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RESEARCH ARTICLE

Cost-utility analysis of vertebroplasty versus thoracolumbosacral orthosis in the treatment of traumatic vertebral fractures

[Analyse coût-utilité de la technique de vertébroplastie versus corset orthopédique dans le traitement des tassements récents post-traumatiques]

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Abstract: In this research we compared the cost-utility of vertebroplasty versus bracing for treatment of post-traumatic fractures. Cost and health outcomes were assessed from a prospective, randomized, non-blinded, single-center study that was carried out between May 2010 and November 2011 at the University Hospital of Clermont-Ferrand, France. The study included 99 patients, aged from 18 years to 70 years, suffering from acute non-osteoporotic vertebral fracture. We compared the costs and Quality-Adjusted Life Years (QALY) and assessed the Incremental Cost-Effectiveness Ratio for the two arm groups. Health insurance and patient perspectives were considered**.** From the health insurance perspective, total cost was €7,267 for the brace group whereas it was €7,365 for the vertebroplasty group (mean difference €75.3; p <0.9). From the patient perspective, total cost was €5,303 for the brace group and €3,435 for the vertebroplasty group (mean difference €-1,900.7; p<0.02). Differences between groups in QALYs were non-significant: 0.01 (95% CI -0.01 to 0.04; p=0.5). The Incremental Cost-Effectiveness Ratio of vertebroplasty was €-12,200 per QALY from the health insurance perspective and €-159,200 per QALY from the patient perspective. While the QALY values do not differ between the two groups, the vertebroplasty technique resulted in significantly lower costs from the patient perspective in France. From the health insurance perspective, we were unable to conclude if vertebroplasty was more cost-effective than bracing.

Keywords: Health economic assessment, cost-utility analysis, QALY, SF-36, SF-6D, vertebroplasty, bracing, clinical practice, France.

Résumé : Nous avons comparé le rapport coût-utilité de la vertébroplastie et du corset orthopédique pour le traitement des fractures post-traumatiques. Les coûts et les résultats d'efficacité ont été évalués à partir d'une étude monocentrique, prospective, aléatoire et non-aveugle, réalisée entre mai 2010 et novembre 2011 au centre hospitalier universitaire de Clermont-Ferrand, France. L'étude a inclus 99 patients, âgés de 18 à 70 ans, souffrant d'une fracture vertébrale aiguë non-ostéoporotique. Nous avons comparé les coûts et le nombre d'années de vie ajustées par leur qualité (QALY), puis évalué le rapport coût-efficacité incrémental pour les deux groupes. Les perspectives prises en compte étaient celles de l'assurance maladie et du patient. Du point de vue de l'assurance maladie, le coût total était de 7267€ pour le groupe corset orthopédique contre 7365€ pour le groupe vertébroplastie (différence moyenne 75,3€; p <0,9). Du point de vue du patient, le coût total était de 5303€ pour le groupe corset orthopédique et de 3435€ pour le groupe vertébroplastie (différence moyenne -1900,7€; p <0,02). Les différences de QALY entre les groupes étaient non significatives: 0,01 (IC à 95% -0,01 à 0,04; p=0,5). Le ratio coût-efficacité différentiel de la vertébroplastie était de -12200€ par QALY selon le point de vue de l'assurance maladie et de -159200€ par QALY selon la perspective du patient. Alors que la différence de QALY ne diffère pas entre les groupes, la technique de la vertébroplastie a entraîné des coûts très inférieurs du point de vue du patient. Pour la perspective de l'assurance maladie, il n'a pas pu être conclu à la supériorité de l'une des deux techniques.

Mots clés : Évaluation économique en santé, analyse coût-utilité, QALY, SF-36, SF-6D, vertébroplastie, corset orthopédique, pratique clinique, France.

Introduction

Post-traumatic vertebral fractures represent 14% of the total number vertebral fracture cases and are painful and disabling [1]. With an annual incidence range between 19 and 88/100,000 inhabitants in developed countries, the people most at risk are active male adults with a mean age of 45 years.

Vertebroplasty is performed with the injection of polymethyl methacrylate resin within the vertebra in order to stabilize and reduce pain. Initially used for osteolytic vertebral metastases, myeloma and vertebral angioma, this technique has been widely adapted [2-7] especially for osteoporotic fractures. However, the treatment success results have not been uniform [8-12]. Vertebroplasty for treatment of non-osteoporotic and/or non-neoplastic fractures is poorly supported by available scientific literature [12-13] and therefore remains controversial [14-16].

Bracing is the established conservative treatment of choice for the treatment of post-traumatic fractures [12]. However, if the efficacy of vertebroplasty is proven, it would be advantageous to estimate the efficiency of using this alternative in a clinical practice.

Objective

The objective of this study was to assess the cost-utility of vertebroplasty compared to bracing for treatment of post-traumatic fractures.

Materials and methods

Study population

This study was based on a single-center, non-blinded, prospective, randomized trial conducted between May 2010 and November 2011 at the University Hospital of Clermont-Ferrand (France) under the approval number 2010-17 of *Comité de protection des Personnes du Sud-Est* ethics committee, whose study methods, including the protocol, patient selection and clinical outcome measures were made available (ClinicalTrials.gov number, NCT01643395). All patients provided written informed consent.

Patients were enrolled by one investigator, a neurosurgeon or a neuroradiologist from the study center. The study included 99 patients from ages 18 to 70 years who suffered from acute (<15 days) Magerl type A non-osteoporotic vertebral fracture. Out of this, 28% of patients had at least one A3 burst fracture. Exclusion criteria were as follows: C1 to T4 fractures, associated posterior arch fracture, substantial retropulsion of bony fragments (medullary canal narrowing above 50 % in lumbar and 30% in thoracic spine), neurological complications, head injury with Glasgow Score <15, long-term painkiller therapy, local or systemic infection, suspected or known malignancy, coagulation disorders, contraindication to general anaesthesia, pregnant women, and no informed consent obtained.

Study methods

Vertebroplasty

The procedures were performed by three experienced interventional neuro-radiologists, with the patients under general anesthesia and prophylactic antibiotic treatment. All the radiologists performed vertebroplasties according to a standardized protocol (http://www.my-spine.com/kyphoplasty-and-vertebroplasty.html). Patients were positioned prone on a fluoroscopy biplane suite's examination table. Pillows were inserted under the chest and pelvis to increase the lordosis and reduce the wedge angle of the fractured vertebral body. A posterolateral approach was performed using a 13G trocar at thoracic levels and a 11G trocar at lumbar levels. The trocar was pushed toward the ventral third of the vertebral body under bi-plane fluoroscopic guidance. Barium opacified polymethyl-methacrylate cement (Osteopal®V, Hereus, Germany or OsteoFirm®, William Cook Europe, Denmark) was injected using Duro-Ject® Vertebroplasty Injector Set (William Cook Europe, Denmark) under fluoroscopic guidance. The procedure was discontinued when the cement reached the dorsal quarter of the vertebral body or when epidural or venous extravasation was observed.

