Interventional procedure overview of direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant

Contents

Table 1 Abbreviations

Abbreviation	Definition
AMP	Amputee Mobility Predictor
BAP	Bone-anchored prosthesis
BMD	Bone-mineral density
CI	Confidence interval
DSF	Direct skeletal fixation
DXA	Dual X-ray absorptiometry
EMG	Electromyography
EQ-5D	EuroQol 5-dimension quality of life questionnaire
HTA	Health Technology Assessment
HRQOL	Health-related quality of life
ILP/EEFP/EEP	Integral Leg Prosthesis; also known as ESKA Endo-Exo Femur-Prosthesis
ITAP	Intraosseous Transcutaneous Amputation Prosthesis
MCS	Mental component summary
NS	Not significant
OFI-C	Curved osseointegration femur implant
OFI-Y	Gamma osseointegration femur implant
OI	Osseointegration
OPRA	Osseointegrated Prosthesis for the Rehabilitation of Amputees
OGA-OPL	Osseointegration Group of Australia-Osseointegration Prosthetic Limb
OTI	Osseointegration tibia implant
PMQ	Prosthesis mobility questionnaire
POP	Percutaneous osseointegrated prosthesis
PRO	Patient-reported outcome
PROM	Patient-reported outcome measure
PWS	Preferred walking speed
PCS	Physical component summary
QOL	Quality of life
Q-TFA	Questionnaire for persons with a Transfemoral Amputation
ROM	Range of motion
RSA	Radio stereometric analysis
RCT	Randomised controlled trial
SF-36	36-Item Short-Form Health Survey
SF-6D	Short-Form 6-Dimension

Abbreviation	Definition
SD	Standard deviation
TFA	Transfemoral amputation
TKR	Total knee replacement
TOFA	Transcutaneous osseointegration for amputees
TOPS	Transcutaneous osseointegrated prosthetic systems
TTA	Trans-tibial amputation
THA	Trans-humeral amputation
TRA	Transradial amputation
TUG	Timed Up and Go
6MWT	6-minute walk test

Indications and current treatment

Limb amputation is traumatic and affects QOL. Lower-limb amputation (above or below the knee) is the most common reason for a person to use a prosthetic limb (customised prosthesis). The most common reason for lower-limb amputation is peripheral vascular disease. Other causes include trauma, infection, diabetes and cancer. Upper-limb amputations are less common and are mainly a result of trauma. A small proportion of people need prosthetic limbs because of congenital limb loss or deformities.

The customised prosthesis is fitted to replace the function of the missing limb and provide cosmesis for major amputations. The type of prosthesis depends on what part of the limb is missing. Conventionally, the prosthesis is attached to the residual stump by belts and cuffs, suction, or by a suspension system. The conventional prosthesis usually has a socket, which is custom made from a plaster cast of the stump. Every effort is made to ensure individuals have sockets that fit well and are comfortable. One of the main problems with this type of prosthesis is rubbing between the stump and the socket. This can cause pain, ulceration and improper distribution of body weight that can affect balance and lead to falls. This may mean the user has limited use of the prosthesis or may have to abandon it for a period because of poor fit.

Unmet need

Conventional socket prostheses with a poor fit can cause a variety of problems, including:

- recurrent skin infections
- ulcers (pressure sores in the socket area)
- fistula formation
- pain
- discomfort
- excessive sweating
- balance problems, and
- falls.

These problems are more common in people with short residual limbs and those with skin problems, and may lead to prosthesis abandonment or restricted mobility. As a result these people may depend on a wheelchair or crutches or both. For most people a conventional prosthesis is appropriate and well tolerated. But, when a conventional socket prosthesis is unsuitable or causes problems, DSF of limb prostheses using an OI implant may be an option for some people.

What the procedure involves

The procedure aims to surgically insert an OI implant, producing a secure connection between the remaining bone and the implant for prosthetic attachment. The implant may be in 1 piece or modular with a separate small metal extension (called an abutment).

The advantages of DSF of an OI implant are:

- proper transfer of load from the prosthesis to the person’s body
- better function and mobility (such as walking)

- improved comfort while sitting
- better balance
- fewer stump problems
- increased prosthesis use, and
- improved QOL.

The potential problems are:

- soft-tissue infection where the skin and the prosthesis meet
- deep infection
- fracture or loosening around the implant, and
- implant failure.

DSF of limb prostheses using an OI implant is done under general or regional anaesthesia (depending on the level of amputation). The procedure can be done all in 1 stage or in 2 stages separated by a period of time. In the first stage, a metallic implant (with either an outer surface threaded like a screw or a press-fit design) is inserted into the medullary cavity of the residual bone. Then, healing components are attached to the implant to secure the bone graft during healing. The second stage of the procedure is typically done about 2 to 6 months later, after the implant has integrated into the bone (osseointegration) and the stump wound is completely closed and healed. It involves surgically removing the healing components and re-exposing the distal end of the implant. It is then attached to an abutment with an abutment screw or bridge component. The wound is closed with the abutment penetrating the skin. The external prosthesis can then be attached to the OI implant using various components, depending on the level of amputation.

A period of extensive physiotherapy and rehabilitation follows the procedures, and the load on the prosthesis is gradually increased until full weight-bearing is allowed a few weeks later.

Outcome measures

The main outcomes included functional outcomes, QOL and adverse events.

The measures used were:

PROMs

- **HRQOL**: A measure of the impact of a person's health status on their QOL. HRQOL tools allow the effects of chronic illness, treatment, and disability on a person's QOL to be measured. It is measured using validated outcome measures such as Q-TFA and SF-36.
- **Q-TFA**: A self-report outcome measure for non-elderly people who have had an above-knee amputation and use a socket or OI implant. It provides a score of 0 to 100 in the following 4 domains:
  - Prosthetic use: The number of days per week the person normally wears their prosthesis, multiplied by the number of hours it is used each day. A score of 100 means the prosthesis is used 7 days a week for more than 15 hours per day.
  - Prosthetic mobility: The ability and performance of the person to move, change and maintain postures when using the prosthesis. A score of 100 indicates the best possible prosthetic mobility. The mobility score is the average of 3 subscores:
    - ◊ capability (12 items)
    - ◊ use of walking aid (2 items), and
    - ◊ walking habits (5 items).
  - Problem score: This measures specific problems related to the amputation and prosthesis and their impact on QOL. A higher score indicates more serious problems (unlike the other domains).
  - Global health score: This measures the person's perception of their functional ability, any problems with the prosthesis, and their overall

circumstances. The score is a summary of 3 questions to which answers are given on a 5-point Likert scale. A score of 100 indicates the best possible overall situation.

- **SF-36**: A generic measure of QOL. The tool has 8 subscales:
  - 4 measure physical health:
    - ◊ physical functioning
    - ◊ role functioning – physical
    - ◊ bodily pain
    - ◊ general health, and
  - 4 measure mental and psychological health:
    - ◊ vitality
    - ◊ social functioning
    - ◊ role functioning – emotional
    - ◊ mental health.

  The results are also captured in 2 summary measures:
  - PCS and
  - MCS.

  In each scale, values run between 0 and 100. A higher score indicates better physical or mental health.
- **PMQ**: A questionnaire with 12 questions about mobility in everyday life, which are answered on a 5-step Likert scale. Higher scores represent better mobility, with the maximum total score of 40.

Healthcare professional outcome measures

- **6MWT**: Measures the distance a person can walk in a 6-minute period and has been shown to reliably measure functional capacity in various populations, including people who have had amputations.

- **TUG test**: A valid test for quantifying functional mobility and useful for following clinical change over time. It is a measure of function that correlates with balance and risk of fall. The test is quick, reliable and measures the time a person takes to rise from a chair, walk 3 metres, walk back, and sit down. The TUG test is interpreted as follows:
  - 10 seconds or less: normal mobility
  - between 10 and 20 seconds: mild mobility impairment, can go out alone, mobile without a gait aid
  - between 20 and 30 seconds: significant mobility problems, cannot go outside alone, needs a gait aid.
- **AMP**: A reliable, valid measure for assessing mobility in people who have had a lower-limb amputation, with or without using a prosthesis (AMPPRO and AMPnoPRO, respectively). It can be used before prosthetic fitting to predict functional ability after prosthetic fitting. AMPPRO scores are presented as K-levels. This is a 5-level rating system used by the US Medicare health insurance program to indicate the extent of a person's disability and their potential for rehabilitation. Ratings range from 0 (no potential to walk independently, even with a prosthesis) to 4 (exceeds basic ambulation skills).
- **Prosthetic activity grades**: Activity is graded between 0 and 4 and combines the extent of prosthetic use, use of walking aids, outdoor walking habits, and other activities using the prosthesis. The activity is captured from Q-TFA items and medical records.
  - 0: Do not use prosthesis; no prosthetic activity
  - 1 (Low): Limited use of prosthesis for standing or walking, use walking aid, no long walks
  - 2 (Average): Uses prosthesis most of the day, with or without walking aid at home, uses walking aid outdoors

- 3 (High): Uses prosthesis for a full day, no walking aid except for longer distances, walks a lot, rarely performs other demanding or high-load activities using the prosthesis
- 4 (Very High): Uses prosthesis for a full day, no walking aid, walks a lot or routinely performs other highly demanding or high-load activities involving the prosthesis (for example, cycling or gym training).

Evidence summary

Population and studies description

This interventional procedures overview is based on 2,708 people from 1 HTA, 3 systematic reviews, 2 retrospective cohort studies, 2 retrospective reviews, and 1 cross-sectional observational study. Of these 2,708 people, 2,606 had the procedure. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 8 studies as the key evidence in table 2 and table 3, and lists 68 other relevant studies in table 5. There is an overlap of studies between the HTA and systematic reviews.

The HTA assessed 2 stage OI implant surgery for people with an amputation above the knee who had problems with socket prosthesis or cannot use a socket, in 9 observational studies (4 retrospective and 5 prospective) with short-term follow up (mean 1 to 5 years). One study reported follow up of 7.5 years. The population sizes ranged from 12 to 96 people. Studies were based in Sweden, the Netherlands, Germany, and Australia. No studies comparing DSF with conventional or no prosthesis were identified in the review. Studies evaluated 3 implants that are used currently (OPRA implant system in 4, ESKA EEFP/ILP in 3, and OGAP-OPL in 1, ILP or OGAP-OPL in 1). All studies reported exclusion criteria and excluded people with peripheral vascular disease and diabetes mellitus, exposure to radiation in the affected limb or past or ongoing chemotherapy. Amputations were mainly due to trauma or tumours. Seven

studies included some people with bilateral amputations and the results were analysed separately. Two studies included only people with unilateral amputations and 1 only on people with bilateral amputations. All the studies included in the HTA were at high risk of bias (when assessed using the ROBINS-I instrument) and certainty about the evidence for functional outcomes and QOL reported was very low when assessed using modified GRADE. Some studies had overlapping patient data. A qualitative synthesis of the included studies was done to summarise outcomes. Authors state that 'it was not clear if problems with sockets and suitability for surgery were assessed in a standard and reliable manner in included studies and whether the studies included all people after being unable to tolerate socket prostheses'.

A systematic review (Atallah 2018) of 12 cohort studies only assessed safety data on BAP (3 types of prostheses) for people with an extremity amputation. A qualitative synthesis of the included studies was done to summarise outcomes. There was a partial overlap of patient data in some of the included studies. Data was analysed separately according to the implant type and level of amputation. Some studies were retrospective and may have underestimated the complication rates.

Another systematic review (Balzani 2020) included 17 case series with several types of implants and varied follow-up times. Amputation at different levels were analysed.

A large prospective cohort study (Hagberg 2020 with OPRA implant and a rehabilitation protocol) was done over 18 years in a single centre and reported results for multiple timepoints (2, 5, 7, 10 and 15 years). People were recruited at different times throughout the study and only small number of people had 15-year follow up. There were insufficient details about the criteria for defining problems related to socket-suspended prosthesis. People were excluded from the study due to death (n=3), lost to follow up (n=6) and implant failures (n=18).

A small retrospective study (Thouvenin 2023 with OPRA implant) with long-term follow up (average 9.4 to 15 years) compared outcomes before and after the procedure.

Two retrospective studies (Hollewarth 2020 and Örgel 2022 both with ILP) focused only on management of periprosthetic fractures.

All the included observational studies in the overview were at high risk of bias and certainty about the evidence for all outcomes was very low.

Table 2 presents study details.

Figure 1 Flow chart of study selection

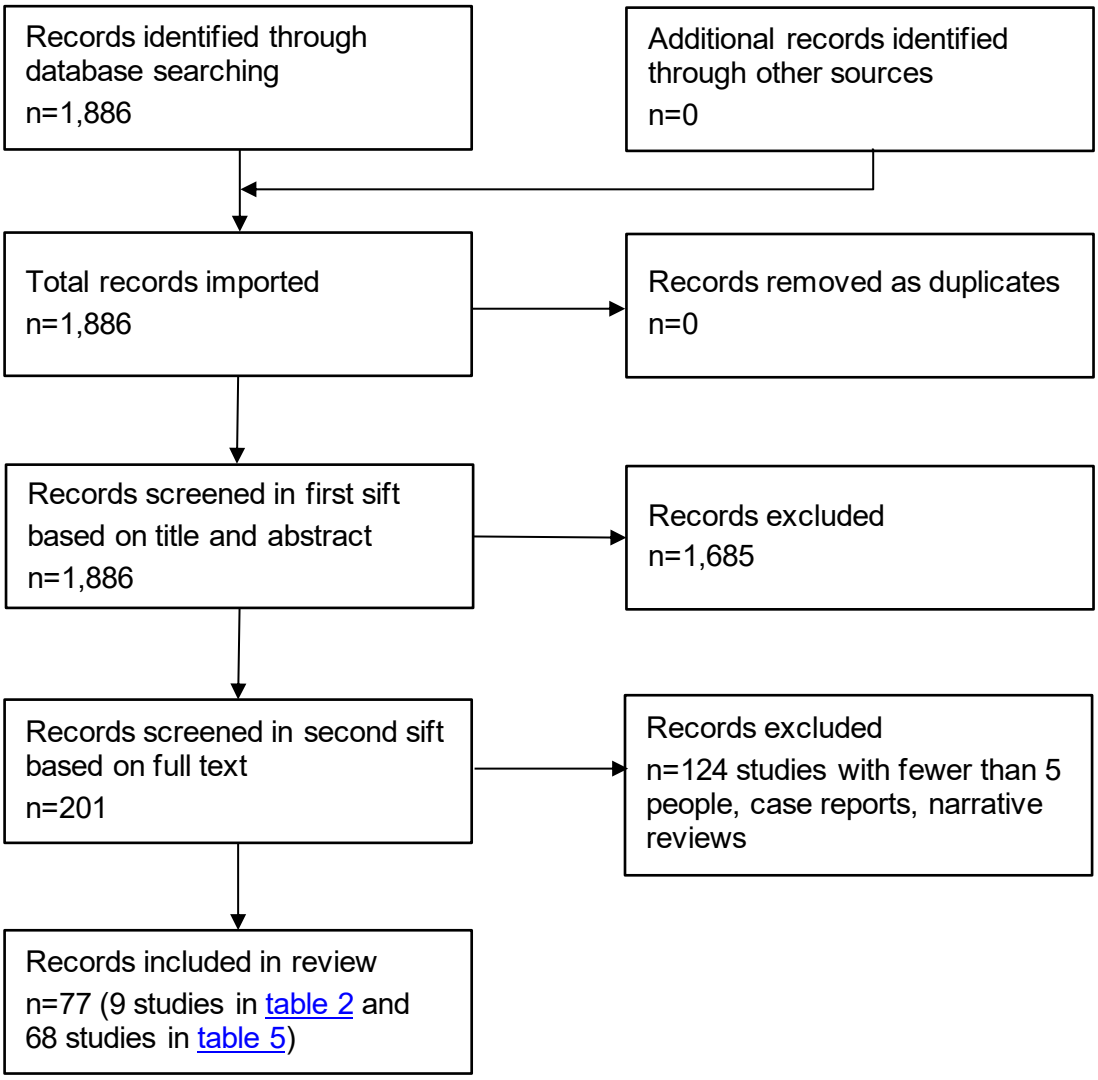

Table 2 Study details

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
1	Ontario, 2019 Canada	n=480 (68.8%:31.2%)	Mean age= 65.7 years	Systematic review and HTA (9 studies for qualitative synthesis and 0 for quantitative synthesis)	Adults with lower-limb amputation due to nonvascular causes who have problems with the use of socket prosthesis or cannot use a conventional socket prosthesis	1. OPRA Implant System, Integrum AB, Sweden 2. EEFP, ESKA Orthopaedic, Germany; also known as ILP 3. OGAP-OPL, Permedica, Italy	Mean/median duration= 1 to 5 years among most studies (1 study had a follow up of 7.5 years but only reported on the risk of osteomyelitis)
2	Atallah, 2018 8 different centres worldwide	n=604 (640 implants, 537 people with a lower- and 67 people with an upper-limb amputation) (426:147) TFA, n=522 TTA, n=15 THA, n=40	Mean age= 45, 47 and 48 years in people with a screw, press-fit or Compress implant	Systematic review (12 cohort studies for qualitative synthesis, 3 prospective, 6 retrospective and 3 undefined design) Of these, 3 studies had 2 separate	RCTs, controlled clinical trials and prospective and retrospective observational studies (including before-after, cohort and case-control	OPRA screw (n=206), ILP or OGAP-OPL press-fit (n=387) or other type of bone-anchored implant (Compress implant, n=11)	Varied follow-up time points (ranged from 1 to 288 months)

