Sex and gender differences in quality of life and related domains for individuals with adult acquired lower-limb amputation: a scoping review

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Purpose: To understand what is known about sex and gender differences in quality of life (QoL) and related domains for individuals with an adult acquired lower limb amputation (LLA).

Methods: A computer-assisted literature search of four online databases was completed. Articles were included if they incorporated sex or gender as part of their data analysis with a focus on QoL-related domains. Data were analyzed using descriptive numerical analysis and thematic analysis.

Results: One hundred and eleven articles were included in this review. Women were under-represented across studies, with most of the participants being men. No articles described the inclusion of trans or non-binary persons. Differences by sex or gender were reported by 66 articles. Articles reporting on gender seldom provided descriptions of how gender was defined. Overall, women/females seemed to have worse outcomes in terms of prosthesis-related outcomes, mental health, and return to occupations.

Conclusion: Articles included in this review were not clear with how gender was defined. In order for more targeted interventions that account for sex and gender differences, studies need to be more forthcoming about how they use and define gender. Future research should seek to include gender non-conforming participants to identify additional needs.

ABSTRACT

Introduction

In the field of disability and rehabilitation, there is growing recognition of the importance of how and to what extent sex and gender may influence outcomes [1]. Sex and gender are terms that are often used interchangeably but are in fact two separate entities. According to the Canadian Institutes of Health Research (CIHR), sex is understood as a set of physical and physiological attributes that are biological in nature [2]. These biological attributes are usually categorized as male or female, but variation is possible in how they are expressed [2]. Gender encompasses the socially constructed roles, behaviours, expressions and identities of girls and boys, women and men, as well as those who identify as gender diverse. Gender influences how people perceive themselves and each other, how they act and interact, and the distribution of power and resources in society [2]. While substantial strides have been made to conduct sex and gender-based analyses in the field of disability and rehabilitation (e.g., traumatic brain injury [3]; Alzheimer’s Disease [4]), several gaps still exist for certain disability groups. Based on a preliminary scan of the literature, this is particularly evident in the field of lower limb amputation (LLA).

LLA is a life-changing event that has recently been deemed the leading cause of global disability [5]. Major LLA (ankle and above) may occur due to trauma, cancer, infection and/or complications from diabetes and/or peripheral vascular disease [6–8]. In addition to mobility impairments, persons with major LLA experience a variety of health challenges, which include phantom limb pain, low back pain, osteoarthritis, heterotopic ossification, cardiovascular disease, anxiety and depression [9–13]. It is therefore not surprising that undergoing LLA has been shown to negatively influence quality of life (QoL) [14,15].

Broadly, QoL may be conceptualized as an individual’s perception of their position in life within the context of which they live (i.e., culture and value systems) as well as in relation to their goals, expectations, standards and concerns [16]. While various
measures of QoL have been used in the LLA population to better understand their experiences living with this condition, it is not well understood how sex and gender influence QoL. Further exploration from a sex and gender lens is warranted since there are known differences in risk factors, health outcomes and experiences post-LLA [17,18]. From an epidemiological perspective, males are more likely to be at risk for an amputation [19,20]. While the reasons for this are not well understood [21], preliminary evidence suggests that males (sex) are less likely to seek timely treatment for a diabetic foot [22] and are more likely to have risk factors associated with amputation such as vascular disease and smoking [20].

Differences in experiences and perceptions of overall wellbeing by gender in LLA have also been reported [18,21]. Women are more likely to experience body image issues, are more likely to live alone as well as are less likely to receive a prosthesis than men [18,23]. However, more critical appraisals of how sex and gender are addressed in the LLA literature are needed to improve the health and QoL of this patient population. This is particularly important for the psychosocial factors of QoL (mental/emotional health, community participation, etc.) as the majority of research in this population has focused on function and mobility [14]. Furthermore, identifying variables that interact with sex and gender will help those developing interventions to better understand under which circumstances specific aspects of the intervention will work and for whom it will work [24].

To advance knowledge of how sex and gender influence QoL post-LLA, a scoping review was undertaken to map the literature [25]. Specifically, we aimed to identify studies that reported on sex and/or gender differences in QoL in people with LLA or that contextualized their findings with respect to sex and gender in the case where only one sex or gender is studied. In addition to extracting key findings as it relates to sex and gender, we also mapped which QoL outcome measures or domains have been studied.

**Materials & methods**

For the present review, the scoping review framework described by Levac et al. [25] was used. This framework builds on the original guidelines developed by Arksey et al. [26] by making specific recommendations and clarifications for each of the five stages [25]. The use of a scoping review is appropriate for examining issues of sex and gender as it relates to QoL and related domains post-LLA since scoping reviews are designed to examine the extent, range and nature of research activity as well identify gaps in the existing literature [26]. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews guidelines [27]. Finally, the protocol for this review was registered with OSF Registries (https://osf.io/89czx).

**Stage 1 – identifying research questions**

The guiding research question for this review was: What is known about sex and gender differences in QoL and related domains for individuals living with an adult acquired LLA? The sub-questions of interest were: 1) How are sex and gender defined/used in the available LLA literature?; 2) What domains and/or tools have been used to measure QoL and related domains with a sex and gender lens?; and 3) What are the major findings with respect to QoL and related domains as it pertains to sex and gender? By addressing these objectives, a better understanding of what gaps exist in the literature with respect to sex and gender analysis will be obtained and can be used to inform future research in the area.

**Stage 2 – identifying relevant studies**

A computer-assisted search of the literature on articles published from 1 January 2000 to 13 July 2020 was conducted. The date of 1 January 2000 was selected as care for individuals with LLA has advanced greatly over time with respect to surgical interventions, rehabilitation, and prosthetic care [28]. Of particular importance is that both rehabilitation [29] and prosthetic care [30] have been shown to impact QoL. Therefore, including studies from the past 20 years would ensure that the most up-to-date information is included in this scoping review. Four online databases were used to search the literature: Medline (OVID), EMBASE (OVID), CINAHL (EBSCO) and PsycINFO (OVID). In addition, key journals (e.g., Journal of Prosthetics & Orthotics, International Journal of Prosthetics & Orthotics, Disability and Rehabilitation) were manually searched to ensure that all relevant articles were identified. For knowledge syntheses (e.g., systematic reviews) that met the inclusion criteria, their reference sections were hand searched for articles that met the inclusion criteria and were not captured by the database searches. Grey literature (e.g., theses and dissertations, clinical trial protocols, key agency reports) was included to avoid publication bias and ensure thoroughness of the review. Websites of key agencies that were searched included the International Society for Prosthetics and Orthotics, Canadian Association of Physical Medicine & Rehabilitation, Trauma Association of Canada, American Academy of Physical Medicine & Rehabilitation, and International Society of Physical and Rehabilitation Medicine. ProQuest Dissertations & Theses Global and ClinicalTrials.gov were also searched. This is in line with recent developments in searching standards for scoping reviews from the Joanna Briggs Institute [31]. In order to search for relevant grey literature, we utilized the Canadian Agency for Drugs and Technologies in Health (CADTH) checklist [32], and the University of Toronto Libraries Grey Literature Documentation template (adapted from Godin et al. [33]).

After a discussion with an expert librarian at the University of Toronto, two key concepts were used to search for relevant studies. First, sex and gender and the associated key terms were included. MESH terms for this concept included: sex characteristics; sex factors; sex distribution or sex ratio; gender identity and gender. The second concept was lower limb loss and associated key terms. These included but were not limited to: lower extremity amputees; amputation or disarticulation; and prosthetics. For a sample of the search strategy for Medline (OVID) please refer to Appendix A. This search strategy was adopted for the remaining databases.

**Stage 3 – selection of relevant studies**

This study sought to include articles that covered overall QoL and related domains. From previous work done in similar reviews on QoL in this population, potential domains relevant to QoL included psychosocial wellbeing, physical functioning, environmental factors and community participation [14,30]. While these are the most commonly reported domains, other areas were included as they arose (e.g., discharge destination, sexual health). Included studies must have met the following eligibility criteria: 1) any study design (e.g., cross-sectional, qualitative, knowledge syntheses), except for clinical case studies, that included sex and/or gender as part of their analysis of the data (e.g., females have
higher QoL than men); 2) had at least one individual with a major LLA (i.e., ankle disarticulation and above) who were older than 18 years of age at the time of their amputation, and their amputation was due to trauma (i.e., accident, burns), dysvascular causes (i.e., diabetes complications or peripheral vascular disease), cancer or infection; 3) articles published in any language since 1 January 2000; and 4) not an opinion piece (e.g., narrative review article) or conference publication.

The resulting list of articles (n = 3,110) was de-duplicated with Endnote using the technique described by Bramer and colleagues [34]. This systematic guideline for removing duplicates in EndNote helped to streamline the article review process. To facilitate the screening process, the systematic reviews software production tool, Covidence, was used. Two members of the study team (SRC and AV) were responsible for the title and abstract screening. A pilot test was conducted where each reviewer independently screened 10 articles after which the agreement was compared. Interrater agreement was 90% which was sufficient to continue the title and abstract screening [35]. All titles and abstracts were screened by both reviewers.

Once the title and abstract screening was completed, full-text screening began. An initial pilot of 10 articles was conducted by the same two reviewers (SRC and AV) and an interrater agreement of 80% was achieved. Each of the full-text articles was screened by both reviewers. Data extraction began once the full-text screening was completed. Two knowledge syntheses articles that met all the inclusion criteria were not included in data extraction. Instead, their references were searched for articles that met the inclusion criteria.

Stage 4 – charting the data

Relevant data (i.e., study information, participant characteristics, outcome measures used, and results pertaining to sex and gender) were extracted using Microsoft Excel. Two members of the research team (SRC and AV) were responsible for extracting the relevant data. First, a pilot extraction was conducted on 10 randomly selected studies. The two reviewers independently collected the data from these 10 studies and met to compare findings. An acceptable level of agreement was obtained between the two reviewers (approximately 90%) [35]. Disagreements and clarifications were discussed in person until consensus was reached. Following the pilot, the remaining articles were split between the two reviewers and full data extraction was completed. For the purposes of this review, a quality assessment of the articles was not conducted. This is consistent with scoping review methodology as the purpose of this type of review is to provide an overview of existing literature regardless of quality [36]. Thus, the articles findings were not classified based on quality and reported results reflect the terminology used by the original authors of the included studies.

