VA/DOD CLINICAL PRACTICE GUIDELINE FOR REHABILITATION OF INDIVIDUALS WITH LOWER LIMB AMPUTATION

Department of Veterans Affairs

Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and the Department of Defense (DOD) guidelines are based on the best information available at the time of publication. The guidelines are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This clinical practice guideline (CPG) is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when providers consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every health care professional using these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DOD policies. Further, inclusion of recommendations for specific testing, therapeutic interventions, or both within these guidelines does not guarantee coverage of civilian sector care.

Version 3.0 – 2024

Prepared by

The Rehabilitation of Individuals with Lower Limb Amputation Work Group

With support from

Office of Quality and Patient Safety, Veterans Health Administration

And

Clinical Quality Improvement Program, Defense Health Agency

Version 3.0 – 2024[1]

Based on evidence reviewed through March 2024

[1] VA/DOD Clinical Practice Guideline. (2024). Rehabilitation of Individuals with Lower Limb Amputation Work Group. Washington, DC: U.S. Government Printing Office.

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I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DOD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the "…Health Executive Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration and Military Health System," by facilitating the development of clinical practice guidelines (CPGs) for the VA and DOD populations.(1) Development and update of VA/DOD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and wellbeing.

In 2017, the VA and DOD published a CPG for the Rehabilitation of Lower Limb Amputation (2017 LLA CPG), which was based on evidence reviewed through July 2016. Since the release of that CPG, the evidence base on LLA has expanded. Consequently, a recommendation to update the 2017 LLA CPG was initiated in 2023. This updated CPG's use of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach reflects a more rigorous application of the methodology than previous iterations.(2) Therefore, the strength of some recommendations might have been modified because of the confidence in the quality of the supporting evidence (see Evidence Quality and Recommendation Strength).

This CPG provides an evidence-based framework for evaluating and managing care for adult patients, 18 years or older, who have experienced LLA, toward improving clinical outcomes. Successful implementation of this CPG will

- Assess the patient's condition and in collaboration with the patient, determine the most appropriate rehabilitation plan;
- Optimize each individual's functional independence, health outcomes, and quality of life.
- Minimize preventable complications and morbidity; and
- Emphasize the use of patient-centered care.

II. Background

A. Epidemiology of Lower Limb Amputation

a. Overview

A 2008 study utilizing data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS) estimated that there were 1.6 million people living with limb loss due to diabetes mellitus (diabetes) or peripheral arterial disease (PAD), trauma, or cancer in the U.S. in 2005, over 1 million of whom had lower limb loss.(3) A 2024 study of insurance claims from a health plan including many Medicaid and Medicare patients estimated that there were over 2.2 million people living with limb loss at any given point from 2016 to 2021.(4)

In the U.S., the most common cause of prevalent lower limb amputation (LLA) is complications from diabetes and/or PAD, which are sometimes grouped together as "dysvascular," and are often

associated with chronic non-healing wounds and osteomyelitis. This is followed by trauma, then cancer.(3) Sepsis or septic shock are estimated to be present in about one-quarter of LLAs at the transmetatarsal level or higher, and about 10% of incident LLAs are considered to be emergency operations.(5)

b. Diabetes Mellitus and Peripheral Arterial Disease

Diabetes affects over 25M people and when present, increases the risk of amputation 10 times higher compared to those without diabetes.(6,7) The overall incidence rate of diabetes and PAD is increasing, and amputation remains a treatment option in these diagnoses once severely diseased limbs are no longer salvageable. (8,9) In this population amputation may be considered as a treatment option for complications such as tissue loss (nonhealing wound or gangrene), infection, or ischemic rest pain when nonoperative management or revascularization do not exist or have failed, or if amputation is deemed to have benefit to the patient over other management strategies (for example, a better chance of healing or return home).(10,11) There may be a choice between multiple levels of amputation.(12)

The age-adjusted incidence rate of nontraumatic lower extremity amputation (NLEA) in adults with diabetes decreased from 2000 to 2009, then increased by 2015.(13,14) The increase in incidence was greater for amputations at the toe or foot level than for higher level amputations. (13,14) These changes were largely driven by increased rates of NLEA among younger and middle-aged adults (18—44 and 45—64, respectively). Rates also increased more prominently in men than women.(13)

There are a multitude of modifiable and non-modifiable risk factors in patients who have sustained limb loss. For example, Black race has been found to be a risk factor for amputation among patients with diabetes or peripheral arterial disease in multiple studies.(15-17) In a study of Medicare beneficiaries diagnosed with peripheral arterial disease, other factors associated with increased risk of amputation included diabetes, renal disease, dementia, congestive heart failure, cerebrovascular disease, and region (East South Central and West South Central, which together included states of the Southeast).(17) In Medicare beneficiaries with critical limb ischemia, risk factors for major amputation included history of smoking, age over 80, rural environments, and region of the U.S. (South, Puerto Rico).(16) In patients with critical limb ischemia, presentation with ulcer or gangrene was a risk factor for amputation in comparison to presentation with rest pain.(16)

While this guideline's focus is on rehabilitation care for patients with LLA, preservation of the residual limb and preservation of the contralateral limb is of utmost importance. In diabetic patients, protective and prophylactic foot care and early detection of any deformity or skin breakdown may prevent the development of ulcers and reduce the risk of amputation (see the VA/DOD CPG for the Management of Diabetes Mellitus in Primary Care [1]). Tobacco cessation and control of cardiovascular risk factors, including glycemic control in diabetics, are additional

[1] See the 2023 VA/DOD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus. Available at: https://www.healthquality.va.gov/

approaches to the prevention of LLA. Due to the systemic nature of PAD and diabetes, patients with these conditions are at high risk for further complications to their amputated residual limb and/or amputation of the contralateral limb. In addition, they are at higher risk for other health problems such as cardiovascular disease, cerebrovascular accident, renal disease, peripheral neuropathy, etc. Preservation of the residual and contralateral limb as well as the patients' general health, wellness, and functional independence remain integral parts of ongoing care.(10)

c. Other Etiologies of Non-traumatic Lower Limb Amputation

Causes other than diabetes, PAD, trauma, and cancer were estimated to account for less than 3% of cases of incident limb loss.(3) Less common causes of amputation include cancer, infection or wounds with primary etiology other than diabetes or PAD (e.g., necrotizing fasciitis, end-stage renal disease, chronic venous stasis, weakness or contractures), non-traumatic orthopedic injuries or complications of orthopedic interventions, frostbite, iatrogenic complications of vascular access procedures for other medical problems, and others. The goal in treating musculoskeletal tumors with the lowest risk of recurrence is to remove the tumor and salvage the limb, while for tumors with high risk of local recurrence or metastasis, amputation is indicated. Complications of total knee arthroplasty such as periprosthetic infection, severe pain, or periprosthetic fracture may also lead to transfemoral amputation.(18)

d. Traumatic Amputation

Trauma is responsible for approximately 13% of prevalent amputation in the U.S., although prevalence can be as high as 45%, as these injuries occur in a younger population.(3,8,19) Limb trauma could lead to amputation by direct mechanical disruption of the limb, vascular injury, compression syndrome, or by complications such as infection.(20) Trauma-related infection could lead to delayed amputation months to years later.(20)

Of particular concern to military and Veteran populations are amputations associated with combat-related injuries, such as those occurring from blast, penetrating, or crush injuries. These injuries are also typically complicated by a multitude of other comorbid conditions (e.g., traumatic brain injury, post-traumatic stress, heterotopic ossification (HO), infection, and other orthopedic and soft tissue injuries).(21) Heterotopic ossification is present in many persons with amputation due to trauma and can significantly affect prosthesis fitting and rehabilitation.(22)

An analysis of the National Trauma Databank of civilian amputations indicated that in the U.S. from 2000-2004, digit amputations were the most prevalent at 76.9%, followed by single limb amputations at 23.1%. Among single limb amputations, LLAs were more common than upper limb amputations (59% versus 41%). Most amputations were caused by blunt injury (83%); 51% of those cases were caused by motor vehicle accidents and 19.4% caused by machinery accidents. Motorcyclists and pedestrians were more likely to sustain LLA, while those involved with motor vehicle collisions were more likely to sustain upper limb amputation.(23) In a study of global incidence and prevalence, two peaks in in age distribution are notable with traumatic amputation: males aged 20-29 and 70-79, and women aged 70-79 years. It is likely that the younger traumatic amputations are associated with occupational and automobile injuries whereas the peak from 70-79 is more likely attributed to falls.(24)

e. Limb Salvage and Delayed Amputation after Trauma

For severe traumatic limb injury, patients and surgeons are often faced with the decision between amputation versus limb salvage and reconstruction. Despite advances in limb salvage management, complications such as infection, chronic pain, or persistent dysfunction may lead to a decision for delayed amputation. In some cases, the decision to attempt limb salvage may result in increased complication rates, increased pain, and more procedures than if a primary amputation had been performed.(25,26) Several scoring systems of injury severity have been developed to inform the decision of whether to amputate or attempt to salvage the limb, for example the Mangled Extremity Severity Score (MESS) and Limb Salvage Index (LSI).(24) As these systems may not accurately predict functional recovery, it has been recommended they be used in combination with other criteria, including clinical judgement and patient preferences.(27)

B. Impact and Outcomes

a. Mortality

An analysis of Medicare data from 2000 through 2008 showed that mortality rates were nearly twice as high for those with PAD who had major LLA compared to similar patients that did not have LLA at 30 days (13.5% versus 6.9%), one year (48.3% versus 24.2%), and three years (70.9% versus 43.2%).(28) Age, Black race, male sex, history of heart failure, kidney disease, cancer, and chronic obstructive pulmonary diseases were all independently associated with higher risk of mortality after major LLA, while Asian race was associated with decreased risk of mortality. Evidence also suggests that individuals with more proximal limb loss (i.e. transfemoral amputation) have a higher risk of death compared to those with more distal amputation.(28)

b. Functional Outcomes

In a single site study of patients with major LLA, less than half of patients were ambulatory with a prosthesis by one year.(29) In a study of patients with LLA due to trauma, less than half of patients had returned to work by seven years after amputation.(30) Among military service members with through-knee or transfemoral amputation, 28.6% and 42.2% reported being fully disabled.(31)

c. Costs

In Medicare beneficiaries with PAD, cost per patient-year after major amputation was $55,700.(16) In a 2007 study of patients with LLA due to trauma, the two-year costs were $91,106, with an estimated lifetime healthcare cost of over half a million dollars.(32)

C. Lower Limb Amputation in the Department of Veterans Affairs and the Department of Defense

a. Department of Veterans Affairs

In fiscal year 2023, 97,024 Veterans with amputation were registered for VA Healthcare. Of these, 43,736 were documented as having major amputations (i.e. amputation proximal to the wrist or ankle).(33) Similar to civilian populations, the number of individuals with amputation(s) cared for in the VA and DOD medical systems has been increasing. The total number of Veterans with LLAs

being seen at VA facilities increased from almost 23,000 in fiscal year 2000 to over 75,000 in fiscal year 2023.(33,34) Annually, the number of patients undergoing a LLA procedure increased from 5,010 in fiscal year 2001 to 6,345 in fiscal year 2023. In fiscal year 2023, 88.6% of patients undergoing LLA had diabetes compared to 76.5% in fiscal year 2001. Some patients underwent multiple amputation procedures, as the total number of LLA procedures in fiscal year 2023 was 12,809.(33)

The VA Amputation System of Care was developed to provide lifelong interdisciplinary care to service members with combat-related amputations and Veterans with amputations from diabetes, PAD, or other causes.(35) To expand the care and treatment of Veteran patients at risk of primary or secondary limb loss, the VA's Prevention of Amputation for Veterans Everywhere (PAVE) program was designed to help prevent or delay limb loss.(36)

b. Department of Defense

The DOD has two distinct groups of amputation populations. One is the general population with over 63,000 beneficiaries in calendar year 2022 with some level of limb absence or loss across all age ranges. The other is the population of those with traumatic amputations related to recent conflicts. The Extremity Trauma and Amputation Center of Excellence database provided data on all conflict and operation-related amputations (excluding fingers, thumbs, or toes) sustained by U.S. service members between January 1, 2001, and December 31, 2023. During this period, 1,746 patients sustained at least one amputation. The majority of these amputations were a result of an improvised explosive device injury. Among this population, 1,446 patients had lower limb loss and 541 involved more than one limb (a combination of both lower limbs or a lower and an upper).(37) This CPG does not specifically address the care of individuals with multiple limb loss. The reader is referred to the textbook *Care of the Combat Amputee* for more information about rehabilitation for patients with multiple limb loss.(38)

D. Factors Affecting Rehabilitation of Lower Limb Amputation

The successful rehabilitation of patients with LLA is influenced by systemic considerations such as availability of the full multi-disciplinary team, structured programs and systems of care such as the VA's Amputation System of Care. Patient level factors include but are not limited to level of amputation, physical conditioning, social support such as a caregiver, comorbidities, cognitive functioning, and psychological factors.(39) Amputations caused by vascular disease generally occur in aging populations with numerous other comorbidities such as cardiovascular disease, hypertension, renal disease, and arthritis.(28) These factors must be considered in order to help patients reach their goals when developing individualized rehabilitation plans for individuals with LLA.

While the pathophysiology of traumatic amputations may be different than non-traumatic amputations, rehabilitation strategies and prosthetic component prescriptions for both should be focused on patient goals. The overall goals of rehabilitation after amputation are to optimize the patient's health status, functional independence, and quality of life.(40,41) Ongoing assessments and therapeutic interventions to address medical, psychosocial, physical, and functional limitations are necessary to achieve these desired outcomes.(42)

III. Scope of This Guideline

This CPG is based on published clinical evidence and related information available through March 15, 2024. It is intended to provide general guidance on best evidence-based practices (see Appendix A for additional information on the evidence review methodology). Although the CPG is intended to improve the quality of care and clinical outcomes (see Introduction), it is not intended to define a standard of care (i.e., mandated or strictly required care).

A. Guideline Audience

This CPG is intended for use by VA, DOD, and community providers and others involved in the health care team assessing and managing adult patients with LLA.

B. Guideline Population

This CPG is designed to assist providers in managing or co-managing patients in rehabilitation for LLA. Moreover, the patient population of interest for this CPG is adults who are eligible for care within the VA and DOD healthcare delivery systems. It includes Veterans as well as Active, Guard and Reserve service members and their adult beneficiaries. This CPG does not provide recommendations for rehabilitation of children or adolescents with LLA.

IV. Highlighted Features of This Guideline

A. Highlights in This Guideline Update

The current document is an update to the 2017 VA/DOD Lower Limb Amputation CPG. The major strength of this CPG is the coordination and collaboration of the multidisciplinary team ensuring a broad representation of providers engaged in LLA. The following significant updates make it important that providers review this version of the CPG:

- Updated Algorithm;
- Updated Routine Care for LLA section;
- Added 12 new recommendations, reviewed and replaced 4 recommendations, reviewed and amended 3 recommendations, carried over 1 recommendation not changed, and carried over 4 recommendations amended from the 2017 VA/DOD LLA CPG.

The methodology used in developing this CPG has been updated since the prior versions and reflects a more rigorous application of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology than previous versions. The result is a refined CPG that includes methodologically rigorous, evidence-based recommendations for the rehabilitation of individuals with LLA.

This CPG also provides expanded recommendations on research needed to strengthen future guidelines.

B. Components of This Guideline

This CPG provides clinical practice recommendations for the care of patients with LLA (see Recommendations). In addition, the Algorithm incorporates the recommendations in the context of the flow of patient care. This CPG also includes Research Priorities which list areas the Work Group identified as needing additional research. To accompany this CPG, the Work Group also developed toolkit materials for providers and patients, including a provider summary, a patient summary, and a quick reference guide, which can be found at: https://www.healthquality.va.gov/index.asp.

C. Racial and Ethnic Demographic Terminology in This Guideline

Demographic terms referring to an individual's race or ethnicity (e.g., Hispanic, Latino or Latina, Asian, Native American, Black, African American, White, Caucasian) can be ambiguously defined and understood, reflecting diverse geographies, histories, cultures, and experiences. Aligned with the recent Executive Order on Further Advancing Racial Equity and Support for Underserved Communities through the Federal Government,[1] the Work Group used terms such as Black rather than African American and White rather than Caucasian to avoid presumptions about ancestry and to promote inclusivity, clarity, and consistency. However, to represent accurately the evidence on which this CPG is based, the Work Group generally deferred to racial and ethnic terminology as reported in the published systematic reviews (SR), clinical trials, and other studies comprising that evidence when summarizing or otherwise referring to those studies. Consequently, usage of demographic terms in this CPG might appear inconsistent.

V. Guideline Development Team

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, Defense Health Agency, identified the following four providers to serve as Champions (i.e., leaders) of this CPG's Work Group: M. Jason Highsmith, PhD, PT, DPT, CP, FAAOP and Jeffrey T. Heckman, DO from VA; and Andrea Crunkhorn, PT, DPT and Tawnee Sparling, MD from DOD. The Work Group comprised individuals with the following areas of expertise: adaptive sports, nursing, occupational therapy, orthotics and prosthetics, pharmacy, physical medicine & rehabilitation, physical therapy, psychology, and social work. Table 1 lists the Work Group and Guideline Development Team members.

This CPG Work Group, led by the Champions, was tasked with

- Determining the scope of the CPG;

[1] Executive Order on Further Advancing Racial Equity and Support for Underserved Communities Through The Federal Government | The White House

- Crafting clinically relevant key questions (KQ) to guide the systematic evidence review;
- Identifying discussion topics for the patient focus group and considering the patient perspective;
- Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence; and
- Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation.

The Sigma Team (Sigma Health Consulting and Duty First Consulting) were contracted by VA to help develop this CPG.

Table 1. Guideline Work Group and Guideline Development Team

Organization	Names*
Department of Veteran Affairs	**M. Jason Highsmith, PhD, PT, DPT, CP, FAAOP (Champion)**
	Jeffrey T. Heckman, DO (Champion)
	Ian Pace, PharmD
	Leif Nelson, PT, DPT, ATP, CSCS
	Aaron Turner, PhD
	Patty Young, MSPT, CP
	Michael Carroll, PhD, CPO, FAAOP
	Rebecca Speckman, MD, PhD
	Teresa Schuck, LCSW
	Yvonne Gallegos, DNP
Department of Defense	**Andrea Crunkhorn, PT, DPT (Champion)**
	Tawnee Sparling, MD (Champion)
	Dixie Lee Johnson, MSN, RN, CRRN, CCM
	Jessica M. Richards, PhD
	Meghan Logeais, OTD, OTR
	Robert J. McGill, MD
	Robert T. Cook, CPO
	Stuart M. Campbell, PT, MPT
	James Sall, PhD, FNP-BC

Organization	Names*
VA Evidence Based Practice, Office of Quality and Patient Safety Veterans Health Administration	René M. Sutton, BS, HCA, FAC-COR II
	Jennifer Ballard-Hernandez, DNP, RN, FNP-BC
	Sarah Davis-Arnold, MSN, RN, NPD-BC, RCIS, EBP-C
	Lisa M. Wayman, PhD, RN, EBP-C
	Kelley Ern
Clinical Quality Improvement Program Defense Health Agency	Isabella M. Alvarez, MA, BSN, RN
	Lynn M. Young, BSN, RN, CIC
	Gwen Holland, MSN, RN
Sigma Health Consulting, LLC	Frances Murphy, MD, MPH
	James Smirniotopoulos, MD
	James Reston, MPH, PhD
	Joann Fontanarosa, PhD
	Kristen D'Anci, PhD
	Aggee Loblack
	Annie Tran, MPH
	Dan Sztubinski
	Sophie Roberts
	Will Wester, MLIS
	Erin Gardner, MPH, PMP
	Jennifer Falgione, MPH
	Ruth Bekele, MPP
	Samantha Speed-Gangitano, MPH
Duty First Consulting	Kate Johnson, BS
	Anita Ramanathan, BA

*Additional contributor contact information is available in Appendix D

VI. Summary of Guideline Development Methodology

The methodology used in developing this CPG follows the Guideline for Guidelines, an internal document of the VA/DOD EBPWG updated in January 2019 that outlines procedures for developing and submitting VA/DOD CPGs.(43) The Guideline for Guidelines is available at http://www.healthquality.va.gov/policy/index.asp. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and strength, management of potential conflicts of interest [COI], interdisciplinary stakeholder involvement, use of SR and external review).(44) Appendix A provides a detailed description of the CPG development methodology.

A. Evidence Quality and Recommendation Strength

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (see Determining Recommendation Strength and Direction).(45)

1. Balance of desirable and undesirable outcomes
2. Confidence in the quality of the evidence
3. Patient or provider values and preferences
4. Other implications, as appropriate, e.g., resource use, equity, acceptability, feasibility, subgroup considerations)

Using these four domains, the Work Group determined the relative strength of each recommendation (*Strong or Weak*). The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which incorporates the four domains.(46) A Strong recommendation generally indicates High or Moderate confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, insufficient evidence exists on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The way this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for an intervention that might be in common practice although it is unsupported by clinical evidence and particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text as shown in Table 2.

Table 2. Strength and Direction of Recommendations and General Corresponding Text

Recommendation Strength and Direction	General Corresponding Text
Strong for	We recommend . . .
Weak for	We suggest …
Neither for nor against	There is insufficient evidence to recommend for or against . . .
Weak against	We suggest against . . .
Strong against	We recommend against . . .

That a recommendation's strength (i.e., Strong versus Weak) is distinct from its clinical importance (e.g., a Weak recommendation is evidence based and still important to clinical care) is important to note. The strength of each recommendation is shown in Recommendations.

This CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations; the determination of the strength of the recommendation is more directly linked to the confidence in the quality of the evidence on outcomes that are critical to clinical decision making. The confidence in the quality of the evidence is assessed using an objective, systematic approach independent of the clinical topic of interest. Therefore, recommendations on topics for which designing and conducting rigorous studies might be inherently more difficult (e.g., randomized controlled trials [RCT]) are typically supported by lower quality evidence and, in turn, Weak recommendations. Recommendations on topics for which rigorous studies can be designed and conducted might more often be Strong recommendations. Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2,47) This stricter standard provides a consistent approach to determining recommendation strengths. For additional information on GRADE or CPG methodology, see Appendix A.

B. Categorization of Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, staying current typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations.(48) For example, the United States Preventative Services Task Force (USPSTF) has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every five years for either an update or reaffirmation.(49)

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England).(50,51) Table 3 lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified, and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The 2024 CPG recommendation categories can be found in Recommendations. Appendix C outlines the 2017 VA/DOD LLA CPG's recommendation categories.

Table 3. Recommendation Categories and Definitions*

Evidence Reviewed*	Recommendation Category*	Definition*
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012) (50) and Garcia, et al. (2014) (51)
Abbreviation: CPG: clinical practice guideline

C. Management of Potential or Actual Conflicts of Interest

Management of COIs for the CPGs is conducted as described in the Guideline for Guidelines.(43) Further, the Guideline for Guidelines refers to details in the VHA Handbook 1004.07 Financial Relationships between VHA Health Care Professionals and Industry (November 2014, issued by the VHA National Center for Ethics in Health Care)(52) as well as to disclosure statements (i.e., standard disclosure form completed at least twice by CPG Work Group members and the guideline development team).(43) The disclosure form inquiries regarding relevant financial and intellectual interests or other relationships with, for example, manufacturers of commercial products, providers of commercial services, or other commercial interests. The disclosure form also inquiries regarding any other relationships or activities that could be perceived to have influenced, or that give the appearance of potentially influencing, a respondent's contributions to the CPG. In addition, instances of potential or actual COIs among the CPG Work Group and the guideline development team were subject to random web-based identification via standard electronic means (e.g., Centers for Medicare & Medicaid Services Open Payments, ProPublica).

D. Patient Perspective

When developing a CPG, consideration should be given to patient perspectives and experiences, which often vary from those of providers.(47) Focus groups can be used to help collect qualitative data on patient perspectives and experiences. VA and DOD Leadership arranged a virtual patient focus group on January 11, 2024. The focus group aimed to gain insights into patient perspectives of individuals who received care in the VA and DOD healthcare systems for amputation of a lower limb and incorporate these insights into the CPG, as appropriate. Topics discussed included the patients' priorities, challenges they have experienced, information they have received regarding their care, and impacts of their care on their lives and their family members' lives.

The patient focus group was comprised of a convenience sample of 9 participants, which included four women and five men. Participants were mixed in terms of receiving care from VA or DOD, with many of them mentioning that at the start of their amputation care/rehabilitation, they received care from DOD and now receive care from VA. The time since amputation ranged from 4 years to over 50 years at the time of the patient focus group. The Work Group acknowledges this convenience sample is not representative of all individuals who have undergone lower limb amputation within the VA and DOD healthcare systems and, thus, findings are not generalizable and do not comprise evidence. For more information on the patient focus group methods and findings, see Appendix E. Patient focus group participants were provided the opportunity to review the final draft of this CPG and provide additional feedback.

E. External Peer Review

The Work Group drafted, reviewed, and edited this CPG using an iterative process. For more information, see Drafting and Finalizing the Guideline. Once the Work Group members completed a near-final draft, they identified experts from VA and DOD health care systems and outside organizations generally viewed as experts in the respective field to review it. The draft was sent to those experts for a 14-business-day review and comment period. The Work Group considered all feedback from the peer reviewers and modified the CPG where justified, in accordance with the evidence. Detailed information on the external peer review can be provided by the VA Office of Quality and Patient Safety.

F. Implementation

This CPG and algorithm are designed for adaptation by individual health care providers with respect to unique patient considerations and preferences, local needs, and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the care of patients who have experienced a LLA. The Work Group submits suggested performance metrics for VA and DOD to use when assessing the implementation of this CPG. Robust implementation is identified in VA and DOD internal implementation plans and policies. Additionally, implementation would entail wide dissemination through publication in the medical literature, online access, educational programs, and, ideally, electronic medical record programming in the form of clinical decision support tools at the point of care.

VII. Approach to Care in the Department of Veterans Affairs and the Department of Defense

A. Patient-Centered Care

Intended to consider patient needs and preferences, guideline recommendations represent a whole/holistic health approach to care that is patient-centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning disabilities. VA/DOD CPGs encourage providers to use a patient-centered, whole/holistic health approach (i.e., individualized treatment based on patient needs, characteristics, and preferences). This approach aims to treat the condition while also optimizing the individual's overall health and wellbeing.

Regardless of the care setting, all patients should have access to individualized evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in providers, and improve treatment adherence.(53,54) A whole/holistic health approach (https:/www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and wellbeing goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to sex, culture, ethnicity, and other differences.

B. Shared Decision Making

This CPG encourages providers to practice shared decision making, a process in which providers, patients, and family/friend/caregiver consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(55) Shared decision making is emphasized in Crossing the Quality Chasm, a 2001 Institute of Medicine report in 2001(56) and is inherent within a holistic health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, expected outcomes, and levels or settings of care or both, especially where patient heterogeneity in weighing risks and benefits might exist. Veterans Health Administration and the Military Health System have embraced shared decision making. Providers are encouraged to use shared decision making to individualize treatment goals and plans based on patient capabilities, needs, and preferences.

C. Patients with Co-occurring Conditions

Co-occurring conditions can modify the degree of risk, impact diagnosis, influence patient and provider treatment priorities and clinical decisions, and affect the overall approach to managing LLA rehabilitation. Many Veterans, active-duty service members, and their families have one or more co-occurring conditions. Because LLA is sometimes accompanied by co-occurring conditions, managing LLA collaboratively with other care providers is often best. Some co-occurring conditions might require early specialist consultation to determine necessary changes in treatment or to establish a common understanding of how care will be coordinated.

D. The Amputation Care Team

A multidisciplinary care team consists of expert clinicians purposefully assembled to provide patient-centered, holistic and precision care. “The core function of a multidisciplinary team (MDT) is to bring together a group of healthcare professionals from different fields in order to determine patients’ treatment plan.”(57) This team paradigm reduces barriers to interdisciplinary communication improving efficiency of diagnosis, treatment planning and comprehensive care. Collocation of the team in specialized centers utilizes coordinated care to decrease the burden of travel and improve access for patients to all members of the team resulting in enhanced outcomes. The experience of the Department of Defense and the Department of Veterans Affairs has utilized this approach for over twenty years.

a. The Members of the Amputation Care Team

As stated by the Massachusetts General Hospital team, “Effective care of amputees is not just limited to surgical intervention; rather, it requires a comprehensive approach that recruits services focused on functional and psychosocial rehabilitation.”(58)

The core amputation clinic team includes a physical medicine and rehabilitation physician (physiatrist), a physical therapist, an occupational therapist, a prosthetist, a licensed social worker, a nurse, and a rehabilitation psychologist. The expanded team includes those from vascular services, orthopedics, plastic surgery, dermatology, wound care, infectious disease, podiatry, and recreational therapy and adaptive sports or others as appropriate. Involvement of an expanded team will be dependent on individual patients or overall clinical population.

a. A physical medicine and rehabilitation physician (physiatrist) is responsible for leading the team through the rehabilitation process including assessment and evaluation, prosthetic planning if applicable, and lifelong management.
b. The physical therapist (PT) and occupational therapist (OT) perform comprehensive evaluations of the patient’s current function and design a rehabilitation program to address functional impairments. The PT and OT then provide education, functional mobility and gait training, safety and falls prevention, self-care management and activities of daily living (ADL) training. These therapists collaborate closely with a prosthetist during all phases of prosthetic care and prosthetic training.
c. The certified prosthetist (CP) performs a comprehensive evaluation of the patient’s residual limb, range of motion and functional goals. The CP is responsible for directing the team on the appropriate componentry based on goals and abilities of the patient. The CP fabricates the limb, provides adjustments and modifications and fitting guidance throughout the rehabilitation process alongside the therapists.
d. Licensed social workers provide adjustment counseling (individual, family and group), complete needs assessments around psychosocial issues, provide resources, assist with navigation of the health system, and provide case management services.
e. Rehabilitation psychologists assess cognitive functioning, provide adjustment counseling services, and further research efforts with the amputation population.
f. Expanded team members provide specialty input to optimize lower limb health and patient function, throughout all phases of rehabilitation.

b. Effectiveness of the Team as an Amputation Care Team

"Working with a specialized multidisciplinary amputation care team is critical to provide patients with the full range of information and resources they need to adapt and thrive following their amputation."(59) The multidisciplinary team is successful when working closely with referring teams such as primary care and surgery teams when it has been determined that the patient will require amputation. A referral from the primary care team provides the opportunity for the multidisciplinary team to educate the patient and their family prior to the surgery. It is during this education session when topics such as preparing the home, estimated timelines and what to post-surgical discharge planning first occur.

In the same article(59), there is emphasis on the importance of collaboration of the surgical team and the other members of the care team prior to amputation: "…it is important for the surgeon to understand some of the basics of prosthetics (sic) and what advances have been made and to have a working relationship with a prosthetist, who as a team, can help provide the patient with the optimum prosthetic (sic)." By creating an environment of multidisciplinary collaboration, the team makes decisions with the patient and their family to ensure the best possible outcomes.

c. Conclusion

Over time, greater familiarity among specialists will serve to improve the provision of amputation care through more robust integration of services and a better understanding of post-operative patient need and expectations.(58)

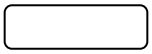
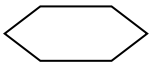
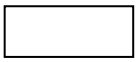
Hence, these professionals should be integrated into amputation care teams. In addition, involving translational research teams should also be considered, as it will help reduce the existing gap between basic research and the daily clinical practice.(57)

VIII. Algorithm

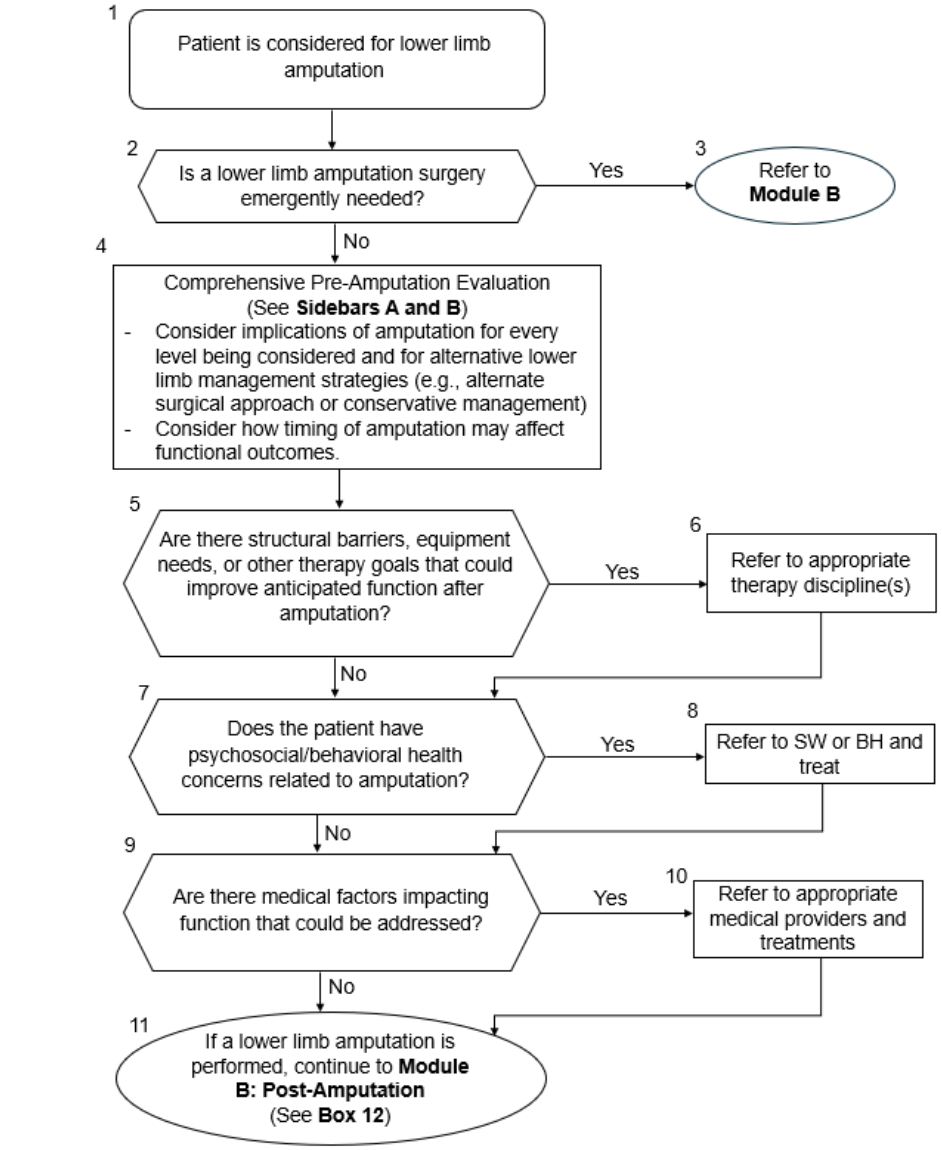
This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in rehabilitation of patients with LLA. This algorithm format represents a simplified flow of the management of patients with LLA and helps foster efficient decision making by providers. It includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

The algorithm is a step-by-step decision tree. Standardized symbols are used to display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.(60) Sidebars provide more detailed information to assist in defining and interpreting elements in the boxes.

