distal radius malunion, from a Dutch societal perspective.

Method: A health state transition model was developed to evaluate the cost-effectiveness of 3D-guided corrective osteotomy versus 2D-planned corrective osteotomy, from a Dutch societal perspective. The outcome of interests were quality-adjusted life-years (QALYs) gained, number of revisions in each strategy, and incremental cost-effectiveness ratio (ICER) per QALY gained. Model inputs, including transition probabilities, costs, and utilities were based on patient data from OCON Orthopaedic clinic in the Netherlands and from published literature. One-way deterministic and probabilistic sensitivity analyses were performed to investigate the impact of parameter uncertainty on the outcomes. Several scenario analyses were performed, including incorporating a hospital perspective and incorporating improved recovery for patients treated with the 3D strategy.

Results: 3D-guided corrective osteotomy led to 0.004 incremental QALYs and reduced costs by €72.36, making the intervention cost-effective. At a willingness to pay threshold (WTP) of €20,000 the probability of the 3D approach being cost-effective was 0.77. Scenario analyses showed that from a hospital perspective, the 3D approach is not cost-effective. Furthermore, the analysis incorporating improved recovery for 3D patients resulted in a higher incremental QALY of 0.085.

Conclusion: This early cost-effectiveness analysis suggests that 3D-guided corrective osteotomy is expected to be cost-effective compared to 2D-planned corrective osteotomy, from a Dutch societal perspective, indicating that 3D-guided corrective osteotomy should be adopted. However, further research into differences in revision rates and patient recovery between the two strategies is necessary to address uncertainties.

Introduction

Fractures of the distal radius are a frequent injury with an incidence between 8% and 17% of all extremity fractures and accounting for up to 75% of all forearm fractures [1, 2]. The majority of patients with distal radius fractures respond well to treatments ranging from simple closed reduction and casting to surgical interventions. However, in about 23% to 31% of the cases complications arise during recovery [1].

Malunion is the most common complication of distal radius fractures with an incidence of approximately 17% [1-6]. Malunion can cause considerable disability, manifesting in symptoms such as wrist pain, limited grip strength, decreased wrist motion, and cosmetic deformity [1, 3-9]. Moreover, it can lead to early-onset osteoarthritis [4, 6, 7]. The impact of malunion is not limited to the patient, it has also consequences for society, as patients suffering from malunion might be temporarily unable to work or only to a limited extent [1, 5].

Conventional treatment of symptomatic malunion consists of corrective osteotomy using two-dimensional (2D) preoperative planning to restore the wrist anatomy and optimize functional outcomes [1-5, 7-9]. Achieving optimal surgical outcomes relies on thorough preoperative planning, which involves obtaining two orthogonal 2D radiographs of the radius to provide details of the deformity and determining the osteotomy plane, fixation method, and in some cases the shaping of a bone graft. Measurements of radial inclination, ulnar variance, and palmar tilt are taken from these 2D radiographs (see Figure 1) [8, 10]. However, the process of planning and executing a corrective osteotomy can be challenging, because the bone is often deformed in multiple planes, including axial rotation which can only be visualized using 3D (see Figure 1) [3, 4, 6-8, 10, 11]. Certain studies indicate that, despite careful preoperative planning, in only 40% of the cases the correction achieves anticipated outcomes including alignment within 5° of the planned correction for angular deformities (radial inclination and palmar tilt) and within 2 mm of the intended ulnar variance [8]. Suboptimal correction can lead to residual functional impairment, pain and joint instability [6, 9].

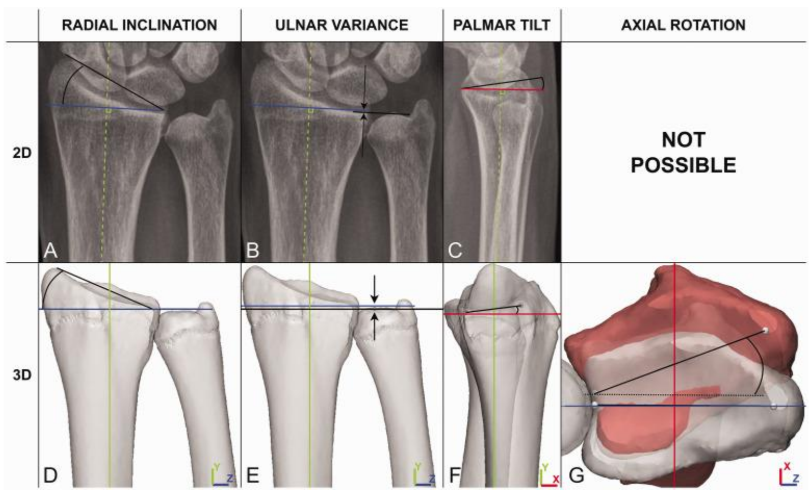

Figure 1. 2D and 3D measurements of the distal radius: (A) 2D radial inclination, (B) 2D ulnar variance, (C) 2D palmar tilt, (D) 3D radial inclination, (E) 3D ulnar variance, (F) 3D palmar tilt, and (G) 3D axial rotation [10]

The use of three-dimensional (3D) computer simulation and patient-specific guides can improve patient outcomes [6-9]. Pre-operative planning of 3D-planned corrective osteotomy comprises three steps. First, a computed tomography (CT) scan is conducted on both the malunited and healthy contralateral forearm to gather detailed information about the deformity. Second, virtual models of both radii are generated using medical image processing software (see Figure 2A). A comprehensive three-dimensional assessment of the location and degree of the deformity is provided by superimposing a mirrored version of the normal contralateral side on the malunited radius (see Figure 2B). Following this, a virtual correction of the present deformity is planned in a computer-aided design (CAD) program (see Figure 2C). Finally, the preoperative plan is translated to the actual surgery using 3D-printed patient-specific drilling and cutting guides (see Figure 2D) and 3D-printed anatomic models of both the malunited radius and the planned post-operative radius [7-9, 11, 12].

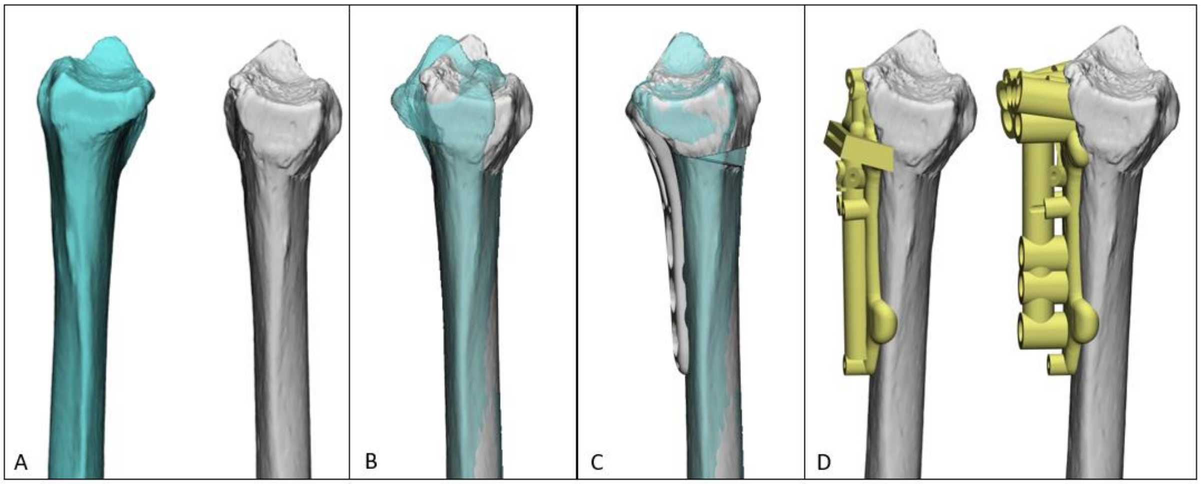

Figure 2. 3D-preoperative planning: (A) virtual 3D models of the malunited radius (grey) and the healthy contralateral side (blue), (B) mirrored version of the healthy radius (blue) on the malunited radius (grey), (C) planned result with plate, and (D) cutting (left) and drilling (right) guides on the malunited radius.

Several studies already reported improvements in patient-reported outcome measures (PROM) and radiographic results using 3D-guided corrective osteotomy [2-4, 6-9, 11, 12]. Especially in complex cases it has added value, as it enables to perform a complex corrective osteotomy which would not have been performed using 2D-planning without patient-specific guides. Complex cases often involve deformities in multiple planes, which cannot be visualized using only 2D images. 3D visualization and the use of guides provides surgeons with greater confidence to undertake these complex procedures [7, 8, 11]. A review conducted by Meesters et al. reported a higher gain in Disability of the Arm, Shoulder and Hand (DASH) score in patients treated with the 3D approach compared to conventional methods, with follow-up periods ranging from a few months to several years [6]. Improvements in wrist motion, grip strengths and pain due to 3D-guided corrective osteotomy were also demonstrated across various studies [3, 6-8, 12]. Research indicated that in 3D preoperative planning 96% of the patients experienced the planned outcomes based on radiographic parameters compared to the 40% in 2D preoperative planning. Additionally, the complication rate decreased from 42% with 2D planning to 16% with 3D planning. The reported complications include implant failure, non-union, loss of alignment and hardware removal [4, 8, 13, 14]. One randomized clinical trial (RCT) was performed to assess whether 3D-guided corrective osteotomy resulted in better patient outcomes compared to traditional 2D planning. The study showed a minimal clinically important difference in favour of the 3D group, however this was not significant due to insufficient study power [3]. Lastly, the use of 3D technology and patient-specific guides reduces surgery duration, resulting in cost savings by decreasing the use of operating room resources and lowering personnel expenses [4, 7, 15].

