CLINICAL PRIORITIES ADVISORY GROUP
20 May 2024

Agenda Item No	5.1
National Programme	Trauma
Clinical Reference Group	Rehabilitation, Disability & Spinal Cord Injury
URN	2206

Title
Clinical Commissioning Policy for Direct Skeletal Fixation for Transfemoral Limb Loss (Adults)

Actions Requested	1. Support the adoption of the policy proposition
	2. Recommend its relative prioritisation

Proposition
Delegation status - Service to be retained Direct Skeletal Fixation is recommended to be available as a routine commissioning treatment option for transfemoral limb loss within the criteria set out in the policy proposition document.

Clinical Panel recommendation
Select appropriate option (*delete prompt and all not applicable statements*): The Clinical Panel recommended that the policy proposition progress as a routine commissioning proposition.

The committee is asked to receive the following assurance:	
1.	The Deputy Director of Clinical Effectiveness confirms the proposition has completed the appropriate sequence of governance steps and includes an: Evidence Review; Clinical Panel Report.

2.	The Deputy Director of Acute Programmes confirms the proposition is supported by an: Impact Assessment; Engagement Report; Equality and Health Inequalities Impact Assessment; Clinical Policy Proposition. The relevant National Programme of Care has approved these reports.
3.	The Director of Finance (Specialised Commissioning) confirms that the impact assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal.
4.	The Director of Clinical Commissioning (Specialised Commissioning) confirms that the service and operational impacts have been completed.

The following documents are included (others available on request):	
1.	Clinical Policy Proposition
2.	Engagement Report
3.	Evidence Summary
4.	Clinical Panel Report
5.	Equality and Health Inequalities Impact Assessment

In the Population what is the clinical effectiveness and safety of the Intervention compared with Comparator?

Outcome	**Evidence statement**
Clinical effectiveness	
Critical outcomes	
Outcome 1 Functional outcome measures **Certainty of evidence:** Very low	Functional outcomes are important to patients as they quantify enablement, independence and active participation. In total, one prospective case series reported non-comparative evidence for functional outcomes at a minimum of one year follow-up after stage one direct skeletal fixation (DSF) surgery (mean follow-up of 21.5 months) in adults with unilateral transfemoral amputation (TFA) and socket or prosthesis-fitting problems. Outcomes reported included timed up and go (TUG)[1] test duration and 6-minute walk test (6MWT)[2] distance. The results were reported separately for pre-operative wheelchair bound patients and prosthetic user patients. At a mean follow-up of 21.5 months: • One prospective case series (Al Muderis et al 2016a) reported a mean TUG duration of 9 (0.56 SD) seconds for patients who had been wheelchair bound pre-operatively (n=14). These patients were not able to complete the TUG test before surgery but the

[1] A valid test for quantifying functional mobility. It 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 = normal; ≤ 20 seconds = good mobility, can go out alone, mobile without a gait aid; < 30 seconds = problems, cannot go outside alone, requires a gait aid

[2] 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 amputees

	authors reported that post-operative scores were comparable with those of the patients who had been walking pre-operatively. **(VERY LOW)** • Al Muderis et al (2016a) also reported a *statistically significant* (p<0.01) improvement in TUG duration for patients who had been prosthetic users pre-operatively (n=36) with a mean TUG duration of 14.59 (5.94 SD) seconds pre surgery and 8.74 (2.81 SD) seconds post surgery. **(VERY LOW)** • Al Muderis et al (2016a) also reported a mean 6MWT distance of 411 (31.44 SD) metres for patients who had been wheelchair bound pre-operatively (n=14). These patients were not able to complete the 6MWT before surgery but the authors reported that post-operative scores were comparable with those of the patients who had been walking pre-operatively. **(VERY LOW)** • Al Muderis et al (2016a) reported a *statistically significant* (p<0.001) improvement in 6MWT distance for patients who had been prosthetic users pre-operatively (n=36) with a mean 6MWT distance of 281 (93 SD) metres pre surgery and 419 (133 SD) metres post surgery. **(VERY LOW)** **This study provided very low certainty evidence that there is a statistically significant improvement in functional outcomes in patients with unilateral TFA and socket or prosthesis-fitting problems undergoing DSF who had been prosthetic users pre-operatively as measured by the TUG test and 6MWT at a mean follow-up of 21.5 months. For those patients who had been wheelchair bound pre-operatively, the authors reported that post-operative scores were comparable with those of the patients who had been walking pre-operatively.**
Outcome 2 **Quality of life** **Certainty of evidence:** Very low	Quality of life is an important outcome to patients as it provides an indication of an individual's general health and self-perceived well-being and their ability to participate in activities of daily living. In total, two prospective case series reported non-comparative evidence for quality of life up to 15 years follow-up after DSF in patients with unilateral TFA and socket or prosthesis-fitting problems. Outcomes reported included the short-form-36 health survey (SF-36)[3] physical component, Q-TFA global score[4], Q-TFA problem score[5] and