Stage 5 – collating, summarizing and reporting the results

Results pertaining only to sex and gender were compared across studies. To analyze the extracted data, two approaches were used: a descriptive numerical analysis and thematic analysis. In addition to these analyses, the extracted data were used to look for gaps in the literature and develop suggestions for future research.

Results

Study information

Following deduplication, N = 2,056 unique articles were included for screening (see Figure 1 for PRISMA diagram). Following the initial title and abstract screening and full-text screening, 111 articles met the inclusion criteria. Of these, 93 were cross-sectional [18,37–128], 16 were longitudinal [129–144] and 2 were intervention studies [145,146]. Grey literature that met the inclusion criteria was not included in the review process.

Figure 1. PRISMA diagram. From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.
criteria included theses/dissertations (n = 3) [123, 126, 144]. Most of the studies were conducted in the United States (n = 30) [37, 38, 40, 49, 54, 58–60, 63, 65, 68, 71, 77, 89, 100, 113–115, 118, 124, 125, 127, 129–131, 134, 135, 140, 143, 145], followed by the United Kingdom (n = 19) [18, 41, 42, 44, 55, 72, 81, 84, 92, 104, 108, 111, 112, 116, 128, 132, 137, 138, 142], Canada (n = 8) [53, 78, 85, 91, 94, 136, 141, 146], Ireland (n = 7) [39, 48, 88, 102, 103, 126, 144], and the Netherlands (n = 6) [66, 79, 80, 90, 97, 117]. The most common method of data collection was questionnaires (n = 61) [43, 45, 46, 48, 51, 52, 57, 60–62, 66, 67, 69, 73, 74, 76, 79, 81, 83–85, 88, 90, 91, 93, 96–108, 111–113, 115, 119–122, 125, 127–129, 131, 132, 135–137, 139, 140, 142–144, 146], followed by chart/data base review (n = 25) [38, 41, 44, 47, 50, 53, 55, 56, 58, 59, 63, 64, 66, 68, 71, 78, 87, 92, 95, 109, 116, 124, 130, 133, 134] and mixed methods (n = 13) [18, 37, 54, 70, 72, 77, 80, 89, 94, 110, 117, 123, 141]. Eight studies used observations (e.g., kinematics, lab studies) [40, 65, 72, 82, 86, 114, 138, 145] and only four were solely qualitative (e.g., interviews or focus groups) [39, 42, 118, 126].

Of the included articles, 42 reported on sex (i.e., identified that they collected sex) [40, 41, 45, 47–51, 54, 60, 61, 66, 68, 69, 71, 72, 79, 80, 85, 87, 95, 100, 104, 105, 107, 111, 113–117, 120, 122, 124, 129, 130, 134, 136, 137, 143, 145, 146] while 69 reported on gender (i.e., identified that they collected gender) [37–39, 42, 43, 46, 52, 53, 55–59, 62–65, 67, 70, 73–78, 82–84, 86, 88–94, 96–99, 101, 103, 106, 108–110, 118, 119, 121, 123, 125, 126, 128, 131, 133, 135, 139–142, 144]. These constructs were collected from demographic questionnaires and from medical charts. For articles that reported on sex, the majority reported study populations that were mostly male or all male (n = 36) [40, 41, 45, 47–51, 54, 60, 61, 66, 68, 69, 71, 72, 79, 80, 85, 87, 95, 100, 104, 105, 107, 111, 113–117, 120, 122, 124, 129, 130, 134, 136, 137, 143, 145, 146] with only 5 studies reported a mostly female population [54, 68, 79, 114, 134]. Further, there was one article that used an equal ratio of males to females [87]. A similar trend is apparent for those articles reporting on gender with 62 reported mostly men or all men [37, 38, 42, 44, 46, 52, 53, 55–57, 59, 62–65, 67, 70, 73–75, 78–82, 84, 86, 88–94, 96–99, 101, 103, 106, 108–110, 119, 121, 123, 125, 126, 128, 131, 135, 139, 140, 142, 144], and only 7 reporting mostly women or all women [39, 43, 58, 74, 118, 133, 141]. No studies that reported gender included information regarding trans or non-binary individuals. Only four studies mentioned how they defined gender [52, 75, 123, 139]. In these articles, gender was defined as ‘male’ or ‘female’ with two studies stating they collected data from “both genders” [75, 139]. One additional study used sex and gender interchangeably [72]. Furthermore, most sex and gender analyses were mostly descriptive (i.e., differences between males and females or men and women) rather than in explanatory. No articles used sex or gender theories as the basis of their analysis.

**Sex and gender-based results**

Fifty-five articles did not find differences on various domains of QoL [41–45, 50, 52–54, 56, 58, 61, 62, 64, 70, 75–78, 80, 83, 84, 86, 88–90, 92, 93, 95, 96, 98, 99, 103, 104, 106, 108–110, 111, 115, 120, 122, 127, 128, 132, 134, 135, 140–143, 146], while 66 reported differences [18, 37–40, 43, 45–49, 51, 54–57, 59, 60, 63, 65–69, 71–74, 79, 82, 85, 87, 89, 91, 94, 97, 100–102, 105, 107, 112–114, 116–119, 121, 123, 125, 126, 128–131, 133, 134, 136–139, 143–145] (see Figure 2). Articles most commonly reported on the more physical aspects of QoL such as physical health, prostheses use/satisfaction or mobility. Psychosocial facets such as mental health, occupations and sexual health were less frequently discussed. For the purposes of this paper, the articles where differences by sex and gender were reported will be described in more detail (see Table 1 for specific article information). To maintain consistency of reporting, for articles that reported sex the terms “male” and “female” will be used while for those articles that reported on gender we will use “men” and “women”. Where terms have been changed from what was originally reported by the article, the terms will be written in italics. For example, if an article said that they collected gender but used male and female when reporting their results, the term will be changed to *man* or *woman*.

**Overall QoL**

Overall QoL differences by gender were described by six studies utilizing the Short-Form-36 (SF-36) [37, 57, 74] and the World Health Organization Quality of Life Questionnaire (WHO QOL-BREF) [74, 121, 123, 144]. Reported findings were mixed with respect to whether men or women had higher scores on either measure. In one study, SF-36 sub-scores for role physical and role emotional were reported to be higher in *women than men* in a dysvascular population [74] however, vitality scores were reported to be higher for *men than women* (reason for amputation not reported) in a second study [37]. On the WHO QOL-BREF, Cox et al. [74] reported that women had better overall QoL scores. However, two others reported that men had higher scores on the overall health, physical health, social relationship domains in a mostly traumatic LLA population [121] and better psychological QoL in persons with dysvascular LLA [144]. An additional study with a mostly dysvascular population highlighted that only men had lower scores on physical health and social relationship domains compared to normative data [123]. No studies reported differences in QoL using subjective measures.

**Physical health**

Based on the included articles, various aspects of physical health such as pain, comorbidities, length of stay, and level of amputation were investigated. For articles that reported on sex, Bosmans et al. [79] noted that there was a protective effect of being male on the incidence of phantom limb pain in a mostly dysvascular LLA population and Ebrahimzadeh et al. [107] found rates of phantom limb pain and sensation to be 87% and 45.1% respectively in a traumatic LLA cohort. This article also reported rates of residual limb pain, chronic back pain and contralateral knee pain (64.5%, 61.2% and 54.8% respectively) [107]. However, articles that reported on gender suggested mixed findings with respect to phantom limb pain. While both studies had all trauma or mostly trauma participants, one study reported men had significantly higher odds of persistent/recurrent pain compared to women [63], while another suggested that the prevalence of phantom limb pain was higher in women than men [43].
Table 1. Descriptive summary of articles that found sex or gender differences (n = 66).

