

Bone-anchored implants for direct attachment of external prostheses for persons with transfemoral amputation: Protocol for a systematic review

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Introduction

Rationale:

Amputation of the lower limb has a severe impact on physical function, psychological well-being, and social participation.¹⁻⁸ Following an amputation, the conventional method of attaching a prosthetic limb to the body is through a custom-designed socket-suspension system to which their prosthetic devices are connected (hereafter called “socket prosthesis”). About 86% of people with a major lower extremity amputation are fitted with a socket prosthesis.⁹ Prosthetic limbs dependent on socket-suspension systems have evolved over the past few decades, with substantial technological advancements, but there still are limitations to their use. The socket is custom-designed for each individual user according to the condition and shape of their residual limb. They rely on suction or strapping of the prosthesis to the residual limb. The socket must fit securely to the residual limb to maximize comfort, to transmit the forces of the skeleton to the ground, and to allow the movement of the residual limb to control the prosthetic limb. The

interface between the residual limb and the socket is one of the most crucial aspects for the success of any prosthesis and continues to be a major limiting factor in prosthetic use. Discomfort and problems related to the fit of the socket are common and have been shown to negatively affect the quality of life and mobility of the user.¹⁰⁻¹³ Lack of comfort, skin ulcers,¹⁴ inadequate or fluctuating suspension,¹⁵ tissue irritation, excessive heat and perspiration,¹⁴ poor control due to the motion of the soft tissue within the socket, and low confidence with mobility¹² are problems that plague many prosthetic users. Between 34% and 63% of socket prosthesis users have chronic skin problems and pain resulting from friction between the residual limb and the prosthesis which lead to reduced prosthetic use and function, reduced quality of life and detrimental body image.^{12,16-19} The socket can also restrict the range of movement of the proximal joint leading to difficulties in sitting or participating in activities of daily living. These issues necessitate frequent refitting in up to three-quarters of socket prosthesis users.¹¹

These problems spurred the development of new techniques of attaching prosthetic components directly to the bone of the residual limb, bypassing the need for a socket interface. This procedure, termed *osseointegration*, has become an established treatment option in several areas of the world. This technology which relies on anchoring the prosthetic devices directly to the bone of the residual limb involves the surgical insertion of a titanium implant into the centre of the residual femur, which extends percutaneously, i.e., through the skin, to allow a direct structural and functional connection to a prosthetic leg.^{20,21} Titanium is naturally biocompatible (non-toxic and non-allergenic) and the titanium implant integrates with living bone tissue. A connector allows for proper attachment of the implant to the prosthesis.

Several types of implants exist and previous reviews on this topic focus separately on clinical outcomes^{22,23} or complications.²⁴ To date, there is no review of the available health economic literature available on this top. Therefore, there needs to be a single resource to which clinicians and policymakers can refer if they need to learn about the evidence on clinical efficacy, adverse events, patient experience, and cost-effectiveness.

Objectives:

The research question guiding this systematic review is:

What is the (a) clinical-effectiveness and safety, (b) patient experience, and (b) cost-

effectiveness of bone-anchored implants that enable attachment of prosthetic devices for persons with above-knee amputations?

Methods:

Eligibility criteria:

Population: Persons with a unilateral or bilateral transfemoral (above-knee) amputation

Intervention: Osseointegrated/bone-anchored implants to which prosthetic legs are attached

Comparator: Socket-suspension systems to which prosthetic legs are attached or no prosthesis

Outcome: Health-related quality of life, mobility, prosthesis usage, safety, patient experiences, health economic outcomes

Time: Experimental or observational studies that have a comparison group

Studies: Peer-reviewed original quantitative and qualitative research studies published in English, but not other health technology assessments, systematic reviews, case reports, opinion pieces, or editorials

Exclusion criteria: Articles not meeting the criteria above will be excluded.

Information sources

The following databases will be searched: Ovid MEDLINE® ALL, including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Embase, Cochrane Library (Wiley), CINAHL (Ebsco), the Core Collection of Web of Science, and PubMed.