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
		TRA, n=14 Thumb amputation, n=13		cohorts based on level of amputation or implant type. So, a total of 15 cohorts assessed	studies) reporting device- or procedure-related complications in people with an upper or lower (or both) extremity amputation (mainly trauma) treated with bone-anchored prostheses		
3	Balzani 2020 Italy	n=634 people (669 implants) TFA, n=586 TTA, n=6 THA, n=37 TRA/TUA, n=24 Thumb or partial amputation, n=12.	Mean age = 44.7 years (range 17 to 84 years)	Systematic review (17 studies for quantitative synthesis)	Studies with upper and lower-limb amputation (major cause trauma in 65%) treated with an osseointegrated prosthesis, with description of procedure, reporting	Osseointegrated prosthetic implants for limb amputation (OPRA implant system in 10 studies, OGAP-OPL in 3 studies, not reported in 1 study, customised 3-dimensional printed titanium implant [AQ Implants] in 1 study and EEFP in 2 studies)	Average 61.4 months, ranging from 10 months to 228 months

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
					clinical outcome and complications		
4	Leijendekkers RA 2017 The Netherlands	n=227 people with TFA mainly due to trauma (110 BAP in cohort studies, 32 BAP versus 185 socket prosthesis in cross-sectional studies)	Cohort studies ranged from 20 to 70 years; cross-sectional studies: BAP group ranged from 26 to 67 years, socket-prosthesis group ranged from 28 to 70 years	Systematic review of 7 studies (5 before and after cohort and 2 cross-sectional studies) conducted in Sweden (n=6) and the Netherlands (n=1)	Studies on people with a lower extremity BAP; comparing bone-anchored prostheses with socket prostheses; evaluating QOL, function, activity or participation level. studies in English, Dutch or German	Bone-anchored prostheses compared with socket prostheses	Varied follow up across studies.
5	Hagberg 2020 Europe	n=111 (78:33)	Mean age= 44.6 years (range 17 to 70)	Prospective cohort study	People with unilateral TFA (mainly trauma) experiencing problems related to a	Bone-anchored transcutaneous prosthesis -OPRA implant system surgery in 2 stages followed by a rehabilitation protocol	18 years Results reported at multiple time points (2 to 15 years)

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
					socket-suspended prosthesis and having mature and sufficient residual skeleton dimensions were enrolled		At 15 years (n=14)
6	Thouvenin 2023 France	n=17 (20 BAPs) (7:10) 3 bilateral amputees Level of amputation: TFA 14, TTA 3 Time between amputation and surgery 8.4 years.	Mean age=32 years (range 15 to 54)	Retrospective cohort study (single centre)	People with lower-limb amputation (mainly due to trauma) eligible for a BAP (between 2007-2021) if they major fitting difficulties with a socket-suspended prosthesis, such as a short stump, skin lesion in the socket, or intractable pain, and more	OPRA implant system	1 to 15 years

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
					than 1 year follow up		
7	Hollewarth 2020	n=458 (519 OI) Upper extremity (n=17, 18 implants, Humerus 16 implants radial 1 implant) Lower extremity (n=441, 500 implants, Femur 347 implants and tibia 153 implants) Bilateral procedures femur 34, tibia 16, humerus 1	Mean age (SD, range) =48.3 years (13.1; 22.6 to 64.5)	Retrospective review	All OI operations done at 4 centres between 2010 and 2018	Osseointegrated Prosthetic Limb/ILP devices	Not reported
8	Örgel 2022 Germany	n=140 (2 centres)	Mean age 48.7 years	Retrospective cohort study	People who had TOPS following TFA between 2010-2019	EEP/ILP device	Not reported
9	Welke 2023	n=37 (20 BAP and 17 socket suspended)	BAP group: Mean age	Cross-sectional observational study	Adults with unilateral TFA, mobility grade 3 'unrestricted	Socket fitting or BAP system	Not reported

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
			(SD) =54 (8.2) Socket group: Mean age (SD) =62 (14.6)		outdoor walker' or 4 'unrestricted outdoor walker with particularly high demands' and initial prosthetic fitting that has been completed for more than 2 years		

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Ontario, 2019 Canada	**Functional Outcomes and HRQOL** **6MWT Score in metres, mean (SD); 2 studies** van de Meent 2013 (n=22 TFA, device ILP) preoperative: 321 m (28), 1-year follow up=423 m (21); p=0.002 Al Muderis 2016 (n=50 TFA, device: ILP and OGAP-OPL) Wheelchair user, preoperative: not reported, mean 1.8-year follow up: 411 (31.44); p=not reported Prosthesis user, preoperative: 281 m (93), postoperative= 419 m (133); p<0.001 **TUG score in seconds, mean (SD); 2 studies** van de Meent 2013 (ILP) preoperative: 15.1 (2.1), 1-year follow up= 8.1 (0.7); p=0.002 Al Muderis 2016 (ILP and OGAP-OPL) Wheelchair user, preoperative: not reported, mean 1.8-year follow up=9.0 (0.56); p=not reported Prosthesis user, preoperative: 14.59 (5.94), postoperative: 8.74 (2.81); p<0.01 **AMP** No studies reported on AMP. However, 1 study (Al Muderis 2016) reported on K-levels based on previously reported AMP scores; K-level improved	**Superficial infection** Brånemark 2014 (OPRA implant system, 2 years follow up): 55% (28 out of 51), incidence=41 episodes. Treated with antibiotics. 5 years follow up: 67% (34 out of 51), 70 episodes; treated with antibiotics, 1 implant loosening and explantation. Juhnke 2015 (ILP, n=39 TFA, mean follow up 2.7 years): none. Al Muderis 2016 (ILP, mean 2.8 years follow up): mild 27% (23 out of 86), severe 1% (1 out of 86), 43 episodes, treated with antibiotics. Al Muderis 2016 (ILP and OGAP-OPL, mean 1.8 years follow up): total 36% (18 out of 50; [mild 26% (13 out of 50) and severe 10% (5 out of 50)]). Refashioning surgery=20%. Al Muderis 2017 (OGAP-OPL, mean 1.2 years follow up): 45.5% (10 out of 22). Refashioning surgery=27% **Deep or bone infections** Tillander 2010 (OPRA implant system, n=39 [TFA 32, TTA1, arm 6], mean 3 years follow up): 18% (6 out of 39) occurred at mean 2.8 years. Surgical reintervention, n=4 (2 revision, 1 debridement, and 1 extraction). Brånemark 2014 (OPRA implant system, 2 years follow up): signs of infection=4% (2 out of 51), positive culture 4% (2 out of 51), occurred immediately after stage-1 to 42 days after stage-2.

	in 60% of people and was unchanged in 40% (p=0.001) **ROM** None of the studies reported on changes in ROM **Q-TFA; 3 studies** Brånemark 2014 (n=51 TFA, 55 implants, device: OPRA implant system) Daily prosthesis use increased from 57% before the procedure to 89% at 2 years follow up. Van de Meent 2013 (ILP) Prosthetic use: preoperative 56 hours per week, at 1-year follow up 101 hours per week, p<0.001 Global health score: preoperative 39 (4.7), at 1-year follow up 63 (5.3), p=0.001 Al Muderis 2016 (ILP and OGAP-OPL) Only reported scores for global health, which showed a statistically significant improvement (preoperative 47.82, at mean 1.8-year follow up 83.52, p<0.001) **SF-36; 2 studies** Brånemark 2014 (OPRA implant system, 2- and 5-years follow up) Physical functioning: baseline 35 (0 to 85), change 23 (−23 to 75; n=45); p<0.001 5 years: 28 (23.1; n=40), p<0.0001 Role-physical: baseline 41 (0 to 100), change 22 (−50 to 100; n=44); p<0.001 5 years: 19 (47.9; n=39), p=0.02	5 years follow up: 22% (11 out of 51), mainly treated with antibiotics, led to 1 implant loosening which was removed 6 months after stage 2 surgery. Tillander 2017 (OPRA implant system, n=96 TFA, mean follow up 7.9 years): Osteomyelitis (occurred at median 2.6 years): overall 17% (16 out of 96), before OPRA protocol 26% (7 out of 27), during and after OPRA protocol 13% (9 out of 69). Extracted 10 and reimplanted 1. Osteitis (diagnosed more than 5 years after implantation): 6% (6 out of 96). Al Muderis 2016 (ILP, mean 2.8 years follow up): abscess formation 5% (4 out of 86). Surgical debridement in all. Al Muderis 2016 (ILP and OGAP-OPL, mean 1.8 years follow up): 6% (3 out of 50). Surgical debridement in all. **Bone fracture** Brånemark 2014 (OPRA implant system, 2 years follow up): femoral fracture, 0. other locations, ipsilateral hip= 6% (3 out of 51), below elbow=2% (1 out of 51) and vertebral compression fracture= 2% (1 out of 51). Juhnke 2015 (ILP for TFA, mean 2.7 years follow up): femoral fracture, 5% (2 out of 39). Other locations not reported. Al Muderis 2016 (ILP, mean 2.8 years follow up): femoral fracture, 3.5% (3 out of 86). Other locations not reported. Al Muderis 2016 (ILP and OGAP-OPL, mean 1.8 years follow up): Femoral fracture, 8% (4 out of 50)

IP overview: Direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.

	Bodily pain: baseline 55 (10 to 100), change 6 (−61 to 59; n=45), p=NS 5 years: 4 (30.7; n=40), p=0.45 General health: baseline 78 (37 to 100), change −1 (−42 to 40; n=45); p=NS 5 years: 3 (22.7; n=40), p=0.31 Vitality: baseline 60 (15 to 90), change 3 (−70 to 45; n=45); p=NS 5 years: 3 (22.1; n=40), p=0.35 Social functioning: baseline 78 (13 to 100), change 1 (−100 to 63; n=45); p=NS 5 years: 1 (31.8; n=40), p=0.96 Role-emotional: baseline 75 (0 to 100), change 0 (0 to 100; n=44); p=NS 5 years: −1 (42.9; n=39), p=1.00 Mental health: baseline 74 (4 to 100), change 2 (−76 to 40; n=45); p=NS 5 years: 1 (22.2; n=40), p=0.56 PCS: baseline 74 (4 to 100), change 2 (−76 to 40; n=44); p<0.001 5 years: 10 (9.9; n=39), p<0.0001 MCS: baseline 53 (19 to 69), change −3 (−44 to 22; n=44); p=NS.	Other locations not reported **Implant removal** Tillander 2010 (OPRA implant system, mean 3 years follow up): 3% (1 out of 69). Reason = deep infection Brånemark 2014 (OPRA implant system, 2 years follow up): 5.8% (3 out of 51). Reason = deep infection: 1 at 6 months and failed integration: 2 at 1.3 and 1.7 months 5 years: 4 implants removed, 3 needed stump revision Implant survival rate 92%; revision-free survival rate was 45% Juhnke 2015 (ILP, mean 2.7 years follow up): 2.6% (1 out of 39). Reason = failed integration Al Muderis 2016 (ILP, mean 2.8 years follow up): 3.5% (3 out of 86). Reason = failed integration in 1, breakage of implant in 2 at 42 and 47 months after stage 1 Al Muderis 2016 (ILP and OGAP-OPL, mean 1.8 years follow up): 4% (2 out of 50). Reason = failed integration at 2 years (n=1) and fatigue failure 3.5 years (n=1) **Intramedullary breakage and extramedullary mechanical issues** Brånemark 2014 (OPRA implant system, 2 years follow up): Implant breakage, 0 5-year follow up: 43 mechanical complications in 15 people, needed replacement of damaged parts Issues with extramedullary parts: changing the abutment or its screws: 8% (4 out of 51; 9 events; 6 occurred in 1 person) Al Muderis 2016 (ILP, mean 2.8 years follow up) Implant breakage, 2.3% (2 out of 86).