| Article                | Sample size | Sample               | Domain                    | Key findings/results related to sex and gender |
|------------------------|-------------|----------------------|---------------------------|------------------------------------------------|
| Bilodeau et al. 2000   | N = 65      | Mean age: 57 years   | Prosthesis Use            | • Prosthesis was used significantly less by women compared to men (p = 0.02). |
| Location: Canada       |             | Gender: 52 Men, 13 Women |                           |                                                 |
|                        |             | Aetiology: All vascular |                           |                                                 |
|                        |             | Level of amputation: |                           |                                                 |
|                        |             | Right TT: 15         |                           |                                                 |
|                        |             | Left TT: 19          |                           |                                                 |
|                        |             | Right TF: 13         |                           |                                                 |
|                        |             | Left TF: 18          |                           |                                                 |
|                        |             | Mean time since amputation: 2.9 yrs | |                                                 |
| Bodenheimer et al. 2000| N = 30      | Mean age: 43.9 years | Sexual Health             | • Majority of participants experienced some problems with sexual functioning. |
| Location: United States|             | Sex: All male        |                           | • 50% of participants were moderately to extremely satisfied with their ability and intensity of orgasm. |
|                        |             | Aetiology: n/r       |                           | • 67% of participants reported moderate to high interest in sex, while 90% reported wanting to have sex more than once a month. |
|                        |             | Level of amputation: |                           | • 63% of participants were satisfied with their relationship with their sexual partners. |
|                        |             | TT: 21               |                           | • No correlation between, prosthesis, pain, or depression on sexual functioning. |
|                        |             | TF: 1                |                           | • Peak CoM displacement did not differ between amputation and control groups (p = 0.052). |
|                        |             | Bilateral TF: 1      |                           | • Individuals with TTA had significantly larger net CoP displacement (p = 0.002) than controls. |
|                        |             | One TT one TF: 1     |                           | • There was a protective effect of being male on the incidence of PLP. |
|                        |             | Median time since amputation: 23 mths | |                                                 |
| Bolger et al. 2014     | N = 10 (5 LLA) | Mean age: 43.9 years | Mobility                  |                                                 |
| Location: United States|             | Sex: All male        |                           |                                                 |
| Bosmans et al. 2010    | N = 85 (73 LLA) | Mean age: 59.8 years | Pain                      |                                                 |
| Location: Netherlands  |             | Sex: 26 Male, 47 Female |                           |                                                 |
| Boulias, et al. 2006   | N = 123     | Mean age: 63.4 years | Driving                   | • Men were more likely to return to driving following LLA (p<.01). |
| Location: Canada       |             | Sex: 93 Male, 30 Female |                           |                                                 |
| Article                          | Sample size | Sample | Amputation-related information | Outcome measure(s) used | Domain                      | Key findings/results related to sex and gender |
|--------------------------------|-------------|--------|--------------------------------|-------------------------|-----------------------------|-----------------------------------------------|
| Bowrey, et al. 2019            | N = 338     |        | Mean age:                       | Aetiology:              | Functional outcome          | Poor functional outcome and non-functional mobility outcome associated with the female sex. |
|                                |             |        | TF: 69.5 years                  | Vascular: 282           | coding & mobility           |                                |
|                                |             |        | TT: 65 years                    | Orthopaedic/Trauma       |                             |                                |
|                                |             |        | Sex:                            | Congenital: 45           |                             |                                |
|                                |             |        | TF: 109 Male, 43 Female         | Cancer: 11               |                             |                                |
|                                |             |        | TT: 144 Male, 42 Female         | Level of amputation:    |                             |                                |
|                                |             |        |                                | TF: 152                  |                             |                                |
|                                |             |        |                                | TT: 186                  |                             |                                |
|                                |             |        | Time since amputation: 12 months|                         |                             |                                |
|                                |             |        |                                |                         |                             |                                |
| Brunelli et al. 2013           | N = 44      |        | Mean Age: 68 years              | Aetiology:              | Prosthesis use & mobility   | Female gender associated with increased probability of not using a prosthesis at 4 years post-hospital discharge (OR = 3.6). |
|                                |             |        | Gender: 29 Male, 15 Female      | Artherosclerosis: 26     |                             |                                |
|                                |             |        |                                | DM: 18                   |                             |                                |
|                                |             |        |                                | Level of amputation:    |                             |                                |
|                                |             |        |                                | TF: 52                   |                             |                                |
|                                |             |        |                                | TT: 12                   |                             |                                |
|                                |             |        | Time since amputation: n/r      |                         |                             |                                |
| Chihuri & Wong, 2018           | N = 255     |        | Mean Age: 55.7 years            | Aetiology:              | Mobility                    | Females were almost 3 × more likely to have a fall-related injury compared to males (OR = 2.90). |
|                                |             |        | Sex: 177 Male, 79 Female        | Vascular: 112            |                             |                                |
|                                |             |        |                                | Non-vascular: 131        |                             |                                |
|                                |             |        |                                | Level of amputation:    |                             |                                |
|                                |             |        |                                | TF/Bilateral TF: 125    |                             |                                |
|                                |             |        |                                | TT/Bilateral TT: 114    |                             |                                |
|                                |             |        | Time since amputation: n/r      |                         |                             |                                |
| Coffey, 2012                   | N = 98      |        | Mean Age: 62.6 years            | Aetiology:              | Overall QoL & Mental Health | Females tended to have lower psychological QoL, poorer general and social adjustment, higher negative affect and greater symptoms of depression compared to men at admission to rehab. |
|                                |             |        | Gender:                         | Chronic (i.e., PVD,    |                             |                                |
|                                |             |        | Time 1: 78                       | DM, cancer): 79%         |                             |                                |
|                                |             |        | Male, 20                         | Trauma: 8%               |                             |                                |
|                                |             |        | Time 2: 59                       | Deep vein               |                             |                                |
|                                |             |        | Male, 16                         | Thrombosis or necrotising fasciitis from intravenous drug use: 13% |                             |                                |
|                                |             |        | Time 3: 52                       | Level of amputation:    |                             |                                |
|                                |             |        | Male, 10                         | Unilateral BK: 48%      |                             |                                |
|                                |             |        | Female                            | Unilateral AK: 44%      |                             |                                |
|                                |             |        |                                | Bilateral: 8%            |                             |                                |
|                                |             |        |                                | Meantime since amputation: |                             |                                |
|                                |             |        |                                | Time 1: 30.32 weeks      |                             |                                |
|                                |             |        |                                | Time 2: 29.79 weeks      |                             |                                |
|                                |             |        |                                | Time 3: 31.92 weeks      |                             |                                |
| Article                  | Sample size | Sample | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain                        | Key findings/results related to sex and gender |
|-------------------------|-------------|--------|--------------------------------|--------------------------------|-------------------------|-------------------------------|-----------------------------------------------|
| Coffey et al. 2014      | N = 98      | Gender: 79 Male, 19 Female | Mean Age: 62.6 years | Aetiology: Chronic (i.e., PVD, DM, cancer): 79% Trauma: 8% Deep vein thrombosis or necrotising fasciitis from intravenous drug use: 13% Level of amputation: Unilateral BK: 47 Unilateral AK: 43 Bilateral: 7 Meantime since amputation: 30.3 weeks | PANAS          | Mental Health            | A greater negative effect was associated with being female but not positive affect. |
| Location: Ireland       |             |        |                                |                                |                         |                               |                                               |
| Cox et al. 2011         | N = 87      | Gender: 35 Male, 52 Female | Mean Age: 62 years | Aetiology: All diabetes Level of amputation: BK: 64 AK: 23 Time since amputation: 1–3 years prior to study | WHO QOL-BREF FIM       | Overall QoL & Functional Outcome | Females had significantly better QoL and FIM scores compared to males (p < 0.0001). |
| Location: Jamaica       |             |        |                                |                                |                         |                               |                                               |
| Davie-Smith et al. 2017 | N = 2145    | Gender: 1112 Men, 623 Women | Mean Age: 69.7 years | Aetiology: PAD with or without DM Level of amputation: Non-DM: Bilateral: 150 TF: 362 TF: 389 DM Bilateral: 214 TF: 434 TF: 186 Time since amputation: n/r | Limb fit or non-limb fit Prosthesis Prescription & LOS |                               | For both TT and TF, significantly more men than women were fit with a prosthetic limb (p = 0.001). Men also were more likely to be fit than women for TT and TF (OR = 1.71 and OR = 2.17, respectively). Rehab LOS for women was significantly longer than men by an average of 3 weeks (p < 0.010). |
| Location: Scotland      |             |        |                                |                                |                         |                               |                                               |
| de Laat et al. 2018     | N = 173     | Gender: 124 Men, 49 Women | Mean Age: 65 years | Aetiology: Vascular: 142 Non-vascular: 31 Level of amputation: Unilateral Higher (HD, TF, KD): 66 Unilateral Lower (TT or Syme): 95 Bilateral: 12 Time since amputation: n/r | FCI            | Physical Health & Mental Health | Females have a higher risk of having lumbago, rheumatoid arthritis or osteoarthritis, or anxiety or panic disorders. |
| Location: Netherlands   |             |        |                                |                                |                         |                               |                                               |
| de Laat et al. 2014     | N = 172     | Gender: 122 Men, 50 Women | Mean Age: 65 years | Aetiology: Vascular: 143 Non-vascular: 29 Level of amputation: Higher (HD, TF, KD): 66 Lower (TT or Syme): 94 Bilateral: 12 Time since amputation: n/r | LCI QR&S       | Mobility                   | Women perceived less independence in rising. |
| Location: Netherlands   |             |        |                                |                                |                         |                               |                                               |

