Washington State Health Care Authority

Microprocessor-controlled Lower Limb Prosthetics (MCP)

Assessing Signals for Update

March 7, 2025

Health Technology Assessment Program (HTA)

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Tables and Figures

Previous Coverage Decision
A Health Technology Assessment titled: Microprocessor-controlled Lower Limb Prostheses, was published on October 12, 2011 by the Health Care Authority. Findings and Coverage Decision was adopted on March 16, 2012. The Committee's Coverage Decision is summarized below.

Health Technology Background

Amputation or loss of a limb is a life-altering condition with profound physical, emotional, and social implications. An estimated 2.3 million[5] people are currently living with limb loss, and that number is expected to grow to 3.6 million by the year 2050[23]. Primary causes of amputation include disease, trauma (accident or injury), cancer (tumor or malignancy), and congenital disorder (birth anomalies). As rates of chronic diseases like diabetes and peripheral vascular disease increase, lower limb amputation increases in a younger and broader population. Lower limb loss is associated with poorer functional performance, reduced mobility, and increased risk of falling.[6,21] Research shows that quality of life is diminished in patients with lower limb amputation, and that prosthesis use improves their quality of life.[21]

Prostheses are devices that replace or compensate for the absence of a body part. Lower limb loss (amputation of the toe, foot, leg, or thigh) notably affects an individual's ability to stand, transfer, and ambulate. A variety of additional functional deficits have similarly been associated with lower limb loss, including compromised balance, increased metabolic requirements for walking, reduced walking speeds, temporal-spatial gait asymmetries, increased fall rates, reduced activity, and difficulties walking over non-level terrain (uneven ground, stairs, or inclines). Lower limb loss has also been associated with an elevated incidence in certain medical conditions, including joint pain, osteoarthritis, osteopenia/osteoporosis. The combination of these functional and medical issues experienced by persons with limb loss is likely responsible for the well documented challenges with community reintegration and returning to work following amputation.

Lower limb prostheses are designed to replace the normal function of the knee and/or ankle. Standard treatment for people with lower limb loss or absence is the provision of prosthesis (artificial limb). A lower limb prosthesis for a person with transtibial (below-knee) limb loss includes, at a minimum, a prosthetic socket, a prosthetic foot, and the adapters necessary to connect these components. A lower limb prosthesis for a person with transfemoral (above-knee) limb loss includes, at a minimum, a socket, knee, foot, and the necessary pylons and/or adapters to connect these components. Microprocessor-controlled lower limb prostheses (MCP) are contemporary devices that include electromechanical sensors, actuators and behavioral logic within the device to detect users' movements and control the position and/or motion of the device. Microprocessor-controlled lower limb prostheses have several potential advantages over traditional prostheses, including reduced energy expenditure, improved ambulation, improved safety, and improved quality of life.

A Health Technology Assessment lower-limb MCPs in 2011. At that time, several MCP knee devices were commercially available but only one MCP ankle/foot device is available. After the 2011 HTA new knee MCPs and upgrades to previously identified knee MCPs are available and there are additional foot and/or ankle MCPs available. There is likely updated evidence on benefits and harms for MPCs.

Health Technology Clinical Committee's Findings and Coverage Decision

HTCC Coverage Determination

Microprocessor-controlled Lower Limb Prostheses (MCP) for the Knee is a **covered benefit** with conditions

Microprocessor-controlled Lower Limb Prostheses (MCP) for the feet and ankle is **not a covered benefit**

HTCC Reimbursement Determination

- **Limitations of Coverage**
  - Microprocessor-controlled Lower Limb Prostheses (MCP) for the knee is a covered benefit when the following conditions are met:
    - Functional levels 3 or 4, level 2 under agency review
    - Experienced user, exceptions under agency review
    - Use within manufacturers' specifications
- **Non-Covered Indicators**
  - Microprocessor-controlled Lower Limb Prostheses (MCP) for the feet and ankle

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and agency and state utilization information. The committee concluded that the current evidence on MCP for the knee demonstrates that there is sufficient evidence to cover with conditions. The committee concluded that the current evidence on MCP for the feet and ankle demonstrates that there is insufficient evidence to cover. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. Based on these findings, the committee voted to cover with conditions MCP for the knee. Based on these findings, the committee voted not to cover MCP for the feet and ankle.

Medicare Decision and Expert Treatment Guidelines

The committee reviewed the Clinical guidelines and Medicare decision. The Centers for Medicare and Medicaid Services have no published national coverage determinations (NCD) for any MCPs.

1. Purpose of Report, Key Questions and Scope

The purpose of this literature signal update review is to determine whether or not there is sufficient high-quality evidence published after the original report that would change the primary conclusions of the prior review and warrant the conduct of a re-review of this technology. The key questions included the following:

The Key Questions (KQs) and scope for the 2011 review were developed with the Washington State Health Technology Assessment Program and are listed below. For purposes of this signal update, only KQs 2 through 5 will be addressed following the same scope as the 2011 HTA.

A. Key Questions (KQs):

When used by people living with lower limb loss in real-world conditions:

Key question 1 (Will not be addressed in this signal update report)

1. What are the expected treatment outcomes of the use of microprocessor-controlled lower limb prostheses? Are there validated instruments related to measurement of outcomes of this technology? Has clinically meaningful improvement in outcomes been defined for use of this technology?

Key question 2

2. What is the evidence of efficacy and effectiveness of microprocessor-controlled lower limb prostheses? Including consideration of validated tools to measure both short term and long-term outcomes.
    a. Energy and cognitive requirements of ambulation
    b. Impact on ambulation: daily step frequency; estimated step distance; performance on level or varied surfaces
    c. Patient perception; QOL; impact on activities of daily living; work; work performance

Key question 3

3. What is the evidence about the safety of microprocessor-controlled lower limb prostheses? Including consideration of
    a. Adverse events type and frequency (mortality, other major morbidity)
    b. Equipment failure
    c. Ulcers, falls, etc.

Key question 4

4. What is the evidence that microprocessor-controlled lower limb prostheses has differential efficacy or safety issues in sub populations? Including consideration of: gender, age, psychological or psychosocial co-morbidities, baseline functional status, other patient characteristics or evidence-based patient selection criteria, provider type, setting or other provider characteristics, payor/ beneficiary type: including worker's compensation, Medicaid, state employees.

Key question 5

5. What is the evidence of cost implications and cost-effectiveness of microprocessor-controlled lower limb prostheses? Including consideration of: costs (direct and indirect)

and cost effectiveness, short term and long term, and ongoing maintenance and replacements for the prosthesis

B. Scope

Inclusion and exclusion criteria from 2011 HTA are in Table 1.

Table 1. Inclusion and exclusion criteria from 2011 HTA

	Inclusion	Exclusion
Participants	▪ Adults >18 ▪ Transfemoral amputee (above knee) ▪ Transtibial amputee (below knee)	▪ Bilateral amputation ▪ Hip/knee disarticulation
Intervention	▪ Microprocessor-controlled knee prosthesis ▪ Microprocessor-controlled foot prosthesis	▪ Powered prosthesis
Comparators	▪ Mechanically controlled prosthesis ▪ Other microprocessor-controlled prosthesis ▪ Anatomically typical (non-amputee)	▪ None
Outcomes	▪ Any outcome assessing use of microprocessor-controlled prostheses in an uncontrolled (e.g., home, work, or community) setting ▪ Adverse events: mortality, other major morbidity, equipment failure, ulcers, falls, etc. ▪ Cost-effectiveness	▪ Outcomes assessing activity in standardized, controlled settings (e.g., lab or obstacle courses) will be summarized.
Study Design	▪ KQ1: All studies included in Questions 2, 3, 4, and 5 ▪ KQ2, KQ3, KQ4: Comparative clinical studies ▪ KQ5: Comparative studies of both costs and outcomes	▪ Case reports ▪ Case series ▪ Cost-only studies ▪ Intervention group n<5 participants
Publication	▪ Full-length studies published in English in peer reviewed journals, published HTAs or publicly available FDA reports ▪ Full formal economic analyses (e.g., cost-utility studies) published in English in a HTAs or in a peer-reviewed journal published after those represented in previous HTAs.	▪ Abstracts, editorials, letters ▪ Duplicate publications of the same study ▪ Single reports from multicenter trials ▪ Studies reporting on the technical aspects of these procedures ▪ White papers ▪ Narrative reviews ▪ Articles identified as preliminary reports when results are published in later versions

2. Methods

2.1 Literature Searches

We conducted an electronic literature search for the period January 1, 2011 to July 3, 2024 with an update search from January 1, 2024 to March 4, 2025. This search included three main databases: PubMed/Medline, Cochrane Library, and EMBASE. Appendix A reports the search methodology for this topic. General, limited google searches to identify technology assessments and new prostheses. ClinicalTrials.gov was searched for on-going trials.

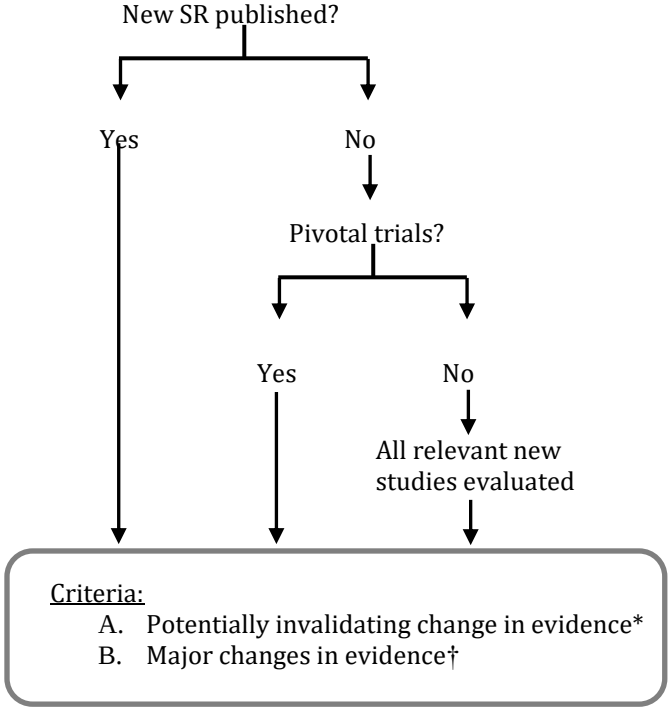
2.2 Study selection

We used the same inclusion and exclusion criteria as the 2011 HTA for KQs 2-5.

2.3 Compilation of Findings and Conclusions

For this assessment we constructed a summary table that included the KQs 2-5, the 2019 conclusions, new sources of evidence, new findings, and new conclusions based on available signals. To assess whether the conclusions might need updating, we used an algorithm based on a modification of the Ottawa method, Figure 1. Signal update reports do not provide a comprehensive search for or comprehensive review of the literature.

Figure 1. Algorithm of the modified Ottawa Method of Identifying Signals for SR Update



*A-1. Opposing findings: Pivotal trial or SR including at least one new trial that characterized the treatment in terms opposite to those used earlier

A-2. Substantial harm: Pivotal trial or SR whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making

A-3. Superior new treatment: Pivotal trial or SR whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm.

†B-1. Important changes in effectiveness short of "opposing findings"

B-2. Clinically important expansion of treatment

B-3. Clinically important caveat

B-4. Opposing findings from discordant meta-analysis or nonpivotal trial

3. Results

3.1 Search

From 220 citations returned from the updated search, 195 were excluded at title/abstract review, 25 were reviewed at the full-text level and ultimately 13 studies in 15 citations were included: five for knee MCPs[1,12,14,18,21] and eight (in 10 publications) for foot or ankle MCPs[2-4,7-9,13,15,16,22] (Figure 2).

For knee MCPs, four systematic reviews (SRs) that included studies published after the 2011 HTA were retained[12,14,18,21]; one of which focused on cost effectiveness[12] and another SR focused on comparing a newer MCP (Genium) with other MCPs.[18] The results of the retained systematic reviews are summarized in Appendix B. In addition, a limited reference list on knee MCPs was published by The Canadian Agency for Drugs and Technologies in Health (CADTH)[1] identified and is briefly described in the results.

For foot or ankle MCPs, no systematic reviews were identified. Three studies (5 publications)[2,3,7,13,16] that employed a randomized cross-over design and five non-randomized trials (NRSI)[4,8,9,15,22] that provided information on patient-reported outcomes in uncontrolled settings or energy cost/expenditure in controlled settings were retained. The data abstraction for included studies are summarized in Appendix B. A full list of studies excluded at full text review and the reasons for exclusions can be found in Appendix C.

Summaries of Medicare Functional Classification Levels (MFCL) and clinical outcomes measures are in Appendix D. Ongoing trials identified from a ClinicTrials.gov search are in Appendix E.