[3] The 36-Item Short Form Health Survey (SF-36) is a generic measure of quality of life. 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 two summary measures: the physical component summary (PCS) and the mental component summary (MCS). In each scale, values run between 0 and 100. A higher score indicates better physical or mental health

[4] The Questionnaire for Persons with a Transfemoral Amputation (Q-TFA) is a self-report measure developed for nonelderly transfemoral amputees using a socket- or osseointegrated prosthesis to reflect use, mobility, problems, and global health, each in a separate score (0-100). Global health is defined as the perception of function and problems with the current prosthesis and the perception of the current overall amputation situation. The score is a summary of three questions to which answers are given on a 5-point Likert scale. A Global score of 100 indicates the best possible overall situation as measured by this instrument

[5] The Questionnaire for Persons with a Transfemoral Amputation (Q-TFA) is a self-report measure developed for nonelderly transfemoral amputees using a socket- or osseointegrated prosthesis to reflect use, mobility, problems, and global health, each in a separate score (0-100). Problems are defined as the extent of specific problems related to the amputation and the prosthesis and their impact on the quality of life. A higher score indicates more serious problems.

	response to a single Q-TFA question on the patient's overall situation as an amputee[6]. At a mean follow-up of 21.5 months: • One prospective case series (Al Muderis et al 2016a) reported a *statistically significant* (p<0.001) improvement in mean SF-36 physical component summary score, from 37.09 (9.54 SD) pre surgery (n=46) to 47.29 (9.33 SD) post surgery (n=49). **(VERY LOW)** • Al Muderis et al (2016a) also reported a *statistically significant* (p<0.001) improvement in mean Q-TFA global score, from 47.82 (17.28 SD) pre surgery (n=46) to 83.52 (18.04 SD) post surgery (n=46). **(VERY LOW)** At 2 years: • One prospective case series (Hagberg et al 2020) reported on the response to a single Q-TFA question on patient's overall situation as an amputee with 0/83 (0%) patients responding "very poor", 7/83 (8%) patients responding "poor", 14/83 (17%) patients responding "average", 38/83 (46%) patients responding "good" and 24/83 (29%) patients responding "very good". At baseline 23/107 (21%) patients responded as "very poor", 29/107 (27%) patients as "poor", 34/107 (32%) patients as "average", 16/107 (15%) patients as "good" and 5/107 (5%) patients as "very good". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* (p<0.001) improvement in response to a single Q-TFA question on the patient's overall situation as an amputee compared with baseline with 62/81 (77%) patients having a better score, 14/81 (17%) patients having an equal score and 5/81 (6%) patients having a worse score. **(VERY LOW)** At 5 years: • One prospective case series (Hagberg et al 2020) reported on the response to a single Q-TFA question on patient's overall situation as an amputee with 0/62 (0%) patients responding "very poor", 2/62 (3%) patients responding "poor", 14/62 (23%) patients responding "average", 25/62 (40%) patients responding "good" and 21/62 (34%) patients responding "very good". At baseline 23/107 (21%) patients responded as "very poor", 29/107 (27%) patients as "poor", 34/107 (32%) patients as "average", 16/107 (15%) patients as "good" and 5/107 (5%) patients as "very good". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* (p<0.001) improvement in response to a single Q-TFA question on the patient's overall situation as an amputee compared with baseline with 47/60 (78%) patients having a better score, 10/60 (17%) patients having an equal score and 3/60 (5%) patients having a worse score. **(VERY LOW)** At 7 years:

[6] This is the third question of the Global health subdomain of the Q-TFA "How would you summarise your overall situation as an amputee?" Responses include Extremely poor (0) Poor (1) Average (2) Good (3) Extremely good (4)

