Review Article

# Low back pain in persons with lower extremity amputation: a systematic review of the literature

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**Abstract**

**BACKGROUND CONTEXT:** Lower extremity amputation (LEA) is associated with an elevated risk for development and progression of secondary health conditions. Low back pain (LBP) is one such condition adversely affecting function, independence, and quality of life.
**PURPOSE:** The purpose of this study was to systematically review the literature to determine the strength of evidence relating the presence and severity of LBP secondary to LEA, thereby supporting the formulation of empirical evidence statements (EESs) to guide practice and future research.
**STUDY DESIGN/SETTING:** Systematic review of the literature.

**METHODS:** A systematic review of five databases was conducted followed by evaluation of evidence and synthesis of EESs.

**RESULTS:** Seventeen manuscripts were included. From these, eight EESs were synthesized within the following categories: epidemiology, amputation level, function, disability, leg length, posture, spinal kinematics, and osseointegrated prostheses. Only the EES on epidemiology was supported by evidence at the moderate confidence level given support by eight moderate quality studies. The four EESs for amputation level, leg length, posture, and spinal kinematics were supported by evidence at the low confidence level given that each of these statements had some evidence not supporting the statement but ultimately more evidence (and of higher quality) currently supporting the statement. The remaining three EESs that addressed function, disability and osseointegrated prosthetic use were all supported by single studies or had comparable evidence that disagreed with study findings rendering insufficient evidence to support the respective EES.

**CONCLUSIONS:** Based on the state of the current evidence, appropriate preventative and, particularly, treatment strategies to manage LBP in persons with LEA remain a knowledge gap and an area of future study.   © 2018 Elsevier Inc. All rights reserved.

# Introduction

Common musculoskeletal derangements of the spine that contribute to low back pain (LBP) include discogenic dysfunction, facet joint syndrome, sacroiliac joint syndrome, spinal instability, and postural syndrome [1]. There are many factors related to spinal derangements including behavioral, congenital, traumatic, disease processes, and others. These derangements and factors can co-exist, leading to varying levels of disability attributed to LBP. Severe lower extremity trauma, including lower extremity amputation (LEA), can further confound and complicate the clinical presentation and management of LBP [2].

The prevalence of LBP is much higher (52%−89%) among persons with LEA as compared to the general non-amputee population (12%−45%) [3−6]. Low back pain has been considered more bothersome than residual and phantom limb pain [4]. In a cross-sectional survey of persons with LEA (n=255), 52% rated their pain as persistent and 25% described their pain as frequent and severely interfering with daily activities [6]. Performance of daily activities with altered anatomy and biomechanics may be related to the development of LBP following LEA [7−10]. Persons with LEA present unique challenges to rehabilitation clinicians managing their LBP. Clinical practice guidelines highlighting efficacious interventions to manage LBP in this group are not available. However, sparse evidence regarding the underlying mechanisms, prevalence, intensity, and management of LBP among those with LEA is available. A systematic review and synthesis of evidence in these areas may inform the development of targeted inventions and lead to improved rehabilitation in this population. Therefore, the purpose of this project was to systematically review and evaluatethe literature, and to formulate empirical evidence statements (EESs) regarding the etiology, epidemiology, and management of patients with LEA and LBP.

# Materials and methods

## Search strategy

A search strategy used in several previous prosthesis- and amputation-related systematic reviews was implemented[11,12]. Five medical literature databases (Medline/Pubmed, CINAHL, EMBASE Elsevier, Web of Science, and Cochrane Clinical Trials Register) were searched on January 1, 2016 based on the following terms (Table 1):

- Primary search terms (target population): *transtibial, transfemoral, lower extremity*, and *amputee*.
- Secondary search terms (target comorbidity): *low back pain, sciatica, lumbago*, back pain, *back disorder, spinal disease*, and *backache*.

Searches were prelimited using the following criteria: English language, abstract available, and peer reviewed. A manual search of included articles' reference lists was also conducted in the event very recent publications or keywords missed important publications in the electronic automated search.

## Screening

Resulting references were exported to EndNote (vX7, Thompson, CA, USA) bibliographic citation software. Two reviewers independently screened resulting references' titles, then abstracts, and finally full text articles according to inclusion/exclusion criteria (listed below). Articles were then classified as either (i) pertinent, (ii) not pertinent, or (iii) uncertain pertinence. Full-text articles were then reviewed for all manuscripts classified as pertinent or uncertain pertinence. Disagreements regarding citations of uncertain pertinence were resolved by having a third reviewer independently review full-text articles, discuss, and reach agreement on ultimate inclusion or exclusion.

Table 1
Selected sample search term sets and from the Medline and CINAHL databases