3.2 Identifying signals for re-review

Table 2 shows the original key questions 2-5, the conclusions of the original report, the new sources of evidence, the new findings, and the recommendations of Aggregate Analytics, Inc. (AAI) regarding the need for update. Appendix B summarizes the results for the included systematic reviews for knee MCP and for new primary studies for foot/ankle MCPs.

Figure 2. Flow chart showing results of literature search

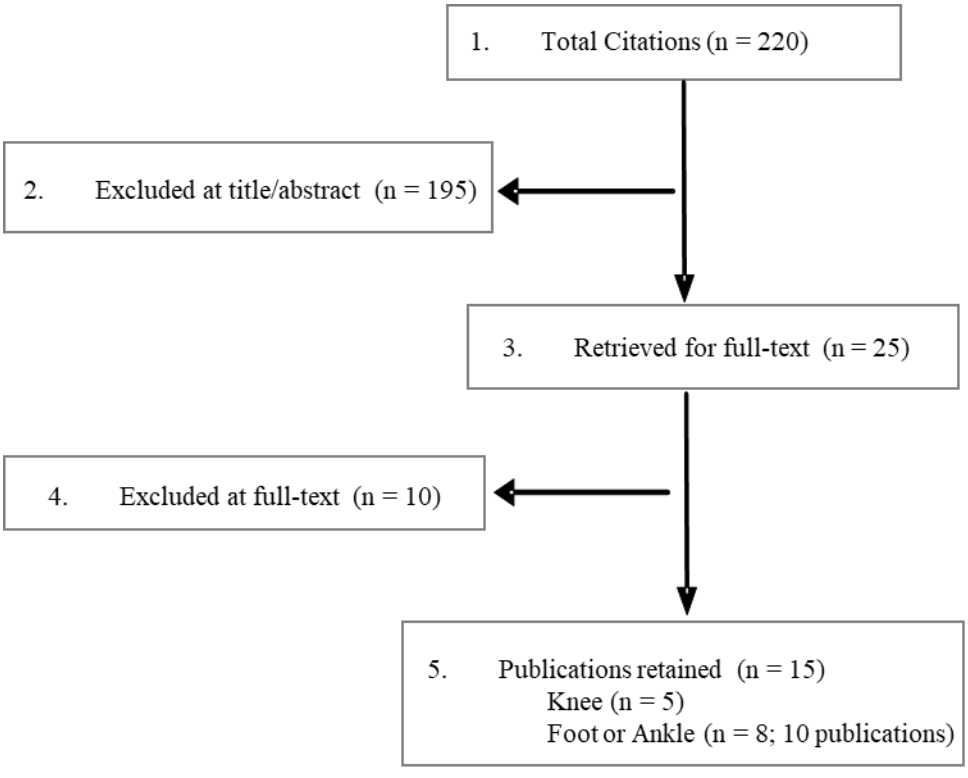


Table 2. Summary Table of Key Questions 2-5

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
Key Question 2. What is the evidence of efficacy and effectiveness of microprocessor-controlled lower limb prostheses? Including consideration of validated tools to measure both short term and long-term outcomes. ***(Evidence from 12 studies)***			
Key Question 2a. Energy and cognitive requirements of ambulation			
Knee • Evidence from two moderate and three low-quality studies consistently suggests that energy/cognitive requirements associated with MCP are improved compared to NMCP in real-life settings. Strength of evidence: LOW **Foot/ankle and combined knee & foot/ankle:** • No evidence	**Knee: Systematic Reviews:** Thibaut 2022[21] Hahn 2022[14] **Foot/ankle Randomized:** Colas-Ribas 2022 (N=45)[7] Agrawal 2013, 2015 (N=10)[2,3] **NRSI** Hanh 2018 (N=70)[15] Delussu 2013 (N=10)[9] Darter 2014 (N=6)[8]	Knee • One SR included a cross-sectional study that reported increased brain activity (pre-frontal and motor cortices) with NMCP vs. MCP while walking which was interpreted as a reduction in cognitive resources required with MCP vs. NMCP however no data are presented in the SR.[19,21] • One SR: MCPs in limited community ambulators (MFCL-2), were associated with better PEQ utility scores (0-100) vs. NMCPs but estimates are imprecise: 3 studies (2 new), N=138, pooled MD 7.76 (95% CI 2.05 to 13.47), I^2=0%.[14] **Foot/ankle** • One randomized cross over trial (N=45) found no difference in energy expenditure cost of ambulation between MCP and standard energy storage and return prosthesis (ESAR) in a controlled setting.[7] • One randomized trial (N=10) reported no differences in their Symmetry in External Work (SEW) measure between MCPs and NMCPs in general but SEW may vary based on incline and functional level.[2,3] • One large (N=70) observational cohort: Similar % of subjects rated the MCP better or much better than their previous NMCP (vs. worse, much worse) for concentration and exertion during walking.[15]	**Knee:** This section of the report remains valid. It could be updated with additional limited evidence in people with MFCL-2 from nonrandomized studies. **Foot/ankle:** New evidence on energy and cognitive

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
		• NRSI (controlled settings): One small NRSI trial (N=10) found MCP foot reduced the energy cost of walking vs. NMCP; another (N=6) found no difference in energy expenditure or energy cost of walking when the MCP was on vs. when it was off.[8,9]	
Key Question 2b. Impact on ambulation: daily step frequency; estimated step distance; performance on level or varied surfaces			
Knee • Evidence from one moderate-quality and six low-quality studies suggests that MCP use is associated with equivalent or improved ability to ambulate compared to NMCP in real-life settings. Strength of evidence: LOW **Foot/ankle and combined knee & foot/ankle:** • No evidence	**Knee - Systematic Reviews:** Hahn 2022[14] Thibaut 2022[21] Mileusnic 2021[18] **Foot/ankle: Randomized cross-over trials:** Colas-Colas-Ribas 2022 (N=45)[7] Kaluf 2020 (N=21)[16] Gailey 2012(N=10)[13] **NRSI** Delussu 2013 (N=10)[9] Thomas-Pohl (N=6) 2021[22] Bai 2018 (N=5)[4]	**Knee** • One SR: MCPs in limited community ambulators (MFCL-2) vs. NMCPs ○ MCPS were associated with improved: ▪ PEQ ambulation scores (0-100), 4 studies (3 new), N=156, MD 9.32 (95% CI 3.61 to 15.03), I^2=7% (results are imprecise). ▪ Walking Speed, 6 studies (4 new including 1 randomized): SMD 0.47 (95% 0.14 to 0.81), I^2=0%.[14] ○ 51% (95% CI 47% to 55%) of subjects increased function from MFCL-2 to MFCL-3 after switching to MCP from NMCP (6 studies, 4 new including 1 randomized). ○ There were no differences between MCP and NMCP for: Activity-based balance scale (ABC), fast walking speed (See data abstraction). • One SR provides qualitative statements only: MCP users presented better functional status and mobility; It is unclear whether more advanced MPCs such as Genium are superior to other MCPs.[21] • One SR states that the newer (Genium) improves gait and mobility vs. "conventional" MCPs (see	**Knee:** This section of the report remains valid but could be updated to reflect additional evidence in people with MFCL-2. Most new studies are nonrandomized. Evidence comparing newer knee MCPs with standard MCPs could be updated but does not trigger a need for re-review. **Foot/ankle:** This section of the report could be updated. (Criterion B-1). However, evidence from randomized studies appears to be sparse; Included studies suggest that MCPs may confer equivalent improvement in patient reported function outcomes compared with NMCPs.

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
		data abstraction).[18] **Foot/ankle** • One randomized trial (N=45) found no difference in total ESAT score or the effectiveness score (1-5 scale) or locomotor capability/activities (PPA-LCI score, 0-3 scale) between MCP and NMCP feet.[7] • One randomized trial (N=21) reported no difference in perceived mobility on the PLUS-M (T-score, range 17.5 to 76.7) and a marginally insignificant improvement in the PEQ-MS (0-100) which may not be clinically significant (MD 0.24 on 0-48 scale).[16] • One randomized trial (N=10) compared amputees with and without PVD but did not directly compare MPC with NMCP across groups. They suggest that the MPC perform differently in those with and without PVD on some measures (e.g., 6-minute walk test) however this trial was underpowered to formally explore differences. In general, authors suggest that there are no differences between MCPs and NMCPS in most measures.[13] • NRSI trial (N=10) found no significant improvement in perceived mobility or walking ability for MCP vs. the NMCP including use on stairs and ramps.[9] • Two small NRSIs in controlled settings provide limited information on patient-reported measures comparing MCPs and NMCPs and statistical analyses were not done. One NRSI reports no difference between devices in walking speed in either ascending or descending slopes; limited patient reported data suggests that mobility, stability, and comfort may be better with the	

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
		MCP.[4] The other NRSI reports that "confidence in balance" and BBS scores may be better with MCPs.[22]	
Key Question 2c. Patient perception; QOL; impact on activities of daily living; work; work; work performance			
Knee • Evidence from two moderate-quality studies and four low quality studies consistently suggests that MCP use is associated with improved quality of life compared to NMCP in real-life settings. Strength of evidence: LOW • Evidence from one moderate quality study and two low quality studies consistently suggests that MCP use is associated with improved activities of daily living compared to NMCP in real-life settings. Strength of evidence: LOW • Evidence from one moderate-quality and one low-quality suggests that MCP use is associated with improved balance confidence compared to NMCP in real-life settings. Strength of evidence: VERY LOW • Evidence from one moderate-quality and two low-quality studies consistently suggest that MCP use is associated with improved comfort and fit compared to NMCP use in real-life settings. Strength of evidence: VERY LOW • Evidence from two moderate-quality and two low-quality studies consistently suggests that MCPs are preferred by users	**Knee - Systematic Reviews:** Hahn 2022[14] **Foot/ankle: Primary studies Randomized cross-over trials**: Colas-Ribas 2022[7] Kaluf 2020[16]	**Knee** • One SR: MCPs in limited community ambulators (MVCL-2): ○ There was no statistically significant difference between MCPs and NMCPs for the following PEQ (0-100) domains however estimates are imprecise: Well-being (3 studies, 2 new), appearance (3 studies, 2 new), sounds (3 studies, 2 new).[14] • One SR states that a newer MCP (Genium) improved performance of ADLs and quality of life (see data abstraction) vs "standard" MCPs.[18] Foot/ankle • One randomized trial (N=45) found the MCP was associated with improved QOL based on SF-36 physical and mental component scores (0-100) and greater comfort (ESAT comfort score, 1-5 scale). They found no differences between prostheses for durability or simplicity of use (ESAT scores 1-5 scale).[7] • One randomized trial (n=21) reported that the MCP socket was more comfortable for walking and standing (SCS comfort score 0-10) vs. NMCP.[16]	**Knee:** This section of the report remains valid and does not need updating; most studies are nonrandomized. Evidence comparing newer knee MCPs with standard MCPs could be updated but does not trigger a need for re-review. **Foot/ankle:** This section of the report could be updated. (Criterion B-1). However, evidence from randomized studies appears to be sparse. Included randomized studies suggest that MCPs may be associated with improved QOL and comfort.

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
compared to NMCPs in real-life settings. Strength of evidence: LOW • Evidence from one moderate-quality and two low-quality studies consistently suggest that MCP use is associated with improved perceived perceptions by others compared to NMCP use in real-life settings. Strength of evidence: VERY LOW **Foot/ankle and combined knee & foot/ankle:** • No evidence			
Key Question 3. What is the evidence about the safety of microprocessor-controlled lower limb prostheses? ***(Evidence from 6 studies)***			
Key Question 3a. Adverse events type and frequency (mortality, other major morbidity)			
Knee • Evidence from one moderate-quality and one low-quality study suggests that MCPs are associated with fewer negative effects on residual limbs compared to NMCPs in real-life settings. Strength of evidence: VERY LOW **Foot/ankle and combined knee & foot/ankle:** • No evidence	**Knee - Systematic Reviews:** Hahn 2022[14] **Foot/ankle:** No new evidence identified	**Knee** • One SR: MCPs in limited community ambulators (MFCL-2) reported no difference between MCPs and NMCPs on the PEQ residual limb score (0-100): 3 studies (2 new) 4.43 (95% CI - 1.29 to 10.14), I^2=4%.[14] **Foot/ankle** • No included study reported adverse events	**Knee:** This section of the report remains valid and does not need updating. New studies are not randomized, estimates are imprecise, and SOE is unlikely to change. **Foot/ankle:** This section of the report remains valid.
Key Question 3b. Equipment failure			
Knee • Evidence from two low-quality studies suggests that there may be fewer incidences of equipment failure or problems with MCPs compared to NMCPs in real-life settings. Strength of evidence: VERY LOW	No new evidence identified	**Knee** • Included SRs did not report on this **Foot/ankle:** • No included study described equipment failure	**Knee:** This section of the report remains valid and does not need updating.

