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Patients with unilateral transfemoral amputation treated with a percutaneous osseointegrated prosthesis

A COST-EFFECTIVENESS ANALYSIS

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Aims

The aim of this study was to compare the cost-effectiveness of treatment with an osseointegrated percutaneous (OI-) prosthesis and a socket-suspended (S-) prosthesis for patients with a transfemoral amputation.

Patients and Methods

A Markov model was developed to estimate the medical costs and changes in quality-adjusted life-years (QALYs) attributable to treatment of unilateral transfemoral amputation over a projected period of 20 years from a healthcare perspective. Data were collected alongside a prospective clinical study of 51 patients followed for two years.

Results

OI-prostheses had an incremental cost per QALY gained of €83 374 compared with S-prostheses. The clinical improvement seen with OI-prostheses was reflected in QALYs gained. Results were most sensitive to the utility value for both treatment arms. The impact of an annual decline in utility values of 1%, 2%, and 3%, for patients with S-prostheses resulted in a cost per QALY gained of €37 020, €24 662, and €18 952, respectively, over 20 years.

Conclusion

From a healthcare perspective, treatment with an OI-prosthesis results in improved quality of life at a relatively high cost compared with that for S-prosthesis. When patients treated with S-prostheses had a decline in quality of life over time, the cost per QALY gained by OI-prosthesis treatment was considerably reduced.

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Routine management following a transfemoral amputation (TFA) has traditionally been to fit patients with a socket-suspended (S-) prosthesis.[1,2] A recent advance is bone-anchored artificial limbs in which the prosthesis is attached without a socket. This may be an option for patients with amputations which are undertaken for nonvascular reasons.[3] The patient-perceived benefits of using a prosthesis which is anchored to bone rather than a S-prosthesis include increased use, less inconvenience, a more reliable attachment, improved mobility, reduced energy cost and improved health-related quality of life (HRQoL).[4-10] However, complications have been reported including implant loosening, deep and superficial infection and mechanical complications.[7,9-12]

A prosthesis which is anchored to bone using osseointegration was first developed in Sweden.[13] Currently, other designs and methods are in use or under development.[3,9,10,14-16] The Swedish treatment uses the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) implant (Integrum AB, Mölndal, Sweden), which has three main components (Fig. 1). The surgical part of the treatment involves two operations, about six months apart,[7] followed by approximately six months of rehabilitation including gradually increased loading of the prosthesis, and its use and activity.[11] Thus, a period of one year is required before the patient is allowed non-restricted weight-bearing on the osseointegrated (OI-) prosthesis. Brånemark et al[7] described the OPRA treatment and reported the outcomes in a prospective study involving 51 patients with a transfemoral amputation followed for two years. They reported a 92% cumulative

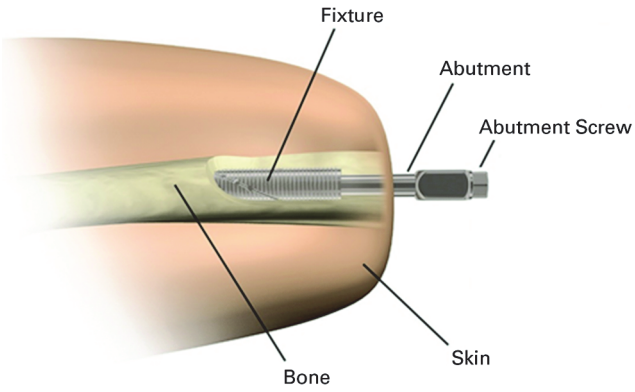

Fig. 1

The Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) Implant System. It includes three main parts: an implanted fixture, an abutment, and an abutment screw. The fixture is implanted into the residual bone at a first operation. At a second operation, about six months later, the percutaneous parts, (the abutment and screw), are installed into the fixture to act as the connection to the artificial limb. These two components can be replaced if needed. The second operation also involves the creation of the percutaneous area where the implant protrudes from the residual limb. This figure is reproduced with permission from **Brånemark R, Berlin O, Hagberg K, et al.** A novel osseointegrated percutaneous prosthetic system for the treatment of patients with transfemoral amputation: A prospective study of 51 patients. *Bone Joint J* 2014;96-B:106-113.