Bracing

Bracing for the purpose of this study consisted of tailor-made rigid thoraco-lumbo-sacral orthoses worn at all times for three months except when lying flat in bed. Compliance in wearing the brace was self-reported by patients at all time-points of the follow-up.

Outcomes and measurement of utility

Outcome measurements were performed at baseline, 1, 3 and 6 months [10,12] by specialist consults, and included spine radiography and Magnetic Resonance Imaging (MRI). A self-assessment questionnaire was used to evaluate the following: pain using a Visual Analogue Scale (VAS); functional disability using the Rolland Maurice Disability Questionnaire (RMDQ) score; and quality of life using the Short-Form Health Survey (SF-36).

The primary endpoint was the quality of life, measured by the Short-Form 36 questionnaire (SF-36) at baseline, 2-days, and 1, 3, and 6 months. The SF-36 questionnaire includes 36 questions exploring eight dimensions of quality of life. It has been validated in France. This questionnaire is considered to have limited application in economic evaluation based upon the criticism that its questions do not rely on individual preferences [17]. However, the SF-6D, developed by Brazier *et al.* [18], enables QALYs to be obtained from the SF-36 for use in cost-utility analysis. This algorithm is considered as having more rigorous methodological and theoretical bases, and more robust results than nine other preference-based algorithms [19]. Although the SF-6D has not been validated in France [17], in the absence of an alternative, we used this scale to estimate QALYs. From the utility scores generated, the number of QALYs was calculated by multiplying the length of time spent in health states by preference scores associated with these conditions [17]. The QALYs gained by the intervention were calculated by the area-under-the-curve method. We used the common assumption of a linear change over time [20-21]. After the intervention period of 6 months, we conservatively assumed a linear decrease of intervention effect returning to baseline level 12 months after onset of the study. The mean value was calculated for each group, and the average utility of the vertebroplasty group was subtracted from the average bracing utility group. The formula used was as follows [22]:

$$
\begin{aligned}
QALY = 1/12 \times (&\alpha \times (SF6D_{baseline} + SF6D_{1month}) \times 1 + \alpha_1 \\
&\times (SF6D_{1month} + SF6D_{3month}) \times 2 + \alpha_2 \times (SF6D_{3month} + SF6D_{6month}) \\
&\times 3 + \alpha_3 \times (SF6D_{6month} + SF6D_{baseline}) \times 6 \\
&- [(\beta \times (SF6D_{baseline} + SF6D_{1month}) \times 1 + \beta_1 \\
&\times (SF6D_{1month} + SF6D_{3month}) \times 2 + \beta_2 \times (SF6D_{3month} + SF6D_{6month}) \\
&\times 3 + \beta_3 \times (SF6D_{6month} + SF6D_{baseline}) \times 6])
\end{aligned}
$$

where α, α_1, α_2, α_3/ β, β_1, β_2, and β_3 correspond to the length of time spent in health states at baseline, 1, 3 and 6 months for the vertebroplasty and bracing groups.

Imbalance in baseline utility must be taken into account for the estimation of mean differential QALY by multiple regression methods [23]. A regression using ordinary least square was used [24], controlling by sex, age, degree of kyphotic angle and the SF-6D at baseline. Selection of variables was made from successive "step by step" iterations, removing non-significant variables associated with QALYs [24]. QALYs derived from this model were used in our main analysis.

Cost estimation

On-site data collection was carried out from October 2013 to March 2014. The costing analysis of one year around the treatment (from June 2010 to July 2011) was performed following the recommendations of IPSOR [25] and the French Health Authority [17,26]. Direct costs related to care and indirect costs associated with cessation of work were considered. However, costs were disaggregated in order to incorporate the recommendations of other international institutions such as the National Health Service in England, Statutory Health Insurance in Germany and Medicare in the United States [27-29].

We considered the health insurance (which is compulsory and public) and the patient perspectives. The cost of production was first estimated to cover: the manufacturing cost of the brace in the brace arm and the cost of vertebroplasty procedure in the second arm. The cost associated with vertebroplasty included the costs of the injected material, utilization of the neuroradiology room, imaging explorations and biology examinations, anesthesia, consultations and acts performed during follow-up. For each technique, the costs of hospitalization, imaging and ambulatory care were included.

Price data for the cost of brace and the cost of injected material are from the imaging center of the University Hospital of Clermont-Ferrand, for which the presented prices are inclusive of value-added tax. The cost of imaging acts, anesthesia and capital facilities were evaluated based on their Relative Cost Index (ICR in French). This index expresses the level of mobilization of human and material resources that are directly necessary to fulfill each act [26]. The cost of an ICR unit of each component was multiplied by the number of necessary ICR corresponding to each patient's act. The cost difference of drugs was not statistically significant and therefore their costs were not included in the analysis. The cost of biological tests was calculated from the agreed Social Security fee. The cost of single use materials and consumables for vertebroplasty was assessed from a standard list prepared by the nursing staff. The cost of hospital stays was evaluated by the French national hospital administrative database *Programme de Médicalisation des Systèmes d'Information* (PMSI) from costs per the French Diagnosis-Related Group (DRG). DRG uses 2011 data from the French National Scale of Costs database, which allows the calculation of complete costs per stay and a full cost by DRG. The French DRG is a composite index of diseases, to the extent that a number of pathologies are related to a DRG while simultaneously the same pathology is found in several DRG [26]. For these reasons, we adopted the "*DRG modified*" approach ("DRG *aménagé*" in French) [26] and replaced the variable medical costs related to anesthesia, imaging, interventional imaging, laboratory tests, consumables, and medical devices by observed cost directly attributable to the implementation of both treatment. For fixed costs, we used data from the French National Scale of Costs.

Daily hospital charges and the cost of follow-up (imaging, physiotherapy and nursing home consultations) were evaluated based on Social Security official tariffs. The cost of a hospital day was multiplied by the number of days of hospitalizations for each patient. Similarly, the costs of a physiotherapy session, nursing consultation and imaging were multiplied by the number of sessions performed for each patient.

Indirect costs related to the potential loss of production were evaluated using the average value of daily allowance paid by health insurance under cessation of work estimated at €31.4 [30]; those related to production losses from the commercial sphere were estimated from the daily average wage income of the French population estimated at €72 for a man and €55 for a woman [31].

The variation in costs and outcomes was undertaken to see if our results were specific to France. All costs were estimated in € (2014), and a discount rate of 4% was applied in accordance with the recommendations of the French Health Authority (HAS) [17].

Cost-effectiveness analysis

The mean difference between the two treatment strategies for the total cost and for each cost component was tested with the student's *t*-test. A nonparametric bootstrap (2,000 replicates) was used to estimate confidence intervals [24,32]. For counteracting the imbalances between the groups, we adopted a generalized linear model (GLM) to estimate the incremental cost [24,33-35], controlling for age, sex, history of existence of vertebral fractures, cement leakage and severity of fracture from the patient's perspective, and the average degree of kyphotic angle, sex, and the SF-6D at baseline from the health insurance perspectives. Independent variables were selected from successive "step by step" iterations by removing non-significant variables associated with costs.