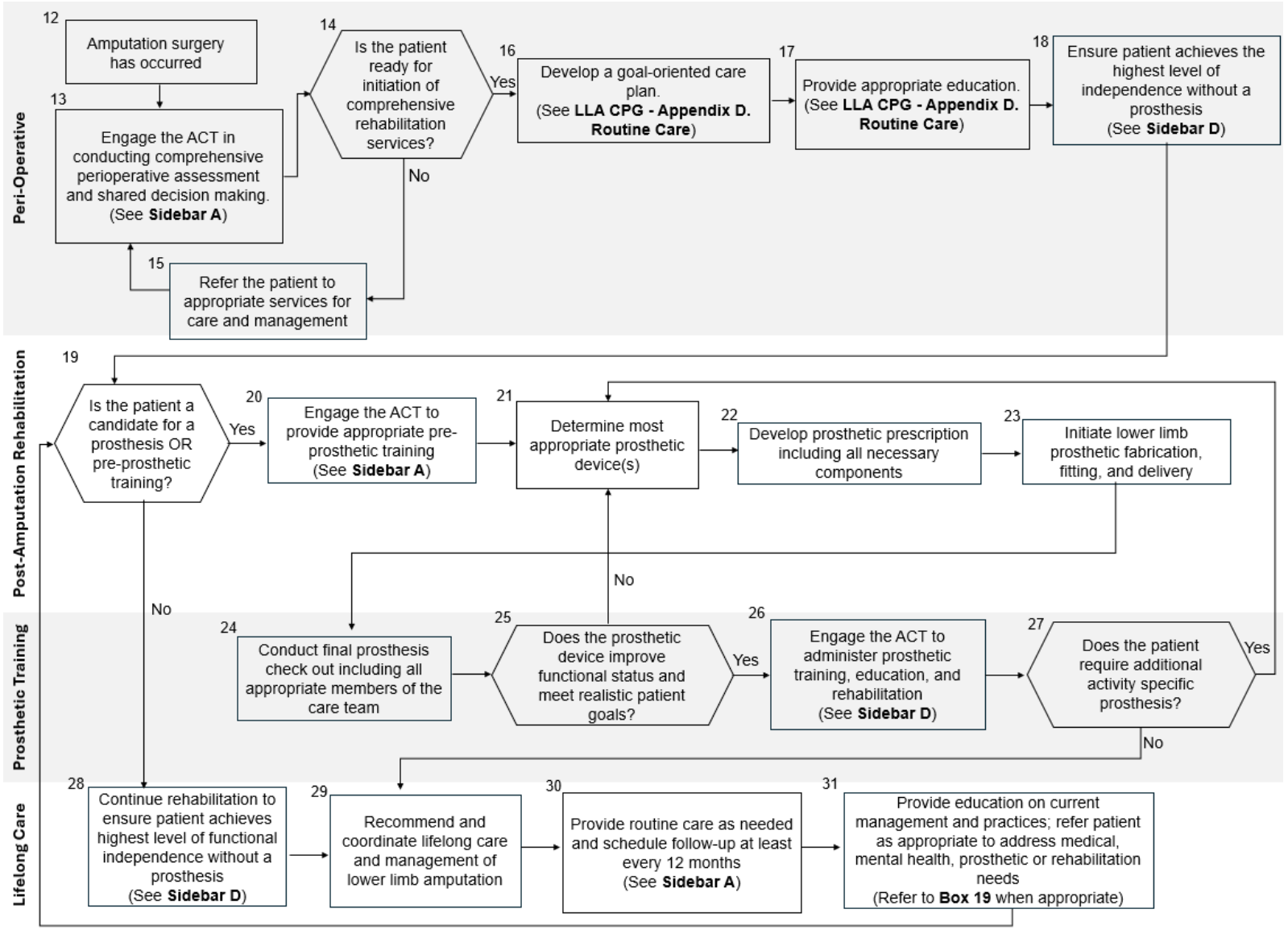
Shape	Description
	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered "Yes" or "No".
	Rectangles represent an action in the process of care.
	Ovals represent a link to another section within the algorithm

Module A. Pre-Amputation



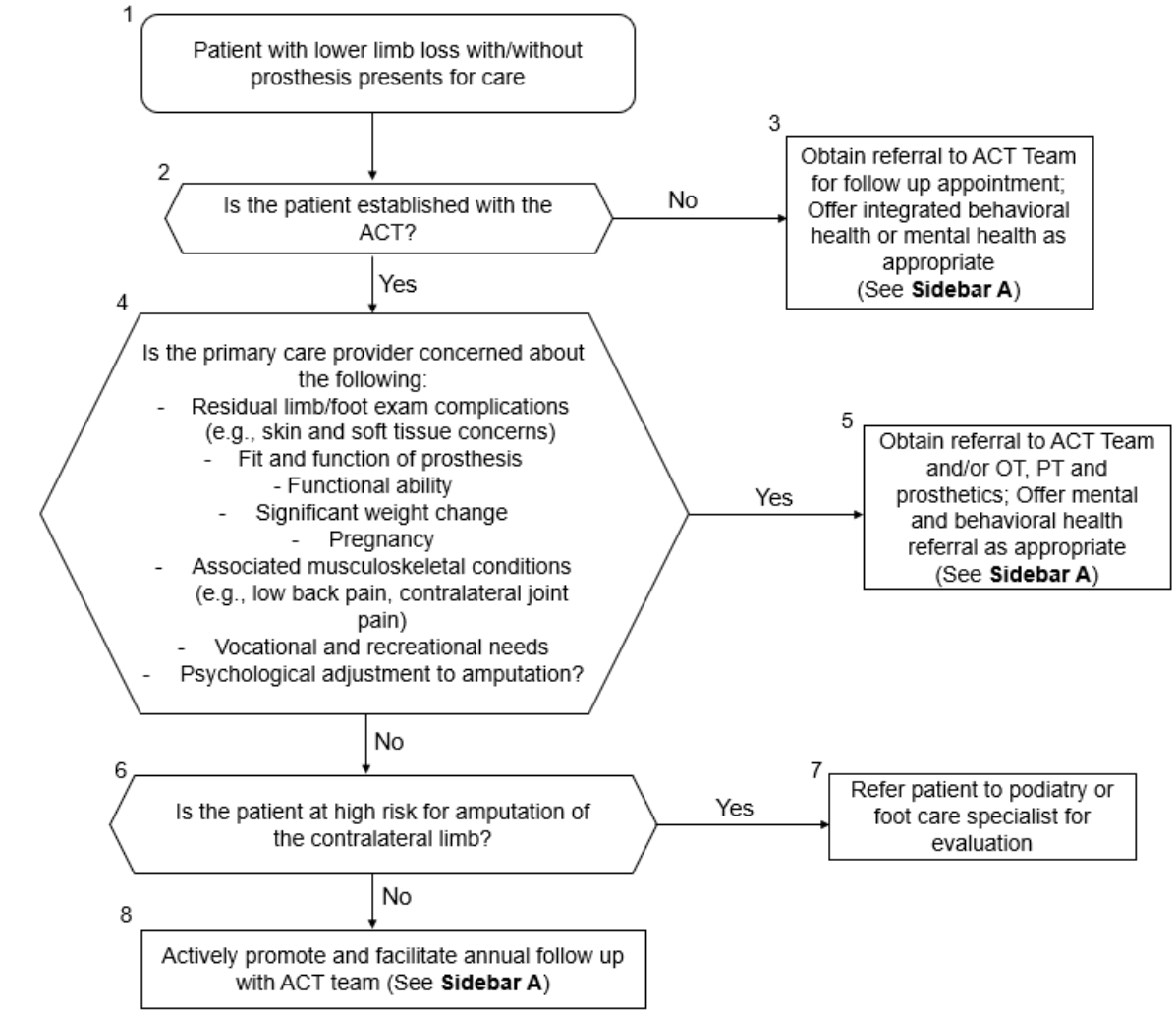
Abbreviations: BH: behavioral health; SW: social work

Module B. Post-Amputation



Abbreviations: ACT: Amputation Care Team; CPG: clinical practice guideline; LLA: lower limb amputation

Module C. Primary Care



Abbreviations: ACT: Transdisciplinary Amputation Care Team; OT: occupational therapy; PT: physical therapy;

Sidebar A: Amputation Care Team (ACT)

The ACT is a physician-led, patient-centered, transdisciplinary approach to provide a comprehensive treatment plan, limb preservation, and ensure lifelong management. The specialists involved may include:

- Rehabilitation physicians
- Pain management specialists
- Surgeons (e.g., vascular, orthopedic)
- Mental and behavioral health providers
- Case managers
- Nurses
- Occupational therapists
- Physical therapists
- Certified prosthetists
- Social workers
- Trained peer visitors
- Recreational Therapists and Adaptive Sports Providers
- Others (e.g., podiatrist, cardiologist)

Abbreviations: ACT: Amputation Care Team

Sidebar B: Comprehensive Pre-Amputation Evaluation

For amputation or other management approaches being considered, assess the following:

- Preliminary prosthesis candidacy
- Functional implications of amputation if not using a prosthesis (applies to all patients at times)
- Equipment or home modification needs to prepare for post-amputation
- Specific rehabilitation goals such as optimizing mobility with the contralateral limb
- Psychosocial and behavioral health
- Medical factors affecting function
- Alternative surgical approaches or conservative management

See **Appendix D** in the full LLA CPG for further recommendations.

Sidebar C: Pain Management

- **Perioperative Pain Management:**
  - Intraoperative placement of a perineural catheter for the post-operative delivery of local anesthetic can reduce pain following amputation surgery. (Recommendation 4)
  - Insufficient evidence to recommend for or against targeted muscle reinnervation or other peripheral nerve surgical management for phantom limb pain (PLP). (Recommendation 3)
- **Residual Limb Pain (RLP) Management:**
  - Insufficient evidence for or against neurostimulation (e.g., peripheral nerve stimulation, or spinal cord stimulation) or neuroablation (e.g., cryoneurolysis, radio frequency ablation) interventions for the management of RLP (Recommendation 21)
- **Chronic Phantom Limb Pain Management:**
  - Perineural catheter delivered anesthetic for the treatment of chronic severe phantom limb pain with functional impairment (Recommendation 22)
  - Consult for mirror therapy, alone or in combination with other therapies, to improve pain, function and quality of life for individuals with phantom limb pain. (Recommendation 11)
  - Insufficient evidence to recommend for or against any systemic pharmacologic intervention for the management of phantom limb pain. (Recommendation 23)
  - Insufficient evidence for or against neurostimulation (e.g., peripheral nerve stimulation, or spinal cord stimulation) or neuroablation (e.g., cryoneurolysis, radio frequency ablation) interventions for the management of phantom limb pain (Recommendation 21)

Sidebar D: Functional Activity List	
Below is a comprehensive list of activities to include throughout the rehabilitation process of individuals with lower limb amputation. *These activities are dependent on patient preference, level of functioning, and overall clinical judgment to ensure safety.* *The goal of this list is to promote the highest level of independence for individuals with and without prosthesis/prostheses.* *Ensure incorporation of appropriate medical equipment as needed to complete tasks safely (prostheses, wheelchair, crutches, walker, etc.).*	
Activities of Daily Living	Bathing and Showering (including transfers)
	Toileting and hygiene (including transfers)
	Grooming (standing or sitting at sink with or without a prosthesis)
	Dressing (managing pants with/without prosthesis, changing shoes on prosthesis)
	Donning/doffing shrinkers/liners/prosthesis
	Cleaning, charging, basic maintenance of prosthesis
	Wound care
Functional Mobility	Fall recovery
	Transfers to/from kneeling/sitting on floor
	Managing a curb
	Stairs
	Managing uneven terrain (rocks, sand, grass)
	Inclines and declines (hills)
	Ambulating while carrying objects
	Wheelchair management
	Managing small spaces (walking backwards, side steps, etc.)
	Quick changes of direction/pivots
Household Tasks	Cooking
	Cleaning dishes (unloading dishwasher, managing high/low cabinets)
	Housework (vacuuming, mopping, dusting, cleaning toilets/tubs)
	Laundry
	Gardening
	Yardwork (mowing the lawn, weed whacking)
	Making the bed/changing sheets
	Taking out the trash/bringing bins to the street
	Painting a room
	Managing a ladder
	Moving furniture/boxes (with or without dolly)
	Hanging a painting
	Retrieving objects under the bed

	Cutting firewood
Caregiving	Child rearing (carrying child, pushing child on swing, carrying car seat, playing on floor)
	Caring for pets and animals (managing dog leash, washing animal, carrying food bag)
	Caring for family members (pushing wheelchair, assisting with transfers)
Community Tasks	Driving
	Managing public transportation (bus, train, etc.)
	Wheelchair management in/out of car or public transportation
	Grocery shopping (pushing cart, carrying bags, loading/unloading car)
	Carrying tray in the cafeteria
	Changing a tire
	Religious activities (managing church pews, kneeling, etc.)
	Managing opening and closing doors
Return to Work	*These tasks will be specific to an individual's job duties. Many jobs can provide a job description that includes the physical requirements.*
Return to Sport/Leisure	Gym Exercises (squats, push-ups, managing gym equipment)
	Backpacking
	Camping (setting up a tent, starting a fire)
	Hiking
	Golfing
	Throwing/catching ball
	Transfers in/out of a boat
	Hunting/fishing
	These tasks will be specific to an individual's interests.
Return to Travel	Managing security at the airport
	Carrying luggage to and through the airport
	Placing luggage overhead
	Managing escalators and moving sidewalks
	Transfers in/out of airplane bathrooms

IX. Recommendations

The evidence-based clinical practice recommendations listed in the table below were developed using a systematic approach considering four domains as per the GRADE approach (see Summary of Guideline Development Methodology). These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences, and other implications (e.g., resource use, equity, acceptability).

A note regarding the 2024 LLA CPG Recommendation Table: While some of the below recommendations may be an element of a single phase of care, others may be relevant to multiple phases or require consideration throughout the entire continuum of care.

Table 4. Evidence-Based Clinical Practice Recommendations with Strength and Category

#	Recommendation	Strength[a]	Category[b]
1.	There is insufficient evidence to recommend one surgical amputation procedure over another.	Neither for nor against	Not reviewed, Not changed
2.	For patients with transfemoral amputation who meet eligibility criteria, we suggest osseointegration as an option to improve prosthesis use.	Weak for	Reviewed, New-added
3.	There is insufficient evidence to recommend for or against targeted muscle reinnervation or other peripheral nerve surgical management for phantom limb pain.	Neither for nor against	Reviewed, New-added
4.	We suggest intraoperative placement of a perineural catheter for the post-operative delivery of local anesthetic to reduce pain following amputation surgery.	Weak for	Reviewed, New-added
5.	Post-transtibial amputation, we suggest application of a rigid or semi-rigid residual limb dressing to promote healing and early prosthesis use as soon as feasible.	Weak for	Not reviewed, Amended
6.	We suggest providing post-operative amputation care in an inpatient rehabilitation facility (IRF) over other settings (e.g., skilled nursing facility (SNF) or home care).	Weak for	Reviewed, Amended
7.	We suggest assessment and treatment to improve behavioral health and psychosocial functioning.	Weak for	Reviewed, New-replaced
8.	We suggest peer support by a trained peer as a component of rehabilitation to improve psychosocial function.	Weak for	Reviewed, Amended
9.	We suggest cognitive assessment to inform rehabilitation goals and prosthetic candidacy.	Weak for	Not reviewed, Amended
10.	We suggest the care team provides patient education throughout amputation rehabilitation.	Weak for	Reviewed, Amended
11.	We suggest mirror therapy, alone or in combination with other therapies, to improve pain, function and quality of life for individuals with phantom limb pain.	Weak for	Reviewed, New-added
12.	We suggest an individualized and skilled rehabilitation program with exercise and gait training to improve functional status, walking ability, and quality of life.	Weak for	Reviewed, New-replaced
13.	We suggest using patient-identified sex to inform individualized rehabilitation plans.	Weak for	Reviewed, New-replaced

#	Recommendation	Strength[a]	Category[b]
14.	We suggest screening for factors associated with rehabilitation outcomes following acquired limb loss, (e.g., smoking, comorbid injuries or illnesses, psychosocial characteristics and physical function).	Weak for	Not reviewed, Amended
15.	For community ambulators, there is insufficient evidence to recommend any specific transfemoral socket design.	Neither for nor against	Reviewed, New-added
16.	For community ambulators, there is insufficient evidence to recommend for or against ischial containment or sub-ischial socket designs.	Neither for nor against	Reviewed, New-added
17.	For prosthetic ambulators, we suggest prescribing microprocessor knee units over non-microprocessor knee units for reducing falls, optimizing functional mobility, and improving patient satisfaction.	Weak for	Reviewed, New-replaced
18.	For prosthetic ambulators, there is insufficient evidence to prescribe any specific energy storing and return (ESAR) or microprocessor foot and ankle component over another.	Neither for nor against	Reviewed, New-added
19.	For prosthetic ambulators, we suggest energy storing and return (ESAR) or microprocessor-controlled foot and ankle components over solid ankle cushioned heel (SACH) feet to improve ambulation and patient satisfaction.	Weak for	Reviewed, New-added
20.	We suggest using patient-reported and performance-based measures with acceptable psychometric properties to assess function.	Weak for	Not reviewed, Amended
21.	There is insufficient evidence to recommend for or against neurostimulation (e.g., peripheral nerve stimulation, or spinal cord stimulation) or neuroablation (e.g., cryoneurolysis, radio frequency ablation) interventions for the management of phantom limb pain or residual limb pain.	Neither for nor against	Reviewed, New-added
22.	We suggest perineural catheter delivered anesthetic for the treatment of chronic severe phantom limb pain with functional impairment.	Weak for	Reviewed, New-added
23.	There is insufficient evidence to recommend for or against any systemic pharmacologic intervention for the management of phantom limb pain.	Neither for nor against	Reviewed, New-added
24.	For prosthesis users with hyperhidrosis, there is insufficient evidence to recommend for or against Botulinum toxin treatment to reduce sweat production, improve prosthetic function, reduce pain, and improve quality of life.	Neither for nor against	Reviewed, New-added
25.	There was insufficient evidence to recommend for or against strategies to prevent re-amputation of the ipsilateral limb or amputation of the contralateral limb.	Neither for nor against	Reviewed, New-added
26.	There is insufficient evidence to recommend for or against any specific intervention to improve intimacy and sexual health.	Neither for nor against	Reviewed, New-added

[a] For additional information, please refer to Determining Recommendation Strength and Direction

[b] For additional information, please refer to Recommendation Categorization

Recommendation

1. There is insufficient evidence to recommend one surgical amputation procedure over another.
   (Neither for nor against | Not reviewed, Not changed)

Discussion

The primary objective of a lower limb surgical amputation procedure is a well-healed and well-shaped residual limb that is free from pain or other complications with excellent function and soft tissue characteristics. While the surgical procedure chosen is most often related to the surgeon's preference and experience or is determined after a conversation between the surgeon and the patient, involving other members of the care team can better align expected surgical outcomes with expected rehabilitation outcomes. For example, if there is uncertainty regarding the optimal length of a residual limb, a pre-operative consultation with an experienced physiatrist or prosthetist should be considered. Of the many contemporary lower limb surgical amputation procedures, only a few (e.g., Burgess versus Ertl, Gritti-Stokes versus traditional transfemoral) have been compared in non-randomized observational studies.(61-66) No one procedure has been shown to be clearly superior to another, or to lead to a clear advantage in prosthesis use or rehabilitation potential. Each procedure has its own advantages and disadvantages. Further research is needed to explore how different surgical techniques impact functional outcomes based on underlying indication for amputation (e.g., trauma, vascular deficiency, infection). Also, more research is needed to further outline the potential strengths and weaknesses of the available procedures beyond expert opinion.

The Work Group considered the assessment of the evidence from the 2017 VA/DOD LLA CPG and did not systematically review the evidence related to this recommendation in this update.(61-66) Therefore, this recommendation is categorized as *Not reviewed, Not changed*. The Work Group's confidence in the quality of the evidence overall was very low. The benefits and harms were balanced as there were no major differences in serious adverse effects between surgical amputation procedures. Patient values and preferences may have large variation. Other implications the Work Group considered included subgroup considerations surrounding patient demographics and the feasibility of training for specific surgical procedures. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

2. For patients with transfemoral amputation who meet eligibility criteria, we suggest osseointegration as an option to improve prosthesis use.
   (Weak for | Reviewed, New-added)

Discussion

Osseointegration, as described by Atallah et al. (2018)(67), is "the direct connection of a 'nonvital' component incorporated in living bone". This procedure originated in the dental field in the 1960s and was integrated into the audiology field through bone-anchored hearing aids in the late 1970s. The introduction of osseointegration as a technique for individuals with limb loss as a bone-

anchored option for prosthesis use, an alternative to traditional socket-based suspension, was introduced world-wide in 1990 but only in the past 10 years in the United States.

Advancements in materials used to design and fabricate prosthetic sockets and the use of materials, such as silicone and urethane to enhance comfort, have helped enhance prosthetic socket comfort and function. Despite those advancements, many individuals experience difficulty with a consistent and accurate fit due to residual limb volume fluctuations, which can be caused by diet, change in activity level, comorbidities such as diabetes or dialysis, or muscle atrophy. A "poor fit can lead to issues regarding prosthetic function, with poor mechanical coupling…making it difficult for the person to use their prosthesis in a precise and confident manner."(68) These challenges can lead to prosthesis intolerance and abandonment, and this alone, may justify the osseointegration procedure as a viable option for many users.

While osseointegration is believed to result in improvements in functional outcomes and health-related quality of life, the procedure is not without risk. Noted complications are infection, both stoma-associated infections and soft-tissue infections, as well as peri-prosthetic fractures and loosening of the implant.(69) Presenting potential candidates with both the benefits and risks of the procedure will ensure the decision is patient-centered and comprehensively explored. The clinician should also consider the potential harms or risks to this procedure including infection and tissue complications, implant loosening and fracture. Infections are common in this population as cited by Atallah et al. (2018) stating an incident of infection of 49% reported in either a scheduled or emergency visit after three years.(67) Balzani et al. (2020) showed an overall infection rate at 32% with the more common infection being superficial in nature and did not require implant removal.(69)

For eligible patients, the potential benefits in overall functional mobility and quality of life may foster a level of lifestyle change with both physical and psychological benefits as noted in Balzani et al. (2020), which reported that "users of osseointegrated prostheses demonstrated improved walking ability when compared to walking prior to the procedure using traditional socket based prosthesis."(69) Other noted benefits, such as ease of donning and the absence of a socket contributed to an improved quality of life. While mobility seems to be a primary focus of many interested in this procedure, often overlooked are the precautions, contraindications, and timeline from time of surgery to discharge from rehabilitation services. Precautions and contraindications may include life-changing activity parameters in high-impact sports, limitation of activities in various bodies of water to prevent potential for infection and avoiding activities requiring excessive movements such as torque or rotation through the bone. And for many, age alone may be a contraindication and reason for not being a candidate for the procedure.

Some osseointegration procedures are one-stage while others adopt a two-stage approach which may span weeks to months of surgery to healing time. In addition to the surgical healing time, the often slow and steady approach to the rehabilitation process may create longer than expected timelines.

The Department of Defense has been integrating osseointegration surgery into their surgical repertoire for almost ten years, most often using the Osseoanchored Prostheses for the Rehabilitation of Amputees (OPRA^{TM}) Implant System created by Dr. Rickard Branemark. This

osseointegration system received FDA approval for the transfemoral level on December 18, 2020, and is commercially available in the US and is a covered benefit for qualifying Veterans at VA. Other bone anchored prostheses are considered experimental to include the eOPRA, a device being developed to restore some sensory function through the osseointegrated component.

The Work Group systematically reviewed evidence related to this recommendation(67,69) and are categorizing it as *Reviewed, New-added*. The Work Group's confidence in the quality of evidence was very low. The body of evidence had some limitations as both studies were systematic reviews which included numerous cohort studies. We believe the benefits and harms/burdens are balanced and, when considering patient values and preferences, there may be patient hesitancy to undergo a procedure such as a bone-anchored prosthesis knowing there is always a possibility of infection and a potential need for additional surgical procedures. The large variation in this population is also supported by the possibility of a lack of expertise in care of the person with osseointegration as many clinicians are largely not familiar with the procedure and the care of the individual with this bone-anchored prosthesis due to lack of access to the intervention and limited training. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

3. There is insufficient evidence to recommend for or against targeted muscle reinnervation or other peripheral nerve surgical management for phantom limb pain.
   (Neither for nor against | Reviewed, New-added)

Discussion

Targeted muscle reinnervation (TMR) involves "transferring distally innervating peripheral nerves from muscles that are no longer present or functional to more proximal available or functional musculature."(70) Emerging research shows additional potential for reduced phantom limb pain (PLP) and residual limb pain, although some of the risks involved in TMR include neuromas of the dissected nerve, local wound problems, and compromised limb/socket interface due to scarring or hypersensitivity.(71) Dumanian et al. (2019)(72) identified TMR as a promising surgical intervention for improving PLP and possibly residual limb pain. However, lower extremity Quality of Life in Neurological Disorders (NEURO-QoL), Numerical Rating Scale (NRS) pain scale scores, and Patient-Reported Outcomes Measurement Information Systems (PROMIS) pain scale scores did not differ between groups at 1 year.

Like treatments in upper limb amputations, a variety of potential treatments (e.g. Regenerative Peripheral Nerve Interface) in addition to TMR were identified as options to help improve outcomes in individuals with LLA. However, many did not meet inclusion criteria for this CPG's systematic evidence review due to potential selection bias, minimal control for potential confounders, and lack of blinding outcomes assessors.

The Work Group systematically reviewed evidence related to this recommendation focusing on TMR effects on PLP and are categorizing it as a *Reviewed, New-added.*(72) The Work Group's confidence in the quality of the evidence was very low. The body of evidence had limitations including small sample sizes and confounders in the analysis. The evidence supporting potential

benefits of the advances, including hardware, software, surgical, technology, or supplemental surgical interventions was limited. Thus, the Work Group decided on a *Neither for nor against* recommendation. Patient values and preferences were similar, as patients have a desire for relief of PLP. The Work Group felt that although TMR is a procedure that is becoming widely acceptable, surgical training in the technique is not yet universal. In addition, the Work Group felt that further research into peripheral nerve management, along with exploration for individuals undergoing amputation surgery due to dysvascular disease was needed. Therefore, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

4. We suggest intraoperative placement of a perineural catheter for the post-operative delivery of local anesthetic to reduce pain following amputation surgery.
   (Weak for | Reviewed, New-added)

Discussion

Evidence suggests that infusion of local anesthetic via perineural catheter (PNC) reduces post-operative pain in patients undergoing LLA. The evidence base for this recommendation was a single SR(73) that contained a total of 10 studies, from which the Work Group paid particular attention to the included individual RCTs.(74-77) A systematic review by Laloo (2021)(73) found that anesthetic administered via PNC for the first 72-96 hours after amputation surgery reduced post-operative acute residual pain and morphine requirements.(74-77) A systematic review by Laloo (2021)(73) found that anesthetic administered via PNC for the first 72-96 hours after amputation surgery reduced post-operative acute residual pain and morphine requirements. However, when only the RCTs were assessed, the impact of PNC delivered anesthetic on pain reduction was maintained with a moderate effect size (SMD -0.6) but there was no clear reduction in morphine requirements. Considering all trials (e.g., retrospective, and prospective RCTs) contained within the SR – average opioid reduction in the PNC arm was 20mg of oral morphine equivalents over the entire post-operative period (e.g., studies ranged from 3-5 days of post-op assessment when evaluating opioid requirements) and this reduction was of uncertain clinical significance.

There are similar values in patient preferences regarding PNC delivered local anesthetic as most patients prefer adequate post-operative pain control. Additionally, the benefits of the intervention slightly outweigh the harm/burden since complications (e.g., leaking, infection) were reported as either rare or easily managed. From a resource utilization standpoint, PNC does require additional training of the healthcare provider, requires supplies, and some patients undergoing LLA may require more than one PNC for adequate anesthetic delivery, but none of these were deemed burdensome by the Work Group.

The Work Group systematically reviewed the evidence related to this recommendation, which included a single SR (73) identified by the evidence review process. Specific focus was given to the four individual RCTs (74-77) contained in this SR and, as such, this recommendation is categorized as a *Reviewed, New-added*. The Work Group's confidence in the quality of evidence was low since the evidence base was limited to a single SR with large heterogeneity in how

outcomes of interest were measured. Benefits are assessed as slightly outweighing harms given that PNC-administered anesthetic improves the outcome of post-operative pain and was not associated with serious adverse effects. Patient values were deemed similar as the patient focus group report good quality pain control of importance. Thus, the Work Group decided upon a *Weak for* recommendation**.**

Recommendation

5. Post-transtibial amputation, we suggest application of a rigid or semi-rigid residual limb dressing to promote healing and early prosthesis use as soon as feasible.
   (Weak for | Not reviewed, Amended)

Discussion

The Work Group did not identify any new evidence on post-surgical dressing options for transtibial or transfemoral amputation that met inclusion criteria.

"Residual limb dressing" is often used to describe dressings that are placed over a local surgical incision, such as sterile gauze. Potential goals of post-operative residual limb management include: to promote healing, promote early prosthesis fitting, promote earlier or improved return to function, or control residual limb or PLP. Ideally, a post-operative residual limb dressing should protect the surgical incision and residual limb from trauma, control edema, prevent knee flexion contracture (if applicable), and shape the limb for prosthesis fitting.(78) There are three categories of post-amputation residual limb dressings(78,79): soft dressings, semi-rigid dressings, and rigid dressings. Terminology varies and categories are not mutually exclusive. For example, in the SR by Kwah et al.(79), semi-rigid dressing is a term sometimes grouped under rigid dressings. Some rigid dressing interventions included the use of a soft, elastic dressing underneath the rigid layer.(80,81)

Soft Dressing

Soft residual limb dressings can be categorized as *non-elastic soft dressings* (e.g., gauze wrapping and/or non-elastic residual limb sock) or *elastic soft dressings* (e.g., elastic bandage or elastic residual limb shrinker sock). Soft dressings are relatively easy to apply and remove, easy to store and order from the manufacturer (therefore easy to replace should soiling occur) and make it easy for clinicians to inspect and address the incision. Elastic bandages, if incorrectly applied, could cause excess pressure at the proximal limb or other location, which could lead to tissue damage and compromised distal blood flow, impaired healing and a suboptimal limb shape.(78,80) Possible disadvantages include dressings falling off if loose, suboptimal protection of the residual limb from trauma, and increased the likelihood of knee flexion contracture.

Semi-Rigid Dressing

A variety of dressings could be considered as "semi-rigid". Some studies use the term to specifically describe dressings that "consist of a bandage imbedded with Unna paste (zinc oxide, calamine, gelatin, and glycerine) which forms a semi-rigid inextensible dressing".(82) Other

dressings that might be considered semi-rigid are constructed with rigid and soft parts, providing some protection and allowing some movement.

Rigid Dressing

Conventional rigid dressings, or *nonremovable rigid dressings,* are plaster shells over soft base layers such as gauze, residual limb sock, and foam or felt padding of the tibial flares and residual limb end, which extend to the thigh and keep the knee in extension. A window is cut for the patella.(78,83) Modern nonremovable rigid dressings may use fiberglass casting tape. Nonremovable rigid dressings are often placed in the operating room or recovery area. A cast saw is needed to remove a nonremovable rigid dressing (unless it has become very loose). Theoretical advantages of nonremovable rigid dressing include protection of the surgical incision and residual limb from trauma, control of edema by creating a hard stop, and prevention of knee flexion contracture. In addition to non-compliance issues, potential disadvantages of nonremovable rigid dressings include the time and clinical expertise needed for application, weight, and impeded access to the residual limb for incision checks or investigation of new concerns. Clinicians should exercise clinical judgement as to which type of dressing they use and consider the pros and cons of each for patients (e.g., patients with high risk of falling may benefit from the protection offered by a rigid dressing; a removable dressing option may be preferred in patients at higher risk of non-adherence for follow-up).

The term "removable rigid dressing" was first used to describe a plaster cast-based dressing up to the knee, secured to the limb by a suspension cuff.(84) This design allowed knee flexion while the cast was in place and potentially removal of the intact cast.(78,79) There are also a variety of orthotic devices, custom-made or off-the-shelf, that are rigid *and* removable. Potential advantages of removable rigid dressings or devices include the ability for clinicians to easily access the residual limb for inspection and management, and the ability to accommodate residual limb volume changes with socks or other measures more frequently. Potential disadvantages of removable rigid orthotic devices are that they may be bulky and heavy (which may lead to pistoning and skin breakdown), and the patients may remove them at times other than as needed for clinical care.

A 2016 SR found evidence that in persons with transtibial amputation, short-cast “removable rigid dressings and semirigid removable dressings with or without combined elastic compression at reducing acute post-amputation edema volume compared with conventional elastic compression alone” and that removable rigid dressings may reduce residual limb healing time and hospitalization time in comparison to soft elastic dressings.(83) This review also found that vacuum-formed removable rigid dressings (short-cast) and conventional short-cast removable rigid dressings had similar time to prosthesis fitting and wound healing, and had similar physical function in follow-up. The study found that use of a polymer gel sock with short-cast removable rigid dressing could lead to earlier decrease in residual limb volume in comparison to conventional nonremovable rigid dressing. This evidence was included in the 2017 LLA CPG.

A 2003 systematic review found that “The literature supports that [thigh-high] rigid plaster cast dressings result in significantly accelerated rehabilitation times and significantly less edema

compared to soft gauze dressings, and prefabricated pneumatic prostheses were found to have significantly fewer post-surgical complications and required fewer higher-level revisions compared to soft gauze dressings."(78) This evidence was included in both the 2007 and the 2017 LLA CPG.