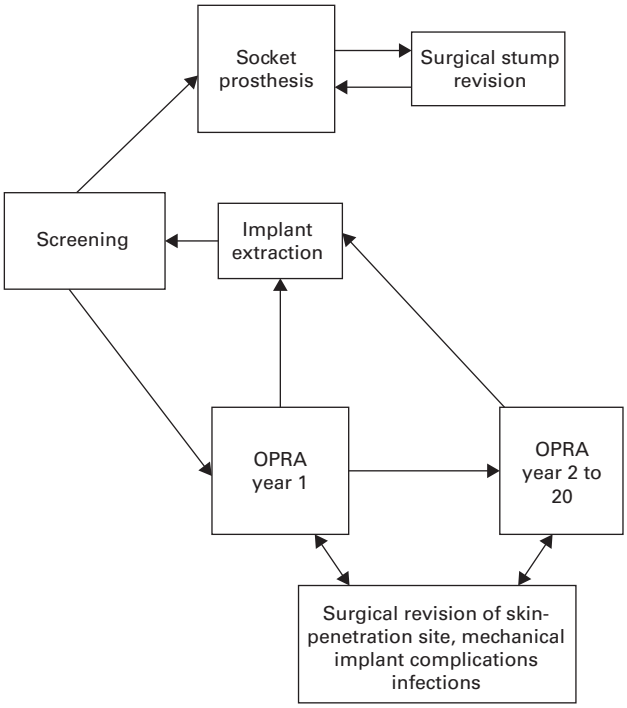

Fig. 2

Flowchart showing a Markov structure. The model contained two arms for the assessment of cost-effectiveness: osseointegrated (OI-) prosthesis and standard-of-care socket (S-) prosthesis.

implant survival rate and important improvements in patient-reported outcomes.[7] Haggstrom et al showed that the annual mean costs of OI-prostheses are comparable with to those of S-prostheses.[17] However, the OPRA treatment incurs additional costs, mainly for the surgery and the implant. The costs of the complications of surgery and adverse events could be significant compared with the cost of a S-prosthesis, and therefore should be considered when determining whether OI-prostheses are cost-effective when compared with S-prostheses.

To our knowledge, no study has yet evaluated the cost-effectiveness of using a OI-prosthesis after TFA, although such research has been called for.[18-20] The aim of this study was to assess the cost-effectiveness and outcome of OI-prostheses compared with the use of routine S-prostheses for patients with a unilateral TFA treated with OPRA in Sweden.

Patients and Methods

A Markov-state transition model was built to represent the two treatment options: OI- and S- prostheses (Fig. 2). It used a specific structure for each arm, rather than one common structure for both arms, in order to allow for differences in the pattern of treatment between interventions.

In the OI-prosthesis arm, patients entered the model having been screened for eligibility. Those deemed not eligible for the OI-Prosthesis were moved to the S-prosthesis arm. Patients deemed eligible (e.g. full skeletal maturity, having problems to use S-prosthesis, amputation due to other reason than severe vascular disease) are fitted with an OI-prosthesis.[7]

This stage consists of two main periods. The first involves a year during which patients have surgery after which the prosthesis is fitted and they undergo rehabilitation. Patients who are successfully treated during this time pass into the second period, in which they have full use of their prosthesis.

The S-prosthesis arm contained one such period and a tunnel health state: those treated with the prosthesis and those requiring revision of the stump. Revision was included in the model because patients seeking OPRA treatment may have soft-tissue-related adverse events that lead to revision. Revisions have an impact on health care resource use for patients in this arm of the study.

All patients in the model are at risk of developing adverse events during the period of the study. The most severe is removal of the implant. Patients who require this move to the first period of the OI-prosthesis arm. They are thus screened for eligibility for a second treatment and may re-enter the model. Patients may develop a superficial or deep infection, mechanical complications related to the abutment and/or abutment screw and/or revision of the soft tissues.[7] None of these complications leads directly to secondary effects but have been modelled as a tunnel state in which patients re-enter the state that they previously were in after incurring treatment costs due to the specific event.

Table I. Baseline demographics of 39 patients with a unilateral transfemoral amputation included in the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) study between 1999 and 2007 and followed for two years

Variable	
No. of patients	39
Gender, male:female	17:22
Mean age at the start of treatment, yrs (SD)	44 (12.4)
Reason for amputation, n	
Trauma	23
Tumour	11
Other	5
Mean age at amputation, yrs (SD)	31 (14.8)
Mean time between amputation and the start of treatment; yrs (SD)	13 (11.7)
Concomitant injuries or defects at the start of treatment*	7
Prosthetic user at inclusion (≥ 1 day per week)	33
Country of residence	
Sweden	21
Other European country	18

*Concomitant injuries in seven patients with at least one additional disability included transtibial amputation (n = 1), foot injury (n = 3), knee injury (n = 1), and paralytic arm (n = 2)