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
Foot/ankle and combined knee & foot/ankle: • No evidence			**Foot/ankle:** This section of the report remains valid and does not need updating.
Key Question 3c. Ulcers, falls, etc.			
Knee • Evidence from two moderate-quality studies and one low-quality studies suggests that MCP use is associated with equivalent or reduced stumbles or falls compared to NMCP use in real-life settings. Strength of evidence: LOW **Foot/ankle and combined knee & foot/ankle:** • No evidence	**Knee** **Systematic Reviews:** Hahn 2022[14] Mileusnic 2021[18] **Foot/ankle:** **Primary studies** **Randomized cross-over trials**: Colas-Ribas 2022[7]	**Knee** • One SR: MCPs in limited community ambulators (MFCL-2) led to a reduction in: o Falls (7 studies, 5 new, n=117; SMD g: –0.59; 95% CI [–0.85, –0.32]; I^2=0%) o Fear of falling (6 studies, 5 new, n=464; SMD g: 1.2; 95% CI [0.55, 1.85]; I^2=80%) o Risk of falling as indicated by the TUG (4 new studies, n=45; SMD g: –0.45, 95% CI [–0.87, –0.02; I^2=0%) o PEQ sounds (3 studies, 2 new, n=69; MD 3.36, 95% CI [–4.65 to 11.37], I^2=0%).[14] • One SR comparing newer Genium MPCs with "conventional" MCPs provides evidence statements based on qualitative synthesis across included studies. They state that Genium improves performance in and safety of conducting ADLs compared to conventional MCPs (see data abstraction).[18] **Foot/ankle:** • One randomized trial (N=45) found no difference in patient perceived safety (ESAT safety score, 1-5 between MCP and NMCP.[7] • Included studies did not report on falls, etc.	**Knee:** There appear to be new data in persons with MFCL-2 suggesting improved safety with MCP vs. NMCP, however most studies were not randomized. This section may benefit from an update with additional evidence in patients with MFCL-2, however, signal criteria are met. **Foot/ankle:** This section of the report is still valid. Evidence from the single trial reports only on patient perception of safety.
Key Question 4: What is the evidence that microprocessor-controlled lower limb prostheses has differential efficacy or safety issues in sub populations? Including consideration of: gender, age, psychological or psychosocial co-morbidities, baseline functional status, other patient characteristics or evidence-based patient selection criteria, provider type, setting or other provider characteristics, payor/ beneficiary type: including worker's compensation, Medicaid, state employees. ***(Evidence from 2 studies)***			

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
Knee • Evidence from one moderate-quality study suggests that benefits of MCP use to energy, ambulation, safety, and quality of life are greater in people at higher baseline function (MFCL-3) compared to NMCP use. However, people at lower function (MFCL-2) may also experience some benefits of MCP use. Strength of evidence: VERY LOW • Evidence from one low-quality study suggests that the quality of life benefits of MCPs may extend to people who are first time prosthesis users. Strength of evidence: VERY LOW **Foot/ankle and combined knee & foot/ankle:** • No evidence	**Systematic Reviews:** Hahn 2022[14] **Primary studies** Randomized cross-over trial – 3 publications in the same population Gailey 2012,[13] Agarwal 2013, 2015[2,3]	**Knee** • One SR reported analyses in limited community ambulators (MFCL-2); results are described in the previous sections as they do not represent true evaluation of modification of treatment effects.[14] **Foot/ankle:** • Three publications of one small randomized cross over trial (N=10) report stratified analyses for patients with and without PVD or by functional level, however data are insufficient to evaluate effect modification in these subgroups.[2,3,13]	**Knee:** This section of the report remains valid and does not need updating. **Foot/ankle**: This section does not need updating.
Key Question 5: What is the evidence of cost implications and cost-effectiveness of microprocessor-controlled lower limb prostheses? Including consideration of: costs (direct and indirect) and cost effectiveness, short term and long term, and ongoing maintenance and replacements for the prosthesis ***(Evidence from 3 studies)***			
Knee • Evidence from three low-quality studies suggests that the cost of MCP purchase and fitting is higher than for NMCP. Strength of evidence: LOW • Evidence from three low-quality studies suggests that the total health care costs of MCP use are higher than for NMCP use. Strength of evidence: VERY LOW • Evidence from two low-quality studies suggests that total societal costs, including productivity, caregiver burden, and costs to patient of MCP use are lower than those	**Systematic Reviews:** Donnelley 2021[12] **Reference List** CADTH[1] **Primary studies** (foot/ankle) No new evidence identified	**Knee** • One SR: 4 CUA (2 new, one in the U.S.) found knee MCPs to be cost-effective vs. NMCPs. ICER range: €3,281 - €40,155/QALY for non-US studies; ICER for U.S. study conducted by the RAND corporation and sponsored by the American Orthotic and Prosthetic Association $11,606/QALY.[12] • Genium was more expensive vs. C-Leg but provided better quality of life when evaluated across an array of functional measures in the same SR.[12] • The CADTH reference list cites one other new economic study which concludes that knee MCP is likely cost-effective vs. NMCP in transfemoral	**Knee:** This section of the report remains valid and does not need updating. **Foot/ankle**: No economic studies were identified.

Conclusions from CER Executive Summary: 2011	New Sources	New Findings: 2025	Conclusion from AAI
associated with NMCP use. Strength of evidence: LOW • Evidence from two low-quality studies suggests that the short-term cost-effectiveness of MCP use ranges from dominant (better outcomes and lower costs) to incremental cost- effectiveness ratios of under €40,000/QALY. Strength of evidence: VERY LOW **Foot/ankle and combined knee & foot/ankle:** • No evidence		amputees with diabetes as well as those without diabetes (data not abstracted).[17] **Foot/ankle:** No studies identified	

AAI: Aggregate Analytics, Inc.; ABC: activity-based balance scale; ADLs: activities of daily living; CADTH: Canadian Agency for Drugs and Technologies in Health; CER: comparative effectiveness review; CI: confidence interval; CUA: cost-utility analysis; ESAR: standard energy storage and return prosthesis; ESAT: Evaluation de la Satisfaction envers une Aide Technique (French translation of the "Quebec User Assessment of Satisfaction with Assistive Technology"; ICER: incremental cost-effectiveness ratio; MCP: microprocessor-controlled prosthesis; MD: mean difference; MFCL: Medicare Functional Classification Level; MCP: microprocessor-controlled knee; NMCP: non-microprocessor-controlled prosthesis; NRSI: non-randomized study of interventions; PEQ: Prosthesis Evaluation Questionnaire; PEQ-M: Prosthesis Evaluation Questionnaire Mobility Scale; PLUS-M: Prosthetic Limb Users Survey of Mobility™; PPA-LCI: Prosthetic Profile of the Amputee Locomotor Capabilities Index; PVD: peripheral vascular disease; QALY: quality-adjusted life years; QOL: quality of life; RCT: randomized controlled trial; SCS: Socket Comfort Score; SEW: symmetry in external work; SF-36: Short Form Health Survey; SMD: standardized mean difference; SOE: strength of evidence; SR: systematic review; TUG: timed up and go test.

Conclusions of the 2025 Signals for Update Assessment on MCP

New Evidence base overview

Knee MCP: We included four SRs of comparative studies published since the 2011 HTA. Confidence in all SRs was considered critically low based on modified AMSTAR-2 criteria[10,11,20] (Appendix F). Reviews included a variety of study designs including two randomized cross-over studies with the remaining studies being non-randomized cross-over, single subject pre-post designs or cross-sectional studies. The 2011 HTA included a similar mix of study designs. Three SRs compared knee MCPs with NMCPs and are the focus of this signal update for knee MCP.[12,14,21] One SR compared newer knee MCPs with older "standard" MCPs and is included for completeness as the original PICOTS included comparison of different MCPs.[18] Many authors of SRs did not clearly describe whether sample sizes represented the number of individual patients or the number of prosthetic fittings over cross-over periods. Many individual studies included in the SRs had small samples sizes (<30). Heterogeneity across included studies in the SRs generally precluded extensive meta-analyses and some SRs provided only qualitative summaries of findings. Studies included in the SRs appear to be from a variety of settings inside and outside of the U.S.; authors do not describe the extent to which studies were in "real life" or "uncontrolled" settings versus observations in controlled settings. One SR focused on economic studies.[12] One SR focused on subanalyses of limited community ambulators (MFCL-2) primarily from nonrandomized studies.[14] In one SR,[18] all studies except for one reported on subjects with mobility grades of MFCL-3 and MFCL-4 and functional level was not clearly described in two other SRs.[12,21]

Foot/Ankle MCPs: No systematic reviews comparing foot/ankle MCPs with standard prostheses were identified. At the time of the 2011 HTA, only one foot/ankle MCP (Proprio-foot, Össur, Reykjavik, Iceland), was available and evidence was considered insufficient, and no evidence was presented. The Proprio-foot assists mobility across terrains during the swing phase between steps but does not provide ankle slope accommodation. In addition to new studies of Proprio-foot, newer MCPs reported in new trials provide slope accommodation and include: Kinnex (Freedom Innovations, Irvine, CA, USA); Elan (Chas A Blatchford & Sons Ltd, Basingstoke, United Kingdom), Raize (Fillauer LLC, Chattanooga, TN, USA), Meridiam (Otto Bock, Duderstadt, Germany). Our summary focuses on three studies published since the 2011 HTA which used a randomization cross-over design and briefly summarizes five nonrandomized studies that provided patient-reported outcomes from uncontrolled settings or energy cost in controlled settings.

Biometric, kinemetric and laboratory data (other than energy cost) are not included in this signal update.

Efficacy

- **Knee MCP:** One SR focused on people with MFCL-2, described as limited community ambulators, found that MCPs were associated with improved function compared with NMCPs for most functional measures and reported that ~50% of patients improved to MFCL-3. Most studies in the SR were not randomized. Sections of the 2011 HTA reporting on the effectiveness of knee MCPs remain valid. Additional evidence in people with MFCL-2 would update these sections but do not signal need for an update.
- **Foot/Ankle MCP:** New evidence comparing foot/ankle MCPs with NMCPs suggests that they may be similar for the following outcomes: energy cost and cognitive function and various patient reported measures of function and mobility. MCPs may be associated with improved quality of life and patient comfort, however evidence from included studies is sparse. This section of the report could be updated. (Criterion B-1).

Safety

- **Knee MCP**: Results from one SR suggest that MCPs led to a reduction in falls, risk of falling and fear of falling and compared with NMCPs. Sections of the 2011 HTA reporting on the safety of knee MCPs remain valid and do not require updating.
- **Foot/Ankle MCP**: Included studies did not report on adverse events or provide data on falls, etc. One trial reported on patients' perceived safety. Evidence from newly included studies remains insufficient. This section of the report remains valid.

Differential Efficacy and Safety

- We identified no new studies formally comparing the differential efficacy, effectiveness, or safety of MCPs for either knee or foot/ankle. One SR focused on studies reporting on people with MFCL-2 function and the 2011 HTA reported subanalysis of this population from one study, however neither study allows for evaluation of effect modification by MFCL level. This section of the report remains valid.

Cost Effectiveness

- **Knee MCP**: New evidence suggests that MCPs are more cost-effective than NMCPs and is consistent with findings of the 2011 HTA. This section of the report remains valid and does not need updating.
- **Foot/Ankle MCP**: No studies were identified. This section of the report remains valid.

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APPENDIX A. SEARCH STRATEGIES

Below is the search strategy for PubMed. Parallel strategies were used to search other electronic databases listed below from January 1, 2011 through March 4, 2025 with the original search conducted from January 1, 2011 through July 3, 2024 and supplemental search conducted from January 1, 2024 through March 3, 2025. Keyword searches were conducted in the other listed resources. In addition, hand-searching of included studies was performed.