| Database | Medline | CINAHL |
|---|---|---|
| General search term set | Dorsalgia[tiab] OR exp Back Pain OR backache[tiab] OR (lumbar pain)[tiab] OR coccyx[tiab] OR coccydynia[tiab] OR sciatica[tiab] OR sciatic neuropathy/ OR spondylosis [tiab] OR lumbago[tiab] | "lumbago" OR (MH "Spondylolisthesis") OR (MH "Spondylolysis") OR (MH "Thoracic Vertebrae") OR lumbar N2 vertebra OR (MH "Lumbar Vertebrae") OR "coccydynia" OR "coccyx" OR "sciatica" OR (MH "Sciatica") OR (MH "Coccyx") OR lumbar N5 pain OR lumbar W1 pain OR "backache" OR (MH "Low Back Pain") OR (MH "Back Pain+") OR "dorsalgia" |
| Amput* string | (((((("Lower Extremity"[Mesh] OR lower extrem*[TIAB] OR lower extrem*[OT] OR lower limb*[TIAB] OR lower limb*[OT] OR leg[TIAB] OR leg[OT] OR legs[TIAB] OR legs [OT] OR hip[TIAB] OR hip[OT] OR hips[TIAB] OR hips [OT] OR thigh*[TIAB] OR thigh*[OT] OR foot[TIAB] OR foot[OT] OR feet[TIAB] OR feet[OT] OR "Knee Joint"[Mesh] OR knee[TIAB] OR knee[OT] OR knees[TIAB] OR knees[OT] OR "Ankle Joint"[Mesh] OR ankle*[TIAB] OR ankle*[OT] OR "Femur"[Mesh] OR femur*[TIAB] OR femur*[OT] OR transfemoral[TIAB] OR transfemoral[OT] OR trans-femoral[TIAB] OR trans-femoral[OT] OR "Tibia"[Mesh] OR tibia*[TIAB] OR tibia*[OT] OR transtibial[TIAB] OR transtibial[OT] OR trans-tibial[TIAB] OR trans-tibial [OT] OR transpelvic[TIAB] OR transpelvic[OT] OR trans-pelvic[TIAB] OR trans-pelvic[OT] OR syme's[TIAB] OR syme's[OT] OR symes[TIAB] OR symes[OT]))) AND (("Amputation"[Mesh] OR amput*[TIAB] OR amput*[OT] OR disarticulat*[TIAB] OR disarticulat*[OT] OR hemipelvectom*[TIAB] OR hemipelvectom*[OT] OR "Amputees"[Mesh] OR "Amputation Stumps"[Mesh] OR "Artificial Limbs"[Mesh] OR artificial limb*[TIAB] OR artificial limb*[OT] OR "Amputation, Traumatic"[Mesh] OR "Prostheses and Implants"[Mesh:noexp] OR residual limb*[TIAB] OR residual limb*[OT] OR limb loss*[TIAB] OR limb loss*[OT] OR prosthe*[TIAB] OR prosthe*[OT] OR stump*[TIAB] OR stump*[OT])))) | ((MH "Lower Extremity+") OR (TI lower extrem* OR AB lower extrem*) OR (TI lower limb* OR AB lower limb*) OR (TI leg OR AB leg) OR (TI legs OR AB legs) OR (TI hip OR AB hip) OR (TI hips OR AB hips) OR (TI foot OR AB foot) OR (TI feet OR AB feet) OR (MH "Knee Joint+") OR (TI knee OR AB knee) OR (TI knees OR AB knees) OR (MH "Ankle Joint") OR (TI ankle* OR AB ankle*) OR (MH "Femur+") OR (TI femur* OR AB femur*) OR (TI transfemoral OR AB transfemoral) OR (TI trans-femoral OR AB trans-femoral) OR (MH "Tibia") OR (TI tibia* OR AB tibia*) OR (TI transtibial OR AB transtibial) OR (TI trans-tibial OR AB trans-tibial) OR (TI transpelvic OR AB transpelvic) OR (TI trans-pelvic OR AB trans-pelvic) OR (TI syme's OR AB syme's) OR (TI symes OR AB symes) OR (TI thigh* OR AB thigh*)) AND ((MH "Amputation+") OR (TI amput* OR AB amput*) OR (TI disarticulat* OR AB disarticulat*) OR (TI hemipelvectom* OR AB hemipelvectom*) OR (MH "Amputees") OR (MH "Amputation, Traumatic") OR (MH "Limb Prosthesis") OR (TI prosthe* OR AB prosthe*) OR (TI artificial limb* OR AB artificial limb*) OR (TI limb loss OR AB limb loss) OR (TI residual limb* OR AB residual limb*) OR (TI stump* OR AB stump*) OR (MH "Prostheses and Implants")) |

Inclusion criteria were as follows: (1) peer-reviewed publication; (2) English language; (3) published within the previous 10 years (2006−2016); and (4) study included subjects with both lower extremity amputation and low back pain;

Exclusion criteria were as follows: publication date outside of the 10-year search window; nonhuman subject research; non-English language; pediatric studies; studies of patients with bilateral lower extremity amputations; case report or case series methodology; studies of digit or partial foot amputation; hypothesis, editorial, classification, or taxonomy papers; thesis, dissertation, and preliminary or pilot level research; and duplicate publication.

*Study data*

Data from each article including demographic, anthropometric, dependent and independent variables, quantifiable outcomes, and conclusions were entered into an Excel database (Microsoft Corporation. Redmond, WA, USA). These data were verified by a multidisciplinary team (ie, physical therapists, prosthetists, chiropractors, and biomechanists) for completeness and accuracy. Data were assessed for the ability to aggregate for descriptive characteristics (ie,

anthropometrics) as well as outcomes (ie kinematic data and pain) and to calculate effect sizes (Cohen *D*) [13]. To prevent double counting of subject data, data from systematic reviews were not included in the extraction and aggregation.

*Quality assessment*

The study design and methodologic quality of those publications meeting eligibility criteria were independently assessed by two reviewers according to the American Academy of Orthotists and Prosthetists (AAOP) State-of-the-Science Evidence Report Guideline Protocol [14]. Prior to assessment, the two raters participated in a prelaunch reliability procedure. Test articles were assigned to the two reviewers for assessment. The process was repeated until 90% agreement was attained regarding use of the AAOP rating tool as scored by a third rater. Reviewers discussed pertinent issues until consensus on study design and methodological quality was obtained for the included publications. Each reviewer rated each study according to the AAOP Study Design Classification Scale that describes the type of study design [14]. The State of the Science Conference Quality Assessment Form [14] was used to rate

methodologic quality of studies classified as experimental (E1−E5) or observational (O1−O6). The form identifies 18 potential threats to internal validity and eight potential threats to external validity. In accordance with the guidelines, examples of criteria are provided and described as not applicable for certain study designs; however, guidelines indicate that provided examples are not exhaustive and that reviewers should use their judgment in determining which criteria are not applicable for certain study designs [14]. Threats were evaluated and tabulated.