An RCT that did not meet inclusion criteria for the SR's used by prior Work Groups compared the use of elastic bandage versus compressive residual limb sock (shrinker).(85) There was reduction in residual limb circumference in both groups, with greater reduction in the elastic bandage group. There was not a statistically significant difference between the groups in patient satisfaction with residual limb appearance. Another RCT that did not meet inclusion criteria for SR's used by prior Work Groups compared the use of nonremovable rigid dressing (cast) or pre-fabricated polyethylene removable protective device, grouped as "rigid dressing," to soft dressing with an elastic bandage and knee immobilizer.(65) This study found that time to healing was faster in the rigid dressing group.

Types of rigid dressing interventions included non-removable plaster cast dressing to the thigh (two studies), short cast removable rigid dressing (five studies), and semirigid dressings with Unna paste (two studies). All but one soft dressing comparison groups included elastic bandaging or self-adherent elastic gauze; one defined the comparison as "customary soft dressings and bandaging." For the main comparison of rigid dressings to soft dressings, the SR found that the time from amputation to wound healing or prosthesis readiness was shorter in patients with rigid or semirigid dressing than with soft dressing, albeit with very low certainty of evidence. There was not conclusive evidence for between-group differences in skin- or non-skin-related adverse events, time from amputation to no pain, or time from amputation to walking. No data was found regarding patient comfort, quality of life, or cost. A 2019 Cochrane Collaboration SR of rigid dressings versus soft dressings for transtibial amputation included nine RCTs or quasi-RCTs, most of which included persons with amputation due to dysvascular disease.(79) All included studies compared one type of rigid dressing to soft dressing.

The 2017 LLA CPG Patient Focus Group valued the use of shared decision making to develop an individualized rehabilitation plan. With respect to residual limb dressing, patient-specific factors should be considered in selecting the management strategy. Clinicians should exercise clinical judgement as to which type of dressing they use and consider the pros and cons of each for patients (e.g., patients with high risk of falling may benefit from the protection offered by a rigid dressing). Resource considerations include the time and expertise required for application of a residual limb dressing or device, cost of the device, and feasibility in changing the dressing for inspection and management of the residual limb or when indicated due to changes in fit. These considerations might vary by the patient's setting for initial post-amputation rehabilitation.

The Work Group considered the assessment of the evidence from the 2017 VA/DOD LLA CPG. No new evidence was found in the 2024 LLA CPG evidence review. Therefore, this recommendation was categorized as *Not reviewed, Amended*. The Work Group's confidence in the quality of the evidence overall was very low. The body of evidence had some limitations including variation in intervention group, small sample sizes, and high risk of bias including selection bias, performance bias, attrition bias, and reporting bias. The potential benefits slightly

outweigh the harms due to improved volume reduction, safety for transfers and non-ambulation activities, facilitation of healing and contracture prevention. Therefore, the Work Group decided upon a *Weak For* recommendation.

Recommendation

6. We suggest providing post-operative amputation care in an inpatient rehabilitation facility (IRF) over other settings (e.g., skilled nursing facility (SNF) or home care).
   (Weak for | Reviewed, Amended)

Discussion

The 2024 update to the 2017 CPG did not find any additional evidence to add to the 2017 evidence synthesis.

A prospective, multi-site cohort study of 297 patients with new dysvascular LLA at the foot level or higher found that rehabilitation in an inpatient rehabilitation facility (IRF) has advantages compared to a skilled nursing facility (SNF).(86) Instrumental variable analysis was used to control for potential confounders including amputation level, comorbidities, baseline disability, post-operative physical or occupational therapy, self-selection into alternative settings, and others. In adjusted analyses of the 149 patient who were fitted with a prosthesis, those who had undergone rehabilitation in an IRF were more likely to be satisfied with their gait than those who had been in a SNF (76.1% vs. 59.3%, p-value < 0.05), and used their prosthesis more on average and experienced less pain related to prosthesis use (0.05 <= P <=0.1). There were not statistically significant differences (at P < 0.1) in skin irritations, wounds, satisfaction with appearance, or satisfaction with gait. In comparison of those who had been in an IRF compared to discharge directly home, there were not statistically significant differences (at P < 0.1) in prosthesis use, skin irritations, wounds, pain related to prosthesis use, or satisfactions with appearance, gait or comfort. Confidence intervals were not reported for any multivariate adjusted rates. In an adjusted analysis of all patients in the Roth et al. study(86), those who had undergone rehabilitation at an IRF had better physical function on several Short Form-36 domains and were less likely to have activities of daily living (ADL) impairment at six-month follow-up.(87) Overall benefit from this intervention exceeds any potential harm from a change in the rehab setting.

Other research not found within either the 2017 or 2024 literature reviews supports the finding of an association between IRF setting and better mobility outcome. A prospective cohort study of 72 individuals with first LLA at the transmetatarsal level or higher by Czerniecki et al., found that those who received care on a IRF within the year after amputation were more likely to achieve mobility success by 12 months after amputation than those who did not receive care on an IRF (adjusted risk difference 0.17, 95% CI 0.09 to 0.25). Mobility success was defined as same or improved mobility at 12 months after amputation compared to premorbid, as measured by the Locomotor Capability Index 5 (LCI-5). Adjusted analysis controlled for potential confounders including amputation level, social support, and total number of therapy visits.(87,88) A study of patients in the Netherlands with new amputation at the ankle or higher due to diabetes or dysvascular disease found that those who were admitted to an IRF after amputation were more likely to return home by one year than those discharged to a nursing home (OR 10.6, 95% CI

2.2—52.3). Those admitted to SNF were also more likely to return home than those discharged to a nursing home, albeit with a smaller magnitude of effect (OR 3.5, 95% CI 1.1—11.1).(89)

Potential contributors to benefit from IRF over SNF include intensity and dosage of therapy and other treatments, the interdisciplinary and comprehensive approach of IRF, and a stronger knowledge base of IRF team members. A mixed methods study of clinicians from skilled nursing facilities found that it was difficult for clinicians to maintain knowledge about amputation. Contributors were thought to be that amputation comprised a small portion of admissions, and resources were spread widely. Participants recommended the use of guidelines in care, and collaboration with specialized team members.(90)

Other considerations for this recommendation include the possible increased resource demands on the healthcare system, family and caregivers, and monetary costs with this referral approach versus SNF or home-based care programs. Resource use, access, feasibility, and subgroup considerations are important factors to consider when discussing rehabilitation settings with patients as IRFs may not be easily accessible to all patients. However, these settings are accessible and feasible for VA and DOD patients. Although neither the 2017 nor the 2024 patient focus groups specifically addressed type of rehabilitation facility following amputation, programs that optimize patient outcomes and achievement of patient goals align well with both the 2017 and 2024 focus group reports. Patients preferred rehabilitation in a setting where treatment was specialized to their needs and recognized the importance of an interdisciplinary amputation care team (which may be readily available to or integrated with an IRF team).

As no new evidence was found, the Work Group systematically reviewed evidence related to this recommendation from 2017 (86-88) and categorized it as *Reviewed, Amended*. The Work Group's confidence in the quality of the evidence was low, with study limitations including imprecision and risk of selection bias. The potential benefits of post-operative amputation care in an IRF over other settings include improved quality of life, better ambulation and confidence in gait, increased prosthetic device use, improved success with mobility overall, and fewer complaints of pain with prosthetic device use. These improved outcomes outweighed the potential harm of increased resource demands across family/caregivers, medical staff, and other resources. Patient values and preferences were similar because patients consistently prefer focused and personalized rehabilitation that optimizes their outcomes. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

7. We suggest assessment and treatment to improve behavioral health and psychosocial functioning.
   (Weak for | Reviewed, New-replaced)

Discussion

Behavioral health includes mental health diagnoses commonly occurring in individuals with limb loss. This includes, but is not limited to, depression, anxiety, and post-traumatic stress disorder as well as behavior that promotes effective self-care including lifestyle factors and self-management. Psychosocial functioning refers to the patient's ability to manage the

psychological and social factors which influence their interpersonal relationships and personally meaningful activities such as work and school. In the case of a patient with LLA, this also refers to how well the patient can participate in these activities despite his or her physical impairment. Behavioral health interventions may be implemented in multiple formats (e.g., individually or in group settings), across different modalities (e.g., in-person or telehealth) and may be freestanding or embedded in other rehabilitation treatments.

Evidence from three studies suggests behavioral health interventions following LLA improve psychosocial function, health behavior, and other rehabilitation outcomes such as balance. Godlwana et al. (2020) compared a 3-month education and home exercise program to usual care.(91) Intervention participants received education on amputation-related care, strengthening, and balance. The intervention also included a behavioral component that included a personal exercise diary, education on lifestyle modification, and telephone reminders for adherence to goals. Intervention participants endorsed greater quality of life and social participation (though the social participation did not endure through extended follow-up). Another study (92) identified in a systematic review by Wijekoon et al. (2023)(93), compared a 3-month behavior change intervention based on cognitive behavioral principles with a comparator intervention focused on health status monitoring. The intervention included targeted and collaborative goal setting surrounding home exercise, walking, and self-management. Participants in the intervention condition exhibited greater increase in physical activity (step counts) and reductions in sedentary behavior. Turner et al. (2021)(94) examined the effectiveness of a structured, group-based self-management program vs. education alone. The self-management intervention included topics related to basic self-management skills, physical health, emotional health, and social relationships and included an amputee peer who contributed to discussion. Participants in the self-management program reported improved psychosocial function (lower depression) and improved quality of life relative to education alone.

One study examined a pre-amputation behavioral intervention. Toygar et al. (2023)(95) examined the impact of a nurse-delivered education program for people with diabetic ulcers requiring amputation. The intervention, based on social cognitive theory, included exercise recommendations, education on amputation and prosthesis self-care, and coping strategies. Participants who received the intervention had better balance scores at 3-days post-amputation.

One additional study(96) not included in the evidence review and not impacting the strength of the recommendation examined a self-management intervention similar to Turner et al. (2021).(94) In this large multi-site trial, participants were recruited from existing support groups across the country and were randomized to receive either a structured, group-based self-management intervention, or continue usual care within their existing support groups. (2021).(94) In this large multi-site trial, participants were recruited from existing support groups across the country and were randomized to receive either a structured, group-based self-management intervention, or continue usual care within their existing support groups. The self-management intervention included topics related to self-management skills, pain, physical

health, emotional health, social communication, working with a healthcare team, and identifying resources. Group classes included an amputee peer. Participants in the self-management condition reported improvements in psychosocial function, physical function, and self-efficacy relative to controls.

Behavioral health is a topic of high importance to Veterans and was a topic frequently mentioned in the VA/DOD patient focus group. Periodic assessments of the patient should include inquiries into behavioral health status and psychosocial functioning (including spiritual beliefs and coping mechanisms). These assessments should be repeated at each phase of care and should be part of long-term management. For patients at risk for suicide[4], major depressive disorder[5], post-traumatic stress disorder and acute stress reaction[6], or substance use disorder[7], see the relevant VA/DOD CPGs. Behavioral interventions are generally well tolerated, have few side effects, and thus have a favorable risk benefit ratio. Care may include, but is not limited to, health behavior counseling and support for adaptation to amputation, as well as the treatment of specific mental health disorders. Individual counseling, pharmacotherapy, and group therapy (including peer support groups) are common therapeutic options. Behavioral health assessment and treatment should be integrated into routine amputation care whenever possible to reduce barriers to care.

The Work Group systematically reviewed evidence related to this recommendation.(91,93-96) Therefore, it is categorized as *Reviewed, New-Replaced*. The Work Group's confidence in the quality of the evidence was low. The body of evidence suggests that behavioral interventions may improve physical activity, balance, psychosocial function, and quality of life. Reviewed studies also had some limitations including small sample size, inconsistent findings for a particular outcome across studies, and the deterioration of treatment effects. The benefits of the assessment and treatment of behavioral health to improve psychosocial functioning outweighed the potential harm of adverse events, which was small. Patient values and preferences were strongly supportive of the need for behavioral health. Routine assessment of behavioral health at all phases of rehabilitation and integration into routine care were identified as ways to reduce barriers to access and participation. Thus, the Work Group decided upon a *Weak for* recommendation.

[4] See the 2024 VA/DOD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. Available at: https://www.healthquality.va.gov/
[5] See the 2022 VA/DOD Clinical Practice Guideline for the Management of Major Depressive Disorder (MDD). Available at: https://www.healthquality.va.gov/
[6] See the 2023 VA/DOD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder. Available at: https://www.healthquality.va.gov/
[7] See the 2021 VA/DOD Clinical Practice Guideline for the Management of Substance Use Disorder (SUD). Available at: https://www.healthquality.va.gov/

Recommendation

8. We suggest peer support by a trained peer as a component of rehabilitation to improve psychosocial function.

(Weak for | Reviewed, Amended)

Discussion

For this 2024 update of the 2017 Recommendation, only one study was retrieved. Turner et al. (2021)(94) examined the efficacy of self-management training following amputation. One hundred and forty-seven subjects were randomized to either the intervention group with the facilitation or to an education group which received standard clinical education and training to include the Amputee Coalition's First Step booklets. Investigators employed trained facilitators (one clinician and one Veteran with amputation) over a 4-week period. Assessments included 1) the impact of the intervention on physical and psychosocial functioning (primary outcomes) and quality of life (secondary outcome) in individuals with amputation and 2) to examine the feasibility and acceptability of the intervention in a large national health care system. Vet's Promoting Amputee Life Skills (VETPALS) consisted of a 4-hour workshop and 4 additional 2-hour sessions addressing self-management skills, health, and activity, managing emotions, communication, and social support, and maintaining goals and gains.

The study's primary outcomes were physical functioning (Short Musculoskeletal Functional Assessment) and psychosocial functioning (Patient Health Questionnaire-9) with secondary outcomes of quality of life (global) and quality of life (satisfaction with health) from the World Health Organization Quality of Life Scale (brief). Assessment was conducted at baseline, 6 weeks (treatment completion), and 6 months (follow-up). Participants randomized to VETPALS reported significantly improved psychosocial functioning and quality of life (satisfaction with health) relative to controls at 6 months with no differences in physical functioning over time between VETPALS and education control at either time point. Among VETPALS participants, treatment initiation was low (56%), but treatment retention (93% attended 4 of 5 classes) and overall satisfaction (100% reported very helpful or better and would recommend to a friend) were high.

Other evidence not included in the evidence allowed within this CPG does exist but did not meet standards for inclusion. Consistently albeit anecdotally, peer support has been identified as a key component in rehabilitation in studies that were not included in the evidence synthesis report. While not of sufficient quality to be included, they provide anecdotal evidence that peer support is both valued and sought by families, caregivers and women Veterans.(97-99) Lee et al. 2018(100) was excluded because it was a poor quality, retrospective comparative study.

While the quality of the evidence is very low, benefits outweigh harms overall, the 2017 recommendation was modified to remove reference to certified peer visitation as no evidence was found to support this aspect of peer support. Additionally, as no evidence was found to specify the timing or dosing of peer visitation or support across the continuum of care, the language was modified to narrow the scope of this recommendation to the evidence provided by Turner et al. (2021).(94) This recommendation is consistent with evidence and guidance from the 2017 CPG

update. While the quality of evidence was also low, it also suggested involvement in some type of support program as beneficial for both the patient and the family/caregiver.(101) Early involvement of family members and contact with other patients with amputations is important for the patient's psychological adjustment.(102) The Commission on Accreditation of Rehabilitation Facilities (CARF) Amputation Specialty Program requirements are consistent with literature suggesting that peer visits work best when the age, sex, and amputation level are considered and matched.(101,103) Patient focus group participants reported that peer support programs are often helpful following amputation as they provide opportunities for patients with amputation to relate to one another as well as share experiences and coping strategies. These factors indicate that the benefits of offering this component of care greatly outweigh the potential harms to the patient.

While initial introductory visits between a new patient and the peer visitor are best done in person, follow-up visits can be done more easily and frequently using phone, e-mail, or text messaging. For patients who are not a reasonable distance from a peer center, or live in an area with low population density, a clinical video telehealth visit (real-time video conference) may also be used to broaden the patient's access to a certified peer visitor or support group.

While the quality of the evidence is very low, benefits far outweigh harm. The patient focus group had a clear consensus on the need for peer support as well as a call for additional interventions. While there are resource implications (staff time, training, facility space, and recruitment of suitable peer support leaders) for peer support programs, the workgroup supports peer support and visitation programs as essential to psychosocial function and long-term health for patients with LLA.

This recommendation is *Reviewed, Amended* from the 2017 CPG. Work Group confidence in the quality of the evidence was very low thus this recommendation is rated as Weak for. The benefits to adopting this recommendation outweigh potential harms and patient values and preferences align positively. Key considerations include the feasibility of developing and sustaining peer support programs in facilities with small amputation populations and equity in access to such programs in rural or economically disadvantaged locations. Although able to be developed with limited resources, these still require staff oversight and leadership which at this point is not a billable activity for reimbursement, thus limiting access. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

9. We suggest cognitive assessment to inform rehabilitation goals and prosthetic candidacy. **(Weak for | Not reviewed, Amended)**

Discussion

Performing cognitive assessment prior to rehabilitation may assist in the development of appropriate goals and tailoring of the rehabilitation care plan. An SR of 30 studies reported that poorer cognitive function is associated with multiple aspects of amputation rehabilitation and subsequent functioning, including lower rates of successful prosthetic device fitting, decreased prosthetic device use, decreased mobility, loss of independence, and increased incidence of

falls, as well as higher mortality rate and an undesirable variation in adherence to medical regimens for individuals with LLA.(104)

The impaired cognitive domains of memory and executive function relate to the reduction of prosthetic device use and decreased functional outcomes. Verbal fluency, a measure of executive function, has been found to be predictive of prosthetic device use.(104) Cognitive status, particularly for individuals without comorbidities, can be predictive of long-term mobility. Memory in the acute phase following amputation is a predictor of long-term perceived health status and activity restriction. Visual memory is a predictor of mobility and locomotion. Dementia prior to amputation is predictive of increased mortality following amputation.(104)
Two other SRs not included in the evidence review and not impacting the strength of the recommendation examined the association between function and outcomes following amputation. One SR of 9 studies examined the association between cognition and prosthesis related outcomes among dysvascular amputees and found poorer cognitive function associated with poorer functional mobility, shorter wearing time, lower likelihood of prosthesis fitting, and poorer performance on multi-factorial prosthesis-related outcome measures. The most recent SR conducted in 2023 focused specifically on dysvascular amputees consisting of 14 studies. The review was consistent with previous reviews noting an association between cognition and prosthesis use, mobility, ADLs.(105) Depending upon the modality (e.g., screening vs. more extensive testing), assessment requires additional resources including time for testing and specific training, but also addresses important individual difference factors for some groups of patients, particularly individuals who are older or have dysvascular etiology. As cognition may affect most aspects of rehabilitation as well as patient outcomes, treatment teams should establish a process whereby any member can identify a concern and recommend additional assessment by a qualified professional (most typically a neuro- or rehabilitation psychologist or speech language pathologist).

The Work Group systematically reviewed evidence from the prior CPG to this recommendation.(104) Therefore, it is categorized as *Not reviewed, Amended*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence supports assessing cognitive function, specifically memory and/or executive function, in patients following LLA. Studies included in the SR had some limitations including small sample size, and widely varying use of assessment tools and specific outcomes, detracting from the ability to summarize findings across studies. The benefits of cognitive assessment, including gaining valuable information that can be used to help establish goals and determine prognosis treatment, outweighed the barriers, which included provider time and availability. Potential harm of adverse events was small. Regular consideration of the need for assessment at all phases of rehabilitation and integrated into routine care were identified as ways to reduce barriers to access. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

10. We suggest the care team provides patient education throughout amputation rehabilitation.
    (Weak for | Reviewed, Amended)

Discussion

Evidence suggests patient education interventions (the timing, format, and content of which varies substantially from study to study) improve functional status/walking ability in the perioperative phase, increases social participation throughout the rehabilitation process, and improves quality of life in patients with LLA.(91,93,95)

An RCT (N = 60; 30 in each group) by Toygar et al. (2023)(95) found that compared to patients who received 15 minutes of routine education pre-surgery, patients who received an hour-long education program based on Bandura's Social Cognitive Learning Theory before surgery showed improved balance/reduced fall risk as measured by scores on the Berg Balance Scale three days post-amputation. Although subgroup analysis revealed no statistically significant difference in balance/fall risk among patients who received major amputations (but a trend in favor of the intervention), the treatment effect on balance/fall risk favoring the intervention persisted for patients with minor amputations.

Evidence from 1 SR(93) that included 1 RCT studying a patient education intervention(91) (N = 154; 77 in each group) showed that compared to Usual Care, a 3-month home education + daily exercise program with daily telephonic reminders improved social participation at 3 months post-op (i.e., Intervention group showed "mild" participation restrictions while Control group showed "moderate" restrictions), but this effect did not persist at 6 months post-op (at which point, both groups were in the "mild" restrictions range). The effects of the intervention on different quality of life outcome measures varied across time points. Specifically, the intervention improved scores on an overall quality of life measure and two of its subscales (i.e., the overall EuroQOL-5D, the Utility subscale, and the Visual Analog Scale (VAS) subscale) at 3 months post-op; however, the treatment effect only remained significant for the VAS subscale at 6 months post-op.

Although not included in the 2024 LLA CPG evidence review, older peer-reviewed publications have consistently concluded that patient education is beneficial for improving patient outcomes specifically following amputation and other invasive surgical procedures. (e.g.,(106,107) Joint Commission requirements (also not included in the 2024 evidence review) further underscore the importance of patient education in health care settings given their emphasis on assessing patient learning needs and tailoring educational materials and training programs accordingly to meet those needs.(106,107) Joint Commission requirements (also not included in the 2024 evidence review) further underscore the importance of patient education in health care settings given their emphasis on assessing patient learning needs and tailoring educational materials and training programs accordingly to meet those needs.(108) Our suggestion to provide patient education throughout the rehabilitation process also aligns with patient values and preferences. The patient focus group emphasized the importance of patient education to better advocate for themselves when developing their care plan. They also discussed the need for easily accessible information and resources for themselves and their loved ones to further optimize care and support for patients living with LLA.

The Work Group considered the resource requirements of training providers and/or peers (see 2024 LLA CPG suggestion for peer support interventions, including incorporation of trained peers in self-management programs) to assess for relevant subgroup considerations (e.g., cognitive status, learning needs, single limb vs. multi-limb amputation) and provide patient education interventions that appropriately meet individual patient needs. The Work Group also discussed that resource use at individual facilities could be offset by incorporating peer educators, digital platforms, app development, and telehealth services to increase feasibility and accessibility to patient education materials and reduce potential inequities regarding the availability of patient education interventions across rehabilitation settings.(109)

The Work Group systematically reviewed evidence related to this recommendation(91,93,95) and it is categorized as *Reviewed, Amended*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations in the methodological quality of the included RCTs, including lack of intention-to-treat analyses, high attrition rates, unclear blinding of patients and study personnel/assessors, and not adequately adjusting for significant differences in baseline characteristics. The strength of evidence was also limited due to imprecision related to wide variability around effect sizes and the inclusion of single small studies.(91,95) Therefore, the recommendation is rated as *Weak For*. Despite the very low quality of the evidence, the benefits of providing patient education throughout amputation rehabilitation (e.g., improved balance, social participation, and quality of life) greatly outweigh the potential harms to the patient. Patient values and preferences were similar because patients want access to information that can aid in advocating for themselves in the development of their care plan and effectively communicating their care/support needs to family members post-amputation. The Work Group acknowledged there are resource requirements involved in training educators to assess individual patient learning needs and provide education that appropriately addresses these needs; however, incorporating trained peers, digital platforms, and/or telehealth services are all options to improve feasibility/accessibility, and reduce potential inequities across rehabilitation settings. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

11. We suggest mirror therapy, alone or in combination with other therapies, to improve pain, function and quality of life for individuals with phantom limb pain.
    (Weak for | Reviewed, New-added)

Discussion

Evidence suggests that mirror therapy (MT), either alone or as a component of an intervention, improves PLP based on two 2 SRs (110,111) and 3 RCTs (112-114) identified during the systematic evidence review. This recommendation is consistent with that of the 2022 VA/DOD Upper Limb Amputation (ULA) recommendation #5, which reads "We suggest the use of mirror therapy for the short-term reduction of phantom limb pain." This ULA recommendation was supported by evidence from Barbin et al. (2016)(115), which similarly found that "mirror therapy resulted in improved pain outcomes when compared to the control patients with ULA at 4 days to 6 weeks follow-up."(116) A key difference from the ULA CPG findings is that many of the

RCTs contained within the SRs in this evidence base for LLA reported on secondary endpoints of PLP reduction at 3 months (114) and 6 months (117-120) suggesting that the effect is durable in LLA.

Improvements in function and/or Quality of Life (QOL) were critical outcomes for the key question related to this recommendation. Overall, studies evaluating function/QOL are less common, and outcome measurement is more heterogenous (e.g., versus a numeric pain rating scale), making inter-trial comparisons difficult. Nonetheless, there was one SR identified by the systematic evidence review (110) that specifically evaluated the impact of MT on functional outcomes in patients with LLA and PLP. The Work Group also considered RCTs identified by the SR (112,114) or RCTs that were contained within SRs (117-120) that included functional outcome information. Lastly, one RCT contained within the Gane 2023 (110) SR was reported as a negative trial; however, upon individual review, MT was the control and MT + phantom limb exercise was the intervention with both arms improving similarly and statistically significantly from baseline in domains of pain, QOL and ambulation.(121)

The evidence base also identified the interventions of Graded Motor Imagery (Limakatso) and virtual reality (122) which were associated with positive findings on the outcomes of interest (e.g. pain and or function). The Work Group did not find sufficient evidence to make any individual recommendations for these two outcomes since the evidence for virtual reality was based on a single small trial and the evidence for Graded Motor Imagery was based on two small trials, both of which reported differing findings on functional outcomes.

All studies identified by the evidence review were deemed very low quality due to small sample sizes, heterogeneity of outcomes, and the difficulty of ensuring blinding with MT. Additionally, control interventions (e.g. “covered” MT, Phantom Limb Exercise, extra physiotherapy, tactile or sensorimotor treatment, etc.) are neither sham nor placebo as they all have some impact via their contextual effect. As such, eliminating bias is difficult in studying MT as an intervention for PLP.

Conversely, there is no evidence of harm with this intervention. The patient focus group identified that interventions which mitigate pain and the presence of multiple options and strategies (e.g. non-pharmacologic option) for pain management were of high importance. Additionally, resource requirements to implement MT are non-burdensome and, as such, this intervention can be broadly applied.

The Work Group systematically reviewed evidence related to this recommendation.(110-114,116-122) Therefore, it is categorized as *Reviewed, New-added*. The Work Group’s confidence in the quality of the evidence was very low (e.g., small sample sizes, heterogenous outcomes reported, inherent difficulties with blinding and placebo control). None-the-less, given the absence of harm for MT when used to improve pain and function/QOL in patient with LLA and PLP, the benefits were assessed to outweigh harms. Patient values were deemed similar as most patients prefer safe, effective, and non-medical management options to treat their PLP. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

12. We suggest an individualized and skilled rehabilitation program with exercise and gait training to improve functional status, walking ability, and quality of life.
    (Weak for | Reviewed, New-replaced)

Discussion

Despite numerous factors that can make it challenging to objectively compare the effectiveness of one rehabilitation intervention over another, there is limited evidence to support that engagement in a rehabilitation program can lead to improvements in functional status, walking ability, and QOL.

The challenges with comparison of rehabilitation interventions arise from a variety of factors including differences in the way a facility defines a rehabilitation program, how, when, and where it is administered; and how it is adapted to suit individual patient needs and goals. These challenges were emphasized by this evidence review, as the results were mixed and observations varied depending on the type of intervention being studied and the outcome measures being used.

For example, evidence from a SR by Wijekoon et al. 2003(93) comparing exercise programs to usual care reported improved QOL. On the other hand, evidence from a SR by Abou et al. 2022(123) found inconsistent results regarding changes in functional status and walking ability when comparing exercise programs to traditional training programs.

Despite the complications surrounding the comparison of rehabilitation interventions, it is generally accepted that the benefits of engaging in a rehabilitation program significantly outweigh the burdens. The general burdens include the need for time commitment, need for skilled rehabilitation providers, and the direct and indirect cost for patients when considering travel and access to the appropriate facilities. While these can present challenges for program implementation, the potential benefits of increasing functional status and QOL make it worth considering implementation of a program. It is important to note that due to patient differences in skill and goals, an individualized approach to the design and implementation of the program should be discussed with a skilled provider.

The Work Group systematically reviewed evidence related to this recommendation.(93,123-126) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including lack of clarity regarding randomization, blinding of patients and/or providers, blinding of outcome assessors, as well as reporting of allocation concealment. The benefits outweigh the harms due to the improvement in functional status, walking ability and QOL compared to the burdens of time for rehabilitation interventions and cost. Patient values and preferences varied some due to patient commitment. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

13. We suggest using patient-identified sex to inform individualized rehabilitation plans. **(Weak for | Reviewed, New-replaced)**

Discussion

We rated the confidence of the evidence as very low. The search identified one SR which included four relevant prospective cohort studies and one individual prospective review comparing female LLA patients to males for several important outcomes. No studies reported on any of the critical outcomes related to female LLA patients versus male LLA patients.

For important outcomes, evidence from 4 prospective cohort studies in 1 SR(127) and 1 individual prospective cohort study(128), reported inconsistent results for function/walking ability. Male LLA patients reported greater mobility per the Craig Handicap Assessment and Reporting Technique (CHART) scale, a lower injury rate from falls per self-report, and greater balance confidence per the Activities-specific Balance Confidence (ABC) scale 1-month post-LLA relative to female patients and female LLA patients reported higher daily activity levels and involvement in housework/shopping during an episode of PLP per a Pain/Coping Diary 1-month post-LLA relative to male patients. In healed patients, male sex was not identified as a variable affecting ADL, measured by the Barthel Index at approximately 5 years post-LLA, in a multivariate analysis. Female sex was not included as a variable.

Evidence from 1 individual prospective cohort study(128) reported unclear results for serious adverse events (SAEs). A higher proportion of male LLA patients had healed wounds at 2 months post-LLA. However, we noted a potential publication error in the data, as the total numbers of healed and non-healed male and female patients do not add to their reported sample sizes. Exact numbers are unknown. In healed patients, male sex was not identified as a variable affecting occurrence of new ulcerations approximately 5 years post-LLA in a multivariate analysis. Female sex was not included as a variable. In healed patients, female LLA patients had a higher mean survival time within an approximately 5-year follow-up period. However, male sex was not identified as a variable affecting mortality in a multivariate analysis. Female sex was not included as a variable.

The evidence did not consistently have accurate pre- and post-intervention results for outcomes, several studies did not have male or female as a variable, and a potential publication error in data was noted in another study. The primary limitations of these studies were a lack of clarity regarding attrition rates and adjustment for confounders.

Sex affirming care is an essential consideration when establishing goals for care of the LLA patient, to avoid assumptions as much as possible in the effort of optimizing and customizing care by opening dialogue with patients around their sex and all related variables, for the patient, and from the patient's perspective. Sex is a variable that has been understudied and underrepresented in the research literature for this population. Sex influences care outcomes, and important considerations for potential areas relevant to QOL include psychosocial wellbeing, physical functioning, environmental factors, and community

participation.(127) In future research and in practice, it would be psychologically beneficial to provide a broad range of sex options for patients to choose from versus only male or female. Providers should ask the patients to identify their preferred sex. Valuing patients' sex preferences will inform care and improve care outcomes in a positive direction due to the ability to customize care. Additionally, by inquiring about sex, the care team will be best directed by the patient to ask additional questions about the importance of appearance, roles, functioning, and QOL as it relates to the patient's identified sex.

In a paper by Randolph et al.,(129) there was emphasis placed on the female sex, relative to poor cosmesis, fewer female specific components, heavy prosthesis weight, and socket fitting issues, as well as psychological adjustment issues that are female specific. It is worth noting that the physical habitus issues commonly associated with the female sex may or may not impact care of all females due to varying physical stature in both males and females. Although attention to habitus is an important aspect when fitting a prosthesis, consideration should also be given to sex issues that go beyond prosthesis use, such as self-perception and roles an individual patient identifies with, which may be a more impactful focus for care teams of LLA patients.

Overall, the evidence comparing outcomes between male and female LLA patients is mixed and limited to measures of function/walking ability and serious adverse events (SAEs). Our searches did not identify studies that evaluated trans-identifying LLA patients or other sex-identifying populations beyond male and female. All 4 relevant prospective cohort studies in the included SR used the terms "sex", "male", and "female" to describe patients.(127) In the individual prospective cohort study, the term "gender" was used despite authors also referring to patients as "male" and "female".(128) Thus, it is unclear whether the intent in Chu et al. (2016)(128) was to record biological sex or gender identification.

Both the included SR(127) and individual study(128) reported inconsistent results for various measures of function/ walking ability with results being greater in male patients 1-month post-LLA. Male patients also self-reported a lower injury rate from falls, and at 5 years follow-up, male identification was not observed as a factor impacting ADL via multivariate analysis. Female patients reported higher activity levels via a Pain/Coping Diary and greater involvement in housework and shopping during an episode of PLP. Female sex was not included as a variable within the multivariate analysis of ADL; therefore, we could not conclude if ADL was impacted by female sex. A higher mean survival time was observed for female versus male LLA patients with a slight overlap in range, indicating that overall, females had more favorable mortality rates within 5 years of amputation. However, statistical test data was not provided and thus, whether this difference is significant remains unknown. Due to methodological limitations, unclear effect sizes, and variability all these studies received a Very Low rating.

Although we were able to find limited evidence in supporting our recommendation, we feel the benefits outweigh the harms/burden. In patient centered care, it is recommended to use an individualized care approach, treating each person with dignity and respect, and involving them in

all decisions about their health. This involves considering each patient's identified sex to optimize their rehabilitation trajectory, prosthesis acceptance, and QOL.

Another notable finding in these studies is the impact sex may have on community reintegration. One study(128) noted that women with LLA were less likely than men to return to work or driving. There is also variation in patient values and preferences. Men reported greater mobility, more confidence with balance, and less falls, while women reported higher daily activity levels in the home and community with ADLs. There are also sub-groups and equity issues that may arise as different sex identities have different needs for fitting and success. As an example, prosthetic components are generally more masculine in appearance and can be heavy and too large for many women to use comfortably.

Although there is limited evidence to support using patient-identified sex to inform individualized rehabilitation plans for LLA, there is sufficient evidence to support individualized patient care models. Individualized care addresses the whole person, which encompasses their physical, mental, and emotional well-being, and QOL. Knowing a patient's identified sex is a key requirement when establishing an individualized rehabilitation plan.