	5 years: 4 (14.4; n=39), p=0.22 Al Muderis 2016 (ILP and OGAP-OPL) PCS: baseline 37.09 (9.54), 1.8-year follow up 47.29 (9.33), p<0.001	issues with extramedullary parts: breakage of safety parts: 29% (25 out of 86; 30 events). Juhnke 2015 (ILP, mean 2.7 years follow up) 0 events **Non-infectious soft-tissue and bone complications** Juhnke 2015 (ILP for TFA, mean 2.7 years follow up) Excess granulation tissue at stoma: 1. Treatment= removed granulations Al Muderis 2016 (ILP, median 2.8 years follow up) • Hypertrophic bone formation: 10% (9 out of 86), treatment = not reported • Redundant soft tissue: 16% (14 out of 86); 23 events, treatment= excised redundant soft tissues • Hypergranulation at stoma: 20% (17 out of 86); 22 events, treatment= treated with chemical cauterisation • Rounding and resorption of distal femoral cortex: 20% (17 out of 86), treatment=not reported
Atallah, 2018	No clinical efficacy results assessed	**Infection** reported in 73% (11 out of 15) cohorts Overall infection rate (implant type): 23% to 49% (with screw implants), 0% to 77% (with press-fit implant) and 0% (with Compress implant) Soft-tissue infections in the skin-penetrating area (grade 1 to 2): 28% (screw implants) and 0% to 57% (press-fit implants) Bone infection (grade 3): 5% to 13% (screw implants) and 0% (press-fit implants) Infections resulting in implant loosening (grade 4): 8% to 11% (screw implants) and 3% to 29% (press-fit implants) Infection rates in relation to amputation level: 0% to 77% (TFA treated with press-fit implants) and 44% (upper extremity amputation). Rates unknown for TTA

		Rate of soft-tissue infections (grade 1 to 2): 0% to 57% (TFA treated with press-fit implants) and 28% (upper extremity amputation) Bone infection (grade 3): 13% (TFA treated with screw implants) and 6% (upper extremity amputation) Implant loosening due to infection (grade 4): 0% to 11% of people with TFA (screw-fit: 11%, press-fit: 0% to 3%), 29% (TTA) and 11% (upper extremity amputation- all trans-humeral) Juhnke 2015. infection rates: from 77% to 0% before and after adaptation of surgical technique and implant designing press-fit transfemoral implants **Soft-tissue complications** Lower-extremity amputation-TFA Stoma hypergranulation: 44% (in those with screw implant), 3% to 20% (with press-fit implants) and 0% (with Compress implant) Stoma-redundant tissue: 0% (with screw implant), 3% to 16% (with press-fit implant) and 9% (with Compress implant) upper extremity amputation: stoma hypergranulation of 44% in people with THA treated with screw implants (in 1 study) TTA: 0% **Periprosthetic bone fracture** reported in 60% (9 out of 15) cohorts 0% (in studies with screw implant), 0% to 10% (in 7 studies with TFA treated with press-fit implant) and 18% (in 1 study

		with TFA treated with Compress implant). 0% in studies with upper extremity implants and in those with implants for TTA Cause of bone fracture: falls (reported in 3 studies) **Device-related complications** **Device Breakage** (fractures of the intramedullary implant, of the abutment [screw] and of the dual-cone adaptor [press-fit]) reported in 53% (8 out of 15) of the cohorts Implant type: 27% to 45% (with screw -fit implant), 0% to 31% (with press-fit implants) and 0% (with Compress implant) amputation level: Intramedullary device breakages: 0% (TFA treated with screw implants), 1% (TFA treated with press-fit implants) and 27% (transradial screw implants). No breakages in those with implants for TTA **Implant Loosening** reported in 60% (9 out of 15) cohorts. Implant type: 3% to 23% (in 2 studies with screw implants), 0% to 29% (in 4 studies with press-fit implants) and 0% (in 1 study with Compress implant) amputation level: loosening occurred in 0% to 3% of people with TFA treated with press-fit implants, 29% of people with TTA treated with press-fit implants, in 13% and 23% of people with trans-humeral and thumb amputation and 0% in those with TRA **Complication-related interventions** **Surgical revision** (for stoma-redundant tissue, infection and hypergranulation) Implant type

		11% (in those with a screw implant), 9% (in those with Compress implant) and 6% to 77% (in those with press-fit implants). **Explantation** (for infection, device breakage, bone fracture, and implant loosening) Implant type Incidence: 14% to 19% (in 5 studies with screw implant), 0% to 57% (in 8 studies with press-fit implant) and 9% (in 1 study with Compress implant) Explantation rate as per level of amputation: TFA: 17% to 18% (screw implant), 0% to 13% (press-fit implant) and 9% (Compress implant) TTA: from 42% to 57% (press-fit implants) THA: 17% to 19% (screw implants) **Reimplantation** reported in 87% (13 out of 15) cohorts Implant type: performed in 6% to 40% (in 4 studies with screw implant), 25% to 100% (in 8 studies with press-fit implant) and 100% (in 1 study with Compress implant) Reimplantation was successful in 33% of people with THA
Balzani 2020	**Lower limb** **SF-36:** MCS postoperative mean value 55.1 PCS postoperative mean value 45.4 Muderis (2016): PCS (p=0.001) Brånemark (2014): general QOL (p<0.0001)	**Complications rates (13 studies)** Overall rate of complications: 75% (164 out of 216) Stoma Hypergranulation: 35% Implant-related complications (including breakage): 27% Periprosthetic fractures/fracture above the implant: 18% Soft tissues redundancy: 8% Aseptic loosening of the implant: 8%

	Atallah (2017): MCS: 57.4 (range 41.2 to 70.3); PCS: 40.8 (range 38.9 to 44.4) Hagberg (2008): MCS: 50; PCS: 44 Hagberg (2014): PF: 60 ± 21,4; PCS: 40.5 ± 9.8 Matthews (2019): improved significantly between preoperative and 2- and 5-years follow up McMenemy (2020): MCS: 58.19; PCS: 54.5 Al Muderis (2016): PCS: mean 47.29 (SD 9.33) **Q-TFA: postoperative mean value of 73.8** Muderis (2016): Significant improvement in Q-TFA global score (p=0.001) Brånemark (2014): Q-TFA scores improved (p<0.0001): prosthetic use, prosthetic mobility, global situation, and fewer problems Atallah (2017): global: 63.2 (58 to 83.3) Hagberg (2008): global: 72.1 (33 to 100) Hagberg (2014): global: mean 76 (SD 17.4) Matthews (2019): significant improvements in all of the main scores, and in 2 out of the 3 subscores for prosthetic mobility, between the preoperative period and 2- and 5-years post implantation Al Muderis (2016): global: mean 83.52 (SD 18.4) Van de Meent (2013): global: 75 (42 to 100) **6MWT (5 studies): average value 388 metres** Muderis (2016): Significant improvements (p=0.001)	Persistent pain: 4% **Infection rates (16 studies)** Overall rate of infections: 32% (201 out of 626) Superficial infections (163 out of 201) Deep skin/bone infections (38 out of 201)

	Muderis (2017): significant improvements, with a mean increase of 128% Atallah (2017): 311 (144 to 433)m McMenemy (2020): 402 m Al Muderis (2016): 419 ± 31.44m Van de Meent (2013): 423 ± 21 **TUG (6 studies): average 11.5 seconds** Muderis (2016): Significant improvements (p=0.01) Muderis (2017): Mean reduction of 30% Atallah (2017): 18.65 (6.28 to 26,8) McMenemy (2020): 10.6 seconds (7.4 to 12.1) Al Muderis (2016): 8.74 ± 2.81 second Van de Meent (2013): 8.1 ± 0.7 second **Upper limb:** no clinical data were reported.	
Leijendekkers RA 2017	**QOL** Q-FTA problem score (in 2 cohort studies: Hagberg 2008, Brånemark 2014) at 1 year follow up and QFTA global score (in 3 cohort studies: van de Meent 2013, Brånemark 2014, Hagberg 2008) at 2 years follow up improved significantly with use of BAP compared with socket prosthesis General QOL (assessed using SF-36 in 2 cohort studies, Hagberg 2008, Brånemark 2014) The scores of physical health (physical functioning score, role-physical functioning score and PCS) improved significantly at 1 year and 2 years	

	follow up with use of a BAP compared with socket prostheses use. SF-36 physical bodily pain subscale score improved significantly using BAP compared with socket prosthesis in one study at 1- and 2-years follow up (Hagberg 2008) but reported no change in another study at 1 year follow up (Brånemark 2014). Scores on other SF-36 subscales (physical general health, all mental health subscales) did not change significantly after BAP at 1- and 2-years follow up. One study (Hagberg 2014) using SF-6D reported an improvement in general health status at 2 years follow up using BAP compared with socket-prosthesis use **Functional level** Q-TFA Prothesis use score (3 cohort studies) All the 3 studies found that prosthesis use improved significantly with BAP compared with socket prosthesis at 1 year (van de Meent 2013, Brånemark 2014) and 2 years follow up (Hagberg 2008). ROM and gait One cross-sectional study (Hagberg 2005) reported that range of hip motion was lower with socket prosthesis compared with BAP use at 2- and 10-years follow up. Another cross-sectional study (Frossad 2010) assessing temporal gait variables (cadence, duration gait cycle and duration support phase) reported that BAP use had a gait more	

	similar to healthy subjects than socket prosthetic use at 1 year follow up. Another cohort study (Tranberg 2011) assessing gait kinematics in the sagittal plane found that during the stance phase use of a BAP increased hip extension and decreased anterior pelvic tilt compared with a socket-prosthesis use and are more similar to that of healthy subjects compared with socket-prosthesis use **Activity level** Q-TFA mobility score (3 cohort studies) All studies found that using a BAP use resulted in significant improvements in overall mobility score, capability sub-score and walking habit sub-score compared with socket prostheses use at 1 (Brånemark 2014) and 2 (Brånemark 2014, Hagberg 2008) years follow up, but there was no change in walking aid sub-score at 2 years follow up. Discomfort when sitting (1 cross-sectional study Hagberg 2005) Evidence shows that using a BAP was associated with less discomfort when sitting than use of a socket prosthesis. Discomfort when sitting was reported in 44% (n=19) in the socket group and was common in people with less than 90 degrees of hip flexion motion (p=0.025). In the BAP group, no subject had less than 90 degrees of flexion and 5% (n=1) reported discomfort when sitting. Walking ability (cohort study van de Meent 2013)	

	Walking ability improved significantly 1 year after BAP use compared with use of a socket prosthesis, both in terms of distance covered in 6-min and time needed to get up from a chair, walk 3-m up and down a walkway and sit again Energy cost of walking (2 cohort studies- van de Meent 2013, Hagberg 2014) Both studies found that use of a BAP reduced the energetic cost of walking significantly compared with use of a socket prosthesis at 1- and 2-years follow up. **Participation level (1 study Hagberg 2008)** Before BAP: 11 of the 18 participants worked, 2 years after BAP use 10 of the 18 participants worked (reason decrease; loosening of the implant). No difference reported	
Hagberg 2020	**Q-TFA at 7-year follow up** **Q-TFA prosthetic use score** (0 to 100): n=54, mean (SD; range) 85 (25.0; 3 to 100), p=0.24 **Q-TFA prosthetic mobility score** (0 to 100): n=54, mean (SD; range) 67 (17.8; 22 to 95), p=0.007 **Q-TFA problem score** (100 to 0): n=54, mean (SD; range) 17 (10.8; 0 to 44), p=0.34 **Q-TFA global score** (0 to 100): n=54, mean (SD; range) 74 (20.6; 17 to 100), p=0.047 **Prosthetic activity grade compared with baseline n (%)**	**Mechanical complications** leading to change in abutment or abutment screw **% (n)** 0 complications: 45% (50 out of 111) 1 complication: 13.5% (15 out of 111) 2 to 5 complications: 22.5% (25 out of 111) 6 to 10 complications: 9% (10 out of 111) More than 10 complications: 10% (11 out of 111) mean (SD; range) 3.3 (5.76; 0 to 26) **Fixture survival** (leading to change in abutment and/or abutment screw**)** At 2 years (n=90): 81% (95% CI 71% to 88%)

	At 2 years (n=85): 50 (59) higher score; 32 (38) equal score; 3 (4) lower score; p<0.001 At 5 years (n=62): 42 (68) higher score; 19 (31) equal score; 1 (2) lower score; p<0.001 At 7 years (n=54): 36 (67) higher score; 17 (31) equal score; 1 (2) lower score; p<0.001 At 10 years (n=32): 22 (69) higher score; 6 (19) equal score; 4 (13) lower score; p<0.001 At 15 years (n=11): 5 (45) higher score; 6 (55) equal score; p=not reported **Change in answer to the single Q-TFA question on people's overall situation as an amputee compared with baseline, n (%):** At 2 years (n=81): 62 (77) better score; 14 (17) equal score; 5 (6) worse score; p<0.001 At 5 years (n=60): 47 (78) better score; 10 (17) equal score; 3 (5) worse score; p<0.001 At 7 years (n=52): 40 (77) better score; 11 (21) equal score; 1 (2) worse score; p<0.001 At 10 years (n=29): 21 (72) better score; 6 (21) equal score; 2 (7%) worse score; p<0.001 At 15 years (n=11): 7 (64) better score; 3 (27) equal score; 1 (9) worse score; p= not reported.	At 7 years (n=55): 32% (95% CI 22% to 43%) At 15 years (n=14): 14% (95% CI 6% to 26%) **Implant replacement and/or refitting** (n=111, follow up 15 years) **Implant revisions** % (n): 16% (18 out of 111) 6% (7 out of 111) due to infection, 5% (6 out of 111) due to aseptic loosening and 5% (5 out of 111) due to fractures **Revision-free survival of the fixture**: At 2 years (n=90): 92% (95% CI 85 % to 96%) At 7 years (n=55): 89% (95% CI 80 % to 94%) At 15 years (n=14): 72% (95% CI 57 % to 83%)
Thouvenin 2023	**Q-TFA at last follow up (mean 9.4, median 8, range 6 to 15) years (n=20 BAP)** **Prosthetic use score** Mean (SD): from 54.8 (26.0) to 91.8 (22.7) Mean difference: +36.5, p<0.001	**Mechanical complications % (n=17)** Total: 59% (10 out of 17), number of events=44 Abutment: 59% (10 out of 17), number of events=43 Intramedullary screw: 6% (1 out of 17), number of events= 1 Bone fractures: 12% (2 out of 17), number of events=2

	Prosthetic mobility score Mean (SD): from 66.8 (19.1) to 82.9 (20.7) Mean difference: +16.1, p<0.001 **Problem score** Mean (SD): from 30.4 (8.2) to 10.2 (5.4) Mean difference: −20.3, p<0.001 **Global score** Mean (SD): 41.7 (17.1) to 71.8 (18.6) Mean difference: +29.9, p<0.001 After 2 years, 75% (n=13) of the people participated in a professional activity; 50% (n=8) participated in a sports activity 12 people referred to their prosthesis using the term 'it's a part of me'	**Infections** Total: 7 6% (13 out of 17), number of events=37 Stage 1 (incisional discharge/fistula): 65% (11 out of 17), number of events=25 (68%) Stage 2: 18% (3 out of 17), number of events=4 Stage 3: 23% (4 out of 17), number of events=6 Stage 4: 12% (2 out of 17), number of events=2 Most treated on an outpatient basis, 8 required hospitalisation Stage 1 had antibiotic therapy; stage 2 to 3 had surgical debridement, abutment change and systemic antibiotic therapy) and stage 4 had implant removal, surgical debridement and antibiotic therapy Stump revision (for excessive soft tissue): 35% (6 out of 17), number of events=10 Neuroma surgery: 29% (5 out of 17), number of events=6 **Implant survival rate** Removal rate: 30% (6 out of 20) 2 were removed at 2 and 3 years due to aseptic loosening or non-osseointegration, which caused pain while walking. 4 were removed because of infection (1 for complications in the stump after 1 year, 3 at 9, 10, and 11 years for chronic infection and permanent pain) The Kaplan–Meier survival curve showed implant survival rates of 90% at 2 years, 70% at 10 years, and 60% at 15 years.