(continued)
| Article                  | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain                      | Key findings/results related to sex and gender |
|-------------------------|-------------|--------------------------------|-------------------------------|-------------------------|-----------------------------|-----------------------------------------------|
| Dillingham & Pezzin, 2008 | N = 2468    | Mean Age: 74.6 years           | Time since amputation: n/r    | Medical stability       | Discharge Destination       | - Females were more likely than males to be discharged to a nursing home. |
| Location: United States |             | Sex: 1216 Men, 1252 Women      | Aetiology: All dysvascular    | Re-amputations          |                             |                                |
|                         |             |                                | Level of amputation:         | Prosthetic device       |                             |                                |
|                         |             |                                | Foot or ankle: 379            | acquisition             |                             |                                |
|                         |             |                                | TT: 949                      |                         |                             |                                |
|                         |             |                                | TF: 1135                     |                         |                             |                                |
| Durmus et al. 2015      | N = 104 (51 LLA) | Mean Age: 36.7 years          | Time since amputation: 12 months | Satisfaction with       | Mental Health & Prosthesis Use | - State anxiety and trait anxiety scores were higher in the LLA group compared to control (p = 0.001). |
| Location: Turkey        |             | Gender: All men                | Aetiology: Weapon injury: 30  | Prosthesis Questionnaire|                             |                                |
|                         |             |                                | Traffic accident: 11          | Phantom Pain VAS        |                             |                                |
|                         |             |                                | Electric shock: 5             | SCL-90-R                |                             |                                |
|                         |             |                                | Industrial accident: 5        | BDI                     |                             |                                |
|                         |             |                                | Level of amputation:          | STAI                    |                             |                                |
|                         |             |                                | Foot-ankle: 9                 | PSQI                    |                             |                                |
|                         |             |                                | TT: 15                        | RSES                    |                             |                                |
|                         |             |                                | KD: 3                         |                         |                             |                                |
|                         |             |                                | TF: 15                        |                         |                             |                                |
|                         |             |                                | HD: 1                         |                         |                             |                                |
|                         |             |                                | Meantime since amputation:    |                         |                             |                                |
|                         |             |                                | 106 months                    |                         |                             |                                |
| Ebrahimzadeh et al. 2009 | N = 31      | Mean Age: 43.25 years         | Aetiology: Land mines: 14     | Questionnaire developed by investigator which include questions about pain, rehab, psychological problems, general condition and family and social functioning. | Pain, Mental Health, & Prosthesis Use | - Phantom sensation and PLP found in 87% and 45.1% of participants. |
| Location: Iran          |             | Sex: All male                  | Shells: 13                    |                         |                             |                                |
|                         |             |                                | Direct bullets: 4             |                         |                             |                                |
|                         |             |                                | Level of amputation: All TF   |                         |                             |                                |
|                         |             |                                | Meantime since amputation:    |                         |                             |                                |
|                         |             |                                | 17.36 years                   |                         |                             |                                |
| Erjavec et al. 2008     | N = 63      | Mean age: 72.5 years          | Aetiology: All PVD            | ROM measurements        | Prosthesis Prescription     | - Gender was able to determine who was fitted with a prosthesis and those who were not (p < 0.000). |
| Location: Slovenia      |             | Sex: 34 Men, 27 Women          | Level of amputation: All TF   | Manual muscle test      |                             |                                |
| Fajarado-Martos et al. 2018 | N = 169    | Mean age: 61.6 years          | Time since amputation: n/r    | 6MWT                    | Mobility                    | - Being male was a predictor for failed prosthetic rehabilitation (unable to complete 45 m walk test). |
| Location: Spain         |             | Gender: 82.8% Men, 17.2% Women| Aetiology: Vascular: 70.4%    | Lower-limb characteristics|                             |                                |
|                         |             |                                | Traumatological: 18.9%        | Successful prosthetic rehabilitation |                             |                                |
|                         |             |                                | Infective: 4.7%               |                         |                             |                                |
|                         |             |                                | Tumoral: 5.3%                 |                         |                             |                                |
|                         |             |                                | Level of amputation:          |                         |                             |                                |
|                         |             |                                | TF: 76                        |                         |                             |                                |
|                         |             |                                | TT: 86                        |                         |                             |                                |
|                         |             |                                | Bilateral: 7                  |                         |                             |                                |
|                         |             |                                | Meantime since amputation:    |                         |                             |                                |
|                         |             |                                | 130.6 days                    |                         |                             |                                |
| Article                  | Sample size | Sample demographic information | Amputation-related information | Outcome measure(s) used | Domain                  | Key findings/results related to sex and gender |
|-------------------------|-------------|---------------------------------|--------------------------------|-------------------------|-------------------------|-----------------------------------------------|
| Gardinier et al. 2018   | N = 20 (10 LLA) | Age range: 26–60 years Sex: All males | Aetiology: Trauma: 9 Dysvascular 1 Level of amputation: All unilateral TT Time since amputation: n/r | Walking performance (energy costs, preferred walking speed) | Mobility | • Preferred walking speed was not significantly changed when using the BIOM. 
  • No significant differences for metabolic costs between BIOM and unpowered conditions or LLA groups vs controls. 
  • Increases in preferred walking speed were associated with decreases in controlled speed ($p = 0.071$) and controlled speed oxygen consumption ($p = 0.076$). 
  • No effect on controlled walking speed on change in controlled speed with BIOM. |
| Gaunaurd et al. 2020    | N = 101 | Mean age: 50.9 years Sex: 47 Men, 54 Women | Aetiology: Trauma: 61 Disease: 29 Tumor: 11 Level of amputation: Unilateral TT: 48 Unilateral TF: 50 Unilateral KD: 3 Meantime since amputation: 101 months | 2MWT | Mobility | • Mean 2MWT distance was farther and gait speed was faster for men than women ($p < 0.05$). |
| George et al. 2017      | N = 43 | Mean age: 65.2 years Sex: 24 Males, 29 Females | Aetiology: Osteoarthritis: 40 Rheumatoid arthritis: 7 Post-traumatic arthritis: 4 Osteochondritis dessicans: 2 Level of amputation: All AK Meantime since amputation: 29 months | Ambulatory status | Mobility | • Male sex was a predictor of better ambulation in univariate ($p = 0.008$) and multivariate ($p = 0.003$) analyses. |
| Highsmith et al. 2016   | N = 294 | Mean Age: 58.9 years Gender: TF: 55 Male, 18 Female TT: 171 Male, 50 Female | Aetiology: n/r Level of amputation: TT: 221 TF: 73 Time since amputation: n/r | Delivery and utilization of cosmetic covers Type of cosmetic cover Prosthesis cover prescription | Prosthesis cover | • Males were less likely to receive a cover for TT and TF ($p = 0.003$ and $p = 0.02$, respectively). |
| Hisam et al. 2016       | N = 52 | Mean Age: 30.7 years Gender: 49 Males, 3 Females | Aetiology: Trauma: 48 Cancer: 2 DM: 2 Level of amputation: TT: 36 KD: 0 TF: 15 HD: 1 Meantime since amputation: 1.9 years | SF-36 | Overall QoL | • Role physical and role emotional scores were higher for females compared to males ($p = 0.024$ and $p = 0.002$, respectively). |

(continued)
| Article          | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used      | Domain                        | Key findings/results related to sex and gender |
|-----------------|-------------|-------------------------------|-------------------------------|-----------------------------|-------------------------------|-----------------------------------------------|
| Huang, 2003     | N = 90      | Mean Age: 71.28 years         | Aetiology: DM: 68             | WHOQOL-BREF Taiwan version  | Prosthesis Use & Overall QoL  | • More prosthesis use associated with female gender (p = 0.008).  
                                                        | Gender: 73 Male, 17 Female | Vascular disease: 18         | SF-36                         |                              |                                               |
                                                        |              |                               | Infection: 2                 |                              |                                               |
                                                        |              |                               | Malignant tumor: 1           |                              |                                               |
                                                        |              |                               | Osteomyelitis: 1             |                              |                                               |
                                                        |              |                               | Level of amputation:         |                              |                                               |
                                                        |              |                               | Unilateral BK: 56            |                              |                                               |
                                                        |              |                               | Unilateral AK: 15            |                              |                                               |
                                                        |              |                               | Bilateral BK: 16             |                              |                                               |
                                                        |              |                               | Bilateral BK & AK: 2         |                              |                                               |
                                                        |              |                               | Bilateral AK: 1              |                              |                                               |
                                                        |              |                               | Meantime since amputation:   |                              |                                               |
                                                        |              |                               | 4.1 years                    |                              |                                               |
| Kelly et al. 2018 | N = 1291    | Mean Age: 54 years            | Aetiology: Dysvascular: 546   | Neuro-Qol, ACGC             | Mobility                      | • Being female was associated with lower  
                                                        | Sex: 764 Male, 319 Female, 3 n/r | Trauma: 666                  | ABC Scale                     | ABC and PLUS-M scores (p < 0.0001  
                                                        |                               | Infection: 44                  | PLUS-M                         | for both).                                   |
                                                        |                               | Congenital: 20                 |                               |                              |                                               |
                                                        |                               | Non-dysvascular etiology: 15   |                               |                              |                                               |
                                                        |                               | Level of amputation:           |                               |                              |                                               |
                                                        |                               | Unilateral BK: 703            |                               |                              |                                               |
                                                        |                               | Unilateral AK: 383            |                               |                              |                                               |
                                                        |                               | Bilateral BK: 135             |                               |                              |                                               |
                                                        |                               | Bilateral AK: 70              |                               |                              |                                               |
                                                        |                               | Meantime since amputation:     |                               |                              |                                               |
                                                        |                               | 4.1 years                     |                               |                              |                                               |
| Knezetic et al. 2016 | N = 263    | Mean Age: 60.8 years          | Aetiology: PAD: 237           | FCI                         | Mobility                      | • Men had a significantly higher  
                                                        | Gender: 218 Male, 45 Female  | Trauma: 16                   | Mobility level                | Mobility level at end of rehabilitation  
                                                        |                               | Other: 10                      |                               | treatment (p = 0.036).                       |
                                                        |                               | Level of amputation:          |                               |                              |                                               |
                                                        |                               | TT: 93                        |                               |                              |                                               |
                                                        |                               | TF: 170                       |                               |                              |                                               |
                                                        |                               | Meantime since amputation:    |                               |                              |                                               |
                                                        |                               | n/r                           |                               |                              |                                               |
| Kurichi et al. 2013 | N = 1536   | Mean Age: 68.2 years          | Aetiology: Chronic osteomyelitis: 96 | Inpatient costs & LOS      | Financial & LOS               | • Women had higher unadjusted total  
                                                        | Sex: 1519 Male, 17 Female    | Device infection: 165         |                               |                               | inpatient costs and lower mean LOS  
                                                        |                               | DM type 1: 257                 |                               |                               | compared to men.                           |
                                                        |                               | DM type 2: 975                |                               |                               |                                               |
                                                        |                               | Local significant infection:  1201 |                               |                               |                                               |
                                                        |                               | PVD: 1340                     |                               |                               |                                               |
                                                        |                               | Previous amputation  
                                                        |                               |                               |                                               |
                                                        |                               | complication: 116             |                               |                               |                                               |
                                                        |                               | Skin breakdown: 981           |                               |                               |                                               |
                                                        |                               | Systemic sepsis: 185          |                               |                               |                                               |
                                                        |                               | Trauma: 202                   |                               |                               |                                               |
                                                        |                               | Level of amputation:          |                               |                               |                                               |
                                                        |                               |                                |                               |                               |                                               |
|                 |             |                               |                                |                               |                               |                                               |