The family function was selected with a Parks Modified-test and tests to assess goodness of fit were performed [24]. These comprised the Pearson correlation test, the Hosmer & Lemeshow modified test (for systematic bias in fit on raw scale), and the Pregibon link test (for linearity of response on scale of estimation). Costs derived from these models were used in our cost-effectiveness analysis. Poisson distribution with a log link was the best fit for the health insurance and patient perspectives. The incremental cost-effectiveness ratios (ICERs) were calculated as follows:

$$ICER = \frac{\text{Incremental difference in total costs}}{\text{Incremental difference in QALYs saved}}$$

The uncertainty was estimated using a nonparametric bootstrap [36] generated by the "recycled predictions" [24]. Commonly applied in cost-effectiveness analyses for balanced data between different groups, this method consists of encoding each patient as if they were part of the control group and predicting the results for each individual, and then encoding each patient as if they were part of the treatment group and predicting the results for each individual.

Cost-effectiveness acceptability curves were constructed [36-38]. The cost-effectiveness acceptability curve showed the probability that the new intervention is more cost-effective compared to the former intervention, based on the willingness to pay of the community [39]. Our confidence statements were based on whether or not the upper and lower confidence interval included the decision threshold. If the confidence interval included the decision threshold, we cannot be confident that the alternatives differ from one another; conversely, if the confidence interval excluded the decision threshold, we can be confident that the alternatives differ from one another [24]. In France, there is no threshold/QALY applied for judging whether or not to adopt a new technology. In England, the threshold €30,000 (£20,000) is generally adopted [29,39]. In Germany too, there is no official threshold, but some health economists use €50,000/QALY [40]. These two thresholds are therefore used in our analysis. The cost/QALY represents the willingness to pay. Data analyses were performed with the STATA/SE12 (StataCorp LP) software.

Sensitivity analysis

To assess the robustness of the results, sensitivity analyses were conducted [25]. In the first sensitivity analysis, we varied the discount rate from 0% [26] to 10% [41], including a discount rate at 2.5% to take into account discussions within the French Health Authority (HAS) about a potential revision of discount rate recommendation and also those of other international institutions. The proper discount rate remains controversial. Often 3%, 3.5% or 5% are suggested in international clinical practice guidelines [25,28-29,42].

Further, we evaluated the effect of different model specifications for the cost estimate. Specifically, we used estimates of the difference in costs arising from the use of ordinary least squares (OLS) regression in order to compare the results derived by the use of a GLM.

As the quality of life was assessed up to six months (see above), we also estimated the QALY until six months and calculated the ICER for this gain in QALY without discount rate.

Results

Study population

Ninety-nine patients were included in the analysis (vertebroplasty: 51; brace: 48). The mean age and the distribution of women were 44.5 years and 41.2% in the vertebroplasty group and 45.3 years and 41.2% in the brace group. Sixty percent of the fractures were type A.1 according to Magerl classification (Tables A1 and A2 in the Appendix). The baseline characteristics of the two groups were similar (Table A1 in the Appendix). Demographic and clinical characteristics were identical between the two groups. In 74% of patients, only one vertebra was fractured. A six month follow-up was obtained for 88 patients (89%). 8 patients in the brace group and 3 in the vertebroplasty group missed their interview. Significant reduction of VAS was observed in the vertebroplasty group at two days post-treatment (VAS 2.3 *versus* 3.4, p<0.05). Functional disability was significantly lower after vertebroplasty compared to bracing at all time-points of the follow-up (RDQ score at one month 7.5 *versus* 11.4, p<0.001). Kyphosis angle increased less after vertebroplasty than after bracing (at 3 months 1.2° for vertebroplasty *versus* 5.8° for bracing, p<0.001). At three months, the quality of life was significantly better after vertebroplasty than after bracing (Mental Health 54.5 *versus* 64.0, p<0.03; Physical Health 50.6 versus 60.1, p<0.02). No clinical complication was observed. No additional compression fracture in adjacent vertebrae was reported. Cement leakage occurred in 57% of the cases.

Analysis of costs

Table 1 shows a higher cost of intervention for the vertebroplasty group than for the brace group. The cost of the occupation of the room was €1131.4 for the vertebroplasty group and €426.3 for the brace group, and the cost for anesthesia was €1832.6 for the vertebroplasty group compared to €0 for the brace group. The average cost of consumables (single-use equipment, cement for vertebroplasty group and brace for brace group) was €932 for the brace group and €525 for the vertebroplasty group (bootstrap 95% CI €-420 to €-361). However, difference in costs of radiology and laboratory exams were not statistically significant between the two groups (bootstrap 95% CI €-35 to €2).

From the health insurance perspective, vertebroplasty was associated with lower cost for patient follow-up (consultations, physiotherapy, and nursing home visits) than the brace group (€311 versus €606, bootstrap 95% CI €-450 to €-115). However, vertebroplasty was associated with a higher cost of imaging act (€134) than the brace group (€103.9) (bootstrap 95% CI €18 to €44). The difference in the average cost/patient between the two arms (bootstrap 95% CI €-1,048 to €1,207) was insignificant. Furthermore, the indirect costs (severance daily wage paid under cessation of work) were not statistically significant between the two groups (€1,652 versus €1,348, bootstrap 95% CI €-1,047 to €407).

When we consider the patient perspective, the cost of hospital fees was significantly lower for the vertebroplasty group (€79.9) than the brace group (€1,067), (bootstrap 95% CI €-1,117 to €-851). The main reason is that vertebroplasty is a free act and therefore fully covered by health insurance, unlike the brace, which is not fully covered by health insurance (80%). The technique of vertebroplasty was also associated with a lower cost of follow-up (physiotherapy and nursing) (€402.5 versus €207.8, bootstrap 95% CI €-300 to €-77). Differences in indirect costs were not statistically significant between the two groups (€3,788 versus €3,090, bootstrap 95% CI €-2,401, €934).