Hollewarth 2020	No efficacy outcomes were reported	**Periprosthetic fractures** Overall rate 4.2% (22 out of 518) Femoral OI 6.3% (22 out of 347) Location of the fracture: Neck of femur 2 Intertrochanteric 14 Subtrochanteric 6 Location relative to implant within 2 cm of the proximal tip of the implant 86.4% (19 out of 22) more than 2 cm proximal of the tip 9% (2 out of 22) more than 2 cm distal of tip 5% (1 out of 22) Mechanism of injury Ground level fall 86% (19 out of 22) Twist 9% (2 out of 22) Kicking 5% (1 out of 22) Implant used for fixation. Dynamic hip screws 45% (10 out of 22) Reconstruction plates 41% (9 out of 22) Blade plate 5% (1 out of 22) Cannulated screws 5% (1 out of 22) Extension nail 5% (1 out of 22) No OI implants required removal

		Prosthesis use for more than 16 hours daily before OI 14% (3 out of 22) post fracture mobility 82% (18 out of 22) People with K-level more than 2 Before OI 23% (5 out of 17) Post fracture 100% (22) Regression analysis identified a 3.89-fold increased risk of fracture for females (p=0.007) and a 1.02-fold increased risk of fracture per kg above a mean of 80.4 kg (p=0.046)
Örgel 2022	No efficacy outcomes were reported	**Periprosthetic fractures: 10.7% (15 out of 140)** Cause of fracture Slipped 13% (2 out of 15) Stumbling 33% (5 out of 15) Malfunction of the prosthesis 6.7% (1 out of 15) Intraoperative fracture (needed no surgical intervention) 46.7% (7 out of 15) Location of fracture Femur neck 2 Intertrochanteric 4 Subtrochanteric 2 Longitudinal split of the femur 5 Distal femur 2 Time to fracture mean 21.8 months

		Treatment of fracture Non-operative 53% (8 out of 15) Dynamic hip screw 46.7% (7 out of 15) 14 healed with no complications after 3 months. One postoperative fracture developed a clinically asymptomatic firm non-union. No devices were removed **Outcomes in periprosthetic facture group compared with control group (with no fractures, n=19) after OI treatment** There was no significant difference for PMQ and K-level between the fracture and control group at follow-up times. However, a significant increase of the PMQ ($p<0.001$) and K-level ($p<0.001$) was observed after OI treatment compared with baseline in both groups. The subgroup analysis showed a significant increase of the PMQ and K-level for both normal weight less than 25 kg/m^2 ($p=0.002$) and overweight more than 25 kg/m^2 people ($p<0.001$).
Welke 2023	**QOL and mobility assessment (6.6 years in BAP group)** **SF-36** **PCS, mean (SD)** BAP group: 46.3 (8.1) Socket group: 46.9 (7.0) p=0.892 **MCS, mean (SD)**	No safety data

	BAP group: 50.2 (7.3) Socket group: 53.7 (3.4) p=0.293 **Q-TFA** **Global score, mean (SD)** BAP group: 69.6 (19.0) Socket group: 74.0 (12.5) p=0.354 **Problem score, mean (SD)** BAP group: 10.3 (7.9) Socket group: 17.3 (11.2) p=0.063 **Prosthetic mobility score, mean (SD)** BAP group: 89.2 (12.7) Socket: 84.8 (12.8) p=0.493 **Prosthetic use scores, mean (SD)** BAP group: 85.0 (20.2) Socket group: 82.1 (13.1) p=0.745 **Functional outcomes** **6MWT, mean (SD)** BAP group: 321.7 (74.0) metres Socket group: 315.5 (70.9) metres	

	p=0.876 **TUG performance, mean (SD)** BAP group: 11.0 (3.3) seconds Socket group: 11.2 (2.6) seconds p=0.626 **Gait analysis.** **ROM** **Hip flexion/extension, mean (SD)** BAP group: 48.2 (6.2), socket group: 44.3 (7.4); p=0.064 **Abduction** BAP group: 23.2 (8.2), socket group: 18.0 (5.5); p=0.03 **Knee flexion/extension, mean (SD)** BAP group: 60.1 (9.9), socket group: 55.6 (11.6), p=0.347 **Abduction** BAP group: 12.7 (5.4), socket group: 6.7 (3.0), p=0.000 **Ankle flexion/extension, mean (SD)** BAP group: 17.5 (4.1), socket group: 15.5 (4.0), p=0.144 **Abduction** BAP group: 8.2 (4.2), socket group: 4.6 (2.1), p=0.003	

	Walking speed, mean (SD) BAP group: 1.15 ± 0.23 m/second Socket group: 1.13 ± 0.25 m/second (p=0.843). **Step width, mean (SD)** BAP group: 0.19 (0.04) metres, Socket group: 0.24 (0.04) metres, (p=0.001).	

Procedure technique

Three different implant systems were used in most of the studies. Evidence was mainly on the latest version of the following systems:

- OPRA implant system (press-fit and screw design, made of titanium in Sweden)
- Endo-Exo-Femur-Prosthesis (press-fit design made of cobalt chromium molybdenum alloy, sealed with a titanium-niobium layer in Germany), and
- OGAP-OPL (press-fit design and made of titanium in Australia).

These implant systems have undergone several design and material changes.

Two stages of surgery were common and the time between the first and the second surgery ranged from 4 to 8 weeks for the press-fit implants (OGAP-OPL and EEFP) and 6 months for the OPRA system (abutment that is press-fit and an abutment screw). Healing period, and time to load the prosthesis varied among the implant systems.

Efficacy

Functional outcomes

6MWT

In a HTA of 9 observational studies, 2 studies reported a statistically significant improvement in 6MWT scores. One of the prospective case series (van de Meent 2013 with ILP implant), reported a statistically significant change in mean score from 321 m before the procedure to 423 m at 1-year follow up (p=0.002). In another prospective case series (Al Muderis 2016d, with ILP and OGAP-OPL implants), the mean scores also improved in people who used a socket prosthesis from 281 m at baseline to 419 m at mean 1.8 years follow up

(p<0.001). Wheelchair users reported a mean score of 411 m (but the preoperative score and p-value were not reported; Ontario Health 2019).

A systematic review of 17 observational studies on OI implants for lower- and upper-limb amputation reported that the average value of 6MWT was 388 m (Balzani 2020).

In a cross-sectional observational study of 20 people with TFA and BAP comparing 17 people with TFA and socket prosthesis, the mean walking distance did not significantly differ between the groups after 6 minutes (BAP group 321.7 m, socket group 315.5 m, p=0.876; Welke 2023).

TUG test

In the HTA of 9 observational studies, 2 studies reported a statistically significant improvement in TUG scores. In one of the prospective case series (van de Meent 2013 with ILP implant), the mean score improved from 15.2 seconds before the procedure to 8.1 seconds at 1 year follow up (p=0.002). In another prospective case series (Al Muderis 2016d, with ILP and OGAP-OPL implants), the mean scores also improved for socket-prosthesis users from 14.59 seconds before the procedure to 8.74 seconds at mean 18 years follow up after the procedure (p<0.01). Wheelchair users had a follow-up score of 9.0 seconds, but the preoperative score and p-value were not reported (Ontario Health 2019).

The systematic review of 17 studies reported that the average value of TUG score was 11.5 seconds (Balzani 2020).

In the cross-sectional observational study of 20 people with TFA and BAP comparing 17 people with TFA and socket prosthesis, there was no statistically significant difference in TUG score between the 2 groups (BAP group 11 seconds, socket group 11.2 seconds, p=0.626; Welke 2023).

In a systematic review of 7 studies in people with a lower-extremity amputation using bone-anchored prostheses compared with socket prostheses, 1 cohort study (van de Meent 2013 with ILP implants and rehabilitation) reported that walking ability improved significantly 1 year after BAP use compared with use of a socket prosthesis, both in terms of distance covered in 6 minutes and time needed to get up from a chair, walk 3 m up and down a walkway and sit again. Two cohort studies (van de Meent 2013, Hagberg 2014 with OPRA implant and rehabilitation) found that use of a BAP reduced the energetic cost of walking significantly compared with use of a socket prosthesis at 1 and 2 years follow up. In the systematic review, 1 study (Hagberg 2008, with OPRA implants and rehabilitation) reported no difference in participation (activity) level (before BAP 11 of the 18 people worked, and at 2 years after BAP use 10 of the 18 people worked; Leijendekkers 2017).

In the same systematic review, 1 cross-sectional study (Hagberg 2005 with OPRA implants and rehabilitation) reported that using a BAP was associated with less discomfort when sitting than use of a socket prosthesis. Discomfort when sitting was reported in 44% (n=19) in the socket group and was common in people with less than 90 degrees of hip flexion motion (p=0.025). In the BAP group, no subject had less than 90 degrees of flexion and 5% (n=1) reported discomfort when sitting (Leijendekkers 2017).

AMP

In the HTA, no studies reported on AMP. But, 1 prospective case series included in the HTA (Al Muderis 2016d) reported on K-levels based on previously reported AMP scores. K-level improved in 60% of people and was unchanged in 40% (p=0.001; Ontario Health 2019).

ROM

In the HTA, none of the studies reported on changes in ROM.

In the systematic review of 7 studies in people with a lower-extremity amputation using bone-anchored prostheses compared with socket prostheses, 1 cross-sectional study (Hagberg 2005, with OPRA implants and rehabilitation) reported that range of hip motion was lower with socket prosthesis compared with BAP use at 2 and 10 years follow up. Another cross-sectional study (Frossad 2010, with OPRA implants and rehabilitation) assessing temporal gait variables (cadence, duration gait cycle and duration support phase) reported that BAP users had a gait more similar to healthy people than socket prosthetic users at 1-year follow up. Another cohort study (Tranberg 2011, with OPRA implants and rehabilitation) assessing gait kinematics in the sagittal plane found that during the stance phase, users of a BAP increased hip extension and decreased anterior pelvic tilt compared with a socket-prosthesis users and are more similar to that of healthy people (Leijendekkers RA 2017).

In the cross-sectional observational study of 20 people with TFA and BAP comparing 17 people with TFA and socket prosthesis, statistically significant differences were observed in the abduction ROM for the hip, knee and ankle between the 2 groups (hip: BAP group 23.2, socket group: 18.0, p=0.03; knee BAP group: 12.7, socket group: 6.7, p=0.000; ankle: BAP group: 17.5, socket group: 15.5, p=0.144; Welke 2023).

HRQOL

Q-TFA

In the HTA of 9 studies, 3 studies reported a statistically significant improvement in Q-TFA scores. In 1 of the prospective case series (Brånemark 2014, with OPRA implant system) the mean score for prosthetic use increased from 47 (of possible 100) before surgery to 79 at 2-year follow up ($p<0.001$). Other domains (mobility, problems, and global health) also improved significantly ($p<0.001$). Another prospective case series (van de Meent 2013 with ILP implant) reported that prosthetic use improved significantly from 56 hours to 101 hours per week

(p<0.001), and the global scores also significantly improved (p=0.001, other domains were not reported). The third study (Al Muderis 2016d) only reported scores for global health, which showed a statistically significant improvement (p<0.001; Ontario Health 2019).

In the systematic review of 17 studies, the postoperative mean score of Q-TFA was 73.8 (Balzani 2020).

In the systematic review of 7 studies in people with a lower-extremity amputation Q-TFA prothesis use score (in 3 cohort studies) improved significantly with BAP compared with socket prosthesis at 1 year (van de Meent 2013 with ILP implant and rehabilitation, Brånemark 2014 with OPRA implant and rehabilitation) and 2 years follow up (Hagberg 2008 with OPRA implant). The problem score (in 2 cohort studies: Hagberg 2008, Brånemark 2014) at 1 year follow up and global score (in 3 cohort studies: van de Meent 2013, Brånemark 2014, Hagberg 2008) at 2 years follow up improved significantly with use of BAP compared with socket prosthesis. Three cohort studies found that using a BAP resulted in significant improvements in overall mobility score, capability sub-score and walking habit sub-score compared with socket prostheses use at 1 year (Brånemark 2014) and 2 years (Brånemark 2014, Hagberg 2008) follow up, but there was no change in walking aid sub-score at 2 years follow up (Leijendekkers RA 2017).

In a prospective cohort study of 111 people with unilateral TFA who had BAP (with OPRA implant system), the Q-TFA scores demonstrated significantly more prosthetic use, better mobility, fewer problems, and an improved global health at 2, 5, 7, and 10 years compared with baseline (p<0.001 for all). At 15 years follow up, the problem score (p=0.020) and global score (p=0.004) significantly improved from baseline. At 7 years follow up (n=55), a higher activity grade (p=0.002) and higher prosthetic mobility score (p=0.007) and global scores (p=0.047) were reported in the group with ‘any mechanical complication’ (n=37) compared with those with ‘no mechanical complication’ (n=18; Hagberg 2020).

In a retrospective cohort study of 17 people (with 20 BAPs) at a mean follow up of 9.4 years, all Q-TFA scores improved statistically significantly. The mean prosthetic use score increased from 54.8 to 91.8 ($p<0.001$), prosthetic mobility score from 66.8 to 82.9 ($p<0.001$) and global score from 41.7 to 71.8 ($p<0.001$). The mean problem score decreased from 30.4 to 10.2 ($p<0.001$). After 2 years, 75% (n=13) of the people participated in a professional activity and 50% (n=8) participated in a sports activity (Thouvenin 2023).

In the cross-sectional observational study of 20 people with TFA and BAP comparing 17 people with TFA and socket prosthesis, the Q-TFA global score did not significantly differ between groups (BAP group 69.6, socket group 74.0, $p=0.354$). No statistically significant differences were found between the groups for the subscores. There were no significant differences reported for prosthetic mobility score (BAP group 89.2, socket group 84.8, $p=0.493$) and prosthetic use scores (BAP group 85, socket group 82.1, $p=0.745$) in both groups, respectively (Welke 2023).

SF-36

In the HTA of 9 studies, 2 studies reported data on the SF-36 health survey, a generic measure of QOL. One prospective case series (Brånemark 2014, with OPRA implant system) reported on all subscales of the SF-36. The improvement in QOL after DSF with an OI implant was significant for the domains of physical functioning and role-physical and PCS ($p<0.001$) but there was no statistically significant improvement for other subscales (bodily pain, general health, vitality, social functioning, role-emotional, mental health). The mean scores for the MCS declined by 3 points, but this result was not statistically significant. Another prospective case series (Al Muderis 2016d, with ILP and OGAP-OPL implant) reported only on the PCS score, which showed a statistically significant improvement (baseline 37.09 to 47.29 at follow up, $p<0.001$) but did not report scores for any of the other subscales of the survey (Ontario Health 2019).

In the systematic review of 17 studies, the most common clinical scores used were MCS and PCS of SF-36 and the postoperative mean values of MCS and PCS related to lower limb were 55.1 and 45.4 respectively (Balzani 2020).

In the systematic review of 7 studies in people with a lower-extremity amputation using BAP compared with socket prostheses, the scores of physical health (physical functioning score, role-physical functioning score and PCS; assessed using SF-36 in 2 cohort studies, Hagberg 2008, Brånemark 2014 both with OPRA implants) improved significantly at 1 year and 2 years follow up with use of a BAP compared with socket prostheses use. SF-36 physical bodily pain subscale score improved significantly using BAP compared with socket prosthesis in 1 study at 1- and 2-years follow up (Hagberg 2008) but reported no change in another study at 1 year follow up (Brånemark 2014). Scores on other SF-36 subscales (physical general health, all mental health subscales) did not change significantly after BAP at 1- and 2-years follow up. One study (Hagberg 2014 with OPRA implant) using SF-6D reported an improvement in general health status at 2 years follow up using BAP compared with socket-prosthesis use (Leijendekkers RA 2017).

In the cross-sectional observational study of 20 people with TFA and BAP comparing 17 people with TFA and socket prosthesis, the PCS and MCS scores did not significantly differ between the groups (PCS: BAP group 46.3, socket group 46.9, p=0.892; MCS: BAP group 50.2, socket group 53.7, p=0.293; Welke 2023).

Safety

Superficial infection

In the HTA of 9 studies, 5 studies reported superficial infections. In 3 prospective case series the rates of 1 or more superficial infections ranged from 28% to 55% at mean 1.2 to 2.8 years follow up (Brånemark 2014, with OPRA implant system,

Al Muderis 2016c with ILP, Al Muderis 2016d with both ILP and OGAP-OPL implants). In another retrospective case series (Al Muderis 2017e with OGAP-OPL), 45% (10 out of 22) people developed superficial infection at a mean follow up of 1.2 years, 3 of which were severe. Refashioning surgery (surgery performed on soft tissue) to control the infection was performed in 2 studies. The retrospective case series by Juhnke (2015) with ILP reported no superficial infections (Ontario Health 2019).

In a systematic review of 12 studies, the occurrence of infection was reported in 73% (11 out of 15) of cohorts assessed. The overall infection rate ranged from 23% to 49% in people who had screw implants compared with 0% to 77% in those who had press-fit implants and 0% in those who had the Compress implant (in 1 study). Soft-tissue infections in the skin-penetrating area (grade 1 to 2) occurred in 28% people who had screw implants and 0% to 57% of people who had press-fit implants, respectively. Bone infection (grade 3) occurred in 5% to 13% of those who had screw implants and 0% with press-fit implants, respectively. Infections resulting in implant loosening (grade 4) occurred in 8% to 11% of those who had screw implants and 3% to 29% of those who had press-fit implants, respectively. Analysis of infections rates according to the level of amputation showed that in people with TFA treated with press-fit implants, the overall infection rate ranged from 0% to 77% and in those with upper extremity amputation it was 44%. The rate of soft-tissue infections (grade 1 to 2) ranged from 0% to 57% in those with TFA treated with press-fit implants and 28% in those with upper extremity amputation. The rates of infection in people with TFA who had screw implants or those who had TTA was unknown (Atallah 2018).