Table II. Transition probabilities in the model

Event	Probability	Source
Being eligible for OPRA treatment	0.6857	Hospital data
Removal of the fixture	0.0029	OPRA study
Proportion of patients receiving new OPRA treatment after removal	0.0519	Assumption; OPRA study
Superficial infection at skin-penetration site	0.0513	OPRA study
Deep infection, year 1 and 2	0.0088	OPRA study
Deep infection, beyond year 1	0.0035	Tillander et al[12] (2010)
Mechanical complications, change of abutment and/or screw	0.0091	OPRA study
Surgical revision of skin-penetration site	0.0044	OPRA study
Revision of stump, S-prosthesis	0.0022	Hospital data

OPRA, Osseointegrated Prostheses for the Rehabilitation of Amputees; S-prosthesis; socket-suspended prosthesis

The model estimated the medical costs and quality-adjusted life-years (QALYs) attributable to a unilateral TFA in Sweden over a 20-year period with a one-month cycle length.

The OPRA study was performed at a single site (Sahlgrenska University Hospital). A total of 51 patients with TFA were treated with 55 OPRA implants.[7] Six had bilateral TFA, and four of these had simultaneous bilateral procedures. The complete costs for each patient were recorded by the hospital and could be accessed using the patient's Social Security number. We have previously reported the details of the patient-reported outcomes for the 39 patients with unilateral TFA at two years postoperatively.[6] The current study used the hospital and utility data for these patients which are summarized in Table I. Probabilities of events used in the model are summarized in Table II.

Screening for eligibility included assessment of radiographs, CT scans, assessment of the residual limb and the patient's overall health and preoperative information. Data from the hospital records revealed that 48/70 (69%) of those assessed during a three year period were selected for treatment.

The most severe complication that could occur was removal of the implant due to aseptic loosening or deep infection. In the OPRA study,[7] four of 55 implants were removed during the two-year follow-up period. Three of these patients were treated with a second OPRA implant at a later date. The most common complication was a superficial infection.[7,12] In the OPRA study, 28 of 51 patients had one or more such infections with a total of 41 infections at any time after the second surgery. During the first year, deep infection was diagnosed in four of 51 patients. These occurred at any time between immediately after the first operation to about six weeks after the second operation.[7] Deep infections can also occur later. Tillander et al[12] reported that seven of 39 patients in their study had a deep infection occurring at a mean of 34 months (11 to 60) postoperatively.

Mechanical complications occurring to the percutaneous parts of the implant involving abutment and/or the screw (Fig. 1) and leading to the need for replacement may occur after the first year. In the OPRA study, four of 51 patients had a total of nine such complications during the second year.[7]

Table III. Utility data in the model, taken from the Short Form 6 Dimensions (SF-6D). All patients in the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) study answered the 36-item Short Form Health Survey (SF-36) at baseline, before treatment start, and at one and two years after the second operation. Detailed results on the 39 patients have been previously reported[6]

Health state	Utility	Source
S-prosthesis	0.653	OPRA study
OPRA, year 1 after second surgery	0.682	OPRA study
OPRA, year 2 and onward	0.692	OPRA study

S-prosthesis; socket-suspended prosthesis

Table IV. Costs in euros (€) using 2009 values and a conversion rate of €1 = 10.41 SEK.

Event	Cost	Source
Cost of screening for eligibility for OPRA treatment	€620	Hospital statistics
Total cost of first surgery	€17 632	Hospital statistics
Total cost of second surgery	€16 470	Hospital statistics
Cost of revision of skin-penetration site	€6401	Hospital statistics
Cost of prosthesis per year, OI-prosthesis	€2910	Häggström et al[17] (2013)
Cost of prosthesis per year, S-prosthesis	€3338	Häggström et al[17] (2013)
Cost to change abutment and/or screw, including surgery and component(s)	€4372	Hospital statistics
Revision of stump, S-prosthesis	€7929	Hospital statistics
Cost of superficial infection, antibiotics, 10 days	€23	Expert opinion
Cost of deep infection, antibiotics, 3 mths	€850	Expert opinion

OPRA, Osseointegrated Prostheses for the Rehabilitation of Amputees; OI-prosthesis, osseointegrated prosthesis; S-prosthesis; socket-suspended prosthesis

Revision of the wound, due to poor wound healing or complications at the skin-penetration site may be required.[7] Thus, six such revisions were required in 39 patients.