(continued)
| Article                      | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain       | Key findings/results related to sex and gender |
|-----------------------------|-------------|-------------------------------|-------------------------------|-------------------------|--------------|-----------------------------------------------|
| Abeyasinghe et al. 2012     | $N = 96$ (40 LLA) | Age range: 18–49 years Sex: All males | Unilateral TT: 477 Unilateral TF: 388 Bilateral TT: 24 Bilateral TF: 647 Time since amputation: n/r | Questionnaire created based on Impact of Event Scale & PTSD Symptom scale. | Mental Health | • 42.5% of LLA participants had symptoms suggestive of PTSD. |
| Location: Sri Lanka          | $N = 47$ | Mean age: Male: 50.6 years Female: 51.7 years Gender: 31 Males, 16 Females | Aetiology: Battlefield injury Level of amputation: 40 LLA Meantime since amputation: 21 years | WHOQOL-BREF | Overall QoL | • Males had significantly higher scores than females on overall health ($p = 0.012$), physical health ($p = 0.007$) and social relationship ($p = 0.024$) domains. |
| Adegoke et al. 2012          | $N = 47$ | Mean age: Male: 50.6 years Female: 51.7 years Gender: 31 Males, 16 Females | Aetiology: DM: 16 Malignancy: 7 Trauma: 20 Infection: 1 PVD: 3 Level of amputation: | Mobility | Mobility | • Males reported greater mobility 1-month post-amputation ($p < 0.01$). |
| Location: Nigeria            | $N = 89$ | Mean age: 44.2 years Sex: 69.7% Male, 30.3% Female | Aetiology: Traumatic: 69.7% DM: 14.6% Infection: 5.6% Level of amputation: BK: 66.3% AK: 18.0% Time since amputation ranges: 3–24 months: 27 25–48 months: 14 49–72 months: 2 > 72 months: 4 | SI Sub-scale of CHART MSPSS CES-D SWLS | Mobility | |
| Williams et al. 2004         | $N = 41$ | Mean Age: 56.9 years Sex: 24 Male, 17 Female | Aetiology: Vascular: 29 Non-vascular: 12 Level of amputation: TF/Bilateral TF: 24 | Self-reported falls/fall-related injury Houghton Scale ABC Scale | Mobility | • Females had a higher injury rate (5.88 x more) from falls than males during the study period. |
| Location: United States      | $N = 100$ | Age Ranges: 20–29 years: 34% 30–40 years: 36% 40–60 years: 30% Sex: 80 Male, 20 Female | Aetiology: Unplanned: Road accidents: 56 Bomb blasts: 9 Electric Shock: 4 Gunshot: 7 Planned: 24 Level of amputation: Major LLA Meantime since amputation: 6.7 years | Psychological Adjustment Scale | Mental Health | • Significant differences were found between males and females on adjustment levels (i.e., females scored higher than males). |
| Ali et al. 2017              | $N = 65$ | Mean Age: 56.7 years Sex: 49 Men, 16 Women | Aetiology: | Psychological Adjustment Scale | Mental Health | |
| Location: Ireland            | $N = 65$ | Mean Age: 56.7 years Sex: 49 Men, 16 Women | Aetiology: | Self-reported falls/fall-related injury | Mobility | |
| Woods et al. 2018            | $N = 65$ | Mean Age: 56.7 years Sex: 49 Men, 16 Women | Aetiology: PVD: 27 DM: 5 | HADS BDI-II BIQLI | Sexual Health | • Greater self-consciousness or anxious attentional focus scores were found to be one standard deviation above the |
| Article                        | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain | Key findings/results related to sex and gender |
|-------------------------------|-------------|--------------------------------|--------------------------------|-------------------------|--------|------------------------------------------------|
| Pereira et al. 2018           | N = 63      | Mean Age: 63 years Sex: 79.4% Male, 20.6% Female | Aetiology: Chronic disease: 74.6% | Brief COPE Scale SWLS Mental health | Women showed greater use of denial coping strategies compared to men (p = 0.025). |
| Cairns et al. 2014            | N = 153     | Age: 78% between 45 & 70 years Gender: 69% Male, 31% Female | Aetiology: Trauma: 33% PVD: 18% Congenital defect: 11% | Amputee satisfaction with cosmeses and importance of cosmesis design features Durability of cosmesis | Compared to males, females were less satisfied with the durability of their cosmesis (p = 0.016). |
| Lee et al. 2020               | N = 90      | Mean Age: 58.7 years Gender: 68 Male, 22 Female | Aetiology: n/r Level of amputation: AK: 43.8% BK: 56.2% | SF-36, version 2 Overall QoL | Vitality scores for males were significantly higher than women (p = 0.04). |
| Lefebvre & Chevan, 2015       | N = 121 587 | Age Ranges: 30–57 years: 30,316 58–68 years: 30 645 69–78 years: 29 820 >78 years: 30 806 Gender: 71 667 Male, 49 899 Female | Aetiology: n/r Level of amputation: TT: 53.9% TF: 46.1% | Secondary analysis of Healthcare Utilization Project Nationwide Inpatient Survey data Physical Health | Males made up a greater proportion of TT, while females made up a greater proportion of TF. Being female was significantly associated with increased odds of having a TF. |
| Legro et al. 2001             | N = 92      | Aetiology: n/r Level of amputation: | PEQ Physical activity | A higher proportion of males vs females completed activities that were | |
| Article | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain |
|---------|-------------|-------------------------------|-------------------------------|-------------------------|--------|
| Location: United States | 759 | Mean age: 55 years Gender: 85.9% Male, 14.1% Female | TT: 63% Meantime since amputation: 18 years | Used data from Department of Veterans Affairs Region database | Physical health |
| Littman et al. 2015 | 75 | Mean age: 55 years Gender: 85.9% Male, 14.1% Female | Aetiology: n/r Level of amputation: PF: 396 TT: 267 TF: 96 Meantime since amputation: n/r | | |
| Majstorovic & Pesta, 2020 | 75 | Mean age: Male: 61.8 years Female: 68.1 years Gender: 55 Men, 20 Women | Aetiology: All PVD Level of amputation: ALL TT Time since amputation: n/r | K-levels classification LCI scale | Mobility |
| Meulenbelt et al. 2011 | 805 | Mean age: 58 years Gender: 59% Male, 41% Female | Aetiology: PAD/DM: 23% Trauma: 44% Oncology: 19% Congenital: 4% Infection: 6% Other: 8% Level of amputation: TT: 49% KD: 11% TF: 32% Hip/pelvis: 2% Bilateral: 6% Meantime since amputation: n/r | Dermatology Life Quality Index | Physical health |
| Miller & Deathe, 2004 | 245 | Mean Age: 60.5 years Sex: 74% Male, 26% Female | Aetiology: Traumatic etiology: 56% Level of amputation: BK: 68% Meantime since amputation: n/r | ABC scale | Mobility |
| Morisaki et al. 2018 | 106 | Mean Age: 77.3% Sex: 63.2% Male, 36.8% Female | Aetiology: DM: 67.9% Coronary artery disease: 36.8% Hemodialysis: 35.8% Congestive heart failure: 22.6% Level of amputation: AK: 66.9% BK: 33.1% Time since amputation: n/r | Risk factors for wound complications | Physical health |

Key findings/results related to sex and gender:
- Categorized as high energy and low energy activities (High: 13.5% vs. 4%, and 29.8% vs. 12%, respectively).
- Females completed more moderate level activities (52% vs. 29.1%) but were also found to have a higher proportion of sedentary activities (24% vs. 20.6%).
- Men with amputation were found to have greater weight gain compared to men without amputation at 2-year follow-up.
- Over time, men with TT or TF saw a greater mean percentage weight change compared to PF (8%–9% vs 3%–6%, respectively).
- Men were found to have higher scores on the different components of the LCI (basic and advanced activities) and K-levels at discharge ($p < 0.01$ to $p < 0.001$).
- Males had a significantly lower mean total score on the Dermatology Life Quality Index compared to females ($p = 0.03$) indicating a smaller effect of skin problems on day-to-day life.
- Being male was independently related to having higher balance confidence.
- Being female was a predictor of having lower balance confidence scores at follow-up.
- Female sex was identified as a risk factor for wound complications ($p = 0.01$).
| Article & Year | Sample size | Socio-demographic Information | Amputation-related Information | Outcome measure(s) used | Domain | Key findings/results related to sex and gender |
|---------------|-------------|--------------------------------|--------------------------------|------------------------|--------|---------------------------------------------|
| Murray & Fox, 2002 | N = 46 | Mean Age: 41.6 years Sex: 54.5% Male, 38.6% Female, 6.8% Unknown | Aetiology: Accident: 36.4% Cancer: 36.4% Congenital: 6.8% PVD: 4.5% DM: 2.3% Other: 13.6% Level of amputation: BK: 50.0% Through knee: 31.8% AK: 13.6% Bilateral: 2.3% PF: 2.3% Meantime since amputation: n/r | TAPES | Body Image, Pain, Prosthesis Satisfaction & Use |
| Nunes et al. 2014 | N = 149 | Mean Age: 60.2 years Gender: 62% Male, 38% Female | Aetiology: Diabetic foot: 45% Trauma: 26% Ischemia: 13% Infections: 11% Others: 5% Level of amputation: Bilateral: 27 Unilateral: 122 Meantime since amputation: 76.8 months | Adaptation to Prosthesis | Prosthesis Use |
| Nunes et al. 2012 | N = 138 | Mean Age: 62.3 years Gender: 57% Male, 43% Female | Aetiology: Chronic: 105 Nonchronic: 33 Level of amputation: Major: 92 Minor: 46 Meantime since amputation: 43 years | SRQ-20 | Mental health |
| Pet et al. 2015 | N = 38 | Mean Age: 42 years Gender: 68% Male, 32% Female | Aetiology: Trauma: 63% Tissue infection or ischemia: 32% Oncologic disease: 5% Level of amputation: TT: 79% TF: 21% Meantime since amputation: 7 years | Absence or presence of persistent or recurrent neuroma-type pain | Pain |