In the systematic review of 17 observational studies, infections were evaluated in 16 studies. The overall rate of infections was 32% (201 out of 626 people); and of these 81% (163 out of 201) were superficial infections (Balzani 2020).

In the retrospective cohort study of 17 people (with 20 BAPs), the overall infection rate was 76% (13 out of 17), with 37 events. Of these, 68% (n=25) were stage 1 infections, 11% (n=4) were stage 2 infections, 16% (n=3) were stage 3 infections, and 12% (n=2) were stage 4 infections (involving septic loosening of the implant). Most infections (n=29) were treated on an outpatient basis without (n=22) or with (n=7) surgery; and 8 (22%) needed hospitalisation and postoperative care (Thouvenin 2023).

Deep or bone infection

In the HTA, one prospective case series (Brånemark 2014 with OPRA implants) reported that 8% (4 out of 51) of people had deep infection at 2 years follow up. The deep infection in one implant led to loosening of the implant, which was extracted 6 months after the second-stage surgery. Another retrospective case series with a mean 7.9-year follow up (Tillander 2017b, with OPRA implants) reported that osteomyelitis developed in 17% (16 out of 96) of people at a median time of 2.6 years from implantation. Of these, 13% (9 out of 69) of people had received an OI during and after the OPRA rehabilitation protocol. All were treated with antibiotics and devices were extracted in 10 and reimplanted in 1 person. Osteitis (treated with antibiotics) was reported in 6% (6 out of 96) of people. Authors also reported a 10-year cumulative risk of implant-associated osteomyelitis of 20% (95%CI 12 to 33). Another prospective case series (Tillander 2010a) with OPRA implants in 39 people with upper and lower-limb amputations, reported that 18% (6 out of 32) of people who had TFA developed a deep infection at mean 2.8 years follow up, all of whom needed surgical intervention. One prospective case series with ILP implants (Al Muderis 2016c) reported that 5% (4 out of 86) of people developed an abscess at a median follow up of 2.8 years. All were treated with antibiotics and surgical debridement. However, no deep infection was reported for ILP implants in another retrospective case series of 39 TFA with a mean follow up of 2.7 years (Juhnke 2015). In another prospective case series (Al Muderis 2016d) 6% (3 of 50) of

people who had ILP or OGAP-OPL implants, developed deep infection at a mean follow up of 1.8 years. All were treated with antibiotics and surgical debridement (Ontario Health 2019).

In the systematic review of 12 studies, bone infection (grade 3) occurred in 13% of people with TFA treated with screw implants and 6% of those with upper extremity amputation. Rates in those with TFA treated with press-fit implants or in those with TTA are unknown. Implant loosening due to infection (grade 4) occurred in 0% to 11% of people with TFA (screw-fit: 11%, press-fit: 0% to 3%), 29% of people with TTA and 11% of those with upper extremity (trans-humeral) amputation (Atallah 2018).

In the systematic review of 17 observational studies, infections were evaluated in 16 studies. The overall rate of infections was 32% (201 out of 626 people); and of these 19% (38 out of 201) were deep infections localised at the bone or causing septic disease (Balzani 2020).

Bone fracture

In the HTA of 9 studies, one prospective case series (Brånemark 2014 with OPRA implant), reported that there were no periprosthetic fractures (around the implant) during the 2-year study period. Four people (8%) had fractures in locations other than the femoral bone. One retrospective case series (Jhunke 2025) reported 2 periprosthetic fractures at 2.5 to 3 years after implantation, and another prospective case series (Al Muderis 2016c) reported 3 femoral fractures at a mean follow up of 2.8 years. One prospective case series (Al Muderis 2016d with both ILP and OGAP-OPL) reported 4 (8%) periprosthetic fractures at a mean follow up of 1.8 years. The retrospective case series on OGAP-OPL alone (Al Muderis 2017e) did not report any fractures at 1 year follow up (Ontario Health 2019).

In the systematic review of 12 studies, the incidence of periprosthetic bone fracture was reported in 60% (9 out of 15) of cohorts. It ranged from 0% to 10% in those who had a press-fit implant (in 7 studies), 18% in those who had a Compress implant (in 1 study) and 0% in people who had a screw implant. In 3 studies, the cause of bone fracture reported was falls. No fractures occurred in people with upper extremity implants and those with TTA who had bone-anchored implants (Atallah 2018).

In the systematic review of 17 studies, postoperative complications were reported in 13 studies and the overall rate was 75% (164 out of 216 implants). Periprosthetic fractures or fractures above the implant were 18% and less frequent (Balzani 2020).

In a retrospective review of 518 OI procedures in 458 people, periprosthetic fractures were reported in 4% (22 out of 518) of procedures. 86% (19 out of 22) of these occurred within 2 cm of the proximal tip of the implant and after a fall. There were no spontaneous fractures. These were most commonly fixed with dynamic hip screws (10) and reconstruction plates (9). None of the implants needed removal. The mobility (K-level) before OI improved to and maintained to a K-level of 2 or higher after fixation of the fractures. All fractures united and 82% (18 out of 22) reported using the prosthesis more than 16 hours daily (Hollewarth 2020).

In another retrospective study of 140 people with OI after TFA, periprosthetic fractures were reported in 11% (15 out of 140) of people. Five of these were intraoperative (not needed any surgical treatment) and 10 were post operative. All these were treated with implant retaining osteosynthesis and no devices were removed. Fourteen fractures healed without complications after a mean of 3 months and 1 postoperative fracture developed a clinically asymptomatic firm non-union. When outcomes in the periprosthetic fracture group (n=15) were compared with the control group (no fractures, n=19), there was no statistically

significant difference for PMQ and K-level between the 2 groups at follow-up times. However, a significant increase of the PMQ ($p<0.001$) and K-level ($p<0.001$) was observed after OI treatment compared with baseline in both groups. The subgroup analysis showed a significant increase of the PMQ and K-level for both normal weight less than 25 kg/m^2 ($p=0.002$) and overweight more than 25 kg/m^2 people ($p<0.001$; Örgel 2022).

Implant removal

In the HTA, 5 studies reported that implants were explanted due to deep infection, failed osseointegration, implant breakage, and fatigue failure (damage to the device due to repeated loading and unloading). Two of these studies with OPRA implant system (Brånemark 2014, Tillander 2010) reported implant removals due to deep infection in 1 each and failed OI in 2 people during 2 years follow up. Two studies with ILP implants (Jhunke 2015, Al Muderis 2016c) reported failed integration in 2 people and implant breakage in 1 person at mean 2.7 years or median 2.8 years follow up. Another prospective case series of 50 people both with ILP and OGAP-OPL implants (Al Muderis 2016d) reported failed integration in 1 person and fatigue failure in another person at mean 1.8 years follow up (Ontario Health 2019).

In the systematic review of 12 studies (15 cohorts assessed), the incidence of explantation (for infection, device breakage, bone fracture and implant loosening) ranged from 14% to 19% in people who had a screw implant, from 0% to 57% in those who had a press-fit implant and was 9% in those who had the Compress implant (in 1 study). The explantation rate in those with TFA was 17% to 18% with a screw implant, 0% to 13% with a press-fit implant and 9% with a Compress implant. Implant loosening and infection were other reasons for explantation of transfemoral implants and occurred in both the screw and press-fit implants but not the Compress implant. Also, the rate of explantation in those with THA was

similar (17% to 19%) with screw implants. The rate of explantation was much higher in people with TTA ranging from 42% to 57% (Atallah 2018).

In the retrospective cohort study of 17 people (with 20 BAP) with a mean follow up of 9.4 years, 30% (6 out of 20) of implants required removal. Two were removed (at 2 and 3 years) for aseptic loosening or non-osseointegration, which caused pain while walking. Four implants were removed because of infectious complications (1 removed after a year for complications in the stump during load bearing, 3 removed at 9, 10, and 11 years for chronic infection and permanent pain). The Kaplan–Meier survival curve showed implant survival rates of 90% at 2 years, 70% at 10 years, and 60% at 15 years (Thouvenin 2023).

Reimplantation

In the systematic review of 12 studies (15 cohorts assessed), the incidence of reimplantation was reported in 87% (13 out of 15) of cohorts. It was successful in 100% of people who had the Compress implant (in 1 study), in 6% to 40% of people who had a screw implant (in 4 studies) and 25% to 100% of people who had press-fit implants (in 8 studies), respectively. Reimplantation was successful in 33% of people with THA (Atallah 2018).

The prospective case series of 111 people reported that 16% (18 out of 111) of people had implant revisions at 15 years follow up. Of these 6% (7 out of 111) were due to infection, 5% (6 out of 111) were due to aseptic loosening and 5% (5 out of 111) were due to fractures. Revision-free survival of the implant ranged from 92% at 2 years to 72% at 15 years follow up. Survival of the implant needing a change of the abutment, abutment screw or both ranged from 81% at 2 years to 14% at 15 years (Hagberg 2020).

Intramedullary and extramedullary breakage

In the HTA, 4 included studies reported breakage of intramedullary or extramedullary components of the osseointegrated prosthetic implant systems. In

1 prospective case series (Brånemark 2014 with OPRA implants), 8% (4 out of 51) of people needed exchange of abutment or abutment screws. In another prospective case series (Al Muderis 2016c with ILP implants), 2 people (2%) had implant breakage and 29% (25 out of 86) had breakage of the safety part that is added to the system to avoid the risk of fracture in case of excessive load. Three studies reported that no intramedullary breakage occurred during follow up (Brånemark 2014, Junke 2015 with ILP, Al Muderis 2017e with OGAP-OPL). (Ontario Health 2019).

In the systematic review of 12 studies (15 cohorts assessed), device breakage (due to fractures of the intramedullary implant, of the abutment [screw] and of the dual-cone adaptor [press-fit]) was reported in 53% (8 out of 15) of the cohorts. Device breakage occurred in 27% to 45% of people with screw implant, 0% to 31% of those with press-fit implants, and 0% with Compress implant, respectively. No intramedullary device breakages were reported in people with TFA treated with screw implants, while it occurred in 1% of those with TFA treated with press-fit implants. No device breakages were reported in those with TTA with BAP. The incidence of intramedullary device breakage was 27% in those with transradial screw implants (Atallah 2018).

In the systematic review of 17 studies, the most common implant-related complication rate, including breakage was 27% (Balzani 2020).

Non-infectious soft- tissue and bone complications

In the HTA, 2 studies reported on non-infectious soft-tissue and bone complications (Junke 2015 with ILP implant and Al Muderis 2016d with ILP and OGAP-OPL implants). These included hypergranulation at the stoma in 20% (17 out of 86) of people, which was treated with chemical cauterisation, hypertrophic bone formation in 10% (9 out of 86) of people, redundant soft tissue in 16% (14 out of 86) of people, which was excised, and rounding and resorption of distal femoral cortex in 20% (17 out of 86) of people (Al Muderis 2016d). Excessive

granulation tissue at the stoma was reported in 1 person, which was removed (Jhunke 2015). It was not clear if other studies reported these adverse events (Ontario Health 2019).

In the systematic review of 12 studies (15 cohorts assessed), soft-tissue complications such as stoma hypergranulation was reported in 44% of TFAs with screw implants, in 3% to 20% TFAs with press-fit implants and 44% of those with THA treated with screw implants (in 1 study). Stoma-redundant tissue was reported in 3% to 16% TFAs with press-fit implants and 9% with Compress implants (Atallah 2018).

In the systematic review of 17 studies, complications assessed in 13 studies reported that the most common complication was stoma hypergranulation in 35% of people. Soft-tissue redundancy was reported in 8% of people (Balzani 2020).

The retrospective study of 17 people (20 BAPs) at a mean follow up of 9.4 years reported that 6 people had surgery for stump remodelling because of excessive soft tissue and 5 people underwent surgery for neuromas (Thouvenin 2023).

Implant loosening

In the systematic review of 12 studies (15 cohorts assessed), the incidence of implant loosening was reported in 60% (9 out of 15) cohorts. It ranged from 3% to 23% in people with screw implants (in 2 studies) and 0% to 29% in people with press-fit implants (in 4 studies), and 0% in those with the Compress implant (1 study), respectively. Implant loosening occurred in 0% to 3% in TFA with press-fit implants, 6% with screw implants; 29% of TTA with press-fit implants and in 13% and 23% of those with upper extremity implants (trans-humeral and thumb amputation treated with screw implants), respectively. Implant loosening was not reported in people with TRA (Atallah 2018).

In the systematic review of 17 studies, complications were analysed in 13 studies and aseptic loosening of the implant was reported in 8% of people (Balzani 2020).

Mechanical complications

In the prospective cohort study of 111 people, 55% (61 out of 111) of people had at least 1 mechanical complication resulting in a change of the abutments (Hagberg 2020).

In the retrospective cohort study of 17 people (20 BAPs) at a mean follow up of 9.4 years, 65% (11 out of 17) people had mechanical complications. Forty-three abutments were changed in 10 people, intramedullary screw changed in 1 and bone fractures treated in 2 people by osteosynthesis (Thouvenin 2023).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They listed the following anecdotal adverse events:

- 2 people ‘died by suicide after their bone-anchored implants had failed because of deep infection, and reimplantation had been refused’
- psychological issues
- osseointegrated components ‘dual-cone’ breakage.

They listed the following theoretical adverse events:

- likely increased risk of injury by being more active and could lead to falls and risk of bone fracture
- bone infections and risk of need for higher amputation
- ongoing management of stoma
- other medical issues and infection in the body.

Eight professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- Most of the evidence was on OI implants for people with above-the-knee amputation. A small number of people with below the knee amputation or upper extremity amputation were included.
- Systematic reviews and HTA included mainly observational studies with high risk of bias and some studies with the same patient populations.
- Follow up ranged from 1 to 15 years. But, long-term results are based only on a small number of people.
- Evidence was mainly on 3 implant systems (OPRA, ILP, OGAP-OPL). Several other OI implant systems are currently under development. These include ITAP (UK), POP (US), Compress (US) and the keep walking advanced (US).
- A 2-stage surgical procedure was commonly used, and this has been modified over time.
- The majority of the studies are done outside the UK, and it is not clear if these results might be generalisable to current practice in the UK.
- There are no RCTs comparing DSF with conventional or no prosthesis.
- Studies reporting on osseoperception are added to other relevant studies section.

Existing assessments of this procedure

The NHS England Clinical commissioning policy: direct skeletal fixation for transfemoral limb loss (adults) was published in 2023. It recommends that direct skeletal fixation is not used as an option in routine commissioning for transfemoral limb loss within the criteria set out in this document. The policy is restricted for use in adults to avoid disruption of the growth plate in younger people.

The NHS England Evidence Review: Direct skeletal fixation for transfemoral limb loss in adults was published in October 2022. The evidence included in this review is insufficient to draw conclusions about the clinical effectiveness and safety of DSF compared with no prosthetic use in people with transfemoral limb loss who are unable to tolerate conventional socket use.

The key limitation to identifying evidence on the effectiveness of DSF compared with no prosthetic use in people who are unable to tolerate conventional socket use is the lack of studies comparing DSF with no prosthetic use in this group. Five case series (3 prospective and 2 retrospective) were identified ranging in size from 50 to 111 people and reporting results at multiple time points up to 15 years. This very low certainty, non-comparative evidence in people with transfemoral limb loss who are unable to tolerate conventional socket use suggests that DSF improves functional outcomes as measured by the TUG test and 6MWT at 2 years, QOL as measured by the SF-36 and Q-TFA up to 10 years, mobility as measured by prosthetic activity grades up to 10 years and wheelchair use up to 3 years follow up. Across the studies, at different time points up to 15 years, rates of implant replacement, refitting or both ranged from 3% to 34%, and extraction due to infection ranged from 6% to 10%. Over half of people experienced an adverse event as reported by 1 study at 2 years, and across the studies the percentage of people experiencing infections at different time points up to 8 years ranged from 17% to 42%.