The internal and external validity of each study was then subjectively rated as "high," "moderate," or "low" based on the quantity and importance of threats present. As a guide for rating the internal and external validity separately, studies achieving ≥80% of applicable criteria were classified as "high." If studies achieved <80% but >50% of applicable criteria, they were classified as "moderate." Studies achieving ≤50% of applicable criteria received a "low" classification. Each study was then given an overall quality of evidence rating of either "high," "moderate," or "low" by combining the ratings of internal and external validity as outlined by the AAOP State-of-the-Science Evidence Report Guidelines [14]. The overall ratings from the AAOP State-of-the-Science Evidence Report Guidelines were used in assigning confidence to the developed EESs described in the *Results* section.

*Empirical evidence statements*

Based on results from the included publications, EESs were developed describing collective findings from included research regarding LBP in persons with LEA. Reviewers rated the level of confidence of each EES as "high," "moderate," "low," or "insufficient," based on the number of publications contributing to the statement; the methodologic quality of those studies and whether the contributing findings were confirmatory or conflicting [14].

**Results**

In total, 302 articles were identified from the search (Fig. 1). Ten articles required eligibility determination by the third rater. In most cases, articles requiring the additional review were studies of the spine in a sample of individuals with amputation but the subjects did not have a history of LBP and thus were excluded.

Ultimately, 17 of the original 302 articles met inclusion criteria. Four articles were published in 2009. Between 2006 and 2016, the mean (standard deviation [SD]) number of articles published per year on the subject of LBP in LEA was 1.5 (1.1) (Fig. 2). Study designs included 13 cross-sectional studies, one controlled trial, and three systematic reviews (Table 2). Manuscripts were published predominantly in physical medicine, rehabilitative, and
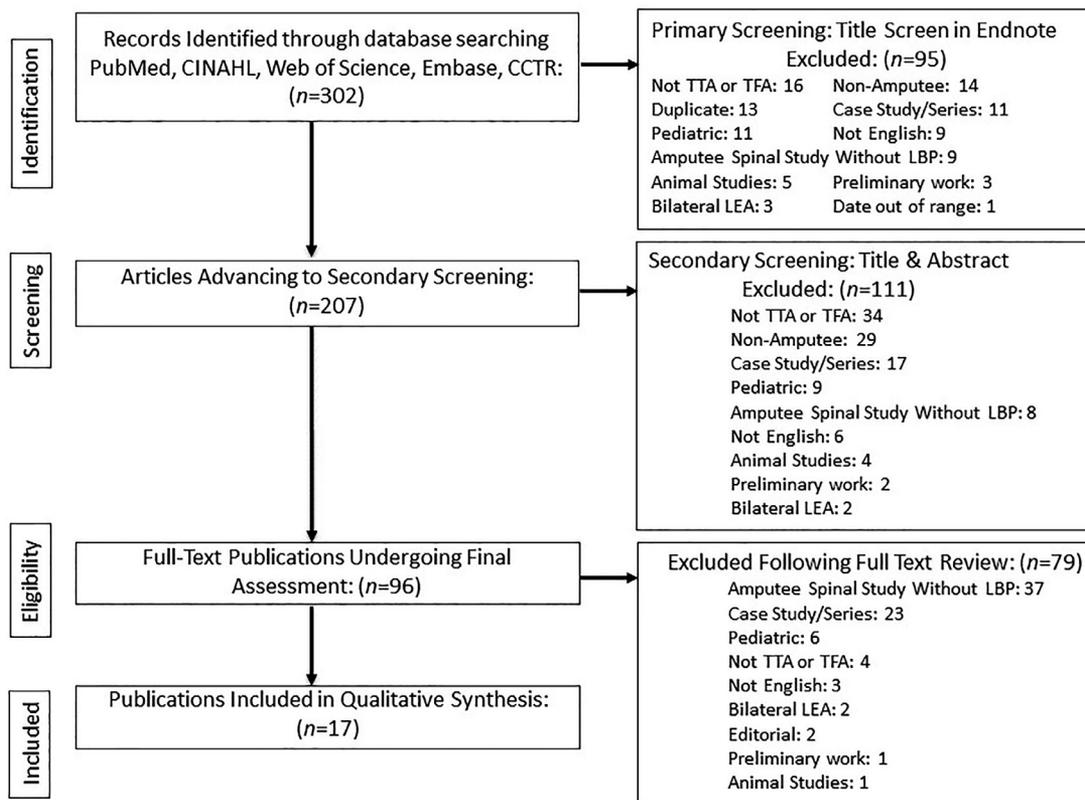


Fig. 1. Results of the literature search and application. TTA, transtibial amputee; TFA, transfemoral amputee; LBP, low back pain; LEA, lower extremity amputation.
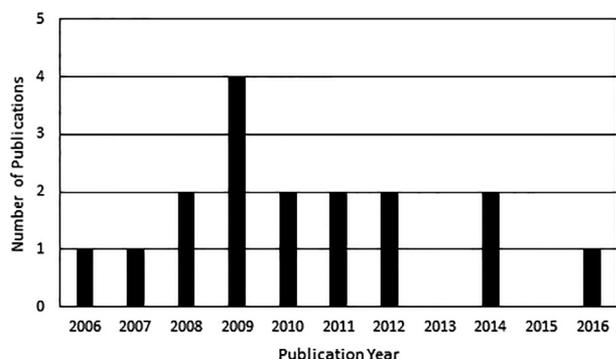
Fig. 2. Included studies by publication year.