(continued)
| Article          | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain                                      | Key findings/results related to sex and gender                                                                 |
|-----------------|-------------|--------------------------------|--------------------------------|-------------------------|---------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| **Pezzin et al. 2004** | N = 935 (841 LLA) | Mean age: 50 years Gender: 61.2% Men, 38.8% Women | Aetiology: Dysvascular: 37.8% Trauma: 38.7% Cancer: 23.4% Level of amputation: BK: 40.4% AK: 38.5% Bilateral: 10.8% Upper limb: 10% | 4-Point Likert Scale Prosthesis satisfaction & prosthettist satisfaction | Domain                                      | - Men were more likely to be satisfied with prosthesis fit ($p = 0.03$), comfort ($p = 0.07$) and appearance ($p = 0.00$) compared to women.  
- Women were more likely to have favourable perceptions about their prosthetists compared to men. |
| **Refaat et al. 2002** | N = 408 (66 LLA) | Mean Age: 52 years Gender: 41 Male, 25 Female | Aetiology: n/r Level of amputation: AK: 52% BK: 29% Pelvis: 8% Hip: 6% Other: 4% Meantime since amputation: n/r | Survival and QoL questionnaire Employment & physical activity | Domain                                      | - Rate of employment for males in the amputation group was higher than females (79% vs. 64%).  
- Engagement in sports was higher for males in the amputation group than for females (45% vs. 32%). |
| **Remes et al. 2009** | N = 210 | Mean Age: 73.6 years Gender: 48% Men, 52% Women | Aetiology: PAD Level of amputation: BK: 31% AK: 62% Bilateral: 7% Time since amputation: 12 years | Predictors for institutional care discharge | Domain                                      | - Female gender was associated with discharge to institutional care. |
| **Sansam et al. 2012** | N = 95 | Mean age: 66.5 years Sex: 66 Males, 29 Females | Aetiology: Dysvascular: 56 Trauma: 16 Neoplasm: 3 Other: 6 Level of amputation: Unilateral TT: 55 Unilateral TF: 29 Bilateral TT: 5 Time since amputation: 31 d | TUG Mobility | Domain                                      | - Completion times for the TUG were longer 15.9% longer for men. |
| **Sansosti et al. 2010** | N = 167 | Mean age: 62.4 years Sex: 77 Male, 52 Female | Aetiology: n/r Level of amputation: Unilateral BK: 74 Unilateral AK: 55 Other: 3 Bilateral: 35 Time since amputation: 12 months | Ambulation in a prosthesis Mobility | Domain                                      | - Males with unilateral BK or AK amputations were more likely to be walking 12 months post-amputation compared to females ($p = 0.030$). |
| **Schaffalitzky, 2010** | N = 24 | Mean age: 63.3 years Gender: 13 Males, 11 Females | Aetiology: Congenital: 1 Trauma: 8 Dysvascular: 8 Cancer: 3 Aneurism: 1 Infection: 4 Level of amputation: BK: 15 AK: 8 | Qualitative Focus Groups analyzed using thematic analysis Body Image | Domain                                      | - Potential gender differences in relation to body image were suggested since men were more likely to display their prostheses in public compared to women. |
| Article | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain | Key findings/results related to sex and gender |
|---------|-------------|-------------------------------|-------------------------------|-------------------------|--------|-----------------------------------------------|
| Sederberg et al. 2020 | N = 229 | Age ranges: 15–29 years: 7%; 30–39 years: 10%; 40–49 years: 18%; 50–64 years: 40%; ≥64: 24%; Gender: 76% Male, 24% Female | Aetiology: Traumatic; Yes: 46%; Level of amputation: BK: 66%; AK: 19%; Upper limb: 5%; Time since amputation: ≥1 year: 44%; < 1 year: 56% | EVS | Physical activity | • Female participants were less likely to achieve ≥150 min of physical activity per week (p = 0.04).  
• Females also reported 1.09 fewer hours of exercise per week compared to males (p < 0.001). |
| Singh et al. 2008 | N = 108 | Mean age: Male: 61.3 years; Female: 66.2 years; Gender: 70 Male, 35 Female | Aetiology: Dysvascular: 88%; Level of amputation: TF: 41%; TT: 59%; Meantime since amputation: 23.6 d | PPAM aid | Prosthesis prescription | • More men than women were successfully fitted with a prosthesis (p = 0.011). |
| Sinha et al. 2014 | N = 368 | Mean age: 43.1 years; Gender: 324 Male, 44 Female | Aetiology: Trauma: 280; DM: 42; Vascular: 17; Cancer: 14; Others: 14; Missing: 1; Level of amputation: AK: 76; Through knee: 11; BK: 281; Meantime since amputation: 12.9 years | TAPES | Mental health | • Males were associated with being more socially adjusted. |
| Stutts et al. 2015 | N = 30 | Mean age: 50 years; Gender: All female | Aetiology: Illness/surgery: 18; Motor vehicle accident: 9; Congenital: 2; Electrocution: 1; Level of amputation: Unilateral BK: 14; Unilateral AK: 11; Bilateral AK: 1; Upper limb: 4; Meantime since amputation: 12.5 years | PTGI Interpretive phenomenological analysis | Mental health | • Qualitative analysis yielded 4 themes: 1) coping easier; 2) coping harder; 3) social support; and 4) discrimination.  
• Social support and having a positive attitude of self were common components of coping easier.  
• Feeling alone/lack of support and experiencing grief/depression was associated with coping harder.  
• 86.7% of the participants reported having 'enough' self-defined social support. However, some women indicated a lack of social support from their spouse/partner.  
• 60% of the women reported experiencing discrimination. Discrimination was felt in general society as well as in employment.  
• 66.7% of women reported high levels of self acceptance.  
• Appearance and motherhood were female-specific challenges highlight by participants. |
| Article                        | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain                     | Key findings/results related to sex and gender |
|-------------------------------|-------------|-------------------------------|-------------------------------|-------------------------|----------------------------|-----------------------------------------------|
| Vogel et al. 2014             | N = 4965    | Age Ranges: 67–75: 1336       | Aetiology: n/r Level of amputation: TM: 490 BK: 1596 AK: 2879 | MDS ADL long-form score | ADLs & physical health | Overall, PTGI scores were reported to be moderate to high. |
| Location: United States       |             | 76–85: 2247                   |                              |                         |                            | Women represented more than half of the AK group (58%, p < 0.001). |
|                              |             | >86: 1382                     |                              |                         |                            | Men had better posthospital ADL scores compared to women (p < 0.001). |
| Sex: 2283 Male, 2882 Female   |             |                              |                              |                         |                            | Women represented more than half of the AK group (58%, p < 0.001). |
| Wan-Nar Wong, 2005            | N = 184     | Mean Age: 74.1 years          | Time since amputation: n/r    | Risk factors for failure to ambulate in the community | Mobility                   | Female sex was associated with failure to community ambulate following LLA. |
| Location: China               |             | Sex: 92 Male, 92 Female       |                              |                         |                            |                                |
|                              |             |                                |                              |                         |                            |                                |
| Ward Khan et al. 2019         | N = 9       | Mean Age: 51 years            | Time since amputation: 12 months | Interpretive phenomenological analysis | Mental health | Three themes were discussed: 1) "I don't like the way that I am"; 2) Broken/not wanted; 3) Same but different. |
| Location: Ireland             |             | Gender: All female            |                              |                         |                            |                                |
|                              |             |                                |                              |                         |                            |                                |
| Wen et al. 2018               | N = 140     | Mean Age: 34.9 years          | Aetiology: 2010 earthquake in Haiti Level of amputation: TT: 69 TF: 68 KD: 2 Meantime since amputation: 23.2 months | TAPES LCI                | Mobility, Pain & Psychosocial Adjustment | Men reported better physical capacity than women according to the TAPES Activity Restriction and LCI Advanced subscale (p < 0.001). |
| Location: Haiti               |             | Gender: 68 Men, 72 women      |                              |                         |                            | Prevalence of PLP was significantly higher in women than in men (p = 0.038). |
|                              |             |                                |                              |                         |                            | Women scored higher on psychosocial adjustment when LCI Advanced and PLP scores were held constant. |
| Article                | Sample size | Socio-demographic information | Amputation-related information | Outcome measure(s) used | Domain       | Key findings/results related to sex and gender |
|------------------------|-------------|-------------------------------|-------------------------------|-------------------------|--------------|------------------------------------------------|
| **Whyte & Carroll, 2002** | N = 315     | Mean Age: 43.8 years          | Aetiology:                    | MPQ                     | Employment   | • Significant differences were found by gender in terms of employment with a greater proportion of the male population remaining in employment compared to females (47.4% vs. 32.5%, respectively, p < 0.001). |
| Location: Scotland     |             | Gender: 73 Male, 27 Female    | Trauma: 47%                   | Prosthesis use per day  |             |                                                |
|                        |             |                               | PVD: 12%                      | and week                |             |                                                |
|                        |             |                               | Illness: 29%                  | Use of health services  |             |                                                |
|                        |             |                               | Cancer: 12%                   | RGSC                    |             |                                                |
|                        |             |                               | Level of amputation: LLA      |                         |             |                                                |
|                        |             |                               | Meantime since amputation: 13.2 years |                      |             |                                                |
| **Whyte & Niven, 2001** | N = 89      | Mean age: 46.1 years          | Aetiology:                   | Pain/Coping Diary       | Physical activity | • Women reported higher daily activity levels compared to men. |
|                        |             | Gender: 53% Male, 47% Female   | n/r                           |                         |             | • Women also reported getting involved in housework or shopping when they had an episode of PLP. |
|                        |             |                               | Level of amputation: LLA      |                         |             |                                                |
|                        |             |                               | Meantime since amputation: n/r |                         |             |                                                |
| **Wong et al. 2020**   | N = 305     | Mean Age: 56 years            | Aetiology:                   | PEQ-MS                  | Mobility     | • Male sex was associated with lower subjective function on the PEQ-MS (p = 0.013). |
|                        |             | Sex: 69% Men, 31% Women        | Vascular: 52%                 | 2MWT                    |             | • Male sex was also associated with a further distance walked on the 2MWT. |
|                        |             |                               | Non-vascular: 42%            |                         |             |                                                |
|                        |             |                               | Level of amputation:          |                         |             |                                                |
|                        |             | AK: 42%                       |                               |                         |             |                                                |
|                        |             | BK: 58%                       |                               |                         |             |                                                |
|                        |             |                               | Meantime since amputation: 6.3 years |                      |             |                                                |