Despite the promising outcomes of this new treatment and the cost savings due to a reduction in surgery duration, 3D planning leads to additional costs, including expenses for developing patient-specific guides and 3D software. This highlight the importance of conducting a cost-effectiveness analysis to investigate whether the additional costs of 3D planning are justified by potential improved patient outcomes and reductions in complication rates. It also aims to incorporate the broader impact on costs, including potential reductions in societal expenses. Currently, the cost-effectiveness of 3D-guided corrective osteotomy compared to

2D-planned corrective osteotomy has not been examined yet [4]. Performing an early cost-effectiveness analysis is crucial for assessing the potential economic and clinical impact of this new approach in treating distal radius malunion. By evaluating cost-effectiveness at an early state, information needed to conduct future research can be identified. This study aimed to assess the cost-effectiveness of 3D-guided corrective osteotomy versus 2D-planned corrective osteotomy for treating distal radius malunion. The central research question is: *"What is the cost-effectiveness of 3D-guided corrective osteotomy compared to 2D-planned corrective osteotomy for the treatment of symptomatic malunion in the distal radius, from a Dutch societal perspective?"*

Method

A health state transition model was developed in R Statistical Software (v4.3.3) [16] to assess the cost-effectiveness of 3D-guided corrective osteotomy compared to 2D-planned corrective osteotomy from a Dutch societal perspective. A time horizon of three years was implemented with three-monthly cycles. The outcomes of interest were number of patients who underwent a revision or hardware removal per strategy, quality-adjusted life-years (QALYs) gained, incremental costs, and the increment cost-effectiveness ratio (ICER) per QALY gained. The ICER was calculated by dividing the incremental costs by the incremental QALYs of the 3D approach compared to the 2D approach. The analysis was based on the R code from Alarid-Escudero et al. [17], which forms the basis for a state-transition model in R for cost-effectiveness analysis. This study has been approved by the ethical committee of the BMS faculty from the University of Twente (nr 240188). The reporting of this study followed the guidelines outlined in the 2022 Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (see Appendix A) [18].

Model structure

The health state transition model consists of eleven health states and six tunnel states (see Figure 3). The tunnel states are incorporated to implement time-dependent transition probabilities and are represented in Figure 3 with dashed lines. Patients cannot stay in this state for more than one cycle. A simulated cohort of 1,000 patients enters the model in the '2D-planned or 3D-guided corrective osteotomy' state. After surgery the patients can either experience acceptable pain and functional disability or not-acceptable pain and functional disability. A patient may undergo a revision, which is categorised into two types. The first type of revision (R1) encompasses non-union and implant failure. Such revisions do not require preoperative planning because it does not involve a re-correction, and are uniform across both strategies. The second type of revision (R2) involves re-corrections required when the initial surgery fails to achieve the desired correction and the patient experiences not-acceptable pain and functional disability. Under the 3D strategy, a new 3D analysis is conducted and new 3D guides are developed. The 2D approach involves creating a new 2D plan. A patient with not-acceptable pain and functional disability can also undergo hardware removal, where the plate and screws are removed. Patients can only stay one cycle in the revision or hardware removal state. After revision or hardware removal, patients transfer to one of the pain and functional disability states. Patients can also stay in one of the pain and functional disability states or can transition between these two states. Transition to the death state is possible from all other health states.

The cut-off value between acceptable and not-acceptable pain and functional disability is based on the patient acceptable symptom state (PASS) of the patient rated wrist/hand evaluation (PRWHE) score [19]. The PRWHE questionnaire is a validated 15-item self-administered questionnaire measuring wrist pain and disability of daily living resulting in a score between 0 and 100. A score of 100 indicates the most severe pain and functional impairment, while 0 signifies no disability [20, 21]. PASS represents the threshold score beyond which patients perceive themselves as fine. A PRWHE score of 30 or lower indicates an acceptable pain and functional disability [19].

Costs were discounted with 3% and effects with 1.5% annually according to Dutch guidelines [22]. The model structure is based in the following assumptions: (1) after hardware removal a patient cannot undergo a revision; (2) the probability of transitioning to revision 1 does not depend on the pain and functional disability of the patient; (3) patients with acceptable pain and functional disability can only undergo revision 1; (4) a patient cannot undergo two revisions; (5) the transition probabilities of transitioning between the pain and functional disability health states remains constant from month 0 to 3 and from 3 to 12 months postoperative; (6) when a patient experiences acceptable pain and functional disability after undergoing hardware removal, the patient cannot transition back to not-acceptable pain and functional disability; (7) 12 months after initial surgery or revision, patients are assumed stable and cannot transition between the pain and functional disability states.

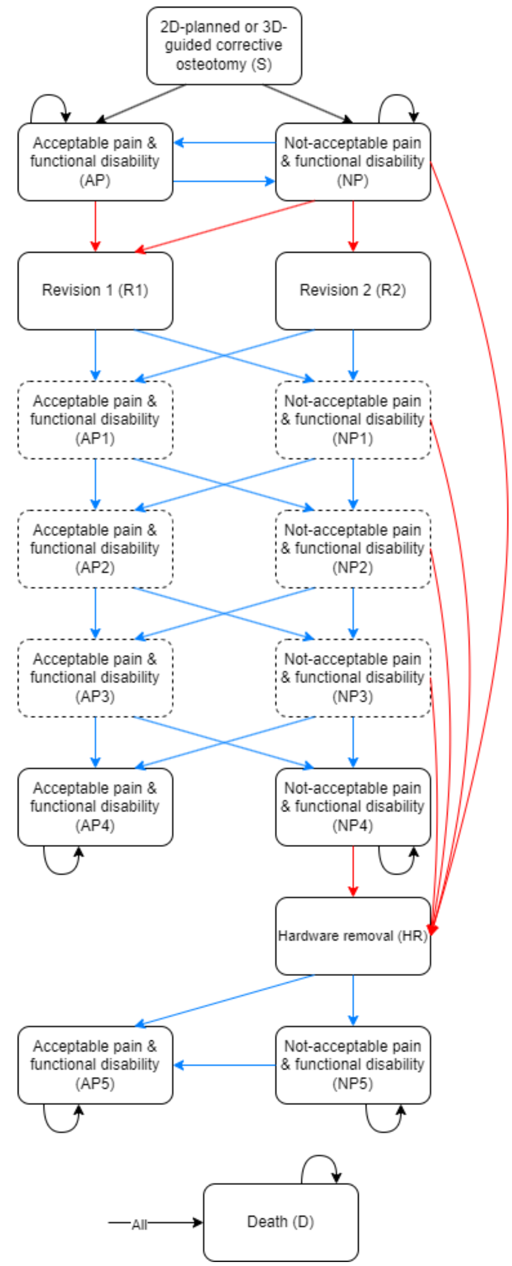

Figure 3. Health state transition model structure. Transitions in red differ between the two strategies in the base case analysis. Transitions in blue are equal for both strategies in the base case analysis, but were adjusted in one of the scenario analyses, resulting in differences between the two strategies in this analysis.

Model inputs

Data for model inputs was collected from Orthopaedic clinic OCON in the Netherlands and from literature. OCON provided the PRWHE scores of patients undergoing 3D-guided corrective osteotomy both preoperatively and three and twelve months postoperatively, along with records of surgery duration and revisions. Meesters et al. conducted a review reporting the number of revisions in each strategy [6]. Furthermore, an RCT documented the PRWHE score preoperatively, three, six and twelve months postoperatively of both strategies [3].

Transition probabilities

Transition probabilities of 3D-guided corrective osteotomy are based on patient data of OCON (Table 1). The transition from corrective osteotomy to one of the pain and functional disability states and the probabilities of transitioning between these two states are based on the PRWHE score. Only patients who had undergone surgery more than one year ago and therefore could participate in the twelve-month follow-up measurement were included. The transition probabilities of revisions and hardware removal were based on the number of events during the follow-up period until 14-03-2024 and the total number of years patients were at risk for undergoing a revision or hardware removal. Age- and gender-specific mortality rates, reflecting the baseline patient average age of 44 years and a female percentage of 76%, were derived from the age-specific Dutch mortality rate in 2022 and were converted into transition probabilities [23].

3D-guided transition probabilities were adjusted into 2D-planned transition probabilities using relative risks (Table 1). Relative risks of undergoing a revision or hardware removal were derived from the number of complications in 3D-guided and conventional surgery reported in a systematic review by Meesters et al [6]. Relative risks for transitioning to one of the pain and functional disability states and between these states were based on the PRWHE scores reported in the RCT by Buijze et al [3]. In the base case analysis, only the probabilities of undergoing a revision or hardware removal were adjusted, resulting in differences in these probabilities between the two strategies. The effect of differences between the two strategies in other transition probabilities was examined during a scenario analysis.

Health effects

Two types of health effects were examined during this study: QALYs gained and number of patients who underwent a revision or hardware removal in each strategy. Health state utility values were established through a mapping function that computes 12-month postoperative utility based on the baseline EQ-5D score and 12-month postoperative PRWHE score (Appendix B) [24]. The baseline EQ-5D required for this mapping function was not available, so a baseline score from another study was used [9]. The mean utility of patients with a 12-month postoperative PRWHE score of 30 or higher was applied to the revisions, hardware removal, and not-acceptable pain and functional disability health states (Table 1). The mean utility of patients with a 12-month postoperative PRWHE score under 30 was applied to the acceptable pain and functional disability health state (Table 1). The utility of the death state was 0. Total QALYs were calculated by multiplying the time spent in each health state by its utility value, then summing the products across all health states.

Disutilities for both the revisions and hardware removal were applied to represent the negative impact on quality of life due to adverse events. These disutilities were obtained from a study about distal radius factures [25]. They were applied for a period of two weeks after the event, corresponding to the duration a patient needs to war a cast, to accurately reflect the temporary decrease in quality of life.