Search strategy

Specific details regarding the search strategy is available in Appendix 1. An experienced medical information specialist (BS) developed and tested the search strategies through an iterative process in consultation with the two of the review authors (MR and TDS). Using the multifile and deduplication tool options in OVID, we will search Ovid MEDLINE® ALL, including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Embase. We also searched the Cochrane Library (Wiley), CINAHL (Ebsco), the Core Collection of Web of Science, and PubMed. Searches were performed on March 14, 2021, and will be updated in mid-2023. The strategies will utilize a combination of controlled vocabulary (e.g., "Bone-Anchored Prosthesis", "Osseointegration", "Bones of Lower Extremity") and keywords (e.g., "OPRA",

"osseo-anchor", "femur"). Vocabulary and syntax will be adjusted across the databases, and no language or date restrictions will be imposed, although animal-only records will be removed where possible. Results will be downloaded and deduplicated using EndNote version 9.3.3 (Clarivate Analytics) and uploaded to Covidence²⁵. Reference lists of the articles selected for full-text or included in this review will also be searched for additional sources.

Study records

Data management:

Covidence will be used to manage the data and carry out the screening procedures for this study.

Selection process:

Title and abstract screening will be carried out by two reviewers (MR and TDS). Full-text review will be carried out by two reviewers (MR and TDS). Any conflicts at these stages will be handled by consensus (between MR and TDS). A third reviewer (JSH) will serve as arbiter when needed.

Data collection process:

Data extraction template will be developed through discussion between three reviewers (MR, TDS, JSH) and will be trialed with two included articles by two reviewers (MR and TDS). Following this, one reviewer (MR) will carry out data extraction which will be validated by discussion with another reviewer (JSH) who is a subject matter expert on prosthesis research.

Data items

Essential characteristics of the studies, including study type, country of the centre publishing the study, funding source, number of patients, sex ratio, laterality, age of participants at treatment, time since amputation, etiology of the patients, length of follow-up, in addition to the outcomes of interest, will be extracted.

Outcomes

Outcomes on clinical efficacy including health-related quality of life, mobility, prosthesis usage, disability, prosthesis satisfaction will be extracted depending on what is available in the literature. Complications and adverse events data will be extracted including types and incidence

of complications/adverse events, and odds of complications. Patient experiences, changes in lived experience and challenges with bone-anchored implants that enable prosthetic fixation will be extracted from the qualitative literature. Health economic variables including study type, costs, outcomes, ICER will be extracted. The above noted variables may change based on what's available in the literature.

Risk of bias evaluation

Risk of bias will be evaluated using appropriate tools based on the study design of the articles included in the final review.

Data synthesis

Data will be presented in a tabular format for evidence on clinical efficacy, complications, patient experiences, and health economic data. A meta-analysis will be carried out if possible. If methodologically not feasible, a narrative summary will be conducted and presented.

Confidence in cumulative evidence

Confidence in the cumulative evidence will be determined based on the available literature, the quality of the literature, and the risk of bias assessments.

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Appendix 1: Literature search