Table 2
Distribution of included studies by study design

| Study design | Number of publications |
|---|---|
| Meta-analysis ($S_1$) | 0 |
| Systematic review ($S_2$) | 3 |
| Randomized control trial ($E_1$) | 0 |
| Controlled trial ($E_2$) | 1 |
| Interrupted time series trial ($E_3$) | 0 |
| Single subject trial ($E_4$) | 0 |
| Controlled before and after trial ($E_5$) | 0 |
| Cohort study ($O_1$) | 0 |
| Case-control study ($O_2$) | 0 |
| Cross-sectional study ($O_3$) | 13 |
| Qualitative study ($O_4$) | 0 |
| Case series ($O_5$) | 0 |
| Case study ($O_6$) | 0 |
| Group consensus ($X_1$) | 0 |
| Expert opinion ($X_2$) | 0 |
| Total | 17 |

Table 3
Distribution of the studies per journal

| Journal | Number of publications |
|---|---|
| American Journal of Physical Medicine & Rehabilitation | 3 |
| Archives of Physical Medicine & Rehabilitation | 1 |
| Bosnian Journal of Basic Medical Sciences | 1 |
| British Journal of Surgery | 1 |
| Disability & Rehabilitation | 1 |
| Gait and Posture | 1 |
| Irish Journal of Medical Science | 1 |
| Journal of Foot & Ankle Surgery | 1 |
| Journal of Orthopaedic Trauma | 1 |
| Journal of Rehabilitation Research & Development | 4 |
| Military Medicine | 1 |
| Prosthetics Orthotics International | 1 |
| Total | 17 |

biomechanical journals (Table 3). Due to heterogeneity in sample size and demography, methods, accommodation periods, outcome measures and design, the calculation of effect sizes and meta-analyses was not possible (Table 4).

### Subjects

The clinical, patient-oriented studies included a total of 1,260 experimental subjects with a mean (SD; range) sample size of n = 79 (94;8−298). These were subjects with the combination of LEA and LBP. The interquartile mean (IQM) (interquartile range [IQR]) age for experimental study subjects (ie, those with LEA and BP) included in the clinical, patient-oriented studies with adequate data to aggregate was 47.2 years (8.2). The absolute age range of experimental subjects was 16 to 93 years. The height and weight of subjects were only reported in one of the 17 studies. Body mass index was reported or could be calculated in three [15−17] of the 17 studies with an IQM (IQR) of 27.1 m/kg$^2$ (0.4), which is considered "overweight" according to the Centers for Disease Control and Prevention.

Of studies sufficiently describing subjects for analysis of amputation level and etiology, the majority of amputee subjects (48.3%) were transfemoral level and 36.7% were transtibial level. The remaining 15% included partial foot amputation and disarticulations of the ankle, knee, and hip. In terms of amputation etiology, when sufficiently described for detailed analysis, the majority of amputations (89.5%) were caused by trauma. Malignancy, vascular disease, illness, and congenital limb difference were the causes for limb loss in the remaining cases.

### Internal validity

Prior to rating, the prelaunch reliability procedure required three test ratings for the two raters to achieve <90% agreement. The most prevalent threats to internal validity in this body of literature include a lack of blinding, lack of use of a control group, no reported consideration for fatigue, learning, accommodation and washout, no reporting of effect size, and lack of random allocation (Table 5). Considering all included studies, the overall assessment favored moderate level internal validity (13/17 studies). Two of 17 had high internal validity [15,18] and two [19,20] had low internal validity. Additionally, seven studies had attrition greater than 20%.

### External validity

The greatest threat to external validity was inadequate descriptions of the study samples. Specifically, amputation levels, sociodemography, and anthropometry were not clearly described. Thus, it is difficult to know whether findings are generalizable to the larger population of persons with LEA and LBP. Nevertheless, the majority of the studies (12/17) had high external validity and five had moderate external validity (Table 5).

Table 4
Participant characteristics, primary outcomes and conclusions extracted from included studies