Costs

Three types of costs were incorporated: costs within the healthcare sector, costs of patients, and family and costs in other sectors. Healthcare sector costs encompass all medical expenses directly related to the condition. Costs of patient and family incorporate travel expenses to the hospital and physiotherapist. Costs in other sectors include expenses associated with loss of productivity.

Medical expenses include costs for hospital visits, diagnostic tests, surgery, medication, cast, brace, follow-up appointments, physiotherapy and any other expenses made necessary for managing the condition. In the 3D strategy, additional costs are incurred for 3D analysis, 3D license, printing of the 3D anatomic models and guides as well as for a multidisciplinary team meeting. Expenses for 2D planning are calculated based on the assumption that a surgeon takes thirty minutes to plan the surgery, with no additional software required for this planning.

Volumes of healthcare consumptions and accompanying unit prices have been collected from OCON, from Dutch guidelines, and from the Dutch National Health Care Institute (Table 1) [26, 27]. Revision 2 requires a new 3D analysis and development of 3D guides or a new 2D analysis based on the strategy. Costs for revision 1 and hardware removal were assumed equal for both strategies. Unit prices have been multiplied by strategy-specific volumes to calculate overall costs.

Operating room (OR) costs were calculated based on the duration of the different types of surgery. The surgery durations for 3D-guided surgery, revision 1, and hardware removal were derived from surgeries performed at OCON. These surgeries include radius corrections as well as double corrections of both the radius and ulna. The duration for 2D-planned surgery was obtained from literature, which reported mean surgery durations and standard deviations (90.6 ± 32.3 minutes) comparable to those at OCON for 3D-guided surgery (90.2 ± 32.09 minutes) [3]. The duration for revision 2 surgery was assumed to be the same as that of the initial surgery.

Productivity losses were calculated using the friction costs method, according to Dutch guidelines [22]. After surgery, patients are assumed to be absent from work for an estimated period of four to twelve weeks, with an average of eight weeks [28]. This period is shorter than the friction period of 16.4 weeks specified in Dutch guidelines [26]. Costs due to productivity losses were calculated by multiplying productivity costs per hour, number of weeks absent, employment rate and average number of hours worked per week in the Netherlands in 2023 [22, 28-30]. In the base case model, the average of eight weeks absent was incorporated and this was varied between four and twelve weeks in the probabilistic sensitivity analysis. Costs due to productivity losses were incorporated in the surgery and revisions health states.

Travel expenses were calculated based on Dutch guidelines and incorporated in the surgery, revisions and hardware removal health state based on the number of hospital and physiotherapy visits during the entire recovery [22].

All costs have been converted to 2023 Euros, using Dutch consumer price index levels [31].

Table 1. Model inputs

	Value	95% CI	Distribution	Reference
3-monthly health state transition probabilities – 3D				
Surgery to AP	0.07	0.01-0.19	Beta (α=3, β=39)	OCON data
AP to NP cycle 1, 2 & 6 till 12	0	Fixed	Fixed	OCON data
AP to NP cycle 3, 4 & 5	0.06	0.01-0.11	Bootstrap	OCON data
NP to AP cycle 1 & 6 till 12	0	Fixed	Fixed	OCON data
NP to AP cycle 2	0.51	0.35-0.68	Beta (α=20, β=19)	OCON data
NP to AP cycle 3, 4 & 5	0.19	0.11-0.28	Bootstrap	OCON data
AP to revision 1	0.01	0.003-0.02	Bootstrap	OCON data

NP to revision 1	0.01	0.003-0.02	Bootstrap	OCON data
NP to revision 2	0.01	0.002-0.02	Bootstrap	OCON data
NP to hardware removal	0.03	0.02-0.04	Bootstrap	OCON data
Revision 1 to AP	0.55	0.39-0.70	Beta (α=23, β=19)	OCON data
Revision 2 to AP	0.55	0.39-0.70	Beta (α=23, β=19)	OCON data
Hardware removal to AP	0.55	0.39-0.70	Beta (α=23, β=19)	OCON data
Mortality rate				
Age 44	0.0012	Fixed	Fixed	[23]
Age 45	0.00122	Fixed	Fixed	[23]
Age 46	0.00133	Fixed	Fixed	[23]
Age 47	0.00143	Fixed	Fixed	[23]
Age 48	0.00134	Fixed	Fixed	[23]
Utilities				
Utility acceptable pain and functional disability	0.81	0.79-0.83	Beta (α=48, β=11)	OCON data
Utility not-acceptable pain and functional disability	0.58	0.54-0.61	Beta (α=25, β=18)	OCON data
Prices				
CT	€195.21	Fixed	Fixed	[26]
X-ray	€85.32	Fixed	Fixed	[26]
Outpatient visit	€124.61	Fixed	Fixed	[26]
Day outpatient care	€347.86	Fixed	Fixed	[26]
One minute of OR	€11.52	Fixed	Fixed	[26]
Anaesthesia		Fixed	Fixed	Internal
OR materials		Fixed	Fixed	Internal
Plate and screws		Fixed	Fixed	Internal
OR instruments		Fixed	Fixed	Internal
Cast + brace		Fixed	Fixed	Internal
Physiotherapy appointment	€40.38	Fixed	Fixed	[26]
3D license per patient		Fixed	Fixed	Internal
Printing 3D guides and models		Fixed	Fixed	Internal
Multidisciplinary team meeting 3D		Fixed	Fixed	Internal
Hourly wage technical physician		Fixed	Fixed	[32]
Travel costs per kilometre	€0.27	Fixed	Fixed	[26]
Parking hospital	€4.07	Fixed	Fixed	[26]
Productivity costs per hour	€41.41	Fixed	Fixed	[26]
Hourly wage surgeon		Fixed	Fixed	[32]
Resources				
Number of X-rays	2	Fixed	Fixed	Internal
Number of outpatient visits for initial surgery	2	Fixed	Fixed	Internal
Surgery duration 3D (minutes)	90.26	79.95-100.08	Bootstrap	Internal
Surgery duration 2D (minutes)	96.9	94.83-98.84	Bootstrap	
Surgery duration revision 1 (minutes)	71.13	36.18-105.31	Bootstrap	Internal
Surgery duration Hardware removal (minutes)	33.91	25.66-42.32	Bootstrap	Internal
Number of physiotherapy appointments	10	8-12	Triangle(8, 10, 12)	Internal

Number of hours 3D analysis + guides	10	±20%[a]	Normal(μ=10, σ^2=2)	Internal
Average number of kilometres to hospital	7.1	Fixed	Fixed	[26]
Average number of kilometres to physiotherapy	2.2	Fixed	Fixed	[26]
Number of hospital visits for initial surgery	5	Fixed	Fixed	Internal
Number of weeks absent from work	8	4-12	Triangle(4, 8, 12)	[28]
Number of hours worked during a week	23.50	Fixed	Fixed	[29, 30]
Number of hours 2D planning	0.5	Fixed	Fixed	Internal
Relative risks 2D				
Revision 1[b]	2.31	0.92-5.80	Log normal (μ=0.10, σ^2=0.37)	[6]
Revision 2[c]	1.12	0.43-2.99	Log normal (μ=0.84, σ^2=0.44)	[6]
Hardware removal [d]	1.10	0.48-2.50	Log normal (μ=0.12, σ^2=0.44)	[6]
NP to AP month 0-3 [e]	0.71	0.49-1.03	Log normal (μ=-0.34, σ^2=0.19)	[3]
AP to NP month 0-3 [f]	1.35	0.93-1.95	Log normal (μ=0.30, σ^2=0.19)	[3]
NP to AP month 3-12 [g]	0.77	0.57-1.02	Log normal (μ=-0.27, σ^2=0.15)	[3]
AP to NP month 3-12 [h]	1.47	0.92-3.26	Log normal (μ=0.39, σ^2=0.24)	[3]
Annual discount rates				
Annual discount rate costs	0.03	Fixed	Fixed	[22]
Annual discount rate effects	0.015	Fixed	Fixed	[22]

CI confidence interval, *AP* acceptable pain and functional disability, *NP* not-acceptable pain and functional disability

[a] Sensitivity values 20% lower and 20% higher compared to base case value.

[b] Relative risk for 2D strategy of undergoing revision type 1 from all possible health states compared to 3D strategy.

[c] Relative risk for 2D strategy of undergoing revision type 2 from not-acceptable pain and functional disability compared to 3D strategy.

[d] Relative risk for 2D strategy of undergoing hardware removal from all possible health states compared to 3D strategy.

[e] Relative risk for 2D strategy of transitioning from not-acceptable pain and functional disability, revision or hardware removal to acceptable pain and functional disability in the first 3 months after surgery compared to 3D strategy.

[f] Relative risk for 2D strategy of transitioning from acceptable pain and functional disability, revision or hardware removal to not-acceptable pain and functional disability in the first 3 months after surgery compared to 3D strategy.

[g] Relative risk for 2D strategy of transitioning from not-acceptable pain and functional disability to acceptable pain and functional disability in months 3 to 12 after surgery compared to 3D strategy.

[h] Relative risk for 2D strategy of transitioning from acceptable pain and functional disability to not-acceptable pain and functional disability in months 3 to 12 after surgery compared to 3D strategy.