	• One prospective case series (Hagberg et al 2020) reported on the response to a single Q-TFA question on patient's overall situation as an amputee with 0/54 (0%) patients responding "very poor", 1/54 (2%) patients responding "poor", 12/54 (22%) patients responding "average", 20/54 (37%) patients responding "good" and 21/54 (39%) patients responding "very good". At baseline 23/107 (21%) patients responded as "very poor", 29/107 (27%) patients as "poor", 34/107 (32%) patients as "average", 16/107 (15%) patients as "good" and 5/107 (5%) patients as "very good". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* (p<0.001) improvement in response to a single Q-TFA question on the patient's overall situation as an amputee compared with baseline with 40/52 (77%) patients having a better score, 11/52 (21%) patients having an equal score and 1/52 (2%) patients having a worse score. **(VERY LOW)** • Hagberg et al (2020) also reported a mean Q-TFA global score of 74 (20.6 SD; 17 to 100 range) and a median score of 75 (58 to 92 IQR) (n=55). **(VERY LOW)** • One prospective case series (Hagberg et al 2020) reported a mean Q-TFA problem score of 17 (10.8 SD; 0 to 44 range) and a median score of 16 (8 to 25 IQR) (n=54). **(VERY LOW)** At 10 years: • One prospective case series (Hagberg et al 2020) reported on the response to a single Q-TFA question on patient's overall situation as an amputee with 1/30 (3%) patients responding "very poor", 4/30 (13%) patients responding "poor", 4/30 (13%) patients responding "average", 10/30 (33%) patients responding "good" and 11/30 (37%) patients responding "very good". At baseline 23/107 (21%) patients responded as "very poor", 29/107 (27%) patients as "poor", 34/107 (32%) patients as "average", 16/107 (15%) patients as "good" and 5/107 (5%) patients as "very good". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* (p<0.001) improvement in response to a single Q-TFA question on the patient's overall situation as an amputee compared with baseline with 21/29 (72%) patients having a better score, 6/29 (21%) patients having an equal score and 2/29 (7%) patients having a worse score. **(VERY LOW)** At 15 years: • One prospective case series (Hagberg et al 2020) reported on the response to a single Q-TFA question on patient's overall situation as an amputee with 1/11 (9%) patients responding "very poor", 0/11 (0%) patients responding "poor", 4/11 (36%) patients responding "average", 3/11 (27%) patients responding "good" and 3/11 (27%) patients responding "very good". At baseline 23/107 (21%) patients responded as "very poor", 29/107 (27%) patients as "poor", 34/107 (32%) patients as "average", 16/107 (15%) patients as "good" and 5/107 (5%) patients as "very good". **(VERY LOW)** • Hagberg et al (2020) also reported the change in response to a single Q-TFA question on the patient's overall situation as an amputee compared with baseline with 7/11 (64%) patients having a better score, 3/11 (27%) patients having an equal score and

	1/11 (9%) patients having a worse score. *Statistical significance* of change not reported. **(VERY LOW)** **These studies provided very low certainty evidence that there is a statistically significant improvement in quality of life in patients with unilateral TFA and socket or prosthesis-fitting problems undergoing DSF as measured by the SF-36 and Q-TFA at 2, 5, 7 and 10 years follow-up**
Outcome 3 **Activities of daily living** **Certainty of evidence:** Not applicable	This outcome is important to patients because it reflects daily functioning and how well people can engage in education, employment and recreational activities. **No evidence was identified for this outcome.**
Important outcomes	
Outcome 4 **Mobility** **Certainty of evidence:** Very low	This outcome is important to patients as it is a useful measure of overall mobility and functional capability. This encompasses patients' individual rehabilitation goals. In total, two prospective case series reported non-comparative evidence for mobility up to 15 years follow-up after DSF in patients with unilateral TFA and socket or prosthesis-fitting problems. Outcomes reported included Amputation Mobility Predictor Prothesis (AMPPRO)[7] scores presented as K-levels[8], Q-TFA mobility scores[9] and prosthetic activity grades[10].