| Author (year) | Population (etiology) | Amputation level (sample size) | Mean (range/SD) age (y) | Mean (range/SD) time since amputation (y) | Primary outcome measure(s) | Conclusions |
|---|---|---|---|---|---|---|
| Kusljugic (2006) | Civilian/military (traumatic) | LEA (37) | 46 (11) | Not reported | Pain prevalence, psychosocial factors | 89% report chronic LBP. Higher levels of social function among civilian versus military |
| Ebrahimzadeh (2007) | Military (traumatic) | LEA (27) | 21 (16−54)* | 17 (15−22) | Pain prevalence, psychosocial factors | 74% report long-term pain and discomfort |
| Smith (2008) | Civilian (trauma, PVD, cong, tumor) | TTA (57), TFA (32) KD (4), HD (2), BLEA (10), AD (2) | 51 (16−83) | 17 (15) | LBP, RLP (periodicity, Frequency, intensity, ADL interference) | 48% had LBP w/ 5/10 intensity and reported activity interference of 3.4-3.8/10 |
| Morgenroth (2009) | Civilian/veterans (traumatic) | TFA w/ (9) and w/out (9) LBP | 51 (12) | 23 (15) | Static and dynamic leg length in single- and double-limb support | Static and dynamic leg length discrepancy not different b/t groups |
| Taghipour (2009) | Military (traumatic) | LEA (141) | 45 (36−63) | 22 (20−27) | Pain prevalence, health-related quality of life | LBP most impactful physical condition reducing quality of life |
| Ebrahimzadeh (2009) | Military (traumatic) | TTA (200) | 23 (14−60)* | 17 (15−22) | Pain prevalence, psychosocial factors | At long-term follow-up (~17 y), 44% reported LBP and 54% had persistent psychological problems |
| Morgenroth (2010) | Civilian/veterans (traumatic) | TFA w/ (9) and w/out (8) LBP, CTR (6) | 50 (30−77) | 23 (3−57) | Lumbar spine kinematics | Larger transverse rotations among LBP group |
| Reiber (2010) | Military (traumatic) | Vietnam (298), OIF/ OEF (283) | 61/29 | 39 (4)/3 (1) | Pain prevalence and psychosocial factors | 36%−42% report chronic LBP, 37%−59% w/ PTSD symptoms |
| Behr (2011) | (Traumatic, vascular) | TFA (14), KD (14), TTA (14) | 55 (36−85) | 12 (0.6−56) | Pain prevalence and activity level | 57% reported LBP that was "troublesome" |
| Hammarlund (2011) | Not specified (traumatic/ tumor) | TFA (19), KD (9), TTA (18) | 48 (19−79) | 23 (3−58) | Pain prevalence, health-related quality of life (RMDQ, SF36) | 87% reported LBP after amputation (vs 20% before); not different by amputation level. Lower quality of life versus normative data |
| Devan (2012) | Civilian (traumatic) | TFA (145) | 57 (18−93) | 27 (1−66) | LBP prevalence, physical activity questionnaires | 64% reported LBP and 39% reported activity restriction due to LBP |
| Esposito (2014) | Military (traumatic) | TFA w/ (9) and w/out (7) LBP, CTR (12) | 28 (22−39) | 2.7 (0.4−5.9) | Trunk-pelvic segmental coordination | Increased coronal in-phase coordination (segmental rigidity) w/ LBP |
| Hagberg (2014) | Not specified (trauma, tumor, other) | TFA (39) | 44 (12) | Not reported | Health-related quality of life (Q-TFA, SF36) | Improved quality of life, prosthesis use, and physical activity 2 y after OI |
| Fatone (2016) | civilian | TFA w/ (12) and w/out (11) LBP | 47 (20−67) | 16 (2−41) | Pelvic and spinal kinematics | Reversal of motion pattern in sagittal/transverse plane w/ and w/out LBP |

W/, with; w/out, without; Y, year(s); SD, standard deviation; LEA, lower extremity amputation; TTA, transtibial amputation; TFA, transfemoral amputation; LBP, low back pain; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; RLP, residual limb pain; ADL, activity(ies) of daily living; AD, ankle disarticulation; KD, knee disarticulation; HD, hip disarticulation; BLEA, bilateral lower extremity amputee; OI, osseointegration; CTR, control (subjects); RMDQ, Roland Morris disability questionnaire; SF36, short form 36 health survey; PTSD, post-traumatic stress disorder; Q-TFA, Questionnaire for persons with transfemoral amputation.
*At the time of injury.

Table 5
Internal and external validity of included studies

| Author (year) | Study design | Internal validity 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | Total | External validity 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kusljugic (2006)[1] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | n/a | • | • | | | | • | Mod | • | | • | • | • | • | • | • | Mod |
| Ebrahimzadeh (2007)[2] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | n/a | • | • | | • | • | • | Low | • | • | • | • | • | • | • | • | High |
| Smith (2008)[3] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | n/a | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Gailey (2008)[4] | S2 | n/a | n/a | n/a | n/a | n/a | n/a | • | • | n/a | n/a | n/a | • | n/a | n/a | | n/a | n/a | • | Mod | • | • | n/a | n/a | n/a | • | • | • | High |
| Morgenroth (2009)[5] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | • | • | • | | • | • | • | High | • | • | • | • | • | • | • | • | High |
| Robbins (2009)[6] | S2 | n/a | n/a | n/a | n/a | n/a | n/a | • | • | n/a | n/a | n/a | n/a | n/a | n/a | | n/a | n/a | • | Low | • | • | n/a | n/a | n/a | • | • | • | High |
| Taghipour (2009)[7] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | n/a | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Ebrahimzadeh (2009)[8] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | n/a | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Morgenroth (2010)[9] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | n/a | • | • | | • | • | • | High | • | • | • | • | • | • | • | • | Mod |
| Reiber (2010)[10] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | n/a | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Behr (2011)[11] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | • | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | Mod |
| Hammarlund (2011)[12] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | • | • | • | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Perkins (2012)[13] | S2 | n/a | n/a | n/a | n/a | n/a | n/a | • | • | n/a | n/a | n/a | n/a | n/a | n/a | • | n/a | n/a | • | Mod | • | • | n/a | n/a | n/a | • | • | • | Mod |
| Devan (2012)[14] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | • | • | • | • | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Russell Esposito (2014)[15] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | • | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Hagberg (2014)[16] | E2 | | • | • | • | n/a | • | • | • | n/a | • | • | • | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | High |
| Fatone (2016)[17] | O3 | n/a | n/a | n/a | n/a | n/a | • | • | • | n/a | n/a | • | • | • | • | | • | • | • | Mod | • | • | • | • | • | • | • | • | Mod |

Scoring: a dot (•) indicates that the criterion was met. A blank space indicates that the criterion was not met. n/a means the item was not applicable in that particular study design. See Table 1 for study design key.



Fig. 3. Distribution of level of confidence for empirical evidence statements (EESs).