Analyses

Total costs and QALYs were calculated for both strategies, the ICER per QALY gained was calculated by dividing the incremental costs by the incremental QALYs of the 3D approach compared to the 2D approach. The number of patients undergoing a revision or hardware removal was calculated by summing the proportion of patients in the revision state and was presented per 1,000 patients. This was performed for both types of revisions and hardware removal. Deterministic one-way sensitivity analyses (DSA) were performed to assess the impact of individual parameter variations on the incremental net monetary benefit (iNMB). The iNMB converts incremental effects and incremental costs into monetary benefits using the WTP threshold. A positive iNMB indicates that the 3D strategy is cost-effective. Values of parameters were individually varied using their 95% confidence intervals or a 20% standard error assumption when no 95% confidence interval could be calculated, according to Dutch guidelines (Table 1) [22]. Results were visually presented in a tornado diagram, identifying parameters with the most impact on the iNMB.

A probabilistic sensitivity analysis (PSA) was conducted to explore the impact of joint uncertainty in all model input parameters on model outcomes. A Monte Carlo simulation with 10,000 iterations, using pre-assigned distributions for each parameter was conducted and presented in an incremental cost-effectiveness plane. A beta distribution was used for probability and utility values, a lognormal distribution for relative risks, and a triangular and normal distribution were used for resource use (Table 1). Revision rates and transition probabilities from month 3 to 12 postoperative were bootstrapped, generating 10,000 values that were converted into 3-monthly probabilities. Surgery durations were also bootstrapped. These bootstraps were used in the PSA. The probability of 3D-guided corrective osteotomy being cost-effective as a function of the willingness-to-pay (WTP) threshold, ranging from €0/QALY to €100,000/QALY, was shown in the cost-effectiveness acceptability curve (CEAC). The disease burden was calculated using the iMTA Disease Burden Calculator (Appendix C) [33]. Reflecting this disease burden, the relevant WTP is €20,000/QALY, based on Dutch guidelines [34].

Expected Value of Perfect Information (EVPI) per person was calculated to assess the potential value of reducing parameter uncertainty through further research and the expected monetary loss due to making a decision under current uncertainty [22]. The results were represented in an EVPI-curve.

Scenario analyses were performed to investigate structural uncertainty associated with important model assumptions and inputs. The influence of using (1) hospital perspective, (2) time horizon of 5 years, (3) alternative transition probabilities for the 2D approach, (4) alternative surgery duration for both strategies, (5) disutilities, (6), 3D surgery duration for only radius corrections, and (7) alternative 3D costs was investigated. A hospital perspective includes only healthcare sector costs, excluding productivity losses and travel expenses. In scenario analysis 3, transition probabilities of transitioning to one of the pain and functional disability states and between these states of the 2D strategy were updated using relative risks based on the RCT by Buijze et al. [3]. This scenario analysis assessed the impact of better and faster recovery with 3D-guided corrective osteotomy compared to 2D on the outcomes. Scenario analysis 4 evaluated the effect of significant differences in surgery duration between the 2D and 3D strategies on outcomes, obtained from Bauer et al [15]. Scenario analysis 5 incorporated the effect of disutilities associated with revision and hardware removal. In analysis 6, the surgery duration for 3D-guided corrective osteotomy obtained from OCON includes only corrections of the radius, excluding double corrections of both the radius and ulna. The final scenario analysis assessed the impact of 3D costs from literature on the iNMB. The base case 3D costs from OCON (€1751.03) were adjusted within a range of €1,800 to €4,000 as reported in literature [3, 12]. A threshold analysis was performed to determine the 3D cost value at which the iNMB becomes negative, indicating that 2D is cost-effective. Appendix D, Table 4 provides an overview of the model inputs that differ from the base case for each scenario analysis.

Validation

Model's structure, assumptions, input and output were face validated by clinical experts, including an orthopaedic surgeon, a technical physician and a hand therapist. Additionally, technical validation was performed. The results of the validation were reported following the AdVISHE checklist [35].

Results

Over a 3-year time horizon, the total cost of 3D-guided corrective osteotomy was €13,936.13 with total effects of 2.225 QALYs per patient, compared to €14,008.49 and 2.221 QALYs per patient for 2D-planned corrective osteotomy (see Table 2). De-aggregated costs are presented in Table 3, where costs are categorized by type of surgery and type of costs. 3D-guided corrective osteotomy prevented 119 revisions of type 1, thirteen of type 2, and fifteen hardware removals per 1,000 patients compared to the 2D approach (Table 4).

Sensitivity analyses

Results of the deterministic base-case analysis are shown in Appendix E Table 5. The findings of the DSA are presented in Figure 4. Results show that the relative risk of revision 1 was the most influential factor on the iNMB. Variations in the following parameters resulted in a negative iNMB: the lower bound of relative risk revision 1, the upper bound of relative risk hardware removal, the lower bound of relative risk revision 2, the lower bound of the number of weeks absent from work, and the upper bound of surgery duration 3D. The probabilistic sensitivity analysis showed that the probability of the 3D approach being cost-effective at a WTP threshold of €20,000 is 0.77 (see Figure 5 & 6). The EVPI is €25.38 per individual (see Appendix E, Figure 1).

Scenario analyses

The probabilistic results of the scenario analyses are shown in Table 2. From a hospital perspective, 3D-guided corrective osteotomy resulted in an incremental QALY of 0.004 at an additional cost of €462.32 per person, resulting in an ICER of €139,524.00 per QALY gained. The results of (2) alternative time horizon of 5 years, (3) different transition probabilities for 2D approach, (4) alternative surgery duration, (5) disutilities, and (6) alternative 3D surgery duration are consistent with the probabilistic base case analysis. Scenario analysis 3, showed an increase in incremental QALYs from 0.004 to 0.085. The CEAC indicates that the probability of the 3D strategy being cost-effective in this scenario analysis is 99.8% at a WTP threshold of €20,000 (see Appendix E, Figure 2 & 3). Scenario analysis 6 resulted in a cost saving of €185.84, with a 92.6% probability that the 3D approach is cost-effective (see Appendix E, Figure 4 & 5). The threshold analysis showed that at a 3D cost value of €1865.29, the 2D approach becomes cost-effective (see Appendix E, Figure 6).

Table 2. Results of probabilistic base-case analysis and scenario analyses. Costs and effects of individuals treated with 3D-guided corrective osteotomy compared with 2D-planned corrective osteotomy, and the incremental cost and effects are presented.

	3D-guided			2D-planned			Incremental			
	Total effects (QALY)	Total costs (€)	Revision & HR (N)	Total effects (QALY)	Total costs (€)	Revision & HR (N)	Effects (QALY)	Costs (€)	Revision & HR (N)	ICER per QALY
Probabilistic base-case analysis	2.225	13 936.13	268	2.221	14 008.49	415	0.004	-72.36	-147	Dominant
Scenario analyses										
1. Hospital perspective	2.225	5 336.28	268	2.221	4 873.96	415	0.004	462.32	-147	139 524
2. Time horizon of 5 years	3.705	14 550.00	398	3.698	14 909.63	602	0.007	-359.63	-204	Dominant
3. Alternative transition probabilities 2D	2.225	13 936.17	268	2.140	14 158.12	461	0.085	-221.95	-193	Dominant
4. Alternative surgery duration	2.225	14 164.58	268	2.221	14 523.82	415	0.004	-359.24	-147	Dominant
5. Disutilities	2.225	13 936.13	268	2.221	14 008.49	415	0.004	-72.36	-147	Dominant
6. Alternative 3D surgery duration	2.225	13 822.65	268	2.221	14 008.49	415	0.004	-185.84	-147	Dominant

QALY quality-adjusted life years, *HR* hardware removal, *ICER* Incremental Cost-Effectiveness Ratio

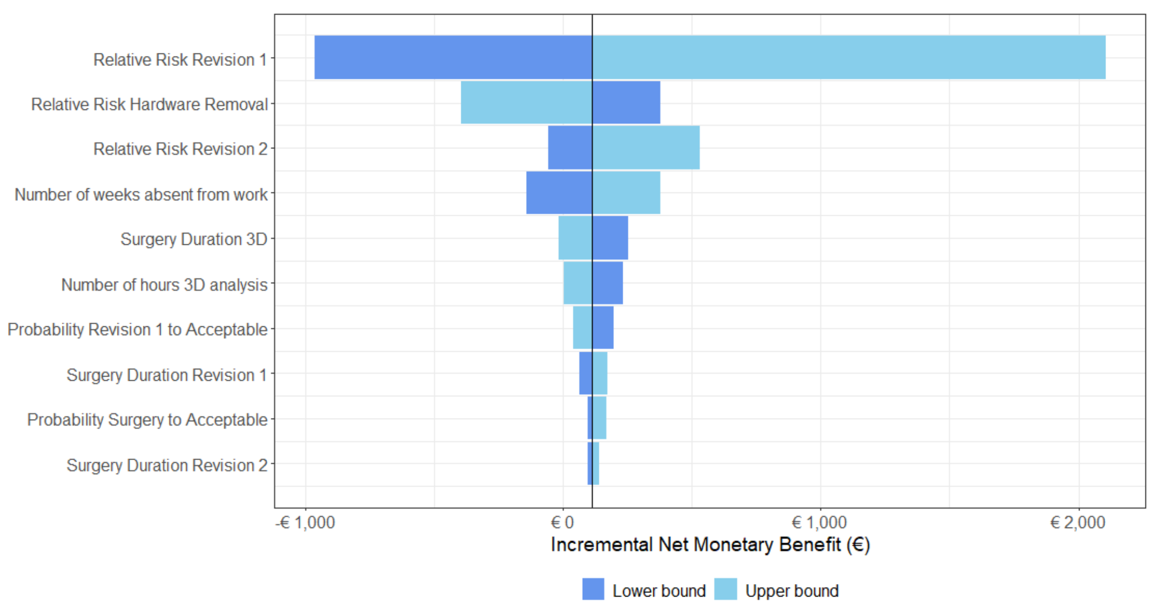

Figure 4. Tornado diagram presenting the results of the deterministic one-way sensitivity analysis. The diagram presents the top 10 parameters with the most influence on the incremental net monetary benefit iNMB). The bars indicate the lower and upper bound of each parameter. The vertical line represents the baseline iNMB of €111.20.