No evidence was identified for particular sub-groups of people who would benefit more from DSF.

Related NICE guidance

NICE guidelines

Rehabilitation after traumatic injury (2022) NG211. (Recommendation complex rehabilitation needs after traumatic injury.)

Professional societies

- British Orthopaedic Association
- British Limb Reconstruction Society
- British Society of Rehabilitation Medicine
- British Society of Physical and Rehabilitation Medicine
- British Association of Plastic, Reconstructive and Aesthetic Surgeons
- British Society for Surgery of the Hand
- British Association of Prosthetists and Orthotists (BAPO)
- Vascular Society of Great Britain and Ireland
- British Society for Chartered Physiotherapists in limb Absence Rehabilitation.

Evidence from patients and patient organisations

NICE received one submission from a patient organisation about direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.

NICE received 17 questionnaires from people who had the procedure (or their carers). See the patient commentary summary for more information.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the interventional procedures technical team and any relevant points have been taken into consideration when preparing this overview.

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8. Örgel M, Petri M, Ranker A et al. (2022) Management, outcome, and novel classification system of periprosthetic fractures in patients with

transcutaneous osseointegrated prosthetic systems (TOPS)-a retrospective cohort analysis. Arch Orthop Trauma Surg. 142 (7):1499-1509.

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Methods

NICE identified studies and reviews relevant to direct skeletal fixation of limb prostheses using intraosseous transcutaneous implants from the medical literature. The following databases were searched between the date they started to 24.06.2024: MEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- People with amputated upper or lower limbs.
- Intervention or test: Direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.
- If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Databases	Date searched	Version/files
MEDLINE ALL (Ovid)	24/06/2024	1946 to June 21, 2024
EMBASE (Ovid)	24/06/2024	1974 to June 21, 2024
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	24/06/2024	Issue 6 of 12, June 2024
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	24/06/2024	Issue 5 of 12, May 2024
International HTA database (INAHTA)	24/06/2024	-

Trial sources searched November 2023

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)

- General internet search

MEDLINE ALL search strategy

Bone-Anchored Prosthesis/
(Intraoss* adj4 Transcut* adj4 Amputat* adj4 Prosthes*).tw.
ITAP.tw.
(intraosse* or intra-osse* or intra osse*).tw.
Osseointegration/
(osseointegrat* or osseoanchor* or OI).tw.
((transcut* or transderm* or transhum* or bionic*) adj4 (implant* or prosthes*)).tw.
((skeleta* or bone*) adj4 (fixat* or anchor* or implant* or prosthes*)).tw.
((Osseo* or Bone*) adj4 (prosthes* or implant*)).tw.
(bone* adj4 anchor* adj4 (prosthes* or implant*)).tw.
or/1-9
exp Amputation/
exp Amputation Stumps/
Amputation surgical/
(Amputat* adj4 (limb* or digit* or finger* or thumb* or stump*)).tw.
(Disarticulat* or Hemipelvect*).tw.
or/12-15
11 and 17
OPRA Implant.tw.
OGAP-OPL.tw.
19 or 20
18 or 21
animals/ not humans/
22 not 23
limit 24 to ed=20231101-20240630

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (table 2 and table 3) are listed in table 5. Studies with fewer than 5 people were excluded.

Table 5 Additional studies identified

Article	Number of people and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Atallah R, van de Meent H, Verhamme L et al. (2020) Safety, prosthesis wearing time and health-related quality of life of lower extremity bone-anchored prostheses using a press-fit titanium osseointegration implant: A prospective one-year follow-up cohort study. PLoS One. 9;15(3): e0230027.	Cohort study n=91 people with lower-limb amputation treated with bone-anchored prostheses using titanium press-fit osseointegration implants (53, 16 and 21 OFI-C, OFI-Y and OTI), OFI-C indicated for a long femoral remnant, OFI-Y indicated for a short femoral remnant, or OTI. 1 year follow up.	Titanium osseointegration implants can be safely used within a 1-year follow-up period. The performance improved compared with the use of a socket-suspended prosthesis.	More comprehensive studies added to evidence summary.
Akhtar MA, Hoellwarth JS, Tetsworth K et al. (2022) Osseointegration following transfemoral amputation after infected total knee replacement: A case series of 10 patients with a mean follow-up of 5 years. Arthroplast Today. 21; 16:21-30.	Retrospective cohort study 10 people who had prior infected TKR had TFA and treated with TOFA press-fit implants systems. Follow up: 2 years	Transfemoral osseointegration confers significantly better mobility and QOL versus knee fusion or a TFA with traditional socket prostheses following infected TKR.	More comprehensive studies added to evidence summary.
Akhtar MA, Hoellwarth JS, Al-Jawazneh S et al. (2021) Trans-tibial	Case series	All people survived through 2 years and reported improvement in mobility and	More comprehensive studies added to

IP overview: Direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.

osseointegration for patients with peripheral vascular disease: A case series of 6 patients with minimum 3-year follow up. JB JS Open Access. 6(2): e20.00113.	n=6 people with peripheral vascular disease and TTA had osseointegration with press-fit custom implant. Follow up: 3 years	QOL. 3 people had superficial soft-tissue infections. One person died from cardiac causes.	evidence summary.
Atallah R, van de Meent H, Verhamme L et al. (2020) Safety, prosthesis wearing time and health-related quality of life of lower extremity bone-anchored prostheses using a press-fit titanium osseointegration implant: A prospective one-year follow-up cohort study. PLoS One. 9;15(3): e0230027.	n=90 people with lower-limb amputation treated with bone-anchored prostheses using titanium press-fit osseointegration implants OFI-C (n=53) indicated for a long femoral remnant OFI-Y (n=16) indicated for a short femoral remnant, or OTI (n=21). Follow up: 1 year	Titanium osseointegration implants can be safely used within a 1-year follow-up period. The performance improved compared with the use of a socket-suspended prosthesis.	More comprehensive studies added to evidence summary.
Atallah R, Li JJ, Lu W, Leijendekkers R et al. (2017) Osseointegrated Trans-tibial Implants in Patients with Peripheral Vascular Disease: A Multicenter Case Series of 5 Patients with 1-Year Follow up. J Bone Joint Surg Am. 99(18):1516-1523.	Case series n=5 people with peripheral vascular disease and TTA had osseointegration with press-fit custom implant. Follow up: 1 year.	The mobility of all people was improved (able to walk and perform daily activities). Four people were pain-free at 12 months. Two people had superficial soft-tissue infection.	More comprehensive studies added to evidence summary.
Al Muderis M, Lu W, Li JJ. (2017) Osseointegrated Prosthetic Limb for the treatment of lower limb amputations: Experience and outcomes. Unfallchirurg. 120(4):306-311.	Retrospective study n=22 people who received the OPL implant. Follow up: 1 year	The results demonstrate that osseointegration surgery using the OPL is a relatively safe and effective procedure for the reconstruction and rehabilitation of lower-limb amputees.	Study included in systematic reviews added to evidence summary

Al Muderis MM, Lu WY, Li JJ et al. (2018) Clinically Relevant Outcome Measures Following Limb Osseointegration; Systematic Review of the Literature. J Orthop Trauma; 32: e64–e75.	Systematic review 21 observational studies 788 lower-limb amputees, 709 OIs observed, and 79 prosthetic socket user controls. (Mainly transfemoral, only 2 studies on upper-limb amputations) Follow up: 1 to 2 years.	Randomised, long-term, trials are needed to prove efficacy of OI compared with socket prosthetic attachment. Osseointegration was equivalent to sockets in most studies. In some cases, it was superior. It is a promising alternative to socket prosthetic attachments for extremity amputees.	More comprehensive studies added to evidence summary.
Al Muderis M, Khemka A, Lord SJ et al. (2016) Safety of osseointegrated implants for transfemoral amputees: a two-center prospective cohort study. J Bone Joint Surg Am. 98(11):900-9.	Prospective cohort study n=86 people (91 implants) Level of amputation: transfemoral. Device used: ILP (press-fit OI) Median follow up 34 months.	Severe infections resulting in septic implant loosening are rare. Mild infection and irritation of the soft tissue in the skin-penetration area are common; these complications can be managed with simple measures. Protocols for adequate surgical management of the peri-implant soft tissue are essential.	Study included in systematic reviews added to evidence summary.
Al Muderis MA, Lu W, Glatt V et al. (2018) Two-stage osseointegrated reconstruction of post-traumatic unilateral transfemoral amputees. Mil Med. 183 (1):496-502.	Prospective case series n=37 post-traumatic unilateral transfemoral amputees. Device used: ILP (press-fit OI) 2-year follow up.	Clinical outcomes were significantly improved. All people were able to ambulate after osseointegrated reconstruction. Sixteen people experienced infection but were managed without implant removal. One periprosthetic fracture occurred due to increased activity and was revised.	Study included in systematic reviews added to evidence summary.
Brånemark R, Berlin O, Hagberg K et al. (2014) A novel osseointegrated percutaneous prosthetic	Prospective cohort study	Cumulative survival was 92%. The Q-TFA showed improved prosthetic use, mobility, global situation and	Study included in systematic reviews added to

system for the treatment of patients with transfemoral amputation: A prospective study of 51 patients. Bone Joint J. 96-B (1):106-13.	n=51 people with 55 TFAs had OPRA system. Follow up: 2 years	fewer problems (all p<0.001). The physical function SF-36 scores were also improved (p<0.001). Superficial infection 55%. The implant was removed in 4 people because of loosening.	evidence summary.
Brånemark RP, Hagberg K, Kulbacka-Ortiz K et al. (2019) Osseointegrated percutaneous prosthetic system for the treatment of patients with transfemoral amputation: A prospective five-year follow-up of patient-reported outcomes and complications. J Am Acad Orthop Surg. 15;27(16): e743-e751	Prospective cohort study n=51 people (55 legs) with TFA had OPRA system. Follow up: 5 years	Cumulative fixture survival rate was 92%, and the revision-free survival rate was 45%. 34 people had 70 superficial infections, 11 had 14 deep infections. 15 had mechanical complications. 4 fixtures were removed. S Significant improvements in use of the prosthesis, better mobility, fewer issues, and improved physical HRQOL (all p<0.0001) compared with baseline reported.	Study included in systematic reviews added to evidence summary
Black GG, Vaeth AM, Chen Y et al. (2023) Osseointegration for lower limb amputation: understanding the risk factors and time courses of soft-tissue complications. Ann Plast Surg. 90 (6S Suppl 5): S452-S456.	Retrospective analysis n=60 people (35 transfemoral and 25 TTAs). Follow up: 22 months	Postoperatively, 25 people developed soft-tissue infections, 5 developed osteomyelitis, 6 had symptomatic neuromas, and 7 required soft-tissue revisions. Soft-tissue infections were positively correlated with obesity and female sex.	More comprehensive studies added to evidence summary.
Corona, PS; Vargas Meouchi, EA; Garcia Hernandez, JM et al. (2024) Single stage transcutaneous osseo integrated prosthesis for above-knee amputations including an antibiotic-loaded hydrogel. Preliminary results of a new surgical protocol. Injury; 55 (4); 111424	Retrospective review of 11 above-knee amputations treated with single-stage transcoutaneous osseointegrated implant together with a rapid-resorbable hydrogel loaded with vancomycin and gentamicin.	The single-stage osseointegration protocol using a rapid-resorbable hydrogel loaded with vancomycin and gentamicin, yields low rates of implant-related deep infection. This protocol consistently delivers high rates of radiological osseointegration, with no hydrogel-associated complications.	More comprehensive studies added to table 2.

	24 months follow-up.		
Davis-Wilson HC, Christiansen CL, Gaffney BMM et al. (2023) Improvements in disability and function in people with lower-limb amputation one year after prosthesis osseointegration. Prosthet Orthot Int. 47(4):343-349.	Cohort study n=12 people (9 transfemoral and 3 TTAs underwent osseointegration with press-fit implants) Follow up: 1 year.	Participants reported less disability and greater function in their prosthesis post-osseointegration.	More comprehensive studies added to evidence summary.
Gaffney BMM, Davis-Wilson HC, Christiansen CL et al. (2023) Osseointegrated prostheses improve balance and balance confidence in individuals with unilateral transfemoral limb loss. Gait Posture.100:132-138.	Cohort study n=10 people with unilateral TFA had osseointegrated prosthesis.	Improvements in postural sway, reductions in gait variability, and greater balance confidence indicate that osseointegrated prostheses improve balance for people with unilateral TFA compared with socket prosthesis.	Biomechanical effect. More comprehensive studies added to evidence summary.
Geiger, Erik J. MD; Hoellwarth, Jason S et al. (2022) Robert MD. Osseointegration of the tibia after a primary amputation. JBJS Essential Surgical Techniques 12(4): p e22.00005,	Review	With the safety of osseointegration demonstrated and the high prevalence of TTAs, it is important that osseointegration be utilised in the rehabilitation and reconstruction offered to people undergoing TTA.	Review
Gerzina C, Potter E, Haleem AM et al. (2020) The future of the amputees with osseointegration: A systematic review of literature. Journal of Clinical Orthopaedics and Trauma 11, S142eS148	Systematic review 9 observational studies (211 to 242 people) 234 to 267 implants, mainly transfemoral, (only 4 transradial, 4 transulnar, 3 trans-humeral, and 1 trans-tibial). Follow up more than 12 months.	Osseointegration is an effective alternative to socket prosthesis in transfemoral amputees. Trans-tibial and upper extremity implants are underreported and clear indication for their effectiveness over socket prosthesis does not exist. Minor complications such as soft-tissue infections are common.	More comprehensive studies added to evidence summary.
Gholizadeh H, Abu Osman NA, Eshraghi A et al. (2014)	Systematic review	No clinical evidence was found as a standard system	More comprehensive

IP overview: Direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.

Transfemoral prosthesis suspension systems: a systematic review of the literature. Am J Phys Med Rehabil. 93:809-823.	n=16 studies (11 prospective and 5 surveys). Level of amputation: mainly transfemoral. Follow up varied.	of suspension and socket design for all transfemoral amputees. However, among various suspension systems for transfemoral amputees, the soft insert or double socket was favoured by most users in terms of function and comfort.	studies added to evidence summary.
Hagberg K, Haggstrom E, Uden M et al. (2005) Socket versus bone-anchored trans-femoral prostheses: hip range of motion and sitting comfort. Prosthetics and Orthotics International 29(2): 153–63.	Non-randomised comparative study n=63 people with unilateral TFA Socket prosthesis =68% (43 out of 63) Osseointegrated BAP OPRA= 32% (20 out of 63) Median follow up (for BAP): 5 years (range 3 to 10 years)	Transfemoral prosthetic socket significantly reduces the ROM of the hip and reported very few problems with discomfort when sitting.	Study included in systematic reviews added to evidence summary.
Hagberg K, Brånemark R, Gunterberg B et al. (2008) Osseointegrated trans-femoral amputation prostheses: prospective results of general and condition-specific quality of life in 18 patients at 2-year follow up. Prosthetics and Orthotics International; 32(1): 29 – 41.	Prospective case series n=18 people with TFA had OPRA OI implanted. Follow up: 2 years	7 out of 18 people used the OI prosthesis; 1 did not due to pain and loosening of the implant. Four of the scales of the SF-36 and all 4 scores of Q-TFA were statistically significantly improved at follow up showing superior general physical HRQOL, increased prosthetic use, better prosthetic mobility, fewer problems and a better global amputation situation.	Study included in systematic reviews added to evidence summary.
Hagberg K, Hansson E, Brånemark R. (2014) Outcome of percutaneous osseointegrated prostheses for patients with unilateral transfemoral amputation at two-year follow up. Arch	Prospective case-control study n=39 people with unilateral TFAs had OPRA OI implantation. Follow up: 2 years	Two years after intervention, people with a unilateral TFA treated with an OPRA implant showed important improvements in prosthetic function and physical QOL. However, walking aids used and the presence of	Study included in systematic reviews added to evidence summary.

