NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 21 December 2022

Intervention: Direct Skeletal Fixation

Indication: Transfemoral limb loss (adults)

URN: 2206

Gateway: 2, Round 1

Programme: Trauma

CRG: Rehabilitation & Disability

Information provided to the Panel

Policy Proposition

Clinical Priorities Advisory Group Summary Report

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment (PIA) Report

Evidence Review by Solutions for Public Health

Evidence Review – IDEAL Evaluation

Evidence to Decision Making Summary

Blueteq™ Form

Policy Working Group Appendix

This Policy Proposition recommends the routine commissioning of direct skeletal fixation (DSF) for adults with transfemoral limb loss – through knee or above, either from birth or due to amputation. These adults are unable to tolerate conventional socket use and have no alternative prosthetic treatment options. DSF is a form of surgery, also known as osseointegration. It involves placing an implant (a rod usually made of titanium) through the skin into the bone which may be carried out in two separate operations or as a single operation. In the first stage, the implant is inserted into the central part of the remaining bone. The second stage of the procedure involves connecting the implant to a small metal extension which goes through the skin, allowing the prosthetic limb to be attached to the implant within the bone.

There is a related NICE Interventional Procedures Guidance (IPG 270) in place which was published in 2008. It states that DSF may have potential advantages for some patients compared with conventional sockets.

Clinical Panel was presented with the evidence review supporting the proposition which included five papers – three prospective and two retrospective case series. The studies included between 50 and 111 patients. Follow-up ranged from 21.5 months to 15 years. Two studies were based in Sweden, one in Australia, one in the Netherlands and one in Australia

and the Netherlands combined. No studies comparing DSF with no prosthetic use were identified.

Reporting **critical outcomes**: One prospective study provided very low certainty evidence of a statistically significant improvement in functional outcomes in patients with unilateral transfemoral amputation (TFA) and socket or prosthesis-fitting problems undergoing DSF. Two prospective studies provided very low certainty evidence of a statistically significant improvement in quality of life in patients with unilateral TFA and socket or prosthesis-fitting problems undergoing DSF. All evidence relating to **important outcomes** were of very low certainty. All studies that reported exclusion criteria excluded patients with peripheral vascular disease, diabetes mellitus, exposure to radiation in the affected limb, or past or ongoing chemotherapy. None of the studies defined the criteria used to assess socket or prosthesis-fitting problems. Adverse events were outlined, including infection, loss of device and fractures.

The IDEAL framework was used to assess the evidence to determine the stage of development of the technique to help inform decision making. The independent evaluators determined this to be stage 2b overall. Some members of the Panel considered this to be stage 2a.

Panel members discussed the proposition and the evidence base at length.

It is estimated that 100 people per year would be eligible for this procedure. It was not clear how this estimate had been arrived at and Panel members considered that the proposition as currently written may allow for a wider population to access.

The proposal for number of centres and facilities required was not clear and would need to be addressed in the commissioning plan, and a provider selection exercise would need to be undertaken.

Three devices were listed in the proposition. The Panel questioned whether one device was superior to another. It is difficult to determine this as there are different methods for attaching a prosthesis. A horizon scanning exercise has previously been completed which did not state this. The latest device technologies were those described in the proposition. Panel members questioned how other new devices could be considered or if current technologies were upgraded.

Panel members discussed whether further research was necessary. This possibility should be explored further.

EHIA – no amendments recommended.
PIA – no amendments recommended.

Recommendation

Clinical Panel recommends this returns to a future Panel meeting with revisions as outlined. A paper outlining possible research options should accompany the proposition.

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Why the panel made these recommendations

Clinical Panel members considered that a decision could not be reached regarding whether this should proceed as routine commissioning or whether there was a possibility of further research. Extensive revisions are required.

Documentation amendments required

Policy Proposition:

- Provide calculations/evidence for the estimated eligible population.
- Analysis required on device superiority.
- Clarification required on the surgical two stage process. Which has the better outcomes – two stage procedures completed at same time or a gap between the stages.
- Could this procedure be for those people needing bilateral surgery or just unilateral?
- Inclusion criteria – needs to state more clearly the type of acquired amputation e.g. trauma, lower limb malignancy.
- Exclusion criteria: – currently phrased in a cumbersome way.
    - Evidence to exclude people with certain conditions, such as diabetes needs to be clear as not seen with the evidence base presented.
    - Smoker – does this mean current or include previous smokers?
    - Regional pain syndrome – it was debated that this is often an issue with amputees and questioned whether this should be an exclusion criterion.
    - Peripheral vascular disease – Policy Working Group to consider inclusion of the cohort of people with popliteal entrapment syndrome.
    - Psychological ability to tolerate implants – the wording is considered to need strengthening and be clearer what this means in reality.
    - Previous radiotherapy – this needs to be more clearly stated that this is related to the area of implementation?
    - Immunosuppression – be clearer of what this is meant by this.
- Stopping criteria – need refining. MDT decision 'not to continue' – this statement needs expansion to clarify what is meant by this.
- Governance arrangements– need to include stronger language regarding data requirements in order to effectively review long term outcomes. Data registry and data linkage needs including.
- Measurement parameters need to be clearly defined.
- Strong element of rehabilitation needs consideration and inclusion in the proposition.