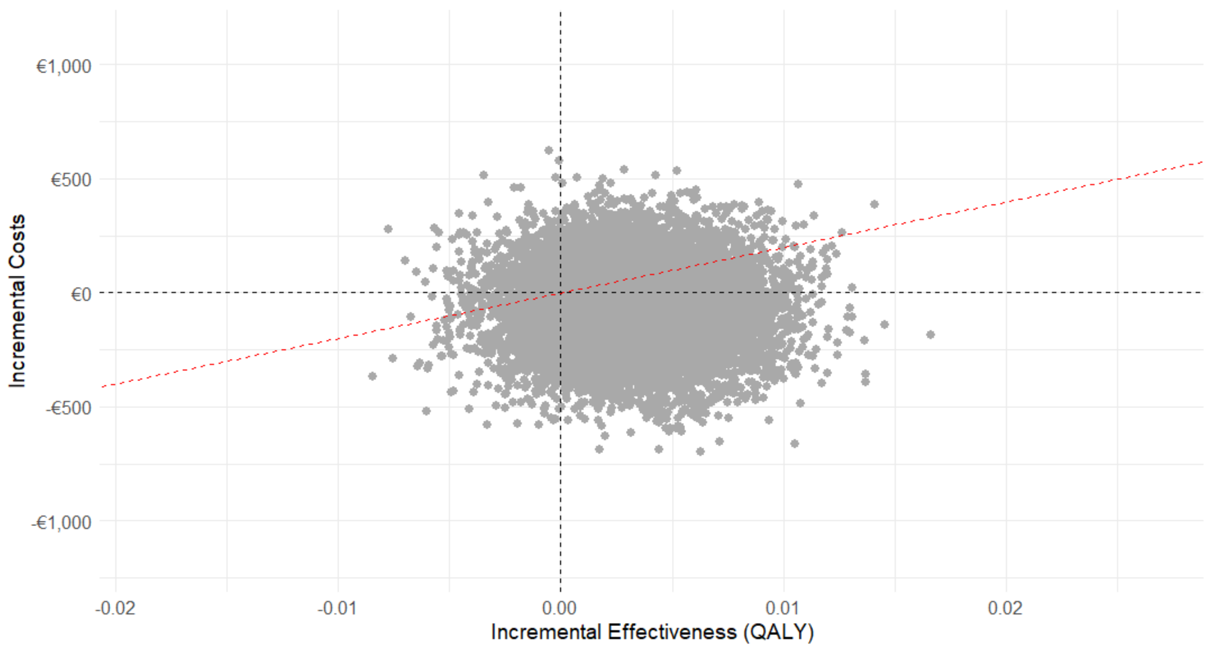

Figure 5. Incremental Cost-Effectiveness Plane (ICE-plane) presenting the results of the probabilistic sensitivity analysis. Each dot represents an incremental cost-effectiveness ratio (ICER) of 3D-guided compared to 2D-planned corrective osteotomy. The dotted red line represents the WTP threshold of €20,000 per QALY gained; dots on or below this line indicate that 3D is cost-effective.

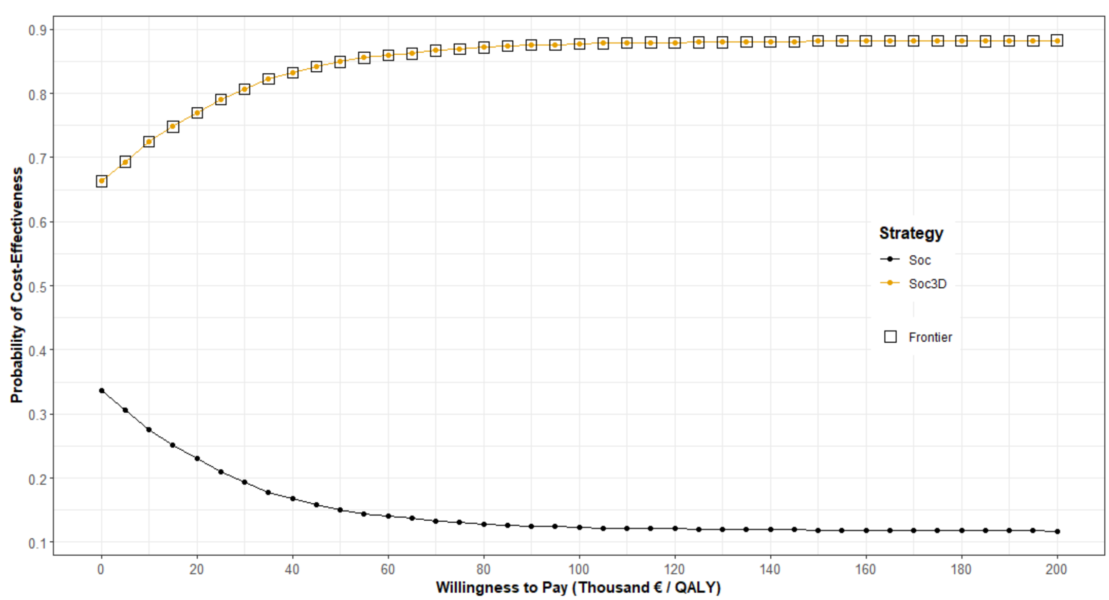

Figure 6. Cost-effectiveness acceptability curve (CEAC) and frontier (CEAF) presenting the results of the probabilistic sensitivity analysis. The black line labelled 'SoC' represents the probability of the 2D strategy being cost-effective across a range of willingness to pay thresholds. The yellow labelled 'SoC3D' represents the probability of the 3D strategy being cost-effective across a range of willingness to pay thresholds.

Table 3. Total discounted costs of each strategy categorized based on surgery type and cost type. Incremental costs of 3D-guided compared to 2D-planned strategy.

	3D-guided (€)	2D-planned (€)	Incremental costs (€)
Initial surgery			
Healthcare costs	4636	3774	862
Productivity losses	7782	7782	0
Travel expenses	52	52	0
Revision 1			
Healthcare costs	376	793	-417
Productivity losses	472	997	-525
Travel expenses	2	2	0
Revision 2			
Healthcare costs	168	140	28
Productivity losses	291	299	-8
Travel expenses	1	1	0
Hardware removal			
Healthcare costs	156	168	-12
Productivity losses	0	0	0
Travel expenses	0	0	0
Total	13 936	14 008	-72

Table 4. Number of revisions and hardware removal in each strategy per 1,000 patients. Incremental number of revisions of 3D-guided compared to 2D-planned strategy.

	3D-guided (N)	2D-planned (N)	Incremental (N)
Revision 1	124	243	-119
Revision 2	38	51	-13
Hardware removal	106	121	-15

Discussion

This study examined the cost-effectiveness of 3D-guided corrective osteotomy compared to 2D-planned corrective osteotomy in treatment of malunion in the distal radius, viewed from the Dutch societal perspective, employing a health state transition model. This is a first, and thus early cost-effectiveness analysis, encompassing significant uncertainty. Based on the current available evidence, the 3D approach was shown to be dominant, with effect gains of 0.004 QALYs and cost savings of €72.36 compared to the 2D approach, over a 3-year time horizon. Furthermore, the 3D approach led to 147 fewer revisions or hardware removals. PSA results showed that the 3D strategy is cost-effective in 77% of the iterations. This suggests a relatively high probability that 3D is cost-effective. However, both incremental QALYs and incremental costs are small. The incremental costs can primarily be attributed to the relative risk of revision 1. This input parameter, derived from literature, led to a lower occurrence of type 1 revisions in the 3D strategy, resulting in reduced costs for this revision (Table 3). Moreover, the decreased frequency of revisions lowered costs due to productivity losses (Table 3). The uncertainty presented in the PSA and the low incremental effects and costs savings indicate the need for further research to provide inputs with less uncertainty.

The results from the DSA (see Figure 4) demonstrate that the relative risk of revision 1 is the most significant parameter affecting the iNMB, indicating that changes in this parameter result in the most substantial variations in iNMB. The lower bound of relative risk revision 1, upper bound of relative risk hardware removal, lower bound of relative risk revision 2, lower bound of the number of weeks absent from work, and the upper bound surgery duration 3D result in a negative iNMB. This suggests that these parameters are critical factors in determining the cost-effectiveness of the intervention and highlights the importance of accurately estimating these parameters.

Dominance was robustly presented in all scenario analyses, except for the analysis from a hospital perspective. This analysis resulted in an ICER of €139,524.00 per QALY gained, indicating that 3D is not cost-effective from a hospital perspective. Excluding productivity losses in the hospital perspective leads to an increase in incremental costs compared to the societal perspective. This is because the 3D strategy incurs relatively higher healthcare costs, while the 2D strategy incurs relatively higher productivity losses. In scenario analysis 3, the impact of better and faster recovery with 3D-guided corrective osteotomy compared to 2D was investigated. Other studies on 3D-guided corrective osteotomy show it results in better plate positioning and alignment, leading to improved patient-reported and functional outcomes compared to conventional treatment [3, 6-8, 12]. This could potentially result in more patients reaching acceptable levels of pain and functional disability and at a faster rate, increasing QALYs. The results of the scenario analysis confirm this assumption, with an incremental QALY of 0.085 observed and a 99.8% probability of the 3D approach being cost-effective. This finding highlights the need to explore this potential improved recovery and obtain more reliable model inputs. The analysis into the effect of significant differences in surgery duration and the analysis based on the surgery duration of 3D procedures limited to radius corrections demonstrated that shorter 3D surgery duration resulted in greater cost savings for 3D and a higher probability of cost-effectiveness. This stresses the need for comprehensive data on surgery duration for both the 2D and 3D approach. The introduction of disutilities has no effect on the outcomes, likely because the disutility is only applied for a period of two weeks. The threshold analysis revealed that the 2D approach becomes cost-effective once the 3D costs exceed €1865.29. This highlights the importance of ensuring that the 3D costs remain below this threshold.