Phys Med Rehabil. 95(11):2120–7.		phantom limb pain and pain in other extremities were unchanged.	
Hagberg K and Brånemark R (2009) One hundred patients treated with osseointegrated transfemoral amputation prostheses—rehabilitation perspective. Journal of Rehabilitation Research & Development, 46 (3), 331-344	n=100 people with 106 OI implants (OPRA) Follow up: 3 months to 17.5 years.	68 people are using their prostheses and 32 are not. The majority of treatment failures occurred in people before we established the OPRA protocol. The implementation of graded rehabilitation is considered to be of utmost importance for improved results.	Study included in systematic reviews added to evidence summary.
Hagberg K (2018): Bone-anchored prostheses in patients with traumatic bilateral transfemoral amputations: rehabilitation description and outcome in 12 cases treated with the OPRA implant system, Disability and Rehabilitation: Assistive Technology.	Prospective cohort study n=12 people with bilateral TFAs had OPRA implanted. Median follow-up time was 7 years (range 1 to 20 years).	Bone-anchored prostheses in people with bilateral TFAs resulted in more prosthesis use during everyday locomotion, due hypothetically to improved comfort while wearing prostheses.	Larger studies with longer follow up included in evidence summary.
Hagberg K, Ghasemi Jahani SA et al. (2022) Osseointegrated prostheses for the rehabilitation of patients with transfemoral amputations: A prospective ten-year cohort study of patient-reported outcomes and complications. J Orthop Translat. 20; 38:56-64.	Prospective cohort study n=51 people with TFAs treated between 1999 and 2007 with the OPRA system. Follow up: 10 years	PROs showed statistically significant mean improvements between baseline and the ten-year follow up with regard to all Q-TFA scores. Eight had implants removed. The revision-free survival rates were 83%. Mechanical complications were 3.9 per 10 person-years. No significant difference in the incidence of deep infections from 5 to 10 years.	Larger studies with longer follow up included in evidence summary.
Haggstrom E, Hagberg K, Rydevik B et al. (2013) Vibrotactile evaluation: Osseointegrated versus socket-suspended transfemoral prostheses. JRRD, 50 (10), 1423-1434.	17 people with TFA tested preoperatively with socket-suspended prostheses and after 2 year with OI prostheses and a control	Differences between the OI and the control groups were found in the highest frequencies in which the OI prosthesis showed reduction of the vibrometric signal.	More comprehensive studies added to evidence summary.

	group (n=17) using socket-suspended prostheses.		
Haidary A, Hoellwarth JS, Tetsworth K et al. (2023) Transcutaneous osseointegration for amputees with burn trauma. Burns. 49(5):1052-1061.	Retrospective review n=5 people (1 unilateral transfemoral amputee (TFA), 1 unilateral trans-tibial (TTA),1 bilateral TFA, and 2 bilateral TTA) had ILP/OPL. Follow up average 3.8 years	No issues of skin compatibility or pain associated with the implant. Three people underwent subsequent surgical debridement, one of whom had both implants removed and eventually reimplanted.	More comprehensive studies added to evidence summary.
Hansen RL, Langdahl BL, Jørgensen PH et al. (2019) Changes in periprosthetic bone mineral density and bone turnover markers after osseointegrated implant surgery: A cohort study of 20 transfemoral amputees with 30-month follow up. Prosthet Orthot Int. 43(5):508-518.	Prospective cohort study n=19 people with TFAs treated with osseointegrated implants -OPRA system Follow up: 30 months.	Implant removal was associated with loss of periprosthetic bone-mineral density and increase in C-telopeptide of type-I collagen in the years following osseointegrated surgery.	More comprehensive studies added to evidence summary.
Hansen CH, Hansen RL, Jørgensen PH et al. (2019) The process of becoming a user of an osseointegrated prosthesis following transfemoral amputation: a qualitative study, Disability and Rehabilitation, 41:3, 276-283,	Descriptive analysis Data were collected through in-depth interviews with 7 participants who had undergone transfemoral implant with osseointegrated prosthesis (OPRA system).	Participants experienced increased action space and a more positive outlook on life. It took determination and stamina to become a user and participants faced several challenges.	More comprehensive studies added to evidence summary.
Handford C, McMenemy L, Kendrew J et al. (2022) Improving outcomes for amputees: The health-related quality of life and	Retrospective health utility and cost analysis of prospectively collected patient-	There is both a quality of life and financial argument in favour of osseointegration in select people with above transfemoral amputations. In	More comprehensive studies added to evidence summary.

cost utility analysis of osseointegration prosthetics in transfemoral amputees. Injury. 53(12):4114-4122	reported health outcome data. n=80 with OGAP-OPL implant from 2 centres. Follow-up 10.5 years.	those unable to mobilise satisfactorily with traditional prostheses and a pre-intervention score of <0.60, a consistent cost effectiveness and quality of life benefit can be seen. Such people should be considered for osseointegration as these people reap the maximum benefit and cost effectiveness of the device.	
Hebert JS, Rehani M, Stiegelmar R (2017) Osseointegration for lower-limb amputation: A systematic review of clinical outcomes. JBJS Rev. 5(10): e10	Systematic review n=14 observational studies (6 prospective and 8 retrospective) n=482 people. Level of amputation: transfemoral in 12 studies (n=467), trans-tibial in 1 study (n=5), and upper and lower extremity in 1 study (transulnar: 4, transradial: 4, trans-humeral: 3). Device used: OPRA in 6 studies, ILP in 5 studies, OPL in 3 studies. Follow up varied in studies (3 months to 17.5 years).	Infection and soft-tissue irritation at the stoma were the most common complications. Changes in implant design, surgical technique, perioperative and postoperative care, and rehabilitation protocols have resulted in improvements in functional outcomes and HRQOL, and reduction in rates of complications.	More comprehensive studies added to evidence summary.
Hoellwarth JS, Tetsworth K, Rozbruch SR et al. (2020) Osseointegration for amputees: current implants, techniques, and future	Review of lower-extremity amputations and osseointegration.	There are different osseointegrated implant designs, surgical techniques, and rehabilitation protocols. The	Review

directions. JBJS Rev.8(3): e0043.		risks, infection and periprosthetic fracture are not frequent.	
Hoellwarth JS, Reif TJ, Henry MW et al. (2022) Unexpected positive intraoperative cultures (UPIC) at index osseointegration do not lead to increased postoperative infectious events. J Bone Jt Infect. 7(4):155-162.	Retrospective chart review 8 people with UPIC and 22 people with negative intraoperative cultures (NIC) who had at least 1 year of post-osseointegration follow up.	UPIC at the time of primary osseointegration with subsequent antibiotic therapy does not appear to predispose to an increased risk of additional infection-related management compared with NIC through 1-year-follow up.	More comprehensive studies added to evidence summary.
Hoellwarth JS, Tetsworth K, Oomatia A et al. (2022) Association between osseointegration of lower extremity amputation and mortality among adults. JAMA Netw Open.5(10): e2235074.	Retrospective cohort study n=485 people with amputation of a lower-extremity (transfemoral and trans-tibial) who underwent TOPS implantation. Follow up: 10 years	4% (19) died at mean 2.2 years,17 were unrelated (cardiac issues) and 2 infectious complications. The findings suggest that people who had TOPS implanted rarely die of problems associated with the procedure but instead usually die of unrelated causes.	More comprehensive studies added to evidence summary.
Hoellwarth JS, Oomatia A, Tetsworth K et al. (2023) Bone density changes after 5 or more years of unilateral lower extremity osseointegration: observational cohort study. Bone Rep. 18:101682.	Registry review of 5 transfemoral and 4 trans-tibial unilateral amputees who had DXA performed preoperatively and after 5 years.	Single-stage press-fit TOPS may facilitate significant BMD improvement to unilateral lower-extremity amputees with local disuse osteoporosis.	BMD changes assessed. More comprehensive studies added to evidence summary.
Hoellwarth JS, Geffner A, Reif TJ et al. (2022) Transcutaneous Osseointegration for Amputees with Short Residual Bone: Is There Increased Risk for Complications? J Limb Lengthen Reconstr. 8(2):115-120.	Retrospective review n=58 people (60 segments) who had transcutaneous osseointegration for amputation (TOFA).	Residual bone length does not appear to be associated with post- TOFA reoperation to address noninfected loosening, periprosthetic fracture, or infection. The “minimum necessary” length of bone to achieve stable transcutaneous osseointegration capable of	More comprehensive studies added to table 2.

		supporting full body weight remains uncertain.	
Jacobs R, Brånemark R, Olmarker K et al. (2000) Evaluation of the psychophysical detection threshold level for vibrotactile and pressure stimulation of prosthetic limbs using bone anchorage or soft-tissue support. Prosthetics and Orthotics International 24: 133–42.	Non-randomised comparative study n=32 limbs Socket prosthesis =47% (15 out of 32; 7 upper limbs, 8 lower limbs) Osseointegrated BAP =53% (17 out of 32; 9 upper limbs, 8 lower limbs) Follow up not reported.	Detection thresholds for pressure and especially vibratory stimulation of prosthetic limbs were generally higher than for control limbs. The outcome was related to the prosthetic limb design with bone-anchored prostheses yielding better perception than socket prostheses.	Study included in systematic reviews added to evidence summary.
Jönsson S, Caine-Winterberger K, Brånemark R. (2011) Osseointegration amputation prostheses on the upper limbs: methods, prosthetics and rehabilitation. Prosthet Orthot Int. 35(2):190-200.	Case series n=37 upper-limb cases were treated and fitted with prosthesis: 10 thumbs, 1 partial hand, 10 transradial and 16 THA	People indicated that function and QOL had improved since osseointegration. It is an important platform for present and future prosthetic technology. The prosthetic situation is improved due to the stable fixation, freedom of motion and functionality.	Surgical procedure description More comprehensive studies added to the summary of evidence.
Juhnke DL, Beck JP, Jeyapalina S et al. (2015) Fifteen years of experience with Integral-Leg-Prosthesis: Cohort study of artificial limb attachment system. J Rehabil Res Dev. 2015;52(4):407-20	Retrospective cohort study n=69 people with TFA were fitted with ILPs Group 1:people fitted with first designs and procedure iterations (n=30) Group 2: people fitted with the final design (n=39)	High rate of stoma-associated infections seen in group 1. No infections in group 2. The reduction in the infection rate was attributed to the clinically based, empirically driven changes in design and surgical techniques.	Study included in systematic reviews added to evidence summary.

	Follow up: 15 years		
Kunutsor S, Gillatt D, Blom A (2018). Systematic review of the safety and efficacy of osseointegration prosthesis after limb amputation. British Journal of Surgery, 105(13), 1731-1741.	Systematic review 13 observational studies (21 articles) included (transfemoral 14, upper arm 7) devices used: mainly OPRA, ILP/EEP, OGAP-OPL Follow up: 1 – 3 years.	Osseointegration of limb amputations confers increased prosthetic use, better sitting comfort, improved walking ability, mobility, gait, and QOL. However, it is associated with an increased risk of soft-tissue infections. Robust evidence from trials is warranted.	More comprehensive studies added to evidence summary.
Leijendekkers RA, van Hinte G, Frölke JP et al. (2019) Functional performance and safety of bone-anchored prostheses in persons with a transfemoral or trans-tibial amputation: a prospective one-year follow-up cohort study. Clin Rehabil. 33(3):450-464.	Prospective cohort study n=40 people who had transfemoral (31) or trans-tibial (9) osseointegration implant procedure followed by a predefined rehabilitation programme. Follow up: 1 year	Strength, prosthetic use, walking distance, HRQOL, and satisfaction level increased significantly at 6- and 12-month follow up compared with baseline ($p \leq 0.002$). The TUG improved significantly at 12-month follow up compared with baseline ($p = 0.005$). Wheelchair-boundedness decreased from 12 out of 40 participants at baseline to 0 at follow ups. The 6MWT and back pain did not change over time. Stump pain was present in 22 out of 40 of people at 12-month follow up, respectively. An uneventful course was completed by 19 out of 31 transfemoral and 4 out of 9 trans-tibial bone-anchored prostheses users.	More comprehensive studies added to evidence summary.
Lennerås M, Tsikandylakis G, Trobos M et al. (2017) The clinical, radiological, microbiological, and molecular profile of the skin-penetration site of transfemoral amputees treated with bone-anchored	Prospective cohort study n=30 TFA people scheduled for abutment exchange or removal.	Relationships exist between clinical, radiological, microbiological, and molecular assessments of the percutaneous area of TFAs. Further long-term studies are required and unravel the role of host-	More comprehensive studies added to evidence summary.

IP overview: Direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.

prostheses. J Biomed Mater Res A. 105(2):578-589.		bacteria interactions in the skin, bone canal and on the abutment for the longevity of percutaneous implants as treatment of TFA.	
Li Y, Brånemark R. (2017) Osseointegrated prostheses for rehabilitation following amputation: The pioneering Swedish model. Unfallchirurg. 120(4):285-292.	Reviews on extremity osseointegration surgeries in Sweden and the development of the OPRA program.	The development of the OPRA program allows for structured rehabilitation with standard surgical techniques to achieve adequate bone–fixture integration.	Review
Li Y, Lindeque B. (2018) Percutaneous Osseointegrated Prostheses for Transfemoral Amputations. Orthopedics. 1;41(2):75-80.	Review on people-centred evaluation, surgical technique, and postoperative rehabilitation protocol.	The outcomes with OPRA and ILP devices have confirmed the tremendous advantages of bone-anchored prostheses over socket prostheses.	Review
Lundberg M, Hagberg K, Bullington J. (2011) My prosthesis as a part of me: a qualitative analysis of living with an osseointegrated prosthetic limb. Prosthet Orthot Int. 35(2):207-14.	Qualitative phenomenological research method n=13 people with unilateral upper or lower-limb amputation (10 transfemoral, 2 trans-humeral, 1 transradial), who had been using OI prostheses for 3 to 15 years.	The most important finding was that the change went beyond the functional improvements, integrating the existential implications in the concept of QOL.	More comprehensive studies added to evidence summary.
Matthews DJ, Arastu M, Uden M et al. (2019) UK trial of the Osseointegrated Prosthesis for the Rehabilitation for Amputees: 1995-2018. Prosthet Orthot Int. 43(1):112-122.	Prospective cohort study n=18 transfemoral amputees received unilateral implants (OPRA system) 12.3 years follow up	This small cohort of people demonstrates osseointegrated prosthesis allows prolonged usage and improves people's QOL compared with conventional prostheses.	Study included in systematic review added to evidence summary.

McMenemy L, Ramasamy A, Sherman K et al. (2020) Direct Skeletal Fixation in bilateral above-knee amputees following blast: 2 year follow up results from the initial cohort of UK service personnel. Injury. 51, 735-743.	Retrospective analysis of a prospective database 7 people (14 femoral amputations) who had undergone implantation with the Australian OGAP-OPL prosthesis. Follow up mean 46 months	At 2 years follow up, the absence of significant infective complications suggests DSF may be utilised in the blast injured despite chronic polymicrobial colonisation. Longer term surveillance of these people is required to assess the long-term suitability of this technique in this cohort of people.	Study included in systematic review added to evidence summary.
Mohamed J, Reetz D, van de Meent H et al. (2022). What Are the Risk Factors for Mechanical Failure and Loosening of a Transfemoral Osseointegrated Implant System in Patients with a Lower-limb Amputation? Clin Orthop Relat Res.1;480(4):722-731.	Retrospective cohort study. n=58 people with TFA had osseointegrated press-fit implant. Follow up: 5 years	34% (20 out of 58) of people had revision surgery. In 12% (7 out of 58), it was due to intramedullary stem failures (6 breakages, 1 septic loosening), and in 22% (13 out of 58) it was due to dual-cone adaptor failure (10 weak-point breakages and 4 distal taper breakages; 1 broke both the weak-point and the dual-cone adapter). Risk factors for implant failure include small stem diameter and high number of infectious events.	Studies reporting similar outcomes added to evidence summary.
Muderis MA; Tan YC; Lu W et al. (2024) Transtibial osseointegration following unilateral traumatic amputation: An observational study of patients with at least two years follow-up. Injury; 55 (6); 111568	Retrospective observational cohort study n=21 people with 2 years of post-osseointegration follow-up.	Trans-Tibial osseointegration (TTOI) is likely to confer mobility and QOL improvements to people dissatisfied with socket prosthesis rehabilitation following unilateral traumatic trans-tibial amputation. Adverse events are relatively infrequent and not further disabling. Judicious use of TTOI seems reasonable for properly selected people.	More comprehensive studies included in table 2.