Table 1: Estimated mean cost per patient (univariate analysis), SF-6D utility scores and QALYs (4% of discount rate)

Cost component	**Bracing (N=48) (SD)**	**Vertebroplasty (N=51) (SD)**	**Difference (95% CI†)**	**P-value**
Occupancy room (1)	426.3 (0)	1,131.4 (235.8)	703.9 (644; 1,935)	<0.001
Anesthesia (2)	0 (0)	1,832.6 (382)	1,831.6 (1,740; 1,941)	<0.001
Exam act (3)	145 (54.3)	118.3 (36.7)	-17.6 (-35; 2)	0.07
Consumables (4)	932.5 (20.7)	524.8 (11.3)	-400.3 (-420; -361)	<0.001
Net DRGs of anesthesia, imaging, interventional imaging, laboratory tests, consumables and medical devices (5)	1,485.6 (76)	1,589.2 (79.8)	51.8 (48,3 ; 55,3)	0.5
Medical device reimbursement by health insurance (6)	2,540.3 (144.9)	1,705.7 (581.9)	-833.5 (-966 ; -642)	<0.001
Reimbursement of hospitalization by health insurance (7)	4,905.2 (1,899.2)	5,571.7 (2,431.4)	641.7 (-181; 1,945)	0.1
Imaging acts (8)	103.9 (38,1)	134.2 (28.5)	30.5 (18; 44)	<0.001
Follow-up consultation (9)	605.5 (423,6)	310.7 (429.4)	-292.3 (-450; -115)	0.002
Daily allowance paid (10)	1,652.1 (2,080)	1,348.1 (1,704)	-318.9 (-1,047; 407)	0.37
Health insurance cost (11) = (1)+(2)+(3)+(4)+ (5) – (6)+(7)+(8)+(9)+(10)	**7,266.7 (3,040)**	**7,364.7 (2,781)**	**75.3 (-1,048; 1,207)**	**0.9**
Lump sum expenses at hospital (Hospital charges) (12)	1,067.5 (477.6)	79.9 (28.4)	985.8 (-1,117; -851)	<0.001
Imaging acts (13)	45.4 (15.1)	57.6 (12.2)	11.9 (7; 17)	<0.001
Follow-up consultation (14	402.5 (282.4)	207.8 (286.2)	-194.9 (-300; -77)	0.002
Production loss of market sphere (15)	3,788 (4,770)	3,090.1 (3,908)	-731.2 (-2,401; 934)	0.4
Patient costs (16)= (12)+(13)+(14)+(15)	**5,303.4 (4,875.3)**	**3,435.4 (3,884.8)**	**-1,900.7 (-3,563; -218)**	**0.02**
SF-6D				
Baseline (SD)	0.670 (.158)	0.689 (0.13)		
One month (SD)	0.527 (0.08)	0.578 (0.09)		
Three months (SD)	0.605 (0.01)	0.628 (0.11)		
Six months (SD)	0.649 (0.11)	0.695 (0.12)		
QALY				
Univariate analysis	**0.445 (0.008)**	**0.458 (0.01)**	**0.013**	**-0.0133; 0.0407**
Multivariate analysis	**0.440 (0.009)**	**0.455 (0.01)**	**0.015**	**-0.0105; 0.0442**

†CIs estimated using 2,000 non-parametric bootstrapping replicates.

QALYs

Table 1 shows the SF-6D scores for each arm at baseline and at one, three and six months. The average QALYs were estimated at 0.440 (SD=0.009) for the brace group and 0.455 (SD=0.01) for the vertebroplasty group. The difference in QALYs between the two groups was not statistically significant during the six months of the study (bootstrap 95% CI -0.0105 to 0.0442). We found similar results for the univariate analysis (bootstrap 95% CI 0.0133, 0.0407).

Although no difference in QALYs was found, we decided to follow the recommendations of international economic evaluation institutions. Glick et al. showed that despite non-significant results, an economic analysis should be performed, insofar as it is possible to have a greater confidence in the joint outcome of costs and QALYs than by either of the outcomes individually [43].

Incremental cost-effectiveness ratio

The ICER was -€12,200 (-183/0.015) for the health insurance perspective and -€159,200 for the patient perspective (-2,388/0.015) (Table 2).

Table 2: Incremental cost, incremental QALY and ICER vertebroplasty versus bracing, GLM analysis (discount rate of 4%)

Perspective	Incremental cost (€, 95 % CI†)	Incremental effect (QALY, 95% CI†)	ICER	Lower confidence interval[††]	Upper confidence interval[††]	% of acceptability	
						€20,000	€50,000
Health insurance	-183 (-1,549; 1,165)	0.015 (-0.01; 0,04)	-12,200	Undefined		72.5%	81.3%
Patient	-2,388 (4,456; -376)	0.015 (-0.01; 0,04)	-159,200	-20,829	181,049	99.8%	99.6%

ICER: Incremental Cost-Effectiveness Ratio. †CIs were estimated using 2,000 non-parametric bootstrapping replicates. [††]This represents the lower and upper boundary of the acceptability curve. The threshold (€20,000 and €50,000) is compared to the Upper and Lower confidence interval in order to assess the probability that vertebroplasty is more cost effective compared to the brace.

Figures 1 and 2 show the results of the bootstrap procedure plotted on a cost-effectiveness plane. These figures represent the differences in costs and differences in QALYs observed in the 2,000 bootstrap replicates from which acceptability curves were plotted (Figure 2). From a health insurance perspective, the dispersions were such that no 95% CI for the ratio could be identified, which means that we can be 95% confident that the two strategies differed from each other in cost effectiveness (Figure 1).

Acceptability curves (Figures 3 and 4) provide a more complete understanding of the degree of confidence that we can have in the comparison between the two strategies. From the patient perspective, the acceptability curve showed that, given a willingness to pay €20,000, there was a 99.8% chance that vertebroplasty was more cost-effective than bracing. Further, there was a 99.6% chance that vertebroplasty was more cost-effective than bracing for a willingness to pay €50,000 (Figure 4). Since the acceptability curves crossed the 97.5% level, we can confirm the superiority of vertebroplasty [43].

However, from a health insurance perspective, the acceptability curve did not cross the acceptability of 2.5% and 97.5% levels (Figure 3). Therefore, we cannot come to a conclusion on the superiority of one or other technique.

Results of our sensitivity analyses are shown in Tables A3 to A7 (Appendix). Modifications in the models' specifications did not change our results, whatever discount rate was used. Specifically, from the health insurance perspective, the 95% CIs were undefined for all models, and acceptability curves remained similar.

When the QALY was considered for 6 months instead of 12 months, our results for the univariate analysis did not change (i.e., the 95% CIs were undefined from the health insurance perspective and we could confirm the superiority of vertebroplasty from the patient perspective). For the multivariate analysis, our results did not change from the health insurance perspective, with undefined 95% CIs for all models, contrary to the patient perspective where 95% of CIs were undefined and did not allow verifying the superiority of vertebroplasty.