Comparison with current evidence

Several studies have shown that 3D-guided corrective osteotomy results in more accurate corrections and improved patient-reported outcomes [2-4, 6-9, 11, 12]. Research indicates that 3D planning achieves the desired outcomes in 96% of cases, compared to 40% with 2D planning, and reduces complications from 42% to 16% [4, 8, 13, 14]. The current study showed a complication rate of 42% in the 2D approach and 27% in the 3D approach. Additionally, 3D technology shortens surgery duration, leading to cost savings by reducing operating room time and personnel expenses [3, 7, 15]. Although a direct cost-effectiveness comparison between 3D-guided and 2D-planned corrective osteotomy is lacking in the current literature, the demonstrated benefits support the inputs based on data from literature in the current study.

An economic analysis into the potential cost saving of 3D printed anatomic models and surgical guides in orthopaedic surgery showed that, despite not being reimbursed, 3D printing has been adopted by several hospitals due to their advantages. The models and guides enable complex procedures, provide surgeons with greater confidence, and reduces surgery duration [36]. Other studies showed that it reduces surgical time, the number of required surgeries, and surgical aggressiveness, while increasing surgeon satisfaction, lowering risks, and shortening recovery time compared to conventional treatment [37, 38].

In other fields, such as plastic surgery, 3D planning has also been proven to be efficient and time saving compared to conventional treatment [39]. A cost-effectiveness analysis of the use of 3D virtual planning in mandible reconstruction demonstrated that 3D planning is cost-effective compared to conventional techniques, reducing surgery duration and operating room costs, and resulting in improved outcomes and incremental QALYs [40]. These findings suggest that 3D planning in corrective osteotomy for the distal radius could similarly reduce surgery duration and operating room costs while improving patient outcomes.

Limitations

The current study has several limitations, primarily the lack of available evidence to inform key parameters, including quality of life, relative risks, and productivity losses. The absence of data introduces uncertainty into the analysis.

To estimate quality of life values, a mapping function with a low R-squared was applied, indicating that only about half of the variability in the data is explained by the predicted regression. Furthermore, the baseline EQ-5D score was taken from another study, introducing significant uncertainty. This could potentially lead to inaccuracies in estimating the quality of life, resulting in an underestimation or overestimation of incremental QALYs.

Ideally, relative risks for undergoing a revision or hardware removal would be derived from an RCT, but instead were based on a systematic review. Relative risks for transitioning to one of the pain and functional disability states and between these states were based in reported PRWHE score in an RCT, but the absence of patient level data in this study prevents the examination of individual transitions between health states. Consequently, relative risks of transitioning to, and between the pain and functional disability states were only applied within a scenario analysis. This analysis showed a more considerable incremental effect than the base case, resulting in a potential underestimation of the incremental effects in the base case analysis. Furthermore, no patient characteristics were reported, preventing correction for potential differences in baseline patient characteristics. This might be a problem because OCON tends to perform more complex surgeries involving deformities in multiple planes. These surgeries may not be representative of all corrective osteotomies performed in the Netherlands, potentially leading to an underestimation of the intervention’s cost-effectiveness.

Resource uses, including duration of work absence to calculate productivity losses and number of physiotherapy appointments, were estimated rather than individually reported. This could lead to either an overestimation or underestimation of physiotherapy costs and costs due to productivity losses. The latter, in particular, can significantly impact the results, as productivity losses have a substantial effect on incremental costs. Furthermore, the surgery durations used in the base case analysis may have led to an underestimation of the cost savings of the 3D approach, as demonstrated in scenario analyses 4 and 6.

Future research

The lack of available evidence stresses the need for further research with more comprehensive data. Ideally, future research should adopt a randomized controlled trial design to capture differences in revision rate and patient recovery between the two strategies. For OCON, it is recommended to conduct a prospective observational study, following patients treated with 3D-guided and 2D-planned corrective osteotomy for a period up until one year after surgery. Various measurements should be taken preoperatively and at three, six, and twelve months postoperatively, including the PRWHE and the EQ-5D-5L questionnaire. This enables the calculation of health-related quality of life and to assess whether 3D leads to better recovery and to what extent. Detailed patient characteristics, including age, gender, dominance of the affected arm, time between the initial injury and osteotomy, initial treatment, and the degree of deformity, should be documented to correct for potential differences between 2D and 3D groups, and prevent selection bias and confounding. Furthermore, it enables to perform subgroup analyses, for example, based on the degree of deformity. The occurrence of revisions should be reported. Patients undergoing a revision should be followed for a period of one year after the revision, conducting the same measurements as after the initial surgery. Documentation of revisions is crucial, as the DSA shows that relative risks of revisions have a big influence on the iNMB, and potentially resulting in different conclusions. Additionally, the duration of work absence for each patient, including their work capacity percentage upon return, the timeline to achieve full capacity, and the work status at baseline should be documented to calculate productivity losses. Recording the number of physiotherapy appointments will aid in updating resource use. Finally, costs for 2D and 3D planning and surgery duration of the 2D and 3D corrective osteotomy needs to be collected.

Conclusion

From a Dutch societal perspective, 3D-guided corrective osteotomy is expected to be cost-effective compared to 2D-planned corrective osteotomy, as it results in a small incremental health effect and a small reduction of costs. Given these findings, 3D-guided corrective osteotomy should be adopted. However, there remains uncertainty around this conclusion, with both incremental health effects and cost savings being small. Future research is necessary to explore differences in revision rates and patient recovery between the two strategies, and the results should be updated as new data becomes available.

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Appendix

A. CHEERS checklist

Table 1. CHEERS checklist

Item		Page number reported
1	Title	1
2	Abstract	2
3	Background and objectives	2-5
4	Health economic analysis plan	5
5	Study population	6
6	Setting and location	6
7	Comparators	2, 3, 6
8	Perspective	5
9	Time horizon	5
10	Discount rate	5
11	Selection of outcomes	5
12	Measurement of outcomes	5-7
13	Valuation of outcomes	5-7
14	Measurement and valuation of resources and costs	7-8
15	Currency, price data, and conversion	8
16	Rationale and description of model	5-6
17	Analytics and assumptions	5-11
18	Characterizing heterogeneity	Not applicable
19	Characterizing distributional effects	Not applicable
20	Characterizing uncertainty	10-11
21	Approach to engagement with patients and others affected by the study	Not applicable
22	Study parameters	8-10
23	Summary of main results	12
24	Effect of uncertainty	12
25	Effects of engagement with patients and others affected by the study	Not applicable
26	Study finding, limitations, generalizability, and current knowledge	15-18
27	Source of funding	Not applicable
28	Conflict of interests	Not applicable

B. Calculations model inputs

Utility values

Mapping function:

EQ5D_12 = 0.623 + 0.344*EQ5D_0 – 0.006*PRWE_12_P – 0.006*PRWE_12_F + 0.000*PRWE_12_PxF [24]

Baseline EQ-5D-5L score: 0.73 [9]

Costs

Costs within the healthcare sector

Table 2. Costs cast OR

Type of resource	Unit price	Number of units	Source
Splint (7.5 cm)		1	Internal
Stocking + cotton wool + pre-tape + adhesive bandage + felt		1	Internal
Cast (7.5 cm)		1	Internal

Table 3. Costs cast brace

Type of resource	Unit price	Number of units	Source
Stocking		1	Internal
Cast		1	Internal
Splint		1	Internal
Velcro		1	Internal
Plaster rivets		1	Internal
Tensoplast sport		1	Internal

Travel costs

Travelling to the hospital:
Average distance to hospital: 7.1 kilometres [26]
Dutch consumer price index (CPI) 2022: 121.43 [31]
Dutch CPI 2023: 126.09[31]
Price per kilometre converted 2023 based on CPI: (€0.26/121.43)*126.09 = 0.27
Mean parking costs per visit: (€3.92/121.43)*126.09 = 4.07 [26, 31]
Total travel and parking costs per hospital visit: 2 * 7.1 * 0.27 + 4.07 = €7.90

Travelling to physiotherapy practice:
Average distance to physiotherapy practice: 2.2 kilometres [26]
Price per kilometre (2023): €0.27 [26, 31]
Total travel cost per physiotherapy visit: 2 * 2.2 * 0.27 = €1.19

Costs due to productivity losses

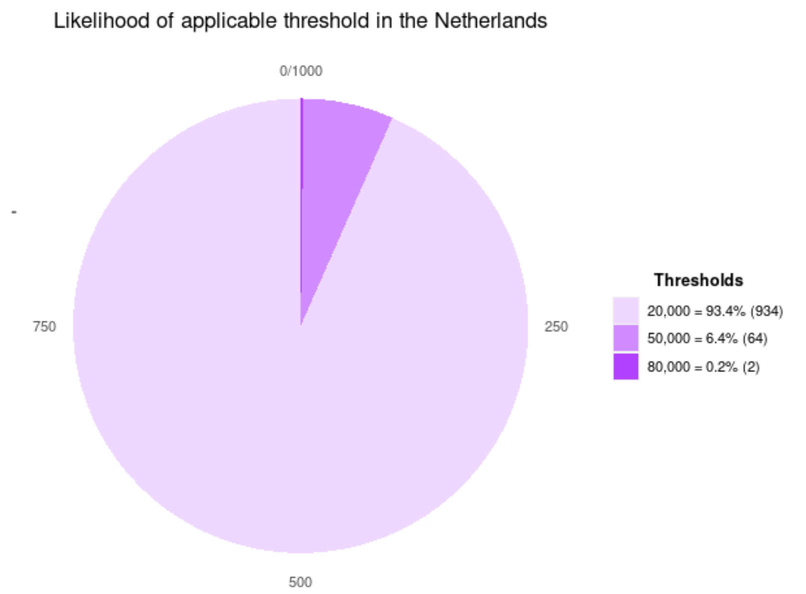
Average number of weeks a patients is not able to work: 8 weeks [28]
Employment percentage in 2023: 73.2% [29]
Average number of hours worked during a week in the Netherlands in 2023: 32.1 [30]
Productivity costs per hour (2023): €41.41 [26]
Costs due to productivity losses: 8*0.732*32.1*41.41 = €7,784.15