Nebergall A, Bragdon C, Antonellis A et al. (2012) Stable fixation of an osseointegated implant system for above-the-knee amputees: titel RSA and radiographic evaluation of migration and bone remodelling in 55 cases. Acta Orthop. 83(2):121-8.	RSA and periprosthetic bone remodelling study n=51 people with transfemoral amputations (55 implants) had osseointegrated implant system (OPRA). RSA and plain radiographs were scheduled at 6 months and at 1, 2, 5, 7, and 10 years after surgery.	The RSA analysis for the OPRA system indicated stable fixation of the implant. The periprosthetic bone remodelling showed similarities with changes seen around uncemented hip stems. It is a promising approach.	More comprehensive studies added to evidence summary. Radiographic analysis
Örgel M, Liodakis E, Jaratjitwilai P et al. (2020) Three-year follow-up of changes of cortical bone thickness after implantation of Endo-Exo-Prosthesis (EEP) for transfemoral amputees. J Orthop Surg Res. 4;15(1):164.	Retrospective cohort study n=37 people with transfemoral amputations had (40 implants - EEP) Follow up: 3 years	Results did not show any significant difference in cortical thickness after implantation. Hypertrophy could be confirmed for 42.5% and atrophy for 37.5%. Some remodelling of the has been reported.	Changes in cortical bone thickness More comprehensive studies added to evidence summary.
Örgel M, Aschoff HH, Sedlacek L et al. (2022) Analysis of Stomal Bacterial Colonialization After Transcutaneous Osseointegrated Prosthetic Systems Surgery. JAMA Netw Open. 1;5(7): e2223383.	Prospective cohort study n=66 above-knee TFAs had TOPs surgery-EEP.	Most bacteria on the stoma of people undergoing TOPS surgery were gram positive. Authors could not detect specific bacterial pathogens prospectively.	Stomal bacterial colonisation after surgery. More comprehensive studies added to evidence summary.
Örgel M, Aschoff HH, Sedlacek L et al. (2022) Twenty-four months of bacterial colonialization and infection rates in patients with transcutaneous osseointegrated prosthetic systems after lower limb amputation-A prospective	Prospective cohort study n=66 people with lower-limb amputations (transfemoral) had TOPS surgery -EEP.	Gram-positive bacteria in the stoma of TOPS people were noted over 24 months. This could be a protective factor for ascending periprosthetic infections and could possibly explain the relatively low infection rates.	Bacterial colonisation of the stoma. More comprehensive studies added to evidence summary.

analysis. Front Microbiol.13:1002211.			
Örgel M, Schwarze F, Graulich T et al. (2022) Comparison of functional outcome and patient satisfaction between patients with socket prosthesis and patients treated with transcutaneous osseointegrated prosthetic systems (TOPS) after transfemoral amputation. Eur J Trauma Emerg Surg. 48(6):4867-4876.	Retrospective comparative analysis n=69 people with TFA had prosthesis (n=36 socket group and n=33 TOPS group) follow up 1 year	Study showed significantly higher scores for mobility and satisfaction. This demonstrates the high potential of TOPS in the prosthetic treatment of people with TFA with regard to their functional abilities in daily life.	More comprehensive studies added to evidence summary.
Örgel M, Elareibi M, Graulich T et al. (2023) Osseoperception in transcutaneous osseointegrated prosthetic systems (TOPS) after transfemoral amputation: a prospective study. Arch Orthop Trauma Surg.143(2):603-610.	Prospective case-control study n=75 people 25 people with EEP, 25 people with socket prostheses, and 25 healthy volunteers.	Significant level of differences in tactile osseoperception between all groups noted ($p<0.001$). EEP can lead to an improvement in tactile sensory perception, QOL and gait safety.	Osseoperception More comprehensive studies added to evidence summary.
Pantall A, Durham S, Ewins D. (2011) Surface electromyographic activity of 5 residual limb muscles recorded during isometric contraction in transfemoral amputees with osseointegrated prostheses. Clin Biomech. 26(7):760-5.	Preliminary study on transfemoral amputees (n=5) with osseointegrated implant (OPRA) with a control group (n=10) assessed surface EMG patterns.	High electromyographic amplitude variability suggests that using residuum muscles singly as a myoprocessor might be challenging. Adductor magnus displayed a different surface EMG profile compared with intact subjects indicating decreased function and neuromuscular changes.	Electromyographic activity assessed. More comprehensive studies added to evidence summary.
Pospiech PT, Wendlandt R, Aschoff HH et al. (2021) Quality of life of persons with transfemoral amputation: Comparison of socket prostheses and osseointegrated prostheses. Prosthet Orthot Int. 45(1):20-25.	Cross-sectional study n=39 people with TFA treated with osseointegration (n=22 endo-exo prosthesis) to socket (n=17) prosthesis users.	People with osseointegration had less prosthesis-associated problems than socket-prosthesis users and had a higher QOL (Q-TFA scores). General QOL (EQ-5D-3L), was not different between groups.	More comprehensive studies added to evidence summary.

IP overview: Direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.

	Follow up: 1 year		
Ranaldi S, Naaim A, Marchis C, Robert T, Dumas R, Conforto S, Frossard L. Walking ability of individuals fitted with transfemoral bone-anchored prostheses: A comparative study of gait parameters. Clin Rehabil. 2023 Dec;37(12):1670-1683.	Retrospective cross-sectional comparative study. n=17 8 people with transfemoral bone-anchored prostheses OPRA versus 9 people with socket prostheses	Bone-anchored and socket-suspended prostheses restored equally well the gait parameters at a self-selected speed. This benchmark data provides new insights into the walking ability of people using transfemoral bionics bone-anchored prostheses.	Gait parameters More comprehensive studies added to evidence summary.
Ranker A, Oergel M, Aschoff HH et al. (2021) Preoperative femoral abduction angle correlates with initial postoperative lateral hip pain after transcutaneous osseointegrated prosthetic system (TOPS) in transfemoral amputees. Eur J Orthop Surg Traumatol. 31(6):1225-1233.	Retrospective analysis Pre- and postoperative long-leg radiographs of 18 unilateral above-knee amputees treated with TOPS (press-fit system) were retrospectively measured after 4 weeks.	The preoperative femoral abduction angle (FAA) strongly correlates with postoperative lateral hip pain (LHP). High risk of LHP can limit prosthetic training and should be realised in the decision meeting. Pre-rehabilitative reduction of the FAA should be taken into consideration.	Radiographic analysis More comprehensive studies added to evidence summary.
Reif TJ, Khabyeh-Hasbani N, Jaime KM et al. (2021) Early Experience with Femoral and Tibial Bone-Anchored Osseointegration Prostheses. JB JS Open Access. 6(3): e21.00072.	Retrospective case series n=31 people who underwent implantation of a press-fit osseointegration implant of the femur (18) or tibia (13) with follow up of at least 6 months. Mean follow up: 21.1 months.	Osseointegration implants improved the overall and functional experience of people compared with socket prosthetics. Complications were present but manageable and were not a deterrent to ongoing support of the technology.	More comprehensive studies added to evidence summary.
Reetz D, Atallah R, Mohamed J et al. (2020)	Retrospective cohort study	Prosthetic use by people and HRQOL improved	More comprehensive

Safety and Performance of Bone-Anchored Prostheses in Persons with a Transfemoral Amputation: A 5-Year Follow-up Study. J Bone Joint Surg Am. 5;102(15):1329-1335.	n=39 people with TFAs had implantation of a press-fit osseointegration implant. Follow up: 5 years.	significantly. Grade-1 and 2 infections were frequent but could be treated. Two broken intramedullary stems were revised successfully.	studies added to evidence summary.
Sinclair S, Beck JP, Webster J et al. (2022) The First FDA Approved Early Feasibility Study of a Novel Percutaneous Bone Anchored Prosthesis for Transfemoral Amputees: A Prospective 1-year Follow-up Cohort Study. Arch Phys Med Rehabil.103(11):2092-2104	Prospective cohort study n=10 people with unilateral TFA had press-fit POP and a minimum of 10 days supervised rehabilitation therapy. Follow up: 1 year	Improvements in bone density, function, and PROs were observed with the POP device when compared with a socket suspension system. This feasibility study established safety and effectiveness of the POP device, supporting further investigation.	More comprehensive studies added to evidence summary.
Saleib MM, Van Lieshout EMM, Verduin D et al. (2023) Activities of daily living in lower limb amputees with a bone-anchored prosthesis: a retrospective case series with 24 months' follow up. Acta Orthop. 10; 94:499-504.	Retrospective case series n=48 people who had transfemoral (n=40) or trans-tibial (n=8) amputations had bone-anchored prosthesis (BAP-OPL press-fit) 24 months follow up.	Objective measurements on activities of daily living positively changed in people with BAP. This effect was also seen in mobility and walking ability at 24 months.	More comprehensive studies added to evidence summary.
Stenlund P, Kulbacka-Ortiz K, Jönsson S et al. (2019) Loads on Trans-humeral Amputees Using Osseointegrated Prostheses. Ann Biomed Eng. 47(6):1369-1377.	Case series n=11 trans-humeral amputees with osseointegrated implants.	The study shows the diversity and uncertainty that exist in a population of trans-humeral amputees treated with bone-anchored prostheses in terms of loading in daily life.	More comprehensive studies added to evidence summary.
Sullivan J, Uden M, Robinson KP et al. (2003) Rehabilitation of the trans-femoral amputee with an osseointegrated prosthesis: the United Kingdom experience. Prosthetics and	Case series n=11 people with transfemoral osseointegrated prostheses. Follow up: 5.5 years	Direct skeletal attachment has led to improvement in candidates' comfort, function and QOL. Importance of an assessment to explore candidates' suitability and	Study included in systematic reviews added to evidence summary.

Orthotics International 27: 114–20.		expectations for the procedure is discussed.	
Tillander J, Hagberg K, Berlin Ö et al. (2017) Osteomyelitis risk in patients with transfemoral amputations treated with osseointegration prostheses. Clin Orthop Relat Res. 475(12):3100-3108	Retrospective cohort study n=96 people with TFA receiving femoral implants - OPRA (102 implants, implant time 95 months)	Implant-associated osteomyelitis was reported in 16 people corresponding to a 10-year cumulative risk of 20% (95% CI 0.12-0.33). Ten implants were extracted owing to osteomyelitis, with a 10-year cumulative risk of 9% (95% CI 0.04-0.20).	Study included in systematic reviews added to evidence summary.
Tillander J, Hagberg K, Hagberg L, Brånemark R. Osseointegrated titanium implants for limb prostheses attachments: infectious complications. Clin Orthop Relat Res. 2010 Oct;468(10):2781-8.	Prospective cohort study n=39 people with arm and leg amputations fitted with transcutaneous osseointegrated titanium implants- OPRA (33 femoral, 1 tibial, 4 ulnar, 4 radial, and 3 humeral implants). Follow up: mean 56 months (range 132 to 133 months).	Infection was 5% at inclusion and 18% at follow up. One person with infection recovered with antibiotic treatment and another person had the implant removed. The most common bacteria in superficial and deep cultures were Staphylococcus aureus and coagulase-negative staphylococci.	Study included in systematic reviews added to evidence summary.
Thesleff A, Brånemark R, Hakansson N et al. (2018) Biomechanical Characterisation of Bone-anchored Implant Systems for Amputation Limb Prostheses: A Systematic Review. Annals of Biomedical Engineering, 46, 3, 377–391.	Systematic review of the biomechanical characteristics of current percutaneous implant systems for direct skeletal attachment of amputation limb prostheses.	Although there are large differences between current implant systems, the 3 clinically available systems (OPRA, ILP, and OPL) have shown functional improvements for people. Recent developments of implant systems, surgical protocols, and safety devices have reduced the rate of mechanical failure and infectious complications.	More comprehensive studies added to evidence summary.

Thomson S, Lu W, Zreiqat H et al. (2019) Proximal Bone Remodeling in lower limb amputees reconstructed with an osseointegrated prosthesis. J Orthop Res. 37(12):2524-2530.	Prospective cohort study n=48 unilateral amputees who received an osseointegrated implant-OPL/ILP (33 transfemoral amputees and 15 trans-tibial amputees) underwent DXA scans of the lumbar spine (L2-L4) and femoral necks at baseline, 1- and 3-years follow ups.	Results suggest that osseointegrated implants induce a physiological response in the femoral neck of recipients and appear to be evidence of restored biomechanical loading in the proximal femur.	Bone-mineral density changes assessed. More comprehensive studies added to evidence summary.
Van Eck CF, and R. L. Mcgough. Clinical outcome of osseointegrated prostheses for lower extremity amputations: A systematic review of the literature. Curr. Orthop. Pract. 26:349–357, 2015.	Systematic review 13 studies (540 people) 3 prospective, 7 retrospective cohort studies, 3 retrospective comparative studies (OI versus socket prosthesis) Devices used: EEP in 5 studies, OPRA in 7 studies and ITAP in 1 study. Mainly TFAs. Follow up varied in studies (from 6 months to 15 years)	82% to 90% of people used prosthesis daily. 95% of people were happy with osseointegrated prosthesis. SF-36 and Q-TFA scores were satisfactory. There was a high complication rate, including skin problems (30% to 54%), skin infections (28% to 55%), implant infections (2% to 41%), loosening (2% to 6%), periprosthetic fracture (0% to 9%), revision surgery (8% to 67%), and explants (3% to 20%).	More comprehensive studies added to evidence summary.
Van de Meent H, Hopman MT, Frölke JP. (2013) Walking ability and quality of life in subjects with transfemoral amputation: a	Prospective case-control study.	Osseointegration is a suitable intervention for persons whose prosthesis use is reduced because of socket-related problems.	Study included in systematic reviews added to evidence summary.

IP overview: Direct skeletal fixation of limb prostheses using an intraosseous transcutaneous implant.

comparison of osseointegration with socket prostheses. Arch Phys Med Rehabil. 94 (11):2174-8.	n=22 with TFA (1 bilateral) had ILP implanted. Follow up: 1 year	Subjects with OI significantly increased their walking ability and prosthesis-related QOL.	
Welke B, Hurschler C, Schwarze M et al. (2023) Comparison of conventional socket attachment and bone-anchored prosthesis for persons living with transfemoral amputation - mobility and quality of life. Clin Biomech. 105:105954.	Cross-sectional study n=37 people with unilateral TFAs (20 with a BAP were compared with 17 with a socket prosthesis)	There were no differences between the groups regarding the QOL, daily mobility, and gait performance. For people who are satisfied with the socket treatment and perform well, BAP may not improve their functional capabilities and QOL.	More comprehensive studies added to evidence summary.
Zaid MB, O'Donnell RJ, Potter BK et al. (2019) Orthopaedic Osseointegration: State of the Art. J Am Acad Orthop Surg. 15;27(22): e977-e985	Review on history, indications, contraindications, implant systems in use, and reported outcomes.	Osseointegration offers the potential for enhanced biomechanical advantage and rehabilitative potential. Multiple percutaneous implant systems exist for clinical use internationally, each attempting to create a stable bone-implant interface while avoiding complications such as infection and loosening.	Review