The Work Group systematically reviewed the evidence related to this recommendation.(127,128) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The benefits outweigh the harms due to the consideration of a patient's identified sex potentially optimizing rehabilitation trajectory, prosthetic acceptance, and QOL, while community reintegration can be impacted by sex. Patient values and preferences varied as the impact of sex related factors in clinical rehabilitation goals and outcomes can vary by individual. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

14. We suggest screening for factors associated with rehabilitation outcomes following acquired limb loss, (e.g., smoking, comorbid injuries or illnesses, psychosocial characteristics and physical function).
    (Weak for | Not reviewed, Amended)

Discussion

Although evidence for this recommendation was not specifically reviewed for the 2024 LLA CPG, evidence pulled forward from the 2017 LLA CPG Evidence Review suggests that several patient-related factors, including smoking, premorbid illnesses, psychosocial characteristics, and physical function are associated with morbidity, mortality, and functional outcomes following an amputation.(130-132) For example, a retrospective cohort study including 4,250 patients demonstrated that the premorbid factors of chronic obstructive pulmonary disease (see the VA/DOD Chronic Obstructive Pulmonary Disease CPG[8]): congestive heart failure, myocardial

[8] See VA/DOD Clinical Practice Guideline – Management of Chronic Obstructive Pulmonary Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/copd/VADoDCOPDCPGFinal508.pdf

infarction within the previous six months, renal disease on dialysis (see the VA/DOD Chronic Kidney Disease CPG[9]), a positive "do not resuscitate" status, and a generally low premorbid functional status were all associated with an increased mortality rate after amputation surgery. (130) Additionally, the evidence from Hasanadka et al.(130) showed an association between smoking and increased wound occurrence.

A cross-sectional study of 368 patients also showed an association between the presence of medical comorbidities and functional outcomes after amputation. This study used the Trinity Amputation and Prosthetic Experience Scales (TAPES) to measure these outcomes, which included subscales for prosthesis satisfaction, psychosocial adjustment, and activity restriction. (131) Moreover, being employed was among the most important factors associated with improved psychosocial adjustment and being less functionally restricted.

Finally, another retrospective cohort study (N = 256) did not find an association between comorbidities and functional outcomes; however, the functional status in this study was only measured during the inpatient phase of rehabilitation (i.e., at admission and discharge). No functional outcomes measures were collected from patients following discharge. Regarding mortality post-discharge, patients who were older at time of rehab admission, had ischemic heart disease, more severe comorbidities, lower functional status at admission, lower functional gains during inpatient rehab stay, and discharged to a place other than home had poorer survival rates over the course of a 96-month post-discharge follow-up period.(132)

While many of the comorbid conditions identified in the evidence review are common for individuals with acquired amputation, their potential impact on the overall health and QOL of the individual following LLA is profound. Similarly, potentially modifiable factors, including smoking, physical fitness, and employment status were also among the most important factors associated with both medical and functional outcomes that were identified in the evidence base, making them essential considerations when designing individualized rehabilitation plans. Thus, the benefits of screening for and addressing these factors greatly outweigh any potential harm.

Although not included in the Evidence Review, one SR(133) offers further support for the association between several patient factors and functional outcomes with specific focus on outcome measures assessing walking ability following LLA. The SR conducted by Kahle et al.(2016)(133), is an update to a previous SR(134) and included a total of 21,490 subjects across the two articles. This updated SR identified factors consistent with earlier literature, including premorbid functioning and medical comorbidities, as important predictors of walking ability. Among the predictive factors most strongly supported in relation to better walking ability outcomes (i.e., supported by at least six of the included studies) were lower amputation level, higher physical fitness, younger age, and fewer medical comorbidities. Additional but relatively less strong factors associated with post-amputation walking ability (i.e., supported by 3-5 of the

[9] See VA/DOD Clinical Practice Guideline – Management of Chronic Kidney Disease. Available at: https://www.healthquality.va.gov/guidelines/CD/ckd/VADoDCKDCPGFinal5082142020.pdf

included studies) included ability to stand on one leg, cognition and mood disturbance, sex, pre-amputation living status, and cause of amputation.

Our suggestion to screen for patient factors associated with rehabilitation outcomes is mostly aligned with patient values and preferences, as positive screens for patient factors associated with poor outcomes could serve as an impetus for offering additional patient education and resources to address/reduce factors associated with poorer outcomes that might otherwise not be offered. Indeed, a strong desire for increased access to educational information and resources was emphasized among patients during the patient focus group. The Work Group acknowledged that there may be some variation in patient preference depending on the number of screeners administered and the frequency of re-administration, as some patients may perceive requests to fill out numerous and/or frequent screeners as burdensome. The Work Group also considered different patient subgroups (e.g., patients with low literacy and/or low English language proficiency) and acknowledged issues of equity given the known racial and socioeconomic health disparities that systematically impact the rates of various patient risk factors (e.g., smoking, unemployment, obesity, medical comorbidities) across patient demographic groups and also function as barriers to effectively address/treat these risk factors.

The Work Group pulled forward and systematically reviewed evidence gathered during the Evidence Review for the 2017 LLA CPG(130-132); however, the evidence for this recommendation was not specifically reviewed again as part of the 2024 LLA CPG Evidence Review process. Therefore, the recommendation is categorized as *Not Reviewed, Amended*. The Work Group's confidence in the quality of the evidence overall was low. The body of evidence pulled forward from 2017 had some limitations in the methodological quality of the included studies which predominantly included retrospective record reviews and cross-sectional studies that precluded the ability to draw any conclusions about the directionality and/or causality of the relationships between identified patient factors and the medical, functional, and adjustment-related outcomes that were measured. Despite the very low quality of the evidence, the benefits of screening for factors that have the potential to profoundly impact patient outcomes following LLA (e.g., identifying patients who screen positive for risk factors, considering these factors in the development of an individualized rehabilitation plan, and intervening to treat and/or mitigate negative impact of risk factors) greatly outweigh the potential harms to patients. The inclusion of screening measures was thought to generally align with patient values and preferences, although some variability may exist depending on the factor being screened (e.g., smoking, obesity, physical fitness) and patient willingness to make behavioral changes to mitigate their level of risk. Other implications the Work Group considered included resource use and feasibility, as the recommended screeners are feasible to perform in the clinical setting and do not require significant resources. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

15. For community ambulators, there is insufficient evidence to recommend any specific transfemoral socket design.
    (Neither for nor against | Reviewed, New-added)

16. For community ambulators, there is insufficient evidence to recommend for or against ischial containment or sub-ischial socket designs.
    (Neither for nor against | Reviewed, New-added)

Discussion

Evidence from one crossover RCT by Fatone et al. (n=25) reported in two publications(135,136) found no difference for a variety of measures of walking ability including sit to stand, the four-square step test, agility, walking speed, step width, and other gait parameters or for functional status (i.e., orthotic prosthetic user survey [OPUS] lower extremity functional status) when comparing an Ischial Containment (IC) socket and a NU-FlexSIV Subischial (Sub-I) Vacuum. Only one test, the prosthesis limb step length, showed a between group difference, favoring the NU-FlexSIV Sub-I Vacuum.

Additionally related to Sub-I socket designs, evidence from another crossover RCT by Kahle et al.(137) (n=15) comparing Sub-I, Dynamic Socket (DS) and ischial ramus containment (IRC) devices, found no difference among groups for most measures of walking ability/gait parameters including sit to stand test, four-square step test, single limb balance, AMP, velocity, cadence, stride width, stance time, and 2 Minute Walk Test (2MWT). A finding of note was sixty days after the completion of the study, approximately half of the participants preferred to use a socket with a design that was different from their baseline socket on which they were successful in ambulating. These studies represent very low strength of evidence and are insufficient evidence to prescribe any specific transfemoral socket design or to recommend for or against ischial containment or sub-ischial socket designs in community ambulators.

Community ambulators in these studies is defined as either a self-reported ability to ambulate a minimum of 20 minutes in the community or a clinician's assessment including use of the Amputee Mobility Predictor with Prosthesis functional outcome measure. The current standard of care is to maintain a socket design on patients that are community ambulators. These studies support clinicians trialing of a variety of prosthetic socket designs. Changing socket design is unlikely to decrease functional outcomes in community ambulators, while patient preference for a specific socket design may change upon trial of different socket designs.

The Work Group systematically reviewed the evidence related to these two recommendations, which were limited to two small sample RCTs. Therefore, the recommendations were both categorized as *Reviewed, New-added*. The body of evidence had some limitations due to only including two RCTs with small sample sizes, and the confidence in this evidence was very low.(135,137) The benefits slightly outweigh harms due to no differences in mobility and safety in two small samples of ambulatory patients using sub-I and other transfemoral level sockets, slightly outweighing risks such as skin complications, compliance, falls and other SAEs. Patient values and preferences were unremarkable between socket types. Thus, the Work Group decided upon two *Neither for nor against* recommendations.

Recommendation

17. For prosthetic ambulators, we suggest prescribing microprocessor knee units over non-microprocessor knee units for reducing falls, optimizing functional mobility, and improving patient satisfaction.
    (Weak for | Reviewed, New-replaced)

Discussion

Falls, stumbles, functional mobility and QOL are compromised in ambulatory patients with transfemoral amputation who use prostheses.(138) For example, transfemoral prosthesis users reportedly ambulate with a walking velocity between 0.97 to 1.04 m/s whereas those with transtibial amputation tend to walk at a velocity as high as 1.22 m/s. In contrast, healthy able bodied individuals walk at 1.31 to 1.47m/s (usual and medium speeds respectively).(139,140) As another example, transfemoral amputees using prostheses have been observed to perform 18-24% lower on physical functional performance tasks than able-bodied controls.(141)

The basis for this recommendation suggesting prescription of microprocessor prosthetic knee (MPK) units over non-microprocessor prosthetic knee (NMPK) units is aimed at reducing falls, optimizing functional mobility, and improving patient satisfaction in ambulators who use transfemoral prostheses. Specifically, evidence favors use of the C-Leg or C-Leg compact MPK over an NMPK on the Assessment of Daily Activity Performance in Transfemoral amputees (ADAPT) assessment tool for patients classified as having intermediate or high functional mobility at baseline. Evidence comparing MPKs to NMPKs favors MPKs for motor and physical function in the stair assessment index, hill assessment index, locomotor capability index, and motor tests (e.g. 6 minute walk test, less sitting time) over a 1 to 3-month follow-up period.(142-145) Additionally MPKs are favored over NMPKs for locomotor ability in longer term, 6 month, follow-up.(146,147)

When determining between specific MPKs, evidence is still unclear. For instance, evidence supports improved gait parameters and functional outcomes, such as a higher Amputee Mobility Predictor (AMP) score or increased step activity, when using the Genium MPK compared to the C-Leg MPK. Conversely, in some instances, use of the C-Leg MPK improved stepping rate compared with the Genium MPK. One large study including 602 MPKs in 448 patients, found no difference in Prosthetic Limb Users Survey of Mobility (PLUS-M) scores between the C-Leg, Rheo, Orion, and Plie MPKs.(138,148-152)

The evidence in this discussion is suggestive of the recommendation being inclusive of most if not all patients that ambulate, and not limiting the recommendation to just those that are classified as community ambulators.

The Work Group systematically reviewed evidence related to this recommendation.(138,153,154) Therefore, it is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence was limited by lack of both rater and participant blinding. Raters includes both data collectors in RCTs and study assessors of SRs. Lack of allocation concealment and intention to treat were other factors limiting study quality and confidence. The benefits of using MPK knee systems generally outweigh the harms due to the improvement in fall reduction, functional mobility, and patient satisfaction in transfemoral

amputees who use prostheses. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

18. For prosthetic ambulators, there is insufficient evidence to prescribe any specific energy storing and return (ESAR) or microprocessor foot and ankle component over another. **(Neither for nor against | Reviewed, New-added)**

19. For prosthetic ambulators, we suggest energy storing and return (ESAR) or microprocessor-controlled foot and ankle components over solid ankle cushioned heel (SACH) feet to improve ambulation and patient satisfaction. **(Weak for | Reviewed, New-added)**

Discussion

The inexpensive SACH foot is a basic type of prosthetic foot with a rigid forefoot, a solid non-articulating ankle block, and a compressible heel wedge. The lower cost of the SACH foot is not typically utilized in the VA nor DOD healthcare systems as clinicians have regularly found improved patient satisfaction and better ambulation outcomes with the alternatives. There are over a hundred energy storing and returning prosthetic feet that are commercially available. Most prevalent are feet with fixed or rigid ankles. Microprocessor-controlled foot and ankle components have an energy storing and returning plantar component and ankle component with either an active dorsiflexion or active dorsiflexion and plantarflexion (push-off). Evidence cited in these recommendations captures these types of feet. Additional energy storing and returning prosthetic feet exist with articulating ankles of varying non-microprocessor controls though no evidence rose to the level of quality to be included in these recommendations.

Evidence from three RCTs and one SR suggests modern energy storing and returning prosthetic feet, with a fixed ankle or microprocessor-controlled foot and ankle component, were preferred by patients and objectively improve prosthetic user ambulation. Additionally, energy storing and returning prosthetic feet and microprocessor-controlled foot and ankles components outperform SACH feet when ambulating, and to a greater degree when ambulating and faster than self-selected speeds.(155)

Runciman et al.(155) found that energy storing and returning prosthetic feet outperformed SACH feet on all biomechanical measures considered including reaching significance for step length ratio (prosthetic side/sound side) which is a measure of gait symmetry. Muller et al.(156) found similar benefits in symmetry in a SR of 28 studies which compared energy storing and returning prosthetic feet and a microprocessor-controlled foot and ankle with powered push-off, with both foot categories performing significantly better than SACH. Morgan et al.(157) found that a novel energy storing and returning prosthetic foot performed comparatively to other energy storing and returning prosthetic feet for walking performance including walking speed, step width, step time, prosthesis-side step length. These findings were supported with functional outcome measures including the six-minute walk test and step activity monitoring. Morgan et al.(157) did report subjective outcome measure differences and situational preferences (e.g., running, ascending inclines and stairs, carrying a heavy load) between same category energy storing and returning

prosthetic feet, favoring a novel energy storing and returning prosthetic foot. This finding supports clinicians trialing of a variety of energy storing and returning prosthetic feet as part of routine clinical care to optimize patient-centered outcomes. Inclusion of microprocessor-controlled foot and ankle components in routine clinical care is supported by findings of Colas-Ribas et al. (2022) (158), who subjectively reported higher QOL for energy storing and returning feet with microprocessor-controlled foot and ankle components compared to energy storing and returning feet. Despite this finding user satisfaction was similar between energy storing and returning prosthetic feet with and without a microprocessor-controlled ankles with users favoring the lighter weight on an energy storing and returning prosthetic foot and the overall comfort provided by a microprocessor-controlled ankle.

Runciman et al.(155) also suggests that progressive orthopedic conditions such as osteoarthritis may be mitigated through use of energy storing and returning feet, although longitudinal evidence is not presently available to support this claim. Muller et al.(156) definitively found biomechanical measurement of push off power may reach levels equal to anatomical limbs for prosthetic ambulators using microprocessor-controlled foot and ankle components specifically with powered push-off feature. Similarly, this SR did not identify current research to correlate this finding with any positive impact on long-term health conditions.

Static balance may improve, and, at a minimum, there is no increased risks of falls or other adverse events when using a microprocessor-controlled foot and ankle components over energy storing and returning feet. No detectible changes in metabolic cost were reported in evidence referenced between energy storing and returning feet and microprocessor-controlled foot and ankle components.

There is some variation in patient preferences regarding types of prosthetic feet, most notable considerations being weight, variation, cosmetic preferences, and footwear choice. Cost of feet does also vary, although this is not a factor when prescribing prosthetic feet in the VA or DOD healthcare systems. Subgroup considerations include prosthetic ambulators who walk household or very limited community distances, as this population is rarely included in the evidence limiting generalization to all prosthetic ambulators. From an equity standpoint, clinical practice in VA and DOD healthcare systems universally provides energy storing and returning feet or microprocessor-controlled foot and ankle components over SACH feet. Prosthetists and other rehabilitation providers must receive some training to effectively provide more technologically complex microprocessor-controlled foot and ankle components. Therefore, training should be provided to remove any barrier to implementation.

The Work Group systematically reviewed evidence related to these two recommendations (155-158) and both recommendations were categorized as *Reviewed, New-added.* The Work Group's confidence in the quality of the evidence was very low for three studies and low for one study, thus very low overall. The body of evidence had some limitations including small sample size, manufacturer funded research and homogenous functional levels of subjects.(155-158) The evidence supports prescription of energy storing and returning prosthetic feet or microprocessor-controlled foot and ankle components over solid ankle cushion heel (SACH) feet to improve walking ability and qualitative outcomes in prosthetic ambulators, without differentiating any one

specific option over another with very low confidence in the quality of evidence. The benefits of prosthetic ambulators receiving energy storing and returning prosthetic feet or microprocessor-controlled foot and ankle components include improved walking characteristics and improved patient satisfaction which outweighed the potential and rarely identified harms. Patient values and preferences varied somewhat because some patients prefer and find satisfaction in different prosthetic foot technology. Thus, the Work Group decided upon *Weak for* (Recommendation 18) and *Neither for nor against* (Recommendation 19) recommendations.

Recommendation

20. We suggest using patient-reported and performance-based measures with acceptable psychometric properties to assess function.
    (Weak for | Not reviewed, Amended)

Discussion

Periodic patient assessments at designated intervals serve as an increasingly important element of evidence-based practice.(159) Because rehabilitative care requires assessment of multiple domains including walking ability, balance, adjustment to prosthetic device use, QOL, patient preference or perception, and others, it is suggested that a combination of psychometrically validated patient-reported and performance-based measures be used to assess outcomes throughout the rehabilitation process.(159,160) Collection of both reported and performed measures offer direct feedback to providers and patients regarding the efficacy of the interventions and progress towards established functional goals.

Amongst the outcome measures that exist, there is variability within the research on which are best.(159,161) As clinicians select from the numerous measures available, priority should be given to identifying psychometrically valid measures that evaluate the constructs of interest while minimizing burden to the patient, provider, and clinic resources.(159,160) Measures that are seen as beneficial to the patient and provider, with minimal burden, are more likely to be performed and put into clinical practice.

While the evidence doesn't support one measure over another, it is important that once selected, future administration is consistent to allow for accurate longitudinal comparison. Establishing a specific interval or timeline for collecting measures can help remind providers to initiate data collection, while communicating the importance and value of the measures can further secure buy-in and compliance from both patients and providers.(161) In addition to quantifying changes for clinical purposes, outcome measures are important for demonstrating the value of the care patients receive. Psychometric measures are increasingly used to justify the need for specific interventions and to quantify changes in the patient's condition to support requests for new treatments or components.(162) Aside from the time burden and risk of survey fatigue, there is minimal drawback to administering outcome measures. When conducting performance-based measures, there is a risk for falls, cardiovascular events, and increased discomfort however these risks are no greater than those typically encountered during ambulatory or rehabilitative tasks.(163)

The Work Group systematically reviewed evidence from the prior CPG related to this recommendation, however new evidence was not found during the scoping review.(159-161) As no new evidence was reviewed, it is categorized as *Not reviewed, Amended*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including few prospective randomized trials with small samples of prosthesis users, as is common in amputation-related research.(83,164,165) The benefits of using a combination of reported and performed psychometrically valid measures (contributing to clinical practice in quantifying changes over the course of treatment, helping justify when new interventions are needed, and assigning value to the care provided) outweighs the potential risk of falls, cardiovascular events, or discomfort. Patient values and preferences had some variation in their perception of outcome measures; however, this is largely remedied though education on how the insights gained from the measure will benefit their care as well as clinician use of the information to inform the treatment plan. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

21. There is insufficient evidence to recommend for or against neurostimulation (e.g., peripheral nerve stimulation, or spinal cord stimulation) or neuroablation (e.g., cryoneurolysis, radio frequency ablation) interventions for the management of phantom limb pain or residual limb pain.
    (Neither for nor against | Reviewed, New-added)

Discussion

The CPG's systematic evidence review identified several potential studies of the effectiveness of neurostimulation or neuroablation interventions on PLP or residual limb pain.

An RCT by Ilfeld et al., (2023) compared the effectiveness of peripheral nerve cryoneurolysis vs. placebo on PLP, residual limb pain, and patient satisfaction/preference in patients with ankle/foot, transtibial, or transfemoral amputation. There were not statistically or clinically significant between-group differences in average PLP or change in PLP, residual limb pain, or Patient Global Impression of Change (PGIC) at 4 months. In post-hoc analyses stratified by amputation level, the average PLP as measured by Brief Pain Inventory (BPI) intensity at 4 months was lower in the treatment group compared to the placebo for patients with transtibial amputation (BPI MD -1.14, 95% CI -2.09 to -0.18) and higher in the treatment group compared to the placebo for patients with foot- or ankle-level amputation (MD 3.00, 95% CI -0.25 to 6.25) or transfemoral amputation (MD 1.28, 95% CI -0.13 to 2.68). The authors speculated that differences in relative location of cryoneurolysis (proximal nerve for transtibial, vs. usually distal nerve for transfemoral) for different amputation levels may have impacted the effectiveness of the intervention. The authors also speculated that for persons with transfemoral amputation, cryoneurolysis of additional nerve might improve the effectiveness of the intervention. On potential adverse event was reported: an occurrence of quadriceps weakness after a more proximal cryoablation of the femoral nerve, which lasted about 12-15 months and may have contributed to a fall.(166)

An RCT by Gilmore et al., (2019, 2020)(167,168) compared the effectiveness of percutaneous peripheral nerve stimulation (PNS) vs. placebo on pain, walking ability, functional status, and patient satisfaction and preference in patient with healed traumatic LLA and moderate-to-severe PLP and/or residual limb pain. The PNS group had a higher proportion of patients with a reduction in BPI and BPI-interference (BPI-I) score by greater than or equal to 50% at 4 and 8 weeks. The average PGIC was higher in the PNS group at the end of the treatment. Strength of evidence was very low (small sample size, with n=14 in each study arm; no measure of dispersion).(167,168)

The CPG's systematic evidence review identified one potential study of the effectiveness of surface neurostimulation. An RCT by Talbot et al. (2017)(169) compared the effects of neuromuscular electrostimulation (NMES) + traditional military amputee rehabilitation program (TMARP) vs. TMARP on lower extremity muscle strength, pain, and mobility in military patients with unilateral transtibial amputation. The NMES intervention was a home-based 12-week course of NMES therapy applied to bilateral quadriceps femoris muscles. There were not clinically or statistically significant between-group differences in pain, functional outcomes, or walking ability. The Work Group ultimately felt that the study design was not optimal for the question of effectiveness in management of residual limb pain or PLP as the study (a) did not use the presence of PLP or residual limb pain as study inclusion criteria, and (b) did not specify the type or location of reported pain. Other limitations included small sample size and study limited to active-duty military amputees.(169)

The patient focus group identified pain management as a core component of their individualized treatment plan. Participants valued a customized approach to pain management that considered different types of pain (e.g., location, nature, intensity) and offered a "toolbox" of different approaches to pain management (e.g., prosthesis adjustments, medications, or alternative therapies). Many patients value pain interventions that are not pharmaceutical. In balancing treatment decisions, pain is a significant risk factor for suicide and can impact participation and return to activities. Potential harms of percutaneous peripheral neurostimulation include bleeding, bruising, lead migration, nerve damage, or infection.(167) Potential harms of peripheral nerve cryoablation include dysesthesia, unintended weakness, and myonecrosis (rarely reported), as well as potential harms of any percutaneous intervention such as bleeding, bruising, or infection.(170) Potential harms could vary by patient characteristics; for example, patients on blood thinners would have higher risk of bleeding. Access to specialized procedures could vary by availability of specialists with the relevant training and experience.

The Work Group systematically reviewed evidence related to this recommendation.(166-169) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including small sample size, imprecision. The potential benefits of neurostimulation or neuroablation (e.g., decreased intensity or interference of PLP or residual limb pain) slightly outweigh the potential harm. Patients had similar values in emphasizing the importance of pain management overall and a toolkit of different approaches to pain management. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

22. We suggest perineural catheter delivered anesthetic for the treatment of chronic severe phantom limb pain with functional impairment.
    (Weak for | Reviewed, New-added)

Discussion

Evidence from a single, moderately sized (n=144) RCT suggests that a continuous infusion of anesthetic via a PNC reduces pain in patients with established (e.g., chronic) PLP. Ilfeld et al.(171) evaluated the effect of a 6-day ambulatory continuous infusion via PNC with ropivacaine versus PNC with saline placebo in individuals with chronic PLP who exhibit a significant amount of pain-related functional impairment. The primary endpoint evaluated was the difference of change in PLP intensity from baseline after ropivacaine infusion versus after placebo infusion at 4 weeks post-intervention. Secondary endpoints included PGIC and impact of intervention on pain interference as measured by the BPI-I. Subjects had a reduction in PLP pain intensity scores measured by a numeric rating scale from 5.4 to 3.0 for ropivacaine versus 5.4 to 4.5 for placebo, a difference in score reduction of 1.5 which would generally be accepted as a clinically important difference. Both secondary endpoints (PGIC and pain interference scores) also improved in the treatment arm versus placebo arm, with BPI-I scores improving greater than 30%, a change which is generally accepted to meet a minimum clinically important difference. Adverse events were rare, with approximately 2% of the cohort (8 of 382 catheters placed) experiencing a catheter related infection, a smaller percentage than has been historically observed with week-long indwelling catheters. All infections resolved upon catheter removal (3 patients required oral antibiotics) and healed without further incident.

There is some variation in patient preferences regarding this treatment. Travel to a medical center to receive the infusion may limit some patients' desire to pursue the intervention. Additionally, the 6-day treatment may be burdensome to patient function and mobility given inability to use a prosthetic leg during this time.

The Work Group systematically reviewed the evidence related to this recommendation, which was limited to a single RCT.(171) Therefore, it is categorized as *Reviewed, New Added*. The Work Group's confidence in the quality of evidence was low (e.g. single RCT), but benefits were assessed as slightly outweighing harms due to the intervention demonstrating a reduction in pain intensity and pain-related interference of function with minimal harms. Patient values varied somewhat as some patients may or may not prefer to travel to a medical center to receive treatment and subsequently not use their prosthesis for several days. Thus, the Work Group decided upon a *Weak for* recommendation.

Recommendation

23. There is insufficient evidence to recommend for or against any systemic pharmacologic intervention for the management of phantom limb pain.
    (Neither for nor against | Reviewed, New-added)

Discussion

The evidence reviewed was insufficient to determine a beneficial impact of systemically acting pharmacotherapies on reducing pain or improving functional outcomes in individuals with LLA with established PLP.(172) The evidence base was limited to a single SR that included 14 small trials with the following results:

- Suggestion for no benefit (memantine, calcitonin, amitriptyline, and intravenous lidocaine)(173,174)
- Conflicting results regarding benefit (gabapentin) (173,174)
- Suggestion for benefit (ketamine, morphine, dextromethorphan)

In the trials suggesting benefit from ketamine, morphine, and dextromethorphan, the Work Group had low confidence in the quality of the evidence. Specifically, the single study evaluating dextromethorphan(175) was very small (n=10) and half of the cohort did not achieve analgesic improvement until the open-label portion of the trial. Two trials, Eichenberger(176) and Nikolajsen(177) that showed a benefit from Ketamine were limited in their duration of effect. Nikolajsen reported pain reduction was limited to the duration of the ketamine infusion(177); while, despite being statistically significant, the pain reduction seen in Eichenberger(176), had waned to less than what would be considered clinically significant by the 48 hour timepoint (VAS less than a 1 point difference for average reported pain ketamine vs. baseline). As such, the Work Group had low confidence that the findings of an immediate analgesic effect of ketamine would be generalizable to more sustained improvement in pain or pain-related functional impairments.

Within the SR, morphine was the other agent with evidence of analgesic benefit assessed in two trials, Huse et al.(178) and Wu et al.(179) both of which reported a clinically meaningful reduction in pain scores. However, this was taken in the context of a) a short timeframe (only 4 weeks) for the primary endpoint assessment of pain reduction; b) unclear benefit (Huse) or impact on function not assessed(179); and c) unclear maintenance of blinding in at least one of the trials.(178) Additionally, the 2022 VA/DOD Opioid Guideline(180) have provided a “strong against” recommendation for initiation of long-term opioid therapy for chronic pain syndromes, largely based on two decades of experience subsequent to these two trials, highlighting the risks of chronic opioid therapy. For all other systemic drugs studied there was either no benefit on pain (memantine, calcitonin, amitriptyline, intravenous lidocaine(172) or, for gabapentin, conflicting evidence regarding pain reduction of uncertain clinical significance, in context of no associated functional improvement.(173,174)

There is large variation in patient preferences regarding systemic pharmacologic intervention for the management of PLP. Although patients have similar preferences regarding a desire for pain control, which was emphasized by the focus group as a core component of individual treatment plans, they oftentimes have variable opinions about whether they prefer non-pharmacologic vs pharmacologic treatments. Much of this is driven by how severe, how frequent, and how functionally impairing the pain is and the side effects of each pharmacologic intervention.

The Work Group systematically reviewed the evidence related to this recommendation, which was limited to a single SR without findings of clinically significant improvements in pain or pain-impaired function.(172) Therefore, the recommendation is categorized as a *Reviewed, New-added*. The body of evidence was limited to a single SR and the Work Group's confidence in the quality of evidence was rated as very low for both the SR and the individual trials contained within the SR, primarily due to small sample size. The benefits and harms were assessed as balanced primarily because no serious harms were reported. Patient preferences varied largely, because some patients prefer not to take medications even if they have evidence of benefit and some patients would prefer to try any pain reducing medication intervention even if evidence suggests it does not work. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

24. For prosthesis users with hyperhidrosis, there is insufficient evidence to recommend for or against Botulinum toxin treatment to reduce sweat production, improve prosthetic function, reduce pain, and improve quality of life.
    (Neither for nor against | Reviewed, New-added)

Discussion

Skin problems in amputees occur with greater frequency than in the non-amputee population. Whereas the non-amputee population experiences dermatologic issues in 7% of all outpatient ambulatory visits, amputees experience dermatoses in 11% to 80% of cases.(181,182) With prosthesis use, sweating and hyperhidrosis are key components leading to the development of inclusion cysts, skin irritation, ulcer, callus, verrucous hyperplasia and other skin problems.

Overall, the evidence on dermatological interventions for skin and soft tissue complications is very limited. Our searches identified 1 SR by Rocha Melo (2023)(183) that studied the comparative effectiveness of botulinum toxins A and B on hyperhidrosis. The SR was comprised of 4 case series, 3 case reports, and 1 RCT which had a small sample size (n=9). The RCT compared botulinum toxin A to control, and 4 case series and 3 case reports observed botulinum toxins A and B's effect on hyperhidrosis. The RCT reported a statistically significant improvement in sweat reduction ($p<0.05$) and prosthesis use ($p<0.05$) following botulinum toxin treatment. Ultimately, the SR reported an improvement in skin condition status after treatment with Botulinum toxins A or B. Given the small sample of the RCT and that the other included studies were case series/studies, the overall recommendation is that the evidence is insufficient to recommend for or against the use of Botulinum toxin treatment to reduce sweat production, improve aesthetic function, reduce pain, and improve QOL. While this evidence is encouraging, more evidence is needed to increase confidence in the evidence supporting the use of Botulinum toxin treatment in these cases. Moreover, more research in dermatologic management is needed to support other options for managing skin maladies in the residual limb of amputees. For instance, ablative fractional laser treatment for the management of scars is a therapy established in non-amputee scars but is still under investigation as it relates to residual limb scars.(184)

The Work Group systematically reviewed the evidence related to this recommendation, which was limited to a single SR. Therefore, the recommendation is categorized as *Reviewed, New-*

added. The body of evidence was limited to a single SR and the Work Group's confidence in the quality of evidence was rated as very low for both the SR and the individual RCT within the SR, primarily due to the small sample size.(183) The benefits and harms were assessed as the benefits slightly outweighing harms due to the therapeutic benefits that outweighed the procedural risks. Patient preferences varied some, because some patients may not tolerate the injection and treatment well and there may be a need for repeat treatments. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

25. There was insufficient evidence to recommend for or against strategies to prevent re-amputation of the ipsilateral limb or amputation of the contralateral limb.
(Neither for nor against | Reviewed, New-added)

Discussion

LLA is a surgical procedure that carries significant morbidity, mortality, and economic burden. Dysvascular LLA is associated with re-amputation more proximally of the ipsilateral limb as well as amputation of the contralateral limb. Unfortunately, there is a lack of consensus on the specific risk factors associated with and the preventive measures against such complications. No evidence was found that met GRADE inclusion criteria for this key question.

One SR(185) that focused on wound healing and rates of re-amputation and two retrospective cohort studies(186,187) that focused on incidence and risk factors for re-amputation were excluded from formal evaluation due to lack of an intervention and comparators of interest. Their results, however, were important and relevant for risk factor determination for wound healing and re-amputation in this patient population. Day et al.(185) reported smoking, nutrition, white blood count, and renal failure as the most significant predictive factors associated with poor healing outcomes. Zambetti et al.(186) and Fard et al.(187) suggest that tobacco use, peripheral artery disease, and bleeding disorders were the most significant predictors of re-amputation.

It has been shown that patients with amputation are at greatest risk for re-amputation within six months after the initial amputation.(188) Zambetti et al.(186) specifically examined factors and outcomes associated with early re-amputation. Predictors of early re-amputation included elderly age (> 60 years old), tobacco use, hypertension, diabetes, end stage renal disease (ESRD), infections/sepsis, and bleeding disorders.(186)

There is little variation in patient preferences regarding prevention of re-amputation of the ipsilateral limb or amputation of the contralateral limb after initial amputation. Patients would prefer not to undergo additional surgery or further amputation. Additionally, peer focus groups continue to express a desire for improved patient education, communication, family/friend/caregiver involvement, and leveraging of peer networks to better support and motivate patients with LLA, all of which could attribute to the avoidance of further surgeries and amputations.

The Work Group systematically reviewed evidence related to this recommendation.(185-187) Therefore, it is categorized as *Reviewed, New-added*.(185-187) Therefore, it is categorized as

Reviewed, New-added. The body of evidence was sparse and limited for this key question. The benefits of identifying specific risk factors and preventative measures to avoid future surgery were balanced with the potential harm of surgical complications of potentially invasive intervention. Patient values and preferences were similar because patients would prefer to not undergo further surgery and further amputations. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

Recommendation

26. There is insufficient evidence to recommend for or against any specific intervention to improve intimacy and sexual health.
    (Neither for nor against | Reviewed, New-added)

Discussion

The evidence search completed for this update of the CPG identified several papers reporting data on sexual activity, anxiety, pain, sexual function and satisfaction, and body image in patients with LLA. No specific interventions to improve intimacy and sexual health were described, so no studies were found to meet inclusion criteria.