C. Results iMTA disease burden calculator

Inputs:

- Age of the population: 44
- Percentage of males in the population: 25%
- Discount rate: 1.5%
- Remaining QALYs: 23.4
- Standard error around PSA QALYs: 5.5

Result:



D. Inputs scenario analyses

Table 4. Model inputs changed for each scenario analyses compared to the base case

Scenario analysis	Model input	Value base case	Value scenario analysis	Reference value scenario analysis
1. Hospital perspective	Price per kilometre	0.27	0	
	Parking hospital	4.07	0	
	Productivity costs per hour	41.41	0	
2. Time horizon of 5 years	Number of cycles	12	20	
3. Alternative transition probabilities 2D approach	Relative risk NP to AP month 0-3	0	0.71	[3]
	Relative risk AP to NP month 0-3	0	1.35	
	Relative risk NP to AP month 3-12	0	0.77	
	Relative risk AP to NP month 3-12	0	1.47	
4. Alternative surgery duration	Surgery duration 3D	90.26	108	[15]
	Surgery duration 2D	96.9	140	
5. Disutilities	Disutility revision 1	0	0.08	[25]
	Disutility revision 2	0	0.11	
	Disutility Hardware removal	0	0.04	
6. Alternative 3D surgery duration	Surgery duration 3D	90.26	81.55	
7. Alternative 3D costs	Costs 3D analysis Costs 3D license per patient Costs printing 3D guides and models Costs CT Costs plate and screws	Total: 1751.03	Range between 1800 and 4000	[3, 12]

E. Results

a. Deterministic base-case analysis

Table 5. Results deterministic base-case analysis. Costs and effects of individuals treated with 3D-guided corrective osteotomy compared with 2D-planned corrective osteotomy, and the incremental cost and effects are presented.

	3D-guided			2D-planned			Incremental			ICER per QALY
	Total effects (QALY)	Total costs (€)	Revision & HR (N)	Total effects (QALY)	Total costs (€)	Revision & HR (N)	Effects (QALY)	Costs (€)	Revision & HR (N)	
Deterministic base-case analysis	2.278	13 905.51	268	2.274	13 955.35	415	0.004	-49.84	-147	Dominant

b. Probabilistic base-case analysis

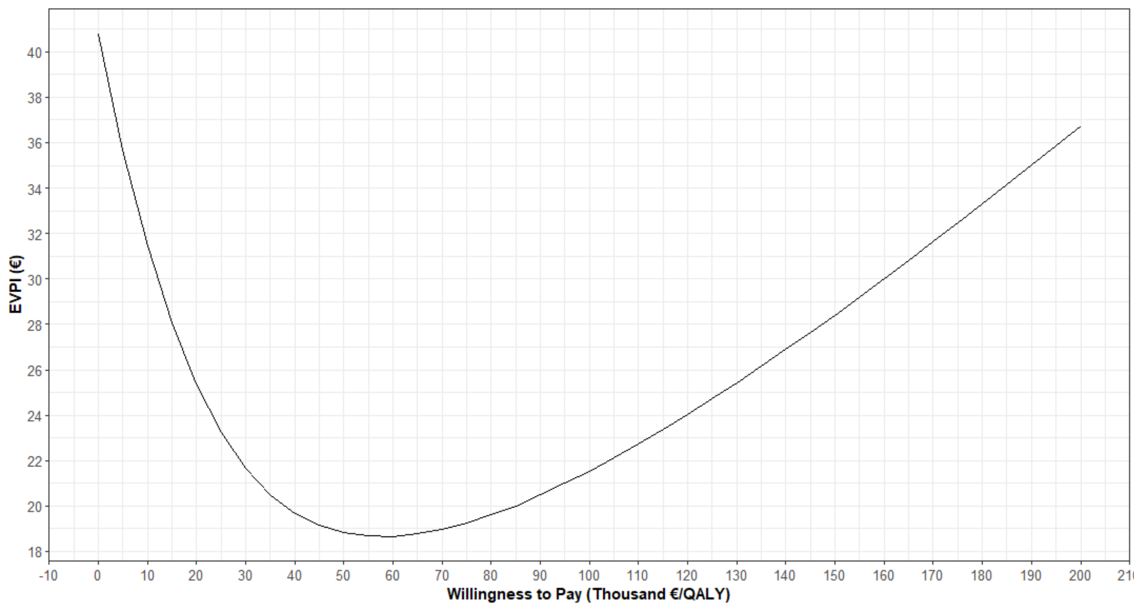


Figure 1. EVPI-curve of the probabilistic base-case analysis presenting the expected value of perfect information per person for a range of willingness to pay thresholds.

c. Probabilistic results of scenario analysis 3

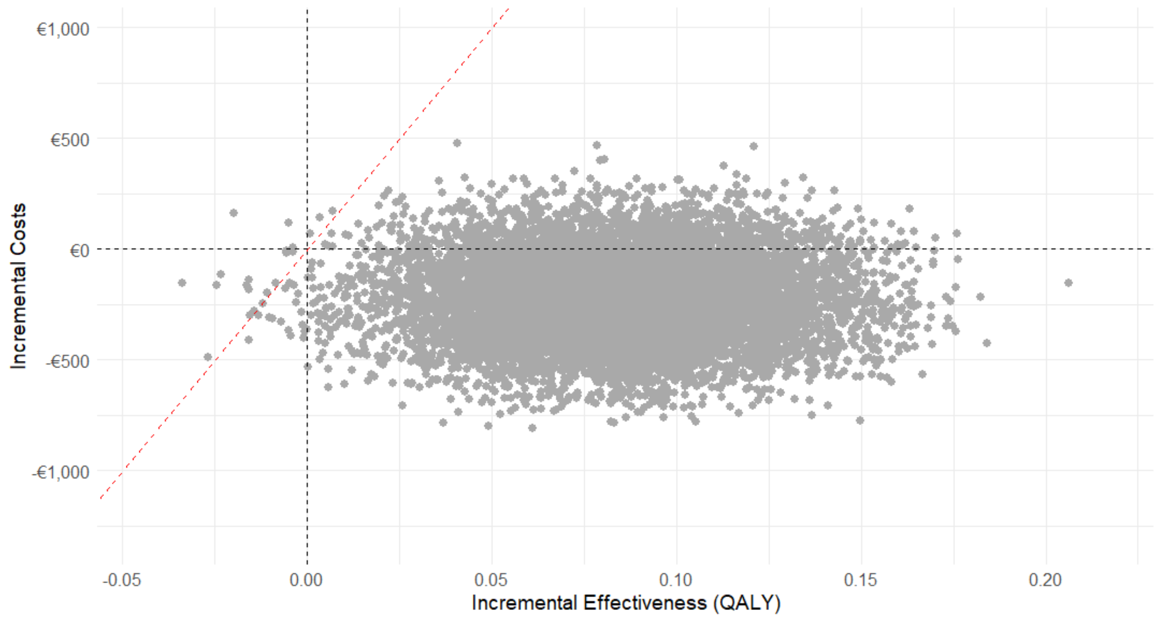


Figure 2. Incremental Cost-Effectiveness Plane (ICE-plane) presenting the results of the probabilistic sensitivity analysis of scenario analysis 3. Each dot represents an incremental cost-effectiveness ratio (ICER) of 3D-guided compared to 2D-planned corrective osteotomy. The dotted red line represents the WTP threshold of €20,000 per QALY gained; dots on or below this line indicate that 3D is cost-effective.

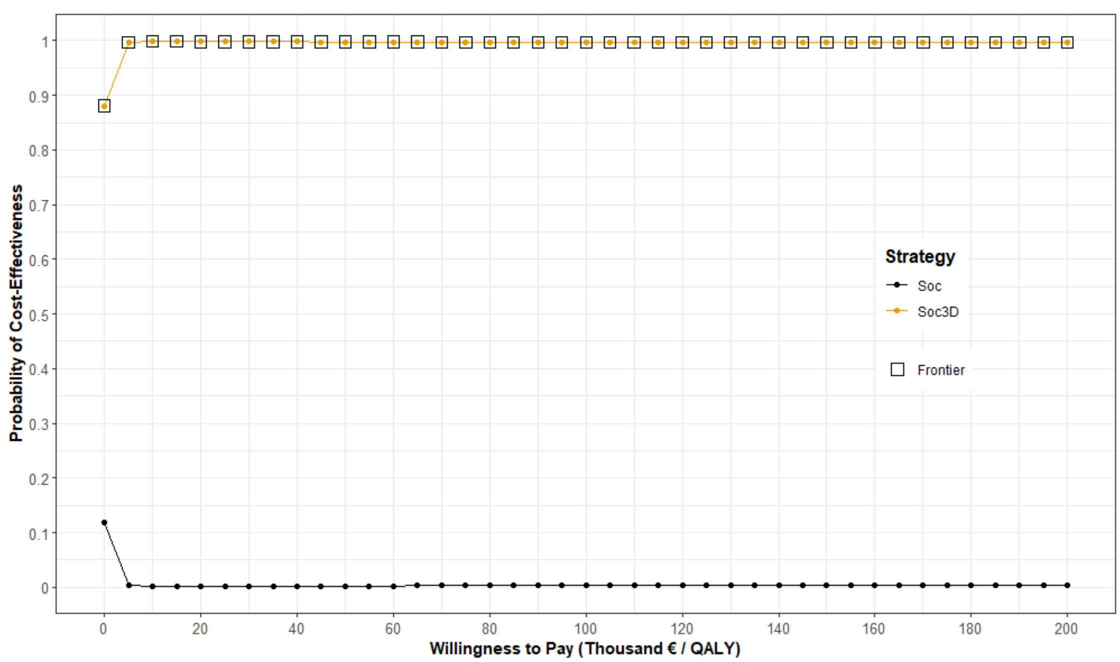


Figure 3. Cost-effectiveness acceptability curve (CEAC) and frontier (CEAF) presenting the results of the probabilistic sensitivity analysis of scenario analysis 3. The black line labelled 'SoC' represents the probability of the 2D strategy being cost-effective across a range of willingness to pay thresholds. The yellow labelled 'SoC3D' represents the probability of the 3D strategy being cost-effective across a range of willingness to pay thresholds.