In patients using a S-prosthesis, revision of the stump may be required in order to achieve a proper fit of the socket or to reduce pain.[21-25]

The current study employs a widely used technique of economic evaluation comparing the incremental cost per QALYs of health care. The QALY combines quantity and quality by assigning a value to quality of life on a zero (for states as bad as being dead) to one (for full health) scale, referred to as a utility value.[26] There are many different methods for obtaining utility values. In this study they were based on the Short Form 6 Dimensions (SF-6D),[27] which is a preference-based, single-index measure of health derived from 11 items in the 36-item Short Form Health Survey (SF-36).[28] The SF-36 data were obtained from the OPRA study for patients treated between 1999 and 2007,[6,7] recorded before treatment and at the one- and two-year follow-ups (Table III).

The costs of revisions and complications are shown in Table IV.

The cost of screening for eligibility for the OI-prosthesis was taken from hospital data. The total cost of surgery included the costs of hospitalization, from admission to discharge, daily costs of care and individual costs. Daily costs include fixed costs (staff salaries, accommodation and administrative costs). Individual costs include patient-specific costs (surgery, the OPRA implant, postoperative care, drugs, laboratory tests and imaging). The cost of a revision of the wound included the costs of surgery, which was usually performed as an inpatient. Change of abutment and/or the screw included fixed costs for surgery as an outpatient and the cost of materials. The cost of treatment for a superficial infection usually included ten days of oral antibiotics, and of a deep infection usually included at least three months of oral antibiotics.

The annual cost of components of OI- and S-prostheses included the cost of the initial components and the requirement of new prostheses, servicing, repairs, adjustments, and maintenance which consisted of workshop salaries, investments in equipment and buildings, and consumer goods based on the cost reported previously by Häggström et al.[17]

Statistical analysis. The base-case analysis estimated the total costs and QALYs for both interventions, to identify the additional cost per QALY gained (the incremental cost-effectiveness ratio (ICER)) for OI-prostheses compared with S-prostheses. Analysis of uncertainty was performed in three parts. First, one-way sensitivity analysis was performed by varying 27 of the parameters in the model individually within an uncertainty range of ± 10% of the mean value. Secondly, probabilistic sensitivity analysis was undertaken to capture the uncertainty in all parameters simultaneously, using 5000 Monte Carlo samples. Parameter uncertainty was defined by probability distributions as recommended by Briggs et al.[29] Depending on the parameter, uncertainty was based on estimates of calculated or reported patient counts, standard errors, or range. Beta distributions were used for changes of probabilities and utility weights, and gamma distributions were used for costs.

Table V. Incremental costs, quality-adjusted life-years (QALYs), and costs per QALY for Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) treatment *versus* conventional care with socket-suspended prosthesis (S-prosthesis; base-case results at 20 years)

Mean per patient	OPRA treatment	Conventional care with S-prosthesis	OPRA treatment *vs* conventional care with S-prosthesis
Total cost per patient	€78 417	€54 825	€23 592
Revision of stump	€1653	€3380	-€1727
Cost of prosthetic components	€48 139	€51 445	-€3307
OPRA treatment	€24 697	N/A	€24 697
Complications related to OPRA treatment	€3928	N/A	€3928
QALYs per patient	10.15	9.87	0.28
Cost per QALY	N/A	N/A	€83 374

N/A, not applicable

Finally, the model was run under alternative scenarios to investigate the impact of uncertainty by varying the time for the analyses and the impact of assumption of decline in utility values over time for patients with S-prostheses.

Quality-control procedures were performed on the final version of the adapted model and included verification of all data with the original sources, a series of diagnostic tests to confirm that the model had correctly applied all formulas, and a review of the calculations and programming.[30] The cost-effectiveness model was programmed in Microsoft Excel 2010 and Visual Basic for Applications (Microsoft Corporation, Redmond, Washington).

The Regional Ethical Review Board (R402-98, T216-03, 737-08) approved the study.

Results

The clinical improvement seen with OI- compared with S-prostheses in previous studies was reflected in a larger gain of QALYs with OI-prostheses (OI-: 10.15; S-: 9.87). The largest proportion of the costs for both strategies was associated with the costs of components, with the S-prosthesis incurring a higher mean cost. However, the higher costs were not enough to offset the increased overall costs related to the OPRA treatment (Table V).

When considering the projected outcomes and costs generated by the model at the end of 20 years, the base-case analysis showed that the OPRA treatment had an ICER of €83 374 per QALY gained, compared with S-prostheses (Table V).

The sensitivity analysis showed that the probability of OPRA treatment being cost-effective was 0.40 for a willingness-to-pay value of €48 000 (500 000 SEK), as presented in Figure 3.

The parameters identified from the one-way sensitivity analysis with the greatest impact on cost-effectiveness were changes to the utility parameters for both S- and OI-prostheses as well as the monthly cost of both prostheses (Supplementary table i).