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- The form needs to include all inclusion criteria and state exclusion criteria as per policy proposition.
- If one or two stage procedure is undertaken, then this could be captured within the form to support future audit.
- Section 3 – language currently cumbersome and needs revising

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Declarations of Interest of Panel Members: One member stated that they undertake amputations as part of their clinical work.

Panel Chair: Anthony Kessel, National Clinical Policy Team Director, Specialised Services

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PWG Post Panel Comments and document amendments

Policy Proposition:

Clinical panel comment	Action
Provide calculations/evidence for the estimated eligible population.	This was discussed by the clinical lead (CL), public health lead (PHL), and lead commissioner (LC). They provided a calculation of the eligible patients using published epidemiological data on the condition which has now been added to the policy. For full calculation please see epidemiology and needs assessment on policy proposition document page 2 and additional references on page 8.
Analysis required on device superiority	This was discussed with CL, who has confirmed there is no evidence between the implants of superiority of one over another. Regardless of the implant, the prosthetic hardware will be the same across all 3 devices. This information and clarification has been added to page 3 of the policy proposition document.
Clarification required on the surgical two stage process. Which has the better outcomes – two stage procedures completed at same time or a gap between the stages	The CL highlighted that the Australian studies (Al Muderis) are one stage whereas some of the European groups in the study (Hagberg) are two stage procedures. Both approaches provided evidence of clinical effectiveness in terms of mobility, functional outcomes and QoL. There is no evidence comparing one over the other and it depends on patient and operator factors. The PWG also clarified that if a two-stage procedure is undertaken the patient is required to be wheelchair bound between both surgeries. This information and clarification has been added to page 3 of the policy proposition document.
Could this procedure be for those people needing bilateral surgery or just unilateral?	The CL and clinical PWG members discussed this and confirmed that the intervention has been used in both and bilateral involvement was not an exclusion criterion on all the papers. The inclusion criteria have been updated with the phrase 'Adult patients who have transfemoral limb loss (unilateral or bilateral)' to reflect this. Please see policy proposition page 4 for updated inclusion criteria.
Inclusion criteria – needs to state more clearly the type of acquired amputation e.g. trauma, lower limb malignancy	The inclusion criteria were discussed with CL and clinical PWG members. Amputations due to diabetes and peripheral vascular disease were excluded from the studies in the evidence review, and therefore the evidence base is only for the intervention in patients where the amputation is due to trauma or malignancy, or there is congenital limb deficiency. The inclusion criteria have therefore been updated to include amputations secondary to trauma OR congenital deficiency OR malignancy only. Please see policy proposition page 4 for updated inclusion criteria
Exclusion criteria: – currently phrased in a cumbersome way.	Phrasing was discussed with and checked by CL, LC and PHL, and has been updated on page 5 of the policy document

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Evidence to exclude people with certain conditions, such as diabetes needs to be clear as not seen with the evidence base presented.	This was discussed with CL, LC and clinical PWG. Because patients with diabetes were excluded from all studies included in the Evidence Review (ER) there is no evidence for the intervention in this patient group. Given the infection risk for the procedure, clinical members of the PWG highlight that diabetes significantly further increases this risk and this is the rationale for these patients being excluded from studies, and from this policy proposition. This therefore remains in the exclusion criteria on page 5 and additional information has been added to the policy on page 5 to justify this.
Smoker – does this mean current or include previous smokers?	CL and clinical PWG discussed this and clarified that current smoking significantly increases infection risk due to associated microvascular disease. For this reason current smokers are also excluded from the Al Muderis studies. The phrase 'current smoker' rather than 'smoker' remains in the exclusion criteria on page 5 and additional information has been added to the policy on page 5 to justify this.
Regional pain syndrome – it was debated that this is often an issue with amputees and questioned whether this should be an exclusion criterion.	CL and clinical PWG discussed this. Clinical consensus considers there is a high risk of CRPS recurrence post-operatively and this risk outweighs the benefit of the procedure in this group. This therefore remains in the exclusion criteria on page 5 and additional information has been added to the policy on page 5 to justify this.
Atherosclerotic peripheral vascular disease – Policy Working Group to consider inclusion of the cohort of people with popliteal entrapment syndrome.	Clinical PWG members discussed this and considered this as an extremely rare cause of transfemoral amputations; in popliteal entrapment syndrome if an amputation is required it is usually at the level of the tibia and therefore these patients do not meet the inclusion criteria. The policy is therefore not being changed.
Psychological ability to tolerate implants – the wording is considered to need strengthening and be clearer what this means in reality	LC and CL discussed this and added this phrase 'Has mental capacity to consent to the procedure, and is fully aware of risks including implant failure, and is able to psychologically tolerate this risk' into the policy proposition on page 4 (inclusion criteria)
Previous radiotherapy – this needs to be more clearly stated that this is related to the area of implementation?	Clinical PWG members discussed and confirmed that radiotherapy involving ipsilateral femur, including the groin, is an exclusion criterion because it significantly increases the risk of implant failure. This therefore has been reflected in the exclusion criteria on page 5 and additional information has been added to the policy on page 5 to justify this
Immunosuppression – be clearer of what this is meant by this	Clinical PWG members discussed what this means and highlighted that immunosuppressed patients were excluded from studies included in the ER; there is therefore very little evidence for the intervention in this