2MWT: 2-min walk test; 6MWT: 6-min walk test; ABC: Activities-specific balance confidence scale; ABIS: Amputee body image scale; ADLs: Activities of daily living; AK: above knee; BBS: Berg balance scale; BESAQ: Body exposure during sexual activities questionnaire; B1: Barthel Index; BDI: Beck depression inventory; BDII: Beck depression inventory-second edition; BIQLI: Body image quality of life inventory; BIOM: Power ankle prosthesis system; BK: below knee; CES-D: Center for Epidemiological Studies depression scale; CHART: Craig handicap assessment and reporting technique; CoM: centre of mass; CoP: centre of pressure; DISF: Derogatis inventory of sexual functioning; DM: diabetes mellitus; EVS: Exerative vital sign; FCI: Functional comorbidity index; FGA: flexible goal adjustment scale; FIM: Functional Independence Measure; GQPLA: Groningen questionnaire problems after leg amputation; GRISS: Golombok rust inventory of sexual satisfaction; HADS: Hospital anxiety and depression scale; HD: hip disarticulation; HS: Houghton scale; HSQ: Health status questionnaire; KD: knee disarticulation; LCI: Locomotor capability index; LLA: lower limb amputation; MDS ADL: Minimum data set activities of daily living; MPQ: McGill pain questionnaire; MSPSS: Multidimensional scale of perceived social support; Neuro-Qol. ACGC: 8 item quality of life in neurological disorders applied cognition – general concerns; NHS: National Health Service; n/r: not reported; PAD: peripheral artery disease; PANAS: positive negative affect schedule; PEQ: Prosthetic evaluation questionnaire; PEQ-MS: Prosthetic evaluation questionnaire mobility subscale; PF: partial foot; PLP: phantom limb pain; PLUS-M: Prosthetic limb users survey of mobility; PPAM aid: Pneumatic post amputee mobility aid; PSQI: Pittsburgh sleep quality index; PTGI: Post-traumatic growth inventory; PTSD: Post-traumatic stress disorder; PVD: peripheral vascular disease; QoL: Quality of life; QRS: Questionnaire rising and sitting down; RGSC: Registrar General’s social classes scale; ROM: range of motion; RSES: Rosenberg self-esteem scale; SAQ: Sexual activity questionnaire; SCL-90-R: Symptom checklist-90-revised; SF-36: Short-form 36; SI: Social integration; SRSQ: Social reporting questionnaire; STAI: State-trait anxiety inventory; SWLS: Satisfaction with life scale; TAPES-R: Trinity amputation and prosthesis experience scale-revised; TGP: Tenacious goal pursuit scale; TF: transfemoral amputation; TT: transtibial amputation; TUG: Timed up and go; VAS: Visual analogue scale; WHOQOL-BREF: World Health Organization Disability Assessment Schedule 2.0; WHOQOL-BREF: World Health Organization Quality of Life Questionnaire.
With respect to comorbidities, three articles reported on sex [47, 117, 130] and one reported on gender [97]. Two studies with predominantly dysvascular cohorts claimed females had a higher risk for wound complications [47] as well as lumbar, rheumatoid arthritis or osteoarthritis [117]. One study claimed that men with amputation had greater weight gain if they had a transfemoral or transmembranous amputation compared to partial foot [130]. For the study reporting on gender, skin problems (e.g., pain, stinging) were claimed to have a larger impact on day-to-day life in women compared to men in a mostly traumatic LLA population [97].

Level of amputation was investigated by two articles, where one reported on gender [131] and the other on sex [68]. Both of these studies did not report the reason for amputation but reported that female sex and women made up a significantly larger proportion of participants with an above-knee amputation [68, 131]. These studies also claimed that being a woman was associated with a higher risk of having a transfemoral amputation [68, 131].

Two studies claimed that length of stay in acute inpatient care and inpatient rehabilitation differed by sex [71] and gender [55]. Kurichi et al. [71] reported that females had a lower mean inpatient length of stay compared to males while Davie-Smith et al. [55] noted that women had a significantly longer rehabilitation length of stay compared to men. Both articles reported on samples comprised mostly or entirely of dysvascular participants.

Prosthesis-related outcomes
Studies reporting on gender and prosthesis use claimed mixed results. These articles had all or mostly dysvascular participants. Three found that women use their prosthesis less often [67, 94, 119] while one suggested that more prosthesis use was associated with being a woman [123]. One additional article reported on prosthesis use and sex [137]. In a cohort of mostly trauma participants, the authors suggested that the number of hours of prosthesis use was correlated with functional satisfaction for males, but all levels of satisfaction (total, functional, aesthetic and weight) for females [137]. The number of hours per day of use was also potentially connected with positive body image for males but not for females in the same study by Murray et al. [137].

Prosthesis prescription was posited to be associated with gender in three studies [18, 55, 82]. These articles reported that men, regardless of the level of amputation, were more often fitted with a prosthesis compared to women in mostly dysvascular cohorts [18, 55, 82]. However, in a study by Highsmith et al. [59], the authors reported prosthesis cover prescription tended to favor women, regardless of the level of amputation. An additional study suggested that the durability of cosmesis was also impacted by gender, where women were less satisfied with durability compared to men [128]. Further, the included articles suggested that satisfaction with prosthesis differed by sex and gender. In terms of sex, a study with mostly non-traumatic participants claimed that lower levels of body image disturbance were correlated with higher levels of functional satisfaction for males but females also required aesthetic and weight satisfaction in addition to function [137]. In another study looking at mostly trauma participants, gender appeared to have an influence on satisfaction with prosthesis fit, comfort and appearance with levels being higher in men than women [89].

Mobility/function
The included articles that described differences in sex and gender on mobility and/or function used a variety of different outcome measures. The most common tools included the Two-minute walk test (2MWT) [147], and the Activities-specific balance confidence (ABC) scale [148]. Few studies used population-specific measures of mobility such as the Locomotor Capability Index (LCI) [149, 150], K-classification levels [151], Trinity Amputee and Prosthesis Experience Scale (TAPES) [152], Prosthetic evaluation questionnaire (PEQ) [153] and Prosthetic limb users survey of mobility (PLUS-M) [154].

Generic measures. Gender differences were identified when results of generic measures were captured based on the included articles. The functional level at the end of rehabilitation was found to be higher for men than women for dysvascular LLA in a study by Knezevic et al. [56]. Two studies reported the opposite in the dysvascular population, with women having better mobility according to the Functional Independence Measure [74] and a 45-meter walk-test [46].

Sex differences were also reported by the included articles in relation to these parameters. Based on the results reported by several studies, being male was associated with better 2MWT scores [40, 114], better ambulatory status [49, 54, 87], mobility [66, 116, 143] and activities of daily living scores [68] in persons with LLA due to trauma, osteoarthritis and dysvascular causes. One article reported conflicting findings, with males having longer Timed-Up-And-Go scores compared to females, suggesting greater mobility impairment [72]. With respect to falls, being female was potentially associated with a higher risk of falls and fall-related injury in persons with vascular LLA in two studies [60, 129]. Balance was also measured using the ABC scale in two studies, with results claiming that males have higher balance confidence compared to females [100, 136].

Lower-limb amputation specific measures. For gender, five studies used population-specific measures. For these studies, men reported better K-levels than women at discharge in persons with dysvascular LLA [139], while a study looking at only trauma LLA found better physical capacity for men according to the TAPES [43]. Similar results were reported with respect to the Locomotor Capability Index in three studies. Specifically, one study claimed that men tended to report less worsening in this score over time [119] and had higher scores than women; suggesting better mobility in both trauma and dysvascular cohorts [43, 139]. With respect to sex, Kelly et al. [100] claimed that scores on the PLUS-M were lower for women than men in a mostly trauma cohort. However, when using the PEQ, Wong et al. [40] posited that male sex was associated with lower perceived functional ability.

Mental health
Mental health outcome measures (e.g., social adjustment, positive/negative affect, depression, post-traumatic stress disorder) varied between studies. As with mobility/function, most of the measures used were not specific to LLA. These included the Positive Negative Affect Schedule (PANAS) [155], Beck Depression Inventory [156, 157], State-trait anxiety inventory [158], Functional comorbidity index [159], Self-reported questionnaire-20 [160], Psychological adjustment scale [161], the Brief COPE scale [162], and the Post-traumatic growth inventory [163]. The only population-specific measures used that determined sex and gender differences were the TAPES. Three additional articles conducted qualitative analyses with two using interpretive phenomenological analysis [39, 118] and one using thematic analysis [126].

Based on the included articles, gender differences were reported when using either generic measures or population-
specific (limb loss) measures. In particular, four studies suggested, that compared to men, women in mostly dyvascular cohorts had higher negative effect [102,144], poorer general adjustment [144] and a higher rate of mental health problems [73], including greater symptoms of depression [144] and moderate-to-high post-traumatic growth scores [118]. However, there is conflicting evidence when it comes to social adjustment. In two articles that utilized the TAPES, one study in a mostly dyvascular population reported that compared to men, women tended to have poorer social adjustment [144], while another with mostly traumatic LLA found women had higher psychosocial adjustment scores when Locomotor Capability Index and phantom limb pain scores were held constant [43]. For the qualitative studies, the notion of body image was most often described by women from mostly dyvascular LLA cohorts [43,118,126]. Although two studies were all women, one indicated that appearance is considered to be a “women specific challenge” [118].

When looking at sex differences, one study of females in a mostly vascular LLA cohort tended to have a higher risk of anxiety or panic disorder [117]. In two studies with all males with traumatic LLA, almost half of participants had symptoms of post-traumatic stress disorder [105] and those with psychological problems tended to have more phantom limb pain [107]. In terms of adjustment, differences depended on the type of adjustment and the measurement tool used. For example, in two studies looking at mostly traumatic LLA, one found that females had higher scores than males on psychological adjustment [51] while another (that used the TAPES) found that males were most socially adjusted [69].

Occupations
The articles included in this review reported that engagement in physical activity was potentially influenced by gender. Of the four studies that reported differences, only one reported a reason for amputation (mostly non-traumatic) [38]. Rates of physical activity were suggested to be higher in men than in women in two studies [38,91] with men reporting higher levels of high energy activities in an additional study [125]. However, in two studies, women were more likely to complete more moderate levels of activities [125] and reported higher daily activity levels than men [138]. Employment was also potentially associated with gender in two studies, with men having a higher rate of employment following LLA [91,112]. Only one article reported sex differences in return to driving in a mostly dyvascular cohort [85]. In this study, the authors claimed that males were more likely to return to driving following their amputation [85].

Sexual health
The two articles that reported differences in sexual health reported on sex rather than gender [48,113]. Sexually active females reported greater self-consciousness than their male counterparts (38% versus 25% respectively) in a study by Woods et al. [48]. In the same article, non-sensuality was measured in the notion of body image was most often described by women from mostly dyvascular LLA cohorts [43,118,126]. Although two studies were all women, one indicated that appearance is considered to be a “women specific challenge” [118].

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Discharge destination
Only two articles reported on sex and gender differences in discharge destination. Both studies focused on dyvascular populations, with one reporting on sex [134] and the other on gender [133]. Both articles found that female sex or being a woman was potentially associated with being discharged to institutional care [133,134].

Discussion
The aim of this scoping review was to highlight the differences that exist between sex and gender for QoL and related domains for persons with an adult acquired LLA. Overall, there were limited details on how these constructs were measured. Thus, while identified studies showed differences across QoL and related domains, it is difficult to parse out whether the differences were by sex or gender. Due to the uncertainty of how these constructs were measured in the included studies, the main findings of differences identified in this review should be interpreted with caution. Although there were mixed findings for many of the domains, it appears that female sex and individuals who identified as a woman experience a greater impact of their LLA on QoL related domains compared to male sex and men. Most notably, potential areas of differences were reported for prosthesis-related outcomes, mental health, return to work and driving.