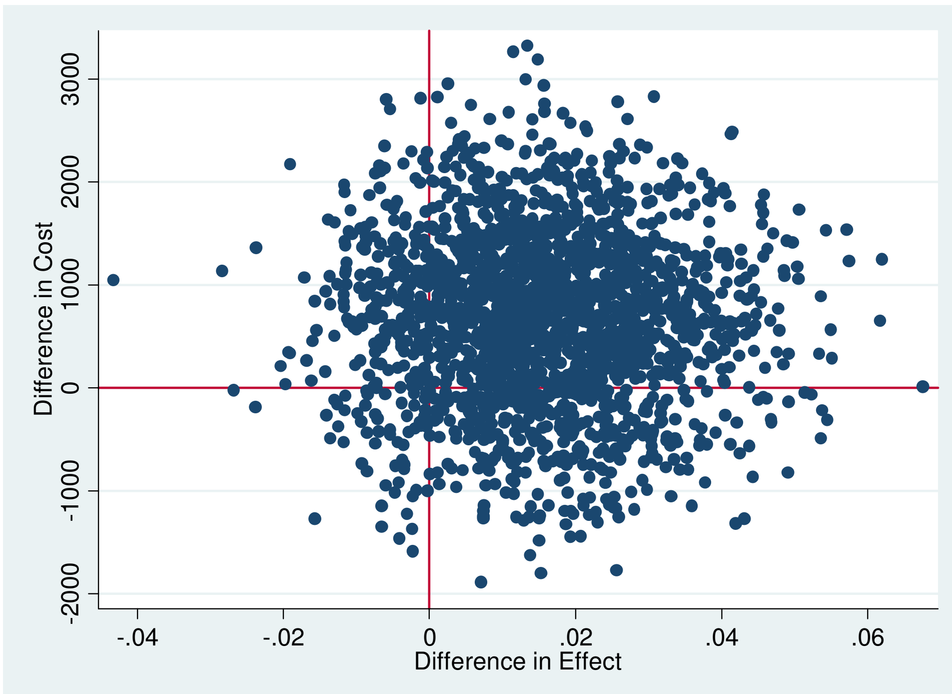

Figure 1: Cost-effectiveness plane, from health insurance perspective

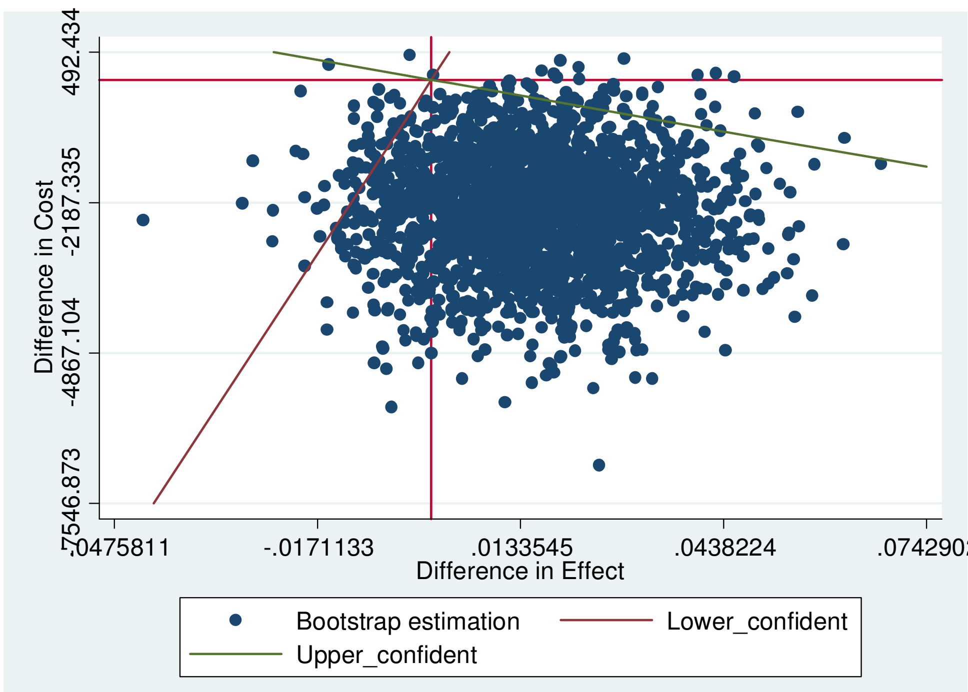

Figure 2: Cost-effectiveness plane, from patient perspective

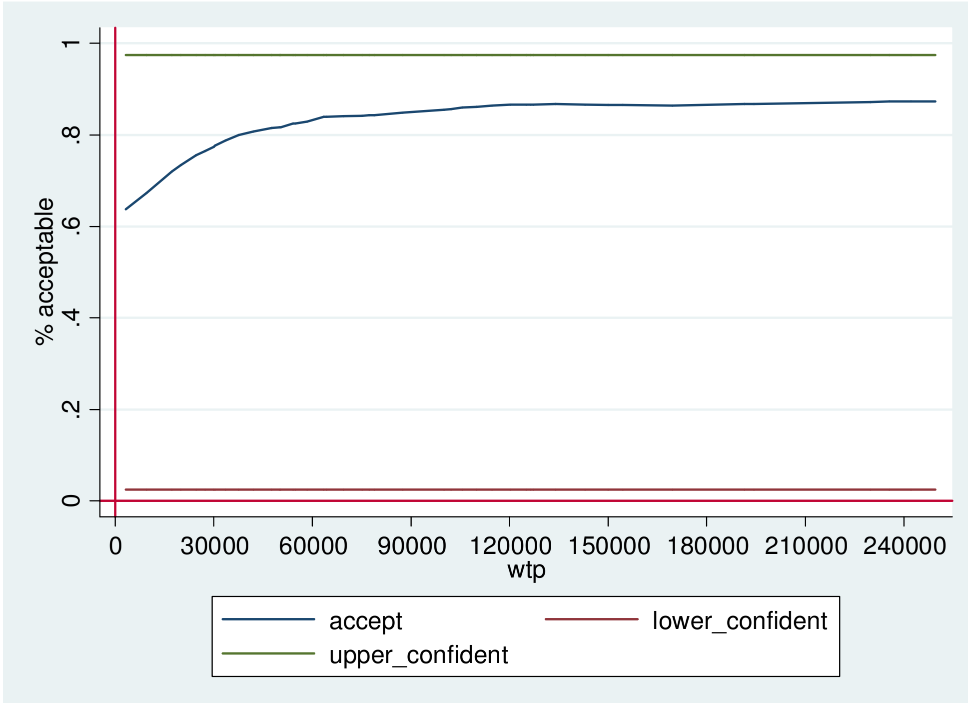

Figure 3: Cost-effectiveness acceptability curve, from health insurance perspective