The model was sensitive to the time horizon, resulting in a cost per QALY gained of €98 519, €243 322, and €2 578 563 when 15-year, five-year, and one-year times were used, respectively, instead of 20 years. When investigating the impact of including decline in utility values for patients with a S-prosthesis over time, an annual decline of utility values of 1%, 2%, and 3% resulted in a cost per QALY gained of €37 020, €24 662, and €18 952, respectively, over a period of 20 years, compared with the €83 374 base case.

Discussion

Our aim was to assess the cost-effectiveness of OI- compared with S-prostheses in the management of patients with unilateral TFA treated with OPRA in Sweden. We found that the OPRA treatment incurs higher costs, from the healthcare perspective, than S-prostheses. The analysis predicted that OPRA treatment would decrease costs related to revisions of the stump and prosthetic components when compared with conventional care. However, due to the cost of the treatment and complications, the OI-strategy had a projected increase in costs of € 23 592 over a period of 20 years. Because this difference is largely composed of the cost of the surgery, this cost is, for most patients, incurred as a one-off cost early in the treatment. Thus, the time under which it is assumed that the patient would benefit from the procedure is important when considering the cost-effectiveness. As the anchorage of prostheses to bone is still a fairly new technology, it is difficult to say how long patients can be assumed to benefit from it. Currently, eight patients from the OPRA study still using the OI-prosthesis have passed their 15-year follow-up. Furthermore, the longer period of time could imply that OPRA treatment should be prioritized to those who would have sufficient time to benefit from it, depending on the level of willingness to pay for a QALY.

A strength of the study is that the healthcare costs are based largely on patient-level data from those treated with a OI-prosthesis. However, a limitation is the fact that societal costs were not included, as the OPRA study included non-Swedish patients, which made the calculation of losses due to sick leave or disability impossible. Difficulties with S-prostheses, such as discomfort related to the socket, affect employment.[31] Higher-level amputations due to trauma, such as TFA result in lower rates of