Search number	Query	Search Details
18	#16 not #17	((("bone anchored prosthesis"[MeSH Terms] OR (("Prostheses and Implants"[MeSH Terms:noexp] OR "Artificial Limbs"[MeSH Terms] OR "Joint Prosthesis"[MeSH Terms] OR "Prosthesis Design"[MeSH Terms] OR ("prosthe*" [Text Word] OR "amput*" [Text Word] OR "artificial limb*" [Text Word]) OR (("limb"[Text Word] OR "limbs"[Text Word]) AND ("miss*" [Text Word] OR "loss"[Text Word] OR "lost"[Text Word] OR "lose"[Text Word]))) AND ("osseointegrat*" [Text Word] OR "osseo integrat*" [Text Word] OR "bone-anchored" [Text Word] OR "bone-anchored" [Text Word] OR "osseoanchor*" [Text Word] OR ("skelet*" [Text Word] AND ("fixed" [Text Word] OR "fixation" [Text Word]))) AND ("bones of lower extremity" [MeSH Terms:noexp] OR "femur" [MeSH Terms] OR "foot bones" [MeSH Terms] OR "leg bones" [MeSH Terms] OR "lower extremity" [MeSH Terms] OR ("ankle" [MeSH Terms] OR "ankle joint" [MeSH Terms]) OR "foot" [MeSH Terms] OR ("knee" [MeSH Terms] OR "knee joint" [MeSH Terms]) OR "leg" [MeSH Terms] OR "thigh" [MeSH Terms] OR ("lower extremit*" [Text Word] OR "lower limb*" [Text Word] OR "ankle" [Text Word] OR "ankles" [Text Word] OR "foot" [Text Word] OR "feet" [Text Word] OR "knee" [Text Word] OR "knees" [Text Word] OR "leg" [Text Word] OR "legs" [Text Word] OR "thigh*" [Text Word] OR "femur" [Text Word] OR "tibia" [Text Word] OR "transfemora*" [Text Word] OR "trans femora*" [Text Word] OR "transtibia*" [Text Word] OR "trans tibia*" [Text Word]))) NOT ("animals" [MeSH Terms] NOT "humans" [MeSH Terms]) NOT ("child" [MeSH Terms] NOT ("adolescent" [MeSH Terms] OR "adult" [MeSH Terms]))
17	child[MeSH] not (adolescent[MeSH] or adult[MeSH])	"child" [MeSH Terms] NOT ("adolescent" [MeSH Terms] OR "adult" [MeSH Terms])
16	#14 not #15	((("bone anchored prosthesis"[MeSH Terms] OR (("Prostheses and Implants"[MeSH Terms:noexp] OR "Artificial Limbs"[MeSH Terms] OR "Joint Prosthesis"[MeSH Terms] OR "Prosthesis Design"[MeSH Terms] OR ("prosthe*" [Text Word] OR "amput*" [Text Word] OR "artificial limb*" [Text Word]) OR (("limb"[Text Word] OR "limbs"[Text Word]) AND ("miss*" [Text Word] OR "loss"[Text Word] OR "lost"[Text Word] OR "lose"[Text Word]))) AND ("osseointegrat*" [Text Word] OR "osseo integrat*" [Text Word] OR "bone-anchored" [Text Word] OR "bone-anchored" [Text Word] OR "osseoanchor*" [Text Word] OR ("skelet*" [Text Word] AND ("fixed" [Text Word] OR "fixation" [Text Word]))) AND ("bones of lower extremity" [MeSH Terms:noexp] OR "femur" [MeSH Terms] OR "foot bones" [MeSH Terms] OR "leg