[7] 21-item performance-based functional test designed specifically for people with lower limb loss to determine functional mobility by evaluating ability in transfers, sitting and standing balance, and gait skills

[8] 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 in individuals with lower-limb amputations. K-levels include: K0 – patient has no ability or potential to ambulate or transfer safely with or without assistance and a prosthesis does not enhance their quality of life or mobility; K1 - patient has the ability or potential to use a prosthesis for transfers or ambulation on level surfaces at fixed cadence - a typical limited or unlimited household ambulator; K2 - patient has the ability or potential for ambulation with the ability to traverse low level environmental barriers such as curbs, stairs, or uneven surfaces - a typical community ambulator; K3 - patient has the ability or potential for ambulation with variable cadence - a typical community ambulator with the ability to traverse most environmental barriers and may have therapeutic or exercise activity that demands prosthetic use beyond simple locomotion; K4 - patient has the ability or potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress, or energy levels - typical of the prosthetic demands of the child, active adult, or athlete

[9] The Questionnaire for Persons with a Transfemoral Amputation (Q-TFA) is a self-report measure developed for nonelderly transfemoral amputees using a socket- or osseointegrated prosthesis to reflect use, mobility, problems, and global health, each in a separate score (0-100). Prosthetic mobility is defined as the ability and performance of the amputee to move and change and maintain postures when using the prosthesis. The score consists of three sub scores, each with a range from 0 to 100: capability (12 items), use of walking aids (2 items), and walking habits (5 items). The average of these three sub scores generates the total mobility score. A higher score indicates better mobility

[10] The activity grade was assigned to each patient at each follow-up by the physiotherapist in the treating team. 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, and 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/walking, use walking aid, no long walks; 2 (Average) = Use prosthesis most of the day, with or without walking aid at home, use 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 in use of prosthesis; 4 (Very High) = Uses prosthesis for a full day, no walking aid, walks a lot and/or routinely performs other highly demanding or high-load activities involving the prosthesis (e.g. cycling, gym training)

	At a mean follow-up of 21.5 months: • One prospective case series (Al Muderis et al 2016a) (n=50) reported an improvement in K-levels post-operatively compared to pre-operatively in 30 patients (K0 to K2 in 2 patients; K0 to K3 in 12 patients; K0 to K4 in 1 patient; K1 to K3 in 1 patient; K2 to K3 in 11 patients; K3 to K4 in 3 patients) and no change in 20 patients (K2 in 2 patients; K3 in 13 patients; K4 in 5 patients). **(VERY LOW)** At 2 years: • One prospective case series (Hagberg et al 2020) reported on prosthetic activity grade with 1/86 (1%) patients graded "no prothesis", 13/86 (15%) patients graded "low", 30/86 (35%) patients graded "average", 24/86 (28%) patients graded "high" and 18/86 (21%) patients graded "very high". At baseline 26/110 (24%) patients were graded "no prothesis", 27/110 (25%) patients graded "low", 39/110 (35%) patients graded "average", 9/110 (8%) patients graded "high" and 9/110 (8%) patients graded "very high". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* (p<0.001) improvement in prosthetic activity grade compared with baseline with 50/85 (59%) patients having a better score, 32/85 (38%) patients having an equal score and 3/85 (4%) patients having a worse score. **(VERY LOW)** At 5 years: • One prospective case series (Hagberg et al 2020) reported on prosthetic activity grade with 2/63 (3%) patients graded "no prothesis", 4/63 (6%) patients graded "low", 25/63 (40%) patients graded "average", 16/63 (25%) patients graded "high" and 16/63 (25%) patients graded "very high". At baseline 26/110 (24%) patients were graded "no prothesis", 27/110 (25%) patients graded "low", 39/110 (35%) patients graded "average", 9/110 (8%) patients graded "high" and 9/110 (8%) patients graded "very high". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* (p<0.001) improvement in prosthetic activity grade compared with baseline with 42/62 (68%) patients having a better score, 19/62 (31%) patients having an equal score and 1/62 (2%) patients having a worse score. **(VERY LOW)** At 7 years: • One prospective case series (Hagberg et al 2020) reported on prosthetic activity grade with 0/55 (0%) patients graded "no prothesis", 8/55 (11%) patients graded "low", 18/55 (33%) patients graded "average", 17/55 (31%) patients graded "high" and 14/55 (25%) patients graded "very high". At baseline 26/110 (24%) patients were graded "no prothesis", 27/110 (25%) patients graded "low", 39/110 (35%) patients graded "average", 9/110 (8%) patients graded "high" and 9/110 (8%) patients graded "very high". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* (p<0.001) improvement in prosthetic activity grade compared with baseline with 36/54 (67%) patients having a better score, 17/54 (31%) patients having an equal score and 1/54 (2%) patients having a worse score. **(VERY LOW)**