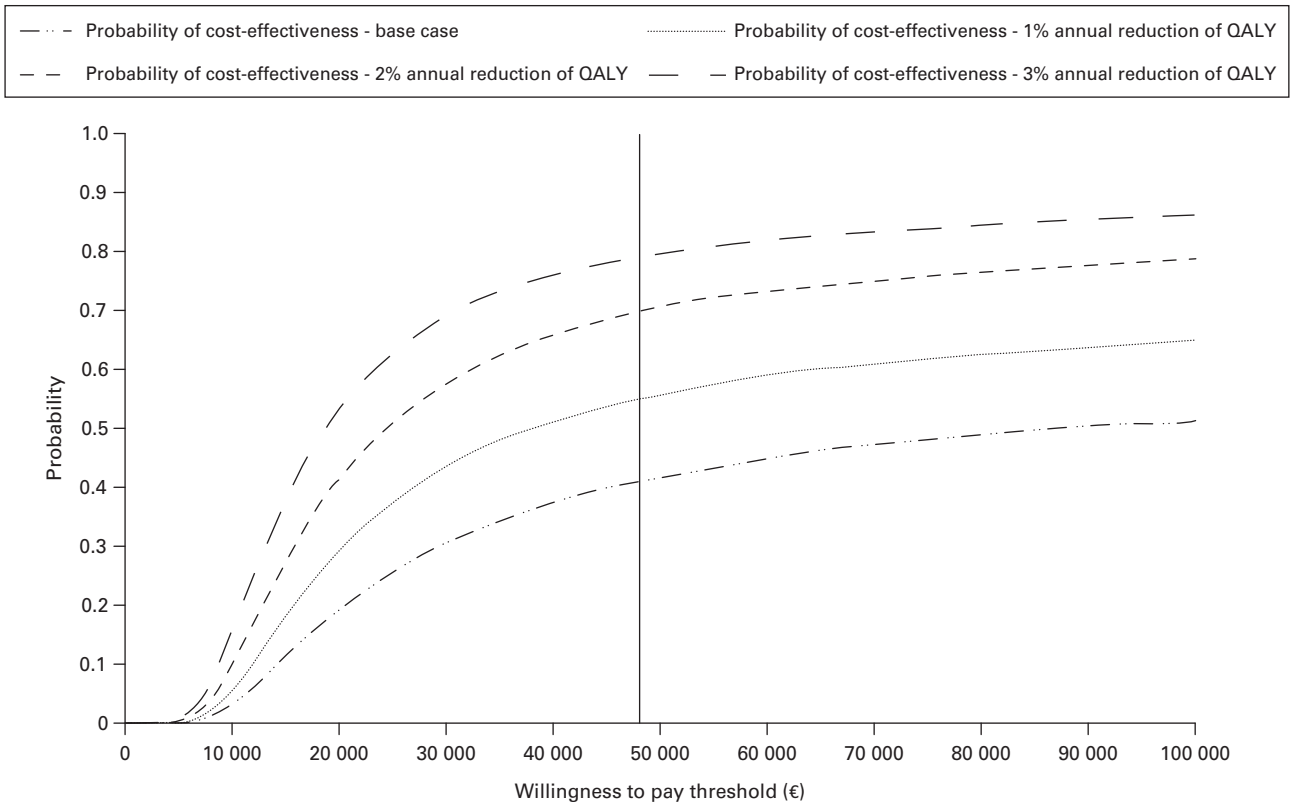

Fig. 3

Cost-effectiveness acceptability curve showing the probability of osseointegrated (OI-) prosthesis being cost-effective for a range of willingness-to-pay values for the base case, as well as scenarios for utility decreases over time for socket-suspended (S-) prosthesis. The scenario with a 3% annual reduction of utility results in a probability of the OI-prosthesis being cost-effective at approximately 80% for conventional willingness-to-pay values for a quality-adjusted life-year (QALY). The vertical line indicates the cost-effectiveness threshold.

employment.[23] It is thus reasonable to assume that a patient supplied with an OI-prosthesis close to the time of amputation would have a better chance of regaining the ability to work, which could decrease societal costs. If the societal perspective could have been included in the study, OPRA treatment would hypothetically reduce the incremental cost of osseointegration and be more cost-effective.

Little information is available about the long-term costs for amputees. A few studies have reported high costs for S-prostheses after traumatic TFA and that a new prosthesis is needed about every 2.5 years.[32,33] As most patients in the OPRA study had their prosthesis serviced at more than one workshop, thus making it difficult to control for between-group differences, prosthetic costs could not be obtained for those patients. Instead, we used costs from a previous publication comparing costs of OI- and S-prostheses in patients in whom all costs could be controlled.[17]

OPRA treatment is intended for amputees who have difficulties using a S-prosthesis.[7] In a recent review article, including 27 studies and 3126 patients with limb loss, at least53% of the patients described heat and/or perspiration when wearing the socket and the authors stated that currently these problems cannot be resolved.[34] Specifically, in patients with a traumatic TFA, limitations of mobility, pain and difficulties affecting the use of the prosthesis have been reported.[23,35] In those with significant symptoms such as an extremely short residual limb and/or poor soft tissues, an OI-prosthesis may be the only alternative. The aim of OPRA treatment is to improve function and comfort when using a prosthesis. The current analysis predicted that OPRA treatment would result in an increase in QALYs gained. QALYs were calculated from the SF-6D scores. This measure allows comparisons among different conditions and is commonly used in health economic studies.[36] However, like other general measures, it is not sensitive enough to capture detailed differences within a group. To our knowledge, the SF-6D has not previously been used in similar groups of amputees. Therefore, the study by Hagberg et al[6] reporting disease-specific measures in the same 39 patients is important, showing significant improvements and fewer problems. Several authors have validated the use of prostheses which are anchored to bone and described the benefits of more prosthetic use, better comfort, improved mobility and improved HRQoL.[4,5,8]

The one-way sensitivity analysis, and the investigations of the impact of decline in utility over time, showed that the utility values for the different treatment options have significant impacts on the results. As patients eligible for OPRA treatment have difficulties using a S-prosthesis, a persistent or worsening of symptoms could cause a continuing decline in HRQoL. Thus, the model was run with the decrease in utility over time for the S-prosthesis strategy. As seen from the results, a hypothetical 1%, 2%, or 3% annual decrease in utility would reduce the cost per QALY considerably. Given the large impact the utility has on the ICER, it would be important to investigate the long-term HRQoL for both groups of patients further. Currently, there is a general lack of such longitudinal studies in amputees[37] regardless of which kind of prosthetic supply.[37] The impact of complications on the use of OI-prostheses[38] also needs to be further investigated.

This study has limitations. Firstly, the number of patients is small, and they were only followed for two years, requiring extrapolation of the effects over time. Secondly, there was no control group. However, a blinded, randomized controlled trial would not be possible in these patients. These limitations mirror the low number of TFAs due to nonvascular causes in Sweden and the low number of patients currently treated with bone-anchored prostheses. Moreover, an appropriate control group should include only those patients with severe difficulties with S-prostheses, to mirror those eligible for OI treatment. To our knowledge, there are no studies involving this particular group of amputees. In fact, the OPRA study is the first controlled, prospective study to report the outcomes for OI-prostheses and thus is the best data currently available. Future cost-effectiveness analyses could be based on longer-term data. Moreover, cost-effectiveness analyses for bone-anchored prostheses, based on data from other forms of treatment and in different health care settings, would be welcomed.