		bones"[MeSH Terms] OR "lower extremity"[MeSH Terms] OR ("ankle"[MeSH Terms] OR "ankle joint"[MeSH Terms]) OR "foot"[MeSH Terms] OR ("knee"[MeSH Terms] OR "knee joint"[MeSH Terms]) OR "leg"[MeSH Terms] OR "thigh"[MeSH Terms] OR ("lower extremit*" [Text Word] OR "lower limb*" [Text Word] OR "ankle" [Text Word] OR "ankles" [Text Word] OR "foot" [Text Word] OR "feet" [Text Word] OR "knee" [Text Word] OR "knees" [Text Word] OR "leg" [Text Word] OR "legs" [Text Word] OR "thigh*" [Text Word] OR "femur" [Text Word] OR "tibia" [Text Word] OR "transfemora*" [Text Word] OR "trans femora*" [Text Word] OR "transtibia*" [Text Word] OR "trans tibia*" [Text Word])) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])
15	animals[MeSH] not humans[MeSH]	"animals"[MeSH Terms] NOT "humans"[MeSH Terms]
14	#10 and #13	("bone anchored prosthesis"[MeSH Terms] OR (("Prostheses and Implants"[MeSH Terms:noexp] OR "Artificial Limbs"[MeSH Terms] OR "Joint Prosthesis"[MeSH Terms] OR "Prosthesis Design"[MeSH Terms] OR ("prosthe*" [Text Word] OR "amput*" [Text Word] OR "artificial limb*" [Text Word]) OR ("limb" [Text Word] OR "limbs" [Text Word]) AND ("miss*" [Text Word] OR "loss" [Text Word] OR "lost" [Text Word] OR "lose" [Text Word]))) AND ("osseointegrat*" [Text Word] OR "osseo integrat*" [Text Word] OR "bone-anchored" [Text Word] OR "bone-anchored" [Text Word] OR "osseoanchor*" [Text Word] OR ("skelet*" [Text Word] AND ("fixed" [Text Word] OR "fixation" [Text Word]))) AND ("bones of lower extremity"[MeSH Terms:noexp] OR "femur"[MeSH Terms] OR "foot bones"[MeSH Terms] OR "leg bones"[MeSH Terms] OR "lower extremity"[MeSH Terms] OR ("ankle"[MeSH Terms] OR "ankle joint"[MeSH Terms]) OR "foot"[MeSH Terms] OR ("knee"[MeSH Terms] OR "knee joint"[MeSH Terms]) OR "leg"[MeSH Terms] OR "thigh"[MeSH Terms] OR ("lower extremit*" [Text Word] OR "lower limb*" [Text Word] OR "ankle" [Text Word] OR "ankles" [Text Word] OR "foot" [Text Word] OR "feet" [Text Word] OR "knee" [Text Word] OR "knees" [Text Word] OR "leg" [Text Word] OR "legs" [Text Word] OR "thigh*" [Text Word] OR "femur" [Text Word] OR "tibia" [Text Word] OR "transfemora*" [Text Word] OR "trans femora*" [Text Word] OR "transtibia*" [Text Word] OR "trans tibia*" [Text Word]))
13	#11 or #12	"bones of lower extremity"[MeSH Terms:noexp] OR "femur"[MeSH Terms] OR "foot bones"[MeSH Terms] OR "leg bones"[MeSH Terms] OR "lower extremity"[MeSH Terms] OR "ankle"[MeSH Terms] OR "ankle joint"[MeSH Terms] OR "foot"[MeSH Terms] OR "knee"[MeSH Terms] OR "knee joint"[MeSH Terms] OR "leg"[MeSH Terms] OR "thigh"[MeSH Terms] OR "lower extremit*" [Text Word] OR "lower limb*" [Text Word] OR "ankle" [Text Word] OR "ankles" [Text Word] OR "foot" [Text Word] OR "feet" [Text Word] OR "knee" [Text Word] OR "knees" [Text Word] OR

		"leg"[Text Word] OR "legs"[Text Word] OR "thigh*"[Text Word] OR "femur"[Text Word] OR "tibia"[Text Word] OR "transfemora*"[Text Word] OR "trans femora*"[Text Word] OR "transtibia*"[Text Word] OR "trans tibia*"[Text Word]
12	"lower extremit*"[tw] or "lower limb*"[tw] or ankle[tw] or ankles[tw] or foot[tw] or feet[tw] or knee[tw] or knees[tw] or leg[tw] or legs[tw] or thigh*[tw] or femur[tw] or tibia[tw] or "transfemora*"[tw] or "trans-femora*"[tw] or "transtibia*"[tw] or "trans-tibia*"[tw]	"lower extremit*"[Text Word] OR "lower limb*"[Text Word] OR "ankle"[Text Word] OR "ankles"[Text Word] OR "foot"[Text Word] OR "feet"[Text Word] OR "knee"[Text Word] OR "knees"[Text Word] OR "leg"[Text Word] OR "legs"[Text Word] OR "thigh*"[Text Word] OR "femur"[Text Word] OR "tibia"[Text Word] OR "transfemora*"[Text Word] OR "trans femora*"[Text Word] OR "transtibia*"[Text Word] OR "trans tibia*"[Text Word]
11	"bones of lower extremity"[MeSH:noexp] or femur[MeSH] or "foot bones"[MeSH] or "leg bones"[MeSH] or Lower Extremity[MeSH] or Ankle[MeSH] or Foot[MeSH] or Knee[MeSH] or Leg[MeSH] or Thigh[MeSH]	"bones of lower extremity"[MeSH Terms:noexp] OR "femur"[MeSH Terms] OR "foot bones"[MeSH Terms] OR "leg bones"[MeSH Terms] OR "lower extremity"[MeSH Terms] OR "ankle"[MeSH Terms] OR "ankle joint"[MeSH Terms] OR "foot"[MeSH Terms] OR "knee"[MeSH Terms] OR "knee joint"[MeSH Terms] OR "leg"[MeSH Terms] OR "thigh"[MeSH Terms]
10	#1 or #9	"bone anchored prosthesis"[MeSH Terms] OR (("Prostheses and Implants"[MeSH Terms:noexp] OR "Artificial Limbs"[MeSH Terms] OR "Joint Prosthesis"[MeSH Terms] OR "Prosthesis Design"[MeSH Terms] OR ("prosthe*"[Text Word] OR "amput*"[Text Word] OR "artificial limb*"[Text Word]) OR ("limb"[Text Word] OR "limbs"[Text Word]) AND ("miss*"[Text Word] OR "loss"[Text Word] OR "lost"[Text Word] OR "lose"[Text Word])) AND ("osseointegrat*"[Text Word] OR "osseo integrat*"[Text Word] OR "bone-anchored"[Text Word] OR "bone-anchored"[Text Word] OR "osseoanchor*"[Text Word] OR ("skelet*"[Text Word] AND ("fixed"[Text Word] OR "fixation"[Text Word])))
9	#7 and #8	("Prostheses and Implants"[MeSH Terms:noexp] OR "Artificial Limbs"[MeSH Terms] OR "Joint Prosthesis"[MeSH Terms] OR "Prosthesis Design"[MeSH Terms] OR ("prosthe*"[Text Word] OR "amput*"[Text Word] OR "artificial limb*"[Text Word]) OR ("limb"[Text Word] OR "limbs"[Text Word]) AND ("miss*"[Text Word] OR "loss"[Text Word] OR "lost"[Text Word] OR "lose"[Text Word])) AND ("osseointegrat*"[Text Word] OR "osseo integrat*"[Text Word] OR "bone-anchored"[Text Word] OR "bone-anchored"[Text Word] OR "osseoanchor*"[Text Word] OR ("skelet*"[Text Word] AND ("fixed"[Text Word] OR "fixation"[Text Word])))