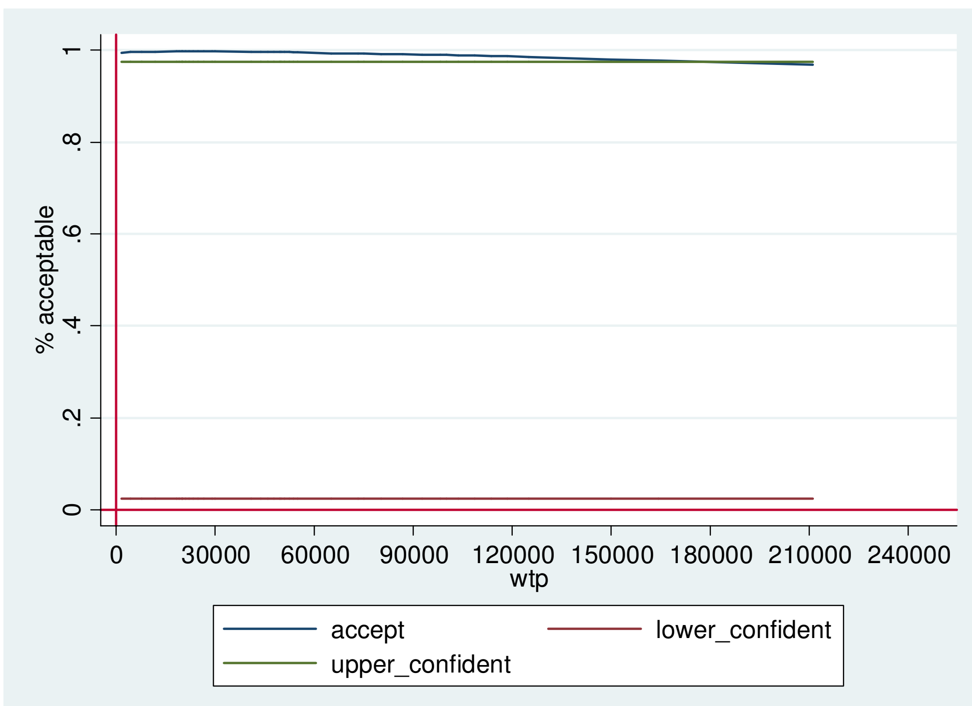

Figure 4: Cost-effectiveness acceptability curve, from patient perspective

Discussion

Our objective was to assess the cost-utility of vertebroplasty in the context of post-traumatic vertebral fractures. This is the first study analysing the relative cost-utility of this technique versus bracing in the context of post-traumatic vertebral fractures. Literature about this technique focuses more on osteoporotic fractures [2-7,44] and many have analyzed vertebroplasty versus kyphoplasty method [45-46] but not with a conservative method such as bracing. We have deliberately chosen to disaggregate perspectives (health insurance and patient) to separate their respective costs and to accommodate recommendations from other institutions for economic evaluations related to the health system or payer perspectives (National Health Service in England, Statutory Health Insurance in Germany and Medicare in the United States).

From the health insurance perspective, we found an incremental cost of €75 in the univariate analysis and a difference of €-183 when multivariate analysis was used. Such a difference can be attributed to the fact that we used multivariate analysis as a tool to assess the influence of some variables (age, sex, average degree of kyphotic angle) in costs. By using this approach, we were able to show that these variables have an impact on cost even if the p-values were not significant. These findings are consistent with the analysis of Glick et al. [24].

The vertebroplasty technique requires higher intervention cost (€2,964) than bracing (€426). That makes sense insofar as vertebroplasty requires expensive equipment and consumables, unlike bracing, for which the main expense is the brace itself. However, vertebroplasty involved less costs for radiology exams at baseline, where a significant, but small, difference of €17 was observed. Moreover, the costs of follow-up were also lower for vertebroplasty (€517.9) than bracing (€1,009.4), where a difference of €487 was observed. However, although the duration of work cessation was significantly longer for the brace group (116 days) than for the vertebroplasty group (82 days), no significant differences in indirect costs were observed. It is likely that such absence of difference in the indirect costs may be directly related to the strong welfare nature of France (i.e. strong social protection). In other countries, like the United States, it is quite improbable that every patient with a post-traumatic fracture would be able to maintain his regular professional income without any decrease for such a lengthy period. It is very likely that the indirect costs of both procedures may be significantly different in such a scenario.

The idea of using threshold values in decision-making encountered some criticism, such as, among others, the risk of uncontrolled growth of health care spending. However, the thresholds represent society's willingness to pay for health care, and for that, this (decision) rule is considered appropriate for policymakers [47]. In France, no threshold value is given by the competent authorities, so we took two different thresholds: €20,000 and €50,000.

Our analysis shows mixed results depending on the chosen perspective. From the patient perspective, vertebroplasty is the preferred strategy in the French context. This is explained by the fact that the patient needs a longer period of bed rest with a brace than for vertebroplasty, which induces faster recovery and a lower cost of follow-up. As there is a gain for the patient, an argument can be provided that health insurance providers increase the budgetary allocation. On the other hand, an argument can be raised that complementary health insurance may assume the cost for the patient to the extent that the cost of vertebroplasty is less than that of bracing. However, this result is no longer verified with the assumption of a linear decrease of intervention effect returning to baseline level after 12 months. Moreover, such results may not lend to generalizations covering other countries' healthcare systems. Indeed, these findings are strongly derived from the situation of the patient population in the French healthcare system where vertebroplasty is a free act fully covered by health insurance, unlike the brace, a decisive fact that influenced the hospital fees of both procedures. For example, in the United States, based on the recently approved Patient Protection and Affordable Care Act, it is expected that a significant amount of the previously uninsured population will be enrolled in cheaper "high- deductible" health plans, where the initial treatment costs before the insurance starts covering the cost is quite high. In such a scenario, it is likely from a patient economic perspective that, either no difference would be found between both therapeutic options, or the vertebroplasty option would lead to higher costs for patients, when the associated costs of such outpatient procedure would not reach the minimum deductible threshold for such plans.

In contrast, there was no difference in relative cost-effectiveness in the two groups from the health insurance perspective. From this perspective, the differences in costs and the differences in QALYs were not significant. However, despite these non-significant results, we nevertheless performed an economic analysis, insofar as it is possible to have a greater confidence by the joint outcome of costs and QALYs than from either of the outcomes individually [47]. From this perspective, we are therefore unable to determine whether vertebroplasty is more effective than bracing.

Sensitivity analysis confirmed the aforementioned results. The disaggregated results allowed us to choose the desired perspective, depending on the institution (health system or payer perspective for England, Germany or the United States). The first drawback of our study was the exclusion of some costs which would have allowed us to have a more complete picture of the cost analysis (presenteeism costs, patient’s family costs etc.), although several studies show a significant impact of these factors on the results [47-49]. This non-inclusion can be explained by the fact that the clinical study had previously been designed without economic evaluation, the choice of integrating a medico-economic component had come at the end of the clinical study. We have thus not been able to establish all the elements necessary for a complete analysis. Similarly, the study of follow-up costs is only limited to hospital prescriptions, omitting any eventual prescriptions made by the family doctors as well as supplementary cessation of work. In the context of cessation of work, we hypothesized that most patients returned to full-time employment while some may have benefited from part-time work arrangements. The second drawback concerns the QALYs calculation. We used the Brazier *al.* algorithm of converting data from SF-36. Despite its rigorous theoretical and methodological bases [18-19], the weighting function for assigning a weight to each of these states was calculated from the United Kingdom population, which does not necessarily reflect the preferences of the French population. The QALYs via VAS could be calculated; however, many health economists do not consider VAS as utilities because they do not require explicit choice and have scales with undesirable properties [50]. The third drawback is the fact that the trial was not blind; patients knew which treatment they were receiving. Awareness of the treatment assigned to them probably influenced patients' responses during evaluations. Finally, the six month follow-up period was too short. A much longer evaluation of these two treatments, especially in terms of costs (re-hospitalization, sick leave, etc.) should be considered.