The studies discussed below are outside the scope of or were excluded from the initial evidence review and do not impact the strength of the recommendation; however, they remain relevant to the topic.

Amputation is life altering and known to have an impact on interpersonal relationships, body image, and self-identity. Sexual activity and intimacy are a significant part of life and related to the overall QOL for many individuals. Unfortunately, health professionals rarely and inadequately discuss topics of sexual health and intimacy with individuals with disabilities, which could be related to lack of education, comfort with the topic, or a lack of clarity regarding which care professional should be addressing sexuality with patients. Patients report a desire for healthcare providers to discuss the impact of LLA on sexual life, educate on strategies to manage dysfunction, and to help accept their new appearance.(189)

In a prospective cohort study of 113 individuals with dysvascular LLA, a majority (54% to 67%) reported that sexual activity was very important to overall life satisfaction.(190) Studies focusing on sexual health report a wide range of sexual dysfunction amongst individuals with LLA, ranging from 13% to 75% of individuals.(191) A multitude of factors can impact sexual function including emotional state, pain sensations, body positioning, movement abilities, and amputation level.(192)

In a 2021 SR focusing on sexuality and sexual health in adults with limb loss (upper and lower), the most common topics addressed were body image, sexual desire, and sexual activity.(193) The SR stated that self-perceived reports of poor body image were associated with higher levels of depression, anxiety, and social restriction/isolation. Sexual dysfunction was associated with performance and/or generalized anxiety, depression, and body self-consciousness during sexual activity.(193,194) In a few studies of lower evidence within the SR by Brooks et al.(193),

greater prosthesis use/satisfaction and being physically active improved body image outcomes. In a prospective cohort study of individuals with dysvascular LLA, greater mobility was associated with increased sexual activity at 4- and 12-months post-amputation.(190) Individuals with transtibial amputations reported significantly higher satisfaction with intercourse as compared to transfemoral.(192) In a cross-sectional study comparing individuals with traumatic LLA and healthy men, amputation related pain was found to have a negative correlation with erectile function and sexual desire.(192)

Limited evidence was found on interventions targeting improving sexual health and intimacy. A study by Srivastava and Chaudhury (2013)(195), reported greater improvement in body image after a two-month intervention incorporating psychological interventions (stages of reassurance, ventilation, acceptance of self, therapeutic milieu, and reintegration) as compared to a control group, although details regarding the specifics of the stages were not reported.

The sexuality within the LLA population remains an understudied and undereducated topic. The injury impacts well beyond the visible physical damage. Although no evidence was found within the evidence report, the CPG working group feels this topic is an essential area to address among the LLA population, including patients and their partners, within the rehabilitation setting and routine care settings.

The Work Group systematically reviewed evidence related to this recommendation and unfortunately no evidence met the criteria. Therefore, it is categorized as *Reviewed, New-added* Although the evidence related to the specific topic was limited, research shows that a majority of the LLA population reported assessment and interventions addressing sexual health and intimacy beneficial within the rehabilitation setting. This topic has a favorable risk benefit ratio as impaired sexual dysfunction is associated with a multitude of behavioral health concerns and broaching this topic with individuals would have few side effects. It is important to consider the various subgroups within the population including the varying needs based on sex and level of amputation. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

X. Research Priorities

There are several areas which require more focused research to provide stronger evidence for further recommendation development across the spectrum of carer recommendations and aid in refining interventions. In summary, the Work Group recommends research on behavioral health, pharmacology and pain management, prosthetic and rehabilitation interventions, as well as the diversification of research populations.

A. Behavioral Health

Future research is needed to further understand which specific behavioral treatments improve psychosocial outcomes. There is also a considerable need for future research to examine the association between factors such as age and amputation etiology with cognitive outcomes. Additionally, the utility of cognitive assessment may differ considerably by demographic characteristics, and future research would benefit from the confirmation of specific domains of

cognition useful in predicting amputation outcomes and prosthetic candidacy, as well as the specific assessment tools best suited to evaluate them.

B. Pain Management and Pharmacology

In patients with LLA, future research should include larger, longitudinal, well-designed trials that address the functional impact of pharmacologic interventions and interference from PLP, as well as looking at outcomes beyond pain intensity or interference. PNC also requires further research, specifically evaluating longer term effects, their ability to reduce reliance on pain medications and confirm a sustained effect on function, as well as the impact that post-operative PNC delivered anesthetic can have on opioid requirements at discharge and for chronic use. Additionally, further research is needed in peripheral nerve management, specifically in the vascular amputee subgroup, as well as neurostimulation and neuroablation for phantom and residual limb pain. Future research into peripheral nerve interventions might consider studies designed to evaluate potential effect heterogeneity by amputation level and studies focused on technological solutions for phantom pain such as central stimulation.

C. Research Populations

Household and limited community ambulators are currently underrepresented in research, and the inclusion of these groups would allow for further investigation into prosthetic components tailored towards them. Other populations of interest include those with concurrent or coexisting conditions.

D. Patient Considerations and Education

In patients with a prior amputation, risk factors and measures to prevent further amputation must be explored to mitigate additional amputation. Current research also lacks comprehensive sub-analyses that distinguishes between male and female participants, which needs to be addressed to utilize patient-identified sex in rehabilitation plans. Patient education interventions require future systematic comparative effectiveness studies to improve outcomes, and further research needs to be done specifically for women including various levels of amputation to improve sexual health and intimacy.

E. Prosthetic Interventions

Assessing the comparative effectiveness of all categories of energy storing and returning feet, including those with articulated ankle components along with the categories studied in current evidence base may provide further evidence by category to drive clinical prescription. Longitudinal research is also required to determine whether general or novel energy storing and returning prosthetic feet, microprocessor-controlled foot and ankle components, or energy storing and returning feet with articulating ankles can positively impact long-term health outcomes and mitigate comorbidities.

Other Topics for Consideration

Other topics for consideration include

- Comparative effectiveness studies on osseointegration versus conventional prosthetic socket use by level of amputation;

- Comparison of different suspension types for all LLA levels;
- Comparison of different socket interfaces for transtibial, joint disarticulation and partial foot amputation levels;
- Consider K level for comparison studies for patient function optimization, safety, and QOL;
- Consider socket design/fabrication utilizing 3D printing vs traditional hand mods as this impacts socket fit, prosthesis acceptance, and resource availability for O&P provider and rehab team; and
- Consider device delivery timeframe/sock ply fit.

Key considerations regarding component studies would be to consider continuing to maximize scientific rigor while the research seeks to determine which components optimize patient function, safety, QOL preference and best mitigate secondary comorbid sequelae.

F. Rehabilitation Interventions

Future rehabilitation research priorities should focus on dosing (timing, intensity and duration) to optimize patient outcomes while husbanding scare resources. Further research is needed to examine the effectiveness of different post-operative amputation rehabilitation options (IRF, SNF, etc.) across differing patient demographics. Additionally, studies comparing the effectiveness of implementation framework-based continuum of care programs versus traditional care on patient outcomes would add to the understanding on how to best support patients and families.

While gold-standard patient-reported and performance-based measures have been identified, there is no research that indicates which outcome measures are best utilized together, nor is there evidence in the literature to identify when to begin outcome measures, how frequently to use outcome measures, and what milestones are to be used to know when to stop a specific outcome or group of outcome measures.

For interventions, investigations into why mirror therapy (MT) is effective and its impact on neural plasticity would be informative. Larger sample sizes are needed to understand optimal utilization of botulinum toxin to address hyperhidrosis plus further investigation into other dermatologic interventions (PRP injection, laser hair removal, fractional laser, microneedling, etc.).

Peer support and peer visitor programs require additional qualitative and quantitative research to explore optimal dosing, training, and management of these programs while also exploring the direct impact on patients, families and caregivers.

G. Surgical Interventions

Additional research is needed to explore how different surgical techniques impact functional outcomes based on the underlying indication for amputation, and to further outline the potential strengths and weaknesses of available procedures.

Appendix A: Guideline Development Methodology

A. Developing Key Questions to Guide the Systematic Evidence Review

To guide this CPG's systematic evidence review, the Work Group drafted 12 KQs on clinical topics of the highest priority for the VA and DOD populations. The KQs followed the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework, as established by the Agency for Healthcare Research and Quality (AHRQ) (see **Table A-1**).

Table A-1. PICOTS (196)

P	Patients, Population, or Problem	Patients of interest. It includes the condition(s), populations or sub-populations, disease severity or stage, co-occurring conditions, and other patient characteristics or demographics.
I	Intervention or Exposure	Treatment (e.g., drug, surgery, lifestyle changes), approach (e.g., doses, frequency, methods of administering treatments), or diagnostic/screening test used with the patient or population.
C	Comparison	Treatment(s) (e.g., placebo, different drugs) or approach(es) (e.g., different dose, different frequency, standard of care) that are being compared with the intervention or exposure of interest described above.
O	Outcome	Results of interest (e.g., mortality, morbidity, quality of life, complications). Outcomes can include short, intermediate, and long-term outcomes.
(T)	Timing, if applicable	Duration or follow-up of interest for the particular patient intervention and outcome to occur (or not occur).
(S)	Setting, if applicable	Setting or context of interest. Setting can be a location (e.g., primary, specialty, inpatient care) or type of practice.

Abbreviation: PICOTS: population, intervention, comparison, outcome, timing, and setting

The Champions, Work Group, and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the systematic evidence review. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. **Table A-4** contains the final set of KQs used to guide the systematic evidence review for this CPG.

a. Population(s)

The KQs are specific to adults (ages 18 years or older) with a lower extremity amputation (unilateral or bilateral and at any level), treated in any clinical setting. The cause of the amputation may be traumatic (combat or non-combat-related) or non-traumatic (dysvascular, neuropathy, neoplasia, or infection).

b. Interventions and Comparators

KQ	Intervention(s)	Comparator(s)
1	▪ Acute inpatient ▪ Acute inpatient rehabilitation	Any of the listed interventions versus another listed intervention

KQ	Intervention(s)	Comparator(s)
	▪ Sub-acute rehabilitation ▪ Skilled Nursing Facility ▪ Nursing home ▪ Outpatient and/or outpatient rehabilitation and/or outpatient therapy ▪ Intensive outpatient program	
2	Socket/ interface ▪ Hip Disarticulation Socket ▪ Transfemoral Socket ◆ Narrow mediolateral (Narrow ML) ◆ Quadrilateral ◆ Ischial Containment (IC) Socket ◆ Ischial Ramus Containment (IRC) Socket ◆ Subischial Socket design ▪ Through Knee Socket/ Knee Disarticulation Socket ▪ Below Knee Socket ▪ Hydrostatic Design (HSD) Socket ◆ Total Contact Socket ◆ Patella or Patellar (PTB) Tendon Bearing Socket ◆ Total Surface Bearing (TSB) Socket Suspension system ▪ Anatomic Fit ▪ Belt / Waist belt ▪ Corset / Thigh corset ▪ Lanyard / Distal locking lanyard ▪ Osseointegration ▪ Pin Suspension/ Pin lock suspension / distal locking suspension / Locking Mechanism ▪ Supracondylar ▪ Suspension Sleeve ▪ Thigh Cuff / Suprapatellar cuff ▪ Vacuum Assisted Suspension/ Elevated Vacuum ▪ Suction suspension / Passive suction suspension Seal-in suction suspension Hip	Different types of prosthetic components compared to other types of components **within the same class**

KQ	Intervention(s)	Comparator(s)
	▪ Hydraulic control ▪ Polycentric axis ▪ Single axis Knee ▪ Extension assist ▪ Friction control ▪ Hydracadence System ▪ Hydraulic control ▪ Hydromechanical/Mechanical ▪ Manual Locking Knee ▪ Microprocessor ▪ Microprocessor Power Assist ▪ Non-Microprocessor ▪ Pneumatic control ▪ Polycentric axis ▪ Single axis: Includes single axis hydraulic knee joint (e.g., Mauch SNS/ Mauch S-N-S) and single axis motorized knee joint (e.g., Intuy Knee) ▪ Swing And Stance Control ▪ Weight Activated Stance Breaking (WASB)/Weight Activated Stance Control Foot, ankle prosthetic components ▪ Activity Specific ▪ Bionic ankle (Biom Foot) ▪ Dynamic Response ▪ Energy Storing (ES) ▪ Energy Storing and Release (ESR or ESAR) ▪ Flex Foot ▪ Flexible Keel ▪ Hydraulic Foot ▪ Microprocessor Foot ▪ Multi-Axial Foot ▪ Power Foot ▪ Powered Dorsiflexion ▪ Powered Plantarflexion ▪ Running Foot ▪ Single Axis Foot	

KQ	Intervention(s)	Comparator(s)
	▪ Solid Ankle Cushioned Heel (SACH) ▪ Torsion ▪ Vertical Shock	
3	▪ Cryoablation ▪ Peripheral nerve stimulator (PNS) ▪ Pulsed radiofrequency ablation (pRF) ▪ Radiofrequency ablation (RFA) ▪ Spinal cord stimulator (SCS) ▪ TENS	▪ Standard of care with or without sham/placebo/attention control ▪ Wait list control
4	Standard of care **plus** specific behavioral health or psychosocial treatments: **Peer Interventions:** ▪ Peer Education ▪ Peer Mentorship ▪ Peer Support ▪ Peer Support Groups ▪ Peer Support Programs ▪ Peer Visitation ▪ Support Groups **Patient education:** ▪ Assertive Communication ▪ Interpersonal Effectiveness ▪ Psychoeducation ▪ Psychological Preparation ▪ Self-Management Training ▪ Social Skills Training ▪ Therapeutic Pain Neuroscience Education **Counseling:** ▪ Accelerated Resolution Therapy (ART) ▪ Acceptance and Commitment Therapy (ACT) ▪ Cognitive Behavioral Therapy (CBT) ▪ CBT for Chronic Pain (CBT-CP) ▪ CBT for Insomnia (CBT-I) ▪ CBT for Suicide Risk Reduction ▪ Cognitive Processing Therapy (CPT) ▪ Dialectical Behavioral Therapy (DBT) ▪ Emotion-Focused Therapy ▪ Eye Movement Desensitization and Reprocessing (EMDR) ▪ Family Counseling ▪ Grief Counseling	▪ Standard of care: Supportive counseling with or without sham/placebo/attention control ▪ Wait list control

KQ	Intervention(s)	Comparator(s)
	▪ Mindfulness-Based Stress Reduction ▪ Motivational Interviewing ▪ Pastoral Counseling ▪ Problem Solving Therapy (PST) ▪ Prolonged Exposure (PE) ▪ Psychoanalysis ▪ Rational Emotive Therapy ▪ Trauma-focused Psychotherapy	
5	▪ Bone bridging (Ertl technique) ▪ Chopart amputation ▪ Gritti-Stokes ▪ Knee disarticulation ▪ Length sparing procedures ▪ Lisfranc amputation ▪ Mazet technique ▪ Modified Bruckner ▪ Myodesis/myoplasty ▪ Skin grafting/flap coverage ▪ Syme's amputation ▪ Transmetatarsal amputation **Myoneural interfaces:** ▪ Agonist antagonist myoneural interface (AMI) ▪ Nerve caps ▪ Regenerative peripheral neural interfaces (RPNI) ▪ Targeted muscle reinnervation (TMR) ▪ Vascularized denervated muscle targets (VDMT) **Intraoperative cyroablation** **Osseointegration:** ▪ Implants (e.g., Compress, electronic osseoanchored prostheses for the rehabilitation of amputees (eOPRA), osseoanchored prostheses for the rehabilitation of amputees (OPRA) ▪ Percutaneous Osseintegrated prosthesis (POP) **Revision surgery:** ▪ Excision of heterotopic ossification (bone spurs) ▪ Fibula/Fibulectomy	▪ Standard of care with or without sham/placebo/attention control: ◆ Guillotine ◆ Fishmouth ◆ Long Posterior Flap/Bruckner/Burgess ◆ Traditional Amputation– transection of major lower extremity bone (i.e., tibia or femur) ◆ 2 stage amputation surgery ▪ Wait list control

KQ	Intervention(s)	Comparator(s)
	▪ Joint replacement ▪ Neuroma/Neurectomy	
6	**Dermatological:** ▪ Ablative fractional resurfacing lasers (AFR) ▪ Ablative laser ▪ Botulinum injections ▪ CO2 lasers ▪ Fractional lasers ▪ Histamine/allergy testing ▪ Iontophoresis ▪ Laser hair removal (LHR) ▪ Microneedling ▪ Microwave ablation/microwave thermolysis (e.g., Miradry) ▪ Pigment laser ▪ Pulsed dye laser (PDL) ▪ Scar resurfacing lasers ▪ Silicon patch/microcolloid ▪ Targeted alkali thermolysis (TAT, e.g., Brella patches) **Regenerative Medicine:** ▪ Platelet rich plasma (PRP) ▪ Stem cells ▪ Tissue engineering	▪ Standard of care with or without sham/placebo/attention control ▪ Wait list control
7	▪ Ankle/foot orthoses ▪ Diagnostic tests such as Computed Tomography Angiography (CTA) or Vascular Ultrasound/vascular screening tests ▪ Dietary interventions/weight loss ▪ Endovascular procedures ▪ Foot management interventions: ◆ Charcot restraint orthotic walker (CROW) ◆ Intrepid dynamic exoskeletal orthosis (IDEO) ◆ Total contact cast/CAM walkers/CROW boot/walker ▪ Foot risk scoring: (PODUS 2020, PAVE) ▪ Limb salvage ▪ Mobility training ▪ Patient education on foot inspection/care ▪ Physical/Occupational Therapy (PT/OT) ▪ Smoking cessation	▪ Standard of care: with or without sham/placebo/attention control ◆ Debridement/self-care ◆ Podiatric care/annual evaluation/professional foot evaluation/care ◆ Routine check-ins with podiatry ◆ Therapeutic footwear inserts ▪ Wait list control

KQ	Intervention(s)	Comparator(s)
8	▪ Couples therapy ▪ Pelvic floor therapy ▪ Psychotherapy (e.g., talk therapy or mindfulness- specific to intimacy) ▪ Sex & Intimacy occupational therapy ▪ Sex therapy ▪ Sexual health apps ▪ Trauma processing	▪ Standard of care with or without sham/placebo/attention control ▪ Wait list control
9	▪ Care Coordinators plus SOC ▪ Care Manager plus SOC ▪ Case Management plus SOC ▪ Integrated Mental Healthcare ▪ Integrated orthotic and prosthetic care ▪ Interdisciplinary team model of care ▪ Multidisciplinary team models of care	▪ Standard of care alone (single provider care) with or without sham/placebo/attention control ▪ Wait list control
10	▪ Activities of daily living training/Daily life activity ▪ Augmented reality: Specific to LLA rehab ▪ Balance training ▪ Compression therapy (e.g., NormaTec) ▪ Electrical stimulation (e.g., H-Wave) ▪ Electromagnetic shielding ▪ Functional training ▪ Gait training ▪ Graded motor imagery ▪ Home exercise program ▪ Mirror therapy ▪ Mobility training ▪ Occupational therapy ▪ Physical therapy ▪ Physiotherapy ▪ Prosthetic use and ambulation ▪ Protective “socks” or sheaths (e.g., Relax Night Care) ▪ Range of motion programs ▪ Recreational therapy ▪ Residual limb management strategies ▪ Transcutaneous electrical nerve stimulation (TENS) Therapeutic exercise ▪ Virtual reality: Specific to LLA rehab	Any of the listed interventions versus another listed intervention

KQ	Intervention(s)	Comparator(s)
11	▪ Female patients with LLA ▪ Transgender patients with LLA ▪ Other gender identification patients with LLA	Patients assigned male at birth and who identify as male with LLA
12	**Pharmacotherapy:** **SNRIs:** ▪ Duloxetine **SSRIs:** ▪ Citalopram ▪ Escitalopram ▪ Fluoxetine **Tricyclics:** ▪ Amitriptyline ▪ Nortriptyline **Opioids:** ▪ Buprenorphine ▪ Codeine ▪ Fentanyl ▪ Hydrocodone ▪ Hydromorphone ▪ Methadone ▪ Morphine ▪ Oxycodone ▪ Oxymorphone ▪ Tramadol **Other:** ▪ Carbamazepine ▪ Clonidine ▪ Dronabinol ▪ Gabapentin ▪ Ketamine (all routes included) ▪ Pregabalin ▪ Mexiletine ▪ Dextromethorphan ▪ Memantine **Topicals:** ▪ Capsaicin ▪ Diclofenac **Injections and nerve blocks:** ▪ Botulinum injection ▪ Corticosteroid injection	Placebo or sham (as appropriate to the type of intervention)

KQ	Intervention(s)	Comparator(s)
	▪ Epidural injection ▪ Nerve block ▪ Neuroma injection ▪ Peripheral nerve injections	

c. Outcomes

KQ	Critical Outcome(s)	Important Outcome(s)
1	▪ Functional status/Walking ability ▪ Prosthetic use ▪ Quality of life	▪ Depression scores ▪ Pain measured by any validated instrument (e.g., VAS) ▪ Patient satisfaction/preference ▪ SAEs /falls
2	▪ Functional status/Walking ability ▪ Prosthetic use	▪ Patient satisfaction/preference ▪ Quality of life ▪ Residual limb health ▪ SAEs/Falls ▪ Pain measured by any validated instrument (e.g., VAS)
3	▪ Functional status/Walking ability ▪ Pain measured by any validated instrument (e.g., VAS)	▪ Falls ▪ Patient satisfaction/preference ▪ Prosthetic use ▪ Quality of life
4	▪ Improved familial/functional/societal reintegration	▪ Depression scores ▪ Functional status/Walking ability ▪ Quality of life ▪ Reduced feelings of stigma/impact on self-esteem/self-consciousness ▪ Self-efficacy ▪ Pain (including neuropathic, residual limb and phantom) measured by any validated instrument (e.g., VAS)
5	▪ Functional status/Walking ability	▪ Pain measured by any validated instrument (e.g., VAS) ▪ Patient satisfaction/preferences ▪ Prosthetic use ▪ Quality of life ▪ SAEs/Falls
6	▪ Functional status/ Walking ability ▪ Skin condition status	▪ Quality of Life ▪ Pain measured by any validated instrument (e.g., VAS) ▪ Patient satisfaction/preference ▪ Prosthetic use/Time worn ▪ SAEs/Falls

KQ	Critical Outcome(s)	Important Outcome(s)
7	▪ Amputation of second limb ▪ Further amputation of affected limb	▪ Functional status/Walking ability ▪ SAEs
8	▪ Increased confidence, desirability and body image ▪ Increase satisfaction with intimate relationships	▪ Decreased anxiety related to sex ▪ Improved communication with partner ▪ Increased desire for sex ▪ Increased frequency of sexual activity ▪ Reduced pain associated with sexual activity
9	▪ Functional status/Walking ability ▪ Patient satisfaction (with treatment outcome)	▪ Quality of life ▪ Life Participation (Return to work/community reintegration/participation in adaptive sports) ▪ Prosthetic use/fitting/cognitive burden ▪ SAE including Falls
10	▪ Functional status/Walking ability ▪ Patient satisfaction/patient preferences ▪ Quality of life	▪ Pain measured by any validated instrument (e.g., VAS) ▪ Prosthetic use ▪ SAE (including Falls, ER visits, hospital readmissions, morbidity) ▪ Strength
11	▪ Prosthesis outcomes (includes satisfaction, cognitive burden and rejection) ▪ Quality of life	▪ Anxiety ▪ Depression ▪ Function/Walking ability ▪ Pain measured by any validated instrument (e.g., VAS) ▪ SAE (including skin integrity, overuse injury, mortality, serious complications)
12	▪ Functional status/Walking ability ▪ Pain/Pain Interference (Pain (residual, neuropathic, phantom limb) intensity change score measured by any validated instrument (e.g., VAS) ▪ Quality of life	▪ Life participation (community reintegration, return to work, adaptive sports) ▪ Patient satisfaction/patient preferences (with outcome of treatment) ▪ Prosthetic use ▪ SAE (includes falls, serious morbidities, dependence/overdose)

d. Timing

KQ	Timing
1 through 11	All
12	Post-operative (Short and long-term)

e. Setting(s)

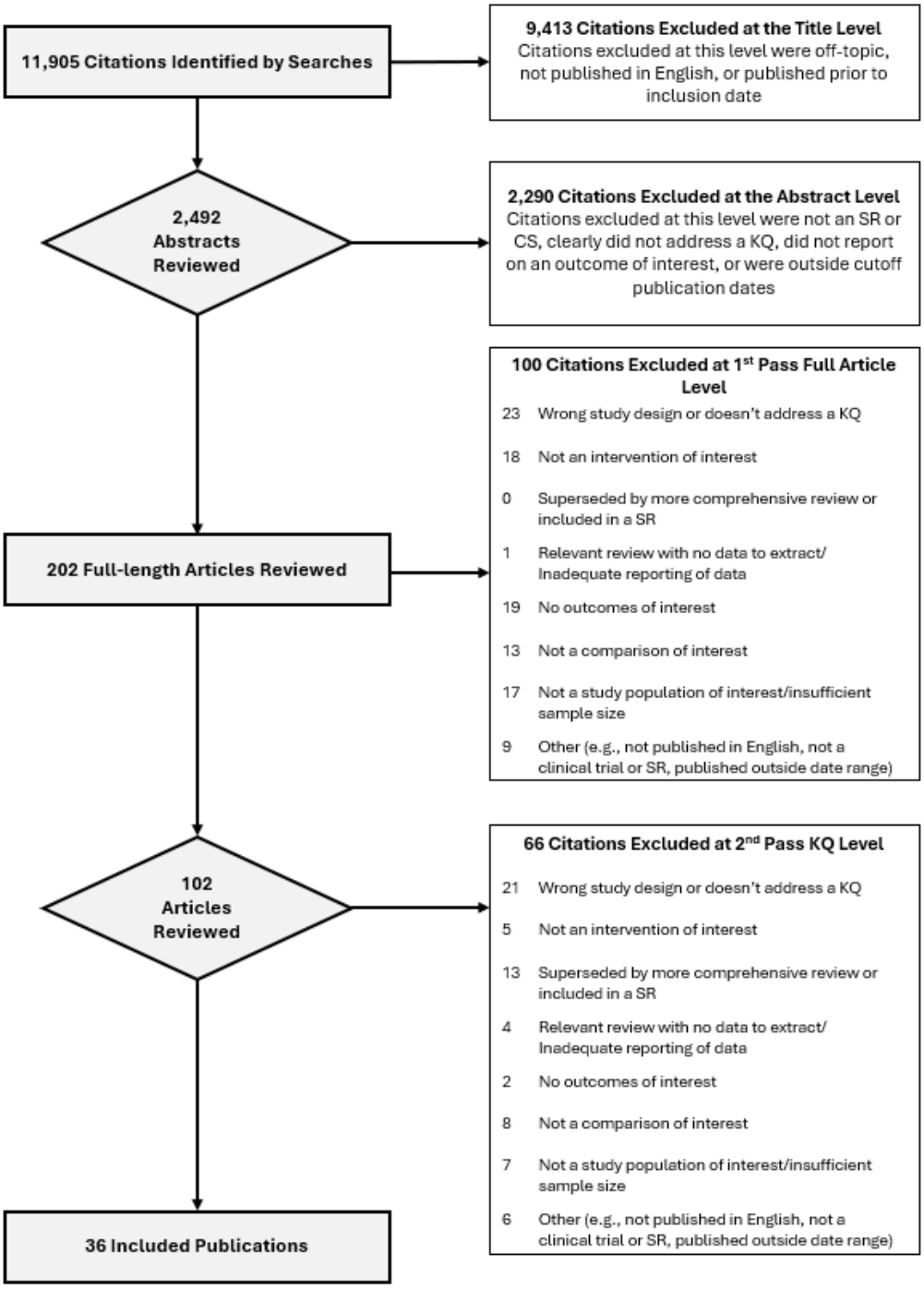
KQ	Setting(s)
1	Any of the intervention settings listed in KQ1
2 through 12	Any

B. Conducting the Systematic Review

Extensive literature searches identified 11,905 citations potentially addressing the key questions of interest to this evidence review. Of those, 9,413 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date, or not a full-length article). Overall, 2,492 abstracts were reviewed with 2,290 of those being excluded for the following reasons: not a systematic review or clinical study, did not address a key question of interest to this review, did not enroll a population of interest, or published prior to July 6, 2016. A total of 202 full-length articles were reviewed. Of those, 100 were excluded at a first pass review for the following: not addressing a key question of interest, not enrolling the population of interest, not meeting inclusion criteria for clinical study or systematic review, not meeting inclusion criteria for any key question, or being a duplicate. A total of 102 full-length articles were thought to address one or more key questions and were further reviewed. Of these, 66 were ultimately excluded. Reasons for their exclusion are presented in **Figure A-1** below.

Overall, 36 publications addressed one or more of the Key Questions and were considered as evidence in this review. **Table A-4** indicates the number of studies that addressed each of the KQs.

Figure A-1. Study Flow Diagram



Abbreviations: CS: comparative study; KQ: key question; SR: systematic review

Alternative Text Description of Study Flow Diagram

Figure A-1. Study Flow Diagram is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion-exclusion process. Arrows point down to boxes that describe the next literature review step and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

1. Box 1: 11,905 citations identified by searches.
    a. Right to Box 2: 9,413 excluded at the title level. Excluded citations were off topic, not published in English, or published prior to inclusion date.
    b. Down to box 3.
2. Box 3: 2,492 abstracts reviewed.
    a. Right to Box 4: 2,290 citations excluded at the abstract level. Citations excluded were not an SR or CS, clearly did not address a KQ, did not report an outcome of interest, or were outside cutoff publication dates.
    b. Down to Box 5.
3. Box 5: 202 full-length articles reviewed.
    a. Right to Box 6: 100 citations excluded at 1st pass full-article level.
        i. 23 wrong study design or doesn't address a KQ.
        ii. 18 not an intervention of interest.
        iii. 0 superseded by more comprehensive review or included in a SR.
        iv. 1 relevant review with no data to extract/inadequate reporting of data.
        v. 19 no outcomes of interest.
        vi. 13 not a comparison of interest.
        vii. 17 not a study population of interest/insufficient sample size.
        viii. 9 other.
    b. Down to Box 7.
4. Box 7: 102 articles reviewed.
    a. Right to Box 8: 66 citations excluded at 2nd pass full-article level.
        i. 21 wrong study design or doesn't address a KQ.
        ii. 5 not an intervention of interest.
        iii. 13 superseded by more comprehensive review or included in a SR.
        iv. 4 relevant review with no data to extract/inadequate reporting of data.
        v. 2 no outcomes of interest.
        vi. 8 not a comparison of interest.
        vii. 7 not a study population of interest/insufficient sample size.

viii. 6 other.

b. Down to Box 9.

5. Box 9: 36 included studies.

Table A-2. Evidence Base for KQs

KQ Number	KQ	Number and Study Type
1	What is the comparative effectiveness of different rehabilitation settings for patients with LLA?	1 SR
2	In patients with LLA, which prosthetic components (socket/interface, suspension system, knee, foot, ankle) optimize patient function, safety, and quality of life for the following amputation levels? a. Hip disarticulation; b. Knee disarticulation; c. Ankle disarticulation; d. Transtibial amputation; e. Transfemoral amputation; f. Partial foot amputation	5 SRs 6 crossover RCTs in 7 publications
3	For patients undergoing LLA, what neurostimulation or ablation interventions are effective for pain management and associated outcomes?	3 RCTs in 4 publications
4	Are behavioral health and psychosocial interventions effective in improving rehabilitation outcomes?	1 SR 2 RCTs
5	In patients with LLA, what initial or revision surgical interventions are effective in improving medical, surgical and rehabilitation (including prosthetic use) outcomes?	1 RCT
6	In patients with LLA who have skin and soft tissue complications, what is the effectiveness of dermatological and regenerative medicine approaches on outcomes?	1 SR
7	In patients with LLA, what preventive measures are effective in reducing the risk of further amputation of the affected limb or amputation of the second limb?	No studies identified
8	What interventions improve intimacy and sexual health in patients who undergo a LLA?	No studies identified
9	What is the effectiveness of different care team models on rehabilitation outcomes?	No studies identified
10	In patients with LLA, what is the comparative effectiveness of specific rehabilitation interventions (all phases)?	7 SRs 4 RCTs
11	What factors need to be addressed specifically for female, transgender, and other sex identification living with LLA? What sex/transgender factors influence the rehabilitation outcomes?	1 SR 1 Prospective Cohort
12	For patients undergoing LLA, what pharmacologic interventions are effective for amputation-related limb pain management and associated outcomes in the post-operative periods?	2 SRs 1 RCT
Total Evidence Base		**38 papers***

*Some papers address more than one KQ, and some studies are reported in more than one paper, therefore the total number for the evidence base is greater than the total number of includes in the study flow diagram and description.
Abbreviations: KQ: key question; RCT: randomized controlled trial; SR: systematic review

a. General Criteria for Inclusion in Systematic Evidence Review

- Randomized control trials (RCTs) or systematic reviews of RCTs published on or after July 6, 2016, through March 15, 2024. If multiple systematic reviews addressed a key question, we selected the most recent and/or comprehensive review.
- Studies had to be published in English.
- Publication had to be a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, research protocols, and other publications that were not full-length clinical studies were not accepted as evidence.
- Systematic reviews had to have searched MEDLINE or EMBASE for eligible publications, performed a risk of bias assessment of included studies, and assessed the quality of evidence using a recognizable rating system, such as GRADE or something compatible (e.g., the one used by the Evidence-based Practice Centers of the Agency for Healthcare Research and Quality). If an existing review did not assess the overall quality of the evidence, evidence from the review must have been reported in a manner that allowed us to judge the overall risk of bias, consistency, directness, and precision of evidence. We did not use an existing review as evidence if we were not able to assess the overall quality of the evidence in the review.
- RCTs needed to assess a pharmacological or non-pharmacological treatment, care management approach or care setting, as specified in the intervention sections above, and have an independent control group. Randomized crossover trials were only included if data from the first period (prior to treatment crossover) was reported separately or an adequate washout period was used.
- If no RCTs were available to address a KQ, prospective, non-randomized comparative studies were included. Similarly, if no systematic reviews of RCTs were available, SRs of eligible non-RCT designs were used.
- Study must have enrolled at least 20 patients (10 per study group for RCTs and 20 for prospective non-randomized studies) unless otherwise noted (see Key Question Specific Criteria below).
- Study must have enrolled at least 85% of patients who met the study population criteria: adults aged 18 years or older with lower limb amputation. If the patient population fell below this threshold but the relevant population of patients with LLA was reported separately, then that study was included.
- To ensure applicability to the VA/DOD healthcare systems, and ensure consistency across the CPG program, inclusion of individual studies was limited to very high Human Development Index (HDI), countries with an index ≥0.8 where standards of healthcare are comparable (e.g., United States, Canada, United Kingdom, Western Europe, Israel, Japan, Hong Kong, Australia, and New Zealand). Inclusion of systematic reviews was limited to those including more than half of the studies from eligible regions.