	• Hagberg et al (2020) also reported a mean Q-TFA mobility score of 67 (17.8 SD; 22 to 95 range) and a median score of 71 (58 to 79 IQR) (n=54). **(VERY LOW)** At 10 years: • One prospective case series (Hagberg et al 2020) reported on prosthetic activity grade with 3/32 (9%) patients graded "no prothesis", 3/32 (9%) patients graded "low", 8/32 (25%) patients graded "average", 14/32 (44%) patients graded "high" and 4/32 (13%) patients graded "very high". At baseline 26/110 (24%) patients were graded "no prothesis", 27/110 (25%) patients graded "low", 39/110 (35%) patients graded "average", 9/110 (8%) patients graded "high" and 9/110 (8%) patients graded "very high". **(VERY LOW)** • Hagberg et al (2020) also reported a *statistically significant* ($p<0.001$) improvement prosthetic activity grade compared with baseline with 22/32 (69%) patients having a better score, 6/32 (19%) patients having an equal score and 4/32 (13%) patients having a worse score. **(VERY LOW)** At 15 years: • One prospective case series (Hagberg et al 2020) reported on prosthetic activity grade with 0/11 (0%) patients graded "no prothesis", 1/11 (9%) patients graded "low", 1/11 (9%) patients graded "average", 4/11 (36%) patients graded "high" and 5/11 (45%) patients graded "very high". At baseline 26/110 (24%) patients were graded "no prothesis", 27/110 (25%) patients graded "low", 39/110 (35%) patients graded "average", 9/110 (8%) patients graded "high" and 9/110 (8%) patients graded "very high". **(VERY LOW)** • Hagberg et al (2020) also reported the change in prosthetic activity grade compared with baseline with 5/11 (45%) patients having a better score and 6/11 (55%) patients having an equal score. *Statistical significance* of change not reported. **(VERY LOW)** **One study provided very low certainty evidence that there is a statistically significant improvement in mobility in patients with unilateral TFA and socket or prosthesis-fitting problems undergoing DSF as measured by prosthetic activity grades at 2, 5, 7, and 10 years follow-up with an improvement also observed at 15 years but no statistical significance of this result reported. One study provided very low certainty evidence that there is an improvement in mobility as measured by AMPPRO scores at a mean follow-up of 21.5 months but no statistical significance of this result was reported. Another study reported Q-TFA mobility scores at 7 years but no baseline result or statistical significance was reported.**
Outcome 5 **Psychological impact** **Certainty of evidence:** Not applicable	This outcome is important to patients because it considers the psychological impact of amputation and rehabilitation. It is important to consider in order to facilitate engagement in rehabilitation programmes. **No evidence was identified for this outcome.**

Outcome 6 **Wheelchair use** **Certainty of evidence:** Very low	This outcome is important to patients as it may reflect issues with functional aspects of the prosthetic. In total, two prospective case series reported non-comparative evidence for wheelchair use at a mean follow-up of 21.5 months and a median follow-up of 34 months after DSF in patients with TFA and socket or prosthesis-fitting problems. At a mean follow-up of 21.5 months: • One prospective case series (Al Muderis et al 2016a) (n=50) reported that all 14 participants that had been wheelchair bound pre-operatively had post-operative K-level scores that were comparable with those of the patients who had been walking pre-operatively (K2 or better). It was not reported whether any participants who were walking pre-operatively became wheelchair bound after surgery. **(VERY LOW)** At a median follow-up of 34 months: • One prospective case series (Al Muderis et al 2016b) (n=86) reported that 25% of the study population was wheelchair-bound before osseointegration, and all of these patients became community ambulators after surgery. It was not reported whether any participants who were walking pre-operatively became wheelchair bound after surgery. **(VERY LOW)** **These studies provided very low certainty evidence that wheelchair use was reduced in patients with TFA and socket or prosthesis-fitting problems undergoing DSF up to a median follow-up of 34 months. One study reported that all patients who had been wheelchair bound pre-operatively became community ambulators after surgery and the other study reported that all patients who had been wheelchair bound pre-operatively had mobility scores comparable with patients who had been walking pre-operatively.**
Outcome 7 **Frequency of implant replacement and/or re-fitting** **Certainty of evidence:** Very low	This outcome is important to patients as it impacts on user comfort and functional use. In total, five case series (three prospective and two retrospective) reported non-comparative evidence on the frequency of implant replacement and/or re-fitting up to 15 years follow-up after DSF in patients with TFA or a knee disarticulation (9% of participants in one study) and socket or prosthesis-fitting problems. At a mean follow-up of 21.5 months: • One prospective case series (Al Muderis et al 2016a) reported that 2/50 (4%) patients underwent revision of an implant. These were due to failure of osseointegration as a result of an undersized device in one patient and implant fatigue failure at 3.5 years in one patient. **(VERY LOW)** At 2 years: • One prospective case series (Hagberg et al 2020) (n=111) reported a revision-free survival of the fixture of 92% (95% confidence interval (CI) 85% to 96%). **(VERY LOW)** • Hagberg et al (2020) (n=111) also reported a survival of the fixture until the first event necessitating a change of the abutment and/or abutment screw of 81% (95% CI 71% to 88%). **(VERY LOW)**