Appendix Table A1: PubMed Search strategy

Construct	Search #	Terms
	#01	Search transtibial or transfemoral
	#02	Search amput* and (foot or knee or ankle)
A. Population	#03	Search #1 or #2
	#04	Search prosthe*
	#05	Search "Artificial Limbs"[Mesh]
B. Prosthesis	#06	Search #4 or #5
	#07	Search microprocessor
	#08	Search “rheo leg”
	#09	Search “intelligent prosthesis”
	#10	Search c-leg
	#11	Search genium
	#12	Search “seattle power knees”
	#13	Search proprio foot
	#14	Search iPED
	#15	Search meridium
	#16	Search elan foot
C. Microprocessor controlled	#17	Search #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16
A and B and C	#18	Search #3 and #6 and #17
Limits		Search Limits: only items with abstracts, Humans, English, 2011/01/01 to 2024/07/03
A and B and C	#21	Search #3 and #6 and #17 and Limits: only items with abstracts, Humans, English
A and B and C	#22	Search #3 and #6 and #17 and Limits: only items with abstracts, Humans, English, 2011/01/01 to 2024/07/03
A and B and C	#23	Search #3 and #6 and #17 and Limits: only items with abstracts, Humans, English, 2024/01/01 to 2025/03/04

Electronic Database Searches

The following databases have been searched for relevant information:

Cochrane Database of Systematic Reviews
Cochrane Registry of Clinical Trials (CENTRAL)
PubMed
ClinicalTrials.gov

APPENDIX B. SUMMARY OF INCLUDED STUDIES

Appendix Table B1. Summary of included systematic reviews: Microprocessor-controlled prosthetic (MCP) knees vs. non-microprocessor-controlled (NMCP) knees

Assessment (year) Search dates Funding/COI	Purpose	Condition	Interventions	Primary Outcomes	Evidence-base Used	Primary Conclusions/Results
Hahn (2022) 13 studies Search Date: July 5, 2021 Funding: None COI: Multiple authors are employees of Ottobock Healthcare Products GmbH Austria	To update the available evidence of the clinical benefits of MCPs in limited community ambulators, i.e., MFCL-2.	Knee disarticulation or above knee or transfemoral amputation and MFCL-2 or equivalent mobility grade (Limited community ambulators) N=2366 patients across studies; n=704 MFCL-2, described as limited community ambulators which is focus of analyses	MCPs vs. NMCPs All patients received both MCP and NMCP	Safety, function, and mobility with prosthesis use and/or of patient-reported outcomes for perceived safety, function, the prosthesis	2 RCTs 1 controlled trial 7 controlled before-and-after trials 1 cohort study 2 cohort/case control studies Methodological quality assessed using the State-of-Science Evidence Report Guidelines of the AAOP. The overall validity was defined as "high" for 9 studies, "moderate" for	**Safety** The use of MCPs in limited community ambulators led to a reduction in (random effects model): - Falls (7 studies, n=117) SMD g: –0.59, 95% CI –0.85 to –0.32, I^2=0% - Fear of falling (6 studies, n=464) SMD g: 1.20, 95% CI 0.55 to 1.85, I^2=80% - Risk of falling as indicated by the TUG (4 studies, n=45) SMD g: –0.45, 95% CI –0.87 to –0.02, I^2=0% **Performance, function, and mobility** Improvement in: - Mobility grade change from MFCL-2 to MFCL-3 (6 studies, n=228 events) SMD 0.51, 95% CI 0.47 to 0.55 - Self-selected walking speed (6 studies, n=71) SMD g: 0.47, 95% CI 0.14 to 0.81, I^2=0%

Assessment (year) Search dates Funding/COI	Purpose	Condition	Interventions	Primary Outcomes	Evidence-base Used	Primary Conclusions/Results
					3 studies, and "low" for one study.	- Fast walking speed (3 studies, n=22) SMD g: 0.40, 95% CI -0.21 to 1.01, I^2=0% - Patient-reported ambulation (4 studies, n=78) MD 9.32, 95% CI 3.61 to 15.02, I^2=7% - Appearance PEQ: (3 studies, n=68) MD 5.24, 95% CI -0.87 to 11.35, I^2=1% - Residual Limb PEQ: (3 studies, n=69) MD 4.43, 95% CI -1.29 to 10.14, I^2=4% - Sounds PEQ: (3 studies, n=69) MD 3.36 95% CI -4.65 to 11.37, I^2=0% - Utility PEQ (3 studies, n=69) MD 7.76, 95% CI 2.05 to 13.47, I^2=0% - Well-Being PEQ: (3 studies, n=68) MD 4.97, 95%CI -1.01 to 10.96, I^2=0% - ABC: (3 studies, n=40) MD 7.55, 95% CI -7.03 to 22.14, I^2=48% MCP associated with greater improvement in mobility grade change, self-selected walking speed, patient-reported ambulation, and utility PEQ compared to NMCP

Assessment (year) Search dates Funding/COI	Purpose	Condition	Interventions	Primary Outcomes	Evidence-base Used	Primary Conclusions/Results
Thibaut (2022) 18 studies Search Date: February 15, 2021 Funding: Part of 2 authors' salaries are paid by the Fonds CNRF, Foundation Léon Frederic, University Hospital of Liège. COI: Authors certify that there is no conflict of interest with any financial organization	To evaluate the impact of the use of all types of MCP on patients' functional status and quality of life.	Unilateral transfemoral limb loss MFCL not clearly reported N=1595	MCP vs NMCP	Gait, ambulation, mobility, ADL performance, physical performance, balance confidence, quality of life (using validated questionnaires/tests)	7 RCTs 6 cross-sectional 5 follow-up studies Study quality was assessed using the Cochrane RoB tool for the RCT, and the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies for the remaining studies.	MCP users presented better functional status, mobility, and quality of life compared to NMCP users. It is unclear whether more advanced MCPs such as Genium are superior to other MCPs such as the C-leg® and the Rheo knee®, especially as these technologies improve over time.* RCTs: Improvement in walking ability and quality of life for MCP compared to NMCP; Similar results for Genium compared to C-Leg; stepping rate was higher for C-Leg.* Follow up trials: Better functional status and quality of life for MCP compared to NMCP. Cross-sectional studies: Improvement in quality of life for MCP compared to NMCP No one MCP outperformed any other MCP in performance or quality of life.

Assessment (year) Search dates Funding/COI	Purpose	Condition	Interventions	Primary Outcomes	Evidence-base Used	Primary Conclusions/Results
Mileusnic (2021) 12 studies Search Date: January 18, 2017 Funding: NR COI: Three authors are employees of Otto Bock Healthcare Products	To evaluate the effect of the Genium knee on ambulation, mobility, ADLs and quality of life compared to standard MCPs.	Transfemoral amputation or knee disarticulation (MFCL-3 and 4) N=1095	Genium knee vs. other "standard" MCPs	Ambulation (level walking, walking on ramps, walking on stairs), mobility, activities of daily living, quality of life	6 RCTs 5 before-and-after 1 cross-sectional Risk of bias was assessed using the State-of-Science Evidence Report Guidelines of the AAOP. Five studies were defined as having "high" validity, 6 of "moderate" validity, and 1 of "low" validity.	Authors present data for individual studies and only provide qualitative synthesis across studies; studies were published after the 2011 HTA. **Level walking:** - Peak knee flexion angle (swing and stance phase) significantly increased ($p<0.05$) with Genium.* **Walking on ramps:** - Peak knee flexion (swing phase) was significantly increased during ramp ascent and descent with Genium.* **Walking on stairs:** - 64% to 80% of patients were able to use step-over-step method when ascending stairs using Genium, resulting in increased range of motion in hip and knee on prosthetic side, and decreased compensations on the sound side.* **Activities of Daily Living:** - Significant improvements in upper body flexibility, balance, endurance, perceived safety and difficulty with Genium.* **Quality of Life:** - Significant improvements in Perceived Response, Social Burden,

Assessment (year) Search dates Funding/COI	Purpose	Condition	Interventions	Primary Outcomes	Evidence-base Used	Primary Conclusions/Results
						Utility, and Well-Being scales ($p<0.05$) on PEQ with Genium.* - No difference found in Ambulation, Frustration, and Residual Limb Health scales.* - Significant improvements in the following physical performance scales using Genium: comfort while standing, walking in tight spaces, walking downstairs, walking steep hills, walking slippery surfaces, satisfaction with walking ($p<0.025$).* **Evidence Statement 1:** "Genium results in more physiological gait, unloading and reduced compensatory mechanisms of the sound side compared to conventional MCPs." (High evidence level) **Evidence Statement 2:** "Genium improves mobility of unilateral TF amputees when compared to conventional MCPs." (Low evidence level) **Evidence Statement 3:** "Genium use improves performance in and

Assessment (year) Search dates Funding/COI	Purpose	Condition	Interventions	Primary Outcomes	Evidence-base Used	Primary Conclusions/Results
						safety of conducting ADLs compared to conventional MCPs." (High evidence level) **Evidence Statement 4:** "Genium further improves prosthesis-related quality of life of unilateral TF amputees as compared to conventional MCPs." (Low evidence level)
Cost-effectiveness only						
Donnelley (2021) 12 studies Search Date: May 2, 2019	To synthesize extant literature on the cost-effectiveness of prosthetic interventions and explore applicability to LMIC settings. No studies in LMIC were identified/included	Lower extremity amputations: transfemoral (9 studies), transtibial (3 studies) N=472	Prosthetic device vs comparison group	Cost difference, utility, ICER, acceptability threshold	3 RCTs 3 non-randomized crossover studies 3 cohort studies 2 lit reviews 1 cost analysis and survey Also Included 3 older RCT/economic	MCPs demonstrated more cost-effectiveness than NMCPs. C-Leg was more cost-effective, less expensive, and had better functional performance than NMCPs. ICER range: €3,281 to €40,155/QALY across 4 studies. One study reported a difference of €6,736 favoring C-leg at 1 year. Genium was more expensive, but provided better quality of life, compared to C-Leg. ICER: $6,000 to 6,522/unit functional improvement

Assessment (year) Search dates Funding/COI	Purpose	Condition	Interventions	Primary Outcomes	Evidence-base Used	Primary Conclusions/Results
					evaluations from the 2011 Critical appraisal and risk of bias assessment using the QHES Instrument, scored studies in the range of 49 to 99.	NMCPs had higher indirect costs than MCPs.

AAOP: American Academy of Orthotists and Prosthetists; ABC: activity-based balance confidence; ADL: activities of daily living; CI: confidence interval; COI: conflict of interest; HTA: health technology assessment; g: hedge's g; ICER: incremental cost-effectiveness ratio; LMIC: low- and middle-income country; MD: mean difference; MFCL: Medicare Functional Classification Level; MCP: microprocessor-controlled prosthesis; NIH: National Institutes of Health; NMCP: non-microprocessor-controlled prosthesis; NR: not reported; PEQ: Prosthetic Evaluation Questionnaire; QALY: quality-adjusted life year; QHES: Quality of Health Economic Studies; RCT: randomized controlled trial; RoB: risk of bias; SMD: standardized mean difference; TF: transferal; TUG: Timed Up and Go test.
* Authors provided qualitative assessments only. Aggregate data NR.

Appendix Table B2. Study characteristics and results of newly identified randomized foot and ankle MCPs vs. NMCPs

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
Colas-Ribas (2022) Randomized crossover trial In controlled (clinic/lab) and uncontrolled (real life use) settings Follow up: Period 1: 34 days (PA*)	Adults with TTA wearing a class II or III ESAR foot for more than 3 months, able to walk outdoors, and with a Houghton score ≥9 (0 to 12 scale, Higher score=greater prosthetic use and confidence) (N=45)	Proprio Foot® (a quasi-active MPA model) vs. standard prescribed ankle prosthesis (PA*) (standard energy	**Energy expenditure† (oxygen uptake [VO_2])** MPA: 19.4 (5.2) $mL \cdot kg^{-1} \cdot min^{-1}$ PA: 19.1 (4.7) $mL \cdot kg^{-1} \cdot min^{-1}$	Proprio Foot® improved balance, quality of life, and patient satisfaction despite no reduction or increase in energy expenditure in comparison with standard energy storage and return prosthesis.	The MPA is intended for patients with TTA with a low to moderate activity level. Funding: NR

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
Period 2: 34 days (PA[*]) - Each foot was worn for 34 days, with 1 week of adaptation and 1 week of follow-up to confirm this adaption and then the foot was worn for the last 20 days in everyday life, with assessments made on the 35th day.	Age: 55.5 (14.4) years Female: 18% Time since amputation (years): 6.1 (6.5) Reason for amputation: Trauma: 66% Vascular: 22% Other: 11% Missing: 7% Level of function/disability: NR Baseline differences noted between groups: - Reason for amputation - Time since amputation	storage and return prosthesis, ESAR)	- No difference in energy expenditure cost of ambulation at the highest performed activity step[‡], p=0.93 **Secondary outcomes[§]** **SF-36 PCS (0 to 100; higher is better)** MPA: 68.5 (19.5) PA: 62.1 (19) significant improvement in MPA compared with PA, p<0.01 **SF-36 MCS (0 to 100; higher is better)** MPA: 72.0 (20.8) PA: 66.2 (20.9) - significant improvement in MPA compared with PA, p<0.01 **PPA-LCI[**] (0 to 56; higher better locomotor capacities and activities)**: MPA: 52.7 (4.8)		COI: None