- These regions of interest are listed in Table 1 of the Statistical Annex of the 2023/24 Human Development Report produced by the United Nations Development Programme.
- Study must have reported on at least one outcome of interest.

b. Key Question Specific Criteria for Inclusion in Systematic Evidence Review

- Because KQ11 could not be addressed by an RCT design, prospective non-randomized studies and SRs of prospective non-randomized studies were sought. All other general inclusion criteria applied to KQ11.

c. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in **Table A-5**, below. Additional information on the search strategies, including topic-specific search terms and search strategies can be found in Appendix G.

Table A-3. Bibliographic Database Information

Name		Date Limits	Platform/ Provider
Bibliographic Databases	The Cochrane Database of Systematic Reviews (Cochrane Reviews)	July 6, 2016, through March 15, 2024	Wiley
	CINAHL	July 6, 2016, through March 15, 2024	Wiley
	EMBASE (Excerpta Medica)	July 6, 2016, through March 15, 2024	Elsevier
	MEDLINE/PreMEDLINE	July 6, 2016, through March 15, 2024	Elsevier
	PsycINFO	July 6, 2016, through March 15, 2024	OVIDSP
Gray Literature Resources	PubMed (In-process and Publisher records)	July 6, 2016, through March 15, 2024	NLM
	AHRQ	July 6, 2016, through March 15, 2024	AHRQ

d. Rating the Quality of Individual Studies and the Body of Evidence

The Sigma Team assessed the methodological risk of bias of individual diagnostic, observational, and interventional studies using the USPSTF method. Each study is assigned a rating of *Good*, *Fair*, or *Poor* based on a set of criteria that vary depending on study design. Detailed lists of criteria and definitions appear in Appendix VI of the USPSTF procedure manual.(197)

Next, the Sigma team assessed the overall quality of the body of evidence for each critical and important outcome using the GRADE approach. This approach considers the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence. The overall quality of the body of evidence is rated as *High*, *Moderate*, *Low*, and *Very Low*.

C. Developing Evidence-Based Recommendations

In consultation with the VA Office of Quality and Patient Safety and the Clinical Quality Improvement Program, Defense Health Agency, and the Sigma Team convened a 3.5 day in-person recommendation development meeting from June 10-13, 2024, to develop this CPG's evidence-based recommendations. Two weeks before the meeting, the Sigma Team finalized the systematic evidence review and distributed the report to the Work Group; findings were also presented during the recommendation development meeting (see Determining Recommendation Strength and Direction).

Led by the Champions, the Work Group interpreted the systematic evidence review's findings and developed this CPG's recommendations. The strength and direction of each recommendation were determined by assessing the quality of the overall evidence base, the associated benefits and harms, patient values and preferences, and other implications.

Determining Recommendation Strength and Direction

Per GRADE methodology, to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:(45)

1. Confidence in the Quality of the Evidence

Confidence in the quality of the evidence reflects the quality of the evidence base and the certainty in that evidence. This second domain reflects the methodological quality of the studies for each outcome variable. In general, the strength of recommendation follows the level of evidence, but not always, as other domains may increase or decrease their strength. The evidence review used for the development of recommendations for LLA, conducted by the Sigma Team, assessed the confidence in the quality of the evidence base and assigned a rate of "High," "Moderate," "Low," or "Very Low."

The elements that go into the confidence in the quality of the evidence include:

- Is there high or moderate quality evidence that answers this question?
- What is the overall certainty of this evidence?

2. Balance of Desirable and Undesirable Outcomes

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid events, resolution of symptoms, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse events, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that most clinicians will offer patients therapeutic or preventive measures if the advantages of the intervention exceed the risks and adverse effects. The certainty or uncertainty of the clinician about the risk-benefit balance will greatly influence the strength of the recommendation.

Some of the discussion questions that fall under this domain include:

- Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?
- Are the desirable anticipated effects large?
- Are the undesirable anticipated effects small?
- Are the desirable effects large relative to undesirable effects?

3. Patient Values and Preferences

Patient values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. More precisely, it refers to the processes that individuals use in considering the potential benefits, harms, costs, limitations, and inconvenience of the therapeutic or preventive measures in relation to one another. For some, the term "values" has the closest connotation to these processes. For others, the connotation of "preferences" best captures the notion of choice. In general, values and preferences increase the strength of the recommendation when there is high concordance and decrease it when there is great variability. In a situation in which the balance of benefits and risks are uncertain, eliciting the values and preferences of patients and empowering them and their surrogates to make decisions consistent with their goals of care becomes even more important. A recommendation can be described as having "similar values," "some variation," or "large variation" in typical values and preferences between patients and the larger populations of interest.

Some of the discussion questions that fall under the purview of values and preferences include:

- Are you confident about the typical values and preferences and are they similar across the target population?
- What are the patient's values and preferences?
- Are the assumed or identified relative values similar across the target population?

4. Other Implications

Other implications consider the practicality of the recommendation, including resources use, equity, acceptability, feasibility and subgroup considerations. Resource use is related to the uncertainty around the cost-effectiveness of a therapeutic or preventive measure. For example, statin use in the frail elderly and others with multiple co-occurring conditions may not be effective and depending on the societal benchmark for willingness to pay, may not be a good use of resources. Equity, acceptability, feasibility, and subgroup considerations require similar judgments around the practicality of the recommendation.

The framework below (**Table A-6**) was used by the Work Group to guide discussions on each domain.

Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgement
Balance of desirable and undesirable outcomes	▪ What is the magnitude of the anticipated desirable outcomes? ▪ What is the magnitude of the anticipated undesirable outcomes? ▪ Given the best estimate of typical values and preferences, are you confident that benefits outweigh harms/burdens or vice versa?	▪ Benefits outweigh harms/burdens ▪ Benefits slightly outweigh harms/burdens ▪ Benefits and harms/burden are balanced ▪ Harms/burden slightly outweigh benefits ▪ Harms/burden outweigh benefits
Confidence in the quality of evidence	▪ Among the designated critical outcomes, what is the lowest quality of relevant evidence? ▪ How unlikely is further research to change the confidence in the estimate of effect?	▪ High ▪ Moderate ▪ Low ▪ Very low
Patient values and preferences	▪ Are you confident about the typical values and preferences and are they similar across the target population? ▪ What are the patient's values and preferences? ▪ Are the assumed or identified relative values similar across the target population?	▪ Similar values ▪ Some variation ▪ Large variation
Other implications (e.g. resource use, equity, acceptability, feasibility, subgroup considerations)	▪ Are the resources worth the expected net benefit from the recommendation? ▪ What are the costs per resource unit? ▪ Is this intervention generally available? ▪ Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? ▪ Is there lots of variability in resource requirements across settings?	Various considerations

D. Recommendation Categorization

1. Recommendation Categories and Definitions

For use in the 2024 LLA CPG, a set of recommendation categories was adapted from those used by the United Kingdom National Institute for Health and Clinical Excellence (NICE).(50,51) These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2017 LLA CPG. The categories and definitions can be found in Table 4.

2. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether they were based on an updated review of the evidence. If evidence had been reviewed, recommendations were categorized as "New-added," "New-replaced," "Not changed," "Amended," or "Deleted."

"Reviewed, New-added" recommendations were original, new recommendations that were not in the 2017 LLA CPG. "Reviewed, New-replaced" recommendations were in the previous version of the guideline but were modified to align with the updated review of the evidence. These recommendations could have also included clinically significant changes to the previous version. Recommendations categorized as "Reviewed, Not changed" were carried forward from the previous version of the CPG unchanged.

Recommendations could have also been designated "Reviewed, Deleted." These were recommendations from the previous version of the CPG that were not brought forward to the updated guideline after review of the evidence. This occurred if the evidence supporting the recommendations was out of date, to the extent that there was no longer any basis to recommend a particular course of care and/or new evidence suggests a shift in care, rendering recommendations in the previous version of the guideline obsolete.

3. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous version of the CPG without an SR of the evidence. Due to time and budget constraints, the update of the LLA CPG could not review all available evidence on rehabilitation of LLA, but instead focused its KQs on areas of new or updated scientific research or areas that were not previously covered in the CPG.

For areas of research that have not changed, and for which recommendations made in the previous version of the guideline were still relevant, recommendations could have been carried forward to the updated guideline without an updated SR of the evidence. The support for these recommendations in the updated CPG was thus also carried forward from the previous version of the CPG. These recommendations were categorized as "Not reviewed." If evidence had not been reviewed, recommendations could have been categorized as "Not changed," Amended," or "Deleted."

"Not reviewed, Not changed" recommendations refer to recommendations from the previous version of the LLA CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations which were modified from the 2007 CPG with the updated GRADE language, as explained above.

Recommendations could also have been categorized as "Not reviewed, Deleted" if they were determined to be out of scope. A recommendation was out of scope if it pertained to a topic (e.g., population, care setting, treatment, condition) outside of the scope for the updated CPG as defined by the Work Group.

The categories for the recommendations included in the 2017 version of the guideline are noted in the Recommendations. Recommendations 6, 8, 9, and 10 were carried forward from the 2017 LLA CPG using this method. The categories for the recommendations from the 2017 LLA CPG are noted in Appendix C.

E. Drafting and Finalizing the Guideline

Following the face-to-face meeting, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2017 LLA CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2017 LLA CPG for inclusion in the update. During this time, the Champions and Work Group also made additional revisions to the algorithms, as necessary.

After developing the initial draft of the updated CPG, an iterative review process was used to solicit feedback on and revise the CPG. Once they were developed, the first two drafts of the CPG were posted on the LLA Wiki Website for a period of 10-20 business days for internal review and comment by the Work Group. Draft 3 was made available for a 14-day peer review and comment period (see External Peer Review). All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG. Following the Draft 3 review and comment period, the Work Group reviewed external feedback and created a final draft of the CPG. The Champions then presented the CPG to the VA/DOD EBPWG for approval, and the final CPG was approved in December 2024. To accompany the CPG, the Work Group produced toolkit products, including a provider summary, quick reference guide, and patient summary.

Appendix B: Evidence Table

Table B-1. 2024 Lower Limb Amputation Evidence Table [1, 2, 3, 4]

#	Recommendation	2017 Strength of Recommendation[1]	Evidence[2]	2024 Strength of Recommendation[3]	2024 Recommendation Category[4]
1.	There is insufficient evidence to recommend one surgical computation procedure over another.	Very low	**Additional References** (61-66)	Neither for nor against	Not reviewed, Not changed
2.	For patients with transfemoral amputation who meet eligibility criteria, we suggest osseointegration as an option to improve prosthesis use.	Not applicable	(67,69) **Additional Reference** (68)	Weak for	Reviewed, New-added
3.	There is insufficient evidence to recommend for or against targeted muscle reinnervation or other peripheral nerve surgical management for phantom limb pain.	Not applicable	(72) **Additional References** (70,71)	Neither for nor against	Reviewed, New-added
4.	We suggest intraoperative placement of a perineural catheter for the post-operative delivery of local anesthetic to reduce pain following amputation surgery.	Not applicable	(73-77)	Weak for	Reviewed, New-added

[1] 2017 Strength of Recommendation column: “Not applicable” indicates that the 2024 VA/DOD LLA CPG recommendation was a new recommendation, and therefore does not have an associated 2017 strength of recommendation.
[2] Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference needed to be identified through a systematic evidence review carried out as part of the initial development or update of this CPG. The second set of references in the evidence column (called “Additional References”) includes references that provide additional information related to the recommendation, but which were not identified through a systematic evidence review. These references were, therefore, not included in the evidence base for the recommendation and did not influence the strength and direction of the recommendation.
[3] 2024 Strength of Recommendation column: The 2024 VA/DOD LLA CPG was developed using the GRADE approach to determine the strength of each recommendation. Refer to the Grading Recommendations section for more information.
[4] Recommendation Category column: Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category

#	Recommendation	2017 Strength of Recommendation[1]	Evidence[2]	2024 Strength of Recommendation[3]	2024 Recommendation Category[4]
5.	Post-transtibial amputation, we suggest application of a rigid or semi-rigid residual limb dressing to promote healing and early prosthesis use as soon as feasible.	Weak for	(65,78,82,83,85,198,199) **Additional References** (79-81,84)	Weak for	Not reviewed, Amended
6.	We suggest providing post-operative amputation care in an inpatient rehabilitation facility (IRF) over other settings (e.g., skilled nursing facility (SNF) or home care).	Weak for	(86-88) **Additional References** (89,90,187)	Weak for	Reviewed, Amended
7.	We suggest assessment and treatment to improve behavioral health and psychosocial functioning.	Not applicable	(91,93-95) **Additional References** (92,96)	Weak for	Reviewed, New-replaced
8.	We suggest peer support by a trained peer as a component of rehabilitation to improve psychosocial function.	Weak for	(94) **Additional References** (97-103,200)	Weak for	Reviewed, Amended
9.	We suggest cognitive assessment to inform rehabilitation goals and prosthetic candidacy.	Weak for	(104) **Additional References** (105)	Weak for	Not reviewed, Amended
10.	We suggest the care team provides patient education throughout amputation rehabilitation.	Weak for	(91,93,95) **Additional References** (106-109)	Weak for	Reviewed, Amended
11.	We suggest mirror therapy, alone or in combination with other therapies, to improve pain, function and quality of life for individuals with phantom limb pain.	Not applicable	(93,110-114) **Additional References** (115-122)	Weak for	Reviewed, New-added
12.	We suggest an individualized and skilled rehabilitation program with exercise and gait training to improve functional status, walking ability, and quality of life.	Not applicable	(93,123-126)	Weak for	Reviewed, New-replaced

#	Recommendation	2017 Strength of Recommendation[1]	Evidence[2]	2024 Strength of Recommendation[3]	2024 Recommendation Category[4]
13.	We suggest using patient-identified sex to inform individualized rehabilitation plans.	Not applicable	(127,128) **Additional References** (129)	Weak for	Reviewed, New-replaced
14.	We suggest screening for factors associated with rehabilitation outcomes following acquired limb loss, (e.g., smoking, comorbid injuries or illnesses, psychosocial characteristics, and physical function).	Strong for	(130-132) **Additional Reference** (133,134)	Weak for	Not reviewed, Amended
15.	For community ambulators, there is insufficient evidence to recommend any specific transfemoral socket design.	Not applicable	(135-137)	Neither for nor against	Reviewed, New-added
16.	For community ambulators, there is insufficient evidence to recommend for or against ischial containment or sub-ischial socket designs.	Not applicable		Neither for nor against	Reviewed, New-added
17.	For prosthetic ambulators, we suggest prescribing microprocessor knee units over non-microprocessor knee units for reducing falls, optimizing functional mobility, and improving patient satisfaction.	Not applicable	(138,153,154) **Additional References** (139-152)	Weak for	Reviewed, New-replaced
18.	For prosthetic ambulators, there is insufficient evidence to prescribe any specific energy storing and return (ESAR) or microprocessor foot and ankle component over another.	Not applicable	(155-158)	Neither for nor against	Reviewed, New-added
19.	For prosthetic ambulators, we suggest energy storing and return (ESAR) or microprocessor-controlled foot and ankle components over solid ankle cushioned heel (SACH) feet to improve ambulation and patient satisfaction.	Not applicable		Weak for	Reviewed, New-added

#	Recommendation	2017 Strength of Recommendation[1]	Evidence[2]	2024 Strength of Recommendation[3]	2024 Recommendation Category[4]
20.	We suggest using patient-reported and performance-based measures with acceptable psychometric properties to assess function.	Weak for	(83,159,161,162,164,165) **Additional References** (162,163)	Weak for	Not reviewed, Amended
21.	There is insufficient evidence to recommend for or against neurostimulation (e.g., peripheral nerve stimulation, or spinal cord stimulation) or neuroablation (e.g., cryoneurolysis, radio frequency ablation) interventions for the management of phantom limb pain or residual limb pain.	Not applicable	(166-169,201) **Additional References** (170)	Neither for nor against	Reviewed, New-added
22.	We suggest perineural catheter delivered anesthetic for the treatment of chronic severe phantom limb pain with functional impairment.	Not applicable	(171)	Weak for	Reviewed, New-added
23.	There is insufficient evidence to recommend for or against any systemic pharmacologic intervention for the management of phantom limb pain.	Not applicable	(172) **Additional References** (173-180)	Neither for nor against	Reviewed, New-added
24.	For prosthesis users with hyperhidrosis, there is insufficient evidence to recommend for or against Botulinum toxin treatment to reduce sweat production, improve prosthetic function, reduce pain, and improve quality of life.	Not applicable	(183) **Additional References** (181,182,184)	Neither for nor against	Reviewed, New-added
25.	There was insufficient evidence to recommend for or against strategies to prevent re-amputation of the ipsilateral limb or amputation of the contralateral limb.	Not applicable	**Additional References** (185-188)	Neither for nor against	Reviewed, New-added
26.	There is insufficient evidence to recommend for or against any specific	Not applicable	**Additional References** (189-195)	Neither for nor against	Reviewed, New-added

#	Recommendation	2017 Strength of Recommendation[1]	Evidence[2]	2024 Strength of Recommendation[3]	2024 Recommendation Category[4]
	intervention to improve intimacy and sexual health.				

Appendix C: 2017 Recommendation Categorization

Table C-1. 2017 Lower Limb Amputation CPG Recommendation Categorization Table [1, 2, 3, 4]

2017 CPG Recommendation #	2017 Recommendation Text[1]	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category[2]	2024 CPG Recommendation Category[3]	2024 CPG Recommendation #
1	We suggest that patient education be provided by the rehabilitation care team throughout all phases of amputation rehabilitation.	Weak for	Reviewed, Amended	Reviewed, Amended	10
2	We suggest an assessment of behavioral health and psychosocial functioning at every phase of amputation management and rehabilitation.	Weak for	Reviewed, Amended	Reviewed, New-replaced	7
3	When assessing pain, we suggest that measurement of the intensity of pain and interference with function should be separately assessed for each pain type and location using standardized tools.	Weak for	Reviewed, Amended	Not reviewed, Deleted	NA
4	We suggest offering a multi-modal, transdisciplinary individualized approach to pain management including transition to a non-narcotic pharmacological regimen combined with physical, psychological, and mechanical modalities throughout the rehabilitation process. For the treatment of chronic pain, the 2017 VA/DOD CPG for the Management of Opioid Therapy for Chronic Pain recommends alternatives to opioid therapy such as self-management strategies, other non-pharmacological treatments, and non-opioids over opioids (see the 2017 VA/DOD OT CPG).[4]	Weak for	Reviewed, New-replaced	Reviewed, New-added	6, 11, 25, 26
5	We recommend providers consider the patient's birth sex and self-identified sex identity in developing individualized treatment plans.	Strong for	Reviewed, New-added	Reviewed, New-replaced	13

[1] The 2017 Recommendation Text column contains the wording of each recommendation from the 2017 LLA CPG.
[2] The Recommendation Category column indicates the way in which each 2017 LLA CPG recommendation was updated.
[3] For recommendations that were carried forward to the 2024 LLA CPG, this column indicates the new recommendation(s) to which they correspond.
[4] See the VA/DOD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: http://www.healthquality.va.gov/guidelines/Pain/cot/.

2017 CPG Recommendation #	2017 Recommendation Text[1]	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category[2]	2024 CPG Recommendation Category[3]	2024 CPG Recommendation #
6	We suggest offering peer support interventions, including visitation by a certified peer visitor, as early as feasible and throughout the rehabilitation process.	Weak for	Reviewed, Amended	Reviewed, Amended	8
7	Prior to surgery, we suggest that rehabilitation goals, outcomes, and other implications be included in shared decision making about residual limb length and amputation level.	Weak for	Reviewed, Amended	Reviewed, New-added	5, 23
8	There is insufficient evidence to recommend one surgical amputation procedure over another.	Not applicable	Reviewed, New-added	Not Reviewed, Not changed	1, 5, 23
9	We suggest the use of a rigid or semi-rigid dressing to promote healing and early prosthetic use as soon as feasible post-amputation in transtibial amputation. Rigid post-operative dressings are preferred in situations where limb protection is a priority.	Weak for	Reviewed, Amended	Not Reviewed, Amended	4
10	We suggest performing cognitive screening prior to establishing rehabilitation goals, to assess the patient's ability and suitability for appropriate prosthetic technology.	Weak for	Reviewed, New-replaced	Not Reviewed, Amended	9
11	We suggest that in the perioperative phase following amputation, patients receive physical rehabilitation and appropriate durable medical equipment/assistive technology.	Weak for	Reviewed, New-replaced	Not reviewed, Deleted	NA
12	We suggest, when applicable, treatment in an acute inpatient rehabilitation program over a skilled nursing facility.	Weak for	Reviewed, New-replaced	Reviewed, Amended	2
13	We suggest the initiation of mobility training as soon as feasible post-amputation. In appropriate patients, this may include ipsilateral side weight-bearing ambulation with a pylon to improve physical function and gait parameters.	Weak for	Reviewed, New-replaced	Reviewed, New-replaced	12
14	We recommend instituting rehabilitation training interventions, using both open and closed chain exercises and progressive resistance to improve gait, mobility, strength, cardiovascular fitness and activities of daily living performance in order to maximize function.	Strong for	Reviewed, New-replaced	Reviewed, New-replaced	12

2017 CPG Recommendation #	2017 Recommendation Text[1]	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category[2]	2024 CPG Recommendation Category[3]	2024 CPG Recommendation #
15	We suggest offering microprocessor knee units over non-microprocessor knee units for ambulation to reduce risk of falls and maximize patient satisfaction. There is insufficient evidence to recommend for or against any particular socket design, prosthetic foot categories, and suspensions and interfaces.	Weak for	Reviewed, New-added	Reviewed, New-replaced	15
16	We recommend the use of valid, reliable, and responsive functional outcome measures, including, but not limited to, the Comprehensive High-level Activity Mobility Predictor, Amputee Mobility Predictor, 10-meter walk test, and 6-minute walk test.	Strong for	Reviewed, New-replaced	Not reviewed, Deleted	NA
17	We suggest the use of a combination of measures with acceptable psychometric properties to assess functional outcomes.	Weak for	Reviewed, New-replaced	Not reviewed, Amended	20
18	We recommend offering further evaluation and interventions for factors that are associated with poorer outcomes such as smoking, comorbidities, psychosocial functioning, and pain.	Strong for	Reviewed, Amended	Not reviewed, Amended	14

Appendix D: Routine Care

The Multidisciplinary Team
A multi-disciplinary team (MDT) provides a coordinated approach to comprehensive care. Members of the team from various areas of specialty provide input based on areas of expertise to ensure all aspects of care are considered. The ideal team should, at the very least, consist of a physician (preferably a physical medicine and rehabilitation physician), a physical therapist, an occupational therapist and a prosthetist. Additional, equally valuable clinicians to include are nurses, social workers, recreational therapists, rehabilitation psychologists, and surgeons.

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post-Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
Focus Areas	MDT team/PM&R consult Functional implications of amputation Home safety evaluation Psychosocial well-being	Pain management Residual limb protection and compression Contralateral foot/limb management	Promote highest level of independence with *and* without prosthesis for all patients. Mobility, ADL, community access goals <u>without</u> a prosthesis (all patients) Pre-prosthesis training (if indicated)	Prosthesis management (donning, doffing, sock ply management, etc.) Gait and other mobility training ADL training Floor recovery techniques	Routine amputation specialty team clinic • Prosthesis fit and function • Durable medical equipment (DME) needs • Functional goals • contralateral limb/foot Psychosocial well-being

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
1. Pain Management	Assess for and manage existing pain Develop a peri-operative pain management plan	Assess and treat residual limb pain (RLP), phantom limb pain (PLP), and phantom limb sensation (PLS) Provide treatment plan for RLP, PLP, PLS, including: patient education, narcotic use, regional anesthesia, psychosocial interventions, non-pharmacologic interventions (i.e., exercises, soft tissue mobilization, tapping, residual limb compression, etc.)	Assess and treat residual limb pain (RLP), phantom limb pain (PLP), and phantom limb sensation (PLS) Provide treatment plan for RLP, PLP, PLS, including: patient education, wean use, psychosocial interventions,non-pharmacologic interventions (i.e., exercises, soft tissue mobilization, tapping, residual limb compression, etc.), Graded Motor Imagery (GMI)	Assess and treat residual limb pain (RLP), phantom limb pain (PLP), and phantom limb sensation (PLS) Provide treatment plan for RLP, PLP, PLS, including: patient education, wean narcotic use, psychosocial interventions, non-pharmacologic interventions (i.e., exercises, massage, etc.), Prosthetic sock ply management, Graded Motor Imagery (GMI)	Reassess and adjust treatment for residual limb pain (RLP), phantom limb pain (PLP), and phantom limb sensation (PLS) Assess and treat contributing musculoskeletal problems

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
2. Medical Management					
2.1. Comorbid and Concurrent conditions	Assess medical risk factors for poor wound healing or re-amputation (e.g., end-stage renal disease on hemodialysis, etc.) Assess medical risk factors for poor functional prognosis (e.g., end-stage renal disease on hemodialysis, tobacco use, diabetes, etc.) Evaluate and consider other medical problems affecting function (e.g., polytrauma)	Complete initial assessment of medical comorbidities and consult experts as appropriate, especially if not addressed preoperatively Initiate medical interventions and education as needed Consider concurrent injuries or conditions that may affect success in rehabilitation	Continue medical interventions and education as needed Evaluate and consider other medical problems affecting function (e.g., polytrauma)	Assess changes in medical comorbidities, and perform interventions and education as needed Assess and optimize medical comorbidities affecting residual limb volume and health	Address musculoskeletal problems and other comorbidities that impact function Reconcile pharmacologic medication list focusing on side effects that may negatively impact function with or without a prosthesis Reinforce preventative care and whole health Refer to specialty care as needed to address comorbidities

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
	Initiate medical interventions, specialty consultations, and education as needed Assess sensation of all extremities				
2.2 Contralateral Lower Limb Management	Contralateral foot/limb assessment Referral to specialists for routine preventive care or evaluation/management of new concerns Prescribe appropriate footwear and orthoses Manage comorbidities affecting foot/limb health and footwear/orthosis fit	Contralateral foot/limb risk assessment and regular skin checks Contralateral foot/limb protection while supine, seated, or weight bearing Referral to specialists as indicated Prescribe appropriate footwear and orthoses	Continued foot/limb evaluation and risk assessment Contralateral foot/limb protection while supine, seated, or weight bearing Referral to specialists as indicated Assess footwear or orthoses as appropriate for functional progression	Continued foot/limb evaluation and risk assessment Contralateral foot/limb protection while supine, seated, or weight bearing Referral to specialists as indicated Assess footwear or orthoses as appropriate for functional progression	Regular foot/limb risk assessment and management; referral to specialists as appropriate Patient education about foot/limb protection and care

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
	Patient education about foot/limb protection and care	Patient education about foot/limb protection and care	Patient education about foot/limb protection and care	Patient education about foot/limb protection and care	
3. Behavioral Health and Psychosocial Function	Perform psychosocial assessment Perform cognitive assessment (may inform prosthesis candidacy, return to driving, etc. Offer counseling for adjustment and other concerns Provide resources based on needs Consider pharmacologic interventions for management of	Evaluate and address psychosocial needs Offer counseling for adjustment and other concerns Consider pharmacologic interventions for management of psychological symptoms or brain injury/dysfunction Offer peer support services Provide education and information on	Continue psychosocial evaluation and address psychosocial needs Complete cognitive assessment (may inform prosthesis candidacy, return to driving, etc.) Offer counseling for adjustment and other concerns Consider pharmacologic interventions for management of	Address psychosocial needs and concerns Provide resources (e.g., transportation, clothing allowance, support groups, community resources) Offer counseling for adjustment and other concerns Consider pharmacologic interventions for management of psychological	Offer counseling for adjustment and other concerns Provide outreach follow-up Provide resources (e.g., transportation, clothing allowance, support groups, community resources) Consider pharmacologic interventions for management of psychological

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
	psychological symptoms or brain injury/dysfunction Offer peer support services Provide education and information on advance care planning	advanced care planning	psychological symptoms or brain injury/dysfunction Offer peer support services Provide education and information on advance care planning	symptoms or brain injury/dysfunction Offer peer support services Provide education and information on advance care planning	symptoms or brain injury/dysfunction Offer peer support services Provide education and information on advance care planning
4. Residual Limb Management	Optimize limb prior to surgery by addressing skin issues, strength limitations, range of motion limitations, etc. Assess functional and prosthetic implications	Local wound care and advanced wound care specialist for surgical incision and other wounds (e.g., negative pressure wound therapy). For complex wound	Continue local wound care, limb shaping, edema management, and protection of the residuum Patient education on residual limb management and	Reinforce use of residual limb compression (e.g., shrinker) when out of prosthesis Progressive prosthesis wear schedule	Assess residual limb condition and intervene as needed Re-emphasize importance of skin checks and pressure points, skin hygiene,

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
	of residual limb length and amputation level Assess sensation of the affected limb and	healing or other vascular challenges, recommend considering a WOCN Consult pre-discharge- in collaboration with surgeon's recs Monitor the surgical wound for signs and symptoms of ischemia or infection Control edema and shape residual limb (e.g., elastic bandage wrapping or shrinker application) Protect residuum using rigid dressings (e.g., rigid cast, rigid removable device, etc.) for transtibial amputations.	desensitization techniques Advance ROM and strengthening of proximal joints and muscles Consider longer term residual limb protection for those with higher fall risk or skin risk (when not using prosthesis or if not a prosthesis candidate)	Consider early prosthesis use only during therapy if there are safety concerns Educate on skin checks and pressure points, skin hygiene, sock ply management, and wear schedule	and sock ply management

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
		Consider for transfemoral amputations. Promote ROM and strengthening of proximal joints and muscles			
5. Patient Education	• Pain management • Manage expectations regarding pain post-amputation (e.g., May not be resolved w/ amputation) • Patient safety/fall precautions • Prevention of complications • Procedural/Recovery Issues • Level of amputation	• Positioning • Rehabilitation process • Pain management • Residual limb care • Edema control • ACE wrapping or shrinker use • Wound care • Prosthetic timeline	• Positioning • Rehabilitation process • Pain management • Residual limb care • Edema control • Application of shrinker • Prosthetic timeline	• Prosthetic goals and expectation management • Pain management • Residual limb care, including edema management • Energy expenditure • Prosthetic education	• Pain management • Equipment needs • Prosthetic goals and expectation management • Prevention of complications • Weight management • Safety and falls prevention

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
	• Prosthetic options • Post-operative dressing • Sequence of amputation care • Equipment • Role of the multi-disciplinary team and members • Psychosocial anticipatory guidance • Expected functional outcomes	• Equipment needs • Coping methods • Prevention of complications • Contracture prevention • Safety and falls prevention	• Equipment needs • Coping methods • Prevention of complications • Continuum of care/annual follow-up • Contracture prevention • Safety and falls prevention	• Donning & doffing • Care of prosthesis • Skin integrity • Sock management • Equipment needs • Coping methods • Weight Management • Contracture prevention • Safety and falls prevention	• Continuum of care/Annual follow-up
6. Prosthesis Management	Patient visit / education Preliminary assessment of prosthesis candidacy by amputation specialty MDT Provide patient and family education addressing	Limb care (see residual limb management) Management of post-operative dressing: • Casting changes • Regular fit checks of rigid removable dressing (RRD)	Re-assessment of prosthesis candidacy by amputation specialty MDT Discussion of realistic goals w/ prosthetic use	Prosthetic fabrication, fitting, alignment, and modification Teach donning/doffing of prosthetic system	Prosthetic fabrication, fitting, alignment and modifications Re-assess prosthesis prescription and functional goals

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
	expectations, timeline and anticipated goals	• Soft dressing	Generate initial prosthetic prescription (if indicated), if cleared for weight-bearing/prothesis fitting by surgical team. Develop and train for safe back-up or alternative mobility and ADL strategies when not using prosthesis (all patients)	Prosthetic gait and ADL training Prosthesis management training (e.g., sock ply management, volume management, skin checks) Suspension and interface training/management Educate on prosthesis maintenance and cleaning (e.g., how to clean liners and sleeves)	Annual visits for assessment of: • Components • Supplies • Socket fit • Activity specific components • Assistive device for prosthetic ambulation
7. Discharge Planning	Discuss and educate the patient and family on potential:	Determine appropriate rehabilitation setting (IRF, SNF, home w/	Develop discharge plan for intermediate care setting,	Establish goals for initial prosthetic training	Implement annual follow-up schedule to address future prosthesis

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
	• DME needs, • Home modifications, • rehabilitation setting options (IRF, SNF, home with home care, home with outpatient care), • timeline of phases of rehabilitation, and • anticipated lifelong care needs.	home care, home w/ outpatient care) Determine caregiver and social support system Initiate discharge care education Arrange peer support/visitation with patient	independent living, etc. Determine caregiver and social support system Continue discharge care education Arrange peer support/visitation with patient Schedule follow up with multidisciplinary team MDT to determine readiness and timeline for prosthesis	Schedule follow up with multidisciplinary team Schedule follow up with prosthetist. Re-engage with PT and OT as goals progress and change	adjustments and replacements Reevaluate goals and functional status and re-engage in PT and OT
8. Rehabilitation					

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
8.1 Range of Motion	Assess ROM in all joints proximal to planned/possible amputation and on contralateral side Treat identified contractures Educate on contracture prevention and initiate full body ROM home exercise program	Initiate full body ROM home exercise program Educate on proper positioning to prevent contractures of hip, knee and ankle contractures	Progress full body ROM home exercise program to include lengthening of specific muscle groups (hip and knee flexors)	Advance stretching program Maximize ROM for prosthetic fit and training and include in home exercise program	Readdress ROM of LE and review home stretching program, if needed
8.2 Strengthening	Assess for preoperative strength deficits of UE and LE Create a home exercise program to strengthen and optimize UE and LE Addressing deficiencies and	Initiate strengthening program to optimize safe functional mobility and in preparation for potential prosthesis use. Target areas prone to overuse injuries (e.g., shoulders, low back, etc.).	Continue strengthening program to optimize safe functional mobility and in preparation for potential prosthesis use (specifically hip and knee musculature).	Progress therapeutic exercise program for all extremities Provide home exercise program when discharged from therapy	Educate on maintenance of strength for long-term activity