Conclusion

Our analysis shows mixed results depending on the chosen perspective. The choice of perspective will depend on what the government wants to prioritize, considering the financial resources of patients to a detrimental impact on the budget, or viewing budgetary considerations as the most important. In France, where the excess for the patient is low (approximatively €290) the government's position will not favor this approach. In contrast, in the United States where health-related costs are very high and the excess for the patient is important, the government's position could be different due to excessive coverage. Finally, in France, those who would encourage the adoption of this technology to facilitate patients' well-being should extend the quality of life observation time beyond six months to confirm the proof of the superiority of this technique.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Appendix

Table A1: Baseline characteristics of the patients

	Brace (N=48)	Vertebroplasty (N=51)
Age (>55 years), N (%)	21 (43.8)	21 (41.2)
Mean age ± sd	45.3 ± 17.2	44.5 ± 16.9
Male sex, N (%)	35 (72.9)	30 (58.9)
Spinal levels treated >1, N (%)	13 (27.7)	14 (26.9)
Fracture type (Magerl's), N (%)		
A1.1, A1.2, A1.3	26 (54.2)	33 (64.7)
A2.1, A2.2, A2.3	6 (12.5)	6 (11.8)
A3.1, A3.2, A3.3	16 (33.3)	12 (23.5)
Other lesions, N (%)	7 (14.6)	12 (23.5)
RMDQ score, mean ± sd	23.8 ± 1	23.7 ± 1.5
Pain intensity, mean ± sd	6.7 ± 1.9	6.7 ± 2.2
SF36		
Mental Health, mean ± sd	73.1 ± 23.3	72.8 ± 20.7
Physical Health, mean ± sd	69.3 ± 27.3	73.1 ± 25.6
Treatment delay days, mean ± sd	4.0 ± 1.9	3.9 ± 2.7

RMDQ: Rolland Maurice Disability Questionnaire; SF36: Short-Form Health Survey.

Table A2: Clinical and anatomical outcomes

	Univariate analysis			Multivariate analysis
	Brace	Vertebroplasty	p-value	Coef [95%CI], p-value
Clinical outcomes				
RMDQ, mean ± sd				
M1 (N=48/51)	11.4 ± 5.3	7.5 ± 5.7	**<0.001**	-3.76 [-5.96; -1.56], **0.001**
M3 (N=44/51)	7.4 ± 6.3	3.8 ± 4.3	**0.001**	-3.25 [-5.33; -1.17], **0.003**
M6 (N=38/47)	4.3 ± 4.5	2.8 ± 4.2	0.13	-1.31 [-3.08; 0.44], 0.14
PAIN INTENSITY, mean ± sd				
D2 (N=46/51)	3.4 ± 2.1	2.3 ± 1.5	**0.004**	-1.08 [-1.81 ; -0.35], **0.004**
M1 (N=48/51)	1.9 ± 2.1	2.4 ± 1.9	0.24	0.50 [-0.28; 1.30], 0.21
M3 (N=44/51)	1.6 ± 1.9	1.6 ± 1.9	0.90	0.07 [-0.70; 0.83], 0.87
M6 (N=38/47)	1.8 ± 2.0	1.3 ± 1.6	0.16	-0.50 [-1.21; 0.21], 0.17
SF36 Mental Health, mean ± sd				
M1 (N=48/50)	50.2 ± 20.6	52.5 ± 20.1	0.58	2.53 [-5.79; 10.86], 0.55
M3 (N=45/50)	54.5 ± 19.9	64.0 ± 21.1	**0.03**	9.19 [0.82; 17.56], **0.03**
M6 (N=38/47)	67.8 ± 20.3	73.5 ± 22.3	0.23	5.73 [-3.29; 14.76], 0.21
SF36 Physical Health, mean ± sd				
M1 (N=48/50)	38.5 ± 11.7	44.8 ± 16.8	**0.03**	6.25 [0.46; 12.03], **0.04**
M3 (N=45/50)	50.6 ± 18.3	60.1 ± 21.5	**0.02**	9.06 [1.11; 17.02], **0.03**
M6 (N=38/47)	61.2 ± 21.4	70.8 ± 24.4	0.06	9.10 [-0.11; 18.31], **0.05**
Anatomical outcomes				
KYPHOSIS ANGLE, mean ± sd				
Inclusion (N=37/39)	10.7 ± 7.0	10.8 ± 6.2	0.96	NP
D2 (N=33/36)	12.3 ± 7.4	10.5 ± 5.8	0.28	-1.88 [-5.22; 1.47], 0.27
M1 (N=39/37)	13.7 ± 7.4	12.0 ± 6.4	0.31	-2.05 [-5.28; 1.17], 0.21
M3 (N=32/38)	15.7 ± 8.1	12.5 ± 7.0	0.08	-3.53 [-7.18; 0.12], 0.06
M6 (N=28/35)	15.0 ± 8.5	12.9 ± 7.4	0.30	-2.09 [-6.25; 2.08], 0.32
ANTERIOR HEIGHT, mean ± sd				
Inclusion (N=44/51)	21.8 ± 3.9	21.5 ±4.1	0.71	NP
D2 (N=41/49)	21.2 ± 4.8	22.6 ± 4.4	0.16	1.35 [-0.58; 3.27], 0.17
M1 (N=45/51)	20.1 ± 4.7	21.8 ± 4.6	0.06	1.83 [-0.03; 3.69], **0.05**
M3 (N=41/51)	19.3 ± 4.9	21.5 ± 4.7	**0.03**	2.45 [0.49; 4.41], **0.02**
M6 (N=36/48)	19.4 ± 4.6	21.3 ± 4.8	0.07	2.01 [-0.05; 4.07], **0.05**
POSTERIOR HEIGHT, mean ± sd				
Inclusion (N=44/51)	26.5 ± 3.2	26.6 ± 3.6	0.93	NP
D2 (N=41/49)	26.9 ± 3.9	26.5 ± 3.6	0.56	-0.21 [-1.82; 1.39], 0.79
M1 (N=45/51)	26.6 ± 4.0	26.6 ± 3.5	0.98	0.17 [-1.37; 1.71], 0.83
M3 (N=41/51)	26.8 ± 4.3	26.5 ± 3.7	0.72	-0.23 [-1.91; 1.44], 0.78
M6 (N=36/48)	26.1 ± 3.4	26.2 ± 3.7	0.85	0.18 [-1.43; 1.78], 0.83

RMDQ: Rolland Maurice Disability Questionnaire; SF36: Short-Form Health Survey; D2: two days after intervention; M1: one month after intervention; M3: three months after intervention; M6: six months after intervention; NP: Not Performed.