	At a median follow-up of 34 months: • One prospective case series (Al Muderis et al 2016b) reported that 1/86 (1%) patient had inadequate osseointegration and underwent implant replacement, 2/86 (2%) patients experienced breakage of the intramedullary component at 42 and 47 months after surgery respectively leading to implant replacement and 25/86 (29%) patients experienced breakage of the pin used for safety in the dual-cone (extramedullary) component on a total of 30 occasions. **(VERY LOW)** At 5 years: • One prospective case series (Mohamed et al 2022) reported that 20/58 (34%) patients underwent revision surgery, 7/58 (12%) were due to a failed intramedullary stem due to breakages (n=6) or septic loosening (n=1) and 13/58 (22%) were due to a broken dual-cone adapter due to weak-point breakages (n=9), broken distal taper of the dual cone (n=3) or broken the weak-point and the distal taper (n=1). **(VERY LOW)** • Mohamed et al (2022) also reported a cumulative implant survival probability after 9 years (n=58) of 78% (95%CI 58% to 89%) and a median implant survival time of 6 years (IQR 4). **(VERY LOW)** At 7 years: • One prospective case series (Hagberg et al 2020) (n=111) reported a revision-free survival of the fixture of 89% (95% CI 80% to 94%). **(VERY LOW)** • Hagberg et al (2020) (n=111) also reported a survival of the fixture until the first event necessitating a change of the abutment and/or abutment screw of 32% (95% CI 22% to 43%). **(VERY LOW)** At a mean follow-up of 7.9 years: • One retrospective case series (Tillander et al 2017) reported that 10/102 (10%) implants were extracted due to osteomyelitis[11]. **(VERY LOW)** • Tillander et al (2017) (n=102) also reported a 10-year cumulative risk of implant extraction due to osteomyelitis of 9% (95% CI 4% to 20%). **(VERY LOW)** At 15 years: • One prospective case series (Hagberg et al 2020) reported that 18/111 (16%) had implant revisions, 7/111 (6%) due to infection, 6/111 (5%) due to aseptic loosening and 5/111 (5%) due to fractures. **(VERY LOW)** • Hagberg et al (2020) (n=111) also reported a revision-free survival of the fixture of 72% (95% CI 57% to 83%). **(VERY LOW)** • Hagberg et al (2020) also reported that 61/111 (55%) patients had at least one mechanical complication resulting in change of the abutment and/or abutment screw. **(VERY LOW)** • Hagberg et al (2020) (n=111) also reported a survival of the fixture until the first event necessitating a change of the abutment and/or abutment screw of 14% (95% CI 6% to 26%). **(VERY LOW)**

[11] Indication for extraction was infection not responsive to conservative treatment or loosening evident in stability testing of the implant