### Funding analysis

Funding was declared in seven of 17 manuscripts (41%). One manuscript indicated private foundation support, two indicated funding through an academic institution, and four manuscripts indicated funding by way of a governmental sponsor. Within the four US government funded studies, three were supported by the US Department of Veterans Affairs and one by the National Institutes of Health. Three of the studies were funded outside of the United States. Support was not declared in nine manuscripts (53%), whereas one manuscript specifically declared that it was unfunded.

### Empirical evidence statements

Eight empirical evidence statements were synthesized. The rate of EES production in this body of evidence was eight EES's per 10 years or a crude rate of 0.8 EES/y. Lack of evidence resulted in insufficient confidence in three of the statements. Evidence supported low confidence in four of the statements and moderate confidence in one EES (Fig. 3). The topical areas covered included epidemiology, amputation level, function, disability, leg length, posture, spinal kinematics, and osseointegrated prosthetic use. Only the epidemiology EES was supported by evidence at the moderate confidence level given that it was supported by eight moderate quality studies. The four EESs for amputation level, leg length, posture, and spinal kinematics were supported by evidence at the low confidence level given that each of these statements had some evidence not supporting the statement but ultimately more evidence (and of higher quality) supporting the statement at the present time. Finally, the remaining three EESs that addressed function, disability, and osseointegrated prosthetic use were all supported by single studies or had comparable evidence (quantity and quality) that disagreed with study findings rendering insufficient evidence to support the respective EES (Table 6).

### Discussion

With regard to study design, 13 of the included studies were observational, one was experimental, and three were

Table 6
Empirical evidence statements, indicating level of confidence and category

| | Empirical evidence statement (EES) | Supporting studies | Level of confidence | Category |
|---|---|---|---|---|
| 1 | Back pain increases following lower extremity amputation | 8 × Mod*[1, 2, 6, 8, 10, 12-14] | Moderate | Epidemiology |
| 2 | Back pain is affected by level of amputation | Support: 4 × Mod*[4, 6, 7, 13]<br>Does not support: 3 × Mod[3, 11, 12] | Low | Amputation level |
| 3 | In persons with lower extremity amputation, function is affected by back pain | Support: 1 × Mod[12]<br>Does not support: 1 × Mod[14] | Insufficient | Function |
| 4 | Frequent bouts of back pain in persons with lower extremity amputation are associated with increased disability | 1 × Mod[12] | Insufficient | Disability |
| 5 | Leg length discrepancy is associated with back pain in persons with lower extremity amputation | Support: 1 × Mod*[4]<br>Does not support: 1 × High[5] | Low | Leg length |
| 6 | Postural asymmetries and postural control issues are associated with back pain in patients with lower extremity amputation | Support: 1 × Mod*[4]<br>Does not support: 1 × High[5] | Low | Posture |
| 7 | Spinal and pelvic kinematics are influenced by low back pain in persons with lower extremity amputation | Support: 2 × Mod[9, 15]<br>Does not support: 1 × Mod[17] | Low | Spinal kinematics |
| 8 | Back pain is not affected by the use of osseointegrated prosthesis | 1 × Mod[16] | Insufficient | Osseointegrated prosthetic use |

*Indicates that the supporting reference is or includes a systematic review.

systematic reviews. Although this is a somewhat heterogeneous blend of study designs, a more optimal body of literature inclusive of prospective, randomized controlled intervention trials may have enabled meta-analyses. Internal validity could have been strengthened in the included studies with minor reporting changes as described by standardized criteria [21,22]. For instance, had the included samples been better described (ie, more uniform reporting of anthropometry and demography), effect sizes been reported, and learning/accommodation and fatigue reported, more of the studies would have likely improved their internal validity ratings from low to moderate or moderate to high. Conversely, external validity was generally high in the selected studies that provide confidence that results have clinical importance despite some methodological weaknesses (ie, threats to internal validity).

In this study, the rate of EES production regarding subjects having LEA and LBP was eight EES's per 10 years (crude rate of 0.8 EES/y). This rate of EES production is considerably low compared to other areas of prosthetic literature. For example, in a previous study of lower extremity prosthetic componentry for persons with transtibial amputation [23], the EES production rate was 1.4 EES/y. More problematic is that in the componentry review, this EES production rate was based upon the use of high-quality evidence, whereas the present review of LBP in LEA is low but is based upon all available quality of evidence. Further, although key sponsors, such as NIH, were notably absent as research supporters in the componentry review, all of the studies included were funded (ie, industry, other governmental departments, nonprofit sponsors, etc.). In the present review, the majority of research available, 53%, was unfunded. This identifies numerous potential issues. For instance, high-quality research can become more difficult to accomplish without adequate funding, which could also decrease interest among researchers in this area. More funding from key research sponsors is needed in this area if the quality and quantity of available research are to become available to fill knowledge gaps related to the care of persons with LEA who suffer from LBP.

Because the majority of this body of evidence was observational by study design, the EESs tended to describe factors that affect or are affected by LBP in persons with LEA. For example, EESs described LBP as increasing following LEA, differences by amputation level, decreased function, increased disability, and altered gait mechanics associated with LBP in persons with LEA. Again, these EESs are predominated by descriptions of LBP and its effects in persons with LEA. Thus, the number of experimental studies was limited to one, minimizing the ability to determine optimal therapeutic intervention choices or their effects in managing persons with LEA who have LBP. Therefore, efficacy of interventions to manage LBP in persons with LEA remains a considerable knowledge gap and an area of future study.