d. Probabilistic results of scenario analysis 6

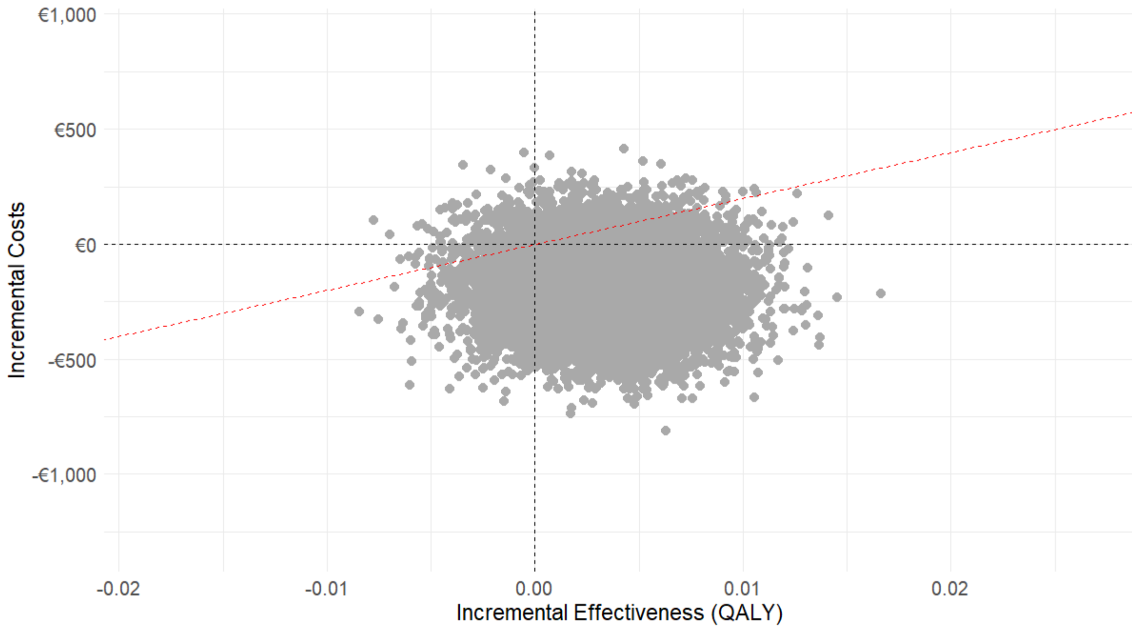


Figure 4. Incremental Cost-Effectiveness Plane (ICE-plane) presenting the results of the probabilistic sensitivity analysis of scenario analysis 6. Each dot represents an incremental cost-effectiveness ratio (ICER) of 3D-guided compared to 2D-planned corrective osteotomy. The dotted red line represents the WTP threshold of €20,000 per QALY gained; dots on or below this line indicate that 3D is cost-effective.

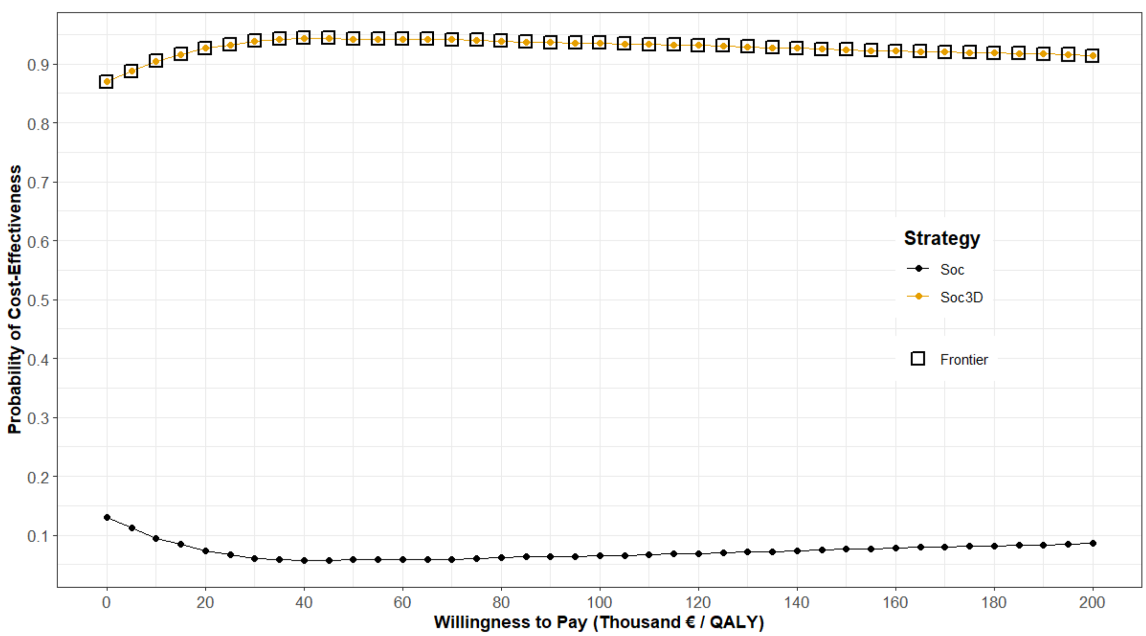


Figure 5. Cost-effectiveness acceptability curve (CEAC) and frontier (CEAF) presenting the results of the probabilistic sensitivity analysis of scenario analysis 6. The black line labelled 'SoC' represents the probability of the 2D strategy being cost-effective across a range of willingness to pay thresholds. The yellow labelled 'SoC3D' represents the probability of the 3D strategy being cost-effective across a range of willingness to pay thresholds.

e. Threshold analysis scenario analysis 7

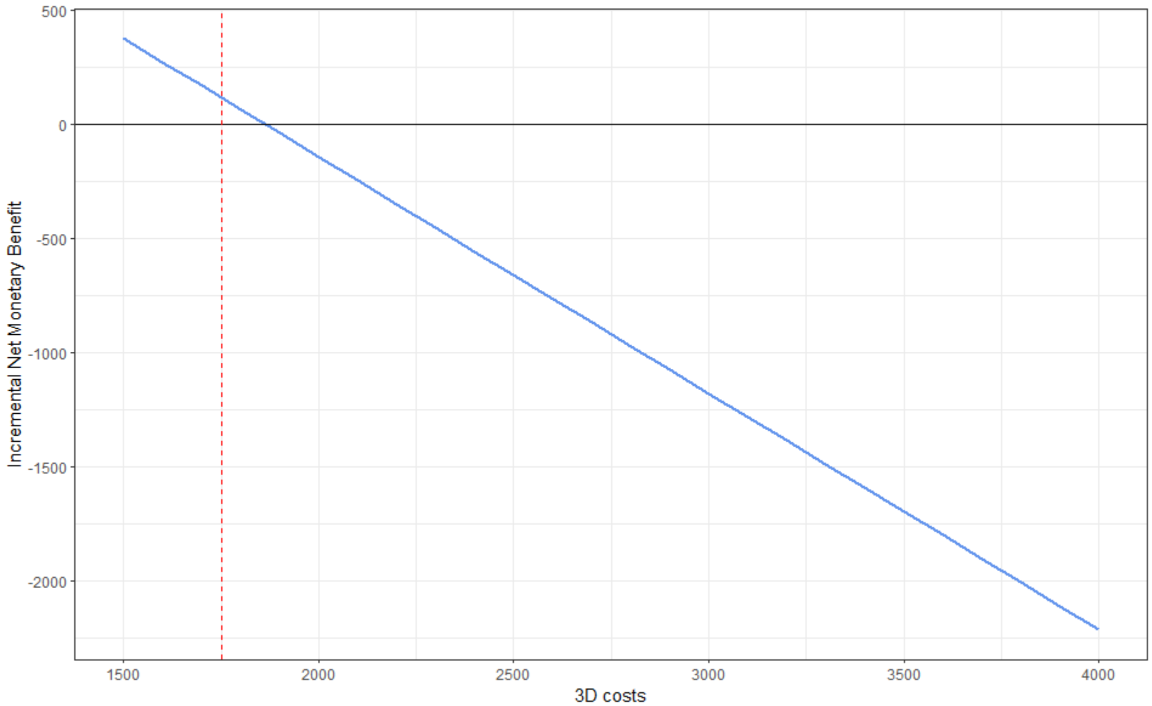


Figure 6. Threshold analysis 3D costs. The vertical red dotted line represents the 3D costs of OCON resulting in an incremental Net Monetary Benefit of €1751.03.