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	patient group. They provided the following definition of immunosuppression: current immunosuppression including but not limited to; chemotherapy/cancer medication, anti-TNF, MTX, Il-6 inhibitors (see policy proposition updates). This has been added to the exclusion criteria on page 5 and additional information has been added to the policy on page 5 to justify this
Stopping criteria – need refining. MDT decision 'not to continue' – this statement needs expansion to clarify what is meant by this.	Clinical PWG members re-discussed the stopping criteria and the phrase 'Non-engagement with limb fitting services or rehabilitation services' has been added to stopping criteria on page 5.
Governance arrangements– need to include stronger language regarding data requirements in order to effectively review long term outcomes. Data registry and data linkage needs including.	Clinical PWG members and the CL discussed the data requirements needed to collect useful information on outcomes and which have been used in the literature. They would require data on the following parameters to be collected: 6 minute walk test or 2 minute walk test if patient is unable to complete 6MWT, Timed up and go test, EQ-5D score, a widely used generic (disease non-specific) quality of life (QoL) instrument. Data on any adverse effects will also be collected, at a minimum: Infection rates and severity, Implant failure. These have been added to page 7, audit requirements
Measurement parameters need to be clearly defined.	See point above
Strong element of rehabilitation needs consideration and inclusion in the proposition.	The CL provided information regarding the rehabilitation programme currently being used in the U.K research cohort (see below), which is based around rehabilitation programmes in the literature. A section of the policy on rehabilitation has been added to page 5 of the policy document.

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- The form needs to include all inclusion criteria and state exclusion criteria as per policy proposition. *Once the PWG had discussed and clarified the exclusion criteria, the prior approval form was updated to correspond.*
- If one or two stage procedure is undertaken, then this could be captured within the form to support future audit. *As per medicines lead and the PWG, this has been added so the number of stages and the device used will now be captured – see prior approval form.*
- Section 3 – language currently cumbersome and needs revising. *Language has been clarified by PWG – see prior approval form.*

Research already undertaken in UK cohorts

Panel heard information that a research cohort of 20 patients with TFAs exists in England who had already undergone this procedure however it was not clear whether these patients were NHS or MoD and how this was funded, or if the outcomes were available

- This intervention has not gone through a commissioning through evaluation process previously. These patients were military veterans with traumatic amputations ONLY and

the research was funded through MoD Libor funding.

- The results from a proportion of this cohort are published here: McMenemy, L., Ramasamy, A., Sherman, K., Mistlin, A., Phillip, R., Evriviades, D., & Kendrew, J. (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*(3), 735–743. https://doi.org/10.1016/J.INJURY.2020.01.006:
    - This paper was not included in the ER as a standalone paper because the same cohort was included in a larger cohort study.
    - The results demonstrate a statistically significant improvement in 6 min walk test by a mean of 154m pre-op to 24 months post op. Pre-op, no patient was able to perform the TUG test. At the last post op review, all patients were able to perform the test with a median time of 10.6 s - comparable to an age matched able bodied person in the literature.
- The results from this cohort were also included in this larger health-realted quality of life and cost utility analysis: Handford, C., McMenemy, L., Kendrew, J., Mistlin, A., Akhtar, A., Parry, M., & Hindle, P. (2022). Improving outcomes for amputees: The health-related quality of life and cost utility analysis of osseointegration prosthetics in transfemoral amputees. *Injury, 0*(0). https://doi.org/10.1016/J.INJURY.2022.10.007
    - This paper was not included in the evidence review because it was published after the ER had been completed.
    - The results were based on EQ5D-HUV and QALY health utility scores calculated from SF-36 questionnaires. Mean pre-operative EQ5D-HUV was 0.64. In those with a starting score of <0.60, there was a consistent improvement in health utility score which was statistically significant at majority of follow ups.

Possible future research options

- The PWG notes that, as above, research has already been undertaken in the UK in a small cohort of relevant patients and demonstrates results that the PWG and PPVs feel are clinically significant. The PWG is however aware that the research already done in the UK has not involved patients with congenital TFAs, or amputations secondary to malignancy, who may meet the inclusion criteria of this policy.

- The evaluative commissioning (previously commissioning through evaluation) route has not been previously used in this cohort and this option was discussed with the EC team. The conclusion of the discussion was that further research could be done via NIHR route if necessary, and the EC route is currently not felt to be appropriate for this intervention. The NIHR route could support, for example, a stepped wedge approach to generate comparative evidence if desired.

- The PWG discussed previous and future research options. Several years ago clinicians with expertise in this area submitted a proposal to NIHR but this was not successful, hence the MoD route for funding the McMenemy trial discussed above. The PWG feel that the best avenue for generating evidence would be through a register using the updated and more specific audit requirements in the policy. This approach is being used in the U.S. to collect data on outcomes. International colleagues are currently in discussion of an international database for these patients although barriers do exist.

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