The first EES indicates that LBP increases following lower extremity amputation. Eight moderate quality studies support the statement ultimately providing moderate confidence in the EES [3,5,19,20,24−27]. The reported prevalence of LBP in the included studies ranged broadly from a minimum of 36% to a maximum of 89% with an interquartile range of 34% [3,25]. The interquartile mean(SD) of the reported prevalence was 62(19)%. These minimum and mean prevalence rates of LBP in persons with LEA are considerably higher than the 15% to 25% prevalence values of LBP reported in the nonamputee general population [25].

One study reported significantly increased LBP after amputation as opposed to before amputation [5]. Furthermore, the characteristics and consequences of this pain in persons with LEA have been described as progressive, disabling, and contributing to limitations in occupation, recreation, and socialization [19,20]. With regard to function, LBP in LEAs has been associated with problems sitting, sleeping, and traveling [3]. Finally, LBP in this population has been associated with decreased health-related quality of life [5].

The second EES states that back pain is affected by level of amputation. Four moderate quality studies support the statement whereas three moderate quality studies do not support it. Ultimately, this yields a low level of confidence in the statement. Importantly, two of the studies supporting the statement were systematic literature reviews [20,28]. Both concluded that persons with transfemoral level amputation reported LBP with a higher prevalence than their transtibial counterparts, which was consistent with two additional clinical studies [27,29]. Perkins et al. suggest that the increased susceptibility to LBP at the higher amputation level may in part be the result of myofascial changes following transfemoral amputation along with gait pattern alterations [27]. Confirming these proposed causes for LBP following LEA through further research could lead to improvements in prevention and management.

Adverse effects of function related to LBP are the subject of the third EES. Hammarlund et al. used the Roland Morris Disability Questionnaire (RMDQ), a valid and reliable measure of functional capacity relative to perceived back pain in a sample of 46 nondysvascular lower extremity amputees [5]. They concluded that nearly all participants with LBP daily or several times per week reported severe or moderate disability on the RMDQ. Devan et al. assessed the relationship of back pain on function in terms of physical activity [26]. Overall, they concluded that there was no relationship between physical activity of LEAs with or without LBP and that there was an equal distribution of persons with LBP in low, medium, and high physical activity groups. They did however find that those reporting activity limitations due to LBP had lower physical activity scores than those with LBP who did not have physical activity limitations. It is important to note that this difference in function related to LBP is potentially confounded by the use of two different outcome approaches and further by the fact that Devan et al. studied those with traumatic transfemoral amputation, whereas the Hammarlund et al. sample was more heterogeneous by amputation level [5,26]. Nonetheless, further evidence is needed to understand which elements of function may potentially be impaired by LBP in persons with LEA.

Increasing frequency of LBP episodes and associated disability is the subject of EES four. A single, moderate-quality study supports EES four with a significant association ($p = .003$) between LEAs who reported LBP daily or several times per week and those reporting moderate or severe disability [5]. Devan et al. studied the relationship

between LBP and physical activity [26]. Their findings create further ambiguity in understanding disability as it relates to LBP in LEAs. That is, they found no association between physical activity in LEAs with or without LBP. One additional systematic review concluded that the majority of LEAs with LBP report minimal to no impact on social, recreational or work activities [20]. Conversely, approximately 25% described their LBP as severely interfering with these activities. These are important findings but do not directly relate to the issue of bout frequency of LBP. Ultimately, although the association identified by Hammarlund et al. was significant, the fact that only a single study supports the conclusion is presently insufficient to confidently support the statement at this time [5].

In EES five, association is made between leg length discrepancy and the presence of LBP in persons with LEA. One clinical study used the RMDQ to identify LEAs with LBP and those without [15]. Motion analysis was then used to determine leg length differences during static standing, dynamically during single and double limb support in gait and with either the prosthetic or sound foot leading. This single, high-quality clinical study did not find a relationship between leg length discrepancy and LBP. Conversely, a systematic literature review [28] indicates that leg length discrepancy among lower extremity prosthetic users is among many contributors to LBP. Further, the review states that those using prostheses that are of the same length as the sound limb have significantly fewer pain symptoms compared to those with length asymmetries between the intact and prosthetic limbs. Postural asymmetries reportedly result from these disparities. For instance, leg length differences of 12.5 mm have been associated with as much as 4° of lateral sacral tilt. It has been further reported that only 15% of LEAs use prostheses of equal length to the sound limb, whereas 34% of prosthesis users have prosthetic leg length differences greater than 20 mm, and that in 79% of cases, the prosthesis is the shorter limb. Given this disagreement between a single clinical study [15] and a systematic literature review [28], there is low confidence in the evidence supporting EES five. This statement indicates an association between leg length discrepancy and back pain in persons with lower extremity amputation. One additional clarifying point is that Morgenroth et al. studied LEAs with chronic LBP as opposed to acute onset cases. Thus, it is not currently possible to determine causation of LBP as a result of leg length discrepancy using these findings. Rather, their study is more useful in assisting to determine whether leg length discrepancy has a role in altering symptoms in chronic LBP cases among those with LEA [15].

Empirical evidence statement six is somewhat related to EES five. Though EES five directly addresses leg length discrepancy, EES six indicates that postural asymmetries and postural control issues are associated with LBP in patients with LEA. Gailey et al. report that persons with LEA tend to stand with increased sway and with increased weight bearing on the sound limb and that this may be

related to the lack of proprioception from the prosthesis [28]. Postural abnormalities observed in those with LEA are numerous including coronal and sagittal compensatory pelvic tilt, increased lumbar lordosis, involved-side hip flexion contracture, lateral trunk asymmetry and more [28]. Morgenroth et al. state that LBP is a common secondary disabling condition affecting TFA and that it is common clinical practice to assess for and correct postural asymmetry in the form of leg length discrepancy [15]. In their sample of subjects with longstanding transfemoral amputation and moderate, persistent LBP, leg length, discrepancies were not different relative to a similar population without LBP. Morgenroth et al. concluded that in longstanding transfemoral amputees with chronic symptoms, their LBP was unlikely to be related to their postural asymmetry [15]. Confidence in EES six is low given support from a systematic review but a lack of support from one clinical study, both of moderate quality.