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
			PA: 52.6 (4.9) no difference, p=0.86 **ESAT scores (1-5; higher is better)** **Overall patient satisfaction** MPA: 4.4 (0.5) PA: 4.3 (0.5) - not statistically significant between groups, p=0.360 **Comfort** MPA: 4.6 (0.6) PA: 4.1 (0.7), - Difference in favor of MPA, p<0.001 **Weight** MPA: 3.8 (1.1) PA: 4.3 (0.7) - Difference in favor of PA, p<0.01 **Safety**: No adverse event was reported for either prosthesis. **ESAT Safety Score (0 to 5; higher is better)** MPA: 4.5 (0.7) PA: 4.3 (0.7)		

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
			no difference between groups, p=0.312		
Kaluf (2020) Randomized crossover trial Follow-up: Group AB received the MPA to use during the first 4-week accommodation period and Group BA received the ESAR foot. Both groups switched to the remaining research ankle-foot configuration following the first accommodation period	Adults with current use of a prosthesis for ≥1 year, wear prosthesis ≥8 hours a day, MFCL K3 or higher, well-fitting and functioning prosthesis, not requiring ambulatory aid (N=23) Age: 51 (NR) years Weight: 88.92 kg Years since amputation: 12.2 (NR) Level of function/disability: MFCL of K3 or higher Reason for amputation: Trauma: 61% Infection:13% Dysvascular: 9% Cancer: 9% Charcot ankle:4% Congenital: 4%	Kinnex microprocessor that receives input from a joint rotation sensor, a combined load/torque sensor, and an inertial measurement unit (MCP) vs. fixed-ankle energy-storing-and-returning (ESAR)	**ABC (0% to 100%)** MCP: 87.52% (8.48%) ESAR: 85.26% (8.48%) – No difference between groups, p=0.376 **PEQ-MS (0 to 48; higher is better function):** MCP: 3.47 (0.39) ESAR: 3.23 (0.39) - Difference in favor of MCP, p=0.0465 **PLUS-M (T-score range from 17.5 to 76.6; higher is greater mobility)** MCP: 58.07 (4.69) ESAR: 55.65 (4.69) - No difference between groups, p=0.102 **SCS (0 to 10, 10 is most comfortable):** **SCS walking: slope ascent**: MCP: 9.14 (1.18)	The 30° range of motion in the MPA can allow greater mobility when ambulating on typical environmental barriers (e.g., uneven terrain, ramps, and stairs) and allow patients to stand and walk on slopes with less socket discomfort. Most participants preferred the MPA. Frequently reported positive and negative aspects of both systems may be useful for patient consultation regarding ankle-foot technology. This study represents the largest known investigation of MPAs, and the results provide evidence of benefits from MPAs over ESAR feet in persons with UTA.	Funding: Industry COI: Dr. Kaluf received funding support from Freedom Innovations LLC

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
			ESAR: 7.71 (1.18) - Difference in favor of MCP, p<0.001 **SCS walking: slope descent:** MCP: 9.09 (1.00) ESAR: 7.52 (1.00) - Difference in favor of MCP, p<0.001 **SCS standing: slope ascent** MCP: 8.91 (1.52) ESAR: 6.74 (1.52) - Difference in favor of MCP, p<0.001 **SCS standing: slope descent** MCP: 9.30 (1.36) ESAR: 6.65 (1.36) - Difference in favor of MCP, p<0.001		
Same patient population					
Gailey[††] (2012) Randomized crossover trial Follow up: - Baseline	Unilateral transtibial amputations caused by diabetes, PVD, trauma, or tumor, comfortably fit with prosthesis for ≥6 months.		Proprio Foot® (MPA) Vs. SACH foot (K1) vs. SAFE foot (K2) vs.	Self-report measures (PEQ-13, LCI-5) did not detect mobility differences after prosthetic gait training or between prosthetic feet. Only AMPPRO identified functional changes post-training. The training helped lower-	Funding: Industry and government COI: Dr. Gailey is an educational consultant

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
- 10-to-14-day initial training - 2-week accommodation period with each prosthetic foot (8 to 10 weeks of testing with all 4 feet)	(N=10; 5 PVD, 5 non-PVD) Age PVD group: 60.60 (2.30) years Non-PVD group: 51 (5.83) years Female: 10% Mean height (cm) PVD group: 179.58 (8.50) Non-PVD group: 169.92 (3.85) Level of function/disability: NR		Talux foot (K3) **LCI-5[**‡‡] (0 to 56; higher better locomotor capacities and activities)** MPA: 54.4 (3.6) SACH: 55.2 (1.8) SAFE: 55.2 (1.8) Talux: 56.0 (0.0) - No difference between groups, p>0.05 **PEQ-13[‡‡] (0 to 130; higher is more functioning)** MPA: 124.02 (8.60) SACH: 112.34 (23.30) SAFE: 121.66 (10.70) Talux: 124.94 (8.30) - No difference between groups, p>0.05 **AMPPRO[‡‡] (0 to 47; higher is greater ambulator level)** MPA: 45.8 (0.4) SACH: 44.0 (1.9)	functioning individuals utilize higher-functioning prosthetic feet. AMPPRO scores and 6MWT distance were higher for the non-PVD group using the Proprio Foot. Self-report measures were ineffective in distinguishing prosthetic feet differences.	with Ossur Americas, and funding was partially supported by Ossur Americas. Ossur Americas had no role in the design or conduct of the study and collection or analysis of the data. The company reviewed the manuscript, but was not permitted to make editorial changes to the results and conclusions set forth.

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
			SAFE: 44.6 (1.5) Talux: 45.0 (1.2) - No difference between groups, p>0.05 **6MWT‡‡ (m)** MPA: 539.94 (79.60) SACH: 495.01 (70.30) SAFE: 488.18 (53.20) Talux: 507.34 (48.10) - No difference between groups, p>0.05 **6MWT Speed‡‡ (m/min)** MPA: 89.99 (13.27) SACH: 82.50 (11.71) SAFE: 81.36 (8.86) Talux: 84.55 (8.01) - No difference between groups, p>0.05 **Steps per day‡‡ (mean)** MPA: 6769 (1623) SACH: 6202 (1527) SAFE: 7465 (3459) Talux: 6321 (1598)		

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
			- No difference between groups, p>0.05 **Hour of Daily Activity‡‡ (mean)** MPA: 4.48 (1.10) SACH: 4.26 (1.20) SAFE: 4.94 (2.10) Talux: 4.80 (1.10) - No difference between groups, p>0.05		
Agrawal (2015); Agrawal (2013) Randomized crossover trial Follow up: - Baseline - 10-14 day initial training - 2-week accommodation period with each prosthetic foot (8-10 weeks of testing will all 4 feet)	Unilateral transtibial amputees (N=10) Female: 10% Age: 55.8 (6.5) years Level of function/disability: K-level-2: 50% K-level-3: 50% Etiology: Trauma: 40% PVD: 50% Tumor: 10%	Proprio Foot (MPA) Vs. SACH foot (K1) vs. SAFE foot (K2) vs. Talux foot (K3)	<u>Ramp ascent:</u> - No significant differences in SEW values between any pair of test feet <u>Ramp descent:</u> K-Level-2 - Higher SEW value with Talux K3 foot ($p<0.05$) compared to K1 and K2 feet. - MPA foot significantly higher SEW than K1 foot ($p<0.05$) - Difference in SEW between MPA foot and - K2 foot did not reach statistical	Prosthetic foot type impacts symmetry in external work more during decline walking than incline. K-Level-2 transtibial amputees achieve better symmetry with K3 dynamic response feet, especially with a J-shaped ankle or microprocessor ankle, when descending ramps. Findings support prescribing K3 feet for K-Level-2 amputees who frequently navigate ramps. K-Level-2 amputees can achieve better work symmetry with training and K3 prosthetic feet. An objective method for categorizing and prescribing prosthetic feet is needed. Gait training and K3 feet with a J-shaped ankle and heel-to-toe footplate may improve prosthetic care, clinician decisions, and reimbursement guidelines.	Funding: Industry and government COI: None

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
			significance (p=0.06). K-Level-3 - SEW values significantly higher with K3 foot (p<0.05) compared to the K1 foot. - K3 foot was not significantly different from K2 foot (p=0.07). - K3 foot had greatest SEW values in 4/5 K-Level-2 patients and 4/5 L-Level-3 patients. - No significant differences between K3 foot and MPA foot. K-Level-2 - Positive work[§§] symmetry[***] was not significantly different between feet - Negative work symmetry of the K3 foot was significantly better than the K1 and K2 feet (p<0.05).		

Author (Year) Study Design	Demographics Mean (SD) or %	Interventions	Results, mean (SD)	Author's Conclusions	Funding COI
			K-Level-3 - Neither positive nor negative work SEW values were significantly different between feet - Difference between K3 and K1 foot approached statistical significance (p=0.08)		

%GC: % gait cycle; 2MWT: two minutes walking test; 6MWT: 6-minute walking test; ABC: Activities Specific Balance Confidence Scale; AHA: articulating hydraulic ankle; AHA-MP: articulating hydraulic ankle with microprocessor; AMPPRO: Amputee Mobility Predictor with a prosthesis; BBS: Berg Balance Scale; BW: body weight; CC: changing cycle; COI: conflict of interest; CoM: change of motion; COP: center of pressure; COT: cost of transport; CV: coefficient of variation; DCF: dynamic carbon foot; EC: energy cost for walking; ECW: energy cost of walking; EE: metabolic energy expenditure; ESAR: energy storing and returning; ESR: energy storing and returning; ESAT: "Evaluation de la Satisfaction envers une Aide Technique" (French translation of the "Quebec User Assessment of Satisfaction with Assistive Technology"); FWT: floor walking test; g: Hedges' g; LCI-5: Locomotor Capabilities Index - modified; MCS: mental component scale; MFCL: Medicare Functional Classification Level; MK: mechanical knee; ML: mediolateral; MPA: microprocessor-controlled ankle; MPF: microprocessor-controlled foot; MCP: microprocessor-controlled prothesis; MTC: minimum toe clearance; NAA: non articulating ankle; NR: not reported; PA: prescribed ankle-foot units; PC: preparing cycle PEQ: Prosthesis Evaluation Questionnaire; PCS: physical component scale; PEQ-13: PEQ mobility scale; PEQ-MS: Prosthesis Evaluation Questionnaire-Mobility Subscale; PLUS-M: Prosthetic Limb User Survey of Mobility; PPA-LCI: Prosthetic Profile of the Amputee-LCI; PVD: Peripheral vascular disease; ROM: range of motion; RPE: rating of perceived exertion; SACH: solid ankle cushion heel; SAFE: stationary attachment flexible endoskeletal; SCS: Socket Comfort Score; SD: standard deviation; SEW: symmetry in external work; SF-36: Short-Form 36 Questionnaire; SSWS: self-selected comfortable walking speed; TP: tripping probability; TSI: trend symmetry index TT: transtibial; TTA: transtibial amputation/amputee; TWT: treadmill walking test; UDS: unified deformable segment; UF: usual foot; W: Kendall's W coefficient.

* Prescribed ankle-foot units consisted of the Proprio-Foot battery-mounted MPA mounted on an ESAR foot unit featuring a position control by imbedded sensors.

† In controlled lab setting.

‡ Step 1: 2 km·h−1 in flat ground; step 2: 2 km·h−1 at 10% incline; step 3: 3.2 km·h−1 at 10% incline [equivalent to a slope 5.71 degrees]; and step 4: 5 km·h−1 at 10%

§ In real life use setting.

** The Locomotor Capabilities Index-5 (LCI-5) and Prosthetic Profile of the Amputee-Locomotor Capabilities Index refer to the same assessment tool.

†† same study and author group as Agrawal 2013 and 2015.

‡‡ Outcomes are also presented for PVD vs. non-PVD groups. Not presented here.

§§ Positive and negative work—resulting from a positive and negative integrand—implied upward and downward CoM [center of mass] displacement, respectively. During gait, negative work is the result of downward CoM displacement, which occurs during weight acceptance and late stance phases of gait. Upward CoM displacement during gait results in positive work.

*** An SEW value of 100% indicates equal work by each limb, whereas values greater than 100% and less than 100% indicate more work by the prosthetic limb and intact limb, respectively.