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
	maximize above ROM strength, balance, etc.		Target areas for strengthening to reduce overuse injuries (e.g., shoulders, low back, etc.). Integrate trunk and core stabilization exercises. Create HEP and provide exercise supplies		
8.3 Cardiovascular	Assess current cardiovascular (CV) fitness for increased energy requirement for prosthetic use Educate regarding increased energy demand in walking with a prosthesis	Incorporate a CV component into the therapy program Reinforce cardiac precautions as determined by cardiology team (heart rate, blood pressure, perceived exertion scales)	Advance CV aspect of program to meet needs of patient Maintain cardiac precautions Encourage reducing risk factors	Increase ambulation endurance to reach community distances and integrate into home exercise program Maintain cardiac precautions	Encourage cardiology and primary care follow up for continuous monitoring of CV fitness Encourage reduction of CV risk factors

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
				Encourage reducing risk factors	
8.4 Balance	Assess preoperative balance considering central and/or peripheral neurologic conditions	Initiate a balance progression in static and dynamic sitting and standing	Progress sitting balance and single limb standing balance	Advance balance activities to equalize weight over bilateral lower extremities Challenge balance with advanced activities	Reassess balance as it relates to gait
8.5 Mobility	Assess current mobility and use of assistive devices and/or DME	Establish upright tolerance Initiate and progress to independent bed mobility, rolling, and transfers	Progress single limb gait from parallel bars to use of assistive device Progress to independent wheelchair mobility	Increase symmetry of weightbearing, maximize weight shift, equalize step length, facilitate trunk rotation, teach reciprocal gait pattern Progress out of parallel bars to use of	Address changes to medical status affecting prosthetic use (e.g., diabetes, heart disease, limb and goals)

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
		Initiate wheelchair mobility Progress to single limb gait in parallel bars	Seating and Mobility evaluation for appropriate custom wheelchair Floor recovery strategies	appropriate assistive device Progress to advanced skills such as climbing/descending stairs, curbs, ramps and gait on uneven terrain Increase ambulation endurance to community distances	Reassess gait and retrain gait as necessary
9. Functional Activities and ADLs	Assess preoperative activity level and independence with basic ADLs and IADLs to help establish post-operative goals and expectations	Promote functional independence with basic ADLs such as eating, dressing, grooming, bathing, toileting. Ensure patient safety with basic transfers, including toilet/bedside	Educate on adaptive techniques for dressing, bathing, grooming, and toileting without a prosthesis. Assess for DME needs to promote functional	Instruct in proper care of prosthesis, suspension system, skin management, and donning/doffing of prosthesis. Promote independence with functional transfers, ADLs, and IADLs	Reassess functional status and educate on adaptive strategies to promote independence as status changes. Educate patient and caregiver on energy conservation, injury prevention, home safety, and DME

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
		commode, wheelchair, bedside chair, car transfers, etc.	independence with ADLs Initiate wheelchair management and safety education. Educate patient and family on understanding that non-prosthesis independence is an important set of functional goals	(laundry, cooking, house management, etc.) with and without prosthesis Educate on fall recovery and functional transitions from floor	needs as patient status changes.
10. Community					
10.1 Vocation and recreation	Obtain preoperative vocation and recreational interests	Offer and promote trained peer visitation	Initiate outings into the community without prosthesis Train in use of public transportation without	Initiate vocational and recreational activities with a prosthesis Train in the use of public transportation	Provide education on opportunities and precautions for long-term sport specific, recreation skills of resources, and prostheses or assistive

	Pre-Amputation: From initial discussion of amputation to admission for amputation	Peri-Operative: From hospitalization admission to discharge to rehabilitation setting	Post Amputation: From acute hospitalization through initial rehab goals	Prosthetic Training: Associated with prosthesis related functional goals	Lifelong Care: From time of discharge from therapy services through to end of life
			prosthesis, if appropriate Complete vocational rehabilitation evaluation Complete recreational training activities without prosthesis	with a prosthesis if appropriate	devices that are available Provide counseling and contact information regarding opportunities in sports and recreation (Paralympics, golfing, fishing, hunting, etc.)
10.2 Home Evaluation	Determine patient's current home set-up, available durable medical equipment, and potential safety concerns. Educate on potential home modifications to promote functional independence and safety.	Assess patient's home for accessibility and safety if not already completed. Provide information on home modifications	Assess patient's home for accessibility and safety if not already completed	Assess prosthetics needs that may improve home safety (e.g., shower leg, shorties)	Continue assessment of DME needs to ensure home accessibility and safety as functional status changes

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
10.3 Transportation and Return to Driving	Educate on potential adaptations needed for return to driving. Educate patient and family on variance between state requirements and insurance policies for driving with LLA.	Provide patient with alternative transportation options if caregivers unable to assist with transportation.	Evaluate patient for adaptations to promote return to driving. Recommend scheduling with Certified Driving Rehabilitation Specialist (CDRS)	Complete driver's training with adaptive equipment as needed Educate patient and family on variance between state requirements and insurance policies for driving with LLA.	Provide resources for alternative transportation options as needed.
11. Equipment	Determine DME and assistive devices available.	Assess living environment including stairs, wheelchair access, and bathroom accessibility for safe discharge to home Educate regarding potential home modifications,	Seating and Mobility evaluation to assess, measure, and order appropriate wheelchair Provide appropriate assistive device to promote	Provide appropriate assistive device for mobility with or without prosthesis	Provide appropriate assistive device and DME for mobility with or without prosthesis Provide appropriate wheelchair if ambulation is no longer an option

	Pre-Amputation: **From initial discussion of amputation to admission for amputation**	**Peri-Operative:** **From hospitalization admission to discharge to rehabilitation setting**	**Post Amputation:** **From acute hospitalization through initial rehab goals**	**Prosthetic Training:** **Associated with prosthesis related functional goals**	**Lifelong Care:** **From time of discharge from therapy services through to end of life**
		including ramp, accessible shower, etc.	independence with mobility Assess for personal equipment Assess for home adaptation and equipment		

Appendix E: Participant List

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Appendix F: Patient Focus Group Methods and Findings

A. Methods

VA and DOD Leadership recruited nine participants for the focus group, with support from the Champions and other Work Group members as needed. A convenience sample was utilized in selection of participants, and therefore the sample of patients used is not generalizable for the entirety of VA and DOD patients who have undergone a LLA. The goal of recruitment for this Patient Focus Group was to have a group of engaging, diverse amputees, who would be able to cogently explain their experience as an amputee receiving VA or DOD healthcare services. Participants were not incentivized for their participation or reimbursed for travel expenses.

The Work Group, with support from the Sigma Team, identified topics on which patient input was important to consider in developing the CPG. The Sigma Team developed, and the Work Group approved and patient focus group guide covering these topics. The focus group facilitator led the discussion used the guide to elicit the patients' perspectives about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all questions were addressed.

B. Patient Focus Group Findings

a. Participants emphasized the importance of pain management as a core component of their individual treatment plan.

- Participants would like their treatment plans to be personalized with multiple options that better serve their activity preferences and pain levels.
- Participants stressed the need for employing effective pain communication strategies to mitigate disconnects with healthcare providers in understanding pain.

b. Participants would benefit from incorporation of behavioral health into their care plans.

- Participants mentioned experiencing stigma post-amputation.
- Participants felt transitional mental health support would be beneficial when adjusting to life after amputation.
- Participants expressed the deep emotional impact that their amputation had on mental and physical health.

c. Participants discussed the value of peer support services and programs as part of their rehabilitation and recovery.

- Participants found peer support encouraging within facilities for rehabilitation.
- Participants emphasized the value of peer support in their wider communities.

d. Participants emphasized the importance of patient education and information resources. They expressed a desire to have access to source(s) of information regarding programs designed for amputees.

- Participants expressed the need for accessible information regarding programs, services, and other amputee resources.

- Participants discussed the importance of patient education in advocating for themselves in their care.
- Participants emphasized the need for better resources to educate family members post-amputation.

e. Participants valued provider communication, care coordination, and continuity of care.

- Participants valued clear and concise communication of treatment from providers.
- Participants expressed the need for coordination of all providers in their overall care plan.
- Participants preferred continuity in their providers and the relationships that are built between them.

Appendix G: Literature Review Search Terms and Strategy

A. Topic-specific Search Terms

The search strategies employed combinations of free-text keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. Strategies for each bibliographic database follow this table.

Table G-1. Concept Tables PubMed and EMBASE

Concept	Controlled Vocabulary	Keywords
Amputation	**EMBASE (EMTREE)** amputee above knee amputation amputation below knee amputation disarticulation foot amputation hemicorporectomy hemipelvectomy knee amputation leg amputation limb amputation traumatic amputation **PubMed (MeSH)** amputees amputation, traumatic amputation stumps amputation, surgical disarticulation hemipelvectomy	amputat* Chopart disarticulation exarticulation hemicorporectomy hemipelvectomy limb loss Lisfranc Syme* *word variations have been searched
Amputation Site	**EMBASE (EMTREE)** amputation stump ankle bones of the leg and foot femur fibula foot foot bone hallux hip joint knee leg	knee* leg legs lower limb* lower extremit* metatarsophalangeal metatars* partial foot patella* phalange* residual limb* supracondylar tansmetatarsal tarsal*

Concept	Controlled Vocabulary	Keywords
	leg bone lower limb metatarsal bone midtarsal joint patella tarsal bone tarsometatarsal joint tibia toe toe phalanx **PubMed (MeSH)** ankle ankle joint femur fibula foot foot bones foot joints hallux hip hip joint hip prostheses knee knee joint knee prosthesis leg leg bones lower extremity metatarsal bones patella tarsal bones tarsal joints tibia toe joint toe phalanges toes	tarsometatarsal thigh* through knee through the knee tibia* toe toes transcondylar transfemoral transmalleolar transmetatarsal transtarsal transtibial unilateral *word variations have been searched
KQ1 Rehabilitation Settings	**EMBASE (EMTREE)** community-based rehabilitation hospital outpatient care rehabilitation rehabilitation center telerehabilitation **PubMed (MeSH)**	acute inpatient rehabilitation ambulatory care inpatient rehabilitation facilit* inpatient subacute intensive outpatient long-term acute care hospital* outpatient rehabilitation skilled nursing facility telerehabilitation

Concept	Controlled Vocabulary	Keywords
	ambulatory care hospitals hospitals, rehabilitation rehabilitation rehabilitation centers telerehabilitation	*word variations have been searched
KQ2 Artificial Limbs/Prosthetics	**EMBASE (EMTREE)** above knee prosthesis ankle prosthesis artificial limb below knee prosthesis dynamic response foot prosthesis electric limb prosthesis foot prosthesis hip disarticulation prosthesis limb prosthesis leg prosthesis lower leg prosthesis prosthesis syme prosthesis talar ankle prosthesis total ankle prosthesis **PubMed (MeSH)** artificial limbs hip prosthesis joint prosthesis knee prosthesis prostheses and implants osseointegration	artificial limb bionic limb prosthes* *word variations have been searched
<u>Socket/Interface</u>		above knee prosthe* below knee prosthe* hip disarticulation prosthe* hydrostatic design prosthe* ischial containment prosthe* ischial ramus containment prosthe* knee disarticulation prosthe* patella tendon bearing design patella* tendon bearing prosthe* prosthe*stump prosthe* through knee prosthe* total contact prosthe* total surface bearing prosthe* VASS prosthe*

Concept	Controlled Vocabulary	Keywords
		*word variations have been searched
Suspension system		anatomic fit belt corset elevated vacuum lanyard locking mechanism osseointegration pin suspension supracondylar suspension suspension sleeve thigh cuff vacuum assisted
Knee		c leg hydracadence hydromechanical knee manual locking knee mauch sns mauch s-n-s microprocessor* non-microprocessor polycentric power knee rheo knee single axis swing and stance weight activated stance *word variations have been searched
Foot/Ankle		ankle biome foot cheetah dynamic response energy storing flex foot flexible keel foot hydraulic foot microprocessor foot multi axial foot power foot

Concept	Controlled Vocabulary	Keywords
		powered dorsiflexion powered plantarflexion PROPRIO foot running foot single axis foot ankle cushioned heel vertical shock
KQ3 Non-surgical Interventions	**EMBASE (EMTREE)** cryoablation nerve stimulation pulsed radiofrequency ablation radiofrequency ablation spinal cord stimulation transcutaneous electrical nerve stimulation **PubMed (MeSH)** ablation techniques cryosurgery spinal cord stimulation transcutaneous electric nerve stimulation	cryoablation peripheral nerve stimulat* pulsed radiofrequency ablation radiofrequency ablation spinal cord stimulat* transcutaneous electric* nerve stimulation *word variations have been searched
KQ4 Biopsychosocial	**EMBASE (EMTREE)** acceptance and commitment therapy assertive training cognitive behavioral therapy cognitive processing therapy counseling systemic desensitization, psychological graded exposure therapy dialectical behavior therapy emotion-focused therapy eye movement desensitization and reprocessing long term exposure mindfulness-based stress reduction motivational interviewing peer group problem solving therapy psychoanalysis psychoeducation psychotherapy rational emotive behavior therapy	accelerated resolution therapy acceptance and commitment therapy cognitive behavioral therapy* cognitive processing therapy counseling dialectical behavior therapy emotion focused therapy assertive communication eye movement desensitization and reprocessing interpersonal effectiveness** problem solving therapy psychoanalysis psychoeducation psychotherapy rational emotive therapy mindfulness based stress reduction motivational interviewing pain reprocessing patient education peer education peer mentor peer support

Concept	Controlled Vocabulary	Keywords
	self care' social competence **PubMed (MeSH)** cognitive behavioral therapy counseling dialectical behavior therapy psychoanalysis psychotherapy desensitization, psychologic	peer visit problem solving therapy prolonged exposure psychoeducation psychological preparation** rational emotive therapy self management** social skills** support group* trauma-focused psychotherapy therapeutic pain** *word variations have been searched **indicates that this term will be searched near 'education or training' in the search statement
KQ5 Surgical Interventions	**EMBASE (EMTREE)** osseointegration revision surgery surgery **PubMed (MeSH)** reoperation surgical procedures, operative	agonist-antagonist-myoneural-interface bone bridg* bone spurs Bruckner Burgess compress implant eopra ERTL excision fibulectomy fishmouth gritti-stokes guillotine heterotopic ossification intraoperative cyroablation joint replacement long posterior flap nerve cap* neural interfaces neurectomy osseointegrat* opra implant regenerative peripheral neural interface reoperation revision surgery surgery targeted muscle reinnervation vascularized denervated muscle target*

Concept	Controlled Vocabulary	Keywords
		*word variations have been searched
KQ6 Dermatological & Regenerative Medicine	**EMBASE (EMTREE)** aboboutlinum toxin a botulinum toxin a dermatological laser incobotulinum toxin a iontophoresis microwave thermotherapy pulsed dye laser stem cell thrombocyte rich plasma tissue engineering xeomin **PubMed (MeSH)** botulinum toxins, type a iontophoresis lasers, dye stem cells tissue engineering	ablative fractional resurfacing laser* ablative laser* botox injection* botulinum injection* brella patches co2 laser* fractional laser* iontophoresis laser hair removal microwave ablation miradry pigment laser* platelet rich plasma pulsed dye laser* scar resurfacing laser* stem cells targeted alkali thermolysis tissue engineering *word variations have been searched
KQ7 Prevention	**EMBASE (EMTREE)** debridement diet therapy endovascular surgery foot care limb salvage occupational therapy orthopedic equipment orthopedic shoe orthosis patient education physiotherapy salvage therapy smoking cessation surgery weight loss program **PubMed (MeSH)** debridement diet therapy endovascular procedures occupational therapy	debridement diet therapy crow boot dietary intervention* endovascular procedure* endovascular surger* foot care** foot inspec** foot risk scor* insert* limb salvage occupational therapy orthopedic equipment orthopedic shoe orthosis patient education physical therapy physiotherapy podiatric care salvage therapy smoking cessation surgery total contact cast

Concept	Controlled Vocabulary	Keywords
	orthotic devices physical therapy modalities salvage therapy smoking cessation weight reduction programs	walker weight loss program *word variations have been searched ** indicates that this term will be searched near 'education or training' in the search statement
KQ8 Sexual Intimacy and Health	**EMBASE (EMTREE)** couples therapy intimacy** mindfulness occupational therapy psychotherapy sex therapy **PubMed (MeSH)** couples therapy mindfulness occupational therapy psychotherapy sex therapy	couples therapy intimacy** mindfulness occupational therapy pelvic floor therapy sex** sex therapy sexual health apps psychotherapy trauma processing ** indicates that this term will be searched near 'mindfulness' or 'occupational therapy' or 'psychotherapy'' in the search strategy
KQ9 Models of Care	**EMBASE (EMTREE)** case management multidisciplinary team **PubMed (MeSH)** case managers	amput* care care manag* ** case manag* ** care model** collaborative care** integrat* inter-disciplinary** mental health care** multi-disciplinary** orthotic care** prosthetic care** *word variations have been searched **indicates that this term will be searched near 'amputation care' or 'rehabilitation'
KQ10 Comparative Effectiveness of Rehab Interventions	**EMBASE (EMTREE)** augmented reality brain depth stimulation graded motor imagery home exercise program kinesiotherapy mirror therapy occupational therapy physiotherapy	activities of daily living ambulation augmented reality balance training daily life activity electromagnetic shielding functional training gait training graded motor imagery

Concept	Controlled Vocabulary	Keywords
	recreational therapy transcutaneous electrical nerve stimulation virtual reality **PubMed (MeSH)** augmented reality mirror movement therapy occupational therapy physical therapy modalities recreation therapy transcutaneous electrical nerve stimulation virtual reality	h wave home exercise program kinesiotherapy mirror therapy mobility training normatech occupational therapy physical therapy prosthetic use range of motion program* recreational therapy relax night care residual limb management therapeutic exercise transcutaneous electrical nerve stimulation virtual reality *word variations have been searched

Concept	Controlled Vocabulary	Keywords
KQ11 Gender	**EMBASE (EMTREE)** male to female transgender gender nonbinary **PubMed (MeSH)** transgender persons	bigender cisgender gender fluid gender nonconforming male male-to-female non-binary transfeminine transgender transwoman two spirit

Concept	Controlled Vocabulary	Keywords
KQ 12 Pharmacological	**EMBASE (EMTREE)** amitriptyline botulinum toxin A' capsaicin carbamazepine citalopram clonidine codeine corticosteroid' dronabinol duloxetine epidural drug administration escitalopram fluoxetine' gabapentin ketamine morphine nortriptyline opiate pregabalin serotonin noradrenalin reuptake inhibitor serotonin uptake inhibitor tramadol **PubMed (MeSH)** Injections, epidural nerve block	amitriptyline botox injection* botulinum injection* capsaicin carbamazepine citalopram clonidine codeine corticosteroid injection* dronabinol duloxetine epidural injection* escitalopram fluoxetine gabapentin hydrocodone hydomorphone ketamine morphine nerve block* neuroma injection* nortriptyline oxycodone peripheral nerve injection* pregabalin qutenza patch tramadol

B. Search Strategies

Table G-2. EMBASE

Set Number	Concept	Search Statement
1	Amputation	('amputation'/exp OR 'amputation stump'/exp OR 'disarticulation'/exp OR 'hemicorporectomy'/exp OR 'hemipelvectomy'/exp OR amputation:ti,ab OR chopart:ti,ab OR disarticulation:ti,ab OR exarticulation:ti,ab OR hemicorporectomy:ti,ab OR hemipelvectomy:ti,ab OR 'limb loss':ti,ab OR lisfranc:ti,ab OR syme:ti,ab) AND [humans]/lim AND [english]/lim AND [2016-2024]/py
2	Amputation Sites	('amputation stump'/exp OR 'ankle'/exp OR 'bones of the leg and foot'/exp OR 'femur'/exp OR 'fibula'/exp OR 'foot'/exp OR 'foot bone'/exp OR 'hallux'/exp OR 'hip joint'/exp OR 'knee'/exp OR 'leg'/exp OR 'leg bone'/exp OR 'lower limb'/exp OR 'metatarsal bone'/exp OR 'patella'/exp OR 'tarsal bone'/exp OR 'tarsometatarsal joint'/exp OR 'tibia'/exp OR 'toe'/exp OR 'toe phalanx'/exp OR 'above knee':ti,ab OR 'above the knee':ti,ab OR 'amputation stump':ti,ab OR ankle*:ti,ab OR 'below knee':ti,ab OR 'below

Set Number	Concept	Search Statement
		the knee':ti,ab OR bilateral:ti,ab OR condyle*:ti,ab OR extremit*:ti,ab OR feet:ti,ab OR femur*:ti,ab OR fibula*:ti,ab OR foot:ti,ab OR hallu*:ti,ab OR hip:ti,ab OR hips:ti,ab OR knee*:ti,ab OR leg:ti,ab OR legs:ti,ab OR 'lower limb*':ti,ab OR 'lower extremit*':ti,ab OR metatarsophalangeal:ti,ab OR metatars*:ti,ab OR 'partial foot':ti,ab OR patella*:ti,ab OR phalange*:ti,ab OR 'residual limb*':ti,ab OR supracondylar:ti,ab OR tansmetetarsal:ti,ab OR tarsal*:ti,ab OR tarsometatarsal:ti,ab OR thigh*:ti,ab OR 'through knee':ti,ab OR 'through the knee':ti,ab OR tibia*:ti,ab OR toe:ti,ab OR toes:ti,ab OR transcondylar:ti,ab OR transfemoral:ti,ab OR transmalleolar:ti,ab OR transmetatarsal:ti,ab OR transtarsal:ti,ab OR transtibial:ti,ab OR unilateral:ti,ab) AND [humans]/lim AND [english]/lim AND [2016-2024]/py
3	Combine Sets	#1 AND #2
4	Rehabilitation Settings	('rehabilitation'/exp OR rehabilitation:ti,ab) AND ('acute inpatient':ti,ab OR 'ambulatory care':ti,ab OR 'nursing home*':ti,ab OR outpatient:ti,ab OR 'skilled nursing facilit*':ti,ab) OR subacute:ti,ab OR 'sub acute':ti,ab
5	Prostheses: Socket	socket*:ti,ab AND ('hip'/exp OR 'knee'/exp OR hip:ti,ab OR knee:ti,ab OR transfemoral:ti,ab OR transtibial:ti,ab)
6	Prostheses: Suspension	suspension:ti,ab AND ('anatomic fit':ti,ab OR belt:ti,ab OR corset:ti,ab OR cuff:ti,ab OR 'elevated vacuum':ti,ab OR lanyard:ti,ab OR 'locking mechanism':ti,ab OR osseointegration:ti,ab OR 'pin lock':ti,ab OR sleeve:ti,ab OR suction:ti,ab OR supracondylar:ti,ab OR 'vacuum assisted':ti,ab)
7	Prostheses: Ankle, Hip, Knee, Foot	'knee prosthesis'/exp OR 'ankle prosthesis'/exp OR 'hip prosthesis'/exp OR 'foot prosthesis'/exp OR 'knee prothesis':ti,ab OR 'ankle prosthesis':ti,ab OR 'foot prothesis':ti,ab OR 'hip prosthesis':ti,ab
8	Non-surgical Interventions	'cryoablation'/exp OR 'nerve stimulation'/exp OR 'pulsed radiofrequency ablation'/exp OR 'spinal cord stimulation'/exp OR 'cryoablation':ti,ab OR 'nerve stimulat*':ti,ab OR 'radiofrequency ablation':ti,ab OR 'spinal cord stimulat*':ti,ab OR 'transcutaneous electric* nerve stimulation':ti,ab
9	Biopsychosocial	'assertive training'/exp OR 'densensitization, psychologic' OR 'eye movement desensitization and reprocessing'/exp OR 'long term exposure'/exp OR 'mindfulness-based stress reduction'/exp OR 'motivational interviewing'/exp OR 'peer group'/exp OR 'psychoanalysis'/exp OR 'psychoeducation'/exp OR 'psychotherapy'/exp OR 'self care'/exp OR 'social competence'/exp OR 'eye movement desensitization and reprocessing':ti,ab OR therapy:ti,ab OR psychoanalysis:ti,ab OR psychotherapy:ti,ab OR 'mindfulness based stress reduction':ti,ab OR peer:ti,ab OR psychoeducation:ti,ab OR 'support group':ti,ab OR ((training OR education) NEAR/2 ('assertive communication' OR 'interpersonal effectiveness' OR 'pain reprocessing' OR 'psychological preparation' OR 'prolonged exposure' OR 'self management' OR 'social skills' OR 'therapeutic pain'))
10	Surgical Interventions	'revision surgery'/exp OR 'surgery'/exp OR reoperation:ti,ab OR 'revision surgery':ti,ab OR surgery:ti,ab
11	Dermatological & Regenerative Medicine	'botulinum toxin a'/exp OR 'dermatological laser'/exp OR 'iontophoresis'/exp OR 'microwave thermotherapy'/exp OR 'pulsed dye laser'/exp OR 'stem cell'/exp OR 'thrombocyte rich plasma'/exp OR 'tissue engineering'/exp OR 'ablative fractional resurfacing laser*':ti,ab OR 'ablative laser*':ti,ab OR 'allergy testing':ti,ab OR 'botox injection*':ti,ab OR 'botulinum injection*':ti,ab OR 'brella patches':ti,ab OR 'co2 laser*':ti,ab OR 'fractional laser*' OR 'histamine testing':ti,ab OR iontophoresis:ti,ab OR 'laser hair removal':ti,ab OR microneedling:ti,ab OR 'microwave

Set Number	Concept	Search Statement
		ablation':ti,ab OR miradry:ti,ab OR 'pigment laser*':ti,ab OR 'platelet rich plasma':ti,ab OR 'pulsed dye laser*':ti,ab OR 'scar resurfacing laser*':ti,ab OR 'silicon patch*':ti,ab OR 'stem cells':ti,ab OR 'targeted alkali thermolysis':ti,ab OR 'tissue engineering':ti,ab
12	Prevention	'endovascular surgery'/exp OR 'debridement'/exp OR 'diet therapy'/exp OR 'foot care'/exp OR 'limb salvage'/exp OR 'occupational therapy'/exp OR 'orthopedic shoe'/exp OR 'orthosis'/exp OR 'patient education'/exp OR 'physiotherapy'/exp OR 'salvage therapy'/exp OR 'smoking cessation'/exp OR 'weight loss program'/exp OR 'charcot restraint orthotic walker':ti,ab OR 'crow boot':ti,ab OR debridement:ti,ab OR 'diagnostic test*':ti,ab OR 'dietary intervention*':ti,ab OR 'diet therapy':ti,ab OR 'endovascular procedure*':ti,ab OR ((education OR training) NEAR/2 foot) OR 'foot risk scor*':ti,ab OR 'limb salvage':ti,ab OR 'occupational therapy':ti,ab OR orthotics:ti,ab OR orthosis:ti,ab OR 'patient education':ti,ab OR physiotherapy:ti,ab OR 'physical therapy':ti,ab OR 'podiatric care':ti,ab OR 'salvage therapy':ti,ab OR 'smoking cessation':ti,ab OR 'total contact cast':ti,ab OR walker:ti,ab OR 'weight loss program':ti,ab
13	Sexual Health and Intimacy	'couples therapy'/exp OR 'psychotherapy'/exp OR 'sexuality'/exp OR 'couples therapy':ti,ab OR psychotherapy:ti,ab OR (intima* NEAR/2 (mindfulness OR 'occupational therapy')) OR 'sex therapy'/exp OR 'sex therapy':ti,ab OR sexuality:ti,ab OR 'pelvic floor therapy':ti,ab OR 'sexual health apps':ti,ab OR 'trauma processing':ti,ab
14	Models of Care	'case management'/exp OR 'multidisciplinary team'/exp OR (rehabilitation NEAR/2 ('care manag*' OR 'case manag*' OR collaborative OR integrat* OR interdisciplinary OR 'multi disciplinary' OR 'mental health care')) OR 'orthotic care':ti,ab OR 'prosthetic care':ti,ab
15	Rehabilitation Interventions	'augmented reality'/exp OR 'brain depth stimulation'/exp OR 'daily life activity'/exp OR 'graded motor imagery'/exp OR 'home exercise program'/exp OR 'mirror therapy'/exp OR 'occupational therapy'/exp OR 'physiotherapy'/exp OR 'recreational therapy'/exp OR 'transcutaneous electrical nerve stimulation'/exp OR 'virtual reality'/exp OR ((ambulation OR mobility) NEAR/2 training) OR 'activities of daily living':ti,ab OR 'augmented reality':ti,ab OR 'balance training':ti,ab OR 'electromagnetic shielding':ti,ab OR 'functional training':ti,ab OR 'gait training':ti,ab OR 'graded motor imagery':ti,ab OR 'h wave':ti,ab OR 'home exercise program':ti,ab OR 'mirror therapy':ti,ab OR normatech:ti,ab OR 'occupational therapy':ti,ab OR 'physical therapy':ti,ab OR 'prosthetic use':ti,ab OR 'range of motion program':ti,ab OR 'recreational therapy':ti,ab OR 'relax night care':ti,ab OR 'residual limb management':ti,ab OR 'therapeutic exercise':ti,ab OR 'transcutaneous electrical nerve stimulation':ti,ab OR 'virtual reality':ti,ab
16	Gender	'male to female transgender'/exp OR 'gender nonbinary'/exp OR 'transgender persons'/exp OR bigender:ti,ab OR cisgender:ti,ab OR 'gender fluid':ti,ab OR 'gender nonconforming':ti,ab OR male:ti,ab OR 'male to female':ti,ab OR 'non binary':ti,ab OR 'trans feminine':ti,ab OR transfeminine:ti,ab OR transgender:ti,ab OR 'two spirit':ti,ab
17	Pharmacology	'amitriptyline'/exp OR 'botulinum toxin a'/exp OR 'capsaicin'/exp OR 'carbamazepine'/exp OR 'citalopram'/exp OR 'clonidine'/exp OR 'codeine'/exp OR 'corticosteriod' OR 'dronabinol'/exp OR 'duloxetine'/exp OR 'epidural drug administration'/exp OR 'escitalopram'/exp OR 'fluoxetine'/exp OR 'gabapentin'/exp OR 'ketamine'/exp OR 'morphine'/exp OR 'nortriptyline'/exp OR 'opiate'/exp OR 'pregabalin'/exp OR 'tramadol'/exp OR amitriptyline:ti,ab OR 'botox injection*':ti,ab OR

Set Number	Concept	Search Statement
		'botulinum injection*':ti,ab OR capsaicin:ti,ab OR carbamazepine:ti,ab OR citalopram:ti,ab OR clonidine:ti,ab OR codeine:ti,ab OR 'corticosteriod injection*':ti,ab OR dextromethorphan:ti,ab OR diclofenac:ti,ab OR dronabinol:ti,ab OR duloxetine:ti,ab OR 'epidural injection*':ti,ab OR escitalopram:ti,ab OR fluoxetine:ti,ab OR hydrocodone:ti,ab OR gabapentin:ti,ab OR hydromorphone:ti,ab OR ketamine:ti,ab OR memantine:ti,ab OR mexiletine:ti,ab OR morphine:ti,ab OR 'nerve block*':ti,ab OR 'neuroma injection':ti,ab OR nortriptyline:ti,ab OR oxycodone:ti,ab OR 'peripheral nerve injection':ti,ab OR pregabalin:ti,ab OR 'quentenza patch':ti,ab OR tramadol:ti,ab
18	Exclude Publication Types	'editorial'/exp OR 'letter'/exp OR 'medical illustration'/exp OR 'book'/exp OR 'poster'/exp OR 'conference abstract'/exp OR 'conference paper'/exp OR 'conferences and congresses'/exp OR 'conference review'/exp OR 'erratum'/exp OR 'symposium'/exp OR 'short survey'/exp OR 'note'/exp OR 'chapter'/it OR 'conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'review'/it OR 'short survey'/it OR abstract:nc OR annual:nc OR conference:nc OR 'conference proceeding':pt OR 'conference review':it OR congress:nc OR meeting:nc OR sessions:nc OR symposium:nc OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR comment:ti OR book:pt OR comment:ab,ti OR annual:ab,ti OR 'conference proceeding':ab,ti OR note:ab,ti OR meeting:ab,ti OR sessions:ab,ti OR 'short survey':ab,ti
19	Combine Sets	#3 AND (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17) NOT #18

Table G-3. PubMed

Set Number	Concept	Search Statement
1	Amputation	"Amputation Stumps"[Mesh] OR "Amputation, Surgical"[Mesh] OR "Disarticulation"[Mesh] OR "Hemipelvectomy"[Mesh] OR amputation[tiab] OR chopart[tiab] OR disarticulation[tiab] OR exarticulation[tiab] OR hemicorporectomy[tiab] OR hemipelvectomy[tiab] OR "limb loss"[tiab] OR lisfranc[tiab] OR syme[tiab]
2	Amputation Sites	"Ankle"[Mesh] OR "Femur"[Mesh] OR "Fibula"[Mesh] OR "Foot"[Mesh] OR "Foot Joints"[Mesh] OR "Foot Bones"[Mesh] OR "Hallux"[Mesh] OR "Hip"[Mesh] OR "Hip Joint"[Mesh] OR "Leg"[Mesh] OR "Leg Bones"[Mesh] OR "Lower Extremity"[Mesh] OR "Metatarsal Bones"[Mesh] OR "Patella"[Mesh] OR "Tarsal Joints"[Mesh] OR "Tarsal Bones"[Mesh] OR "Tibia"[Mesh] OR "above knee"[tiab] OR "above the knee"[tiab] OR "amputation stump"[tiab] OR ankle*[tiab] OR "below knee"[tiab] OR "below the knee"[tiab] OR bilateral[tiab] OR condyle*[tiab] OR extremit*[tiab] OR feet[tiab] OR femur*[tiab] OR fibula*[tiab] OR foot[tiab] OR hallu*[tiab] OR hip[tiab] OR hips[tiab] OR knee*[tiab] OR leg[tiab] OR legs[tiab] OR "lower limb*"[tiab] OR "lower extremit*"[tiab] OR metatarsophalangeal[tiab] OR metatars*[tiab] OR "partial foot"[tiab] OR patella*[tiab] OR phalange*[tiab] OR "residual limb*"[tiab] OR supracondylar[tiab] OR tarsal*[tiab] OR tarsometatarsal[tiab] OR thigh*[tiab] OR "through knee"[tiab] OR "through the knee"[tiab] OR tibia*[tiab] OR toe[tiab] OR toes[tiab] OR transcondylar[tiab] OR transfemoral[tiab] OR transmalleolar[tiab] OR transmetatarsal[tiab] OR transtarsal[tiab] OR transtibial[tiab] OR unilateral[tiab]
3	Combine Sets	#1 AND #2