Relative to EES seven, there is limited (n = 3 studies) evidence reporting alterations in trunk, spinal, and pelvic motions among persons with LEA with LBP (EES seven). Although LBP is multifactorial, repeated exposures to altered trunk-pelvic motions is a purported risk factor for the onset or recurrence of LBP secondary to LEA [7,9,30−33]. The presence of LBP among persons with (transfemoral) LEA is associated with larger axial rotations of the lumbar spine [18], more rigid (in-phase) trunk-pelvic coordination strategies [16], and an apparent (albeit underpowered) trend toward a reversal in patterns of trunk-pelvic motion in the sagittal and transverse planes [17]. Such findings begin suggesting linkage of specific trunk/spinal and pelvic kinematic patterns with LBP secondary to LEA. However, the presence and magnitude of LBP has been inconsistently characterized using a variety of approaches, including binary yes/no, visual analog scale (0−10), question(s) within the Prosthesis Evaluation Questionnaire, and the Grade Questionnaire. Thus, there is a clear need for more consistent and comprehensive quantification of LBP in future work. For example, using the NIH task force for chronic LBP questionnaire that aims to classify LBP by its impact (ie, intensity, interference, and physical function), or using a minimal dataset to describe participants and reporting responder analyses in addition to mean outcomes could be useful [34]. Moreover, considerable prior work among non-amputation individuals have identified substantial influences of LBP on trunk and pelvic motions[35−37], begging the question of the relative contributions of LBP and LEA on the observed movement patterns. To that end, additional biomechanical metrics are needed to understand the underlying factors driving the movement patterns.

A single moderate quality study of 39 subjects supports the final EES [38]. This statement indicates that back pain is not affected by use of an osseointegrated prosthesis. Interfacing the prosthesis with a socket has been associated with adverse effects to skin, comfort, and function [23]. For example, skin erosions of varying

degrees, pain, and unreliable suspension can all potentially emerge related to socket use [39]. Anchoring the prosthesis to the residual limb via osseointegration purportedly mitigates some of the aforementioned complications. Another issue potentially associated with socket use is that gait pattern alterations due to pain or instability could also lead to LBP. Hagberg et al. surveyed LBP in a single item from the Questionnaire for Persons with Transfemoral Amputation [38] finding that at 2 years following osseointegration, approximately 40% of subjects reported reduced LBP, nearly 40% were unchanged, and nearly 20% reported an increase in their LBP symptoms. Compared with baseline, these differences were not statistically significant. Of note, the authors indicated the small sample size and reliance solely upon subjective outcomes limited the strength of evidence. Findings were also confounded by the fact that prosthetic components were changed throughout the 2-year follow-up period. More research is needed to identify and characterize the relationships between osseointegrated prosthetic use and LBP.

Clinical practice guidelines (CPGs) for primary care management of LBP in the general population usually recommend focused history and examination, limited use of diagnostic imaging, self-care, brief education, nonsteroidal anti-inflammatory drugs, manual therapy, and exercise [40]. The US Department of Defense (DoD) and the US Department of Veterans Affairs (VA) similarly have CPGs for persons with LEA and for those with LBP [41,42]. None of the articles uncovered in this systematic review assessed the appropriateness of these recommendations for patients with LEA suffering from LBP. Whether the LBP CPGs can be applied to LEAs or if modifications in the treatment approach are needed is unknown. Further, the recommendations in the VA/DoD include measuring the intensity of LBP but also to initiate a strengthening program for the upper and lower extremities as well as the core to prevent the development of LBP [42]. These recommendations in the second version of the VA/DoD CPG were forwarded from the original CPG and were largely based in expert opinion. These recommendations remain untested in this population. Future research is needed to clarify clinical decision-making processes for management of LBP in lower extremity amputees.

*Limitations*

This body of literature only included a single experimental study [38] and a single study with high internal and external validity [15]. The majority of the included studies were observational, of moderate overall quality, and unfunded. Viewed in aggregate, the subjects studied were somewhat heterogeneous with regard to age, LEA etiology, time since LEA, and included both military and civilian sectors; the methodological quality could be improved with standardized reporting in most cases [21,22]. An example

may include more thorough sample descriptions. Additionally, incorporating blinding (ie, raters, statisticians) would also improve internal validity. Further, important factors are missed due to reporting omissions in many cases such as gender, race or ethnic considerations. Finally, this review uncovered three potential etiologies of LBP in LEA, namely, leg length discrepancy (ESS five), postural asymmetries and control issues (ESS six), and altered spinal kinematics. However, a causal relationship between these potential etiologies and LBP in LEA has not been established and requires further research.

## Conclusions

Because the majority of this body of evidence was observational instead of experimental, the EESs produced tended to describe factors affecting or that are affected by LBP in persons with LEA. More specifically, the EESs supported observationally have concluded that back pain in LEAs has relationships with the following phenomena: increased experiences, level of LEA, leg length differences, postural issues as well as spinal and pelvic kinematics. With only a single experimental study, the ability to determine optimal therapeutic intervention choices or their effects in managing LEAs who have LBP is greatly limited. Therefore, efficacy of interventions to manage LBP in persons with LEA remains a considerable knowledge gap and an area of future study.

## Acknowledgments

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