Appendix Table B3. Study characteristics and results of newly identified non-randomized trials for foot and ankle MCP vs. NMCPs

Author (Year) Study Design	Demographics, mean (SD) or %	Intervention	Results , mean (SD) or % (n/N)	Author's Conclusions	Funding COI
Non-Randomized – uncontrolled environment					
Hahn (2018) Observational cohort Follow up: - Baseline - Interim (after 60 days of Meridium use) - End (after 100 days of Meridium use)	TTA, TFA, or knee disarticulation (N=70/86 with data from at least 1 questionnaire for analysis; 36% had complete data)[†] TFA patients do not all use the same knee in this study. Age: 45.6 (13.7) years Female: 33% Amputation level Transtibial: 64% Transfemoral or knee disarticulation: 36% Level of function/disability: K3: 63% K4: 37% Etiology Trauma: 66% Tumor: 13% Vascular disease: 13% Infection: 5% Congenital: 3%	Meridium foot MCP vs. Previous[‡] feet: carbon fiber feet (85%), MPF (7%), Solid Ankle Cushion Heel (SACH) feet (4%), Solid Ankle Flexible Endoskeletal (SAFE) feet (2%), and single-axis feet	Outcomes: Participant retrospective comparison with and perception of Meridium with their prior foot; ratings were worse, much worse, neutral, better, much better; **Ambulation[*] (% responders; ratings of better or much better**: - Improvement in level walking (54%; 37/68), walking on uneven terrain (82%; 56/68), ascending (97%; 65/67), descending (91%; 61/67), standing on ramps (86%; 45/67) **Patients favored toe clearance offered by Meridium[*]** (53%; 36/68), ascending stairs (37%; 25/68), descending stairs (52%; 35/68) **Comfort[*]**	Users who prefer the Meridium foot report improved safety, comfort, and a more natural walking experience. While many perceive significant advantages on uneven terrain and slopes, this perception only moderately correlates with overall preference. Personalized assessment and trial fittings may be key to identifying those who will benefit most.	Funding: None COI: None reported; one or more authors appear to be employed by Ottobock Healthcare Products

Author (Year) Study Design	Demographics, mean (SD) or %	Intervention	Results , mean (SD) or % (n/N)	Author's Conclusions	Funding COI
			- Rated more comfortable: walking (60%; 40/68), standing (53%; 36/68), sitting (67%; 46/68) **Pain*** No difference between MCP and prior foot in either residual or sound limb pain or back pain; similar proportions of patients were responders and non-responders with most indicating "neutral"/no difference **Concentration and perceived exertion*** No difference between MCP and prior foot for concentration or exertion. **Safety and stability*** Perceived increase during walking and standing (45%; 30/68) **Stumbles*** 35% (24/68) reported fewer stumbles, 32% (22/68) reported no change, and 33% (22/68) reported		

Author (Year) Study Design	Demographics, mean (SD) or %	Intervention	Results , mean (SD) or % (n/N)	Author's Conclusions	Funding COI
			increase in number of stumbles with Meridium. **Falls*** 23% (16/68) reported fewer falls, 72% (49/68) reported no difference, and 5% (3/68) reported more falls **Overall user satisfaction*** 50% (34/68); 40% (27/68) prefer Meridium over their previous foot.		
Nonrandomized: Controlled Environment					
Delussu (2013) Nonrandomized crossover Follow up: Phase 1 (P1): patients fit with dynamic carbon fiber foot and Seal In X5 for 7 weeks Phase 2 (P2): patients fit with Seal In X5 and Proprio Foot, 1 h after delivery to the patient) Phase 3 (P3): after 30 days of Proprio Foot use	Unilateral transtibial amputees (N=10) Age: 44.2 (10.1) years Female: 0% Mass: 81 (16) kg Height: 173.8 (7.3) cm Level of function/disability: K-level 3: 40% K-level 4: 60% Eiotology Trauma: 80% Infection: 10%	Bionic foot - MCP (Proprio Foot) vs. Dynamic carbon foot	**Energy cost of walking** Floor walking test: - significant reduction in ECW after 90 days of using the Proprio Foot compared with DCF/ Seal In X5 suspension system (P1 vs P5: p=0.002) and compared to P0 (P0 vs P5: p=0.005) -ECW on floor was lower than ECW on the treadmill (i.e. TWT -5%, 0% and 12%), p<0.005 Treadmill walking test:	Proprio Foot may reduce the energy cost of walking (ECW) for transtibial amputees (TTAs), despite its increased weight, compared to DCF.	Funding: Industry COI: None

Author (Year) Study Design	Demographics, mean (SD) or %	Intervention	Results , mean (SD) or % (n/N)	Author's Conclusions	Funding COI
Phase 4 (P4): after 60 days of Proprio Foot use Phase 5 (P5): after 90 days of Proprio Foot use	Vascular disease: 10%		- ECW for all slopes showed a trend toward improvement **LCI-5 (0-56; higher is better)** P0: 51.8 (10.9) P1: 53.9 (4.3) P5: 52.4 (6.1) - No trend of statistical significance, p>0.05		
Bai (2018) Nonrandomized crossover Follow up: IP (single day experiment)	Unilateral transfemoral amputees (N=5) Age: 42 (17) years Female: 0% Weight with prostheses: 107 (16) kg Height: 1.83 (0.02) m Level of function/disability: NR Nonamputees (N=14; 5 males and 9 females, Age: 26 (2) years Female: 64% Weight: 68 (15) kg Height: 1.69 (0.08) m	Esprit non articulating ankle (FIX) vs. Elan articulating hydraulic ankle with microprocessor (MPC-HY) vs. Echelon articulating hydraulic ankle (nMPC-HY)	**Walking speed**: - No significant difference found in either ascending slope (p=0.993) or descending slope (p=0.254) among the three devices	Hydraulic ankle-foot devices improve ankle motion, ROM, and walking safety on slopes for TFAs versus FIX. MPC-HY allows customized adjustments, but differences from nMPC-HY were not widely perceived. Overall, hydraulics enhance slope adaptation, with MPC-HY better suited for users needing frequent adjustments in demanding conditions.	Funding: Non-profit/Charity COI: Blatchford & Sons Ltd. provided ankle-foot devices and contributed to the University of Surrey for David Ewins' employment costs. They had no role in study design, data collection, analysis, interpretation, writing, or publication decisions. This does not affect compliance with PLOS ONE data-sharing policies.
Darter (2014)	Traumatic unilateral transtibial amputees (N=6)	Customary device vs.	**Metabolic energy expenditure:**	Adaptive ankle motion did not provide significant	Funding: Government COI: None

Author (Year) Study Design	Demographics, mean (SD) or %	Intervention	Results , mean (SD) or % (n/N)	Author's Conclusions	Funding COI
Nonrandomized crossover ≥ 3 weeks acclimation between testing with each foot	Age: 30 (4) years Height: 1.74 (0.14) m Weight: 85.4 (16.9) kg Time since amputation: 34 (14) months Level of function/disability: NR	Microprocessor-controlled device (Pon) vs. Identical Proprio device deactivated (Poff)	- Nonsignificant interactions between the prosthetic foot type and the walking speed for each of the slope conditions, p>0.05. - Customary foot on average 13.5% higher for slope descent than Pon (p<0.05) and 10.3% more than Poff (p<0.05) - No statistically significant differences among feet during level walking for slope ascent, p>0.05 **Energy cost for walking:** - Nonsignificant interactions for all slope conditions and significant effect for prosthetic foot type (p<0.01) during slope descent only. **Rating of perceived exertion:** - Significant device effect for slope ascent and descent (p<0.01). - RPE values decreased with Pon by an average of 2.2 on the 6 to 20	physiological benefits during slope walking. However, the Proprio required less effort than the standard device for descending slopes, likely due to differences in mechanical properties between the prosthetic feet.	

Author (Year) Study Design	Demographics, mean (SD) or %	Intervention	Results , mean (SD) or % (n/N)	Author's Conclusions	Funding COI
			scale compared to customary ($p<0.01$) and 1.8 with Poff compared to customary device ($p<0.01$). - No significant changes in RPE for level walking, $p>0.05$ - Decrease in RPE of 1.4 with Pon was significantly lower than customary device ($p<0.01$). - No difference between Pon and Poff for each walking condition, $p>0.05$.		
Thomas-Pohl (2021) Nonrandomized crossover Follow up: 3-week wash out period with usual foot between each MPA, followed by 15-day acclimatization period with test MPA	Transtibial amputation for traumatic reasons (N=6) Age: 36 years (range 29 to 64 years) Female: 17% Time since amputation: 46 (NR) months Level of function/disability: NR	Elan (MPA1) vs. Proprio Foot (MPA2) vs. Meridium (MPA3) vs. ESR/UF foot	**Standing on level ground and slope** MPAs improved posture and reduced residual knee moment on positive and negative slopes compared to ESR. Results also indicate that MPA2 provides the best control of the CoP in all situations. **Clinical function:** - 2MWT: no functional differences among feet, $p>0.05$	An increased ankle mobility is associated with a better posture and balance on slope. Gait analysis would complete these outcomes. Findings show that while MPAs adjust their range of motion, these adaptations affect propulsion energy, which should be considered based on user activity. Selecting the right prosthetic foot requires balancing	Funding: NR COI: None

Author (Year) Study Design	Demographics, mean (SD) or %	Intervention	Results , mean (SD) or % (n/N)	Author's Conclusions	Funding COI
			- Gait speed (5.9km/h) higher than reported in literature (3.1 km/h)	comfort, propulsion, durability, and compensatory needs.	

2MWT: two minutes walking test; COI: conflict of interest; COP: center of pressure; CTSA: Clinical and Translational Science Award**;** DCF: dynamic carbon foot; EC: energy cost for walking; ECW: energy cost of walking; EE: metabolic energy expenditure; ESR: energy storing and returning; FIX: Esprit non articulating ankle; IP: immediately post-treatment; LCI-5: Locomotor Capabilities Index - modified; MPA: microprocessor-controlled ankle; : microprocessor-controlled foot; MPC-HY: Elan articulating hydraulic ankle with microprocessor; MCP: microprocessor-controlled knee; nMPC-HY: Echelon articulating hydraulic ankle; NR: not reported; ROM: range of motion; RPE: rating of perceived exertion; SACH: solid ankle cushion heel; SAFE: stationary attachment flexible endoskeletal; SD: standard deviation; TFA: transfemoral amputation/amputee; TTA: transtibial amputation/amputee; TWT: treadmill walking test; UF: usual foot.

* No comparison group. Patients were compared to their existing prosthetic foot. Results are patients' perceptions compared to previous feet used.

† Population drawn from convenience sample of patients having initial routing fitting for Meridium MCP.

‡ Study relies on patients' retrospective comparison of MCP with their previous foot.

APPENDIX C. EXCLUDED STUDIES AT FULL TEXT REVIEW

Excluded	Reason
SRs	
Kannenberg A, Zacharias B, Pröbsting E. Benefits of microprocessor-controlled prosthetic knees to limited community ambulators: systematic review. J Rehabil Res Dev. 2014;51(10):1469-96.	Updated by Hahn 2022 SR
Sawers AB, Hafner BJ. Outcomes associated with the use of microprocessor-controlled prosthetic knees among individuals with unilateral transfemoral limb loss: a systematic review. J Rehabil Res Dev. 2013;50(3):273-314.	Older; overlap with prior report; no new RCTs
Samuelsson KA, Töytäri O, Salminen AL, Brandt A. Effects of lower limb prosthesis on activity, participation, and quality of life: a systematic review. Prosthet Orthot Int. 2012 Jun;36(2):145-58.	Older; only one new RCT from 2014
RCTs	
Davot J, Thomas-Pohl M, Villa C, Bonnet X, Lapeyre E, Bascou J, Pillet H. Experimental characterization of the moment-angle curve during level and slope locomotion of transtibial amputee: Which parameters can be extracted to quantify the adaptations of microprocessor prosthetic ankle? Proc Inst Mech Eng H. 2021 Jul;235(7):762-769.	No clinical outcomes
Ernst M, Altenburg B, Bellmann M, Schmalz T. Standing on slopes - how current microprocessor-controlled prosthetic feet support transtibial and transfemoral amputees in an everyday task. J Neuroeng Rehabil. 2017 Nov 16;14(1):117.	No clinical/patient outcomes
Ernst M, Altenburg B, Schmalz T, Kannenberg A, Bellmann M. Benefits of a microprocessor-controlled prosthetic foot for ascending and descending slopes. J Neuroeng Rehabil. 2022 Jan 28;19(1):9.	No clinical/patient outcomes
Kim J, Wensman J, Colabianchi N, Gates DH. The influence of powered prostheses on user perspectives, metabolics, and activity: a randomized crossover trial. J Neuroeng Rehabil. 2021 Mar 16;18(1):49.	Assesses “powered” prostheses rather than MCP
Riveras M, Ravera E, Ewins D, Shaheen AF, Catalfamo-Formento P. Minimum toe clearance and tripping probability in people with unilateral transtibial amputation walking on ramps with different prosthetic designs. Gait Posture. 2020 Sep;81:41-48.	No clinical/patient outcomes
Schmalz T, Altenburg B, Ernst M, Bellmann M, Rosenbaum D. Lower limb amputee gait characteristics on a specifically designed test ramp: Preliminary results of a biomechanical comparison of two prosthetic foot concepts. Gait Posture. 2019 Feb;68:161-167.	No clinical/patient outcomes
Struchkov V, Buckley JG. Biomechanics of ramp descent in unilateral trans-tibial amputees: Comparison of a microprocessor controlled foot with conventional ankle-foot mechanisms. Clin Biomech (Bristol). 2016 Feb;32:164-70.	No clinical/patient outcomes