This health economics study is the first to report cost-effectiveness for patients treated with prostheses which are anchored to bone. The results showed that OPRA treatment in patients with TFAs treated in Sweden had an ICER of €83 374 per QALY gained over a projected 20 year period. However, if patients treated with S-prostheses had a decline in quality of life over time, the cost per QALY gained by treatment with a OI-prosthesis was considerably reduced. The clinical implication is that, from a healthcare perspective, treatment with prostheses which are anchored to bone after a TFA results in improved quality of life at relatively high costs.

Take home message:

- In patients with a transfemoral amputation, the clinical improvement seen with bone-anchored prostheses, compared with socket-suspended prostheses, was reflected in a larger gain of QALYs but at a relatively high cost.
- If patients treated with S-prostheses had a decline in quality of life over time, the cost per QALY gained by treatment with a OI-prosthesis was considerably reduced.

Supplementary material

Table showing model parameters is available alongside the online version of this article at www.bjj.boneandjoint.org.uk

References

1. **Kapp SL.** Transfemoral socket design and suspension options. *Phys Med Rehabil Clin N Am*2000;11:569–583, vi.
2. **Gholizadeh H, Abu Osman NA, Eshraghi A.** Effect of vacuum-assisted socket and pin suspensions on socket fit. *Arch Phys Med Rehabil*2012;93:921.
3. **van Eck CF, McGough RL.** Clinical outcome of osseointegrated prostheses for lower extremity amputations: a systematic review of the literature. *Curr Orthop Pract*2015;26:349–357.
4. **Hagberg K, Häggström E, Uden M, Brånemark R.** Socket versus bone-anchored trans-femoral prostheses: hip range of motion and sitting comfort. *Prosthet Orthot Int*2005;29:153–163.
5. **Lundberg M, Hagberg K, Bullington J.** My prosthesis as a part of me: a qualitative analysis of living with an osseointegrated prosthetic limb. *Prosthet Orthot Int*2011;35:207–214.
6. **Hagberg K, Hansson E, Brånemark R.** Outcome of percutaneous osseointegrated prostheses for patients with unilateral transfemoral amputation at two-year follow-up. *Arch Phys Med Rehabil*2014;95:2120–2127.
7. **Brånemark R, Berlin O, Hagberg K, et al.** A novel osseointegrated percutaneous prosthetic system for the treatment of patients with transfemoral amputation: A prospective study of 51 patients. *Bone Joint J*2014;96-B:106–113.
8. **Van de Meent H, Hopman MT, Frölke JP.** Walking ability and quality of life in subjects with transfemoral amputation: a comparison of osseointegration with socket prostheses. *Arch Phys Med Rehabil*2013;94:2174–2178.
9. **Juhnke DL, Beck JP, Jeyapalina S, Aschoff HH.** Fifteen years of experience with Integral-Leg-Prosthesis: Cohort study of artificial limb attachment system. *J Rehabil Res Dev*2015;52:407–420.
10. **Al Muderis M, Khemka A, Lord SJ, Van de Meent H, Frölke JP.** Safety of osseointegrated implants for transfemoral amputees: A two-center prospective cohort study. *J Bone Joint Surg [Am]*2016;98-A:900–909.
11. **Hagberg K, Brånemark R.** One hundred patients treated with osseointegrated transfemoral amputation prostheses--rehabilitation perspective. *J Rehabil Res Dev*2009;46:331–344.
12. **Tillander J, Hagberg K, Hagberg L, Brånemark R.** Osseointegrated titanium implants for limb prostheses attachments: infectious complications. *Clin Orthop Relat Res*2010;468:2781–2788.
13. **Brånemark R, Brånemark PI, Rydevik B, Myers RR.** Osseointegration in skeletal reconstruction and rehabilitation: a review. *J Rehabil Res Dev*2001;38:175–181.
14. **Jeyapalina S, Beck JP, Bloebaum RD, Bachus KN.** Progression of bone ingrowth and attachment strength for stability of percutaneous osseointegrated prostheses. *Clin Orthop Relat Res*2014;472:2957–2965.
15. **Muderis MA, Tetsworth K, Khemka A, et al.** The Osseointegration Group of Australia Accelerated Protocol (OGAAP-1) for two-stage osseointegrated reconstuction of amputated limbs. *Bone Joint J*2016;98-B:952–960.
16. **Chimutengwende-Gordon M, Pendegrass C, Blunn G.** The in vivo effect of a porous titanium alloy flange with hydroxyapatite, silver and fibronectin coatings on soft-tissue integration of intraosseous transcutaneous amputation prostheses. *Bone Joint J*2017;99-B:393–400.
17. **Haggstrom EE, Hansson E, Hagberg K.** Comparison of prosthetic costs and service between osseointegrated and conventional suspended transfemoral prostheses. *Prosthet Orthot Int*2013;37:152–160.
18. **Maniadakis N, Gray A.** Health economics and orthopaedics. *J Bone Joint Surg [Br]*2000;82-B:2–8.
19. **Dougherty PJ, Smith DG.** One step forward, but a need for caution: Commentary on an article by Munjed Al Muderis, MB ChB, FRACS, FAOrthA, et al: "Safety of osseointegrated implants for transfemoral amputees. A two-center prospective cohort study". *J Bone Joint Surg [Am]*2016;98-A:48.
20. **Frossard L, Debra. Merlo G, Quincey T, Burkett B.** Cost comparison of socket-suspended and bone-anchored transfemoral prostheses. *Journal of Prosthetics and Orthotics*2017;29:150–160.
21. **Tintle SM, Keeling JJ, Shawen SB, Forsberg JA, Potter BK.** Traumatic and trauma-related amputations: part I: general principles and lower-extremity amputations. *J Bone Joint Surg [Am]*2010;92-A:2852–2868.