Set Number	Concept	Search Statement
4	Rehabilitation Settings	("Rehabilitation"[Mesh] OR rehabilitation[tiab]) AND ("Ambulatory Care"[Mesh] OR "acute inpatient"[tiab] OR "ambulatory care" [tiab] OR "outpatient" [tiab] OR "skilled nursing facilit*"[tiab] OR "subacute"[tiab] OR "sub-acute"[tiab])
5	Prostheses: Socket	(socket*[tiab]) AND ("Hip"[Mesh] OR "Knee"[Mesh] OR hip[tiab] OR knee[tiab] OR transfemoral[tiab] OR transtibial[tiab])
6	Prostheses: Suspension	suspension[tiab] AND ("anatomic fit "[tiab] OR belt[tiab] OR corset[tiab] OR cuff[tiab] OR "elevated vacuum "[tiab] OR lanyard[tiab] OR "locking mechanism "[tiab] OR osseointegration[tiab] OR "pin lock "[tiab] OR sleeve[tiab] OR suction[tiab]OR supracondylar[tiab] OR "vacuum assisted "[tiab])
7	Prostheses: Ankle, Hip, Knee, Foot	"Knee Prosthesis"[Mesh] OR "Hip Prosthesis"[Mesh] OR "knee prosthesis"[tiab] OR "hip prosthesis"[tiab] OR "ankle prosthesis"[tiab]
8	Non-surgical Interventions	Ablation Techniques"[Mesh] OR "Cryosurgery"[Mesh] OR "Spinal Cord Stimulation"[Mesh] OR "Transcutaneous Electric Nerve Stimulation"[Mesh] OR cryoablation[tiab] OR "nerve stimulat*"[tiab] OR "radiofrequency ablation"[tiab] OR "spinal cord stimulation"[tiab] OR "transcutaneous electric* nerve stimulation"[tiab]
9	Biopsychosocial	"Counseling"[Mesh] OR "Psychoanalysis"[Mesh] OR "Psychotherapy"[Mesh] OR "eye movement desensitization and reprocessing "[tiab] OR therapy[tiab] OR psychoanalysis[tiab] OR psychotherapy[tiab] OR "mindfulness based stress reduction "[tiab] OR peer[tiab] OR psychoeducation[tiab] OR "support group "[tiab] OR ((training[tiab] OR education[tiab]) AND ("assertive communication"[tiab] OR "interpersonal effectiveness"[tiab] OR "pain reprocessing"[tiab] OR "psychological preparation"[tiab] OR "prolonged exposure"[tiab] OR "self management"[tiab] OR "social skills"[tiab] OR "therapeutic pain"[tiab]))
10	Surgical Interventions	"Surgical Procedures, Operative"[Mesh] OR "Reoperation"[Mesh] OR "revision surgery"[tiab] OR surgery[tiab] OR reoperation[tiab]
11	Dermatological & Regenerative Medicine	"Botulinum Toxins, Type A"[Mesh] OR "Stem Cells"[Mesh] OR "Tissue Engineering"[Mesh] OR "Iontophoresis"[Mesh] OR "Lasers, Dye"[Mesh] OR "ablative fractional resurfacing laser*"[tiab] OR "ablative laser*"[tiab] OR "botox injection*"[tiab] OR "botulinum injection*"[tiab] OR "brella patches"[tiab] OR "co2 laser*"[tiab] OR "fractional laser*" OR iontophoresis[tiab] OR "laser hair removal"[tiab] OR "microwave ablation"[tiab] OR miradry[tiab] OR "pigment laser*"[tiab] OR "platelet rich plasma"[tiab] OR "pulsed dye laser*"[tiab] OR "scar resurfacing laser*"[tiab] OR "stem cells"[tiab] OR "targeted alkali thermolysis"[tiab] OR "tissue engineering"[tiab]OR "ablative fractional resurfacing laser*"[tiab] OR "ablative laser*"[tiab] OR "botox injection*"[tiab] OR "botulinum injection*"[tiab] OR "brella patches"[tiab] OR "co2 laser*"[tiab] OR "fractional laser*" OR iontophoresis[tiab] OR "laser hair removal"[tiab] OR "microwave ablation"[tiab] OR miradry[tiab] OR "pigment laser*"[tiab] OR "platelet rich plasma"[tiab] OR "pulsed dye laser*"[tiab] OR "scar resurfacing laser*"[tiab] OR "stem cells"[tiab] OR "targeted alkali thermolysis"[tiab] OR "tissue engineering"[tiab] OR"allergy testing"[tiab] OR "histamine testing"[tiab] OR microneedling[tiab] OR"silicon patch*"[tiab]
12	Prevention	"debridement"[Mesh] OR "Diet Therapy"[Mesh] OR "Endovascular Procedures"[Mesh] OR "Occupational Therapy"[Mesh] OR "Orthotic Devices"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Salvage Therapy"[Mesh] OR "Smoking Cessation"[Mesh] OR "Weight Reduction Programs"[Mesh] OR "charcot restraint orthotic walker"[tiab] OR "crow

Set Number	Concept	Search Statement
		boot"[tiab] OR debridement[tiab] OR "diagnostic test*"[tiab] OR "dietary intervention*"[tiab] OR "diet therapy"[tiab] OR "endovascular procedure*"[tiab] OR ((education OR training) AND foot) OR "foot risk scor*"[tiab] OR "limb salvage"[tiab] OR "occupational therapy"[tiab] OR orthotics[tiab] OR orthosis[tiab] OR "patient education"[tiab] OR physiotherapy[tiab] OR "physical therapy"[tiab] OR "podiatric care"[tiab] OR "salvage therapy"[tiab] OR "smoking cessation"[tiab] OR "total contact cast"[tiab] OR walker[tiab] OR "weight loss program"[tiab]
13	Sexual Health and Intimacy	"Couples Therapy"[Mesh] OR "Psychotherapy"[Mesh] OR Sexuality[MeSH] OR "couples therapy"[tiab] OR psychotherapy[tiab] OR (intima* AND(mindfulness OR "occupational therapy")) OR "sex therapy"[Mesh] OR "sex therapy"[tiab] OR sexuality[tiab] OR "pelvic floor therapy"[tiab] OR "sexual health apps"[tiab] OR "trauma processing"[tiab]
14	Models of Care	"Case Management"[Mesh] OR ("Rehabilitation"[Mesh] or rehabilitation[tiab] AND ("care manag*"[tiab] OR "case manag*"[tiab] OR collaborative[tiab] OR integrat*[tiab] OR interdisciplinary[tiab] OR "multi disciplinary"[tiab]OR "mental health care"[tiab])) OR "orthotic care"[tiab] OR "prosthetic care"[tiab]
15	Rehabilitation Interventions	"Activities of Daily Living"[Mesh] OR "Augmented Reality"[Mesh] OR "Mirror Movement Therapy"[Mesh] OR "Occupational Therapy"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Transcutaneous Electric Nerve Stimulation"[Mesh] OR "Virtual Reality"[Mesh] OR ((ambulation OR mobility) AND training) OR "activities of daily living"[tiab] OR "augmented reality"[tiab] OR "balance training"[tiab] OR "electromagnetic shielding"[tiab] OR "functional training"[tiab] OR "gait training"[tiab] OR "graded motor imagery"[tiab] OR "h wave"[tiab] OR "home exercise program"[tiab] OR "mirror therapy"[tiab] OR normatech[tiab] OR "occupational therapy"[tiab] OR "physical therapy"[tiab] OR "prosthetic use"[tiab] OR "range of motion program"[tiab] OR "recreational therapy"[tiab] OR "relax night care"[tiab] OR "residual limb management"[tiab]
16	Gender	"Transgender Persons"[Mesh] OR "Male"[Mesh] OR "Female"[Mesh] OR "Gender Identity"[Mesh]bigender[tiab] OR cisgender[tiab] OR "gender fluid"[tiab] OR "gender nonconforming"[tiab] OR male[tiab] OR "male to female"[tiab] OR "non binary"[tiab] OR "trans feminine"[tiab] OR transfeminine[tiab] OR transgender[tiab] OR "two spirit"[tiab]
17	Pharmacology	amitriptyline[tiab] OR "botox injection*"[tiab] OR "botulinum injection*"[tiab] OR capsaicin[tiab] OR carbamazepine[tiab] OR citalopram[tiab] OR clonidine[tiab] OR codeine[tiab] OR "corticosteriod injection*"[tiab] OR dextromethorphan[tiab] OR diclofenac[tiab] OR dronabinol[tiab] OR duloxetine[tiab] OR "epidural injection*"[tiab] OR escitalopram[tiab] OR fluoxetine[tiab] OR hydrocodone[tiab] OR gabapentin[tiab] OR hydromorphone[tiab] OR ketamine[tiab] OR memantine[tiab] OR mexiletine[tiab] OR morphine[tiab] OR "nerve block*"[tiab] OR "neuroma injection*"[tiab] OR nortriptyline[tiab] OR oxycodone[tiab] OR "peripheral nerve injection*"[tiab] OR pregabalin[tiab] OR "quentenza patch*"[tiab] OR tramadol[tiab]
18	Exclude Publication Types	"comment"[Publication Type] OR "editorial"[Publication Type] OR "letter"[Publication Type] OR "news"[Publication Type] OR "Book Illustrations"[Publication Type] OR "animal*"[Title/Abstract] OR "rat"[Title/Abstract] OR "rats"[Title/Abstract] OR "mouse"[Title/Abstract] OR "mice"[Title/Abstract] OR "goat*"[Title/Abstract] OR "pig"[Title/Abstract] OR "pigs"[Title/Abstract] OR "cadaver*"[Title/Abstract] OR "dog"[Title/Abstract]

Set Number	Concept	Search Statement
		OR "dogs"[Title/Abstract] OR "monkey*"[Title/Abstract] OR "ape"[Title/Abstract] OR "apes"[Title/Abstract] OR "annual"[Title/Abstract] OR "book"[Title/Abstract] OR "conference"[Title/Abstract] OR "conference abstract"[Title/Abstract] OR "conference paper"[Title/Abstract] OR "conference proceeding"[Title/Abstract] OR "conference review"[Title/Abstract] OR "congress"[Title/Abstract] OR "editorial"[Title/Abstract] OR "erratum"[Title/Abstract] OR "letter"[Title/Abstract] OR "note"[Title/Abstract] OR "meeting"[Title/Abstract] OR "sessions"[Title/Abstract] OR "short survey"[Title/Abstract] OR "symposium"[Title/Abstract]
19	Combine Sets	(#3 AND (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17)) NOT #18

Table G-4. CINAHL

Set Number	Concept	Search Statement
	Limits	Limiters - Publication Date: 20160101-20240331; Peer Reviewed; Human; Language: English
1	Amputation	TI (amputation OR chopart OR disarticulation OR exarticulation OR hemicorporectomy OR hemipelvectomy OR "limb loss" OR lisfranc OR syme) OR AB (amputation OR chopart OR disarticulation OR exarticulation OR hemicorporectomy OR hemipelvectomy OR "limb loss" OR lisfranc OR syme) OR MM ("Amputation Stumps" OR "Amputation, Surgical" OR "Disarticulation" OR "Hemipelvectomy")
2	Amputation Sites	TI ("above knee" OR "above the knee" OR "amputation stump" OR ankle* OR "below knee" OR "below the knee" OR bilateral OR condyle* OR extremit* OR feet OR femur* OR fibula* OR foot OR hallu* OR hip OR hips OR knee* OR leg OR legs OR "lower limb*" OR "lower extremit*" OR metatarsophalangeal OR metatars* OR "partial foot" OR patella* OR phalange* OR "residual limb*" OR supracondylar OR tarsal* OR tarsometatarsal OR thigh* OR "through knee" OR "through the knee" OR tibia* OR toe OR toes OR transcondylar OR transfemoral OR transmalleolar OR transmetatarsal OR transtarsal OR transtibial OR unilateral) OR AB ("above knee" OR "above the knee" OR "amputation stump" OR ankle* OR "below knee" OR "below the knee" OR bilateral OR condyle* OR extremit* OR feet OR femur* OR fibula* OR foot OR hallu* OR hip OR hips OR knee* OR leg OR legs OR "lower limb*" OR "lower extremit*" OR metatarsophalangeal OR metatars* OR "partial foot" OR patella* OR phalange* OR "residual limb*" OR supracondylar OR tarsal* OR tarsometatarsal OR thigh* OR "through knee" OR "through the knee" OR tibia* OR toe OR toes OR transcondylar OR transfemoral OR transmalleolar OR transmetatarsal OR transtarsal OR transtibial OR unilateral) OR MM ("Ankle" OR "Femur" OR "Fibula" OR "Foot" OR "Foot Joints" OR "Foot Bones" OR "Hallux" OR "Hip" OR "Hip Joint" OR "Leg" OR "Leg Bones" OR "Lower Extremity" OR "Metatarsal Bones" OR "Patella" OR "Tarsal Joints" OR "Tarsal Bones" OR "Tibia")
3	Rehabilitation Settings	TI (rehabilitation AND ("acute inpatient" OR "ambulatory care" OR "outpatient" OR "skilled nursing facilit*" OR "subacute" OR "sub-acute")) OR AB (rehabilitation AND ("acute inpatient" OR "ambulatory care" OR "outpatient" OR "skilled nursing facilit*" OR "subacute" OR "sub-acute")) OR MM ("Rehabilitation" AND "Ambulatory Care")
4	Rehabilitation Interventions	TI (((ambulation OR mobility) N/2 training) OR "activities of daily living" OR "augmented reality" OR "balance training" OR "electromagnetic

Set Number	Concept	Search Statement
		shielding" OR "functional training" OR "gait training" OR "graded motor imagery" OR "h wave" OR "home exercise program" OR "mirror therapy" OR normatech OR "occupational therapy" OR "physical therapy" OR "prosthetic use" OR "range of motion program" OR "recreational therapy" OR "relax night care" OR "residual limb management" OR "therapeutic exercise" OR "transcutaneous electrical nerve stimulation" OR "virtual reality") OR AB (((ambulation OR mobility) N/2 training) OR "activities of daily living" OR "augmented reality" OR "balance training" OR "electromagnetic shielding" OR "functional training" OR "gait training" OR "graded motor imagery" OR "h wave" OR "home exercise program" OR "mirror therapy" OR normatech OR "occupational therapy" OR "physical therapy" OR "prosthetic use" OR "range of motion program" OR "recreational therapy" OR "relax night care" OR "residual limb management" OR "therapeutic exercise" OR "transcutaneous electrical nerve stimulation" OR "virtual reality") OR MM ("Activities of Daily Living" OR "Augmented Reality" OR "Mirror Movement Therapy" OR "Occupational Therapy" OR "Physical Therapy Modalities" OR "Transcutaneous Electric Nerve Stimulation" OR "Virtual Reality")
5	Prevention	TI ("charcot restraint orthotic walker" OR "crow boot" OR debridement OR "diagnostic test*" OR "dietary intervention*" OR "diet therapy" OR "endovascular procedure*" OR ((education OR training) N/2 foot) OR "foot risk scor*" OR "limb salvage" OR "occupational therapy" OR orthotics OR orthosis OR "patient education" OR physiotherapy OR "physical therapy" OR "podiatric care" OR "salvage therapy" OR "smoking cessation" OR "total contact cast" OR walker OR "weight loss program") OR AB ("charcot restraint orthotic walker" OR "crow boot" OR debridement OR "diagnostic test*" OR "dietary intervention*" OR "diet therapy" OR "endovascular procedure*" OR ((education OR training) N/2 foot) OR "foot risk scor*" OR "limb salvage" OR "occupational therapy" OR orthotics OR orthosis OR "patient education" OR physiotherapy OR "physical therapy" OR "podiatric care" OR "salvage therapy" OR "smoking cessation" OR "total contact cast" OR walker OR "weight loss program") OR MM ("Debridement" OR "Diet Therapy" OR "Endovascular Procedures" OR "Occupational Therapy" OR "Orthotic Devices" OR "Physical Therapy Modalities" OR "Salvage Therapy" OR "Smoking Cessation" OR "Weight Reduction Programs")
6	Sexual Health and Intimacy	TI ("couples therapy" OR psychotherapy OR (intima* N/2(mindfulness OR "occupational therapy")) OR "sex therapy" OR "sex therapy" OR sexuality OR "pelvic floor therapy" OR "sexual health apps" OR "trauma processing") OR AB ("couples therapy" OR psychotherapy OR (intima* N/2(mindfulness OR "occupational therapy")) OR "sex therapy" OR "sex therapy" OR sexuality OR "pelvic floor therapy" OR "sexual health apps" OR "trauma processing") OR MM ("Couples Therapy" OR "Psychotherapy")
7	Gender	TI (bigender OR cisgender OR "gender fluid" OR "gender nonconforming" OR male OR "male to female" OR "non binary" OR "trans feminine" OR transfeminine OR transgender OR "two spirit") OR AB (bigender OR cisgender OR "gender fluid" OR "gender nonconforming" OR male OR "male to female" OR "non binary" OR "trans feminine" OR transfeminine OR transgender OR "two spirit") OR MM ("male to female transgender " OR "gender nonbinary " OR "transgender persons ")
8	Combine Sets	S1 AND S2
9	Combine Sets	(S1 AND S2) AND (S3 OR S4 OR S5 OR S6 OR S7)

Table G-5. PsychINFO

Set Number	Concept	Search Statement
	Limits	Limiters - Publication Date: 20160101-20240331; Peer Reviewed; Human; Language: English
1	Amputation	TI (amputation OR chopart OR disarticulation OR exarticulation OR hemicorporectomy OR hemipelvectomy OR "limb loss" OR lisfranc OR syme) OR AB (amputation OR chopart OR disarticulation OR exarticulation OR hemicorporectomy OR hemipelvectomy OR "limb loss" OR lisfranc OR syme) OR MM ("Amputation Stumps" OR "Amputation, Surgical" OR "Disarticulation" OR "Hemipelvectomy")
2	Amputation Sites	TI ("above knee" OR "above the knee" OR "amputation stump" OR ankle* OR "below knee" OR "below the knee" OR bilateral OR condyle* OR extremit* OR feet OR femur* OR fibula* OR foot OR hallu* OR hip OR hips OR knee* OR leg OR legs OR "lower limb*" OR "lower extremit*" OR metatarsophalangeal OR metatars* OR "partial foot" OR patella* OR phalange* OR "residual limb*" OR supracondylar OR tarsal* OR tarsometatarsal OR thigh* OR "through knee" OR "through the knee" OR tibia* OR toe OR toes OR transcondylar OR transfemoral OR transmalleolar OR transmetatarsal OR transtarsal OR transtibial OR unilateral) OR AB ("above knee" OR "above the knee" OR "amputation stump" OR ankle* OR "below knee" OR "below the knee" OR bilateral OR condyle* OR extremit* OR feet OR femur* OR fibula* OR foot OR hallu* OR hip OR hips OR knee* OR leg OR legs OR "lower limb*" OR "lower extremit*" OR metatarsophalangeal OR metatars* OR "partial foot" OR patella* OR phalange* OR "residual limb*" OR supracondylar OR tarsal* OR tarsometatarsal OR thigh* OR "through knee" OR "through the knee" OR tibia* OR toe OR toes OR transcondylar OR transfemoral OR transmalleolar OR transmetatarsal OR transtarsal OR transtibial OR unilateral) OR MM ("Ankle" OR "Femur" OR "Fibula" OR "Foot" OR "Foot Joints" OR "Foot Bones" OR "Hallux" OR "Hip" OR "Hip Joint" OR "Leg" OR "Leg Bones" OR "Lower Extremity" OR "Metatarsal Bones" OR "Patella" OR "Tarsal Joints" OR "Tarsal Bones" OR "Tibia")
3	Rehabilitation Settings	TI (rehabilitation AND ("acute inpatient" OR "ambulatory care" OR "outpatient" OR "skilled nursing facilit*" OR "subacute" OR "sub-acute")) OR AB (rehabilitation AND ("acute inpatient" OR "ambulatory care" OR "outpatient" OR "skilled nursing facilit*" OR "subacute" OR "sub-acute")) OR MM ("Rehabilitation" AND "Ambulatory Care")
4	Biopsychosocial	TI ("eye movement desensitization and reprocessing " OR therapy OR psychoanalysis OR psychotherapy OR "mindfulness based stress reduction " OR peer OR psychoeducation OR "support group " OR ((training OR education) AND ("assertive communication" OR "interpersonal effectiveness" OR "pain reprocessing" OR "psychological preparation" OR "prolonged exposure" OR "self management" OR "social skills" OR "therapeutic pain"))) OR AB ("eye movement desensitization and reprocessing " OR therapy OR psychoanalysis OR psychotherapy OR "mindfulness based stress reduction " OR peer OR psychoeducation OR "support group " OR ((training OR education) AND ("assertive communication" OR "interpersonal effectiveness" OR "pain reprocessing" OR "psychological preparation" OR "prolonged exposure" OR "self management" OR "social skills" OR "therapeutic pain"))) OR MA ("Counseling" OR "Psychoanalysis" OR "Psychotherapy")
5	Prevention	TI ("charcot restraint orthotic walker" OR "crow boot" OR debridement OR "diagnostic test*" OR "dietary intervention*" OR "diet therapy" OR "endovascular procedure*" OR ((education OR training) N/2 foot) OR "foot

Set Number	Concept	Search Statement
		risk scor*" OR "limb salvage" OR "occupational therapy" OR orthotics OR orthosis OR "patient education" OR physiotherapy OR "physical therapy" OR "podiatric care" OR "salvage therapy" OR "smoking cessation" OR "total contact cast" OR walker OR "weight loss program") OR AB ("charcot restraint orthotic walker" OR "crow boot" OR debridement OR "diagnostic test*" OR "dietary intervention*" OR "diet therapy" OR "endovascular procedure*" OR ((education OR training) N/2 foot) OR "foot risk scor*" OR "limb salvage" OR "occupational therapy" OR orthotics OR orthosis OR "patient education" OR physiotherapy OR "physical therapy" OR "podiatric care" OR "salvage therapy" OR "smoking cessation" OR "total contact cast" OR walker OR "weight loss program") OR MM ("Debridement" OR "Diet Therapy" OR "Endovascular Procedures" OR "Occupational Therapy" OR "Orthotic Devices" OR "Physical Therapy Modalities" OR "Salvage Therapy" OR "Smoking Cessation" OR "Weight Reduction Programs")
6	Sexual Health and Intimacy	TI ("couples therapy" OR psychotherapy OR (intima* N/2(mindfulness OR "occupational therapy")) OR "sex therapy" OR "sex therapy" OR sexuality OR "pelvic floor therapy" OR "sexual health apps" OR "trauma processing") OR AB ("couples therapy" OR psychotherapy OR (intima* N/2(mindfulness OR "occupational therapy")) OR "sex therapy" OR "sex therapy" OR sexuality OR "pelvic floor therapy" OR "sexual health apps" OR "trauma processing") OR MM ("Couples Therapy" OR "Psychotherapy")
7	Gender	TI (bigender OR cisgender OR "gender fluid" OR "gender nonconforming" OR male OR "male to female" OR "non binary" OR "trans feminine" OR transfeminine OR transgender OR "two spirit") OR AB (bigender OR cisgender OR "gender fluid" OR "gender nonconforming" OR male OR "male to female" OR "non binary" OR "trans feminine" OR transfeminine OR transgender OR "two spirit") OR MM ("male to female transgender " OR "gender nonbinary " OR "transgender persons ")
8	Combine Sets	S1 AND S2
9	Combine Sets	(S1 AND S2) AND (S3 OR S4 OR S5 OR S6 OR S7)

Appendix H: Alternative Text Descriptions of Algorithm

The following outline narratively describes the Rehabilitation of Individuals with LLA Algorithm. An explanation of the purpose of the algorithm and description of the various shapes used within the algorithm can be found in the Algorithm section. The sidebars referenced within this outline can also be found in the Algorithm section.

Module A: Pre-Amputation

1. Module A begins with Box 1 in the shape of a rounded rectangle: “Patient is considered for lower limb amputation”
2. Box 1 connects to Box 2, in the shape of a hexagon: “Is a lower limb amputation surgery emergently needed?”
    a. If the answer is “Yes” to Box 2, then Box 3, in the shape of an oval: “Refer to **Module B**”
    b. If the answer is “No” to Box 2, then Box 4, in the shape of a rectangle: “Comprehensive Pre-Amputation Evaluation (See **Sidebars A and B**):
        - Consider implications of amputation for every level being considered and for alternative lower limb management strategies (e.g., alternate surgical approach or conservative management)
        - Consider how timing of amputation may affect functional outcomes.”
3. Box 4 connects to Box 5, in the shape of a hexagon: “Are there structural barriers, equipment needs, or other therapy goals that could improve anticipated function after amputation?”
    a. If the answer is “Yes” to Box 5, then Box 6, in the shape of a rectangle: “Refer to appropriate discipline(s)”, then connects to Box 7 in the shape of a hexagon: “Does the patient have psychosocial/behavioral health concerns related to amputation?”
    b. If the answer is “No” to Box 5, then Box 7, in the shape of a hexagon: “Does the patient have psychosocial/behavioral health concerns related to amputation?”
        i. If the answer is “Yes” to Box 7, then Box 8, in the shape of a rectangle: “Refer to SW or BH and treat”, and connects to Box 9, in the shape of a hexagon: “Are there medical factors impacting function that could be addressed?”
        ii. If the answer is “No” to Box 7, then Box 9, in the shape of a hexagon: “Are there medical factors impacting function that could be addressed?”
            i. If the answer is “Yes” to Box 9, then Box 10 in the shape of a rectangle: “Refer to appropriate medical providers and treatments”, then connects to Box 11 in the shape of an oval: “If a lower limb amputation is performed, continue to **Module B: Post-Amputation** (See **Box 12**)”

ii. If the answer is "No" to Box 9, then Box 11 in the shape of an oval: "If a lower limb amputation is performed, continue to **Module B: Post-Amputation** (See **Box 12**)"

Module B: Post-Amputation

1. Module B begins with Box 12, in the shape of a rectangle: "Amputation surgery has occurred"
2. Box 12 connects to Box 13, in the shape of a rectangle: "Engage the ACT in conducting comprehensive perioperative assessment and shared decision making (See **Sidebar A**)"
3. Box 13 connects to Box 14, in the shape of a hexagon: "Is the patient ready for initiation of comprehensive rehabilitation services?"
    a. If the answer to Box 14 is "Yes", then Box 16 in the shape of a rectangle: "Develop a goal-oriented care plan (See **LLA CPG** – **Appendix D. Routine Care**)"
    b. If the answer to Box 14 is "No", then Box 15 in the shape of a rectangle: "Refer the patient to appropriate services for care and management"
        i. Box 15 connects to Box 13, in the shape of a rectangle: "Engage the ACT in conducting comprehensive perioperative assessment and shared decision making. (See **Sidebar A**)"
        ii. Box 13 connects to Box 14, in the shape of a hexagon: "Is the patient ready for initiation of comprehensive rehabilitation services?"
            1. If the answer to Box 14 is "Yes", then Box 16 in the shape of a rectangle: "Develop a goal-oriented care plan (See **LLA CPG** – **Appendix D. Routine Care**)"
            2. If the answer to Box 14 is "No", then Box 15 in the shape of a rectangle: "Refer the patient to appropriate services for care and management"
4. Box 16 connects to Box 17, in the shape of a rectangle: "Provide appropriate education (See **LLA CPG** – **Appendix D. Routine Care**)"
5. Box 17 connects to Box 18, in the shape of a rectangle: "Ensure patient achieves the highest level of independence without a prosthesis (See **Sidebar D**)"
6. Box 18 connects to Box 19, in the shape of a hexagon: "Is the patient a candidate for a prosthesis OR pre-prosthetic training?"
    a. If the answer to Box 19 is "Yes", then Box 20 in the shape of a rectangle: "Engage the ACT to provide appropriate pre-prosthetic training (See **Sidebar A**)"
        i. Box 20 connects to Box 21, in the shape of a rectangle: Determine most appropriate prosthetic device(s)."
        ii. Box 21 connects to Box 22, in the shape of a rectangle: "Develop prosthetic prescription including all necessary components."
        iii. Box 22 connects to Box 23, in the shape of a rectangle: "Initiate lower limb prosthetic fabrication, fitting, and delivery."
        iv. Box 23 connects to Box 24, in the shape of a rectangle: "Conduct final prosthesis check out including all appropriate members of the care team."

v. Box 24 connects to Box 25, in the shape of a hexagon: "Does the prosthetic device improve functional statis and meet realistic patient goals?"
    1. If the answer to Box 25 is "Yes", then Box 26, in the shape of a rectangle: "Engage the ACT to administer prosthetic training, education, and rehabilitation (See **Sidebar D**)
    2. If the answer to Box 25 is "No", then Box 21 in the shape of a rectangle: "Determine most appropriate prosthetic device(s)"

b. If the answer to Box 19 is "No", then Box 28, in the shape of a rectangle: "Continue rehabilitation to ensure patient achieves highest level of functional independence without a prosthesis (See **Sidebar D**)
c. Box 28 connects to Box 29, in the shape of a rectangle: Recommend and coordinate lifelong care and management of lower limb amputation"

7. Box 26 connects to Box 27, in the shape of a hexagon: "Does the patient require additional activity specific prosthesis?"
    a. If the answer to Box 27 is "Yes", refer back to Box 21 in the shape of a rectangle: "Determine most appropriate prosthetic device(s)"
    b. If the answer to Box 27 is "No", then Box 29, in the shape of a rectangle: Recommend and coordinate lifelong care and management of lower limb amputation"
8. Box 29 connects to Box 30, in the shape of a rectangle: "Provide routine care as needed and schedule follow-up at least every 12 months (See **Sidebar A**)"
9. Box 30 connects to Box 31, in the shape of a rectangle: "Provide education on current management and practices; refer patient as appropriate to address medical, mental health, prosthetic or rehabilitation needs (refer to **Box 19** when appropriate)"

Module C: Primary Care

1. Module C begins with Box 1, in the shape of a rounded rectangle: "Patient with lower limb loss with/without prosthesis presents for care"
2. Box 1 connects to Box 2, in the shape of a hexagon: "Is the patient established with the ACT?"
    a. If the answer is "No" to Box 2, then Box 3, in the shape of a rectangle: "Obtain referral to ACT Team for follow up appointment; Offer integrated behavioral health or mental health as appropriate (See **Sidebar A**)"
    b. If the answer is "Yes" to Box 2, then Box 4, in the shape of a rectangle: "Is the primary care provider concerned about the following:
        - Residual limb/foot exam complications (e.g., skin and soft tissue concerns)
        - Fit and function of prosthesis
        - Functional ability
        - Significant weight change
        - Pregnancy
        - Associated musculoskeletal conditions (e.g., low back pain, contralateral joint pain)

- Vocational and recreational needs
- Psychological adjustment to amputation?"

i. If the answer is "Yes" to Box 4, then Box 5, in the shape of a rectangle: "Obtain referral to ACT Team and/or OT, PT and prosthetics; Offer mental and behavioral health referral as appropriate (See **Sidebar A**)"
ii. If the answer is "No" to Box 4, then Box 6, in the shape of a hexagon: "Is the patient at high risk for amputation of the contralateral limb?"
    1. If the answer is "Yes" to Box 6, then Box 7, in the shape of a rectangle: "Refer patient to podiatry or foot care specialist for evaluation"
    2. If the answer is "No" to Box 6, then Box 8, in the shape of a rectangle: "Actively promote and facilitate annual follow up with ACT team (See **Sidebar A**)"

Appendix I: Abbreviation List

Abbreviation	Definition
ABC	Activities-specific Balance Confidence Scale
ADL	activities of daily living
AHRQ	Agency for Healthcare Research and Quality
AMP	Amputee Mobility Predictor
BKA	below knee amputation
BPI	Brief Pain Inventory
BPI-I	Brief Pain Inventory Interference
CARF	Commission on the Accreditation of Rehabilitation Facilities
CDC	Centers for Disease Control and Prevention
CDRS	Certified Driving Rehabilitation Specialist
CI	confidence interval
CO2	carbon dioxide
COI	conflict of interest
CP	certified prosthetist
CPG	clinical practice guideline
CS	comparative study
CV	cardiovascular
DoD	Department of Defense
DME	durable medical equipment
EBPWG	Evidence-Based Practice Work Group
FDA	Food and Drug Administration
FY	fiscal year
GMI	Graded Motor Imagery
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HEP	home exercise program
IADL	instrumental activities of daily living

Abbreviation	Definition
IRC	Ischial Ramus Containment
IRF	inpatient rehabilitation facility
K(0-4)	Medicare functional levels
KQ	key question
LCI	Locomotor Capabilities Index
LLA	lower limb amputation
m	meter(s)
md	median
MDT	multidisciplinary team
MeSH	Medical Subject Headings
mn	mean
MPK	microprocessor prosthetic knee
NIH	National Institutes of Health
NMPK	non-microprocessor prosthetic knee
OPUS	Orthotic Prosthetic User Survey
OPRA	Osseoanchored Prostheses for the Rehabilitation of Amputees
OT	occupational therapy
OR	odds ratio
PAD	Peripheral artery disease
PAVE	Prevention of Amputation for Veterans Everywhere
PGIC	Patient Global Impression of Change
PICOTS	population, intervention, comparison, outcome, timing and setting
PLP	phantom limb pain
PLS	phantom limb sensation
PROMIS	Patient-Reported Outcomes Measurement Information Systems
PRP	platelet rich plasma
PM&R	physical medicine and rehabilitation

Abbreviation	Definition
PNC	perineural catheter
PT	physical therapy
PVD	peripheral vascular disease
QOL	quality of life
RCT	randomized controlled trial
RLP	residual limb pain
ROM	range of motion
SACH	solid ankle cushioned heel
SAE	serious adverse event
sec	second(s)
SMD	standardized mean difference
SNF	skilled nursing facility
SOC	standard of care
SR	systematic review
TAPES	Trinity Amputation and Prosthesis Experience Scales
TENS	transcutaneous electrical nerve stimulation
TFA	transfemoral amputation
TMR	targeted muscle reinnervation
TTA	transtibial amputation
TUG	timed up and go test
UE	upper extremity
ULA	Upper limb amputation
U.S.	United States
USPSTF	United States Preventive Services Task Force
VA	Department of Veterans Affairs
VAS	Visual Analog Scale
VETPALS	Vet's Promoting Amputee Life Skills

Abbreviation	Definition
VHA	Veterans Health Administration

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