APPENDIX D. FUNCTIONAL CLASSIFICATION AND OUTCOMES MEASURES

Appendix Table D1. Definitions of Medicare Functional Classification Levels

MFCL	Description	HCPCS modifiers	Feet*	Ankles	Knees
Level 0	Does not have the ability or potential to ambulate or transfer safely with or without assistance and a prosthesis does not enhance their quality of life or mobility.	K0	NA	NA	NA
Level 1	Has the ability or potential to use a prosthesis for transfers or ambulation on level surfaces at fixed cadence. Typical of the limited and unlimited household ambulator.	K1	A SACH foot for persons whose functional level is 1 or above. An external keel SACH foot or single axis ankle/foot for persons whose functional level is 1 or above.	NA	A single axis constant friction knee and other basic knee systems for persons whose functional level is 1 or above.
Level 2	Has the ability or potential for ambulation with the ability to traverse low level environmental barriers such as curbs, stairs or uneven surfaces. Typical of the limited community ambulator.	K2	A flexible-keel foot or multi-axial ankle/foot for persons whose functional level is 2 or above.	An axial rotation unit for persons whose functional level is 2 or above.	See above
Level 3	Has the ability or potential for ambulation with variable cadence. Typical of the community ambulator who has the ability to traverse most environmental barriers and may have vocational, therapeutic, or exercise activity that demands prosthetic utilization beyond simple locomotion.	K3	A flex foot system, energy storing foot, multi-axial ankle/foot, dynamic response foot with multi-axial ankle, shank foot system with vertical-loaded pylon or flex-walk system or equal for persons whose functional level is 3 or above.	Microprocessor-controlled ankle-foot prostheses (e.g. PowerFoot BiOM, iWalk, Bedford, MA; Proprio Foot, Ossur, Aliso Viejo, CA) for persons whose functional level is 3 or above.†	A fluid or pneumatic knee for persons whose functional level is 3 or above. A fluid, pneumatic, or electronic/microprocessor knee for persons with a knee disarticulation amputation, a trans-femoral amputation, or a hip disarticulation amputation whose functional level is 3 or above.

Level 4	Has the ability or potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress, or energy levels. Typical of the prosthetic demands of the child, active adult, or athlete.	K4	See above	See above	A high-activity knee control frame for persons whose function level is 4.

HCPCS: Healthcare Common Procedure Coding System; MFCL: Medicare Functional Classification Levels; NA: not applicable; SACH: solid ankle cushion heel; SAFE: stationary attachment flexible endoskeletal.

* Additional notes for feet prostheses:

1. A use-adjustable heel height feature is considered not medically necessary.
2. Foot covers (foot shells) are included in the reimbursement for a prosthetic foot component and are not separately payable. Repair or replacement of a foot cover for appearance, comfort, convenience or individual abuse, misuse or neglect is considered not medically necessary. Repair or replacement of a damaged foot cover should be billed using HCPCS repair code L7510. No more than 1 foot cover replacement per prosthetic foot is considered medically necessary once per year.

† Prosthetic shoe for a partial foot amputation when the prosthetic shoe is an integral part of a covered basic lower limb prosthetic device.

Appendix Table D2. Outcome Measures

Outcome Measure Intent	Assessed By	Components	Score Range	Interpretation	MCID
Most common measures					
General measures* of walking speed, walking distance, rising from or sitting in a chair, ascending stairs or inclines, walking outside on a variety of surfaces, Locomotive performance in stress tests, Metabolic energy expenditure per minute, Energy cost for walking per minute, etc.	Clinician	Varies	Varies	Varies	NR
Prosthesis Evaluation Questionnaire (PEQ) Subscale: Ambulation, Appearance, Residual Limb Health, Sounds, Utility, Well Being, Frustration, Perceived Response, Social Burden.	Patient	VAS scale	0 to 100	Higher the score corresponds with a more positive response.	Not established, but ≤10 improvement is used
Prosthesis Evaluation Questionnaire-Mobility Scale (PEQ-13)	Patient	Focuses on the perceived potential for mobility,	0 to 130	Higher score indicates higher functioning	NR

Outcome Measure Intent	Assessed By	Components	Score Range	Interpretation	MCID
Describes the perception of difficulty in performing prosthetic function and mobility by assessing prosthetic function, mobility, psychosocial aspects, and well-being.		ambulation, and transfers while using a prosthetic device, as a 13-question subset of the PEQ, through a formatted VAS			
Prosthesis Evaluation Questionnaire-Mobility Scale (PEQ-MS) Measure of prosthetic mobility for lower-limb loss	Patient	A 12-question revision of the PEQ-13, with 5-level ordinal response options	0 to 48	Higher score indicates higher functioning	NR
Activities-Specific Balance Confidence Scale (ABC) Measure of perceived balance	Clinician	Includes 16 items, each scored from 0% to 100%, with average score reported	0% to 100%	Higher percentage indicates higher balance	NR
Four Square Step Test (FSST) Examines the ability to step over small objects and to change direction within a clinical setting.	Clinician	Consists of a timed measure that requires individuals to step over canes placed in a crosswise pattern on the floor.	Varies by population	Lower time indicates higher function	NR
Timed Up and Go Test (TUG) Designed to assess aspects of balance, gait, and physical function	Clinician	Tests the ability to rise from a chair, walk 3 meters, turn around, return to the chair, and return to a seated position	Varies	Lower time indicates higher function	NR
Prosthetic Limb user Survey of Mobility (PLUS-M) Measures perceived mobility with a prosthesis in different environments	Patient	Questions beginning with “are you able to…” followed by a description an various activities. No time frame is provided and respondents’ current perception of their mobility is implied.	T-Score with mean 50 and SD=10, with score ranging from 17.5 to 76.6	Higher score indicates greater mobility	NR

Outcome Measure Intent	Assessed By	Components	Score Range	Interpretation	MCID
Amputee Mobility Predictor with a prosthesis (AMPPRO) Evaluates the functional mobility of individuals to help clinicians determine Medicare Functional Classification Levels (K-levels)	Clinician	Consists of 21 tasks evaluating balance, transfers, gait quality, and functional mobility, with scores based on task performance.	0 to 47	Higher score indicates greater ambulator level	NR
Prosthetic Socket Fit Comfort Score (SCS) Rates the current socket comfort	Patient	Measures the comfort level on a scale of 0-10.	0 to 10.	Scores <5 indicate significant discomfort which require adjustments or a new socket; 5-7 suggest moderate comfort but may indicate minor issues; 8-10 indicate excellent comfort and fit.	NR
Quebec User Assessment of Satisfaction with Assistive Technology (QUEST) *Evaluation de la Satisfaction envers une Aide Technique* (ESAT) is French translation of QUEST Assesses user satisfaction with a device	Patient	12 items: eight items concern patient satisfaction on the device and four focus on services surrounding the device.	Each items scored 1-5	Higher score indicates greater satisfaction	NR
Symmetry in External Work (SEW) Assesses the symmetry of mechanical energy expenditure between prosthetic and intact limbs. Provides insight into gait efficiency and asymmetries in locomotion	Clinician	Calculates the changes in energy of center of mass with the intact limb and prosthetic limb, and determines the index of symmetry.	Expressed as a ratio or percentage	Lower values indicate more symmetrical gait and energy distribution, higher values suggest greater asymmetry, which may lead to higher metabolic cost, muscle	NR

Outcome Measure Intent	Assessed By	Components	Score Range	Interpretation	MCID
				strain, and increased fall risk.	
Prosthetic Profil of the Amputee Locomotor Capability Index-5 (PPA-LCI or LCI-5) Evaluates ambulatory skills	Patient	14 items, measuring the ability to perform a number of motor tasks.	Each tasks scored from 0 to 4. Scores range from 0 to 56	Higher score indicates more independence	Change of 7 points
BERG Balance Test (BERG)[†] Assesses the balance and risk of falling in individuals	Clinician	Consists of tasks, including: Sitting to standing, standing unsupported, sitting unsupported, transfers, standing with eyes closed, turning to look behind, picking up an object from the floor, turning 360°, standing on one leg, tandem standing	Each task scored from 0 to 4, with total score being 0 to 56	Score 41-56: low fall risk Score 21-40: medium fall risk Score 0-20: high fall risk	4 to 7
Satisfaction (satisfactory alignment, general satisfaction with device, etc.)	Patient	General satisfaction, % (n/N)	0% to 100%	Proportion of patients satisfied with the device	NR
Subject's perception on task (walking, walking on uneven terrain, ascending, descending, standing on ramps, etc)	Patient	Patients' perception of improvement doing tasks, number experiencing improvement % (n/N)	0% to 100%	Proportion of patients that improved while doing tasks	NR
Likert scale ratings (pain in the back, pain in the sound limb, pain in the residual limb, necessary concentration during walking, perceived exertion during walking)	Patient	Increase or decrease in domains Much more, more, less, much less	-100% (much more) to 100% (much less)	Percentage increase or decrease in the specific domains	NR
Assessment of Daily Performance in Transfemoral Amputees Test (ADAPT)	Patient	Patients perform a set of standardized stimulated ADL, based on activities	0 to 100	Higher score means activity is more difficult	Not established, but some use ≤10 point difference

Outcome Measure Intent	Assessed By	Components	Score Range	Interpretation	MCID
Designed specifically for transfemoral amputees, evaluates the ability to perform ADL while using a prosthetic limb		that are considered difficult to carry out while using a leg prosthesis.			
Houghton Scale Measures the time spent wearing the prosthesis and its functional use	Patient	1. Time spent using the prosthesis 2. How the prosthesis is used 3. The need for an assistive device 4. The individuals perception of stability while walking outside on a variety of terrains	0 to 12	Higher score indicates greater prosthetic use and confidence	NR
Hill Assessment Index (HAI) Evaluates the ability to walk down a ramp	Clinician	Focuses on quality of movement while descending a ramp, with observations focused on: the use of a prosthesis, gait pattern and control, balance and stability, and confidence and independence during the task.	1 to 11	Higher score indicates better performance and greater functional ability	NR
Stair Assessment Index Evaluates the quality of gait by observing use of a handrail and other assistive devices and foot placement while descending 12 steps	Clinician	Assesses the use of handrails or assistive devices, gait pattern, foot placement on each stair, and safety and balance	1 to 13	Higher scores indicate a better functional performance	NR
Amputee Mobility Predictor (AMP)	Clinician	Includes 21 tasks and scores the ability to perform each, ranging	0 to 47	Higher scores indicate greater functional	NR

Outcome Measure Intent	Assessed By	Components	Score Range	Interpretation	MCID
Performance-based outcome measure of current and future functional capabilities.		from 0 to 2 points per item		mobility and potential for prosthetic use 0-18: non-ambulatory 19-26: limited indoor ambulation 27-36: limited community ambulation 37-42: community ambulator, able to navigate most terrains 44-47: higher active ambulator, typically athletes	
Continuous-Scale Physical Functional Performance-10 Assessment (CS-PFP-10) Scores 10 ADL	Clinician	Scores 10 ADL using time, distance, and mass, with raw data reflecting the physiologic domains of function, and then converted into summary scores and individual domain scores (upper-body strength, upper-body flexibility, balance and coordination, lower body strength, and endurance)	0 to 100	Higher scores indicate better physical functional performance	NR
Modified Falls Efficacy Scale (MFES) Assesses confidence in performing daily activity without falling, adapted from the original Falls Efficacy Scale.	Patient	Incudes 14 items that evaluate confidence in performing specific activities such as walking indoors, reaching for objects, navigating stairs, walking on uneven surfaces, getting in and	0 to 140	Higher score indicates greater confidence in performing activities without falling	NR

Outcome Measure Intent	Assessed By	Components	Score Range	Interpretation	MCID
		out of a car, and community ambulation.			

ADL: activities of daily living; MCID: minimal clinically important difference; NR: not reported; VAS: visual analogue scale.
* Includes measures such as 10-minute walk test, 6-minute walk test, 2-minute walk test, which were reported often.
† Also referred to as the Berg Balance Scale (BBS).

APPENDIX E. ONGOING TRIALS

Characteristics of current ongoing studies registered in clinical trials.gov assessing the efficacy of MCP.