Articles that reported on prosthesis-related outcomes reported findings by sex and gender. The results of the included studies suggest that less prosthesis prescription and lower prosthesis satisfaction for both female sex and being a woman (gender) compared to male sex and men (gender). It is possible that this discrepancy in prosthesis prescription may be due to the increased risk of a higher level of amputation for female sex and women [68,131]. In general, above knee prostheses tend to be heavy and difficult to use. From a biological perspective, females tend to be smaller and may not have sufficient strength to effectively use this type of device. Concerns with weight were also identified from the patient perspective, where the weight of the prosthesis was a more important factor for prosthesis satisfaction in women than in men [137]. In addition, comorbidities may also play a role in prosthesis prescription as it was suggested that women tended to have higher rates of comorbidities that may impact prosthesis prescription (e.g., osteoarthritis [117]). These biological differences may result in clinician hesitancy to prescribe women this type of prosthesis due to safety concerns (e.g., increased risk of fatigue resulting in falls). More work is needed to understand why prescription rates between sexes and genders are different.

Issues of mental health and its associations with sex and gender were described. Overall, the findings from the included studies suggested that compared to men and males, women and females experienced a higher rate of mental health problems including depression and anxiety [73,117,144]. However, none of the studies that reported these differences provided potential explanations for why women are experiencing increased symptoms of mental health challenges. One potential explanation may be related to issues of body image. Three qualitative studies included in this review reported that challenges with body image were most commonly discussed by women [43,118,126]. It has been shown that body image in women impacts levels of depression and anxiety [164]. It is important that these sex and gender considerations are taken into account moving forward if rehabilitation aims to address these mental health concerns in women.

Finally, we identified in this review that studies on return to work and return to driving accounted for sex and gender; albeit
there is minimal work in this domain. The included studies claimed that men (gender) were more likely to return to work [91, 112] and males (sex) were also more likely to return to driving following their LLA [85]. Unfortunately, the authors of these studies did not provide reasoning for why sex and gender disparities exist for returning to work and driving. With respect to employment, potential reasons include differences in prosthesis prescription and level of amputation. Those with a prosthesis [165] and those with a lower level of amputation (e.g., below the knee) [166,167] were found to be potentially more likely to return to work. There may be a relationship between return to work and return to driving. Those who return to work may also be more likely to want to return to driving in order to continue working. For example, in persons with a spinal cord injury, those who had the ability to drive were also more likely to be employed [168]. Since women are less likely to return to work, it is possible that they do not see the need to return to driving and therefore, choose not to undergo the relicensing process. However, research is needed to explore this potential connection between gender, return to work and driving following LLA as none of the included studies in this review described such a phenomenon.

In addition to these domains, more work is needed in other areas such as sexual health and sexuality [169,170]. Only two studies that were included in this review suggested differences by sex for sexual health [48,113]. The limited findings on sexual health are in line with a recent systematic review on sexuality and sexual health in persons with limb loss [171]. The authors of this review highlight that more targeted efforts are needed to better understand sexuality and sexual health in women since most of the literature was focused on males/men [171]. It is important for researchers who are exploring sexuality and sexual health in LLA to take into account sex and gender when identifying challenges faced in this population in order to develop interventions that are sex and gender-specific. Not only do biological differences exist by sex, but there are also more social aspects of sexuality and sexual health that may come into play. For example, the more physical aspects of sexual health (e.g., sexual performance) may be more difficult for men, as links have been shown between sexual functioning and men's identities [172]. On the other hand, there are societal implications that women must face that are not the same as in men, including issues of sexual pleasure [173]. These aspects need to be explored in order to provide more nuanced interventions for improving sexuality and sexual health in persons with LLA by sex and gender.

Interestingly, mixed findings for objective QoL measures were reported by the included articles. While none of the studies reported differences by gender in overall QoL scores on the SF-36, specific sub-domains (e.g., role physical or role emotional), were posited to be significantly different by gender. Furthermore, more differences were identified for sub-domains on the WHOQOL-BREF, rather than the overall score (three studies compared to one). This is important as it highlights how the subscales of these generic QoL measures appear to be sensitive to differences in the LLA population, but not the overall scores. However, it is a well-known issue with generic measures that they fail to capture population-specific issues such as satisfaction with mobility aids, accessibility and transportation which have been shown to influence community participation and thus the quality of life [88, 174]. This may account for the discrepancy of gender findings and the lack of significant findings for overall scores on these generic measures.

In this review, we identified an important limitation in the existing research in the reporting of sex and gender. Only four of 69 articles made clear how they defined the term gender. All four of these articles identified that gender was collected by indicating if the participant was a man or woman. While the rest of the 69 articles did not provide a definition, results were only presented using the same man/woman binary. Furthermore, no information was presented regarding the inclusion of trans or non-binary individuals. Taken together, these findings are indicative of measurement issues when it comes to collecting gender. It is possible that the literature included in this review may be using the terms sex and gender interchangeably. However, this should be understood with the caveat that most of the included articles were not clear on how gender was collected. For example, whether participants were asked more specific questions of their gender, but no responses were received or if participants were not provided the opportunity to give a response outside of the man/woman binary was not made explicit. It is also unclear whether binary trans participants (i.e., trans individuals who identify with binary gender identities) were included.

To ensure a clear understanding of sex and gender differences in LLA QoL research, it is pertinent to understand how participants are being asked about their gender. If participants were asked to provide their gender with the options “male or female”, there is no way to understand how someone who identifies as non-binary would answer this question [175]. It is possible that these participants may indicate their sex assigned at birth, choose the option that they find the least offensive or choose to abandon the survey altogether [175]. Phrasing questions about gender this way may even be difficult for binary trans participants since it is unclear whether researchers are asking about their gender identity or sex assigned at birth [175]. Currently, there are no validated and reliable measures that exist to collect gender identities that are inclusive of trans and non-binary participants [176]. However, this should not excuse research from providing participants with a broader range of gender identity options or allowing participants to self-identify their gender to ensure ethically responsible research [175]. In order to ensure that gender is captured properly, future work should seek to make a broad range of gender options available to participants to choose from. This way, participants will be able to self-report their gender identity with the most accuracy. Furthermore, researchers should be explicit with how participants are asked about their gender, in order for those reviewing the literature to have a clear understanding of who is being included and what conclusions can be drawn.

There are also clinical implications regarding a lack of information on trans and non-binary individuals. In a recent study by Baldwin et al. [177] patients who identified as transgender or genderqueer highlighted positive and negative interactions with their healthcare provider. Among the key themes of this qualitative study, participants who had negative experiences noted that they experienced misgendering, the clinician had a lack of knowledge about gender diverse individuals and/or experienced transphobia [177]. The lack of information on trans and non-binary participants may stem from the paucity of research that is inclusive of gender-diverse participants. While this study may not be focused on persons with LLA, it is important that future research in LLA that aims to inform clinical care make explicit the inclusion of gender diverse participants, in order to generate ethical best practices for this population [175]. Furthermore, it is necessary to establish the prevalence of LLA in trans and non-binary persons in order to identify population-specific needs and inform gender-specific interventions.
**Limitations**

As with all scoping reviews, there is the possibility that not all relevant literature was included in the review due to human error. However, every effort was taken to ensure that a rigorous selection process was followed to ensure that unintended omissions were kept to a minimum. This included double screening at each stage of the screening process,grey literature searching and reference searches. A second limitation of the current review involves the scope of the results. While it was not the purpose of this review, it is important to consider the intersectional nature of QoL and its related domains. Future research should seek to include intersectional analyses to highlight the differences by sex and gender in conjunction with other sociodemographic information such as race in order to get a better understanding of specific population group needs. Finally, the included studies were not assessed for quality. A lack of quality assessment, although not required for scoping reviews [36], leaves room for questions about methodological implications. It is possible that some of the findings from this review stem from articles that have methodological issues. Therefore, it is important that the quality of these articles is assessed in the future in order to draw stronger conclusions from the currently available literature.

**Conclusion**

Sex and gender differences are suggested for QoL and related domains for individuals with adult acquired LLA. Overall, findings tended to be more positive for men/males than women/females based on findings of the included studies. Articles included in this review were not clear with how gender was defined. In order for more targeted interventions that account for sex and gender differences, studies need to be more forthcoming about how they use and define gender. This will ensure that we are capturing relevant data and develop more definitive understandings of how sex and gender impact QoL. Furthermore, information regarding gender-diverse persons should be made explicit in future research. The needs of this population are currently not well understood and are therefore necessary in order to ensure we are providing equitable care to improve long-term health and well-being.

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Appendix A.

Search strategy used in Medline (OVID Interface). Results are as of 13 July 2020.

| # | Searches | Results |
|---|----------|---------|
| 1 | Sex characteristics/ | 54119 |
| 2 | Gender identity/or femininity/or masculinity/ | 19620 |
| 3 | Sex factors/ | 263303 |
| 4 | Sex distribution/or sex ratio/ | 64082 |
| 5 | Gender*.tw,kf. | 332000 |
| 6 | (sex adj3 factor* or characteristic* or distribut* or ratio*).tw,kf. | 42560 |
| 7 | (male* adj3 female*).tw,kf. | 321145 |
| 8 | (feminin* or masculin*).tw,kf. | 12899 |
| 9 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 | 893128 |
| 10 | exp Lower extremity/ | 165971 |
| 11 | Amputees/ | 3514 |
| 12 | Amputation/ or disarticulation/ | 21119 |
| 13 | Amputation stumps/ | 3099 |
| 14 | Amputation, traumatic/ | 4756 |
| 15 | Artificial limbs/ | 6853 |
| 16 | 11 or 12 or 13 or 14 or 15 | 32229 |
| 17 | 10 and 16 | 10540 |
| 18 | Hemipelvectomy/ | 475 |
| 19 | Hemipelvectomy*.tw,kf. | 655 |
| 20 | 17 or 18 or 19 | 11239 |
| 21 | (lower or leg or legs or ankle* or foot or feet) adj3 (amput* or loss or prosth*).tw,kf. | 15522 |
| 22 | 20 or 21 | 23165 |
| 23 | 9 and 22 | 1165 |
| 24 | Limit 23 to yr=“2000-Current” | 951 |