	These studies provided very low certainty evidence that the percentage of implant replacement and/or re-fitting after DSF ranged between 3% to 4% at around 2 to 3 years to 34% at 5 years and 16% at 15 years in patients with TFA or a knee disarticulation and socket or prosthesis-fitting problems. One study reported that 10% of implants were extracted due to osteomyelitis at a mean follow-up of 7.9 years and another study reported that 6% were extracted due to infection at 15 years. One study reported a 10-year cumulative risk of implant extraction due to osteomyelitis of 9%. One study reported that 5%of implants were extracted due to fractures at 15 years. One study reported that revision-free survival of the fixture ranged from 92% at 2 years to 72% at 15 years, and a survival of the fixture until the first event necessitating a change of the abutment and/or abutment screw ranging from 81% at 2 years to 14% at 15 years. Another study reported a cumulative implant survival probability after 9 years of 78% and a median implant survival time of 6 years.
Abbreviations 6MWT: 6-Minute Walk Test; AMPPRO: Amputation Mobility Predictor Prothesis; CI: Confidence Interval; DSF: Direct Skeletal Fixation; IQR: Interquartile Range; Q-TFA: Questionnaire for Persons with a Transfemoral Amputation; SD: Standard Deviation; SF-36: 36-Item Short Form Health Survey; TUG: Timed Up and Go Test	
Safety	
Outcome 1 **Adverse events** **Certainty of evidence:** Very low	These outcomes are important to patients because they will impact on the patient's treatment choices, recovery and could have long term sequelae. In total, three case series (two prospective and one retrospective) reported non-comparative evidence on adverse events up to a mean follow-up of 7.9 years after DSF in patients with TFA and socket or prosthesis-fitting problems. At a mean follow-up of 21.5 months: • One prospective case series (Al Muderis et al 2016a) reported that 27/50 (54%) patients experienced an adverse event. **(VERY LOW)** • Al Muderis et al (2016a) also reported that 21/50 (42%) patients experienced one or more infections, 13 of which responded to oral antibiotics alone, 5 responded to intravenous antibiotics and 3 required surgical soft tissue debridement of infected soft tissues. **(VERY LOW)** • Al Muderis et al (2016a) also reported that 4/50 (8%) patients sustained periprosthetic fractures as a result of falls, three of whom were previously wheelchair bound with severe osteoporosis. All four fractures were managed by open reduction and internal fixation with a dynamic hip screw and cables as necessary, without interfering with the osseointegration of the implant. All fractures healed within three months. **(VERY LOW)** At a median follow-up of 34 months: • One prospective case series (Al Muderis et al 2016b) reported that 29/86 (34%) patients experienced one or more infections:

	23/86 (27%) patients had Grade 1A[12] infection (low-grade soft-tissue infection cellulitis with signs of inflammation treated with oral antibiotics); 1/86 (1%) had Grade 1B infection (severe cellulitis and intense pain treated with parenteral antibiotics); 1/86 (1%) had Grade 1C infection (severe cellulitis and intense pain treated with parenteral antibiotics followed by local debridement); 4/86 (5%) had Grade 2C[13] infection (high-grade soft-tissue infection with abscess formation that needed surgical debridement). No patient developed a serious (grade 3[14] or 4[15]) infection. **(VERY LOW)** • Al Muderis et al (2016b) also reported that 17/86 (20%) had stoma hypergranulation (22 events). **(VERY LOW)** • Al Muderis et al (2016b) also reported that 14/86 (16%) had redundant soft tissue (23 events). **(VERY LOW)** • Al Muderis et al (2016b) also reported that 3/86 (3%) had a proximal femoral fracture (3 events. All patients underwent surgical stabilisation of the fracture without the need of implant removal. **(VERY LOW)** At a mean follow-up of 7.9 years: • One retrospective case series (Tillander et al 2017) reported that 16/96 (17%) patients developed osteomyelitis (12 definitive, 3 probable, 1 possible). The clinical presentation of osteomyelitis was subacute or acute in 8 patients and chronic with or without fistulas in 8 patients. The clinical outcome for patients with osteomyelitis was recovery[16] after antibiotics with or without minor debridement (n=4); recovery and later relapse (n=1); successful re-implantation (n=1); recovery after extraction (n=9); and chronic with fistula (n=1). The prosthetic use[17] at the time of diagnosis of osteomyelitis was reported to be unable to use prostheses (n=2); moderately restricted prosthetic use (n=6); no impairment (n=2); and not assessed as patient in the early rehabilitation phase (n=6). **(VERY LOW)** • Tillander et al (2017) (n=96) also reported a 10-year cumulative risk of implant-associated osteomyelitis[18] of 20% (95% CI 12 to 33). **(VERY LOW)** • Tillander et al (2017) (n=96) also reported a median time from implantation to osteomyelitis of 2.6 years (0.3 to 13.8 range). **(VERY LOW)** These studies provided very low certainty evidence on adverse events after DSF in patients with TFA and socket or prosthesis-fitting problems undergoing DSF. One study reported that 54% of patients