Table A3: Incremental cost, incremental QALY and ICER vertebroplasty versus bracing, univariate analysis

Perspective	Incremental cost (€, 95 % CI†)	Incremental effect (QALY, 95% CI†)	ICER	Lower confidence interval††	Upper confidence interval††	% of acceptability	
						€20,000	€50,000
Discount rate 0%							
Health insurance	-94.2 (-1,087; 1,333)	0.014 (-0.01; 0.06)	-6,729	Undefined		61%	72.7%
Patient	-2,008 (-3,764; -230)	0.014 (-0.01; 0.06)	-143,428	-13,920	93,652	99.3%	99.2%
Discount rate 2.5%							
Health insurance	-92.5 (-1,042; 1,282)	0.016 (-0.013; 0.05)	-5,781	Undefined		61.2%	73.2%
Patient	-1,339.8 (3,636; -222)	0.016 (-0.013 ; 0.05)	-83,687	-13,920	93,652	99.3 %	99.2%
Discount rate 4%							
Health insurance	-75.3 (-1,048; 1,207)	0.016 (-0.013; 0.04)	-4,706	Undefined		61.3%	73.2%
Patient	-1,901 (-3,563; -218)	0.016 (-0.013; 0.04)	-118,812	-13,920	93,652	99.3%	99.2%
Discount rate 10%							
Health insurance	-65.4 (-978; 1,146)	0.016 (-0.009; 0.04)	-4,087	Undefined		61.9%	73.3%
Patient	-1,757 (-3,294; -133)	0.016 (-0.009; 0.04)	-109,812	-13,920	93,652	99.3%	99.2%

ICER: Incremental Cost-Effectiveness Ratio. †CIs were estimated using 2,000 non-parametric bootstrapping replicates. ††This represents the lower and upper boundary of the acceptability curve. The threshold (€20,000 and €50,000) is compared to the Upper and Lower confidence interval in order to assess the probability that vertebroplasty is more cost effective compared to the brace.

Table A4: Incremental cost, incremental QALY and ICER vertebroplasty versus bracing, multivariate analysis OLS

Perspective	Incremental cost (€, 95 % CI†)	Incremental effect (QALY, 95% CI†)	ICER	Lower confidence interval††	Upper confidence interval††	% of acceptability	
						€20,000	€50,000
Discount rate 0%							
Health insurance	-176 (-1,573; 1,114)	0.016 (-0.01; 0.06)	-11,000	Undefined		73.1%	81.7%
Patient	-3098 (-2,882; -331)	0.016 (-0.01; 0.06)	-175,375	-18,100	173,293	99.8%	99.5%
Discount rate 2.5%							
Health insurance	-172 (1,517; 1,166)	0.014 (-0.009; 0.04)	10,731	Undefined		73.3%	81,8%
Patient	-2,243 (-4,181; -340)	0.014 (-0.009; 0.04)	-140,187	-18,100	173,293	99.8%	99.5%
Discount rate 4%							
Health insurance	-175.5 (-1,505; 1,147)	0.016 (-0.01; 0.06)	-12,536	Undefined		73.5%	82%
Patient	-2,198 (-4,097; -333)	0.016 (-0.01; 0.06)	-157,000	-18,100	173,293	99.8%	99.5%
Discount rate 10%							
Health insurance	-174.7 (-1,417; 1,056)	0.014 (-0.009; 0.04)	-12,479	Undefined		73.8%	82.1%
Patient	-2,032 (-3,788; 308)	0.014 (-0.009; 0.04)	-145,142	-18,100	173,293	99.8%	99.5%

ICER: Incremental Cost-Effectiveness Ratio. †CIs were estimated using 2,000 non-parametric bootstrapping replicates. ††This represents the lower and upper boundary of the acceptability curve. The threshold (€20,000 and €50,000) is compared to the Upper and Lower confidence interval in order to assess the probability that vertebroplasty is more cost effective compared to the brace.

Table A5: Estimated mean (SE) cost for patient (univariate analysis), SF-6D utility scores and QALY (discount rate of 0%) at six months

Cost component	**Bracing (N=48) (SD)**	**Vertebroplasty (N=51) (SD)**	**Difference (95% CI†)**	**P-value for difference**
Health insurance cost	**7,669.6 (444.33)**	**7,825.1 (407.58)**	**155.51 (-1,054; 1,400)**	**0.78**
Patient cost (16)= (12)+(13)+(14)+(15)	**5,604.9 (4,875.3)**	**3,426.5 (3,884.8)**	**-1,978 (-3,796; -91)**	**0.03**
SF-6D				
Baseline (SD)	0.698 (0.03)	0.672 (0.02)		
One month (SD)	0.416 (0.01)	0.460 (0.01)		
Three month (SD)	0.154 (0.03)	0.157 (0.04)		
Six month (SD)	0.334 (0.01)	0.360 (0.01)		
QALY				
Univariate analysis	**0.436 (0.008)**	**0.492 (0.01)**	**0.064**	**-0.004; 0.11**
Multivariate analysis	**0.467 (0.05)**	**0.51 (0.53)**	**0.038**	**-0.0105; 0.0442**

Table A6: Incremental cost, incremental QALY and ICER vertebroplasty versus bracing, univariate analysis at six months (discount rate of 0%)

Perspective	Incremental cost (€, 95 % CI†)	Incremental Effect (QALY, 95% CI†)	ICER	Lower confidence interval††	Upper confidence interval††	% of acceptability	
						€20,000	€50,000
Health insurance	-19.59 (-1,642; 1,448)	0.055 (-0.004; 0.11)	-356.18	Undefined		17.76%	15.20%
Patient	-1978.48 (-3,796; -91)	0.055 (-0.004; 0.11)	-35,972	-4,653	370,712	99.5%	99.4%

ICER: Incremental Cost-Effectiveness Ratio. †CIs were estimated using 2,000 non-parametric bootstrapping replicates. ††This represents the lower and upper boundary of the acceptability curve. The threshold (€20,000 and €50,000) is compared to the Upper and Lower confidence interval in order to assess the probability that vertebroplasty is more cost effective compared to the brace.

Table A7: Incremental cost, incremental QALY and ICER vertebroplasty versus bracing, multivariate analysis at six months (discount rate of 0%)

Perspective	Incremental cost (€, 95 % CI†)	Incremental effect (QALY, 95 % CI†)	ICER	Lower confidence interval††	Upper confidence interval††	% d'acceptabilité	
						€20,000	€50,000
OLS							
Health insurance	-19.59 (-1642.5;1448.4)	0.038 (-0.11; 0.07)	-515.52	Undefined		17.8%	15.2%
Patient	-1761.5 (-4,598; 732)	0.038 (-0.11; 0.07)	-46,355	Undefined		81.29%	46.29%
GLM							
Health insurance	-26,78 (-61.9; 8.33)	0.038 (-0.04; 0.36)	-704.73	Undefined		39.7%	18.5%
Patient	-1810 (-3,827; -10.7)	0.038 (-0.11; 0.07)	-47,631	Undefined		81.21%	47.3%

ICER: Incremental Cost-Effectiveness Ratio. †CIs were estimated using 2,000 non-parametric bootstrapping replicates. ††This represents the lower and upper boundary of the acceptability curve. The threshold (€20,000 and €50,000) is compared to the Upper and Lower confidence interval in order to assess the probability that vertebroplasty is more cost effective compared to the brace.