8	#5 or #6	"osseointegrat*"[Text Word] OR "osseo integrat*"[Text Word] OR "bone-anchored"[Text Word] OR "bone-anchored"[Text Word] OR "osseanchor*"[Text Word] OR ("skelet*"[Text Word] AND ("fixed"[Text Word] OR "fixation"[Text Word]))
7	#2 or #3 or #4	"Prostheses and Implants"[MeSH Terms:noexp] OR "Artificial Limbs"[MeSH Terms] OR "Joint Prosthesis"[MeSH Terms] OR "Prosthesis Design"[MeSH Terms] OR ("prosthe*"[Text Word] OR "amput*"[Text Word] OR "artificial limb*"[Text Word]) OR (("limb"[Text Word] OR "limbs"[Text Word]) AND ("miss*"[Text Word] OR "loss"[Text Word] OR "lost"[Text Word] OR "lose"[Text Word]))
6	skelet*[tw] and (fixed[tw] or fixation[tw])	"skelet*"[Text Word] AND ("fixed"[Text Word] OR "fixation"[Text Word])
5	osseointegrat*[tw] or osseo-integrat*[tw] or "bone-anchored"[tw] or "bone anchored"[tw] or osseo-anchor*[tw] or osseoanchor*[tw]	"osseointegrat*"[Text Word] OR "osseo integrat*"[Text Word] OR "bone-anchored"[Text Word] OR "bone-anchored"[Text Word] OR "osseanchor*"[Text Word]
4	(limb[tw] or limbs[tw]) and (miss*[tw] or loss[tw] or lost[tw] or lose[tw])	("limb"[Text Word] OR "limbs"[Text Word]) AND ("miss*"[Text Word] OR "loss"[Text Word] OR "lost"[Text Word] OR "lose"[Text Word])
3	prosthe*[tw] or amput*[tw] or artificial limb*[tw]	"prosthe*"[Text Word] OR "amput*"[Text Word] OR "artificial limb*"[Text Word]
2	"Prostheses and Implants"[MeSH:noexp] or "Artificial Limbs"[MeSH] or "Joint Prosthesis"[MeSH] or "Prosthesis Design"[MeSH]	"Prostheses and Implants"[MeSH Terms:noexp] OR "Artificial Limbs"[MeSH Terms] OR "Joint Prosthesis"[MeSH Terms] OR "Prosthesis Design"[MeSH Terms]
1	Bone-Anchored Prosthesis [MeSH]	"bone anchored prosthesis"[MeSH Terms]