22. **Harris AM, Althausen PL, Kellam J, et al.** Complications following limb-threatening lower extremity trauma. *J Orthop Trauma*2009;23:1–6.
23. **Perkins ZB, De'Ath HD, Sharp G, Tai NR.** Factors affecting outcome after traumatic limb amputation. *Br J Surg*2012;99(Suppl 1):75–86.
24. **Sehirlioglu A, Ozturk C, Yazicioglu K, et al.** Painful neuroma requiring surgical excision after lower limb amputation caused by landmine explosions. *Int Orthop*2009;33:533–536.
25. **Bourke HE, Yelden KC, Robinson KP, Sooriakumaran S, Ward DA.** Is revision surgery following lower-limb amputation a worthwhile procedure? A retrospective review of 71 cases. *Injury*2011;42:660–666.
26. **Dolan P.** Modeling valuations for EuroQol health states. *Med Care*1997;35:1095–1108.
27. **Brazier J, Roberts J, Deverill M.** The estimation of a preference-based measure of health from the SF-36. *J Health Econ*2002;21:271–292.
28. **Ware JE Jr, Sherbourne CD.** The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*1992;30:473–483.
29. **Briggs AH, Weinstein MC, Fenwick EA, et al.** Model parameter estimation and uncertainty analysis: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force Working Group-6. *Med Decis Making*2012;32:722–732.
30. **Eddy DM, Hollingworth W, Caro JJ, et al.** Model transparency and validation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. *Med Decis Making*2012;32:733–743.
31. **Burger H, Marincek C.** Return to work after lower limb amputation. *Disabil Rehabil*2007;29:1323–1329.
32. **Bhatnagar V, Richard E, Melcer T, Walker J, Galarneau M.** Lower-limb amputation and effect of posttraumatic stress disorder on Department of Veterans Affairs outpatient cost trends. *J Rehabil Res Dev*2015;52:827–838.
33. **MacKenzie EJ, Jones AS, Bosse MJ, et al.** Health-care costs associated with amputation or reconstruction of a limb-threatening injury. *J Bone Joint Surg [Am]*2007;89-A:1685–1692.
34. **Ghoseiri K, Safari MR.** Prevalence of heat and perspiration discomfort inside prostheses: literature review. *J Rehabil Res Dev*2014;51:855–868.
35. **Ebrahimzadeh MH, Moradi A, Bozorgnia S, Hallaj-Moghaddam M.** Evaluation of disabilities and activities of daily living of war-related bilateral lower extremity amputees. *Prosthet Orthot Int*2016;40:51–57.
36. **Burton M, Walters SJ, Saleh M, Brazier JE.** An evaluation of patient-reported outcome measures in lower limb reconstruction surgery. *Qual Life Res*2012;21:1731–1743.
37. **Sinha R, Van Den Heuvel WJ.** A systematic literature review of quality of life in lower limb amputees. *Disabil Rehabil*2011;33:883–899.
38. **Tillander J, Hagberg K, Berlin Ö, Hagberg L, Brånemark R.** Osteomyelitis risk in patients with transfemoral amputations treated with osseointegration prostheses. *Clin Orthop Relat Res*2017;475:3100–3108.

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