[12] Grade 1 - Low-grade soft-tissue infection cellulitis with signs of inflammation (redness, swelling, warmth, stinging pain, pain that increases on loading, tense) treated with oral antibiotics (Grade 1A), parenteral antibiotics (Grade 1B) or surgical intervention (Grade 1C)

[13] High-grade soft-tissue infection with pus collection, purulent discharge, raised level of C-reactive protein treated with oral antibiotics (Grade 2A), parenteral antibiotics (Grade 2B) or surgical intervention (Grade 2C)

[14] Bone infection with radiographic evidence of osteitis (periosteal bone reaction), radiographic evidence of osteomyelitis (sequestrum and involucrum)

[15] Implant failure with radiographic evidence of loosening

[16] Infections were considered resolved if patients were symptom-free 12 months or more after discontinuation of antibiotics

[17] Prosthetic use at the time of osteomyelitis was retrospectively assessed by a team physiotherapist and assigned a simple 1 to 3 score (unchanged = 1, impaired = 2, and no prosthetic use owing to infection = 3)

[18] Evidence of infection involving implant-surrounding bone and/or bone marrow, supported by positive percutaneous bone biopsy or aspirated bone marrow cultures, and classified as definite, probable, or possible

	experienced an adverse event at a mean follow-up of 21.5 months. The percentage of patients experiencing infections reported by the studies included 42% at a mean follow-up of 21.5 months, 34% at a median follow-up of 34 months and 17% at a mean follow-up of 7.9 years. One study reported a 10-year cumulative risk of implant-associated osteomyelitis of 20% and a median time from implantation to osteomyelitis of 2.6 years. One study reported that 8% of patients sustained periprosthetic fractures at a mean follow-up of 21.5 months and another study reported that 3% had proximal femoral fractures at a median follow-up of 34 months. One study reported that 20% had stoma hypergranulation and 16% had redundant soft tissue at a median follow-up of 34 months.

In the Population what is the cost effectiveness of the Intervention compared with Comparator?

Outcome	Evidence statement
Cost effectiveness	**No evidence was identified for cost effectiveness.**

From the evidence selected, are there any subgroups of patients that may benefit from the intervention more than the wider population of interest?

Outcome	Evidence statement
Subgroups	**No evidence was identified for subgroups.**

Patient Impact Summary
The condition has the following impacts on the patient's everyday life: • **mobility:** severe problems in walking about/are unable to walk about • **ability to provide self-care:** severe problems in washing or dressing/ unable to wash or dress • **undertaking usual activities:** severe problems in doing their usual activities/are unable to do their daily activities • **experience of pain/discomfort:** Patients have moderate to severe pain or discomfort • **experience of anxiety/depression:** Patients may slightly to extremely anxious or depressed depending on their individual circumstances
Further details of impact upon patients: patients with transfemoral amputations (TFAs) who are unable to tolerate conventional sockets currently have no alternative prosthesis options, so may either need crutches or be reliant on a wheelchair which significantly negatively impacts mobility. Infections caused by skin problems or skin breakdown due to conventional sockets can lead to patients

being unable to use the prosthesis which again results in a reliance on crutches or a wheelchair reducing the patient's mobility. This will severely impact on their ability to carry out their usual activities, activities of daily living, their ability to care for dependants (socially and financially) and there is an increased risk of loss of employment and financial dependence on the state or a carer/family member. They also may be experiencing a spectrum of physical issues with their current sockets, including pain (residual limb pain) due to skin intolerance, due to scaring or sensitive skin, skin breakdown or infection and psychological issues associated with the impact on their mobility and body image. Mental health problems, including or compounded by loneliness and isolation can be a consequence of a lack of mobility. Changes in body image can also cause psychological stress and impact mental health.

Further details of impact upon carers: Those living with and caring for people with TFAs who cannot wear a prosthesis are at increased risk of becoming the main care provider, helping with activities of daily living, as well as hospital appointments, rehabilitation attendances and/or emergency attendances if the patient is experiencing socket fit issues. They may also have increased responsibility for childcare, school attendance of school age children and financial security. This requires a lot of additional time and organisation whilst trying to balance their own responsibilities such as employment or childcare. Research has indicated that this can place strain on the relationship and on the care giver.

Considerations from review by Rare Disease Advisory Group
Not applicable.

Pharmaceutical considerations
Not applicable.

Considerations from review by National Programme of Care
1) The proposal received the full support of the Trauma PoC on the 16th June 2023