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
University Medical Center Groningen NCT06031922 12-31-2024 (Recruiting)	**Comparing the Effectiveness and Cost-effectiveness of Conventional Mechanical Knees and Microprocessor-controlled Knees: a Prospective Cohort Study**	**Inclusion Criteria:** 1. At least one year post amputation 2. Unilateral transfemoral amputation or knee-disarticulation 3. Eligible for a trial on an MCP 4. Able to read and write in Dutch 1. Use a prosthesis with a socket **Exclusion Criteria:** 1. Bilateral amputation 2. Osseointegration 3. Previous experience with an MCP	**Intervention:** Microprocessor-controlled Knees (MCP) **Control:** Conventional Mechanical Knees (CMK)	**Primary:** 6 Minute Walking Test (6MWT) **Secondary:** 1. Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) 2. Timed Up and Go test (TUGtest) 3. Activities-Specific Balance Confidence Scale Nederlands (ABC-NL) 4. Cost-questionnaire 5. Prosthesis Evaluation Questionnaire (PEQ) 6. Utrecht Scale for Evaluation of Rehabilitation Participation (USER-P) 7. Activity tracking for physical activity (Activ8)
Proteor Group NCT06017024	**Evaluation of a New Microprocessor-Controlled Prosthetic Knee : A Prospective, Multicentered, Randomized Cross-over Trial**	**Inclusion Criteria:** 1. Able to understand and give informed consent 2. Man or woman, more than 18 y.o	**Intervention:** New MCP **Control:** Current MCP	**Primary:** Personal goal achievement **Secondary:** 1. Functional walking test - mobility capacity

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
08-31-2025 (Recruiting)		3. Lower limb amputee KD or AKA, unilateral or bilateral 4. K3/K4 activity level 5. Already fitted with FR-reimbursed MCP 6. Being comfortable in their socket (SCS>=5) **Exclusion Criteria:** 1. Protected person 2. Pregnant or breast feeding lady 3. Person having pathologies affecting their sensitivity 4. Using walking aids 5. Weighting more than 136kg 6. Insufficient hip joint or pelvic voluntary muscle control 7. Insufficient cognitive ability to charge the knee and care for the device		2. Functional walking test - fast walking speed 3. Functional test - ability to walk downhill 4. Functional test - ability to walk downstairs 5. Questionnaire to assess comfort in the socket 6. Questionnaire to assess satisfaction 7. Questionnaires to assess quality of life 8. Prosthesis Evaluation Questionnaire
YourResearchProject Pty Ltd NCT05870267 06-2024 (Recruiting)	**Biomechanical Assessment of Load Applied on Residuum of Individuals With Limb Loss Fitted With a Prosthetic Limb**	**Inclusion Criteria:** 1. be willing to participate to this project of research, 2. be able to be fitted with common bionic prosthetic components (e.g., Knee, feet), 3. be willing to comply with protocol, 4. have a lower limb amputation more than 12 months prior testing,	**Intervention:** 1. Power Knee with bone anchored suspension 2. C-Leg 3. Rheo Knee XC **Control:**	**Primary:** 1. Cadence 2. Magnitude of loading pattern 3. Maximum moments in gait cycle **Secondary:** 1. The variability of datasets 2. Factor of safety

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
		5. have a clearance of at least 6 cm between residuum and prosthetic joint, 6. have completed rehabilitation program, 7. be free of injuries on the day of the recording session, 8. weigh less than 121 kg, 9. be able to walk 200 meters independently, 10. be between 18-80 years of age. **Exclusion Criteria:** 1. not be able to give informed consent, 2. have bilateral amputation, 3. have self-reported pain levels greater than 4 out of 10 at study outset, 4. have experienced a fall within the last 8 weeks before assessment, 5. have mental illness or intellectual impairment, 6. have injuries involving contralateral (intact) limb, 7. have major uncorrected visual deficit, 8. have history of epilepsy or recurrent dizziness, 9. present signs of infection 2 weeks prior testing session.	1. Usual MCPs (e.g., C-Leg, Genium) 2. Non-MCPs	3. Prosthesis efficacy

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
Liberating Technologies, Inc. NCT05267639 04-30-2025 (Recruiting)	**Clinical Outcomes With Passive MCPs vs. Powered Prosthetic Knees by K4-level Transfemoral Amputees**	**Inclusion Criteria:** 1. Are at least 18 years old 2. Unilateral transfemoral prosthesis user (limb absence between the knee and hip) 3. Current user of a microprocessor-controlled knee (MCP) 4. Have adequate clearance between distal end and ground for necessary knee and foot components 5. Medicare Functional Classification Level (K-Level): 4 6. Socket-Comfort Score: 6 or above to ensure adequate socket fit 7. PLUS-M T-score of 55 or above 8. Six months or more experience on a prosthesis 9. Body weight between 50kg and 116kg (110lbs - 256lbs) **Exclusion Criteria:** 4. Present injuries to residual limb or contralateral leg affecting functional ability 5. Socket issues/changes in the last 6 weeks 6. Users with bone-anchored implants	**Intervention:** Ossur Power Knee **Control:** Passive MCP	**Primary:** 1. [Mobility Primary Outcome]: daily number of steps taken 2. [Safety Primary Outcome]: Activities-Specific Balance Scale 3. [Wellbeing Primary Outcome]: PEQ-Well-Being (PEQ-WB) **Secondary:** 1. Six Minute Walk Test (6MWT) – Measuring change from baseline 2. Stair Assessment Index (SAI) 3. Hill Assessment Index (HAI) 4. Timed Up and Go Test (TUG) 5. Patient Reported Outcomes Measures Information System – Physical Function (PROMIS-PF) 6. PLUS-M Version 3.0 – Measuring change from baseline 7. Borg Rating of Perceived Exertion (RPE)

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
				8. Physiological Cost Index (PCI) 9. PROMIS – Fatigue (PROMIS-FAT) 10. Self reported falls 11. PROMIS-29 12. Oswestry Disability Index (ODI) 13. PROMIS – Ability to Participate in Social Roles and Activities (PROMIS-APSRA)
Synchro Motion LLC NCT05955378 07-31-2024 (Recruiting)	**Assessment of a Microprocessor Ankle for Low Mobility Individuals**	**Inclusion Criteria:** 1. Adults aged 18-89 years 2. Patients who have a unilateral transtibial amputation who are able to use a prosthesis and who currently use a passive, non-MPC prosthesis 3. K2 level ambulators **Exclusion Criteria:** 1. Pregnant women 2. Children (<18 years old) 3. Prisoners or institutionalized individuals 4. Individuals who have the inability to give informed consent 5. Participants unable to walk for 2 minutes without an assistive device	**Intervention:** Damping, Stiffness, and Repositioning (DSR) ankle **Control:** Predicate ankle	**Primary:** 1. Minimum Foot Clearance 2. Time to Foot Flat 3. Maximum Lyapunov Exponent 4. Weight Bearing Symmetry 5. Center of Pressure RMS Velocity **Secondary:** 1. Orthotics Prosthetics User Survey (OPUS) 2. Numerical Pain Rating Scale (NPRS) 3. Borg Rating Scale (RPE) 4. Modified Falls Efficacy (mFES)

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
		6. Participants with complicating health conditions that interfere with the study 7. Inability to read and understand the English language. As this is a pilot study with a small sample size, it is prohibitive to translate Study documents to other languages as recruitment will be from a sample of convenience.		5. 10 Meter Walk Test (10 MWT) 6. Six Minute Walk Test (6 MWT) 7. Berg Balance Test (BBS) 8. Functional Gait Assessment (FGA) 9. Hill Assessment Index (HAI) 10. Timed Up and Go (TUG)
Otto Bock Healthcare Products GmbH NCT04784429 12-31-2026 (Active, not recruiting)	**Assessing Outcomes With Microprocessor Knee Utilization in a K2 Population**	**Inclusion Criteria:** 1. Unilateral transfemoral or knee disarticulation amputation 2. Received prosthesis between 4 - 24 months prior 3. Currently uses prosthesis 4. K2 ambulator status 5. Able to speak English or Spanish language 6. Age ≥ 65 years at Baseline Assessment (one month after enrollment) 7. Minimum Socket Comfort Score (SCS) of 6/10 **Exclusion Criteria:** 1. Unilateral transfemoral or knee disarticulation amputation 2. Received prosthesis between 4 - 24 months prior 3. Currently uses prosthesis	**Intervention:** MCP (Kenevo or C-Leg 4) **Control:** Non microprocessor controlled knee (NMCP)	**Primary:** 1. Fear of Falling Avoidance Behavior Questionnaire (FFABQ) **Secondary:** 1. PROMIS-29 2. PROMIS-APSRA 3. 12-month fall count from bi-weekly fall journal 4. Average daily step counts 5. 10-meter Walk Test (10mWT) 6. Timed Up and Go (TUG)

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
		4. K2 ambulator status 5. Able to speak English or Spanish language 6. Age ,â• 65 years at Baseline Assessment (one month after enrollment) 7. Minimum Socket Comfort Score (SCS) of 6/10		
Shirley Ryan AbilityLab NCT03204513 12-2024 (Active, not recruiting)	**Impact of Powered Knee-Ankle Prosthesis Leg on Everyday Community Mobility and Social Interaction**	**Inclusion Criteria:** 1. Unilateral transfemoral level limb loss or limb difference 2. K2/K3/K4 level ambulators 3. Required to use a microprocessor knee on their prosthesis **Exclusion Criteria:** 1. Over 250 lbs body weight 2. Inactive, physically unfit 3. Cognitive deficits or visual impairment that would impair their ability to give informed consent or to follow simple instructions during the experiments 4. Pregnant women 5. Co-morbidity that interferes with the study (e.g. stroke, pace maker placement, severe ischemia cardiac disease, etc.)	**Intervention:** Vanderbilt Powered Knee-Ankle Prosthesis **Control:** Microprocessor (MP) Knee Prosthesis	**Primary:** 1. Change between devices of the Modified Graded Treadmill Test 2. Change in Biomechanical Assessment [Gait Parameters and Surface Electromyography (EMG) Activation] Between Devices **Secondary:** 1. Change in Manual Muscle Test (MMT) 2. Change in Passive Range of Motion (PROM) 3. Change in Active Range of Motion (AROM) 4. 6 Minute Walk Test (6MWT) with COSMED K4B2 Metabolic unit 5. Hill Assessment Index (HAI) 6. Stair Assessment Index (SAI)

Study Sponsor NCT ID Completion date	Title	Inclusion/exclusion	Intervention	Outcomes
				7. Cross Walk Blinking Signal Test 8. GAITRite® Data Capture 9. 5 Times Sit to Stand Test (5XSST) 10. 4-Square Step Test 11. Talks While Walking Test (TWWT- Dual task test) 12. Outdoor Uneven Surfaces Test 13. Amputee Mobility Predictor 14. Mini Mental State Exam (MMSE)

APPENDIX F. SUMMARY OF AMSTAR-2 ASSESSMENTS OF NEW SYSTEMATIC REVIEWS/QUALITY ASSESSMENT TOOLS

Criteria for assessing systematic reviews based on AMSTAR-2.

Item*	Donnelley 2021	Hahn 2022	Mileusnic 2019	Thibaut 2022
1: Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	Yes	Yes	Yes
2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Yes	Yes	Yes	Yes
3: Did the review authors explain their selection of the study designs for inclusion in the review?	Yes	Yes	Yes	Yes
4: Did the review authors use a comprehensive literature search strategy?	Yes	Yes	Yes	Yes
5: Did the review authors perform study selection in duplicate?	Yes	Yes	No	Unclear
6: Did the review authors perform data extraction in duplicate?	Yes	Yes	Unclear	Unclear
7: Did the review authors provide a list of excluded studies and justify the exclusions?	No	No	No	No
8: Did the review authors describe the included studies in adequate detail?	Yes	Yes	Yes	Yes
9: Did the review authors use a satisfying technique for assessing the RoB in individual studies that were included in the review?	Yes	Yes	Yes	Yes
10: Did the review authors report on the sources of funding for the studies included in the review?	No	No	No	Yes
11: If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	No	Yes	No	No
12: If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Yes	Yes	Yes	Yes
13: Did the review authors account for RoB in individual studies when interpreting or discussing the results of the review?	Yes	Yes	Yes	Yes
14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes	Yes	No	No
15: If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	No	No	No	No
16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	No	Yes	Yes	Yes

Item*	Donnelley 2021	Hahn 2022	Mileusnic 2019	Thibaut 2022
Overall AMSTAR†	**Critically Low**	**Critically Low**	**Critically Low**	**Critically Low**

PICO=population, intervention, comparison, outcome; RoB=risk of bias.
* Bold questions represent critical items.
† Score Criteria
High: No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.
Moderate: More than one non-critical weakness: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.
Low: One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.
Critically low: More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.
- Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence.