WASHINGTON STATE HEALTH CARE AUTHORITY

Microprocessor-controlled Lower Limb Prostheses

Health Technology Assessment

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Health Technology Assessment

FINAL REPORT

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1 EXECUTIVE SUMMARY

Amputation or loss of a limb is a life-altering condition with profound physical, emotional, and social implications. In 2005, 1.6 million people were living with limb loss; the majority of these were lower limb amputees. The rates of lower limb amputation are increasing. Prostheses are devices that replace or compensate for the absence of a body part present at birth, or due to illness or trauma. Lower limb prostheses are designed to replace the normal function of the knee and/or ankle. Microprocessor-controlled lower limb prostheses (MCP) are contemporary devices that include sensors to detect users' movements and computers to adjust behavior of the limb during gait. Several MCP knee devices are commercially available. At this time, only one MCP ankle/foot device is available.

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. Existing literature has demonstrated that MCP knees are likely associated with improved outcomes, including ambulation, safety, and user preference in controlled or laboratory settings. The breadth and quality of evidence of their performance, including effectiveness and safety, in real-world settings is unclear. In 2011, the Washington State Department of Health, Health Care Authority, Health Technology Assessment Program selected microprocessor-controlled prostheses for lower limbs as a topic for health technology assessment.

Appraisal

The aim of this report is to systematically review, critically appraise and summarize evidence on five key questions (KQ) formulated by the WA Health Technology Assessment Program related to use of MCPs by people living with lower limb loss: (KQ1) the outcomes used in assessing MCP performance, (KQ2) comparative clinical efficacy, effectiveness, (KQ3) safety, (KQ4) evidence of differential effectiveness in subgroups, and (KQ5) cost-effectiveness of microprocessor-controlled lower limb prostheses. Based on the available evidence from existing reviews and assessments of the performance of MCPs in laboratory settings, our critical appraisal of evidence is focused on outcomes assessed in microprocessor-controlled lower limb prosthesis users in real-world, uncontrolled (home or community) settings.

Methods

We conducted a systematic review of the scientific literature on outcomes assessed of the performance of MCP knee or foot devices in adults living with unilateral lower limb amputations, either transfemoral (above knee) or transtibial (below knee). We noted and summarized outcomes assessed in controlled settings (laboratory or obstacle course). We critically appraised clinical and economic outcomes assessed in real-world, uncontrolled settings (home, work, community) using methods based on recommendations from the Centre for Evidence-based Medicine, precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group, and recommendations made by the Agency for Healthcare Research and Quality (AHRQ; US Department of Health and Human Services), and the Quality of Health Economic Studies rating scale.

We included or excluded studies based on a priori criteria, extracted data on study design, population, and results. We then rated each included study according to one of four levels of evidence (LoE)--I (good quality) through IV (very poor quality) according to assessment of features of the study design and implementation. Based on the findings of our systematic

review, we provide conclusion statements in answer to each key question. We also provide summaries of the evidence for each aim along with an assessment of the strength of evidence of HIGH, MODERATE, LOW, or VERY LOW for each statement based on the quality, quantity, and consistency of the findings reported.

Results

We identified 24 articles meeting our inclusion criteria, all assessing MCP knee devices. Of these, 12 studies assessed only outcomes in controlled (i.e. lab) settings and so were noted and their findings summarized. The remaining 12 studies, representing a total of 614 people, assessed at least one outcome in uncontrolled (real-life) use; these were included for critical appraisal. Two studies (using the same study population) employed randomized order of knee assessment. Length of follow-up varied from 7 days to 15 months of use of the MCP knee.

Nine of 12 studies assessed patient use of the C-Leg (Otto Bock); two studies assessed use of Intelligent Prosthesis (IP), and one of the Adaptive Knee. All 12 studies used non-microprocessor-controlled prostheses (NMCP) as the comparison, though the models of NMCP varied. Percent of participants completing follow-up varied from 27% to 100%.

Of the 12 studies critically appraised, three were Level II (moderate quality) and nine were Level III (low quality). Common quality issues were lack of random assignment, lack of concealment of sequence allocation, lack of blinded assessment, and failing to control for possible confounding.

Summary of evidence

Microprocessor-controlled prosthetic FEET

There is insufficient evidence to evaluate the comparative effectiveness, safety, or cost effectiveness of microprocessor-controlled foot devices.

Microprocessor-controlled prosthetic KNEES

The evidence on MCP knee use in real-world settings consistently suggests improvement or equivalence associated with MCP knee use compared to NMCPs. No studies suggested that NMCP knees were associated with clearly improved outcomes. The strength of evidence for all conclusions is either low or very low, most often reflecting the quality of study designs and the quantity of studies available rather than the consistency of findings. Future research into the development of valid and reliable patient-centered methods for assessing the performance of microprocessor-controlled prostheses (MCPs) in real-world settings, studies designed to prospectively assess the effects of MCPs on users' function and health over time, studies that include participants of diverse population demographics and functional levels, and long-term studies that examine the costs and outcomes of MCP from a societal perspective will provide valuable evidence toward understanding the performance of MCPs.

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

KQ1. What are the expected treatment outcomes of 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?

Evidence: The majority of the outcomes assessed of community use of MCPs are single item questions. Of six patient-reported outcome measures used in trials assessing MCP

use, three are generic instruments and three condition-specific. Two instruments demonstrate some evidence of reliability and/or validity. Three scales of the Prosthesis Evaluation Questionnaire (PEQ) demonstrated adequate content, criterion and construct validity and five subscales demonstrated adequate test-retest reliability. There were no validity data available for the 50-Question Survey, and its reliability testing was inadequate. Clinically meaningful improvement has not been established for any of the condition-specific measures used.

KQ2. What is the evidence of efficacy and effectiveness of microprocessor-controlled lower limb prostheses?

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

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

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 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

KQ3. What is the evidence about the safety of microprocessor-controlled lower limb prostheses? Including consideration of adverse events type and frequency (mortality, other major morbidity), equipment failure, ulcers, falls, etc.

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

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

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

KQ4. 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 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

KQ5. 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 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 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

2 Appraisal

2.1 Rationale

Amputation or loss of a limb is a life-altering condition with profound physical, emotional, and social implications. In 2005, 1.6 million people were living with limb loss; this number is expected to double by 2050. Sixty five percent (65%) of these are lower limb amputees.

Prostheses are devices that are used to compensate for the absence of a body part (present at birth, or due to illness or trauma). Prosthetic lower limbs are designed to replace the normal function of the knee and/or ankle.

Microprocessor-controlled lower limb prosthetic (MCP) devices include a computer and sensors that detect movement and timing of gait/swing to adjust resistance during movement. Several microprocessor-controlled knee prostheses are approved by the FDA. Coverage by private payers varies, and may specify a minimum level of function for eligibility.

MCPs have several potential advantages over traditional prostheses, including: reduced energy expenditure, improved ambulation, improved safety, and improved quality of life. They are also more expensive to purchase and fit than non-microprocessor-controlled prostheses (NMCP).

The aim of this report is to systematically review, critically appraise and summarize comparative evidence on the clinical efficacy, effectiveness, safety, and cost-effectiveness of MCPs and other alternatives. The critical appraisal of evidence is focused on outcomes assessed on MCP use in uncontrolled (home or community) settings. Outcomes assessed in controlled settings (laboratory or obstacle course) are summarized only.

2.2 Key questions

This report is designed to provide evidence-based responses to a series of Key Questions (KQ) formulated by the Washington State Health Care Authority's (HCA) Health Technology Assessment Program (HTAP) (Table 1).

2.3 Considerations highlighted by clinical experts

How do MCPs perform in real-life use? There is increasing demand for evidence about patient use of technologies in real-world settings. [1] In the context of MCPs, there has appropriately been substantial research on the use of MCPs in controlled or laboratory settings to establish safety and efficacy of the devices. However, real-world use of MCPs has been less evaluated, [2] and there is little standardized use of outcomes measures. [3, 4]

Can MCPs improve function? The role of function as a predictor of performance post-limb loss is well known: people with higher baseline function are more likely to show success with prosthesis. [5] However, there is some suggestion that MCPs can actually help people improve function. [6-8] Evidence supporting this remains scant, though as an idea has some support in the literature. [9] [10]

Table 1: Key questions (KQ)

When used by people living with lower limb loss:

KQ1. What are the expected treatment outcomes of 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?

KQ2. 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.

- **KQ2a. Energy and cognitive requirements of ambulation**
- **KQ2b. Impact on ambulation: daily step frequency; estimated step distance; performance on level or varied surfaces**
- **KQ2c. Patient perception; QOL; impact on activities of daily living; work; work performance**

KQ3. What is the evidence about the safety of microprocessor-controlled lower limb prostheses? Including consideration of

- **KQ3a. Adverse events type and frequency (mortality, other major morbidity)**
- **KQ3b. Equipment failure**
- **KQ3c. Ulcers, falls, etc.**

KQ4. 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.

KQ5. 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.

2.4 Washington State utilization and cost data

The information in this section is provided by the Washington State HCA/HTAP.

State Agency data for 2007-2010 on Microprocessor Controlled Prosthetics (MCP) for Lower Limbs is presented below. As a comparison, data for all other lower limb prosthetics (Non-MCP) is also presented. Note that all identified MCP in claims data are for knee replacement, while the Non-MCP include knee replacements as well as other lower limb prostheses.

State Agency Data 1a: 4 Year Combined Agency Costs, 2007-2010

Agency Experience	PEB	L&I	Medicaid	All Agencies
MCP				
Payments	$482,271	$812,966	$166,234	$1,461,471
Member Count	14	8	15	37
Average Payment/Member*	$43,569	$101,621	$11,082	$39,499
Annual Average Payment/Member*	$10,892	$25,405	$2,771	$9,874
Non-MCP				
Payments	$1,273,586	$7,838,247	$10,067,406	$19,179,239
Member Count	186	350	1844	2380
Average Payment/Member*	$9,735	$22,395	$5,460	$8,059
Annual Average Payment/Member*	$2,434	$5,599	$1,365	$2,014
MCP/Non-MCP Prosthetics Combined				
Payments	**$1,755,857**	**$8,651,212**	**$10,233,639**	**$20,640,708**
Member Count	**200**	**358**	**1859**	**2417**
Average Payment/Member*	**$12,579**	**$24,165**	**$5,505**	**$8,540**
Annual Average Payment/Member*	**$3,145**	**$6,041**	**$1,376**	**$2,134**

**PEB averages do not include claims where PEB was secondary payer, as this primary payer claims are more representative of the average per prosthetic patient for comparison between agencies. In Table 1b below, PEB averages for all patients, including secondary payer claims, are displayed.*

State Agency Data 1b: PEB Annual Prosthetic Costs and Counts, 2007-2010

Year	2007	2008	2009	2010	4 Year Total*
Microprocessor Controlled Lower Limb Prosthetics					
Payments	$76,698	$162,183	$69,840	$173,550	$482,271
Member Count	6	8	8	10	14
Average Paid/Member	$12,783	$20,273	$8,730	$17,355	$34,448
Average PEB 100% Paid	$15,306	$25,619	$13,907	$24,969	$43,569
Max Paid	$36,362	$54,109	$44,685	$46,489	$58,378
Min Paid	$167	$441	$138	$236	$1,016
Median Paid	$2,033	$8,568	$3,132	$10,533	$40,452
Standard Deviation	$17,939	$21,371	$14,980	$17,235	$20,677
Other Lower Limb Prosthetics					
Payments	$261,716	$400,667	$351,898	$259,305	$1,273,586
Member Count	86	97	105	79	186
Average Paid/Member	$3,043	$4,131	$3,351	$3,282	$6,847
Average PEB 100% Paid	$4,764	$5,413	$4,965	$5,180	$9,735
Max Paid	$16,458	$24,846	$29,868	$22,675	$53,814
Min Paid	$0	$0	$0	$9	$0
Median Paid	$1,429	$1,752	$1,376	$1,132	$3,180
Standard Deviation	$3,903	$5,314	$5,116	$4,699	$8,923
Overall Prosthetics					
Payments	**$338,414**	**$562,850**	**$421,738**	**$432,855**	**$1,755,857**
Member Count	**92**	**105**	**113**	**89**	**200**
Average Paid/Member	**$3,678**	**$5,360**	**$3,732**	**$4,864**	**$8,779**
Average PEB 100% Paid	**$5,840**	**$7,145**	**$5,524**	**$7,761**	**$12,579**

PEB – Public Employees Benefits

**4 Year Total/Member Counts represent distinct members counted over the period and are not usually equal to the sum of the annual member counts.*

State Agency Data 1c: L&I Annual Prosthetic Costs and Counts, 2007-2010

Year	2007	2008	2009	2010	4 Year Total*
Microprocessor Controlled Lower Limb Prosthetics					
Payments	$41,306	$264,496	$247,110	$260,054	$812,966
Member Count	6	8	5	8	8
Average Paid/Claim	$6,884	$33,062	$49,422	$32,507	$101,621
Max Paid	$15,641	$120,663	$103,993	$89,583	$129,489
Min Paid	$1,557	$1,536	$449	$1,346	$57,309
Median Paid	$9,525	$31,371	$10,447	$74,837	$105,467
Standard Deviation	$6,304	$48,405	$43,745	$45,070	$24,049

Other Lower Limb Prosthetics					
Payments	$1,935,998	$1,956,523	$1,824,617	$2,121,109	$7,838,247
Member Count	205	214	208	206	350
Average Paid/Claim	$9,444	$9,143	$8,772	$10,297	$22,395
Max Paid	$73,612	$50,719	$43,381	$50,335	$152,207
Min Paid	$40	$10	$12	$13	$10
Median Paid	$7,701	$6,525	$6,366	$8,499	$17,247
Standard Deviation	$10,386	$9,664	$8,697	$9,498	$21,414
Overall Prosthetics					
Payments	**$1,977,303**	**$2,221,019**	**$2,071,727**	**$2,381,163**	**$8,651,212**
Member Count	**211**	**222**	**213**	**214**	**358**
Average Paid/Claim	**$9,371**	**$10,005**	**$9,726**	**$11,127**	**$24,165**

**4 Year Total /Member Counts represent distinct members counted over the period and are not usually equal to the sum of the annual member counts.*

State Agency Data 1d: Medicaid Annual Prosthetic Costs and Counts, 2007-2010

Year	2007	2008	2009	2010	4 Year Total*
Microprocessor Controlled Lower Limb Prosthetics					
Payments	$27,266	$49,927	$54,270	$34,770	$166,234
Claimant Count	6	10	11	8	15
Average Paid/Claimant	$4,544	$4,993	$4,934	$4,346	$11,082
Max Paid	$10,533	$15,856	$29,360	$7,773	$52,989
Min Paid	$282	$214	$165	$2,334	$2,881
Median Paid	$3,962	$3,574	$3,091	$3,638	$7,282
Standard Deviation	$3,452	$4,585	$8,229	$1,966	$12,947
Other Lower Limb Prosthetics					
Payments	$2,173,649	$2,257,335	$2,931,813	$2,704,609	$10,067,406
Claimant Count	738	714	837	810	1844
Average Paid/Claimant	$2,945	$3,162	$3,503	$3,339	$5,460
Max Paid	$30,430	$27,489	$35,568	$37,137	$77,569
Min Paid	$0	$0	$0	$0	$0
Median Paid	$1,381	$1,431	$1,508	$1,452	$2,552
Standard Deviation	$3,819	$4,242	$4,413	$4,480	$7,297
Overall Prosthetics					
Payments	**$2,200,915**	**$2,307,262**	**$2,986,084**	**$2,739,379**	**$10,233,639**
Claimant Count	**744**	**724**	**848**	**818**	**1859**
Average Paid/Claimant	**$2,958**	**$3,187**	**$3,521**	**$3,349**	**$5,505**

**4 Year Total /Member Counts represent distinct members counted over the period and are not usually equal to the sum of the annual member counts.*

State Agency Data 2a: PEB Prosthetic Payment Categories*, 2007-2010

Prosthetic Payment Category*	Prosthetics	Addons	Services	Micro-processor Component	Modifi-cations	Replace-ment	Grand Total
Microprocessor Controlled Lower Limb Prosthetic Patients							
Total Payments	$25,498	$215,816	$470	$195,484	$0	$45,003	$482,271
Member Count	9	14	1	13	0	11	14
Average	$2,833	$15,415	$470	$15,037		$4,091	$34,448
Maximum	$5,275	$27,793	$470	$21,257		$12,882	$58,378
Median	$3,527	$17,043	$470	$19,388		$1,781	$40,452
Standard Deviation	$1,899	$9,346		$7,591		$4,201	$20,677
Non-MCP Prosthetic Patients							
Total Payments	$193,238	$867,465	$34,547	$0	$3,484	$174,852	$1,273,586
Member Count	125	152	29	0	8	83	186
Average	$1,546	$5,707	$1,191		$436	$2,107	$6,847
Maximum	$8,204	$44,345	$6,008		$968	$14,719	$53,814
Median	$794	$3,170	$592		$507	$1,011	$3,180
Standard Deviation	$1,658	$6,520	$1,238		$288	$2,630	$8,923

**CPTs associated with categories are listed in Related Medical Codes at the end of this section*

State Agency Data 2b: L&I Prosthetic Payment Categories*, 2007-2010

Prosthetic Payment Category*	Prosthetics	Addons	Services	Micro-processor Component	Modifi-cations	Replace-ment	Grand Total
Microprocessor Controlled Lower Limb Prosthetic Patients							
Total Payments	$33,695	$371,835	$0	$361,526	$0	$45,909	$812,966
Member Count	4	8	0	8	0	5	8
Average	$8,424	$46,479		$45,191	$0	$9,182	$101,621
Maximum	$9,759	$60,996		$56,760		$16,085	$129,489
Median	$9,644	$49,697		$47,727		$10,990	$105,467
Standard Deviation	$2,520	$10,532		$10,853		$7,176	$24,049
Non-MCP Prosthetic Patients							
Total Payments	$956,129	$5,871,716	$94,414	$0	$18,681	$1,147,948	$8,088,887
Member Count	232	315	37	0	25	194	350
Average	$4,121	$18,640	$2,552		$747	$5,917	$23,111
Maximum	$17,401	$123,610	$4,950		$1,400	$27,038	$152,494
Median	$3,159	$15,543	$2,436		$670	$4,492	$17,719
Standard Deviation	$2,516	$16,632	$1,079		$244	$5,367	$22,032

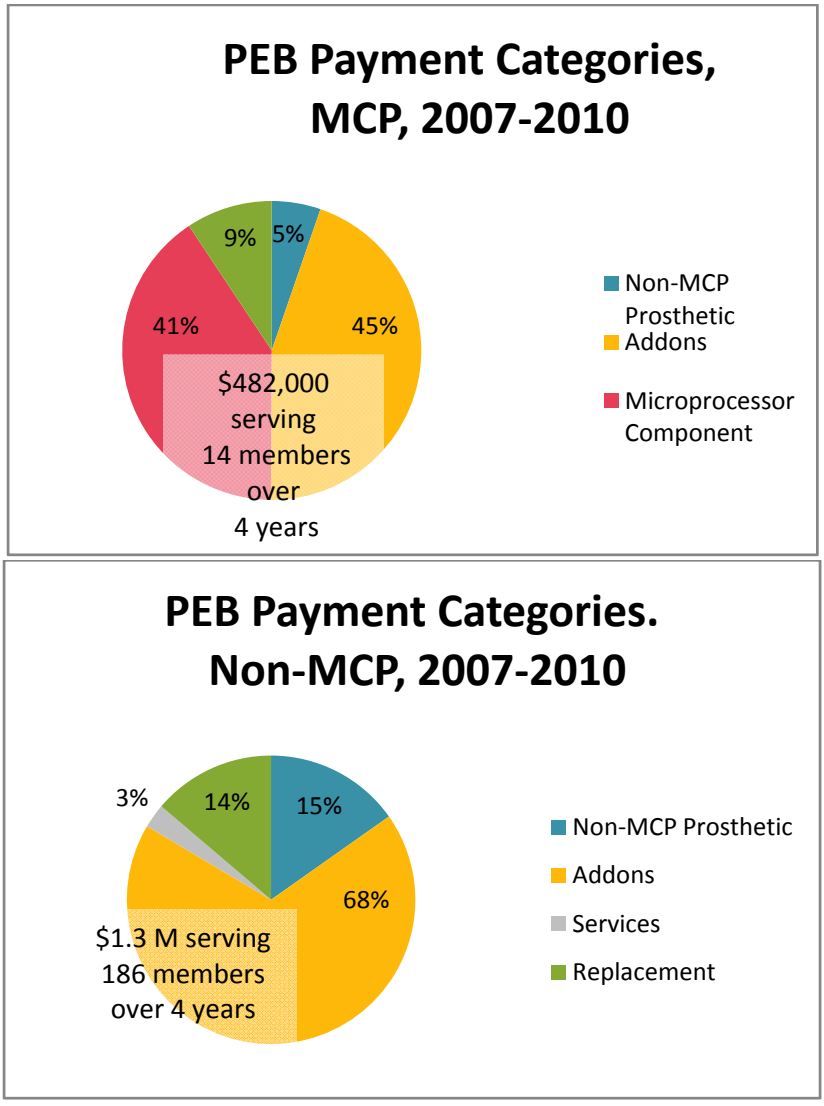
**CPTs associated with categories are listed in Related Medical Codes at the end of this section*

State Agency Data 2c: Medicaid Prosthetic Payment Categories*, 2007-2010

Prosthetic Payment Category*	Non-MCP Prosthetics	Addons	Services	Micro-processor Component	Modifi-cations	Replace-ment	Grand Total
Microprocessor Controlled Lower Limb Prosthetic Patients							
Total Payments	$11,921	$97,005	$1,402	$38,773	$0	$17,133	$166,234
Member Count	8	13	3	15	0	10	15
Average	$1,490	$7,462	467.42	$2,585		$1,713	$11,082
Maximum	$3,718	$41,414	831.87	$4,960		$5,191	$52,989
Median	$805	$4,596	422.77	$2,637		$846	$7,282
Standard Deviation	$1,331	$10,978	344.3033	$1,448		$1,818	$12,947

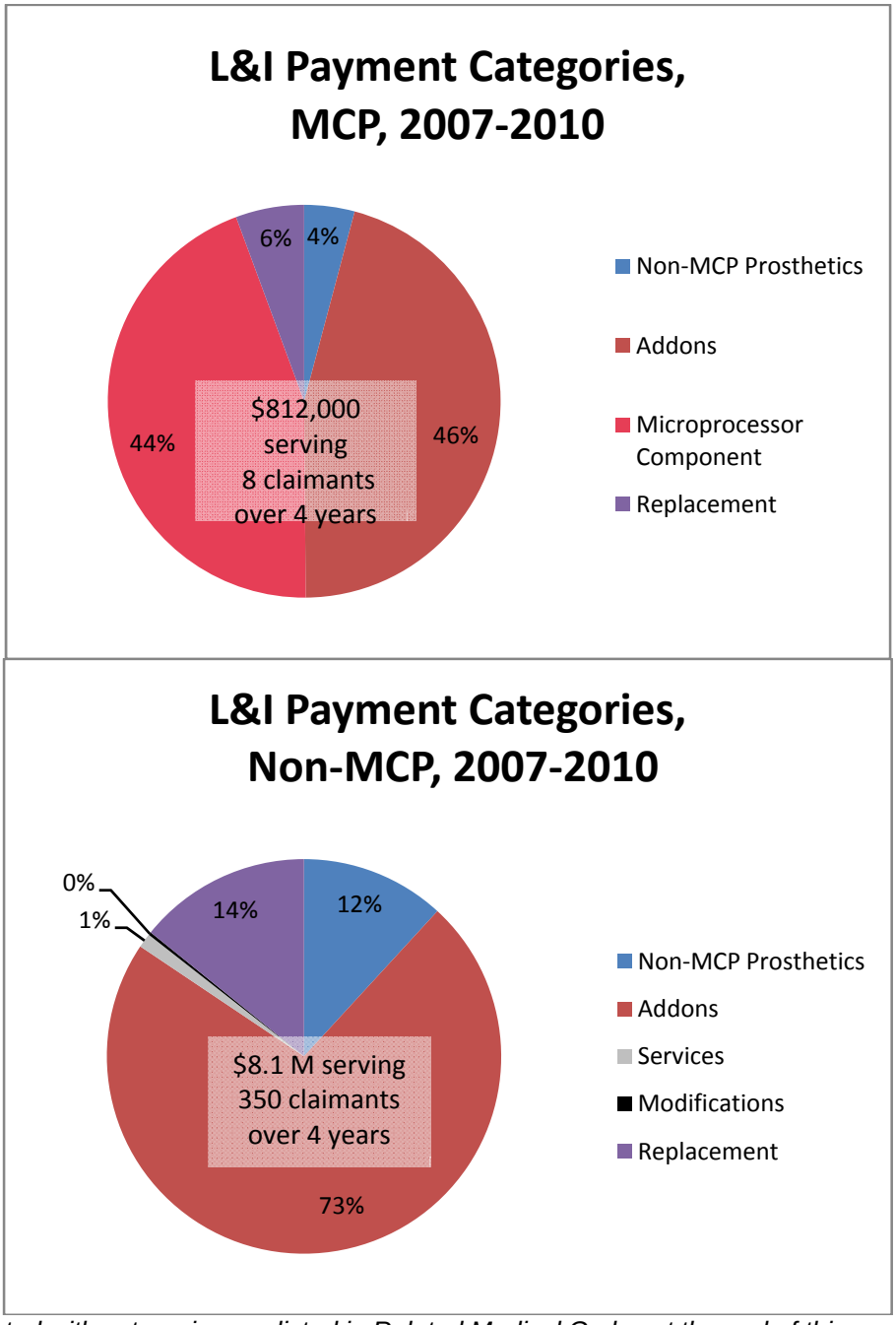
Non-MCP Prosthetic Patients						
Total Payments	$2,063,715	$6,843,932	$363,798	$29,883	$1,409,138	$10,710,466
Member Count	1360	5687	422	67	772	1861
Average	$1,517	$1,203	$862	$446	$1,825	$5,755
Maximum	$16,890	$26,546	$12,383	$2,145	$15,915	$78,498
Median	$646	$542	$354	$803	$803	$2,675
Standard Deviation	$1,683	$1,829	$1,054	$7,622	$2,267	$7,622

State Agency Data 3a: PEB Payment Categories* for Microprocessor Controlled Prosthetics (MCP) and Non-MCP, 2007-2010



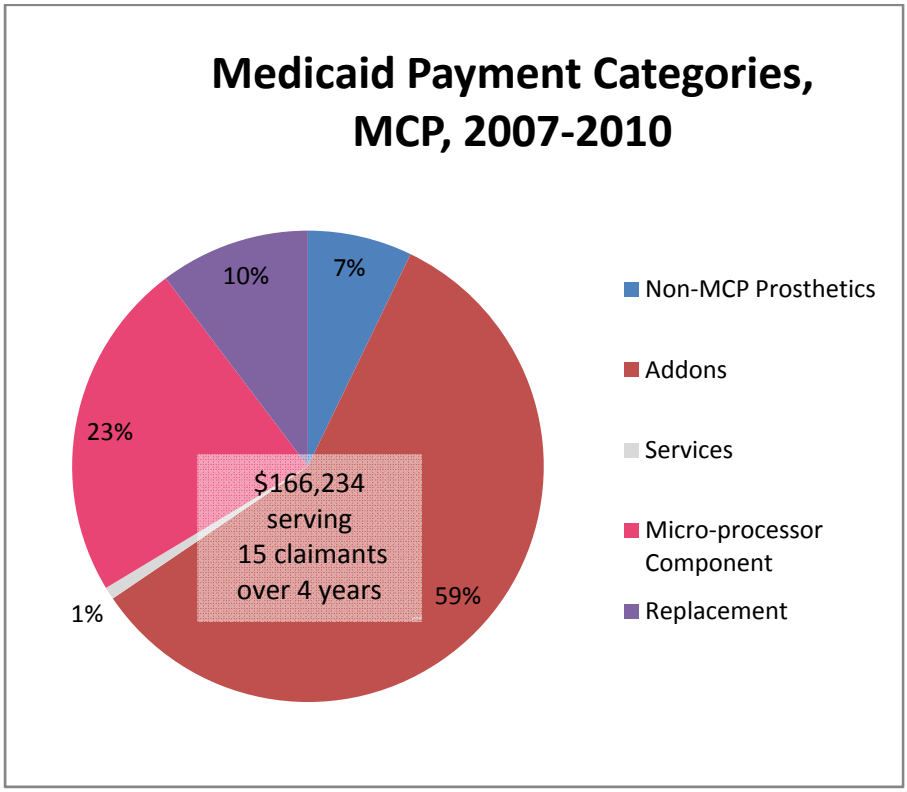
**CPTs associated with categories are listed in Related Medical Codes at the end of this section*

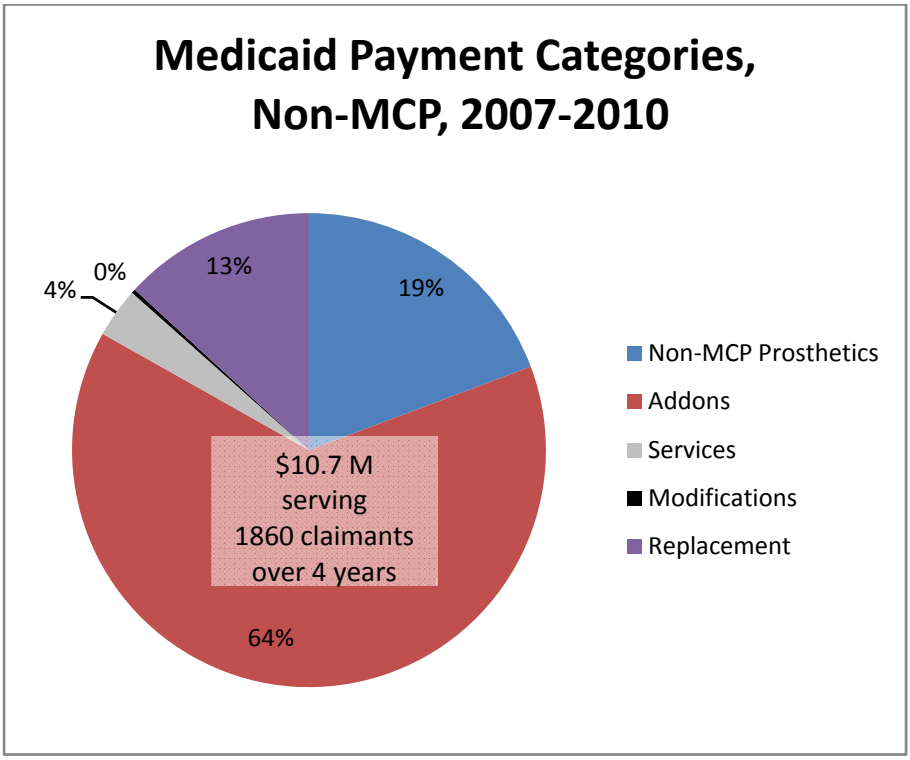
State Agency Data 3b: L&I Payment Categories* for Microprocessor Controlled Prosthetics (MCP) and Non-MCP, 2007-2010



**CPTs associated with categories are listed in Related Medical Codes at the end of this section*

State Agency Data 3b: L&I Payment Categories* for Microprocessor Controlled Prosthetics (MCP) and Non-MCP, 2007-20





State Agency Data 4a: PEB Lower Limb Prosthetics by Gender and Age Group, 2007-2010

Gender/ Age Group	Payments					Counts				
	2007	2008	2009	2010	Grand Total	2007	2008	2009	2010	Grand Total*
Microprocessor Controlled Prosthetics										
FEMALE	**$2,916**	**$106,563**	**$53,447**	**$57,184**	**$220,110**	**1**	**4**	**2**	**2**	**5**
36-50		$97,590	$44,685	$10,695	$152,970		3	1	1	3
51-65	$2,916	$8,973		$46,489	$58,378	1	1		1	1
66+			$8,762		$8,762			1		1
MALE	**$73,782**	**$55,620**	**$16,393**	**$116,366**	**$262,161**	**5**	**4**	**6**	**8**	**9**
36-50	$649		$714	$29,943	$31,306	1		1	1	1
51-65	$72,966	$47,591	$10,569	$73,294	$204,420	3	3	3	5	6
66+	$167	$8,029	$5,110	$13,129	$26,435	1	1	2	2	2
Non-MCP Prosthetics										
FEMALE	**$72,685**	**$80,140**	**$98,520**	**$63,876**	**$315,221**	**28**	**26**	**37**	**27**	**62**
0-18		$6,413	$1,345	$13,594	$21,352		1	1	2	2
19-35	$2,248	$1,324	$2,690	$8,283	$14,545	2	2	1	1	2
36-50	$15,252	$97	$21,876	$649	$37,874	5	1	4	2	7
51-65	$48,651	$63,161	$62,664	$32,042	$206,518	13	14	22	15	32
66+	$6,534	$9,145	$9,945	$9,308	$34,932	8	8	9	7	19
MALE	**$189,031**	**$320,527**	**$253,378**	**$195,429**	**$958,365**	**61**	**74**	**70**	**52**	**124**
0-18	$2,649	$6,810	$21,393		$30,852	1	2	3		3
19-35		$10,638	$846	$20,360	$31,844		2	1	2	4
36-50	$24,206	$100,323	$103,488	$56,737	$284,754	9	12	11	8	22
51-65	$95,018	$164,486	$91,358	$71,451	$422,313	18	30	25	17	43
66+	$67,158	$38,270	$36,293	$46,881	$188,602	33	28	30	25	52

**Grand Total Member Counts represent distinct members counted over the period and are not usually equal to the sum of the annual member counts.*

State Agency Data 4b: L&I Lower Limb Prosthetics by Gender and Age Group, 2007-2010

Gender/ Age Group	Payments					Counts				
	2007	2008	2009	2010	Grand Total	'07	'08	'09	'10	Grand Total*
Microprocessor Controlled Prosthetics										
FEMALE	**$9,525**		**$21,043**	**$74,837**	**$105,405**	**1**		**1**	**1**	**1**
36-50	9524.69		$21,043	$74,837	$105,405	1		1	1	1
MALE	**$31,781**	**$264,496**	**$226,067**	**$185,217**	**$707,561**	**6**	**7**	**7**	**4**	**8**
19-35		1536.29	$103,993		$105,529		1	1		1
51-65	$31,781	$184,438	$103,155	$95,775	$415,148	4	4	4	3	5
66+		$78,521	$18,920	$89,443	$186,884	2	2	2	1	2
Non-MCP Prosthetics										
FEMALE	**$175,505**	**$178,973**	**$227,923**	**$246,870**	**$829,271**	**13**	**21**	**17**	**18**	**32**
19-35	$20,964	$16,049	$20,555	$25,782	$83,351	2	1	2	2	3
36-50	$138,749	$80,353	$154,945	$144,405	$518,451	9	13	10	10	18
51-65	$960	$56,446	$14,702	$60,813	$132,921	1	5	3	5	9
66+	$14,832	$26,125	$37,722	$15,870	$94,548	1	2	2	1	2
MALE	**$1,714,414**	**$1,727,233**	**$1,574,452**	**$1,837,432**	**$6,853,531**	**185**	**187**	**186**	**183**	**348**
0-18	$3,808	$1,739	$14,411	14078.48	$34,036	3	3	3	1	6
19-35	$216,540	$165,760	$151,645	$179,571	$713,517	21	20	16	21	32
36-50	$710,088	$678,984	$562,992	$524,498	$2,476,562	59	66	56	47	101
51-65	$541,587	$661,275	$584,794	$979,398	$2,767,055	71	70	81	88	152
66+	$242,390	$219,475	$260,610	$139,886	$862,361	31	28	30	26	57

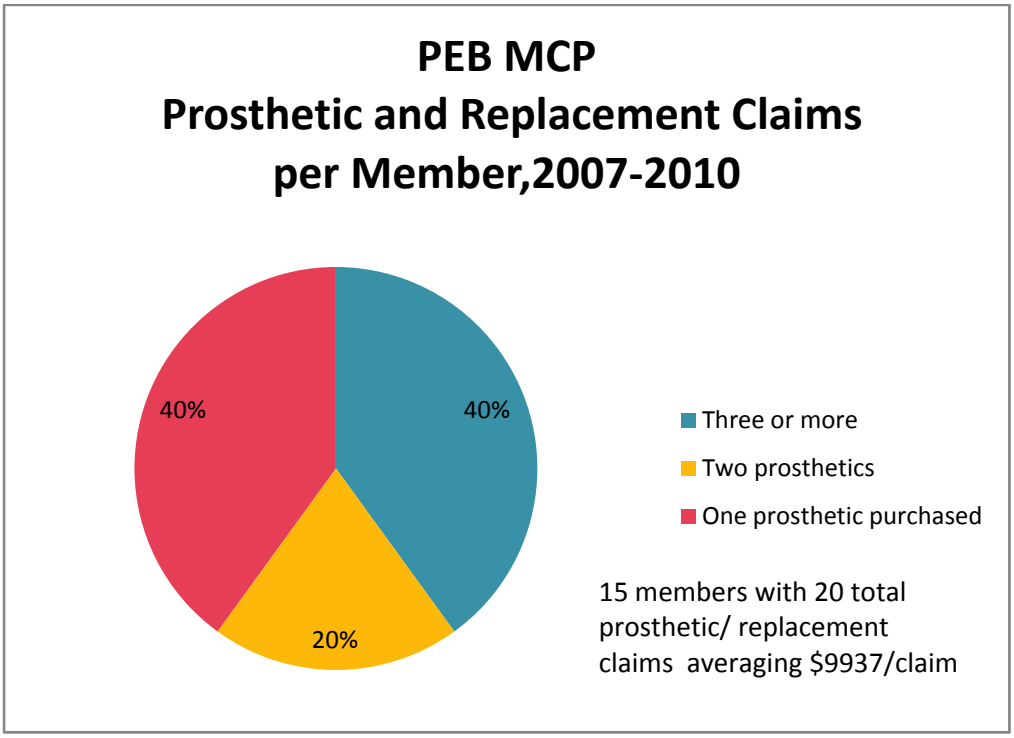
**Grand Total Member Counts represent distinct members counted over the period and are not usually equal to the sum of the annual member counts.*

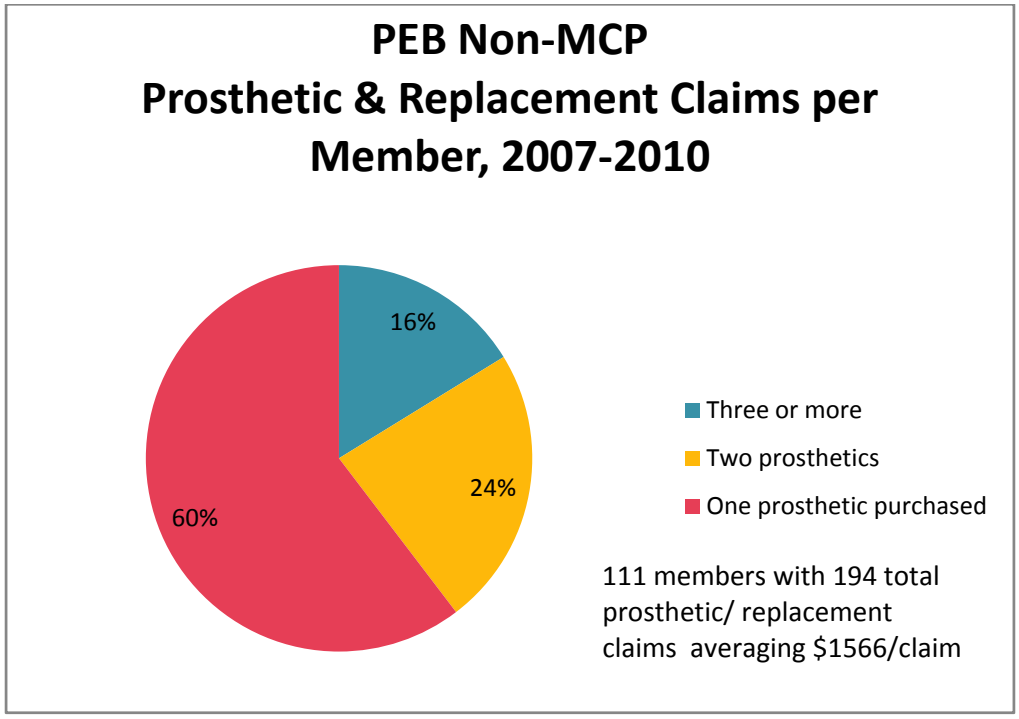
State Agency Data 4c: Medicaid Lower Limb Prosthetics by Gender and Age Group, 2007-2010

Gender/ Age Group	Payments					Counts				
	2007	2008	2009	2010	Grand Total	'07	'08	'09	'10	Grand Total*
Microprocessor Controlled Prosthetics										
F	**$3,291**	**$5,153**	**$329**	**$7,179**	**$15,952**	**2**	**2**	**1**	**2**	**7**
19-35		$2,881			$2,881		1			1
36-50	$282	$2,273	$329	$7,179	$10,063	1	1	1	2	5
51-65	$3,009				$3,009	1				1
M	**$23,975**	**$44,774**	**$53,941**	**$27,591**	**$150,281**	**4**	**8**	**10**	**7**	**29**
19-35		$4,191	$3,091		$7,282		1	1		2
36-50	$4,846	$25,982	$34,854	$14,276	$79,958	1	3	3	4	11
51-65	$19,129	$14,601	$8,328	$258	$42,316	3	4	4	1	12
66+			$7,668	$13,057	$20,725			2	2	4
Non-MCP Prosthetics										
F	**$827,735**	**$780,417**	**$1,001,097**	**$856,064**	**$3,465,313**	**280**	**268**	**292**	**289**	**1129**
0-18	$65,622	$40,951	$115,744	$84,064	$306,381	13	13	16	12	54
19-35	$97,563	$125,884	$46,465	$82,501	$352,412	19	22	19	25	85
36-50	$293,066	$245,602	$331,384	$197,816	$1,067,869	78	72	83	72	305
51-65	$292,510	$270,676	$426,554	$427,471	$1,417,210	105	92	116	120	433
66+	$78,974	$97,304	$80,950	$64,213	$321,441	65	69	58	60	252
M	**$1,346,209**	**$1,476,918**	**$1,930,716**	**$1,847,511**	**$6,601,353**	**459**	**446**	**545**	**521**	**1971**
0-18	$95,201	$52,822	$148,462	$95,567	$392,053	15	12	18	12	57
19-35	$255,179	$225,494	$299,235	$256,203	$1,036,110	57	48	53	50	208
36-50	$371,086	$464,317	$551,403	$487,186	$1,873,992	125	135	135	116	511
51-65	$522,463	$629,208	$770,548	$822,549	$2,744,768	173	169	231	239	812
66+	$102,280	$105,078	$161,068	$186,005	$554,431	89	82	108	104	383

**Grand Total Member Counts represent distinct members counted over the period and are not usually equal to the sum of the annual member counts.*

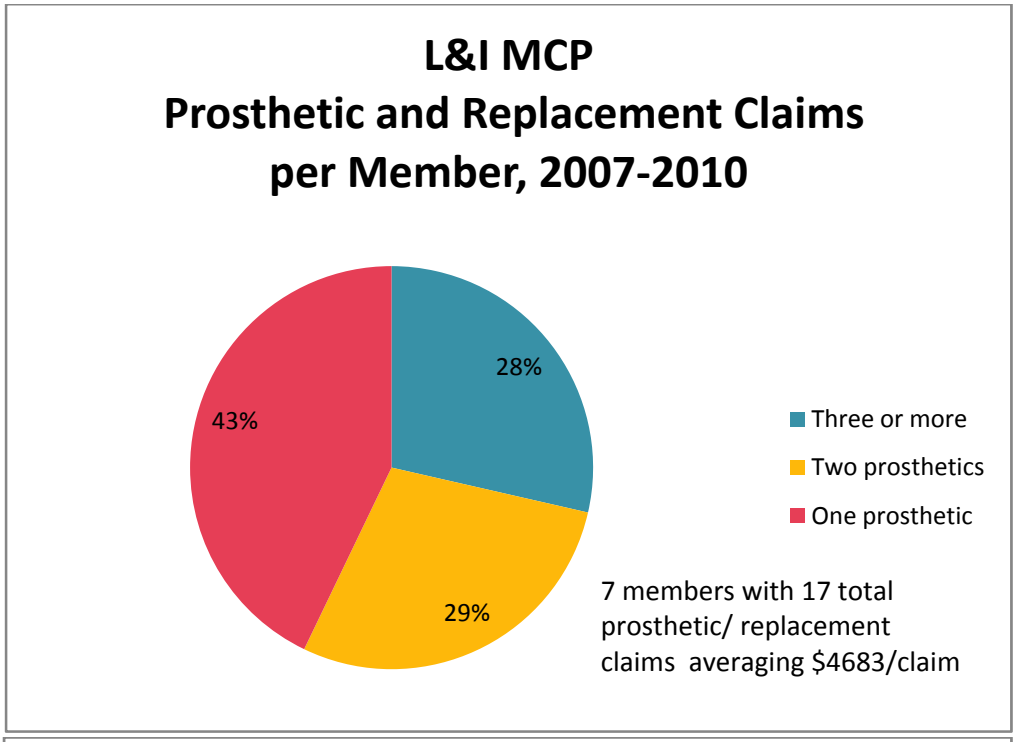
State Agency Data 5a: PEB Prosthetics and Replacements, 2007-2010

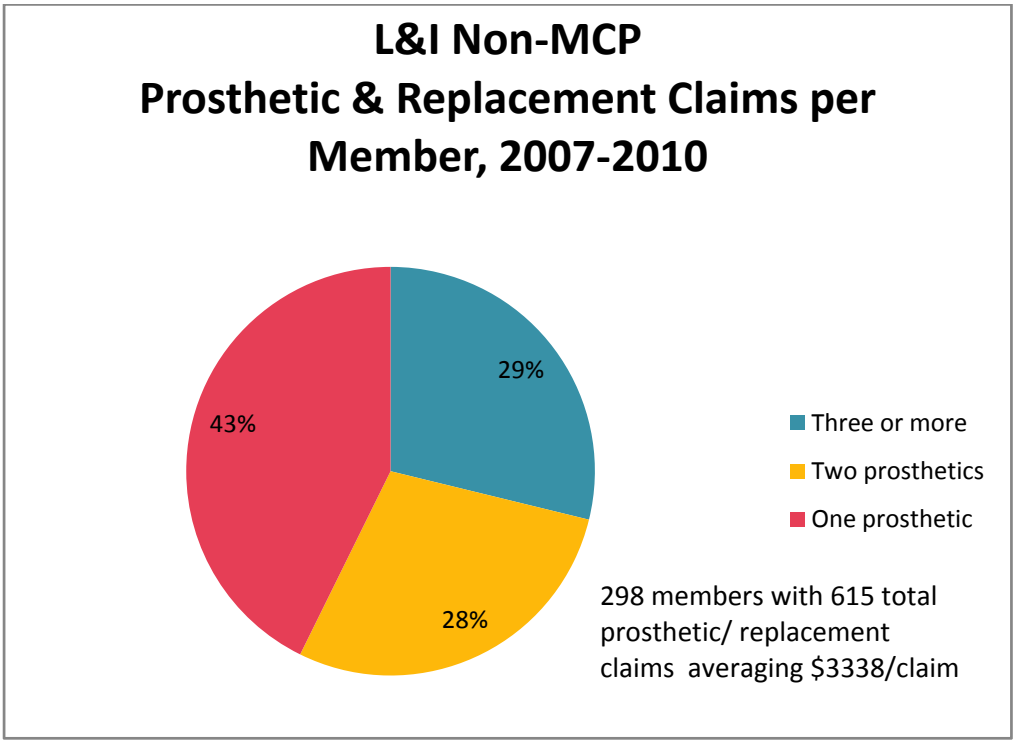




67 or 33.5% of the total 200 members who used prosthetic services during 2007-2010 did not have a claim for either a prosthetic or prosthetic replacement. In Non-MCP members, 12 members had claims for more than 3 distinct prosthetics or replacement prosthetics during 2007-2010.

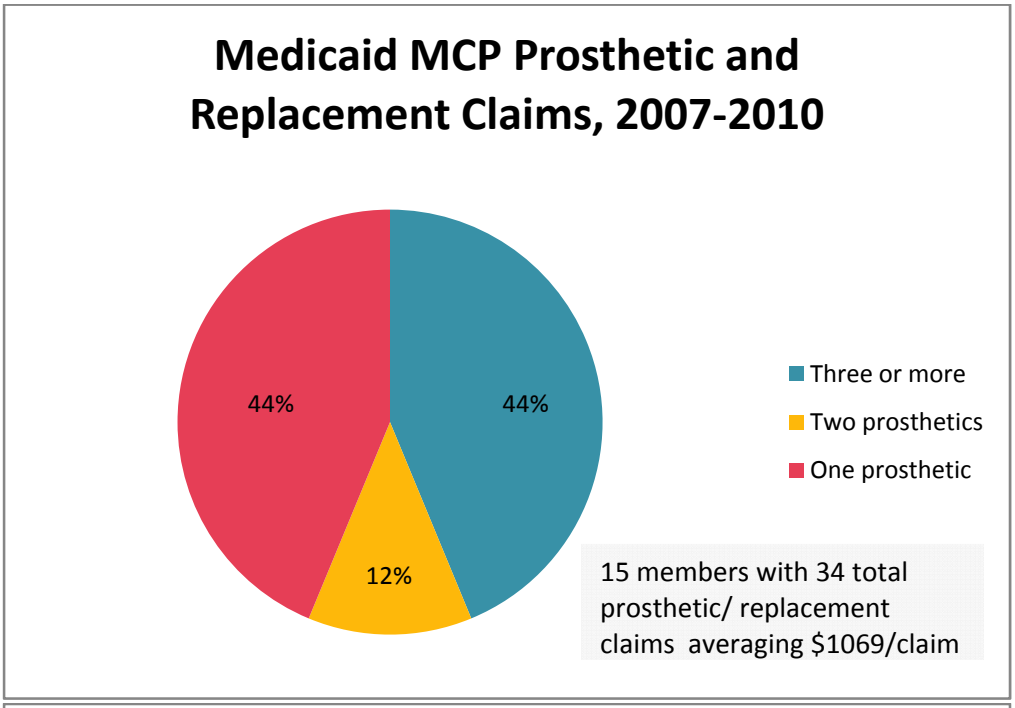
State Agency Data 5b: L&I Prosthetics and Replacements, 2007-2010

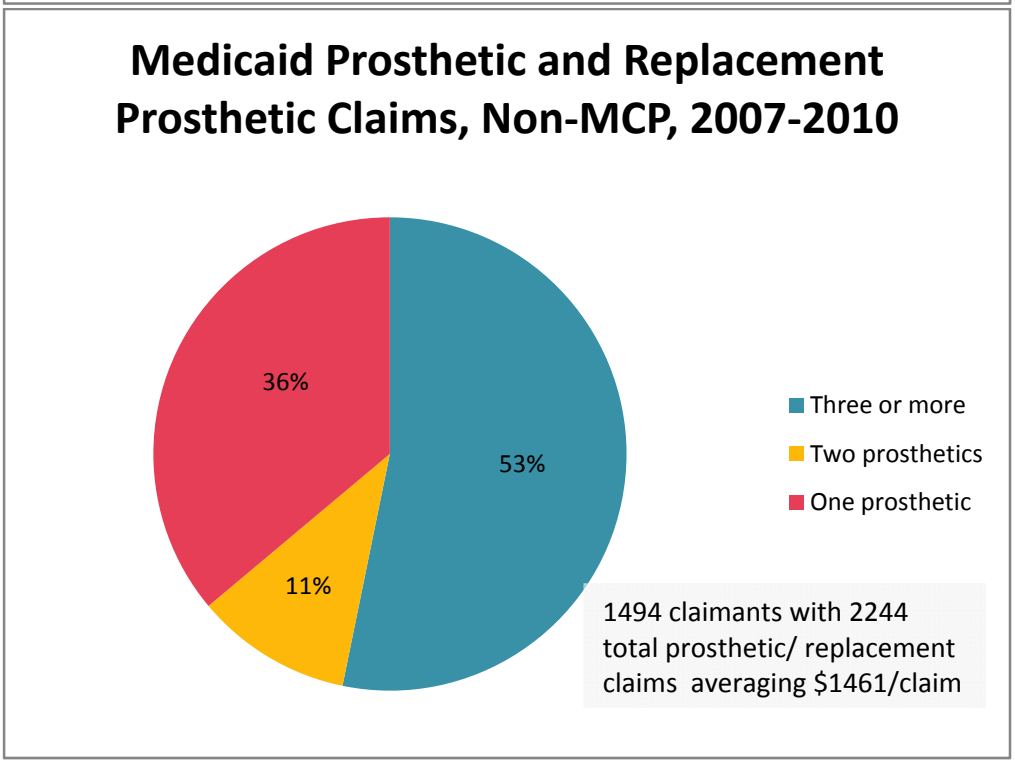




53 or 14.8% of the total 358 members who used prosthetic services during 2007-2010 did not have a claim for either a prosthetic or prosthetic replacement. In Non-MCP members, 47 members had claims for more than 3 distinct prosthetics or replacement prosthetics during 2007-2010.

State Agency Data 5c: Medicaid Prosthetics and Replacements, 2007-2010





350 or 5.3% of the total 1859 members who used prosthetic services during 2007-2010 did not have a claim for either a prosthetic or prosthetic replacement. In MCP claims, 3 claimants had more than 3 distinct prosthetics/replacements compared to 62 in Non-MCP claims.

Related Medical Codes, Prosthetic Categories

CPTs from	*to*	*Description*	*Category*
L5000	*L5020*	*Partial Foot*	*Prosthetic*
L5050	*L5060*	*Ankle*	*Prosthetic*
L5100	*L5105*	*Below Knee*	*Prosthetic*
L5150	*L5160*	*Knee Disart*	*Prosthetic*
L5200	*L5320*	*Above Knee*	*Prosthetic*
L5250	*L5270*	*Hip Disart*	*Prosthetic*
L5280	*L5300*	*Hemipelvectomy*	*Prosthetic*
L5300	*L5301*	*Endo Below Knee*	*Prosthetic*
L5310	*L5311*	*Endo Knee Disart*	*Prosthetic*
L5320	*L5321*	*Endo Above Knee*	*Prosthetic*
L5330	*L5331*	*Endo Hip Disart*	*Prosthetic*
L5340	*L5341*	*Endo-Hemipelv*	*Prosthetic*
L5400	*L5460*	*Early Fitting PS*	*Services*
L5500	*L5505*	*Initial Pros*	*Services*
L5510	*L5595*	*Prep Pros*	*Services*
L5600	*L5617*	*Addns to Lower Extrem*	*Addons*
L5618	*L5629*	*Addns to Test Socket*	*Addons*
L5630	*L5653*	*Addns Socket Var*	*Addons*
L5654	*L5699*	*Addns Socket Insert*	*Addons*
L5700	*L5707*	*Pros Replacement*	*Replacement*
L5710	*L5782*	*Addns Exo Knee-shin*	*Addons*
L5785	*L5795*	*Pros Mods*	*Modifications*
L5810	*L5999*	*Addns Endo Knee-Shin*	*Addons*

Related Medical Codes			
Code Type	***Codes***	***Short Description***	***Additional Info***
ICD9 Diagnosis	*ICD-9*		
	896.0-897,1	*Traumatic amputation of foot or leg*	*Expected Diagnosis*
	897.2-7	*Traumatic amputation of leg(s); code range for above the knee amputations (7/20/2007)*	*Expected Diagnosis*
	V49.7-V49.77	*Lower Leg amputation status*	*Expected Diagnosis*
	V43.65	*Organ or tissue replaced by other means; knee (added 7/20/2007)*	*Expected Diagnosis*
Microprocessor	*CPT*		
	L5856	*Addition to lower extremity prosthesis, endoskeletal knee-shin system, microprocessor control feature, swing and stance phase, includes electronic sensor(s), any type*	*MCLLP*
	L5857	*Addition to lower extremity prosthesis, endoskeletal knee-shin system, microprocessor control feature, swing phase only, includes electronic sensor(s), any type*	*MCLLP*
	L5858	*Addition to lower extremity prosthesis, endoskeletal knee-shin system, microprocessor control feature, Stance phase only, includes electronic sensor(s), any type*	*MCLLP*
	L5973	*Endoskeletal ankle foot system, microprocessor controlled feature, dorsiflexion and /or ploantar flexion control, includes power source (added 1/2010)*	*MCLLP*
	L5000-L5999	*Lower Limb Prostheses*	*MCLLP*
	L7510/L7520	*Parts and labor for repair of prosthetic*	*Adverse Event*

3 Background

3.1 Epidemiology and burden of condition

An estimated 1.6 million persons with limb loss and more than 620,000 persons with major lower limb loss (amputation through the leg, thigh, or hip) reside in the United States[11]. Increases in limb loss prevalence observed more than a decade ago[12] are projected to grow at an even faster rate in the next four decades, due largely to the rising incidence of health conditions such as diabetes, dysvascular disease, and obesity.[11]

Primary causes of amputation include disease, trauma (accident or injury), cancer (tumor or malignancy), and congenital disorder (birth anomalies).

Peripheral vascular disease (PVD) is a progressive circulatory disorder of blood vessels throughout the body (outside the heart). Vascular insufficiencies caused by PVD commonly affect the distal limbs, notably the legs and feet. PVD accounts for more than half of all amputations including amputation of digits (fingers and toes) and more than three-quarters of major (excluding digits) limb amputations.[11, 12] PVD is by far the most common cause of lower limb amputation, accounting for more than 80% of major lower limb amputations.[11] Although PVD is often associated with diabetes, it also presents independently.[13] However, approximately 70% of amputations performed as a result of dysvascular disease include a comorbidity of diabetes. [11] Major risk factors for PVD include hypertension, dyslipidemia, diabetes, atherosclerosis, use of tobacco products, and age over 60 years.[14] More than one-third of persons undergoing an initial amputation due to PVD do not survive longer than 12 months.[15]

Trauma. Traumatic amputations result from a variety of causes, including vehicle accidents, work-related accidents, gunshots, explosions, burns or electrocution.[13] Traumatic amputations account for approximately 45% of all amputations (including digits) and one-fifth of all major limb amputations. An estimated 17% of non-digit amputations are due to trauma in the lower limb.[11] Traumatic lower limb loss is most commonly related to blunt trauma such as vehicle collisions (51.0%) and machinery accidents (19.4%).[16] Traumatic amputations are also significantly more common in men than in women.[12, 16]

Cancer. Tumors account for about 1% of all amputations, about 2% of all limb (non-digit) amputations and about 2% of all major lower limb amputations.[11] Tumors that necessitate limb amputation may develop from many different types of cancer, such as osteosarcoma, carcinoma, chondrosarcoma, histocytofibroma, or fibrosarcoma[17] However, most limb amputations are due to osteogenic sarcoma (osteosarcoma)[13, 17-19] which traditionally occurs in the long bones of the limb (femur or tibia) during periods of rapid growth.[13] The most common level of amputation following a lower limb tumor resection is transfemoral, though the location of tumors may also necessitate amputation at more proximal (hip disarticulation) and distal (knee disarticulation or transtibial) levels. [17, 19]

Congenital disorders. The presence of limb deformities (anomalies related to formation, differentiation, duplication, over- or undergrowth, constriction, or skeletal abnormalities) may present as limb absence or require amputation surgery in cases where a limb is severely deformed. The direct causes of congenital disorder are often unclear, and a variety of biochemical, mechanical, genetic factors may be responsible.[20] Current prevalence of congenital amputations or amputations related to birth anomalies is unknown. Incidence rates of emerging congenital amputations suggest that rates of amputation due to congenital disorders are comparable to amputations due to cancer (0.8% per 100,000 live births, on average, over

the period from 1988 to 1996). Evidence also suggests that approximately 40% of congenital limb deficiencies occur in the lower limb. [12]

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, [21-26] elevated cognitive demands for standing and walking, [26-28] increased metabolic requirements for walking,[29-32] reduced walking speeds, [31-34] temporal-spatial gait asymmetries,[33-36] increased fall rates,[23, 37, 38] reduced activity,[39-41] and difficulties walking over non-level terrain (uneven ground, stairs, or inclines).[42-46] Lower limb loss has also been associated with an elevated incidence in certain medical conditions,[47] including joint pain,[48, 49] osteoarthritis,[48-50] osteopenia/osteoporosis,[49, 51-54] low back pain,[52, 55] and obesity.[56] 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[57-60] and returning to work[61-63] following amputation.

3.2 Treatment: Lower limb prostheses

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.

Selection of prosthetic components is the responsibility of the rehabilitation team with input from a clinical prosthetist.[64] Patient factors such as age, weight, cause of amputation, health status, medical history, personal goals and motivation, and medical coverage are considered when assembling the prosthetic prescription.[6] Determining the most appropriate prescription for an individual patient can be challenging, particularly given the variety and large number of components available to the rehabilitation team. More than 50 different prosthetic feet[65] and more than 220 prosthetic knees[66] are commercially available.

Table 2: Medicare functional classification levels (MFCL) for amputees

Level*	Description
0	The patient 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.
1	The patient 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.
2	The patient 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.
3	The patient has the ability or potential for ambulation with variable cadence. Typical of the community ambulator who has the ability to transverse most environmental barriers and may have vocational, therapeutic or exercise activity that demands prosthetic utilization beyond simple locomotion.
4	The patient has the ability or potential for prosthetic ambulation that exceeds the basic ambulation skills, exhibiting high impact, stress, or energy levels, typical of the prosthetic

	demands of the child, active adult, or athlete.

*Also called "K-level"
Center for Medicare and Medicaid Services (2005)[67]

Selection of specific prosthetic components also depends on the patient's anticipated functional ability with the prosthesis. The Medicare Functional Classification Level (MFCL) or "K-level" descriptors[67] are commonly used by clinical prosthetists and other members of the rehabilitation team to classify or describe patients' ability and/or potential to ambulate with a prosthesis (Table 2).

The descriptions of functional ability denoted by the MFCLs are used both in clinical decisions about prosthetic components for individual patients and by prosthetic manufacturers and reimbursement agencies to classify existing and emerging prosthetic products based on the mechanical features they include. For example, prosthetic knees that contain a fluid (e.g., pneumatic or hydraulic) control system are known to be "cadence responsive" as the compression (pneumatic) or flow (hydraulic) of the fluid through the knee changes in response to the rate of loading (the speed at which the user walks). Therefore, knees that include these features are often recommended for MFCL-3 patients (or higher), as they have the "ability or potential for ambulation with variable cadence". [67]

3.3 Prosthetic knees

For people with transfemoral limb loss, the prosthetic knee is a key component of the prosthetic prescription.[68] The prosthetic knee is commonly selected to provide both the stability (safety) and agility (responsiveness) required by the user. Although more than 220 prosthetic knees are commercially available,[66] no universal classification system has been adopted to describe the mechanical features, performance characteristics, or expected behaviors of modern knees. In general, prosthetic knees are described according to the hinge joint and control systems present in the knee.[68, 69]

Knee hinge joints. Prosthetic knee joints are available with single-axis or polycentric (multiple axis) joint designs. Single-axis designs pivot about a fixed position while polycentric knees flex about an instant center of rotation that follows a curvilinear path called the centrode.[70] The behavior of the prosthetic knee at any point in time is determined by the phase of gait, how the knee is loaded with respect to the joint's center of rotation, and the presence (if any) of a knee control mechanism.

Knee control systems. Prosthetic knees may also include control systems that determine the knee's performance in stance and swing. Many knees have independent stance (when the knee is at rest) and swing (when the knee is in motion) phase control systems. Therefore, these characteristics may be individually considered when classifying or describing a specific knee. Stance (stability) behavior may be controlled by an intrinsic mechanism, such as a lock, a mechanical friction brake, or a hydraulic piston is integrated into the prosthetic knee unit. Similarly, swing behavior of the knee may be controlled by a mechanical friction brake, an elastomeric extension assist, or a pneumatic/hydraulic cylinder.

3.3.1 Technology: Microprocessor-controlled prosthetic knees

Microprocessor-controlled prosthetic (MCP) knees have the ability to monitor, switch, and/or adjust the control system present in the knee. The microprocessor can perform a variety of functions, from switching between the stance and swing control systems to perpetually adjusting

the performance of the knee under different conditions. MCP knees gather information (e.g., position, time, velocity, forces, moments, etc.) from electromechanical sensors located in or around the knee unit and dynamically change the knee's resistance to flexion and extension within or between individual steps.[71] Perpetual, autonomous control of the knee unit, as provided by these described microprocessor knee technologies, is believed to benefit users in many ways. Balance; confidence while walking; ability to change walking speeds or carry objects; ability to walk over stairs, ramps, uneven terrain, and long distances; and safety are all claimed to be improved with use of a MCP knee.[72]

Multiple prosthetic knee products incorporate microprocessor technology; there are subtle but meaningful differences between the products. These differences relate primarily to the control systems present in the knee (e.g., pneumatic fluid, hydraulic fluid, etc.), which knee mode(s) (stance and/or swing) are switched on or off by the microprocessor, and which (if any) of the control systems are adjusted by the microprocessor. For example, the Endolite (Miamisburg, OH) Intelligent Prosthesis (IP) includes a geometric stance phase control system and a pneumatic swing phase control system. The IP microprocessor dynamically adjusts the pneumatic control system during that phase.[73] The IP microprocessor does not switch the knee into swing or stance phase or adjust the knee resistance during the stance phase of gait. The Otto Bock (Duderstadt, Germany) C-Leg includes hydraulic swing and stance phase control systems. The C-leg microprocessor switches the knee back and forth between stance and swing modes and adjusts the knee resistance to extension in the swing phase of gait. In general, the more switching and adjustments made by the microprocessor, the greater the sophistication and cost of the MCP knee. Commercially-available MCP knees and the phase(s) of gait in which the microprocessor is active are shown in Table 3.

The Össur (Reykjavik, Iceland) Power Knee is the only commercially-available prosthetic knee unit to include an electromechanical motor capable of providing active knee flexion and extension. The Power Knee microprocessor uses data provided from multiple sensors (e.g., gyroscopes, accelerometers, torque sensors, and a load cell) to control the behavior of the motor. Motorized control of the knee joint is purported to address functional limitations associated with activities that require active knee extension, such as stair/incline ascent and rising from a chair.[9, 74]

Table 3 Types of microprocessor-controlled prosthetic knees

Prosthetic knee (manufacturer)	Stance control system	Swing control system	Function of microprocessor			
			Adjusts knee resistance during stance	Adjusts knee resistance during swing	Switch to stance	Switch to swing
Rheo (Össur)	Magneto-rheological fluid	Magneto-rheological fluid	yes	yes	yes	yes
Genium (Otto Bock)	Hydraulic fluid	Hydraulic fluid	yes	yes	yes	yes
C-Leg*(Otto Bock)	Hydraulic fluid	Hydraulic fluid	no	yes	yes	yes
Compact (Otto Bock)	Hydraulic fluid	Hydraulic fluid	no	no	yes	yes
Orion (Endolite)	Hydraulic / pneumatic fluid	Pneumatic fluid	yes	yes	yes	yes
Smart Adaptive (Endolite)	Hydraulic / pneumatic fluid	Pneumatic fluid	yes	yes	yes	yes
Smart IP(Endolite)	Mechanical friction (weight-activated)	Pneumatic fluid	no	yes	no	no
IP+ (Endolite)	Mechanical friction (weight-activated)	Pneumatic fluid	no	yes	no	no
Single Axis Power / Intelligent(Trulife) /	Mechanical friction (weight-	Pneumatic fluid	no	yes	no	no

(Nabtesco)	activated)					
4-Bar Power / Intelligent**(Trulife) / (Nabtesco)	Geometric	Pneumatic fluid	no	yes	no	no
Fusion Power / Hybrid (Trulife) / (Nabtesco)	Hydraulic fluid	Pneumatic fluid	no	yes	no	no
Plié*(Freedom Innovations)	Hydraulic fluid	Hydraulic fluid	no	no	yes	yes
REL-K (Fillauer)	Hydraulic fluid	Hydraulic fluid	yes	yes	yes	yes

3.3.1.1 Indications and contraindications

Indications. MCP knees are generally indicated for persons with transfemoral limb loss, knee disarticulation, or hip disarticulation of low-to-high activity (Medicare Functional Classification Level 2, 3, or 4). Additional indications include an ability to ambulate at variable cadence, good strength and balance, and a cognitive ability to use and charge the knee. MCP knees may also be used bilaterally.[72] MFCL-2 patients with sufficient cardiovascular reserve, strength and balance may be appropriate for select types of MCP knees.[72]

Contraindications. Contraindications to the use of MCP knees include a patient weight greater than the weight limit specified by the knee manufacturer (typically 220lbs to 330lbs); low activity (Medicare Functional Classification Level 0, 1, or 2); poor balance; large (greater than 20 degrees) hip flexion contractures; poor socket fit, suspension, or tolerance to the weight of the MCP knee prosthesis; a desire or need to run long distances (or run competitively); or a desire to use a knee under select environmental conditions such as excessive moisture or dust.[72]

3.3.2 Comparator: Non-microprocessor-controlled prosthetic knees

Non-microprocessor-controlled prosthetic (NMCP) knees include control systems that must be manually set and adjusted to obtain the desired behavior of the knee. At the time of prosthetic fitting, the performance of the NMCP knee's control system is individualized to the patient by the prosthetist using manual, mechanical adjustments to the knee unit. These adjustments will dictate the knee's resistance to flexion and extension across different activities. Once adjustments to a NMCP knee's control system have been made, they generally cannot be changed until the prosthetist adjusts them again at another appointment.

In clinical practice, MCP knees are considered an alternative to other prosthetic knees that are appropriate for MFCL-3 patients. This includes prosthetic knees with control systems that provide cadence-responsive (fluid-based) swing control systems.[75] In scientific study, MCP knees have been compared to commercially-available NMCP knees. Most often, the comparator used is the Össur (Reykjavik, Iceland) Mauch knee.

3.3.3 Emerging technologies

Future prosthetic knee technologies will likely include enhancements or advancements related to sensors, actuators, batteries and/or control algorithms. Emerging lower limb products are expected to include devices that provide powered control of the knee[76, 77] as well as those that provide simultaneous powered control of the knee and foot.[78-81] Control of and coordination between both prosthetic joints (the knee and ankle) is notable as it mimics the inter-joint kinematic chain present in the intact limb. One such device, developed by Vanderbilt University[78-81] has been recently licensed to Freedom Innovations (Irvine, CA) and is expected to be commercialized in coming years.[82] Emerging lower limb prosthetic technologies may also include volitional control of the prosthetic knee and/or foot.[78, 83, 84] The volitional control strategies presently under study rely primarily upon surface electromyography (EMG) signals

obtained from residual thigh muscles to command flexion/extension of the knee[78, 84] or plantarflexion /dorsiflexion of the ankle.[84] Although strategies for control of a passive lower limb prosthesis have been previously explored, [85-89] advancements in prosthetic technology have made volitional control of an active prosthesis a potential reality. These recent studies suggest that emerging transfemoral (or transtibial) prostheses may rely upon EMG signals to control the position of the prosthetic limb using methods analogous to those employed in modern myoelectric upper limb prostheses.[90]

3.4 Prosthetic feet

A prosthetic foot is a component in both transtibial and transfemoral lower limb prostheses. The purpose of a prosthetic foot is to replace, to the degree possible, the physical presence and function of the anatomical foot-ankle complex.[91] Given the complexity of the human foot and ankle, it is not surprising that prosthetic feet are, at present, unable to fully replicate all of the functions of those structures. Instead, contemporary prosthetic feet rely upon varying physical designs and mechanical properties of passive foot components (e.g., heel or forefoot) to mimic the behavior of the anatomic foot-ankle complex. Today, there are more than 50 different prosthetic feet available.[65]

Determination of an appropriate foot for a specific patient requires careful consideration of a wide variety of patient characteristics (e.g., weight, personal goals, activity level, length of residual limb, occupation, cosmesis, motivation, contralateral limb involvement and strength) and clinical factors (e.g., compatibility with other components, experience with the device, and durability).[92] As with prosthetic knees, no universally-adopted classification system exists, but prosthetic feet have historically been grouped into clinical categories representative of their mechanical designs.[64, 93]

Non-articulated or solid-ankle feet. Non-articulated feet, such as the SACH (solid ankle, cushioned heel) rely upon compression of the foot materials to simulate anatomical motion of the ankle joint.[75, 93] Non-articulated feet are inexpensive, durable and lightweight. However, because of their fixed-ankle design and rigid keel, non-articulated feet do not well accommodate uneven ground or high levels of activity. As such, they are generally recommended for persons of low activity, such as new amputees or household ambulators.[64, 93]

Articulated, single-axis, or multiaxial feet. Articulated feet include one or more mechanical joints that allow for motion at the ankle. Sagittal and/or coronal plane motion may be provided, depending on the configuration of the foot. The behavior of the joint(s) is generally determined by the presence and stiffness of elastic bumpers within in the foot. A primary advantage of articulated feet is their ability to accommodate to non-level surfaces.[93] Articulated feet are heavier and required more maintenance than non-articulated feet. Articulated feet are therefore indicated for persons who expect to walk over uneven terrain.[64]

Elastic or flexible keel. Elastic keel feet incorporate a compliant forefoot that flexes under load to simulate flexion at the ankle without the need for an articulated ankle joint. The stiffness of the elastic foot keel gradually increases as the keel flexes, mimicking the windlass effect that occurs in the anatomical foot.[93] This encourages a smooth rollover and provides some stability in late stance.[64] The flexible keel foot is not responsive when loaded rapidly, and may therefore be most indicated for persons who primarily walk or need to accommodate to uneven terrain and cannot tolerate the weight or maintenance required by an articulated foot.[64, 93]

Dynamic response, energy storing, or energy storage and return feet. Dynamic response feet integrate flexible composite materials (e.g., carbon fiber, Delrin®) into the heel and keel of the foot. These materials store energy as the foot is loaded in early stance, then release it as the foot is unloaded in late stance.[64, 93] The storage and release of energy provided by dynamic response feet offers a variety of perceived and biomechanical benefits to users when compared to non-articulated feet.[94] As such, dynamic response feet are indicated for most moderate to high activity users.

Hybrid feet. Feet may also incorporate traits from different prosthetic foot categories (e.g., a multiaxial foot with an energy storing keel). These feet are referred to as "hybrid" feet. Indications for hybrid feet vary, based upon the inherent design and associated function of the foot.

3.4.1 Technology: Microprocessor-controlled prosthetic feet

Microprocessor-controlled or "bionic" prosthetic feet include active components to control the motion of the foot with respect to the leg (shank) and simulate the motion of the active muscles of the anatomical ankle.[77] Like MCP knees, microprocessor-controlled prosthetic (MCP) feet integrate electromechanical sensors, actuators, and behavioral logic within the device to control the motion and/or position of the device. At the time of this review, only one MCP foot or foot-ankle device, the Össur Proprio,[95] is commercially available. A number of MCP feet are under development.[77]

The Proprio foot is a "quasi-passive prosthetic ankle" capable of modifying the ankle angle (plantarflexion and dorsiflexion) of the foot during gait.[96] The Proprio uses information from integrated sensors to control the orientation of the foot with respect to the ankle (and ground) during the swing phase of gait. During stance phase, the ankle position is fixed and the foot behavior is determined by the behavior of the carbon fiber foot material. Step-by-step positioning of the foot during the swing phase of gait is purported to improve ambulation over uneven terrain (e.g., stairs, ramps, or other non-level surfaces). Further, because the Proprio foot lifts the toes of the foot (dorsiflexes the foot) during each step, it may reduce stumbles and/or falls.

3.4.1.1 Indications and contraindications

Indications. According to Össur's product guidelines, the Proprio foot is indicated for persons with transtibial (below-knee) amputation of low-to-moderate activity (Medicare Functional Classification Level 3). Because the ankle can accommodate a variety of heel heights, it is also indicated for persons who wish to wear shoes with different heel heights (e.g., athletic shoes and formal footwear).

*Contraindications.*The Össur Proprio foot is contraindicated for persons who weigh more than 256 pounds or wish to participate in activities that will place impacts or high loads on the device, such as jumping, sprinting, or other sporting activities. The Proprio requires at least 7 inches of clearance below the prosthetic socket and may therefore not be appropriate for persons with long residual limbs.

3.4.2 Comparator: Non-microprocessor-controlled prosthetic feet

In clinical practice, the Össur Proprio foot is considered an alternative to other prosthetic feet that are appropriate for MFCL-3 patients. This includes a wide variety of dynamic response or energy-storing prosthetic feet.[75] In scientific study, the Össur Propio foot has been compared to several commercially-available prosthetic feet (Otto Bock Trias+, Trulife Seattle Lite, and

Kingsley SACH foot)[97] and has been evaluated for biomechanical performance in both an "adaptive mode" (microprocessor on) and a "neutral mode" (microprocessor off).[96, 98, 99]

3.4.3 Emerging technologies

Emerging prosthetic foot-ankle products, such as the iWalk PowerFoot BiOM[100-106] and the College Park iPED[107, 108] are in development but are not yet commercially available. These devices differ from the Össur Proprio foot in that they incorporate power-generating features that function in the stance phase as well as in the swing phase of gait. Prototype ankle-foot designs, such as the controlled energy storage and return (CESR) foot are being developed to recycle and return energy during the appropriate phase of gait.[109, 110] Scientific and clinical evaluations of emerging prosthetic foot technologies are ongoing, and evidence on their efficacy, effectiveness, and safety are likely forthcoming.

3.5 Potential complications/harms

Any prosthetic limb, microprocessor-controlled or not, may pose potential complications to the user. First, skin problems may develop on the residual limb (stump) such as eczema, psoriasis, infections, pressure ulcers, wounds, abrasions and blisters are commonly reported among prosthesis users.[111-113] Second, use of a prosthetic limb may induce strain on the joints of the extremities, back and residual limb, which can result in pain and joint degeneration over prolonged use.[23, 48, 49, 52, 55, 114, 115] Third, stumbles, falls, or other difficulties ambulating are common when using a prosthetic limb.[23, 37, 116]

Problems specific to a MCP limb may develop if there is a breakdown in function due to device malfunction, battery loss, or damage from environmental factors such as moisture or dust. MCPs often warn the user of an impending battery drain or failure through auditory and vibratory feedback. In the event of battery failure, MCPs (e.g., the Otto Bock C-leg) may default to a "safety mode" that will provide the user with excessive stability until the battery can be recharged or replaced.[72]

3.6 Clinical guidelines

We searched several literature databases including the National Guideline Clearinghouse, INAHTA, and other databases to identify publicly available clinical practice guidelines, systematic reviews and health technology assessments. We also identified coverage policies from the Centers for Medicare and Medicaid Services (CMS) and several other payer policies related to MCPs for people with lower limb loss. After identifying relevant documents, we summarized their conclusions relating to the key questions of this report.

3.6.1 National Guideline Clearinghouse (NGC)

One guideline addressed rehabilitation of lower limb amputation.[117] In the guideline, a microprocessor knee joint is listed as one of the prescription options for a transfemoral amputation; no specific guidance is given for the use or prescription of the microprocessor-controlled prosthesis. No guidelines were found that specifically addressed microprocessor-controlled prostheses for lower limbs.

3.6.2 National Institute for Health and Clinical Excellence (NICE)

No guidelines specifically addressed microprocessor-controlled prostheses for lower limbs from the National Institute for Health and Clinical Excellence (NICE), which provides guidance on health technologies and clinical practice for the National Health Service in England and Wales

3.6.3 NIH Consensus statements

No consensus statement was found for lower limb prostheses or microprocessor-controlled prostheses for lower limbs.

3.6.4 Professional societies/other (Not indexed in NGC)

We found no guidelines in the following resources: Institute for Clinical Systems Improvement; American Academy of Orthopaedic Surgeons; US Food and Drug Administration (FDA); US Army Institute of Surgical Research; American Association of Hip and Knee Surgeons; The Clinical Orthopaedic Society; American Orthotic and Prosthetic Association; International Society for Prosthetics and Orthotics.

3.7 Previous technology assessments

To date, systematic reviews and technology assessments of lower limb prosthetic technologies have focused primarily on MCP knees. No systematic reviews or technology of assessments of MCP feet (or foot-ankle devices) have been identified. We identified four previous technology assessments of microprocessor-controlled lower limb prostheses and one literature review conducted and reported in brief form by a health technology assessment body. One evidence report was not publicly available.[118] The conclusions of three publicly available technology assessments are listed here and described in more detail in the Appendix.

California Technology Assessment Forum (2007)[119] The California Technology Assessment Forum conducted an assessment of MCP knees for people with transfemoral amputation. The assessment was designed to answer whether five criteria were met: (1) the technology has approval from appropriate government bodies, (2) the scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes, (3) the technology must improve net health outcomes, (4) the technology must be as beneficial as any established alternatives, and (5) the improvement must be attainable outside of the investigational setting. The report concluded that all five of these criteria are met for safety, effectiveness, and improvement in health outcomes, and recommended use of MCP knees in people at functional level 3-4 with amputation from nonvascular cause for whom the prosthesis could be fit by a trained and qualified prosthetists. The CTAF subsequently voted unanimously in favor of the recommendation.

Efficacy: Mixed results regarding energy expenditure: many studies found participants walked more quickly using the MCP compared to an NMCP, one study found no difference when comparing the C-Leg with an NMCP, and two studies found no difference when comparing different MCPs. Many studies found superior function in walking speed/walking dynamics using a MCP compared with an NMCP. Several studies reported significantly improved gait biomechanics with the MCP compared with an NMCP. Few studies reported on functional outcomes: improved function found on stair/hill descent for C-Leg compared with an NMCP, no difference found in cognitive function while walking for C-leg, and significantly improved balance with SOT found using a C-Leg.

Safety: One study found significantly fewer self-reported stumbles and falls with the C-leg compared with an NMCP. Many of the study authors inferred that the results of assessing walking speed/walking dynamics indicate that microprocessor-controlled prostheses have a higher level of function with fewer falls and better ability to navigate complex terrain.

Economic data were not presented.

State of Washington Department of Labor and Industries, Office of the Medical Directory (2002)[120] In 2002, the State of Washington conducted an assessment of MCP knees, in response to a request from Occupational Nurse Consultants. At the time of the review, two unpublished studies were available on the C-Leg and four published studies on the Intelligent Prosthesis, all summarized in the report.

The report concluded that the majority of MCP knees were perceived as favorable by users. However, the overall conclusion of the report was that evidence of broad of effectiveness remained inconclusive, due to mixed evidence of MCPs to facilitate walking on uneven ground and stairs and reduce cognitive demand required for walking. Computerized knees may reduce energy expenditure.

Neither safety nor economic data were presented.

VA Technology Assessment Program (VATAP) (2000)[121] This technology assessment was designed to assess the available evidence in three areas: (1) energy costs of walking for computerized prostheses, (2) patient perceptions of improvements attributable to Intelligent Prosthesis, and (3) factors influencing return to normal living after amputation. The report included ten published studies. It found that the existing literature was very small and that published studies included highly selected participants who were already fit and active and without other medical problems, which may confound the results and limit generalizability to a VA population.

The report concluded that the available evidence suggested there was decreased energy requirements for MCP for speeds other than normal speed; mixed results for MCP in navigating uneven ground, stairs or inclines; step length more symmetrical with IP; that the majority of participants preferred MCPs; and that user perception may be particularly important in evaluating a prosthesis. Mechanical failure of MCPs appears rare.

Economic data were not presented.

Canadian Agency for Drugs and Technologies in Health, Health Technology Inquiry Service (HTIS). C-Leg Prostheses: Clinical and Cost-Effectiveness and Guidelines for Use. 2009.[122] This review was conducted by CADTH in response to the relatively new status of the C-Leg and its high cost. The research questions were focused on (1) clinical effectiveness, (2) cost effectiveness, and (3) previous guidelines. One technology assessment, two subsequent observational studies, and two cost-effectiveness studies were included. No previous guidelines were included. Detailed methods and results were not provided in publicly available documents.

The review concluded that the C-Leg prosthesis may provide better quality of life to healthy and active amputees and appear to be cost-effective from a health care system perspective. The review noted the results may not be generalizable to older amputees with chronic disease, but that the existing evidence appears to support positive health outcomes at an acceptable cost to the health care system.

3.8 Previous systematic reviews

We found one systematic review published in the peer-reviewed literature and one publicly available systematic review repeated in 2003 and 2008. Both were exclusively on the C-Leg MCP knee.

Highsmith (2010)[9] The purpose of this review was to systematically review the literature and provide recommendations on the comparative safety, energy efficiency, and cost effectiveness of the C-Leg prosthesis for transfemoral amputees. The authors conducted a systematic review and quality assessment of methodologic quality and risk of bias of a total of 18 studies.

Energy efficiency: Seven of eight studies reported improvements in energy efficiency compared to NMCP, two were statistically significant. No detriments to energy efficiency were reported.

Safety: Five of seven studies suggest consistent, statistically significant improvements in self-reported stumbles and falls with C-Leg compared to NMCP. No adverse effects or safety concerns were reported.

Economic: Two of two studies were done in Europe from the healthcare systems and from the societal perspective. Both studies were found to have limitations, but the review concluded that there is evidence to suggest that C-Leg is cost-effective from societal perspective and provides positive improvement in outcomes.

Overall, the review concluded that there was sufficient evidence to suggest increased efficacy with respect to energy efficiency, safety, and cost for the C-Leg compared to NMCPs.

WorkSafeBC Evidence-Based Practice Group (2009 update to 2003 report)[123] This systematic review was conducted as an update to WorkSafeBC's 2003 report on the Otto Bock C-Leg (below). The objectives of the report were (1) to assess the effectiveness of C-Leg compared to conventional prosthetic knees, (2) to review existing practice guidelines, and (3) to review their 2003 recommendations. The authors conducted a literature review and summary of the reports available on the Otto Bock website.

The authors identified 37 articles that discussed some aspect of the C-Leg. The authors noted methodological issues in participant selection and study design. The report concluded that there is evidence for reduced (improved) energy expenditure with the C-Leg and conflicting results regarding the speed at which the prosthesis is more energy efficient. Most studies showed improved gait biomechanics and balance and reduced number of stumbles and falls with the C-Leg. There were mixed results regarding walking speed, cognitive function, and walking on uneven ground, slopes, and stairs.

The review concluded that decision on prosthetic application/coverage should be individually based, considering the properties of various prosthetic devices, the amputee's existing health, physical and cognitive capacity, geographic accessibility to prosthetic services, mobility level and future plans (vocational, recreational, etc), and resources for reimbursement. The report recommended continued coverage for C-Leg and other microprocessor-controlled legs, using parameters and guidelines developed by the US Department of Veterans Affairs.

WorkSafeBC Evidence-Based Practice Group (2003)[124] This report found that limited research on MCP knees was available at time of report. Existing studies enroll a select group of participants, who are fit and active with no additional medical problems, likely confounding results of existing non-randomized studies. Existing studies do not conclusively show the effectiveness of the prostheses regarding energy expenditure or walking speed/dynamics. The report recommended the use of the parameters and guidelines for microprocessor-controlled knees developed by the US Department of Veteran Affairs.

3.9 Medicare and representative private insurer coverage policies

More detailed description of bell-whether coverage policies are in the Appendix (page 107). In summary:

The Centers For Medicare and Medicaid Services have no published National Coverage Determinations (NCD) for MCPs.[125] A relevant local coverage determination (LCD) (LCD11453) by CMS contractor Noridian Administrative Services has two relevant excerpts that specify coverage of prostheses beyond "basic", including MCPs, are to be considered for coverage based on participant function of 3 or above[126]:

> "Basic LOWER extremity PROSTHESES include a single axis, constant friction knee. Other prosthetic knees are considered *for* coverage based upon functional classification. … A fluid, pneumatic, or electronic knee (L5610, L5613, L5614, L5722-L5780, L5814, L5822-L5840, L5848, L5856, L5857, L5858) is covered for patients whose functional level is 3 or above."
>
> "Basic LOWER extremity PROSTHESES include a SACH [solid ankle cushion heel] foot. Other prosthetic feet are considered for coverage based upon functional classification. … A microprocessor-controlled ankle foot system (L5973), energy storing foot (L5976), dynamic response foot with multiaxial ankle (L5979), flex foot system (L5980), flex-walk system or equal (L5981), or shank foot system with vertical loading pylon (L5987) is covered for patients whose functional level is 3 or above."

AETNA considers microprocessor-controlled leg prostheses medically necessary under the following conditions[127]:

- For otherwise healthy, active community ambulating adults 18 years of age or older,
- For patients of functional level 3 or 4,
- Who have a knee disarticulation amputation or trans-femoral amputation from a non-vascular cause, and
- For whom the prosthesis can be fitted and programmed by a qualified prosthetist.

Microprocessor-controlled ANKLE-FOOT prostheses are considered to be experimental and investigational due to inadequate evidence of their effectiveness.

CIGNA considers microprocessor-controlled KNEE prostheses medically necessary for transfemoral amputees when ALL of the following criteria are met[128]:

- The patient is of functional level 3 or 4,
- Absence of a significant cardiovascular, neuromuscular, or musculoskeletal condition that would be expected to adversely affect the use of the device,
- A gait analysis demonstrates the ability to ambulate at a rate faster than baseline using a standard prosthetic device with swing and stance control, and
- The patient requires an ambulatory rate/stance control not achievable with a basic lower limb device for use outside the home on a regular basis.

Microprocessor-controlled ANKLE-FOOT prostheses are considered to be experimental, investigational, or unproven.

PREMARA BLUE CROSS (Washington and Alaska) considers microprocessor-controlled KNEE prostheses medically necessary in amputees when ALL of the following criteria are met[129]:

- Demonstrated need for long distance ambulation at variable rates, regular ambulation on uneven terrain, or regular use on stairs,
- Physical ability for ambulation at faster than normal walking speed, and
- Adequate cognitive ability to master the use and care requirements for the device.

Indications for patient use include adequate cardiovascular and pulmonary reserve, strength and balance, and cognitive ability; functional level 3 or 4, or of functional level 2 in specific circumstances; and hemi-pelvectomy through knee-disarticulation level of amputation, including a bilateral lower extremity.

The POWERED KNEE and microprocessor-controlled or powered FOOT are considered investigational.

3.10 Other significant evidence

A number of clinical trials are being conducted on the use of prostheses for transfemoral and transtibial amputees. Active randomized controlled trials listed in the NIH Reporter as of July 2011 are described below.

Active Knee Prosthesis Study for Improvement of Locomotion for Above Knee Amputees (NCT00771589). Massachusetts Institute of Technology. The study's objective is to compare the performance of a commercially-available knee prosthesis (e.g. C-Leg or Ossur Rheo) with an experimental, biomimetic prosthetic knee device that mimics muscle activity using a double series-elastic actuator (SEA) system.

Comparison of Prosthetic Knee Performance During Sitting and Standing (NCT00421356). University of South Florida. In this completed observational, Phase 0 trial, 28 transfemoral amputees were compared with 7 intact controls on their performance while standing up from a chair. Participants used one of the following types of prosthesis: the Power Knee (Ossur), a stance control prosthesis (C-Leg, Rheo, Adaptive), a non-microprocessor stance control prosthesis (Mauch, Catech), or a non-microprocessor/non-stance control prosthesis (WASB, polycentrics, pneumatics). Associated publication: Highsmith, M.J., et al., Kinetic asymmetry in transfemoral amputees while performing sit to stand and stand to sit movements. Gait Posture, 2011. 34(1): p. 86-91.

Effects of Wearing a Powered Ankle-Foot Prosthesis on Amputee Walking (NCT00869947). This small (n = 20) RCT is underway at the Department of Veterans Affairs in collaboration with the Massachusetts Institute of Technology. Energy requirements and characteristics of walking will be compared for amputees wearing either a conventional prosthesis or the MIT Powered Ankle-Foot (PAF) prosthesis and matched non-amputees.

Dynamic Management of Excess Residual Limb Pressure With New Smart Socket Technology (NCT01108536) This RCT is underway at the University of Wisconsin, Milwaukee, and was scheduled to be completed in November, 2009, with an estimated enrollment of 60 participants. Participants are fitted with the SMART socket and radiographic imaging is used to study the behavior of bones and soft tissue of the socket-stump interface during walking.

3.11 Summary

Existing clinical guidelines and reviews tended to conclude benefits of MCP knees based primarily on measures of laboratory-based performance measures of activity, cognitive demand and safety. Payer policies tended to base coverage of MCP knees on baseline function, most

requiring Medicare Functional Classification Level 3 or more. Most policies reviewed considered MCP feet investigational. Several studies that are active or not yet published are examining the use of powered prosthetic knees or feet.

All reviews and assessments noted that more studies of improved methodological quality are needed, even though prosthetic research has inherent challenges. Studies to date tend to enroll participants who are physically active, generally without serious co-morbidities, and long-term users of standard prostheses, limiting generalizability of study results to the total population of people living with lower limb loss.

4 The evidence

4.1 Methods of the systematic literature review

4.1.1 Defining inclusion and exclusion criteria (PICO)

After initial literature review we developed a set of inclusion criteria using the PICO format (Participants, Intervention, Comparison, and Outcomes). Studies were considered eligible if they were comparative clinical studies, included adults with unilateral lower limb amputations, either transfemoral (above knee) or transtibial (below the knee), and had microprocessor-controlled prostheses (MCP) as an intervention (Table 4).

All outcomes were eligible for inclusion in this report. However, after reviewing the literature on individual studies, previous health technology assessments, systematic reviews, and an unpublished review[130] we determined that there is sufficient evidence of laboratory performance of MCPs to justify focusing our critical appraisal on the performance of MCPs in real-world settings. Therefore, we focused our critical appraisal in this report on outcomes measured in real-world, uncontrolled settings (home or community use).

Table 4. PICO: Summary of inclusion and exclusion criteria

	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 (eg 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 (eg 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 publically 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

4.1.2 Search strategy

Article selection took place in four stages. First, we designed a search strategy (Appendix page 97) and conducted a systematic literature search using PubMed, other relevant electronic databases and targeted searches of relevant journals. Second, two reviewers independently reviewed the titles and abstracts of all results. Articles meeting our *a priori* criteria based on the inclusion/criteria (Table 4) were included. Articles not easily included or excluded from the title or abstract were included for full text review. Third, we retrieved full text of remaining articles. Fourth, two independent reviewers read the full text of each article and recommended inclusion or exclusion based on our *a priori* inclusion criteria. Disagreements were resolved by consensus. Reference lists of all eligible studies were also hand-searched to identify any additional eligible articles. Articles selected form the evidence base for this report.

Electronic databases searched included PubMed, the NIH Reporter, the Grey Literature Report from the NY Academy of Medicine, *The Cochrane Library*, AHRQ, and INAHTA. The search strategies used for PubMed are shown in Appendix A (page 97) . Articles excluded at full-text review are listed in the Appendix (page 99).

4.1.3 Data extraction.

Reviewers extracted the following data from the included clinical studies: study population characteristics, study type, patient demographics, study interventions, follow-up time, study outcomes and cost-effectiveness information. In studies appearing or reporting data from the same study population from multiple time points, such as baseline and follow-up data, the outcomes assessed for the longest time period was included.

4.1.4 Analysis and quality assessment

Outcome measures. For each outcome measure used in the included articles, we noted whether each was patient-reported or clinician-assessed and measured in uncontrolled (eg home or community) or controlled settings (eg laboratory or obstacle course), used single-item or summary scores for measuring outcomes, and was condition-specific to use of prostheses by amputees or a generic measure of health/quality of life.

For each outcomes measure, we searched the published literature for studies of reliability or validity in people using lower limb prostheses. We looked for evidence of content validity (do the questions capture all relevant aspects of the outcome?), criterion validity (do scores correlate with a “gold standard” measure?), construct validity (does the instrument measure what it intends to measure?), reliability (do repeated measures show consistent results?), internal consistency (are conceptually similar items correlated?), reproducibility, responsiveness (does the instrument detect change over time?), floor or ceiling effects (do scores cluster at the high or low ends of the scale?) and evidence establishing minimal clinical important difference (MCID).

Clinical evidence. Based on *a priori* criteria, we rated each included study according to one of four levels of evidence (LoE)—I (good quality) through IV (very poor quality). Our methods for assessing the quality of clinical evidence of individual studies and the overall quality of evidence incorporates aspects of the rating scheme from the Oxford Centre for Evidence-based Medicine[131], precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group,[132]and recommendations made by the Agency for Healthcare Research and Quality (AHRQ).[133, 134] Details of the Level of Evidence (LoE) methodology are in the appendix (page 101).

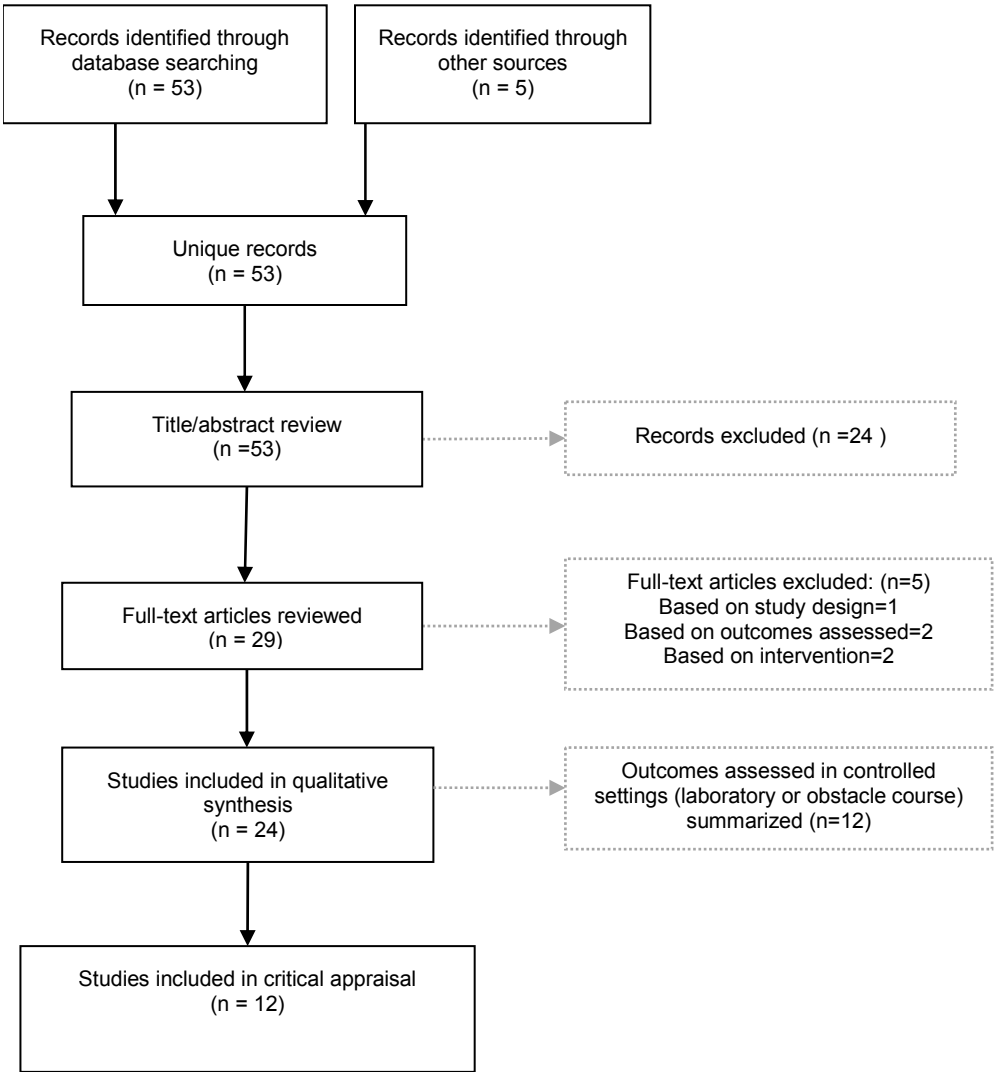
We considered randomized controlled trials as providing evidence on clinical efficacy. For crossover studies, we considered random-order assignment of type of prosthesis necessary to meet the RCT requirement. Crossover studies that did not provide random-order assignment of prosthesis type but attempted to simulate real-life conditions (e.g., switching from the current use of NMCP to the new MCP) provided evidence on clinical effectiveness.

Economic evidence. For each included economic study, two reviewers independently rated the quality of the study using the Quality of Health Economic Studies rating scale[135] as a guide, with concurrent assessment of the clinical evidence provided in each study as described above. The Quality of Health Economics Studies (QHES) facilitates quality rating of study methodology, perspective, time horizon, uncertainty analysis, inputs of both costs and outcomes (in the absence of long-term data from a randomized trial, modeling methods are often employed), and statement of funding. We also assess the quality of the clinical data in economic studies vis-a-vis the evidence for efficacy and effectiveness in other sections of this report. More detailed description on our analysis methods is provided in the Appendix (page 100).

Strength of evidence. Based on the findings of our systematic review, we provide conclusion statements in answer to each key question. We also provide an assessment of the **strength of evidence** of HIGH, MODERATE, LOW, or VERY LOW for each statement based on the quality, quantity, and consistency of the findings reported. One co-author of this report (BJH) was also an author of an included study so did not participate in the critical appraisal process.

4.2 RESULTS OF SYSTEMATIC REVIEW

Figure 1: Article selection process



The literature search resulted in 53 unique citations. Of these, we reviewed the full text of 29 articles. A total of 12 articles were included for critical appraisal based on their inclusion of outcomes assessed in uncontrolled settings. An additional 12 articles met the inclusion criteria based on their assessment of outcomes in controlled settings; those articles are summarized (Figure 1). [136]

Several articles contained results relevant to more than one key question. Of the 12 critically appraised articles, all were considered for KQ1 (outcomes); 12 were relevant for KQ2, seven for KQ3 (safety), two for KQ4 (subgroups) and three for KQ5 (economics) (Table 5). Several studies also assessed different outcomes in both uncontrolled and controlled settings. In these cases, the outcomes in uncontrolled settings were critically appraised and those in controlled settings were summarized.

All eligible articles were assessed outcomes in microprocessor-controlled KNEES. No articles on microprocessor-controlled FOOT prostheses met the inclusion criteria.

Table 5: Included articles

	KQ1 Outcomes	KQ2 effectiveness	KQ3 Safety	KQ4 Subgroups	KQ5 Economics
A. OUTCOMES CRITICALLY APPRAISED (uncontrolled settings)^					
Hafner, BJ et al (2009)[6]*^	■	■		■	
Kahle, JT, et al (2008) [8]^	■	■	■		
Kaufman, KR, et al (2008)[7]^†	■	■	■		
Berry, D et al (2009)[137]	■	■	■		
Datta, D et al (1998)[138]	■	■			
Williams, RM, et al (2006)‡[139]^	■	■			
Klute, GK, et al (2006)‡[140]	■	■			
Kirker (1996)[141]^	■	■			
Jepson, F, et al (2008)[142]^	■	■	■		
Gerzeli, S, et al (2009)[143]	■	■	■		■
Seelen HAM et al (2009)[144]	■	■		■	■
Brodtkorb TH et al,(2008)[145]	■	■	■		■
B. OUTCOMES SUMMARIZED (assessed in controlled settings only)					
Hafner, BJ, et al (2007)[146]*	■	■	■		
Heller, BW, et al (2000)[147]§	■	■			
Datta, D, et al (2005)[148]§	■	■			
Orendurff, MS, et al (2006)[149]‡	■	■			
Seymour, R, et al (2007)[150]	■	■			
Chin, T et al (2003)[30]	■	■			
Bellmann, M, et al (2010)[151]	■	■	■		
Johansson, JL, et al (2005)[152]	■	■			
Schmalz (2002)[153]	■	■			
Maaref (2010)[154]	■	■			
Blumentritt (2009)[155]	■		■		
Kaufman, KR, et al (2007)[156]†	■	■			

^Assessed outcomes both in controlled and uncontrolled settings. Outcomes assessed in controlled settings were summarized only.
*Same study population
†Same study population
‡Same study population
§Same study population

4.3 Summary of study design and populations studied

Design. Twelve (12) articles are included for critical appraisal, representing a total of 614 people. All clinical studies employed within-subjects design except for the economic studies. No studies used blinded designs. Two studies (using the same study population) employed

randomized order of knee assessment. Length of follow-up varied from 7-days to 15 months of use of MCP knee (Table 6).

Nine of 12 studies assessed patient use of the C-Leg (Otto Bock); two studies assessed use of Intelligent Prosthesis (IP), and one of the Adaptive Knee. All 12 studies used non-microprocessor-controlled prostheses (NMCP) as the comparison, though the models of NMCP varied (Table 6). Percent of participants completing followup varied from 27% to 100%.

Table 6 Summary of study designs

	Study design	Intervention	Comparison	Random assignment?	Longest followup	% followup
Datta, D and J Howitt (1998)	Crossover	Intelligent Prosthesis	Endolite PSPC	No	≥ 7 months	100
Hafner, BJ and DG Smith (2009)*	Crossover with repetition	C-Leg	Passive, NMCP	No	15.2 months	81.0
Kahle, JT, et al (2008)	Crossover (A-B)	C-Leg)	Passive, NMCP	No	7 months	90.5
Kaufman, KR, et al (2008)	Crossover with repeated measures	C-Leg	Mauch SNS hydraulic knee	No	9 months	NR
Jepson (2008)	Crossover	Adaptive	Endolite with hydraulic Catech knee	No	6 months	100
Berry (2009)	Crossover (A-B)	C-Leg	Various passive NMCP	No	6-9 months	51% response rate
Klute (2006)	Crossover (A-B-A-B)	C-Leg	Mauch SNS hydraulic knee	Yes	7 days	27.8†
Williams (2006)	Crossover	C-Leg	Mauch SNS hydraulic knee	Yes	3 months	44.4‡
Kirker (1996)	Crossover	Intelligent Prosthesis	Endolite PSPC	No	NR	87.5/37.5§
Brodtkorb 2008	Crossover	C-Leg	NMCP	No	12 months	NR
Gerzeli 2009	Cross-sectional	C-Leg	NMCP	No	12 months	100%
Seelen 2009	Retrospective cohort	C-Leg	NMCP	No	12 months	NR

NMCP: non-microprocessor-controlled prosthesis; NR: not reported; PSPC: pneumatic swing phase control.
*An earlier study using the same population and outcomes collected at earlier time points was not included (Hafner et al 2007).
†Same study population as Williams 2006. Initially, 18 participants gave consent: 4 withdrew voluntarily (time commitment), 3 withdrew due to unrelated medical issues, 3 did not complete the protocol (problems fitting or acclimating to MCP, and 3 were excluded (did not wear the study prosthesis for the full duration of the protocol). Therefore 5/18 completed the study.
‡Same study population as Klute 2006. Initially, 18 participants gave consent: 4 withdrew voluntarily (time commitment), 2 withdrew because the C-leg could not be correctly fit for them, 1 withdrew due to problems acclimating to the C-leg, and 3 withdrew due to unrelated medical issues. Therefore 8/18 completed the study.
§Percent follow-up for: questionnaire/ treadmill testing (gait symmetry, energy expenditure).

Population. Overall, the populations studied were most likely to be male (63% to 88%) and with amputations of traumatic etiology (46% to 96%). Mean age varied from 36 to 54 years, spanning the ages of 18 to 85 years. Years since amputation was reported for all studies. Most reported 10 to 20 years since amputation, with from 3-4 years to 44 years as the range. One study included a range of 0.2 to 78.7 years since amputation[137](

Table 7).

Table 7: Summary of populations studied

	N	% male	Mean age ±SD years	Cause of amputation (%)	Years since amputation (±SD or range)	Medical coverage	Function/ activity level at baseline
Datta (1998)	22	63.6	39.9 (range 25–72)	72.7 traumatic 22.7 cancer 4.6 osteomyelitis	19.2 (5–53)	NR	Fit and generally fairly active; no stump problems
Hafner (2009)	17	76.5	49.1 ± 16.4	58.8 traumatic 17.6 cancer 11.8 infection 5.9 vascular 5.9 congenital	17.6 ± 18 (2–67)	NR	MFCL-2: 47.1% (n = 8) MFCL-3: 52.9% (n = 9)
Kahle (2008)	19	NR	51 ± 19	36.8 traumatic 21.1 diabetes 21.1 congenital 15.8 vascular 5.3 cancer	10 ± 9 (4–37)	NR	MFCL 2, 3, or 4
Kaufman (2008)	15	80.0	42 ± 9	46.7 traumatic 40.0 cancer 6.7 vascular 6.7 congenital	20 ± 10 (3–36)	NR	MFCL 3 or 4
Jepson (2008)	5	NR	41.2 (range, 28.8–55.7)	NR	12.2 (0.8–35.7)	NR	Medically fit to do walking required for study
Berry (2009)	368	78.5	54.7± 15.6	50.3 traumatic 13.9 cancer 11.1 vascular 2.2 congenital 22.5 other	18.5 (0.2-78.7)	NR	MFCL 3
Kirker (1996)	14	83.3	36.5 (range, 29–44)	NR	16.5 (7–44)	NR	Overall good health; wore leg all day and regularly walked at different speeds
Brodtkorb (2008)	20	58.8	41.0 ± 2.5	NR	16.0 ± 2.6	NR	Generally active
Gerzeli (2009)	100	88.0	45.4 ± 11.9	96.0 traumatic 4.0 other	13.5 ± 1.9	NR	NR
Seelen (2009)	26	80.8	47±12	61.5 traumatic 19.2 cancer 19.2 vascular	C-leg:13.2±12.9 NMCP: 11.4±11.7	NR	Daily use of prosthesis 12.6 hours/day
Williams (2006)*	8	87.5	48.5 ± 10.2	NR	NR	VA	Use of prosthesis >8 hours/day for at least 3 years; walk without use of upper-extremity aids; could walk up and down 3 flight of stairs
Klute (2006)*	5	NR	48 ± 12	80.0 traumatic 20.0 cancer	21 ± 11	VA	Could walk without use of upper-extremity aids; could walk up and down 3 flight of stairs

MFCL: Medicare Functional Classification Level; NR: not reported; SD: standard deviation; VA: Veteran's Administration.
*Same study population

4.4 Methodologic quality of included studies (Level of evidence)

Of the 12 studies critically appraised, we appraised three as Level II (moderate quality) and nine as Level III (low quality) (Table 8). No studies were determined to be Level I (high quality) or Level IV (very low quality). Most downgrades in quality were assigned for lack of random assignment, lack of concealment of sequence allocation, lack of blinded assessment, and failing to control for possible confounding (Table 23; Table 24).

Measurement bias. Several studies assessed patient recall of previous prosthesis as the comparison group.[138, 141] One measured comparison by asking participants to assess a

hypothetical scenario (imagine if they had not been given a MCP)[145]. Results from these studies should be interpreted with caution, as there is potential for several types of bias. Even if recall bias is minimized by a short time between use of the previous knee to the new knee, there is potential for expectation bias, which would favor the new or experimental knee.

Generalizability. Overall, the included studies assessed patients of relatively high baseline function (e.g., MFCL 3 or 4 only or "all day" use of prosthesis).[156] [141] No studies selected patients that could be described as "limited" ambulators. As such, the findings of these studies are of unknown generalizability to more limited ambulators so the ability of MCPs to improve function in a lower-functioning population is difficult to assess.

Heterogeneity of outcomes. Several studies created one or more survey items to assess outcomes. For example, the two studies by Hafner et al.[6, 146] created an addendum to the PEQ called the PEQ-A and Kirker et al. assessed "effort" needed to complete various ambulation tasks.[141] These items provide potentially extremely helpful information in the assessment of the effectiveness and safety of MCPs. However, in the absence of comparison to community norms or psychometric assessment to establish validity, reliability, and clinically meaningful differences, the results of these heterogeneous outcomes are difficult to assess in total.

Length of follow-up. The longest follow-up of real-life use of MCPs was three years; most were less than one year. Considering that people most likely to receive an MCP are of functional level of at least 3, they are also relatively young and most likely to be living with an amputation of traumatic etiology. Thus it is likely that users of MCPs could be users for many decades. The studies included here do not permit evaluation of the long-term outcomes related to MCPs.

Loss to follow-up: In several studies, there was significant loss to followup. For example, in the studies by Klute et al. and Williams et al., of 18 people consented 10 did not complete the study. Of these, six were related to problems fitting or acclimating to the MCP (n=3) or to people who did not wear the MCP for the duration of the study (n=3).[139, 140] In the Brodtkorb study, the population includes 20 current C-leg users who had been NMCP users previously.[145] The main reason for having changed was dissatisfaction with the NMCP, which potentially biases the results. Since these problems may be directly relevant to the potential performance of MCPs in real-life settings, such results should be interpreted with caution.

Table 8: Level of evidence of included articles

	I	II	III	IV
Hafner, BJ et al (2009)[6]		■		
Kahle, JT, et al (2008)[8]		■		
Kaufman, KR, et al (2008)[7]			■	
Berry, D (2009)[137]			■	
Datta, D (1998)[138]			■	
Kirker (1996)[141]		■		
Klute, GK, et al (2006)[140]			■	
Williams et al (2006[139])			■	
Jepson, F, et al (2008)[142]			■	
Gerzeli, S, et al (2009)[143]			■	
Seelen HAM et al (2009)[144]			■	
Brodtkorb TH et al,(2008)[145]			■	

I: high quality; II: moderate quality, III: low quality, IV very low quality

4.5 KQ1: Outcome measures

KQ1. a. What are the expected treatment outcomes of use of microprocessor-controlled lower limb prostheses? b. Are there validated instruments related to measurement of outcomes of this technology? c. Has clinically meaningful improvement in outcomes been defined for use of this technology?

KQ1. a. What are the expected treatment outcomes of use of microprocessor-controlled lower limb prostheses?

Outcomes expected with use of a lower limb prosthesis differ according to the type of control provided by the microprocessor (Background section, page 31). Microprocessor control of the *swing* (the period of time when the limb is in the air) features of the prosthesis are expected to provide increased responsiveness and an ability to adapt to different walking speeds. Microprocessor control of the *stance* (the period of time when the foot is on the ground) features of the prosthesis are expected to provide increased stability and safety.

Lower limb prostheses with microprocessor control of *swing* phase are purported to offer users an ability to increase walking speed and quickly transition between different walking speeds (faster or slower).[72] Because the microprocessor is able to adjust how the knee swings, the user may require less energy to walk. These types of knees do not possess microprocessor control of the stance phase of gait and rely on the mechanical control system to provide stance control. Therefore, the expected outcomes are likely similar to NMCPs in regards to stability and safety, such as the ability to walk with variable cadence and to walk long distances (energy savings).[72]

Prostheses with microprocessor control of *stance* phase are purported to improve users balance and provide a greater degree of confidence in the stability of the prosthesis.[72] Because microprocessor control is able to put the knee into a high resistance mode, users are able to walk without fear of the knee collapsing. The safety features provided by microprocessor control of stance are also believed to reduce the likelihood of a fall.[72] Given the high incidence of falls among persons with lower limb loss,[23, 38] safety is often considered a primary outcome from use of a MCP with microprocessor control of stance. This is especially important when additional or unexpected forces are placed on the prosthesis, such as when a user walks down a hill, down stairs or over uneven terrain.[72]

MCPs with microprocessor control of *both stance and swing* inherit the traits from both types of control strategies. Therefore, they are likely to be associated with the following outcomes:

- The ability to walk with variable cadence
- The ability to walk long distances (energy use)
- The ability to walk on uneven terrain
- The ability to descend stairs
- The ability to descend ramps
- The ability to walk while carrying heavy objects
- The ability walk in crowded places
- The ability to get into and out of a car
- The ability to sit down
- The ability to stand in a stationary position
- The ability to resist falls

These expected impacts on ambulation may also lead to several improvements in activity, function, and quality of life, for example:

- Total energy expenditure, including step counts and increased physical activity
- Condition specific quality of life (amputation- or prosthesis-specific), including appearance, fit and comfort, satisfaction, and social function
- Global quality of life
- Activities of daily living

Additionally, if users of MCPs are experience higher global functioning and quality of life, theoretically benefits are possible at a societal level, for example:

- Improved productivity of amputees
- Reduced caregiver burden

The outcomes assessed in the studies included in this report are in Table 9.

Table 9: Outcomes assessed in MCP use

Setting	1. Instrument- or investigator- assessed	2. Patient-reported
A. Controlled or semi-controlled	Controlled (eg lab or clinic): ▪ Energy use: oxygen use cost/rate ▪ Cognitive demand: Serial subtraction test; controlled oral word association test (COWAT); category test ▪ Impact on ambulation: walking speed; stair assessment index (SAI); standardized walking obstacle course (SWOC); Montreal rehabilitation performance profile (MRPP) Semi-controlled (eg obstacle course) ▪ Walking speed ▪ Time to complete ▪ Hill assessment index (HAI) ▪ Cognitive demand: Reverse numbers test "walk and talk"	▪ Borg Rating of Perceived Exertion (RPE)
B. Uncontrolled (eg home/ community)	Doubly labeled water ▪ **Total daily energy expenditure (TDEE)** ▪ **Physical-activity related energy expenditure (PAEE)** Step activity monitor ▪ **Steps per day** ▪ **Minutes of activity per day**	Generic measures: ▪ **SF-36** ▪ EQ-5D Condition-specific measures: ▪ **Prosthesis evaluation questionnaire (PEQ)** ▪ **50-question survey** ▪ Prosthetic cognitive burden scale (PCBS) Individual items: ▪ Stumbles ▪ Falls ▪ Walking speed, distance, style ▪ Stair ascent/descent ▪ Slopes and hills ▪ Rough/uneven roads ▪ Energy level ▪ Device reliability ▪ Overall assessment

		▪ Satisfaction ▪ Patient selection of prosthesis

Bold type indicates measures with that have been assessed for validity or reliability.

KQ1b. Are there validated instruments related to measurement of outcomes of this technology?

Instrument- or investigator-assessed outcomes. Two investigator-assessed outcomes were assessed in real-world settings. Kaufman et al (2008) used a method of doubly labeled water, where participants consumed water containing isotopes of oxygen and hydrogen and oral doses of deuterium and oxygen-18.[7] Energy expenditure was then calculated via clearance of the isotopes in a series of urine samples over 10 days of community activity. This method is acknowledged as the "most accurate and robust" method available to assess energy expenditure in daily living settings.[7] Klute et al (2006) used the StepWatch activity monitor, an instrument the size of a pager and worn on the ankle.[140] Measures of activity are obtained after being calibrated for the individual's height/weight, stepping rate, walking speed, and motion. The SAM has been shown to be reliable and valid for measuring long-term activity.[157]

Patient-reported outcomes. In general, patient-reported outcomes were described in one of two categories: summary scores obtained from outcomes instruments (either as a total score or a scale score) or proportions or means from individual questions. We did not find any psychometric testing on individual questions.

With respect to outcomes measures used in the microprocessor-controlled lower limb patient population, we identified three generic and four condition-specific patient-reported outcomes assessed in real-world settings. Generic measures included two measures of health related quality of life, the SF-36 and the EQ-5D, and one of perceived exertion (Borg Rating of Perceived Exertion, RPE). Population norms for people with lower limb loss have been published by the creators of the SF-36.[158] The EQ-5D has been assessed previously in people with amputations from diabetes[159, 160]; efforts to establish population norms for a US population are ongoing.[161] Of the three condition-specific measures, we located evidence of validity and/or reliability for two: the Prosthesis Evaluation Questionnaire (PEQ) and the 50-Question Survey. The third, prosthetic cognitive burden scale (PCBS), has not undergone any psychometric testing.

We assessed the psychometric properties of the two instruments, the PEQ and the 50-Question Survey, tested in the limb loss population.[162, 163] Appendix C (page 100) contains a detailed description of our methods (Table 12).

Prosthesis Evaluation Questionnaire (PEQ).

Legro et al[164] developed the PEQ as a condition-specific self-reported instrument for persons with lower limb amputations and measure small differences in prosthesis function and major life domains related to the prosthesis function. Seven of the nine scales address the relationship of the amputee to his/her prosthesis or perception of his/her prosthesis. The other two, Ambulation scale and Well-Being scale, address the amputee's function or well-being. Each scale is scored on a 0–100 scale, where higher scores indicate better scores.

The PEQ is a self-administered questionnaire consisting of 82 items with a linear analog scale response format. Forty-two items are grouped into 9 scales (Table 10). The scales can be used independently. The remaining 40 items consist of individual questions and are not grouped into scales.

*Validity***.** Content validity was demonstrated for the PEQ by the original developers in a population where only 25% had transfemoral amputations.[164] The purpose of the PEQ is clearly delineated: to measure small differences in prosthesis function and major life domains related to the prosthesis function. The target population is lower extremity amputees. There were no stated inclusion or exclusion criteria, though the authors refer to those "eligible". Items were selected based on the input from clinicians, researchers, participants in a support group for persons with amputations and from an Internet group for persons with amputations. In an iterative process, both content and format were pilot tested with local patients.

Criterion validity was demonstrated in three scales in two studies.[23, 164] Criterion validity was assessed in the initial cohort of 92 patients[164] by the association between the ambulation scale and SF-36 physical function subscale (r=0.61); between the social burden scale and the SF-36 social function subscale (r=0.59) and SIP social subscale (r=0.52); and the well-being scale and the Profile of Mood States (POMS-SF) total score (r=0.49). Mobility (ambulation scale and transfers) was able to predict the current status of patients based on the use of mobility devices, walking distance and automatic walking.[23] Construct validity was demonstrated in four scales in three different studies.[23, 164, 165]

Table 10: Prosthesis Evaluation Questionnaire (PEQ) domains

PEQ Domain	Constructs assessed in domain
Ambulation	Ability to walk (general), in close spaces, upstairs, down stairs, up steep hill, down steep hill, sidewalks and streets, slippery surfaces
Appearance	Look, damage to clothing, damage to prosthesis, clothing choice limited, shoes of choice,
Frustration	Frequency, most frustrated time
Perceived response	Desire to avoid strangers, partner response, how affected relationship, family member response
Residual limb	Sweat, odor, swelling, rash, ingrown hairs/pimples, blisters/sores
Social burden	Hindered socially, burden on family members, ability to care for others
Sounds	Squeaking, clicking, belching, how bothersome
Utility	Weight, fit, comfort, felt off balance, energy requirements, feel on residual limb, ease of putting on
Well-being	How things have worked out since amputation, self-rated quality of life

Legro et al (1998)[164]

Convergent validity was demonstrated in the initial cohort of 92 patients[164] by demonstrating whether the scales could differentiate between groups of people whose scale scores would be expected to be different. The residual limb health and frustration scales have the ability to differentiate between groups based on age; ambulation and social burden scales differentiate between groups based on sex, and the ambulation scale differentiates between groups based on comorbidities. Convergent validity of the mobility scale (ambulation and transfers) was subsequently tested in 329 patients (72% who had transfemoral amputations).[23] The Pearson correlation coefficients between the Mobility subscale and the 2 minute walk test, the Time Up and Go Test (TUG), the Activities-specific Balance Confidence Scale (ABC) and the Prosthetic Profile of the Amputee Locomotor Capabilities Index(PPA-LCI) were 0.50, 0.50, 0.82 and 0.77, respectively. The Italian language version of the PEQ demonstrated convergent validity in 95

patients by correlating the PEQ mobility score (PEQ-MO) with the Locomotor Capabilities Index (from the Prosthetic Profile of the Amputee), r=0.81.

Reliability. Internal consistency was high in all scales in one study.[164] (Cronbach's α range from 0.73 to 0.89) Questions pertaining to transfers were assessed and had a low value, α = 0.49. In a second study evaluating the mobility scale (ambulation and transfers), the internal consistency was high, α = 0.95.[23] The Italian version demonstrated high internal consistency in all scales (α = 0.72 to 0.95) except for the appearance scale (α = 0.64). Note that the internal consistency for transfers in the Italian version had an α = 0.95.

Test-retest reliability was conducted in three studies.[23, 164, 166] The intraclass correlation coefficient (ICC) for the PEQ total score was 0.77.[23] The ICCs were ≥0.70 in the following scales: utility, ambulation, transfers, residual limb health, appearance, sounds and well-being.

Floor/ceiling effects. Two studies report on the floor/ceiling effect for the PEQ; one reports a ceiling but no floor effect for well-being and transfer scales and no ceiling or floor effect for the remaining scales,[166] and one reports no floor or ceiling effect for the mobility scale.[23]

Responsiveness. One study tested for responsiveness and found that all PEQ scales were responsive.[166]

Minimal clinically important difference (MCID). We found no studies evaluating the MCID of the PEQ.

50-Question Survey

The 50-Question Survey is a self-administered questionnaire created to assess 6 dimensions of prosthetic knee rehabilitation[137] (Table 11):

Table 11: 50-question survey domains

50-question survey domain	Constructs assessed in domain
Socket fit	Comfort in the proximal brim and distal end, suspension, ease of getting the socket off and on, and overall socket comfort
Confidence/security	Ability of the knee to keep up with gait, ease of standing up and sitting down in chair, overall balance, confidence walking in large crowds or unfamiliar places, overall confidence, need of cane or crutches to get around, fear knee may buckle while standing, allowance of normal daily and special activities
Gait/maneuverability with the prosthesis	Ability to walk at slow and fast pace, ability to jog or run, ability to change speeds while walking, stability on uneven surfaces, and ability to walk down stairs or ramps with confidence
Physical attributes of prosthesis	Weight, cosmetic appearance, resemblance to sound leg, fit of prosthetic foot in shoe, and ability to wear clothing items
Physical effects of prosthesis	Socket is hot/causes sweating or produces rash, residual limb volume fluctuates, pressure points in socket, muscle fatigue, cramps or phantom pain in residual limb, tired at the end of the day, low back or hip pain
Safety/negative attributes of prosthesis	Knee buckles while standing, prosthesis feels heavy, knee does not keep up when walking fast, avoidance of going up or down stairs or ramps, walking in crowds produces unstable feeling, stooping to rest when out in public, use of disabled/handicap parking

Berry (2009)[137]

*Validity***.** We found no studies evaluating the validity of the 50-Question Survey.

Reliability. One study[137] assessed the test-retest reliability of the questionnaire on 30 individuals two weeks apart. The authors report that the percent agreement was 94% and that the remaining 6% had a ±1 (scale of 1-5) response.

Floor/ceiling effects. We found no studies evaluating the floor/ceiling effect of the 50-Question Survey.

Responsiveness. We found no studies evaluating the responsiveness of the 50-Question Survey.

MCID. We found no studies evaluating the MCID of the 50-Question Survey.

4.5.1 Summary

Expected treatment outcomes for use of MCPs include improvements to ambulation, energy use, quality of life, activities of daily living, and improved productivity and burden on caregivers. Most outcomes assessing MCP performance in real-life settings are patient-reported. Two investigator-assessed measures were available: doubly labeled water to assess energy use and a step activity monitor to assess daily step count and activity.

Out of six outcomes measures and more than twenty individual items used to assess patient-reported outcomes of MCPs, two have undergone psychometric analyses in people living with limb loss: the Prosthesis Evaluation Questionnaire (PEQ) and the 50-Question Survey. The PEQ primarily evaluates the users' relationship with and perception of their prosthesis with respect to items such as fit and appearance. Only two subscales measure physical function: ambulation and transfers.

- Validity: Three scales of the PEQ demonstrated adequate content, criterion and construct validity: ambulation, transfers, and social burden. Other scales on the PEQ had inconsistent results or were not tested. There are no validity data available for the 50-Question Survey.
- Reliability was adequate in five of the PEQ scales: utility, residual limb health, sounds, ambulation, and well-being. The reliability testing for the 50-Question Survey was inadequate.
- We found no studies were found that defined a minimal clinically important difference for either the PEQ or the 50-Question Survey.

Table 12: Reliability and validity of patient-reported outcomes

Instrument	Content validity	Criterion validity	Construct validity	Internal consistency	Reproducibility	Floor/ceiling	Responsiveness	MCID
PEQ								
Utility	+	-	-	+	+	+	+	-
Residual limb health	+	+	-	+	+	+	+	-
Appearance	+	-	-	+/-	+	+	+	-
Sounds	+	-	-	+	+	+	+	-

Ambulation	+	+	+	+	+	+	+	-
Transfers	+	+	+	+/-	+	+/-	+	-
Frustration	+	-	-	+	+/-	+	+	-
Perceived response	+	-	-	+	-	+	+	-
Social burden	+	+	+	+	+/-	+	+	-
Well-being	+	-	+	+	+	+/-	+	-
50-Question Survey	-	-	-	-	+	-	-	-

4.6 KQ2: Efficacy/effectiveness

KQ2. What is the evidence of efficacy and effectiveness of microprocessor-controlled lower limb prostheses?

4.6.1 KQ2a: Energy and cognitive requirements of ambulation

Controlled settings

Oxygen (O2) cost. Bellmann et al (2010)[151] conducted two within-subject crossover experiments to measure differences in O2 costs between MCPs (Otto Bock C-Leg as compared to Nabtesco Hybrid and C-Leg compared to Össur Rheo). Each experiment was conducted in a single day; the second experiment was conducted approximately one year after the first. In each test experiment, participants (n=9) with non-vascular etiologies were provided with two different MCPs and approximately two hours to accommodate to each test prosthesis. A telemetric spiroergometric system was used to measure O2 costs as participants walked across a flat, level laboratory at three walking speeds (0.6–0.8 m/s, 0.8–1.0 m/s, and 1.0–1.2 m/s). At 0.8–1.0 m/s, C-Leg users required significantly lower O2 costs than when they wore the Rheo knee. All other comparisons (C-leg compared to Rheo at other speeds or C-leg compared to Hybrid knee) showed no significant differences in O2 costs. Results suggest that O2 cost may not change substantially with use of different MCPs at moderate walking speeds on a level surface.

Kaufman et al (2008)[7] conducted a within-subject crossover study to assess differences in O2 costs between a MCP (Otto Bock C-Leg) and a NMCP (various designs). Interventions were ordered (participant's existing NMCP first) and participants (n=15) were allowed to accommodate to the MCP as long as they deemed necessary (a range of 10–39 weeks). Participants of mixed etiologies walked at three controlled speeds (0.45, 0.90, and 1.35 m/s) on a treadmill. A respiratory mass spectrometer was used to assess breath-by-breath O2 costs. At all speeds, participants showed non-significant decreases in O2 costs after transitioning to the MCP. These results similarly suggest that O2 costs may not differ significantly between MCPs and NMCPs at moderate walking speeds on a level surface.

Seymour and colleagues (2007)[150] conducted a within-subject crossover experiment to assess differences in energy expenditure between a MCP (Otto Bock C-Leg) and a NMCP (various designs). All participants (n=10) were of non-vascular amputation etiology, had experience with both prostheses, and were currently wearing the MCP. Interventions were randomized and participants were not provided an extended period of accommodation. Participants were tested at self-selected and fast walking speeds on a motorized treadmill. Breath-by-breath O2 costs were measured with a metabolic stress test system. Results showed that use of the MPC significantly reduced O2 costs at both self-selected and fast walking speeds (by 3.4% and 8.7%, respectively). In contrast to other studies, these results suggest energy demands may be reduced with use of a MPC at moderate and fast walking speeds.

Orendurff et al (2006)[149] conducted a within-subject crossover study to measure gait efficiency using a standardized MCP (Otto Bock C-leg) and NMCP (Össur Mauch SNS). Interventions were randomly assigned and participants (n=8) with traumatic etiology were provided three months to accommodate to each prosthesis prior to testing. Oxygen costs were measured on a level walkway at four speeds (self-selected walking speed, 0.8 m/s, 1.0 m/s, and 1.3 m/s) with a portable telemetric metabolic measurement system. No significant differences in O2 cost were measured between the prosthetic conditions at any speed.

Datta and colleagues (2005)[148] conducted a within-subject crossover study to measure differences in oxygen costs between a single NMCP (Endolite ESK) and MCP (Endolite IP). The order of interventions was fixed (NMCP always tested first) and participants (n=10) of non-vascular etiology were provided six weeks of accommodation before testing the MCP condition. O2 costs were averaged over 3-minute intervals at five different treadmill speeds (ranging from 0.7 m/s to 1.25 m/s) using a cardiopulmonary gas exchanges system. At speeds below 0.9 m/s, use of the MCP required significantly lower O2 costs than the NMCP. This suggests that MCPs with microprocessor swing control may provide reduced energy requirements at speeds below self-selected walking speed.

Chin et al (2003)[30] conducted a between-groups study to assess the O2 costs associated with walking in persons with traumatic amputation (n=8) using a MCP (Endolite IP) compared to healthy controls (n=14). Oxygen cost was measured as participants walked over level ground at five walking speeds (0.5, 0.83, 1.16, 1.5, and 1.83 m/s) using a portable telemetry system. MCP users were young (mean age 22.5 years), physically fit, and skilled in the use of the prosthesis. MCP users expended significantly (20.1% to 33.1%) greater energy than the healthy controls across the tested speeds. The greatest differences in O2 costs between groups were at slower speeds. These results suggest that, even with use of a MCP, relatively large differences in energy demands required for walking exist between persons with amputation and healthy controls.

Oxygen (O2) rate. The previously described study by Seymour et al (2007)[150] reported O2 rate as well as O2 cost. Results similarly showed that O2 rate was reduced at both self-selected and fast walking speeds (by 7.1% and 7.5%, respectively). This again suggests that metabolic energy requirements may be reduced with use of the MPC at moderate and fast walking speeds in persons with non-vascular amputations.

Johansson et al (2005)[152] conducted a within-subjects crossover study to assess differences among two MCPs (Otto Bock C-leg and Ossur Rheo) and a NMCP (Össur Mauch SNS). The order of interventions was randomly assigned. Participants (n=8) with non-vascular etiologies were provided approximately 10hrs of accommodation to each knee prior to each test sessions. Breath-by-breath O2 rate was measured as prosthesis users walked at self-selected speed along a quarter-mile indoor track with a telemetered system. Results showed a 3%, significant decrease in O2 rate with the Rheo MCP and a 2%, non-significant decrease with the C-leg MCP, as compared to the NMCP. Results suggest that magnetorheological control of a MCP may reduce metabolic demands compared to NMCPs at self-selected walking speeds on level ground.

Chin et al (2003)[30] also reported differences in O2 rate between MCP (Endolite IP) users (n=8) and healthy controls (n=14). As noted, MCP users expended significantly greater energy across all walking speeds than the healthy controls.

Schmalz and colleagues (2007)[167] conducted a within-subject crossover experiment to measure differences in energy expenditure between a MCP (Otto Bock C-Leg) and a NMCP (Otto Bock 3C1). Six active, young (average age = 37.9 years) participants with non-traumatic etiologies were asked to wear both prostheses within a single test session. Oxygen rate was assessed as participants walked on a treadmill at three speeds (0.80 m/s, 0.94 m/s, and 1.16 m/s) with cardiopulmonary system. Thirty minutes of rest were provided between test conditions. Significant reductions (approximately 6%) in O_2 rate were measured at the two slowest speeds when participants wore the MCP. This suggests that metabolic demands may be decreased with use of MCP at moderate-to-low walking speeds.

Kirker et al (1996)[141] conducted a within-subject crossover experiment to measure differences in energy expenditure between a NMCP (Endolite PSPC) and a MCP (Endolite IP). Participants (n=6) with non-vascular amputations had previously worn both prostheses and were currently wearing the MCP. Oxygen rate was measured in both prostheses in a single session; practice time was provided, as needed. Testing was performed on a treadmill at three speeds (self-selected normal, fast, and slow), determined by the limits of the NMCP. Consumed oxygen was measured using a closed reservoir filled with O2 and a CO_2 absorber. No significant differences between prostheses or speeds were detected, suggesting that swing-only MCPs may not reduce energy requirements of walking in a narrow range around the self-selected walking speed.

Physiological cost index (PCI). Jepson et al (2008)[142] reported prosthesis users' energy expenditure using a MCP (Endolite Adaptive) and a hydraulic NMCP (Catech SNS). Energy expenditure was measured with the physiological cost index (PCI).[168] Although the validity of the PCI as a proxy for energy expenditure in persons with stroke[169, 170] and healthy controls[171, 172] has been debated, it has also been suggested to be adequate for measuring O2 cost among prosthetic users.[173] No significant differences in PCI were detected between knees, three of four participants showed improved PCI in the MCP. The small sample size (n=4) makes it difficult to assess the impact of microprocessor control on the PCI.

Rating of perceived exertion (RPE). Kaufman et al (2008)[7] reported users' perceived energy expenditure walking with a MCP (Otto Bock C-Leg) and a non-standardized NMCP (various prosthetic knee designs). Perceived energy was assessed with the Borg rating of perceived exertion(RPE).[174] Fifteen participants with transfemoral amputation rated their exertion after walking on a treadmill for several minutes at three walking speeds (0.45, 0.90, and 1.35 m/s). Users' RPE scores were significantly lower in the MCP than in the NMCP. This data suggests that users may perceive improvement in energy expenditure gained from using an MCP, even when assessed energy efficiency is not significantly improved.

Cognitive requirements of ambulation. Studies by Hafner et al[6, 146] examined the cognitive demand associated with ambulation in a MCP (Otto Bock C-Leg) and a NMCP (various designs) in a within-subject crossover trial. Interventions were ordered, but were alternated at least two times. Participants were allowed to accommodate as-needed until basic safety criteria were met. Participants were assessed using an ad hoc measure designed by the investigators to assess the mental energy required to walk two sides of a city block. Participants (n=17) were asked to walk at a comfortable pace while a secondary, reverse numbers test was administered over a cellular phone. Average walking speed and test accuracy were reported as measures of cognitive demand. Early data[146]showed non-significant increases in speed in the MCP, but increasing accuracy in the reverse numbers test. The authors suggested this may allude to a potential learning effect in the selected secondary task. Later analysis with additional assessments[6] showed that the difference in dual-task walking speed between the MCP and

NMCP conditions was significant. Further, the authors suggested that participants rated as MFCL-2 showed greater improvements in cognitive demand (dual-task walking speed) than those rated as MFCL-3. Given the ad hoc nature of this test, results must be taken with caution, but suggest MCPs may reduce the cognitive burden associated with ambulation.

Williams et al (2006)[139] explored the cognitive performance associated with walking using a standardized NMCP (Össur Mauch SNS) and MCP (Otto Bock C-Leg) in a within-subject (n=8) crossover trial. The order of interventions (MCP or NMCP) was randomly assigned and users were assessed after three months accommodation to each prosthesis. The cognitive burden associated with walking was evaluated through self-selected walking speed, measures of objective cognitive performance (e.g., serial subtraction[175], the Controlled Oral Word Association Test (COWAT),[176] and the Category Test[177]) and ad hoc measures of subjective cognitive burden (three scored questions asked of participants following cognitive performance each test). Walking speed, objective cognitive performance scores, and most subjective cognitive burden scores were comparable between knee conditions. Response to the subjective question, "how much of your attention was focused on walking" was significantly better in the MCP than in the NMCP. The results suggest few differences in cognitive burden between MCPs and NMCPs.

A study by Heller et al (2000)[147] examined the cognitive demand of participants (n=10) using a single NMCP (Endolite ESK) and a MCP (Endolite IP). The order of interventions was fixed (NMCP always tested first) and six weeks of accommodation time were provided before testing the MCP condition. Whole body sway, measured as the motion (velocity and ratio of MCP sway to NMCP sway) of a marker placed on participants' foreheads, was used to infer the cognitive demand required for ambulation. Body sway was measured as participants walked and completed one of two secondary tasks, a simple counting task and the Stroop test.[178] The Stroop test has been shown to be cognitively demanding and is resistant to learning effects.[179] Results showed that individuals varied as two participants showed increased sway velocity, two participants showed no change, and six participants showed decreased sway velocity while wearing the MCP. On average, participants experienced reduced sway velocity while wearing the MCP, though this result was not significant. These data suggest that use of different knees may or may not affect sway. However, the connection between sway and cognitive burden is unclear.

Uncontrolled settings (Table 13)

Five studies assessed outcomes in uncontrolled settings related to the energy/cognitive requirements of ambulation.[6, 7, 138, 139, 141] The PEQ Utility subdomain, which includes a measure of "how much energy" required to ambulate, detected different scores between MCP and NMCP knees in two studies, both more favorable for MCPs.[6, 7] However, it should be noted that this domain also includes measures of weight, fit, comfort, feeling off balance, feeling on residual limb and the ease of putting the prosthesis on. As such the PEQ Utility domain may not be sensitive enough to detect specific energy requirements.

Two studies used objective, investigator-assessed measures to assess energy use in real-world setting. Kaufman et al (2008)[7] used a method of doubly labeled water, where participants consumed water containing isotopes of oxygen and hydrogen and oral doses of deuterium and oxygen-18. Energy expenditure was then calculated via clearance of the isotopes in a series of urine samples over 10 days of community activity. The results found that use of C-Leg was associated with higher energy expenditure; this difference was not statistically significant. Williams et al (2006)[139] designed several items to assess subjective cognitive burden; these items were completed by participants at home three times during the week of the laboratory assessment. Participants reported improved cognitive burden with MCP use, though this was

inconsistent with tests of cognitive demand in laboratory setting in the same study. The authors suggest that the cognitive tasks selected may not have been sufficiently challenging to detect the perceived differences in cognitive burden described by study participants.

Hafner et al (2009)[6] employed several single-item measures of the cognitive requirements of ambulation. Patient reported mental energy expenditure and difficulty with concentration were not significantly different between C-Leg and NMCP knees, while MCPs were associated with a significantly improved patient report of ability to multitask while walking.

Kirker et al (1996)[141] reported patient assessment of effort required to walk at various conditions with a MCP compared to NMCP. Significant improvements were indicated for "normal speed", "fast" speed, "outdoors at work" and "down slopes"; no improvement was indicated for slow speed, walking up slopes or walking up/down stairs. One study reported a single item measure of whether walking was more or less tiring between MCP and NMCP knees and found that most (21/22) rated the MCP as "a lot less tiring".[138] However, this study used patient recall of previous prosthesis as comparison so the potential for recall bias is high.

Table 13: KQ2a energy/cognitive requirements of ambulation (uncontrolled settings)

Measure/outcome	Study	N	% male	Mean age (years)	MCP Model	Follow-up (months)	Results*		
							MCP	NMCP	*P*-value
Outcomes Instrument: Domain									
PEQ: Utility (mean)	Hafner 2009 Kaufman 2008	17 15	76.5 80.0	49.1 42.0	C-Leg C-Leg	12 9	**76.1**† **71**‡	68.9† 66‡	ns .02
Prosthetic Cognitive Burden Scale (mean ± SD)	Williams 2006	8	87.5	48.5	C-Leg	7	**2.1 ± 0.4**	3.2 ± 0.4	< .001
Single items									
Mental energy expenditure (mean; VAS, 0–100)	Hafner 2009	17	76.5	49.1	C-Leg	12	**67.9**†	53.3†	0.02
Difficulty with concentration (mean; VAS, 0–100)							**85.6**†	77.2†	0.07
Difficulty multitasking while walking (mean; VAS, 0–100)							**85.4**†	69.0†	0.002
Walking much less tiring (%)	Datta 1998	22	63.6	39.9	IP	≥ 7	**95.5**§	0§	NR
Total daily energy expenditure (MJ/d; mean)**	Kaufman 2008	15	80.0	42.0	C-Leg	9	**14.1**	13.0	.02
Physical activity-related energy expenditure							**5.5**	4.4	.04
Thermic effect of food							**1.4**	1.4	ns
Basal metabolic rate							**7.2**	7.2	ns
Effort needed to walk at: (mean, 0-100, higher is greater effort)	Kirker 1996	14	83.3	36.5	IP	NR			
Normal speed							**28**	47	< .05
Fast speed							**31**	76	< .01
Slow speed							**35**	46	ns
Outdoors/at work							**31**	64	< .01
Down slope							**47**	69	< .05
Up slope							**55**	67	ns
Up steps							**61**	68	ns
Down steps							**47**	54	ns

IP: Intelligent Prosthesis; MCP: microprocessor-controlled prosthesis; NMCP: non-microprocessor-controlled prosthesis; NR: not reported; ns: not statistically significant; PEQ: Prosthesis Evaluation Questionnaire; VAS: visual analog scale.
Bold type indicates more favorable results of compared treatment groups.
†Mean scores for the entire population (MFCL 2 + MFCL 3) were calculated using weighted means.
‡Means estimated from figures provided in the article.
§1/22 (5.0%) reported no difference.

**Estimated using the doubly labeled water (DLW) method.

4.6.2 KQ2b. Impact on ambulation

Controlled settings

Impact on ambulation. Assessments of walking performance are often conducted in controlled environments such as clinics or laboratories.[180] Such locations are well-suited to the study of biomechanical performance as well as evaluations of intervention efficacy. However, these settings are often limited in size and their ability to replicate natural home or community environments. To address these limitations, studies of MCP performance have used portable instrumentation designed to assess participants' ambulation in their lived environments. [6, 140, 146] Investigators have also explored the use of standardized indoor[150] or outdoor[6, 8] obstacle courses to reflect the "real world" conditions that may be present in prostheses users' lived environments. Investigators have attempted to integrate non-level environmental barriers such as ramps, hills, or stairs into motion analysis laboratories[151] to better evaluate the outcomes associated with use of contemporary prosthetic technologies.

Daily step frequency among persons with limb loss is typically assessed using pedometers[181] or portable step activity monitors.[39, 42, 157, 181] These devices are worn at the waist or attached to the prosthesis and monitor activity in the participants' lived environments over selected periods of time (typically 7 days or more). As such, daily step activity is not well suited to evaluation in a controlled setting and no studies were identified that measured step activity in this fashion.

Estimated step distance may be derived from measurement of daily step frequency and a measurement or estimate of stride length.[182] Like daily step frequency, estimated step distance is obtained with use of a pedometer or step activity monitor and reflects performance in the lived environment. As such, no studies were identified that measured estimated step distance in a controlled environment.

Level terrain. Kahle and colleagues (2008)[8] conducted a within-subject crossover study to evaluate outcomes associate with use of a MCP (Otto Bock C-leg) compared to a NMCP (various prosthetic knee designs). Interventions were ordered (participants were tested after 90 days in their existing NMCP first) and participants (n=19) were allowed to accommodate to the MCP for 90 days. Investigators assessed participants' ability to walk on level, even terrain over short (6-meter) and long (75-meter) distances. Participants were asked to walk the short and long distances in the shortest time possible. In both cases, participants required significantly less time (17% and 15%, respectively) to walk the described distance in the MCP than in the NMCP.

Uneven terrain: Seymour and colleagues (2007) [150] measured performance of participants walking over indoor, uneven terrain using the Standardized Walking Obstacle Course (SWOC)[183] while using a MCP (Otto Bock C-Leg) and again while using a NMCP (various designs). The SWOC has been used to assess walking performance among healthy adults,[183] elderly persons with arthritis,[183] healthy children,[184] and children with cerebral palsy.[185] Study participants were tested both in a hands-free condition and when carrying a 10-pound basket. Results showed that participants completed the SWOC under both conditions in significantly less time and with significantly fewer "step-offs" in the MCP.

In contrast to Seymour et al, Hafner et al[6] and Kahle et al[8] measured prosthesis users' performance on ad hoc outdoor obstacle courses. Both investigators compared a standardized MCP (Otto Bock C-leg) to various types of NMCPs. Neither obstacle course was validated by

the investigators, but both included natural terrain, such as grass, rocks, and sand. Kahle et al measured fastest possible walking speed over a 38m obstacle course. Results showed that significantly less (21%) time was required to complete the course in the MCP (Otto Bock C-leg) compared to the NMCP (various designs). Hafner et al similarly measured performance over a 75 meter course. Results also indicted significantly less time was required to complete the obstacle course in the MCP, particularly for those of lower mobility (those rated as Medicare Functional Classification Level 2).

Hill and ramps. The studies by Hafner et al[6, 146] included assessments of hill descent using an ad hoc observational scale called the Hill Assessment Index (HAI).[186] Hill descent was assessed on a steep (19-degree), outdoor, 28-meter sidewalk. The HAI is an investigators-assigned rating of the quality of movement on a hill, such as stepping pattern, independence, and assistive device use. Results showed that participants were rated significantly higher in the MCP (Otto Bock C-leg) than in the NMCP (various designs). Participants also descended the hill in significantly less time in the MCP. These results suggesting an improved ability to descent hills with use of a MCP, though further evidence is needed to collaborate this finding.

In their comparative study of four MCPs, Bellmann et al (2010)[151] noted that use of a hand rail in ramp descent varied, based on the MCP. Users of the Adaptive 2 knee relied upon the hand rail in 100% of the tests, while C-leg users did so only 22% of the time. This may suggest that different MCPs offer varying amounts of security to users in ramp or hill descent.

Stairs: Studies by Hafner et al (2009, 2007)[6, 146] also included a measure of stair descent, the Stair Assessment Index (SAI)[186]. Like the HAI, the SAI is an investigator-assessed rating of the stepping pattern, independence, and assistance used by participants as they descended a flight of stairs. The investigators rated participants as they descended a standard, indoor staircase. Users scored significantly higher on the SAI using the MCP (Otto Bock C-leg) than they did in the NMCP (various designs), suggesting an improved ability to descend stairs. However, as the SAI has not been tested by other investigators, its evidence of validity is limited and these results should be interpreted with caution.

Kahle et al (2008)[8] also included an assessment of stair performance. The investigators used the Montreal rehabilitation performance profile (MRPP)[187] to quantify performance on a six-stair staircase. It should be noted that the MRPP was originally developed for children and has, to-date, not been validated in the amputee population. The MRPP includes a composite score that reflects stepping pattern, cueing, time of stair descent, and assistance. Results were qualitatively analyzed and the authors reported that 12 of 19 participants improved their quality of stair descent when using the MCP (Otto Bock C-leg).

Bellmann and colleagues (2010)[151] reported data that suggests MCP users more often relied upon use of a handrail in stair descent than in ramp descent. The frequency of use also varied with the type of MCP. For example, while wearing the Adaptive 2 MCP, users elected to use the handrail 100% of the time. When wearing the C-Leg MCP, users elected to use the handrail 44% of the time. As with ramp descent, this may suggest that security of the prosthesis may be related to the type and/or model of the microprocessor knee present.

Stopping and standing safety. Kaufman et al (2007)[156] conducted a within-subject crossover study to assess differences in perturbed balance related to use of a MCP (Otto Bock C-Leg) and a non-standardized NMCP (various prosthetic knee designs). Interventions were ordered (participants were tested in their existing NMCP first) and participants (n=15) were allowed to accommodate to the MCP as long as they deemed necessary (a range of 10-39 weeks).

Participants' balance was measured with the Sensory Organization Test (SOT) and administered using a computerized dynamic posturography platform.[188] The SOT includes six test conditions that challenge participants' somatosensory, visual, and vestibular systems. The SOT has been reported to be reliable in persons with transtibial amputation[189] but may not accurately identify those susceptible to falling.[190] The validity of the SOT among persons with transfemoral amputation is unknown. The authors reported that the MCP showed significantly improved SOT scores across all six conditions (and the composite score) compared to the NMCP. These results suggest that MCPs may improve balance, but more evidence is needed to confirm these findings.

Adaptation to different walking speeds. Mâaref et al (2010)[154] conducted a between-groups retrospective analysis of walking gait parameters collected for MCP (Otto Bock C-leg) users (n=14), NMCP (various designs) users (n=15) and able-bodied controls (n=15). Groups were predominantly men and included participants with similar ages. Characteristics of prosthesis users were combined, so comparability of intervention groups was difficult to assess. All prosthesis users had at least one month experience with their device prior to testing. Walking speed was evaluated by tracking reflective markers placed on participants' sacra with a motion analysis laboratory. A minimum of three trials were collected for each participant on level, indoor terrain. Results showed that, although amputee participants walked significantly slower than the control group, self-selected walking speeds were significantly greater in the MCP group (mean = 1.13 m/s) as compared to the NMCP group (mean = 0.96 m/s). Results suggest that use of a MCP may allow users to walk at greater self-selected walking speeds. However, given the small group sizes, heterogeneity of the intervention group and poor definition of group characteristics, these results should be taken with caution.

Kahle and colleagues (2008)[8] assessed participants' ability to vary speed over 75 meters of level terrain. Participants were asked to walk at self-selected and fastest-possible speeds. Results showed that both self-selected and fastest-possible speeds significantly increased (17.2% and 14.3%, respectively) after users transitioned to the MCP. Results indicate that prosthetic users were able to rather substantially increase their customary and fast-paced walking speeds when using the MCP.

Orendurff et al (2006)[149] explored the interactions in walking speeds and metabolic energy demands in MCP (Otto Bock C-leg) and NMCP (Össur Mauch SNS) users. Although no significant differences in O_2 cost were detected across the study population (n=8), the investigators reported that self-selected walking velocity was significant faster in the MCP than in the NCMP and that this increased speed was not associated with an increased O_2 cost. Data from this study presented by Segal et al 2006[191] indicated that participants also adopted a significantly faster walking speed in the MCP (1.30 m/s) compared to the NMCP (1.20 m/s). Thus, use of an MCP may allow users to adopt faster walking speeds without affecting the energy required to do so. This conclusion is further supported by feedback offered by the study participants who reported that the MCP improved their ability to adapt to different walking speeds.

Kirker et al (1996)[141] examined users' ability to walk at self-selected, slow, and fast walking speeds along a 100-meter corridor using a MCP (Endolite PSPC and a MCP (Endolite IP). Results showed that participants (n=6) adopted a range of walking speeds (average of 1.01 m/s to 1.45 m/s), but that self-selected speeds did significantly differ between knee conditions. This suggests that the magnitude of self-selected speeds on indoor, level terrain may not be significantly affected by use of a MCP with microprocessor control of swing phase.

Uncontrolled settings (Table 14)
Two studies reported the Ambulation domain of the PEQ, which includes patient report of ability to walk on various surfaces and at various speeds and slopes.[7, 146] Both studies reported improvement (0-100 scale, higher is better ambulation) associated with use of MCP knees; both study found this difference to be statistically significant.

Berry and colleagues (2009)[137] reported results of a 50 question survey with a gait/maneuverability subset that also included measures of ability to walk at various speeds on various surfaces. The maximum score for this subset was 35, indicating most favorable outcome. The MCP knee group reported higher scores on this set of questions than the NMCP group (20.2 vs 11.8). P-values were not reported. Gerzeli reported significantly better physical mobility as measured by the EQ-5D.[143]

Datta et al (1998)[138] asked several questions of MCP users about the comparative use of MCP vs NMCP knees. The majority of respondents reported that MCP use improved walking at different speeds, distance, stairs, slopes, uneven ground, and overall walking style. These results should be interpreted with some caution since they are based on patient recall of former knee prosthesis.

Jepson et al (2008) reported results of a series of single items in a questionnaire sent to participants after use of the Adaptive knee. JEPSON. It is unclear from the description of methods, but it appears the questionnaire was conducted at the time of lab-based assessment and again 6 months later. Of five participants, four reported reduced ability to walk in several conditions at the 6-month time point. For example, in response to a question about flat walking for 1000 meters, one reported no change at 6 months, two reported lower results, and two reported better results. Actual responses were not reported and statistical tests were not performed (n= 5), making it difficult to interpret the actual impact on ambulation. However, these data lend some support to the idea that use of MCPs in extended community use may vary over time.

In one study[8] the authors conducted a secondary analysis of functional classification. Of nine participants initially rated as MFCL-2 (lower function), four were re-classified by study clinicians at the end of the study as MFCL-3. Though no data on the system of reclassification was provided (eg blinding of raters), these data provide support for the idea that MCP knees may in some circumstances improve function significantly enough as to change their MFCL level.

Klute et al[140] conducted a within-subject crossover study to measure community-based activity using a standardized MCP (Otto Bock C-leg) and NMCP (Össur Mauch SNS). Interventions were randomly assigned and participants (n=8) with traumatic etiology were provided three months to accommodate to each prosthesis prior to testing. Daily activity was measured over one week with a step activity monitor (SAM), a portable device worn about the ankle of the prosthesis. The SAM was used to measure the total number of steps taken and the duration of activity (minutes per day) in each prosthesis. Results showed no significant differences in steps or duration of activity between the MCP and NMCP conditions.

Table 14: KQ2b impact on ambulation (uncontrolled settings)

Measure/outcome	Study	N	% male	Mean age (years)	MCP Model	Follow-up (months)	Results*		
							MCP	NMCP	*P*-value
Outcomes Instrument: Domain									
PEQ: Ambulation (mean)	Hafner 2009	17	76.5	49.1	C-Leg	12	**75.7**†	64.4†	0.008
	Kaufman 2008	15	80.0	42.0	C-Leg	9	**75**‡	61‡	.02
50-question survey: gait/maneuverability (mean ± SD)	Berry 2009	363	78.5	54.7	C-Leg	6-9	**20.2 ±6.6**	11.8 ±3.6	< .0001
EQ-5D: physical mobility	Gerzeli 2009	100	88.0	45.4	C-Leg	12			
No problems walking about (%)							**64**	44	.045
Individual Questions									
Walk different speeds (easier/much easier, %)	Datta 1998	22	63.6	39.9	IP	≥ 7	**95.5**	5.0	NR
Walk distance (further/much further, %)							**81.8**	5.0	NR
Ascending stairs (easier/much easier, %)							**22.7**	0	NR
Descending stairs (easier/much easier, %)							**22.7**	0	NR
Walking on slopes and hills (a lot easier, %)							**59.1**	5.0	NR
Walking on rough/uneven ground (easier/a lot easier, %)							**63.6**	5.0	NR
Walking style (more/a lot more normal, %)							**95.5**	0	NR
Flat walking 500 m (easier/much easier, %)§	Jepson 2008	5	NR	41.2	Adaptive	6	20.0	**40.0**	NR
Flat walking 1000 m (easier/much easier, %)§							20.0	**40.0**	NR
Walking up slopes (easier/much easier, %)§							**40.0**	0	NR
Walking down slopes (easier/much easier, %)§							20.0	20.0	NR
Walking up stairs (easier/much easier, %)§							20.0	20.0	NR
Walking down stairs (easier/much easier, %)§							0	**60.0**	NR
Instrument-assessed measure									
Steps per day over 7 days (mean ± SD)**	Klute 2006	5	NR	48	C-Leg	7 days			
Weekdays only							2708 ± 704	**2710 ± 947**	ns
Weekends only							2527 ± 840	**2587 ± 1093**	ns
All days							2657 ± 737	**2675 ± 976**	ns
Minutes per day of activity over 7 days (min/day, mean ± SD)**									
Weekdays only							**272 ± 5 6**	253 ± 95	ns
Weekends only							273 ± 89	**280 ±115**	ns
All days							**273 ± 65**	260 ±100	ns

EQ-5D: European Quality of Life-5 Dimensions; IP: Intelligent Prosthesis; MCP: microprocessor-controlled prosthesis; n/a: not sapplicable; NMCP: non-microprocessor-controlled prosthesis; NR: not reported; ns: not statistically significant; PCS: Physical Component Score; PEQ: Prosthesis Evaluation Questionnaire; SF-36: Short Form-36 questionnaire.

***Bold type** indicates more favorable results of compared treatment groups

†Mean scores for the entire population (MFCL 2 + MFCL 3) were calculated using weighted means.

‡Means estimated from figures provided in the article.

§Description of how the questionnaire was administered and scored was not in the article. This is our best interpretation of the scores given the lack of specific information regarding scoring.

**Measured via the StepWatch 2 activity monitor that was affixed to the distal end of each participant's prosthetic limb. The sampling interval was set to record the number of step occurring in 1-minute intervals for a period of 1 week.

4.6.3 KQ2c. Patient perceptions, quality of life, impact on daily activities.

Controlled settings
Patient perception; quality-of-life (QoL); impact on activities of daily living, work, and work performance are outcomes that traditionally occur in the lived, uncontrolled environment over extended periods. No studies were identified that included assessment of these outcomes in a controlled setting.

Uncontrolled settings (Table 15, Table 16)

Quality of life. Several studies reported overall measures of health related quality of life. Hafner (2007) reported that the SF-36 subdomain results were not significantly different between MCP and NMCP users, but results were not provided.[146] Seelen (2009)[144] used the SF-6D to calculate utility scores for both MCP and NMCP users (0-1, 1 is perfect health), and found that MCP users had a significantly higher score ($p<0.01$); this is likely a clinically meaningful difference.[192] However, this outcome was assessed early in the rehabilitation process and may not reflect quality of life measures over time.

Seymour (2007) assessed quality of life using the SF-36 in MCP users and compared the results to community norms (not NMCP users). They found that SF-36 scores were consistent with national norms and with those of people with limb loss SEYMOUR. In the absence of objective measures of SF-36 of NMCP users, this is technically not a comparative outcome so it is not included in our critical appraisal and the results should be interpreted with caution.

The Gerzeli and Brodtkorb studies both reported utility scores calculated from the EQ-5D, and both found that MCPs were associated with improved health (Gerzeli $p<0.01$, Brodtkorb p value not reported).[143, 145] These studies detected improvements in EQ-5D of 12% and 36%, above the suggested "rule of thumb" of 5%-10% improvement in scores on this instrument considered clinically significant.[192-194] The Brodtkorb result should be noted with a caution to consider a high potential for bias, as a hypothetical scenario was used to assess outcome, asking participants to picture if they had not received a MCP knee.[145]

Gerzeli also reported results of each subdomain on the EQ-5D (physical mobility, self-care, usual activities, pain/discomfort, and anxiety/depression).[143] MCP users were more likely to report higher function in each of these areas but were not statistically significant except for physical mobility ($p=0.045$).

Two studies reported subscales of the PEQ related to overall patient perceptions and quality of life: Well-being; Frustration; Perceived response; and Social Burden[6, 7] Both studies found that the C-Leg was associated with higher well-being, reduced frustration, and improved social burden. Scores on the perceived response domain, relating to reactions of others to the prosthesis, were equivalent in both studies. Kahle reported additive summary scores on the first 15 questions of the PEQ;[8] this interpretation is inconsistent with the recommended measurement of subdomains, so are very difficult to interpret and not possible to interpret compared to other studies.

Confidence. Two studies included assessments of confidence while using MCPs, both using single item measures.[6, 137] The Berry study assessed several questions about confidence, and the pooled category scores indicated that MCPs were associated with significantly higher confidence than NMCPs. The Hafner study (2009) also reported statistically significantly higher confidence while walking in MCP users and reduced fear of falling.[6] No information on the clinical relevance of this scope of difference is available.

Table 15: KQ2c Quality of life (uncontrolled settings)

Measure/outcome	Study	N	% male	Mean age (years)	MCP Model	Follow-up (mos)	Results*		
							MCP	NMCP	*P*-value
QUALITY OF LIFE									
SF-6D utility score (mean ± SD)	Seelen 2009	26	80.8	47.0	C-Leg	12	**0.69 ±0.08**	0.58 ±0.09	0.005
EQ-5D utility score (mean ± SD)	Gerzeli 2009	100	88.0	45.4	C-Leg	12	**0.75 ± 0.12**	0.66 ± 0.20	0.007
	Brodtkorb 2008	34	58.8	41.0	C-Leg	12	**0.83**	0.53	NR
PEQ (first 15 questions, mean ± SD)	Kahle 2008	19	NR	51.0	C-Leg	7	**1184.1 ± 243.1**	942.3 ± 269.3	0.007
PEQ (mean):									
Well-being	Hafner 2009	17	76.5	49.1	C-Leg	12	**81.6**†	76.0†	0.016
	Kaufman 2008	15	80.0	42.0	C-Leg	9	**81**	70	0.02
Frustration	Hafner 2009	17	76.5	49.1	C-Leg	12	**79.0**†	67.9†	ns
	Kaufman 2008	15	80.0	42.0	C-Leg	9	**60**	56	0.02
Perceived response	Hafner 2009	17	76.5	49.1	C-Leg	12	**95.8**†	91.8†	ns
	Kaufman 2008	15	80.0	42.0	C-Leg	9	89	**90**	ns
Social burden	Hafner 2009	17	76.5	49.1	C-Leg	12	**90.0**†	88.5†	ns
	Kaufman 2008	15	80.0	42.0	C-Leg	9	**88**	76	0.02
Comments by others re: walking style (very positive/favorable, %)	Datta 1998	22	63.6	39.9	IP	≥ 7	**86.3**‡	0‡	NR
Confidence									
Outcomes Instrument: Domain									
50-question survey: confidence and security (mean ± SD)	Berry 2009	368	78.5	54.7	C-Leg	6-9	**39.8 ± 9.7**	27.1 ± 7.9	< 0.0001
Individual Questions									
Confidence while walking (mean; VAS, 0–100)	Hafner 2009	17	76.5	49.1	C-Leg	12	**84.2**†	71.4†	0.001
Activities of daily living									
Outcomes Instrument: Domain									
EQ-5D:	Gerzeli 2009	100	88.0	45.4	C-Leg	12			
Usual activities (%)									
No problems performing activities							**64**	44	ns
Self-care (%)									
No problems washing/dressing							**82**	66	ns
Anxiety/depression (%)									
None at all anxious/depressed							**78**	60	ns
Comfort/fit									
PEQ (mean)									
Appearance	Hafner 2009	17	76.5	49.1	C-Leg	12	76.0†	74.0†	ns
	Kaufman 2008	15	80.0	42.0	C-Leg	9	**69**	60	.02
Sounds	Hafner 2009	17	76.5	49.1	C-Leg	12	74.8*	63.3*	ns
	Kaufman 2008	15	80.0	42.0	C-Leg	9	**70**	56	.02
50-question survey: Socket fit and comfort (mean ± SD)	Berry 2009	368	78.5	54.7	C-Leg	6-9	**21.6 ± 5.2**	17.0 ± 5.3	< .0001

EQ-5D: European Quality of Life-5 Dimensions; IP: Intelligent Prosthesis; MCP: microprocessor-controlled prosthesis; MCS: Mental Component Score; n/a: not applicable; NMCP: non-microprocessor-controlled prosthesis; NR: not reported; ns: not statistically significant; PCS: Physical Component Score; PEQ: Prosthesis Evaluation Questionnaire; SF-36: Short Form-36 questionnaire; SF-6D: Short Form-6 Dimensions.

***Bold type** indicates more favorable results of compared treatment group.

†Mean scores for the entire population (MFCL 2 + MFCL 3) were calculated using weighted means.

‡3/22 (13.6%) reported no comments from others.

Preference. The Appearance and Sounds domains of the PEQ were reported by two studies. [6, 7] Both studies indicated higher scores on both domains for MCP than for NMCP users. The questionnaire developed by Berry (2009) indicated improved scores on the "socket fit and comfort" category.[137]Several studies reported measure of subjective preference or actual prosthesis choice. All measures of C-Leg and IP knees suggest patient preference for MCP knees[6, 8, 138, 141] The study on the Adaptive knee prosthesis were more mixed.[142]

Table 16: KQ2c: patient preferences

Measure/outcome	Study	N	% male	Mean age (years)	MCP Model	Follow-up (months)	Results*		
							MCP	NMCP	*P*-value
Prosthesis preference									
% patients	Kahle 2008	19	NR	51.0	C-Leg	7	**73.7**	26.3	NR
	Datta 1998	22	63.6	39.9	IP	≥ 7	**95.5**	5.0	NR
Higher score (mean) = preference for MCP	Kirker1996	14	83.3	36.5	IP	NR	86	n/a	< .001
Overall rating improved/much improved (%)	Datta 1998	22	63.6	39.9	IP	≥ 7	**100**	0	NR
Use of NMCP since getting MCP (% yes)	Datta 1998	22	63.6	39.9	IP	≥ 7	27.3	n/a	
Use of MCP 6 months post-fitting (% yes)‡	Jepson 2008	5	NR	41.2	Adaptive	6	40.0	n/a	NR
Would revert back to NMCP (% no)‡							60.0	n/a	NR
Opinion about weight of leg (light/average, %)‡							**40.0§**	20.0§	NR
Comfort (comfortable, %)‡							0**	**20.0****	NR

IP: Intelligent Prosthesis; MCP: microprocessor-controlled prosthesis; n/a: not applicable; NMCP: non-microprocessor-controlled prosthesis; NR: not reported.
***Bold type** indicates more favorable results.
†2/17 had no preference.
‡Description of how the questionnaire was administered and scored was not in the article. This is our best interpretation of the scores given the lack of specific information regarding scoring.
§2/5 (40.0%) reported no change in weight of leg.
**2/5 (40.0%) reported no change in comfort and 2/5 (40.0%) reported less comfort with NMCP.

4.6.4 Summary

*KQ2a. 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*

*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*

*KQ2c. 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** as measured by the EQ-5D 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 suggests 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 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*

4.7 KQ3. Safety/adverse events

KQ3. What is the evidence about the safety of microprocessor-controlled lower limb prostheses? Including consideration of adverse events type and frequency (mortality, other major morbidity), equipment failure, and ulcers, falls, etc.

Controlled settings

Evidence of the safety provided by MCPs is limited. Adverse events such as falls or skin problems occur with typical use of any prosthesis.[23, 38, 111] Two studies of MCPs that included safety outcomes collected in a controlled environment were identified.

Blumentritt et al.[155] described a pilot study of three participants asked to wear three different prosthetic knees, including two NMCPs (Otto Bock 3C1 and 3R80) and one MCP (Otto Bock C-Leg). Participants had previously worn each prosthetic knee and were provided approximately 30 minutes to accommodate to each test prostheses. Whole body forces and motions (kinetics and kinematics) were collected as participants randomly performed five different types of activities: (1) level walking, (2) stopping, (3) sidestepping to the prosthetic side, (4) stepping on an obstacle, and (5) interrupted swing (tripping). Results of this study suggest that stopping, sidestepping, stepping on an obstacle, and interrupted swing activities may put a NMCP user at risk for stumbles or falls. These conditions often caused the NMCP to enter swing mode, which allowed the knee to flex rather than provide the stability need for the user to bear weight and regain their balance. Conversely, the MCP was maintained stability in each situation and allow users to immediately weight bear on the prosthesis. These data suggest that MCPs with microprocessor control of a hydraulic stance phase control system may resist unwanted transitions into swing phase and prevent falls and/or fall-related injuries under these conditions.

Bellmann and colleagues[151] also compared the safety of four MCPs (Otto Bock C-Leg, Nabtesco Hybrid, Össur Rheo, Endolite Adaptive2) using the protocol described by Blumentritt.[155] These MCPs included prosthetic knees with different types of microprocessor-based control systems (e.g., pneumatic, hydraulic, or magnetorheological of the swing and/or stance control systems). Similarly, results showed that participants wearing MCPs with microprocessor control of a hydraulic stance phase control system (Otto Bock C-Leg and Nabtesco Hybrid knee) experienced no problems in the stopping, sidestepping, or obstacle activities. Participants (n=9) wearing a MCP with microprocessor control of a magnetorheological (Össur Rheo) stance phase control system required compensatory motions to avoid falling. Participants wearing a MCP with microprocessor control of a hydraulic/pneumatic (Endolite Adaptive2) stance phase control system experienced inadvertent

knee joint collapse in stopping and sidestepping activities. Results of the interrupted swing tests showed that MCPs were resistant to stumbles, but to varying degrees. The C-Leg and Rheo knees appeared most resistant to swing interruptions at shallow flexion angles; the C-Leg and Hybrid knee seemed most resistant to interruptions at greater angles. The results of this study indicate that MCP with microprocessor control of a hydraulic stance phase control system may offer greater safety to users than other types of MCPs.

Uncontrolled settings (Table 17)

Mortality/morbidity. None of the articles in this review reported evidence of mortality or any other major morbidity as a result of MCP use.

Equipment characteristics. Very few studies reported any measures of mechanical performance of MCPs. Datta et al[138] found that the majority of MCP users found the device to be mechanically reliable. The economic evaluation by Brodtkorb included estimates of "problems per year" with MCPs and NMCPs, estimating that MCPs would have fewer problems/year (2.25 vs 0.24) and that duration of problems was similar.[145]

Comfort and fit. The Residual Limb domain of the PEQ includes patient assessment of sweat, odor, rash, ingrown hairs/pimples, and blisters/sores. The two studies reporting results on this domain had overall mixed results, though in both studies differences between groups were relatively small.[6, 7] The Berry study (2009)[137] reported highly statistically significantly better scores in the MCP group for the "safety/negative attributes" (including falls and buckling) and "adverse effects" (including socket temperature and pressure, rash, residual limb effects, muscle fatigue/cramping, phantom limb, low back and hip pain) domains.

Stumbles and falls. Hafner and colleagues developed questions on stumbles and falls as an addendum to the PEQ.[6, 146] In the 2009 study, MCP use is associated with fewer stumbles, semi-controlled and uncontrolled falls, and less frequent stumbles, as well as improved frustration and embarrassment with falling. Kahle also suggested that stumbles and falls were less common with MCP use.[8] Jepson found more mixed results;[142] this study was on a different MCP (Adaptive) than the other two studies (Table 17).

4.7.1 Summary:

Evidence from two moderate-quality and one low-quality studies suggests that MCP use is associated with equivalent or improved ***stumbles or falls*** *compared to NMCP use in real-life settings. Strength of evidence: LOW*

Evidence from one moderate-quality and one low-quality studies suggests that MCPs are associated with fewer negative ***effects on residual limbs*** *compared to NMCPs in real-life settings. Strength of evidence: VERY LOW*

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*

Morbidity/mortality: INSUFFICIENT evidence to evaluate.

Table 17: KQ3 Safety, adverse events (uncontrolled settings)

	Study	N	% male	Mean age (years)	MCP Model	Follow-up (months)	Results*		
							MCP	NMCP	P-value
SAFETY/ADVERSE EVENTS									
Outcomes Instrument: Domain									
PEQ: Residual limb (mean)	Hafner 2009	17	76.5	49.1	C-Leg	12	79.5†	81.2†	ns
	Kaufman 2008	15	80.0	42.0	C-Leg	9	**69**	65	.02
50-question survey (mean ± SD)	Berry 2009	368	78.5	54.7	C-Leg	6-9			
Negative attributes/safety							**33.0 ± 7.0**	25.2 ± 6.8	< .0001
Physical effects of prosthesis							**33.5 ± 7.0**	30.8 ± 7.3	< .0001
EQ-5D pain =”no pain” (%)	Gerzeli 2009	100	88.0	45.4	C-Leg	12	**16**	14	ns
Individual Questions									
Stumbles (frequency)	Hafner 2009	17	76.5	49.1	C-Leg	12	**82.2**†	66.8†	
Stumbles (number)							**3.2**†	5.7†	
Semi-controlled falls(frequency)							**93.7**†	84.9†	
Semi-controlled falls (number)							**0.7**†	2.3†	
Uncontrolled falls (frequency)							**97.9**†	93.4†	
Uncontrolled falls (number)							**0.2**†	0.5†	
Frustration with falling (mean; VAS, 0–100)							**94.7**†	78.3†	
Embarrassment with falling (mean; VAS, 0–100)							**88.7**†	84.8†	
Stumbles (number last 60 days)	Kahle 2008	19	NR	51.0	C-Leg	7	**3 ± 4**	7 ± 6	.006
Falls (number last 60 days)							**1 ± 2**	3 ± 3	.03
Falls in last 8 weeks (no.)‡	Jepson 2008	5	NR	41.2	Adaptive	6	**0**	3	NR
Stumble while walking (often/sometimes, %)‡							**20.0**	40.0	NR
Fall because knee has given way‡							40.0	**0**	NR
EQUIPMENT									
Individual Questions									
Mechanically reliable (%)	Datta 1998	22	63.6	39.9	IP	≥ 7	**63.6§**	5.0§	NR
Problems per year	Brodtkorb 2008	34	58.8	41.0	C-Leg	12	**0.24**	2.25	NR
Duration of problem							0.16	0.15	NR
Survival time of prosthesis (year ± standard error)							NR	2.0 ± 0.18	n/a

EQ-5D: European Quality of Life-5 Dimensions; IP: Intelligent Prosthesis; MCP: microprocessor-controlled prosthesis; n/a: not applicable; NMCP: non-microprocessor-controlled prosthesis; NR: not reported; ns: not statistically significant; PEQ: Prosthesis Evaluation Questionnaire.

****Bold type indicates more favorable results**

†Mean scores for the entire population (MFCL 2 + MFCL 3) were calculated using weighted means.

‡Description of how the questionnaire was administered and scored was not in the article. This is our best interpretation of the scores given the lack of specific information regarding scoring.

§7/22 (31.8%) reported no difference.

4.8 KQ4. Differential efficacy/safety in sub-populations

KQ4. What is the evidence that microprocessor-controlled lower limb prostheses has differential efficacy or safety issues in sub populations?

Controlled settings

In general, controlled-setting study results were presented in aggregate (data in the MCP group or condition were averaged and compared to averaged data in the NMCP group or condition). Presentation of complete individual or sub-group data were rarely included in the reviewed studies, thereby restricting assessments of differential efficacy or safety. In most cases, participant-level demographic, physical, medical, psychological, psychosocial, and/or financial data was provided, but individual outcomes were absent.[146, 149-152] Conversely, two studies presented individualized outcomes but did not include the participant-level information needed to assess differential efficacy.[142, 147] Others presented neither the individual information nor the participant-level outcome data necessary to assess differential efficacy[7, 30, 138, 139, 156, 167]

Hafner and Smith[6] presented a subgroup analysis of study participants' function and safety outcomes by Medicare Functional Classification Level (MFCL). Study participants classified as MFCL-2 (n=8) or MFCL-3 (n=9) were evaluated in both non-standardized NMCPs (various designs) and a standardized MCP (Otto Bock C-Leg) using a in a non-randomized crossover study with repetition (six time points). The MFCL subgroups were deemed comparable at baseline. Age, time since amputation, general health, self-reported well being, accommodation time, number of required physical therapy visits, and number of required prosthetic adjustments were not significantly different. The MFCL-3 group presented with a significantly higher Amputee Mobility Predictor (AMP)[195] score, indicating greater strength and balance than the MFCL-2 group. In functional tests, all participants showed increases in performance (when using the MCP compared to the NMCP) when walking down stairs, walking down hills, walking across an obstacle course, and walking while distracted. MFCL-2 participants showed greater improvements in stair mobility, hill mobility, obstacle course speed, and distracted walking speed than did those classified as MFCL-3.

Assessment of participants' functional level upon conclusion of the 2-year study showed that four MFCL-2 participants and three MFCL-3 participants were re-classified one level higher; one MFCL-2 and one MFCL-3 participant were re-classified one level lower. These results suggest that persons with low-to-moderate functional ability may derive similar benefits when using a MCP to those of moderate-to-high functional ability. In some performance tasks, such as stair and hill descent or walking over uneven terrain or while distracted, lower activity persons may benefit more from use of the MCP than do higher activity users. These data also suggest that MCPs have the potential to improve users' functional level after an extended period of use.

Uncontrolled settings (Table 18)

There was limited analysis and/or discussion of subgroups that might have differential outcomes of MCP use in uncontrolled settings. A summary of our findings on differential performance of MCPs in potential sub-populations:

Gender: No evidence located. The majority of participants in all studies were male.

Age: No evidence located.

Psychological or psychosocial morbidities: No evidence located.

Provider type, setting, or other provider characteristics: No evidence located.

Payor/beneficiary type: No evidence located.

Baseline functional status: Two studies reported findings supporting that of baseline function may be associated with differential effectiveness of MCPs. In Hafner et al 2009, nonrandomized crossover trial in 21 unilateral transfemoral amputees; 17 of whom completed the trial (also reported above in Hafner 2007), the authors conducted a separate analysis of function and safety between people at Medicare Functional Classification Levels (MFCL) 2 and 3.[6] Seventeen (81.0%) of the participants completed the trial over a follow-up period of 12 months. Males comprised 75.0% and 77.8% of the groups, respectively, and mean ages were 57.1 years and 41.9 years. Trauma was the primary cause of amputation for both groups (62.5% and 55.6%, respectively) and mean time since amputation was 17.0 years for the MFCL-2 group and 18.2 years for MFCL-3. All participants began the study in the NMCP and after 2 months normal wear were transitioned into the MCP. Participants were allowed to accommodate to the MCP on an individual basis and were given as much time as needed to demonstrate functional proficiency. Functional outcomes were assessed using the Hill Assessment Index (HAI) score, hill self-selected walking speed, Stair Assessment Index (SAI) score, obstacle course speed, attentional demand speed, and attentional demand accuracy. All mean scores while participants wore the MCP were improved compared to the NMCP for both MFCL groups.[146]

Table 18: KQ4 subgroups (uncontrolled settings)

Measure/outcome	Male	Mean age (years)	MCP	Follow-up (mo.)	Results		
					MCP	NMCP	*P*-value
Hafner 2009: Medicare functional level 2 (MFCL)* (N=8)	6/8	49.1	C-Leg	12			
PEQ (mean ± SD)							
Ambulation					**72.7 ± 12.3**	67.9 ± 11.2	ns
Appearance					**77.6 ± 14.7**	76.1 ± 17.7	ns
Frustration					**71.6 ± 15.8**	71.0 ± 15.7	ns
Perceived Response					**95.1 ± 4.7**	92.0 ± 9.0	ns
Residual Limb					**79.5 ± 13.1**	80.9 ± 11.7	ns
Social Burden					**88.6 ± 13.2**	87.2 ± 14.9	ns
Sounds					**68.9 ± 21.6**	65.6 ± 26.6	ns
Utility					**72.7 ± 14.5**	71.9 ± 17.5	ns
Well-being					**82.8 ± 7.7**	77.7 ± 12.8	ns
Mental energy expenditure					**60.1±9.6**	51.1±23.6	ns
Stumbling (frequency)					**85.6±9.1**	74.0±14.7	0.05
Stumbles (number)					**2.7±2.2**	4.0±2.7	ns
Semi-controlled fall (frequency)					**93.1±6.5**	83.8±16.8	ns
Semi-controlled falls (number)					**0.6±0.3**	1.6±1.5	ns
Uncontrolled fall (frequency)					**98.1±1.9**	93.9±3.3	0.01
Uncontrolled falls (number)					**0.0±0.1**	0.5±0.5	0.01
Confidence while walking					**86.1±4.3**	76.2±12.5	ns
Difficulty multitasking while walking					**85.8±7.0**	70.8±18.9	0.04
Frustration with falling					**94.5±6.3**	76.6±21.9	ns (0.06)
Embarrassment with falling					**82.9±14.3**	78.0±20.7	ns
Difficulty with concentration					**82.3±10.0**	74.1±25.0	ns
Seelen 2009: First time prosthesis users (N=11)	**NR**	**NR**	**C-Leg**	**12**			
SF-36 (mean ± SD)							
Physical functioning					**84.0 ± 11.4**	65.0 ± 27.2	ns
Social functioning					**82.0 ± 40.2**	73.0 ± 32.0	ns
Role limitation (physical)					**65.0 ± 28.5**	54.2 ± 36.8	ns
Role limitations (emotional)					**100.0 ± 0**	66.7 ± 42.2	0.041
Mental health					**93.6 ± 8.3**	68.7 ± 18.1	0.007
Vitality					**83.0 ± 17.2**	60.8 ± 20.1	0.049
Bodily pain					**83.0 ± 21.7**	67.8 ± 25.6	ns
General health					**72.0 ± 22.5**	57.5 ± 30.9	ns

Health transition/ improvement	**55.0 ± 20.9**	29.2 ± 29.2	ns

Bold type indicates more favorable results
MCP: microprocessor-controlled prosthesis; NMCP: non-microprocessor-controlled prosthesis; NR: not reported; ns: not statistically significant; PEQ: Prosthesis Evaluation Questionnaire.
*MFCL-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.

Analysis of the lower-function MFCL 2 group alone (n=8) showed that use of MCP knee was associated with improved PEQ scores of at least 5% on the satisfaction, ambulation, sounds, and well-being domains, though these were not statistically significant. Self-assessed measures (PEQ-A) of mental energy expenditure, confidence while walking, multitasking while walking, and difficulty with concentration improved from 10% to 21% in MFCL-2 individuals; only the multitasking domain achieved statistical significance. People with MFCL-2 classification also reported improved falls and stumbles, frustration and embarrassment with falls; stumble frequency and uncontrolled fall frequency (very low for both prosthesis types) achieved statistical significance; frustration with falls approached significance at p=0.06. Analysis of the higher-function MFCL-3 group showed results of similar direction as the MFCL-2 group but of higher magnitude HAFNER 2009 (Table 32 in Appendix).[6] These results are difficult to interpret since tests of interaction were not performed. However, the data from this single study suggests that patients of both MFCL-2 and MFCL-3 may benefit from a MCP knee, though the benefits appear greater in people with MFCL-3.

First time prosthesis user. One study provided secondary analysis suggesting differential effectiveness of MCPs according to whether it is the patient's first use of a prosthesis. Seelen (2009)[144] reported post-hoc subgroup analysis of SF-36 scores for people who were wearing their "first prosthesis" (n=11). Compared to the total group (n=26), who saw significant improvements in all domains of the SF-36 for MCP compared to NMCP, first users did not experience gains of nearly the same magnitude, though there were mean improvements in all subdomains. Role limitations (emotional), mental health, and vitality subdomains all achieved statistical significance. These data are of limited usefulness and are perhaps not surprising given the effort required to learn how to use any prosthetic limb for the first time, but lend support to the idea that even first-time users of prostheses can achieve quality of life benefits from MCP knees.

4.8.1 Summary

KQ4. Evidence from one moderate-quality study suggests that benefits in energy, ambulation, safety and quality of life are greater in people at higher baseline function (MFCL-3) but people at lower function (MFCL-2) may also experience some benefits. 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

4.9 KQ5: Economic considerations

KQ5. What is the evidence of cost implications and cost-effectiveness of microprocessor-controlled lower limb prostheses? Including consideration of:

a. Costs (direct and indirect) and cost effectiveness

b. Short term and long term

c. Ongoing maintenance and replacements for the prosthetic

Controlled settings
No studies of cost implications or cost effectiveness of MCP use in controlled settings were identified in this review.

Uncontrolled settings (Table 19)
Economic evaluations identify and compare appropriate alternatives, their incremental impact on health outcomes, and their incremental costs. There are several types of economic evaluation. Cost minimization studies consider the cost differences between alternatives of equal effectiveness. Cost benefit studies consider both costs and benefits in monetary terms. Cost effectiveness studies consider differences in costs and differences in effectiveness, but effectiveness is measured variably between studies. Cost utility studies consider differences in costs and outcomes for quality-adjusted survival, most often using the quality adjusted life year (QALY). Cost utility studies have the advantage of providing an incremental cost effectiveness ratio (ICER) expressed as 'cost per quality adjusted life year' (cost per QALY) that eases comparison across multiple studies. Studies that report only costs or do not compare alternatives are not considered full economic evaluations and are not included in this report.

Brodtkorb (2008) conducted a cost utility analysis comparing C-Leg to NMCP in people who had recently switched from NMCP to C-Leg. The study took a Swedish health care system perspective and used a Markov model to simulate costs and outcomes for 8 years post-C-leg fitting, set to coincide with the stated durability of the C-Leg. Parameters were derived from interviews with C-Leg patients, prosthetists, or prosthesis manufacturers; clinical judgment is considered one of the least reliable data sources. The authors found the C-Leg to be both more effective and more costly than NMCP, with an incremental cost-utility ratio of €3218 per QALY.[145]

We appraised this study to be of low quality (QHES of 58/100). Strengths were the inclusion of societal-level costs, including patient/family productivity costs, and the longer-term time horizon of 8 years. A major limitation was the method of outcome measurement, which consisted of patient completion of the EQ-5D with use of an MCP compared to their imagined answers to the same questions "if they had not been given" the MCP. This method introduces high potential for expectation bias, and this variable proved to most significantly alter the cost-effectiveness ratio, though the authors did conduct a sensitivity analysis with utility equal at 0.83, and the ICER was still under €30,000/QALY. As with the other two studies, the generalizability of these cost and cost-effectiveness estimates to a US or Washington State setting is unknown.

Gerzeli et al (2009)[143] conducted a cost utility analysis of the C-Leg compared to mechanical prostheses in a population of users of each technology selected from the Italian Workers Compensation Authority records. They calculated the incremental cost utility over five years of the C-leg from two different perspectives: health care, reflecting a choice by a health care system, and societal, reflecting health care costs as well as lost productivity, informal caregiver needs. Quality of life outcomes were derived using results from the EQ-5D. From the health care perspective, the authors found an incremental cost utility ratio of €35,971 per QALY; from the social perspective both costs and outcomes were very similar. The results of this study provide support for the idea that MCP knees are of higher costs initially but are associated with decreased costs and improved quality of life over time.

We judged this to be a moderate quality study (QHES 77/100). Strengths included the random selection of patients from a database and use of person-level data, the modeling of costs and effects to 8 years, and the inclusion of societal costs. Limitations included possible selection bias as there were some baseline demographic differences between MCP vs NMCP users and

only people with traumatic amputations were included in the study. The generalizability of these cost and cost-effectiveness estimates to a US or Washington State setting is unknown.

Seelen et al (2009)[144] conducted a cost consequences analysis of intervention, health care, patient/family, and productivity costs between a group of C-leg users and a group of users of various NMCPs who were seen at a rehabilitation center in the Netherlands. They used a 12-month time horizon and a societal perspective. The results suggest that the total costs for both group were similar (€39,350 vs €46,086, p=0.332) and the utility score was higher in the C-Leg group (0.687 vs 0.584, p=0.005).

We judged this to be a low-quality study (QHES 54/100). Strengths were in the use of person-level data and the societal perspective. Limitations include the short term time horizon of one year, which limits any analysis of longer-term outcomes. The measurement of outcome with the SF-36 is problematic. First, it was assessed early in rehabilitation, which may itself be problematic and subject to change over time. Second, it was assessed retrospectively so has high potential for recall bias. Realizing this potential bias the authors also retrieved information on function from medical records, but it is not stated how or if these data were included in the results. As with the other two studies, the generalizability of these cost and cost-effectiveness estimates to a US or Washington State setting is unknown.

KQ5a. Costs (direct and indirect) and cost effectiveness.

We found no evidence on cost or cost-effectiveness that was collected in a US or Washington State setting, and how economic studies done in Europe would transfer to a US setting is unknown. However, in the absence of US data, some the trends of results from the three included studies may be noted.

Costs. All studies found the costs of the actual prostheses and their fitting to be more expensive for MCPs, from 1.3 to 5 times more than NMCPs. Four analyses of costs were presented in three articles; two from a healthcare perspective[143, 145] and two from a societal perspective, including patient/family, caregivers, and productivity[143, 144]. The two analyses that used a healthcare perspective found that MCPs and their fitting result in higher costs (MCP 44% and 200% higher than NMCP), while the two that used a societal perspective found MCPs to be associated with lower costs than NMCPs (1% and 15% lower than NMCPs), reflecting in both cases increased non-healthcare costs associated with NMCP use. In one, rehabilitation, patient/family costs, and productivity costs were all significantly higher for NMCPs, which balanced against the increased cost of the MCP.[144] In the other, productivity losses with NMCPs countered the increased cost of the MCP.[143] These data provide some support for the idea that the initial increased cost of MCPs may be tempered over time and when indirect/societal costs are included.

Cost effectiveness. All analyses found that MCP use was associated with higher quality of life than NMCPs on generic quality of life measures. Of the two analyses of cost-effectiveness using a health care perspective, both found that the cost per quality-adjusted life year was less than €40,000 often considered an acceptable threshold of cost effectiveness [143, 145]. Of the two analyses from a societal perspective, one found that MCP was both less expensive and associated with improved outcomes (MCP "dominated" NMCP)[143] The other also found that MCP was less expensive and associated with improved outcomes.[144] None of the sensitivity analyses, though of varying quality, suggested anything that would significantly alter the direction of these results.

KQ5b. Short term and long term. The longest time horizon assessed was 8 years. The longest term of real-data collected (not modeled) was 1 year. As such all the analyses reported

here should be considered "short term". There is insufficient data to evaluate the economic implications of MCP use over the long term.

KQ5c. Ongoing maintenance and replacements for the prosthesis. Gerzeli estimated the maintenance and repair of MCP to be slightly less than for NMCP (€2597 vs €2230, difference €367).[143] Brodtkorb included costs of yearly maintenance of MCP based on the manufacturer's warranty at €125 per year for the first three years in prosthetists time and an additional €1417-€2278 per year for years 4-8 for additional optional per-year warranty purchase.[145] Seelen et al did not report costs of maintenance, repair, or replacement.[144]

Table 19: KQ5 economic considerations

	Costs per patient (±SD)			Effectiveness (QALY)			Incremental cost effectiveness ratio (ICER)
	MCP	NMCP	Difference (95% CI)	MCP	NMCP	Difference	
Brodtkorb 2008 (Sweden, health care perspective)							
Prosthesis and fitting	€17,003	€6635	€10,368				
Total	€25,146	€17,488	€7657 (NR)	5.98	3.60	2.38	€3,218/QALY
Gerzeli 2009 (Italy)							
Prosthesis and fitting	€18,616	€3600	€15,016	3.55	3.13	0.42 (0.12 to 0.73)	
Total (**health care perspective**)	€22,744	€7,449	€15295 (€13321 to €17269)				€35,971/QALY
Total (**societal perspective**)	€66,669	€66,927	-€258 (NR)				MCP dominates NMCP**
Seelen 2009 (Netherlands, societal perspective)							
Prosthesis and fitting	€29,044 ± 13,734	€22,656± 16,325	€6388	0.687 ± 0.082*	0.584 ± 0.086	0.103	NR
Total	€39,350 ± 29,064	€46,086 ± 32,218	-€ 6,736 (NR)				

*SF-6D utility score (0-1, 1 indicates perfect health)
**MCP is both lower cost and improved outcomes

4.9.1 Summary

*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 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*

*There is insufficient evidence to evaluate the **long-term costs** (beyond eight years) of MCP use.*

*There is insufficient evidence to evaluate the costs or cost-effectiveness of MCP use in a **United States setting.***

5 Summary of evidence by key question

5.1 Microprocessor-controlled prosthetic feet

There is insufficient evidence to evaluate efficacy, effectiveness, safety, subgroups, or economic considerations for microprocessor-controlled prosthetic feet.

5.2 Microprocessor-controlled prosthetic knees

The evidence on MCP knee use in real-world settings consistently suggests improvement or equivalence associated with MCP knee use compared to NMCPs. No studies suggested that NMCP knees were associated with clearly improved outcomes. The strength of evidence for all conclusions is either low or very low, most often reflecting the quality of study designs and the quantity of studies available rather than the consistency of findings (Table 20).

Future research into the development of valid, reliable, and patient-centered methods for assessing the performance of microprocessor-controlled prostheses in real-world settings and studies that can prospectively assess the effect of MCPs on health and function over time will provide valuable evidence. Also, studies that include participants of more broadly defined population demographics and function and long-term studies of the costs and outcomes of MCP use from a societal perspective will enhance understanding the performance of microprocessor-controlled prostheses.

Table 20: Summary of evidence by key question

Key question	Evidence	Strength of evidence	Quality	Quantity	Consistency
KQ1. Outcomes	The majority of the outcomes assessed of community use of MCPs are single item questions. Of six patient- reported outcome measures used in trials assessing MCP use, three are generic instruments and three condition-specific. Two instruments demonstrate some evidence of reliability and/or validity. Three scales of the Prosthesis Evaluation Questionnaire (PEQ) demonstrated adequate content, criterion and construct validity and five subscales demonstrated adequate test-retest reliability. There were no validity data available for the 50-Question Survey, and its reliability testing was inadequate. Clinically meaningful improvement has not been established for any of the condition-specific measures used.	N/A	na	na	na
KQ2 a. Energy/ cognitive requirements of ambulation	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.	LOW	-	+	+
KQ2b. Impact on ambulation	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.	LOW	-	+	+
KQ2c. Patient perceptions:					
Quality of life	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.	LOW	-	+	+
Activities of daily living	Evidence from one moderate quality study and two low quality studies consistently suggests that MCP use is associated with improved activities of daily living as measured by the EQ-5D compared to NMCP in real-life settings.	LOW	-	+	+
Confidence	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.	VERY LOW	-	-	-
Comfort/fit	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	VERY LOW	-	-	+
Preference	Evidence from two moderate-quality and two low-quality studies consistently suggests that MCPs are preferred by users compared to NMCPs in real-life settings.	LOW	-	+	+

Key question	Evidence	Strength of evidence	Quality	Quantity	Consistency
Perceptions by others	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	VERY LOW	-	-	+
KQ3. Safety/adverse events					
Stumbles/falls	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.	LOW	-	+	+
Effects on residual limb	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.	VERY LOW	-	-	-
Equipment failure	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.	VERY LOW	-	-	+
KQ4 subgroups					
Baseline function	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.	VERY LOW	-	-	-
First time prosthesis users	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.	VERY LOW	-	-	-
Gender, age, psychological or psychosocial morbidity, provider characteristics, payor/beneficiary type	Insufficient evidence to evaluate.	INSUFFICIENT			
KQ5. Economics					
Prosthesis costs	Evidence from three low-quality studies suggests that the cost of MCP purchase and fitting is higher than for NMCP.	LOW	-	+	+
Total costs (health care)	Evidence from three low-quality studies suggests that the total health care costs of MCP use are higher than for NMCP use.	VERY LOW	-	-	+

Key question	Evidence	Strength of evidence	Quality	Quantity	Consistency
Total costs (societal)	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 associated with NMCP use.	LOW	-	+	+
Cost-effectiveness	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.	VERY LOW	-	-	+
Long-term costs	Insufficient evidence to evaluate	INSUFFICIENT			
Costs or cost-effectiveness in US setting	Insufficient evidence to evaluate	INSUFFICIENT			

na:not applicable
Quality: At least 80% of the studies are LoE I or II
Quantity: There are at least three studies which are adequately powered to answer the study question
Consistency: Study results would lead to a similar conclusion (similar values, in the same direction) in at least 70% of the studies

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APPENDIX A. SEARCH STRATEGIES

Below is the search strategy used to search PubMed. Parallel strategies and/or keyword searches were used to search other electronic databases listed below.

Table 21: Search strategy: PubMed

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*
	#06	Search "Artificial Limbs"[Mesh]
B. Prosthesis	#07	Search #4 or #6
	#08	Search microprocessor
	#09	Search rheo leg
	#10	Search intelligent prosthesis
	#13	Search c-leg
C. Microprocessor-controlled	#15	Search #8 or #9 or #10 or #13
Limits	#20	Search Limits: only items with abstracts, Humans, English
A and B	#21	Search #3 and #7 and #20 Limits: only items with abstracts, Humans, English
	#17	Search #3 and #15
A and C	#22	Search #3 and #15 and #20 Limits: only items with abstracts, Humans, English
	#18	Search #15 and #7
B and C	#24	Search #15 and #7 and #20 Limits: only items with abstracts, Humans, English
	#19	Search #15 and #7 and #3
A and B and C	#23	Search #3 and #15 and #7 and #20 Limits: only items with abstracts, Humans, English

The following databases have been searched,:

- PubMed (1975 through Jun 1, 2011)
- NIH Reporter
- Agency for Healthcare Research and Quality (AHRQ)
- Cumulative Index to Nursing and Allied Health (CINAHL)
- Cochrane Library (through June 2011)
- Database of Reviews of Effectiveness (Cochrane Library) (through June 2011)
- Informational Network of Agencies for Health Technology Assessment (INAHTA)
- NHS Economic Evaluation Database (Cochrane Library through June 2011)
- HSTAT (Health Services/Technology Assessment Text)
- Grey Literature Report (New York Academy of Medicine)
- Canadian Agency for Drugs and Technologies in Health
- Centers for Medicare and Medicaid Services (CMS)
- Food and Drug Administration (FDA)
- Google
- Institute for Clinical Systems Improvement (ICSI)

- National Guideline Clearinghouse

APPENDIX B. EXCLUDED ARTICLES

The following articles were excluded at the full text review stage.

Study	Reason for exclusion
Theeven, P., B. Hemmen, et al. (2010). "Feasibility of a new concept for measuring actual functional performance in daily life of transfemoral amputees." J Rehabil Med 42(8): 744-51.	Does not address outcomes of interest
Alimusaj, M., L. Fradet, et al. (2009). "Kinematics and kinetics with an adaptive ankle foot system during stair ambulation of transtibial amputees." Gait Posture 30(3): 356-63.	Powered prosthesis
Fradet, L., M. Alimusaj, et al. (2010). "Biomechanical analysis of ramp ambulation of transtibial amputees with an adaptive ankle foot system." Gait Posture 32(2): 191-8.	Powered prosthesis
Segal, A. D., M. S. Orendurff, et al. (2006). "Kinematic and kinetic comparisons of transfemoral amputee gait using C-Leg and Mauch SNS prosthetic knees." J Rehabil Res Dev 43(7): 857-70.	Does not address outcomes of interest
Wolf, S. I., M. Alimusaj, et al. (2009). "Pressure characteristics at the stump/socket interface in transtibial amputees using an adaptive prosthetic foot." Clin Biomech (Bristol, Avon) 24(10): 860-5	Does not address outcomes of interest

APPENDIX C. DETAILED METHODS

6.1 KQ1: Methods for assessing the validity and reliability of outcomes measures.

Validity: Does the instrument measure what it was intended to measure? We evaluated three aspects of validity:

Content validity evaluates whether the outcomes of interest are comprehensively represented by the questions in the instrument.[162, 163] We gave the studies credit if there was a clear description of each of the following: the aim of the outcome measure, the target population, the concepts being assessed, and the method by which the items were selected. In addition, the population of interest (and either investigators or experts) should have been involved in item selection.

Criterion validity refers to whether the scores relate to a "gold standard" on the same theme. We looked for a correlation with the gold standard of at least 0.70.[162]

Construct validity evaluates whether scores relate to other measures in accordance with specific hypotheses that are theoretically derived. The instrument of interest and another related outcome measure may have convergent (high correlation if they measure similar concepts) or divergent (low correlation if they measure different concepts) validity with one another. Specific hypotheses need to be stated, and 75% or more of the results should be consistent with these hypotheses as tested in at least 50 patients[162, 163]

Reliability: How well do repeated measurements in stable patients (test-retest) yield similar responses? [162, 163]

Internal consistency assesses whether the items in the questionnaire are correlated, in that they evaluate the same concept. Questions should correlate highly with one another and with the overall (sub)scale score. Factor analysis should be performed on a at least 100 patients to determine whether the construct is uni- or multidimensional; Cronbach's alpha should range from 0.70 to 0.95 for each subscale to indicate good internal consistency.

Reproducibility measures whether patients can be differentiated from each other in spite of measurement error (relative measurement error). To be considered reliable, the ICC (intraclass correlation coefficient) or weighted Kappa coefficient should be ≥ 0.70 when measured in at least 50 patients. The Pearson correlation coefficient is not an adequate measurement of reliability, as it does not account for systematic differences.[162, 163]

Responsiveness: Does the instrument detect clinically important changes over time? (the score changes with the status of the patient).[162, 163] One of the following should be demonstrated:

Smallest detectable change (SDC) is less than the minimal important change. The SDC is the smallest intraperson change in score that can be interpreted as "real" change greater than measurement error. Smallest detectable change (SDC) = 1.96 x √2 x SEM (standard error of measurement). Minimally important change (MIC) is "the smallest difference in score in the domain of interest which patients perceive as beneficial and would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient's management". MID may also be written as MCID (minimal clinically important difference) or MIC (minimal important change). MIC should be outside the limits of agreement (LOA), which is the mean change in

scores of repeated measurements ± 1.96 x standard deviation of the changes; RR (responsiveness ratio) > 1.96

AUC (area under the ROC (receiver operating characteristics) curve) ≥ 0.70 of measures whether a questionnaire is able to differentiate between people whose scores have and have not changed, as measured by some other criteria, usually the patient's own perception of change.

Floor or ceiling effects may be present if either the lowest or highest possible score is detected in more than 15% of patients. Floor/ceiling effects are considered absent if none are found in a sample size of 50 patients or more.[162]

MCID (minimal clinically important difference) is reported for the questionnaire based on comparisons with patient-reported evaluation of overall outcome (function).

6.2 KQ2-KQ5: Methods for assessing quality of clinical and economic evidence

Determining level of evidence for individual studies. Each study was rated against pre-set criteria that resulted in an evidence rating (Level of Evidence I, II, III, or IV) and presented in a table. The criteria are listed in the Tables below.

Table 22: Criteria for assessing level of evidence (LoE)

Level	Study design	Criteria
I	Good quality crossover trial	Study design: • Random sequence generation (AB/BA) • Sequence allocation concealed • Intent-to-treat analysis Other methods • Blind or independent assessment for important outcomes • Co-interventions applied equally • F/U rate of 80%+ • Adequate sample size • Duration of acclimation to the intervention considered • Use of paired statistics
II	Moderate quality crossover trial	• No violation of random sequence generation, but violation of one or two of the other criteria for good quality crossover trial or • Violation of random sequence generation, but no more than one violation of the other methods criteria
III	Poor quality crossover trial	• Violation of random sequence generation or • Violation of three or more of the other criteria

For crossover studies, we assessed whether the sequence for the intervention was randomly assigned and whether this sequence was concealed. In crossover trials, a "washout" period is an important internal validity component. However, in this technology where all components of the prosthesis remained the same except for the knee joint, no appreciable carryover from one knee to the next was expected. Rather, it was felt that duration of acclimation to the different knees was more important in the critical appraisal assessing internal validity. Since the studies varied in this accommodation time, we assessed whether or not authors specified a period of accommodation with the test knee.

Table 23: Level of evidence: crossover studies

Methodological principle	Berry 2009	Brodtkorb 2008	Datta 1998	Hafner 2009	Hafner 2007	Jepson 2008	Kahle 2008	Kaufman 2008	Kirker 1996	Klute 2006	Williams 2006
Crossover trial											
Random sequence generation	–	–	–	–	–	–	–	–	–	+	+
Sequence allocation concealed	–	–	–	–	–	–	–	–	–	–	–
Independent or blind assessment	–	–	–	–	–	–	–	–	–	–	–
Complete follow-up of ≥ 80%	–	–	+	+	+	+	+	–	+	–	–
Adequate sample size	+	+	+	+	+	–	+	+	+	–	–
Duration of acclimation considered	+	–	–	+	+	+	+	+	+	+	+
Use of paired statistics	+	–	–	+	+	+	+	+	+	-	-
Evidence class*	III	III	III	II	II	III	II	III	II	III	III

*Level II: MODERATE; Level III: LOW

Table 24: Level of evidence: non-crossover studies

Methodological principle	Gerzeli 2009	Seelen 2009
Study design		
Randomized controlled trial		
Cohort study		
Prospective		
Retrospective		■
Cross-sectional study	■	
Case-series		
Statement of concealed allocation*		
Intent-to-treat*		
Independent or blind assessment	–	–
Complete follow-up of > 80%	+	–
Adequate sample size	+	+
Controlling for possible confounding	-	–
Evidence class**	III	III

*Applies to randomized controlled trials only
**Level III: LOW; Level IV: VERY LOW.

Determining overall strength of evidence (SOE)

Following the assessment of the quality of each individual study included in the report, an overall "strength of evidence" for the relevant question or topic is determined. Methods for determining the overall strength of evidence are variable across the literature and are most applicable to evaluation of therapeutic studies.

SRI's method incorporates the primary domains of quality (LoE), quantity of studies and consistency of results across studies as described by AHRQ.

The following definitions are used by SRI to determine whether or not the body of evidence meets the criteria for each domain:

Table 25 Framework for assessing overall strength of evidence

Domain	Definition/Criterion for clinical studies	Criterion for economic studies
Quality	At least 80% of the studies are LoE I or II	The majority of quality indicators described in the QHES are met AND the methods of patient/claim selection, patient population considerations are consistent with a high quality design
Quantity	There are at least three studies which are adequately powered to answer the study question	There are at least three formal economic evaluations
Consistency	Study results would lead to a similar conclusion (similar values, in the same direction) in at least 70% of the studies	Study results would lead to a similar conclusion (similar values, in the same direction) in at least 70% of the studies

Based on the criteria described above, the possible scenarios that would be encountered are described below. Each scenario is ranked according to the impact that future research is likely to have on both the overall estimates of an effect and the confidence in the estimate. This ranking describes the overall "Strength of Evidence" (SoE) for the body of literature on a specific topic. The method and descriptions of overall strength are adapted from the system described by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group and recommendations made by the Agency for Healthcare Research and Quality (AHRQ).[131-134]

Table 26: Strength of evidence criteria

SoE	Description	Impact of further research	Domain Criterion Met		
			Quality	Quantity	Consistency
1	High	Very unlikely to change confidence in effect estimate	+	+	+
2	Moderate	Likely to have an important impact on confidence in estimate and may change the estimate	+	-	+
			+	+	-
3	Low	Very likely to have an important impact on confidence in estimate and likely to change the estimate	+	-	-
			-	+	+
4	Very Low	Any effect estimate is uncertain	-	+	-
			-	-	+
			-	-	-

Assessment of economic studies. Full formal economic analyses evaluate both costs and clinical outcomes of two or more alternative interventions. The four primary types are cost minimization analysis (CMA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA), and cost-benefit analyses (CBA). Each employs different methodologies, potentially complicating critical appraisal, but some common criteria can be assessed across studies.

No standard, universally accepted method of critical appraisal of economic analyses is currently in use. A number of checklists are available to facilitate critique of such studies. The Quality of Health Economic Studies (QHES) instrument developed by Ofman, et al. embodies the primary components relevant for critical appraisal of economic studies. It also incorporates a weighted scoring process and which was used as one factor to assess included economic studies. This

tool has not yet undergone extensive evaluation for broader use but provides a valuable starting point for critique.

In addition to assessment of criteria in the QHES, we assessed the clinical evidence used in economic articles as described above. Assessment of the overall strength of evidence for formal economic analyses does not appear to be documented in the literature. For this report, we determined overall strength using the definitions of quality, quantity, and consistency listed in Table 25.

Table 27: Quality of health economic studies (QHES) instrument

Questions	Points
1. Was the study objective presented in a clear, specific, and measurable manner?	7
2. Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4
3. Were variable estimates used in the analysis from the best available source (ie, randomized controlled trial - best, expert opinion - worst)?	8
4. If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1
5. Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9
6. Was incremental analysis performed between alternatives for resources and costs?	6
7. Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5
8. Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7
9. Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8
10. Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included?	6
11. Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7
12. Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8
13. Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7
14. Did the author(s) explicitly discuss direction and magnitude of potential biases?	6
15. Were the conclusions/recommendations of the study justified and based on the study results?	8
16. Was there a statement disclosing the source of funding for the study?	3
TOTAL POSSIBLE	100

Chiou 2003[135]

Interpreting cost effectiveness results. The results of cost utility studies are often depicted visually in the form of a cost effectiveness plane (Figure 2). When comparing changes in costs to changes in outcomes between two alternatives, those in the upper right quadrant are associated with increased costs and improved outcomes and results can be reported in terms of a cost-effectiveness ratio. Those results in the upper left and lower right quadrants denote scenarios where the costs and benefits both favor either the intervention (intervention "dominates") or the comparator (intervention "is dominated by" the comparator). Those results in

the lower left indicate results where an intervention has decreased costs but also is less effective.

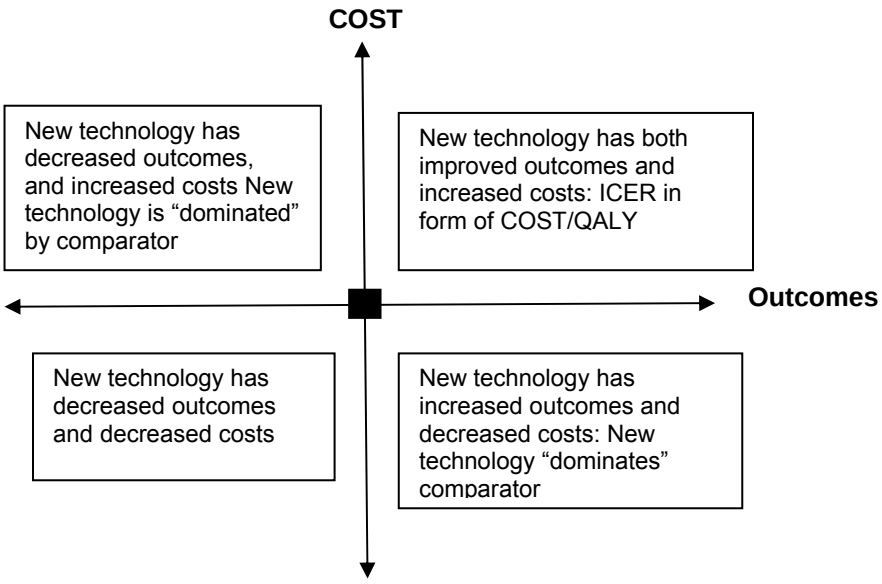

Figure 2: Cost effectiveness plane

APPENDIX D. CLINICAL PEER REVIEWERS

Reviewer	Role/Responsibility	Experience
Joe Czerniecki, MD Interim National Director, VA National Amputation System of Care Associate Director, VA Research Center of Excellence in Limb Loss Prevention and Prosthetic Engineering, Seattle, WA. Professor, Department of Rehabilitation Medicine, University of Washington, Seattle, WA	Consultant/Peer review	Research and clinical practice in post amputation disability; modifiable risk factors that contribute to poor outcome post lower extremity amputation in veterans with peripheral vascular disease and diabetes.
Daniel C. Abrahamson, C.P.O. University of Washington	Consultant/Peer review	Lecturer and certified prosthetist/orthotist with UW Department of Rehabilitation Medicine; expertise in amputation/limb loss, prosthetics and orthotics, rehabilitation medicine
Brian Hafner, PhD Assistant Professor, University of Washington	Co-author	Assessment of performance, function, and quality-of-life in persons with amputation and the associated influence of orthotic and prosthetic intervention on clinical outcomes; development of valid and reliable patient reported outcome measures for users of lower limb prosthetic limbs and the evaluation of outcomes associated with the use of advanced prosthetic knee technologies among individuals with above-knee amputations. Dr. Hafner is also pursuing the development tools and instrumentation suited to measuring outcomes in users' free-living environments.

APPENDIX E. Payer policies

Below is a summary of four publicly available payer policies (as of June 2011).

Table 28: Select payer policies

Payer (year)	Evidence base available*	Policy	Rationale/comments
Centers for Medicare and Medicaid Services (CMS) Medicare Prosthetic Benefit, IOM 100-2, Chapter 15, Sections 120 and 130 [CMS, 2011]	N/A	• Microprocessor-controlled devices are not mentioned in the NCD. • CMS will cover lower limb prostheses to replace all or part of the function of a permanently inoperative or malfunctioning internal body organ. Replacement of prostheses will be covered without regard to continuous use or useful lifetime restrictions.	• N/A
Aetna (2010) *Clinical Policy Bulletin: Lower Limb Prostheses* *Number 0578, 9/17/2010* [Aetna, 2010]	• 3 Technology Assessments • 1 Evidence Review • 4 RCTs • 2 RCT cross-over studies • 1 Comparative study • 2 Case-control studies • 3 Descriptive studies • 1 undefined study type	Microprocessor-controlled leg prosthesis are considered medically necessary for: • otherwise healthy, active community ambulating adults ≥ 18 years of age, • of functional level of 3 or 4, • with a knee disarticulation amputation or trans-femoral amputation from a non-vascular cause, • for whom the prosthesis can be fitted and programmed by a qualified prosthetist. Microprocessor-controlled ankle-foot prosthesis is considered to be experimental and investigational due to inadequate evidence of their effectiveness.	▪ Evidence reviews have identified limitations in current studies of microprocessor-controlled knees. Although some studies focused on functional outcomes, the majority of studies evaluated intermediate outcomes. However, most of these studies showed improvement in outcomes when the microprocessor-controlled knee is compared to a traditional prosthesis. ▪ Standard lower limb prostheses policy is based on Medicare DMERC criteria. ▪ HCPCS codes if selection criteria is met: L5000, L5780, L5785-L5999.

Payer (year)	Evidence base available*	Policy	Rationale/comments
Cigna (2010) *Lower Limb Prosthestic Devices (Including Vacuum-Assisted Socket System and Microprocessor/ Computer-Controlled Lower Limb Prostheses)* *Coverage Policy Number 0194, 8/15/2010* [Cigna, 2010]	• 3 Technology Assessments • 1 Evidence Review • 1 RCT • 1 RCT cross-over study • 3 Comparative/ comparative cross-over studies • 1 Case-control study • 1 undefined study type	Microprocessor-controlled/computer-controlled knee prosthetic devices are considered medically necessary for above-the-knee amputee when ALL of the following criteria are met: • Functional level 3 or 4, *and* • Absence of significant cardiovascular, neuromuscular, or musculoskeletal condition that would be expected to adversely affect the use of the device, *and* • A gait analysis demonstrates the ability to ambulate at a rate faster than baseline using standard prosthetic device with swing and stance control, *and* • The patient requires an ambulatory rate/stance control not achievable with basic lower limb device for use outside the home on a regular basis. Microprocessor-controlled ankle-foot prosthesis is considered to be experimental, investigational, or unproven.	▪ Evidence supporting the use of the microprocessor-controlled knee prosthesis is primarily from small-group case studies and few RCTs. Most patients in these studies were in good health and with no other medical conditions. ▪ Although there is no strong evidence in published, peer-reviewed scientific literature of this prosthesis as being superior to standard devices for performing ADL, there is evidence that supports effective use of this prosthesis for limited populations. ▪ HCPCS codes if selection criteria is met: L5856, L5857, L5858.
Premara Blue Cross (WA and AK) (2010) *Microprocessor-Controlled Prostheses for the Lower Limb* *Number CP.MP.BC.1.01.25,* *4/13/2010* [Premara,2010]	• 1 Technology Assessment • 2 RCTs • 2 RCT cross-over studies • 3 other cross-over studies • 5 Comparative studies • 1 Descriptive study • 1undefined study type	Premara considers a microprocessor-controlled knee medically necessary in amputees when ALL of the following criteria are met: • Demonstrated need for long distance ambulation at variable rates, regular ambulation on uneven terrain, or regular use on stairs, *and* • Physical ability for ambulation at faster than normal walking speed, *and* • Adequate cognitive ability to master use and care requirements for the device. Indications for patient use include the following: • Adequate cardiovascular and pulmonary reserve, strength and balance, and cognitive ability, • Functional level 2 in specific circumstances, • Functional levels 3 or 4, • Hemi-pelvectomy through knee-disarticulation level of amputation, including bilateral lower extremity. A powered knee and microprocessor-controlled or powered foot are investigational.	▪ A microprocessor-controlled knee may provide incremental benefit for some patients. Patients most likely to benefit have a potential and actual need for frequent ambulation at variable pace, on uneven terrain, or on stairs. A high functional level with the device includes having appropriate physical and cognitive ability to use the device. ▪ Published data on this type of prosthesis is limited, with the majority of literature focused on the Intelligent Prosthesis. ▪ HCPCS codes if selection criteria is met: L5856, L5857, L5858.

APPENDIX F. DETAILED STUDY DESIGN

Table 29 Detailed study design: Clinical studies

Study	Participants	Intervention	Outcomes
Berry (2009) (U.S.A) Study design: nonrandomized crossover (A-B design) Total length of follow-up: 9 months Funded by: NR Author declaration of conflict: No conflictss	Total, n = 368 ▪ Type of amputation: TF ▪ % male: 78.5 ▪ Age: 54.7 ± 15.6 (range,15–85) ▪ Weight and height: NR ▪ MFCL: 3 ▪ Reason for amputation: accident (109); trauma (54); tumor (51); vascular (41); infection/gangrene (32); gunshot/combat (22); not noted (18); blood clot (15); congenital (8); medical (8); other (6); surgical (4) ▪ Time since amputation (years): 18.5 (0.2–78.7) ▪ Type of prosthesis at recruitment: variable cadence NMCP knee ▪ Time using prosthesis: variable; < 6 months (9); < 1 year (29); ≥ 1 year (130) ▪ Medical coverage: NR (patients recruited from private clinics) ▪ Patient selection: NR Inclusion: ▪ Unilateral TF amputees ▪ MFCL 3 ▪ Wore a variable cadence NMCP ▪ ≤ 275 lbs. ▪ ≥17in from heel pad to knee center	Intervention ▪ Brand of prosthesis: C-Leg (Otto Bock) ▪ Fitted by certified prosthetist ▪ Time in use on intervention: 6–9 months Comparison Same participants ▪ Brand of prosthesis: NR, variable cadence NMCP ▪ Fitted by certified prosthetist ▪ Time in use (years): 3.5 ± 3.7 (0.1–42) ▪ Crossover to C-Leg	Self-Administered Questionnaire (50 questions) ▪ Assessed 6 dimensions of prosthetic knee rehabilitation: socket fit, confidence/security, gait/maneuverability, prosthesis attributes, physical effects of prosthesis, safety/negative attributes.

Study	Participants	Intervention	Outcomes
	▪ ≥ 2 in from knee center to distal residual limb		
Datta et al, 1998 (United Kingdom) Study design: questionnaire survey Total length of followup: none Funded by: NR Author declarations of conflict: NR	Total n= 22 (14 male, 8 female) ▪ Type of amputation: TF ▪ %male = 64 ▪ Age: 39.9 (range 25-76 yrs) ▪ Weight: NR ▪ Height: NR ▪ MFCL/ general health: no stump problems, otherwise fit, and generally fairly active ▪ Reason for amputation: 16 trauma, 5 malignancy, 1 osteomyelitis ▪ Time since amputation: 19.2 (range: 5-53 yrs) ▪ Type of prosthesis at recruitment: Endolite prosthesis with PSPC (pneumatic swing phase control) ▪ Time using prosthesis: NR ▪ Medical coverage: NR ▪ Patient selection by NR Exclusion criteria: ▪ Age <18	Intervention ▪ Brand of prosthesis: Endolite PSPC ▪ Fitted by prosthetist ▪ Time in use on intervention: 8-10 weeks ▪ Crossover to: microprocessor-controlled intelligent knee joints (IP) Comparison Same participants ▪ Brand of prosthesis: IP ▪ Brief description of function: microprocessor (provides varying damping action for flexion/extension of the knee joint depending on gait speed) ▪ Fitted by prosthetist ▪ Time in use: 17.4 (7-41) months	Patient-reported*: ▪ Walking at different speeds ▪ Walking distance ▪ Ascending stairs ▪ Descending stairs ▪ Walking on slopes and hills ▪ Walking on rough / uneven ground ▪ Gait pattern ▪ Mechanical reliability ▪ Learning to walk ▪ Gait pattern observed by others ▪ Overall comments ▪ Use of PSPC after wearing IP (microprocessor) *5 choices (A lot easier, easier, no difference, difficult, a lot more difficult) Function (assessed in lab/by study team): ▪ None Assessed in community-based activity: ▪ None Other ▪ None
Hafner et al, 2007 (USA) Study design: controlled, non-randomized (A-B-A-B) reversal design Total length of followup: 35-66 weeks (100%) ▪ 8 wks NMP use ▪ 2 wks NMP data	Total n=17* (13 males, 4 females) ▪ Type of amputation: TF ▪ %male: 76 ▪ Age: 49 ± 16 years ▪ Weight: NR ▪ Height: NR ▪ 8 MFCL 2s and 9 MFCL 3s ▪ Reason for amputation: 10 trauma, 1 dysfunction (from polio), 3 malignancy, 2 infection, 1 vascular disease ▪ Time since amputation: 17.6	Intervention ▪ Brand of prosthesis: mechanical prosthesis (NMP – non-microprocesser use) ▪ Fitted by prosthetist ▪ Time in use on intervention: 8 weeks NMP use then 2 weeks NMP-1 data collection ▪ Crossover to Microprocessor use (MP) Comparison Same participants	Patient-reported: ▪ Prosthesis Evaluation Questionnaire Score ▪ Medical Outcomes Study 36-Item Short-Form Health Survey score ▪ Frequency of stumbles and falls ▪ Concentration required for ambulation Function (assessed in lab/by study team): ▪ Stair rating: Stair Assessment Index (0-13, higher is better) ▪ Hill rating and time: Hill Assessment Index (0-11, higher is better) ▪ Obstacle course time

Study	Participants	Intervention	Outcomes
collection ▪ 1-32 wks MP accommodation ▪ 8 wks MP use ▪ 2 wks MP data ▪ 2 wks NMP use ▪ 2 wks NMP data ▪ 8 wks MP use ▪ 2 wks MP data Supported by Otto Bock HealthCare Author declarations of conflict: no conflicts	±18 years ▪ Type of prosthesis at recruitment: mechanical prosthesis ▪ Time using prosthesis: 8 weeks ▪ Medical coverage: NR ▪ Patient selection by research prosthetist and PT Exclusion criteria: ▪ Chronic residual limb skin breakdown ▪ Secondary health problems that would prohibit participation in the study activities Inclusion criteria: ▪ 18 years or older ▪ unilateral TF amputation ▪ MFCL 2 or 3 ▪ Min of 2 years postamputation ▪ Current use of a mechanical control knee *21 participants recruited, 2 withdrew because of medical complications, 1 voluntarily withdrew for personal reasons, and 1 could not obtain an equivalent socket and was withdrawn by the researchers	▪ Brand of prosthesis: Microprocessor control Otto Bock C-Leg (model 3C99) ▪ Brief description of function: microprocessor control in both the swing and stance phases of gait ▪ Fitted by prosthetist ▪ Time in use: 1-32 weeks accommodation, then 8 weeks of MP use, followed by 2 weeks of MP-1 data collection Crossover back to NMP use for 2 weeks, then NMP-2 data collection for 2 weeks Crossover back to MP use for 8 weeks, then MP-2 data collection for 2 weeks	▪ Divided attention task accuracy and time ▪ Amputee Mobility Predictor score ▪ Step activity Assessed in community-based activity: ▪ None Other ▪ None
Hafner et al, 2009 (USA) ▪ Nonrandomized crossover trial with repetition ▪ Total length to follow-up: 12 months	n= Total: 17 MFCL-2: 8 MFCL-3: 9 ▪ Type of amputation: TF ▪ % male = 76.5 ▪ Age (SD): Total: 49.1 (16.4)	Intervention: ▪ Passive-control ▪ Fitted by prosthetist ▪ 2 months ▪ Crossover to active-control prosthesis	Patient-reported: ▪ Mental Energy Expenditure (VAS, 0-100) ▪ Confidence While Walking (VAS, 0-100) ▪ Multitasking While Walking (VAS, 0-100) ▪ Difficulty with Concentration (VAS, 0-100) ▪ Satisfaction (VAS, 0-100) ▪ Ambulation (PEQ Score, 0-100)

Study	Participants	Intervention	Outcomes
▪ Baseline ▪ 4 months (% follow-up NR) ▪ 8 months ▪ 12 months ▪ This material was based on work supported by a research grant from Otto Bock HealthCare, LP. ▪ No author declarations of conflict.	MFCL-2: 50.8 (23.9) MFCL-3:41.9 (14.3) ▪ Weight: NR ▪ Height: NR ▪ MFCL/general health: MFCL-2 and MFCL-3, all of good general health ▪ Reasons for amputation: Trauma, Dysfunction, Infection, Vascular disease, Malignancy ▪ Time since amputation (years): Total: 17.6 MFCL-2: 17 MFCL-3: 18.2	Comparison: ▪ The same participants were included in the crossover for this study. ▪ Otto Bock C-Leg, Model 3C98 ▪ Fitted by prosthetist ▪ Time in use on intervention: 2 months ▪ Crossover to passive-control prosthesis	▪ Appearance (PEQ Score, 0-100) ▪ Frustration (PEQ Score, 0-100) ▪ Perceived Response (PEQ Score, 0-100) ▪ Residual Limb (PEQ Score, 0-100) ▪ Social Burden (PEQ Score, 0-100) ▪ Sounds (PEQ Score, 0-100) ▪ Utility (PEQ Score, 0-100) ▪ Well-Being (PEQ Score, 0-100) ▪ Function (assessed in lab/by study team): ▪ Obstacle course outcome measures (Instrument, Range): ▪ Stair Mobility (SAI, 0-13) ▪ Hill Mobility (HAI, 0-11) ▪ Hill Speed (m/s, 0 →) ▪ Obstacle Course Speed (m/s, 0 →) ▪ Attention Speed (m/s, 0 →) ▪ Attention Accuracy (% correct, 0-100) ▪ AMP Score ▪ SF-36 General Health ▪ PEQ Well-Being Assessed in community-based activity: ▪ None Other ▪ None
Kirker et al, 1996 (United Kingdom) Study design: nonrandomized crossover (significance of test order was considered however) Total length of study: Follow-up: Treadmill testing, 38% (n = 6/16)	n = 14 (demographics reported only for the 6 patients who underwent treadmill testing) ▪ Type of amputation TF ▪ % male: 83 ▪ Age (mean): 36.5 years (range, 29–44) ▪ Weight and height: NR ▪ MFCL/ general health: overall good health and wore their leg all day and regularly walked at different speeds ▪ Reason for amputation: trauma or congenital	Intervention ▪ Brand of prosthesis: IP (NABCO; Kobe, Japan) ▪ Fitted by: NR ▪ Time in use on intervention: ≥ 4 months ▪ Crossover to pneumatic swing phase controlled (PSPC) prosthetic Comparison ▪ Same patients ▪ Brand of prosthesis: Blatchford PSPC knee joint ▪ Fitted by: NR	Functional (lab assessed): ▪ Walking speed ▪ Step length ▪ Oxygen consumption Community-based (patient-reported questionnaire: ▪ Effort needed to walk at various speeds on level ground, outdoors or at work, up and down stairs or slopes; confidence in prosthesis ▪ Confidence in prosthesis ▪ Preference

Study	Participants	Intervention	Outcomes
Questionnaire, 88% (n = 14/16) Funding: NR Author declaration of conflict: NR	abnormality ▪ Time since amputation (mean): 16.5 years (range, 7–44) ▪ Type of prosthesis at recruitment: IP MCP ▪ Time using prosthesis prior to study entry (mean): 5.0 months (range, 4–7) ▪ Medical coverage: NR ▪ Patient selection by: NR Inclusion criteria: ▪ Between 18 and 66 years old ▪ Could manage a free knee ▪ Using IP for at least 1 month Exclusion Criteria ▪ NR	▪ Time in use on intervention: patients were allowed to practice walking for as long as they wanted	
Jepson et al, 2008 (United Kingdom) Nonrandomized comparison study with crossover. Total length of follow-up: Four-week accustomization period followed by short-term gait testing Funded by: NR	n = 5 • Type(s) of amputation: TF • % male: NR • 41.2 (range, 28.8 - 55.7) • 88 • 180 • Medically fit to undergio the length of walking necessary to complete tests • Reason(s) for amputation: NR • Time since amputation (mean years): 12.2 (range, 0.8 - 35.68 years) • Type(s) of prosthesis at recruitment: Endolite prosthetic system with a hydraulic Catech knee joint • Time using prosthesis: NR • Medical coverage: NR • Patient selection by	• Endolite prosthetic system with a hydraulic Catech knee joint • Fitted by prosthetist • Time in use on intervention: NR • Crossover to Adaptive knee joint Comparison: • Same participants • Adaptive knee joint • Fitted by prosthetist • Time in use on intervention: 4 weeks	Patient-reported: • Amputee questionnaire Function (assessed in lab/by study team): • Gait analysis (assessing symmetry and temporal symmetry) • Physiological cost indest (PCI) Assessed in community-based activity: • None Other: • None

Study	Participants	Intervention	Outcomes
	consultant physician and prosthetist Exclusion criteria: • Specific stump problems • Awaiting resoultion of compensation claims		
Seymour et al, 2007 (USA) • Nonrandomized short-term crossover trial comparing Non-microprocessor-controlled prosthesis to C-leg microprocessor-controlled prosthesis • No long-term follow-up, just short-term obstacle trials and baseline questionnaires • Funding and author declarations of conflict not reported	Total n= 13 ▪ Type of amputation: 12 TF, 1 knee disarticulation amputation ▪ % male: 84.6 ▪ Age (SD): 46.2 (13.1) ▪ Weight: 79.2 ▪ Height: 174.6 ▪ MCFL-4 for all participants ▪ Reason for amputation: Non-vascular causes ▪ Time since amputation (years): NR ▪ Type of prosthesis at recruitment: Microprocessor-controlled C-leg ▪ Time using prosthesis: 16.2 ▪ Medical coverage not reported ▪ Patient selection by certified prothestists ▪ Exclusion criteria: ▪ NR	Intervention ▪ Brand of prosthetist: C-leg ▪ Fitted by prosthetist ▪ Time in use on intervention: 2-44 months ▪ Crossover to NMCP Comparison: ▪ Crossover included the same participants as those in the c-leg group ▪ NMCP ▪ Fitted by prosthetist ▪ Used during intervention only ▪ Crossover to C-leg prosthesis	Patient-reported: • Quality of Life through SF-36v2: • Physical Compnent Score (PCS) • General Health (GH) • Bodily Pain (BP) • Role Physical (RP) • Physical Functioning (PF) • Mental Component Score (MPS) • Vitality (VT) • Social Functioning (SF) • Role Emotional (RE) • Mental Health (MH) Assessed in lab/by study team): • Energy expenditure (self-selected fast walking on a treadmill): • Heart rate (bpm) • Oxygen consumption (ml/kg/min) • Oxygen consumption (ml/kg/m) Four trials on functional obstacle course: • Steps • Time • Step-offs • Stumbles Assessed in community-based activity: • None
Kaufman et al, 2008 (USA) Study design: repeated measures design to evaluate comparative functional outcomes (mechanical vs.	Total n=15 ▪ Type of amputation: TF ▪ %male= 80 ▪ Age: 42 (9) ▪ Weight: NR ▪ Height: NR ▪ MFCL: 3 or 4 ▪ Reason for amputation:	Intervention ▪ Brand of prosthesis: Otto Bock C-Leg ▪ Fitted by experienced prosthetist ▪ Time in use on intervention: 18±8 weeks (range, 10-39 wks) ▪ Crossover to none	Patient-reported: ▪ Borg Rating of Perceived Exertion (RPE) during walking testing (measuring oxygen cost) ▪ Prosthesis Evaluation Questionnaire (PEQ): composed of 9 validated scales Function (assessed in lab/by study team): ▪ Energy efficiency (oxygen cost)

Study	Participants	Intervention	Outcomes
microprocessor-controlled prosthetic knees) Total length of followup 10-39wks ▪ Baseline ▪ 18 (±8wks) (100% F/U) Funded by the National Center for Research Resources; the National Institutes of Diabetes and Digestive and Kidney Diseases; and Otto Bock Healthcare Inc. Author declarations of conflict: none	trauma (7), cancer (6), peripheral vascular disease (1), and congenital (1) ▪ Time since amputation: min. 2 yrs ▪ Type of prosthesis at recruitment: mechanical fulid controlled knee prosthesis (11 Mauch SNS, 2 CaTach, 1 Black Max, 1 Century 2000) ▪ Time using prosthesis: 20±10y (range, 3-36y) ▪ Medical coverage: NR ▪ Patient selection by consensus Inclusion criteria: ▪ Unilateral transfemoral amputation ▪ 18 and older ▪ Amputation for any reason ▪ Min. of 2 yrs postamputation ▪ Medicare functional classification level 3 or 4 ▪ Current use of a hydraulic control mechanical prosthetic knee Exclusion criteria: ▪ Chronic residual limb skin breakdown ▪ Secondary medical conditions that would prevent participation in the study	Comparison Same participants ▪ Brand of prosthesis: nonmicroprocessor (mechanical) ▪ Brief description of function: controls both swing and stance phase via a hydraulic unit ▪ Fitted by: experienced prosthetist ▪ Time in use: 20±10 years (range, 3-36 yrs) -Tested participants with their nonmicroprocessor knee (been using for 20±10 years, range, 3-36 years) -Switched to C-Leg -Acclimated for as long as necessary (18±8 weeks, range, 10-39 weeks) -Retested	▪ Total Daily Energy Expenditure (TDEE)- estimated using the DLW method (taking urine samples) Assessed in community-based activity: ▪ None Other ▪ None

Table 30 Economic studies: study design

Study (country)	Intervention	Comparison	Outcome (Utility)	Time horizon and perspective	Data sources	Methods of analysis
Brodtkorb 2008 (Sweden/ Denmark) **Cost utility analysis (2008 € per QALY)**	C-Leg Parameters: Utility:0.83 Reduced utility during problems with device: 18% Number of problems per year:0.24 Duration of problem: 0.16	NMCP Parameters: Utility:0.53 Reduced utility during problems with device: 18% Number of problems per year:2.25 Duration of problem: 0.15	Calculation of quality adjusted life years (QALY) from EQ-5D	8 years Swedish health care perspective	Outcomes: Interviews with patients of current use of C-leg and recall/hypothetical use of NMCP; interviews with patients' prosthetist; interviews with manufacturers (for cost data)	Two-state Markov model: Sensitivity analysis: One-way (utility values varied according to distribution) Two-way (cost effectiveness acceptability curve)
Gerzeli 2009 (Italy) **Cost utility analysis**	C-Leg Parameters: Lifespan of device: 5 years Costs: C-leg plus trial period, and 3-year guarantee Assumption: foot and socket same for both groups C-Leg users (=50) ▪ Age: 45.8 ±11.8 y ▪ Married: 86%* ▪ Traumatic etiology (49/50) ▪ Time since amputation: 13.74 ±1.7 years ▪ Daily use of prosthesis 13.5 (2.6) hours*	NMCP Parameters: Lifespan of device: 5 years Cost: Prosthesis plus estimated repairs and replacements NMCP users (=50) ▪ Age: 45.0 ±12.0 y ▪ Married 56%* ▪ Time since amputation: 13.3 ±2.0 years ▪ Daily use of prosthesis 11.7 (4.0) hours*	Calculation of quality adjusted life years (QALY) from EQ-5D	5 years Costs and outcomes past 12 months assumed constant and discounted 3% Two perspectives: (1) Healthcare Prosthesis acquisition and fitting, hospitalization, drugs, specialist visits, rehabilitation, diagnostic/lab exams (2) Social Also included transportation, overnight stays, informal care, productivity loss	Observational, cross-sectional study with questionnaire and administrative data extraction (EQ-5D, productivity losses, informal caregiver time) Expert panel (prosthesis lifespan and repair/replace rates) Market values (pharmaceutical treatment) National fee schedules (Diagnostic and labs) National Agreement for Home Labour Services (informal caregiver cost) Published literature (primary care visits) Banca d'Italia (annual	Incremental cost-effectiveness ratio calculated with 95% confidence intervals Sensitivity analyses: Discount rate varied to 0% and 5%

Study (country)	Intervention	Comparison	Outcome (Utility)	Time horizon and perspective	Data sources	Methods of analysis
					wages)	
Seelen 2009 (Netherlands) **Cost consequences study**	C-Leg users (n=13) ▪ Transfemoral amputation 12/13 ▪ Age: 47(12) ▪ Male 12/13 ▪ Traumatic etiology 9/13 ▪ Time since amputation 13.2 years (12.9) ▪ C-leg use: 2.4 years (1.2)	NMCP users (n=13) ▪ Transfemoral amputation 10/13 ▪ Age 47 (11) ▪ Male 9/13 ▪ Time since amputation 11.4 years (11.7)	SF-36 SF-6D utility score calculated from SF-36 (score 0-1)	1 year No discounting Societal perspective Intervention costs: Prosthesis, rehabilitation, nurse, paramedical staff Health care costs: Post-clinical care (GP, hospitalization, outpatient care) Patient/family costs (housekeeping help, transportation, house adaptation)	Administrative data: intervention; health care resource use; daily function Questionnaire with patients: Productivity loss; patient/family resource Costs: Dutch Manual for Economic Evaluations	Between group differences assessed using non-parametric statistics Sensitivity analyses: One-way: prosthesis costs; tumour etiology; first-time prosthesis users
NMCP: Non-microprocessor prosthesis ***p<0.05**						

APPENDIX G. DETAILED RESULTS

Table 31: Controlled setting assessment for primary studies comparing MCP with NMCP

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
Berry (2009)	**50-question survey/questionnaire (6 domains)**			
	Domain summaries with use of MPK (%)			
	Socket fit/comfort (n = 361)			
	Worse	21.3		
	Same	5.8		
	Better	72.9		
	Confidence/security in the prosthesis, % (n = 363)			
	Worse	10.5		
	Same	1.4		
	Better	88.1		
	Gait/maneuverability with the prosthesis (n = 363)			
	Worse	10.5		
	Same	1.1		
	Better	88.4		
	Physical/cosmetic attributes of prosthesis (n = 363)			
	Worse	27.5		
	Same	6.6		
	Better	65.8		
	Physical effects of prosthesis (n = 361)			
	Worse	33.5		
	Same	5.0		
	Better	61.5		
	Negative attributes/limiting factors of prosthesis (n = 361)			
	Worse	11.9		
	Same	2.8		
	Better	85.3		
	Mean scores (± SD) by Domain (n = 363)			
	Socket fit/comfort	21.6 ± 5.2	17.0 ± 5.3	< .0001
	Confidence/security in the prosthesis	39.8 ± 9.7	27.1 ± 7.9	< .0001
	Gait/maneuverability with the prosthesis	20.2 ± 6.6	11.8 ± 3.6	< .0001
	Physical/cosmetic attributes of prosthesis	22.1 ± 5.6	18.9 ± 4.9	< .0001
	Physical effects of prosthesis	33.5 ± 7.0	30.8 ± 7.3	< .0001

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	Negative attributes/limiting factors of prosthesis	33.0 ± 7.0	25.2 ± 6.8	< .0001
	Differences between means with NMPK vs. MPK			
	Socket fit/comfort (n = 361)	4.6 ± 7.0		< .0001
	Confidence/security in the prosthesis (n = 363)	12.7 ± 10.8		< .0001
	Gait/maneuverability with the prosthesis (n = 363)	8.4 ± 6.9		< .0001
	Physical/cosmetic attributes of prosthesis (n = 363)	3.2 ± 6.7		< .0001
	Physical effects of prosthesis (n = 361)	2.7 ± 8.0		< .0001
	Negative attributes/limiting factors of prosthesis (n = 361)	7.7 ± 7.9		< .0001
Brodtkorb (2008)	**Utility (EQ-5D)**	0.83	0.53	NR
	Number of problems per year with prosthesis	0.24	2.25	NR
	Duration of problem with prosthesis	0.16	0.15	NR
	Decrement in utility when having a problem (%)	18	18	NR
Datta (1998)*	**Walking at different speeds (%) (vs. NMPK)**			
	A lot easier/easier	95.4 (21/22)	Referent	NR
	A lot easier	66.7 (14/21)	Referent	NR
	Walking distance (%) (vs. NMPK)			
	A lot further/further	81.8 (18/22)	Referent	NR
	A lot further	27.8 (5/18)	Referent	NR
	Stairs (%) (vs. NMPK)			
	Ascending, no difference	77.2 (17/22)	Referent	NR
	Descending, no difference	77.2 (17/22)	Referent	NR
	Walking on slopes and hills - a lot easier (%) (vs. NMPK)	59.1 (13/22)	Referent	NR
	Walking on rough/uneven ground (%) (vs. NMPK)			
	A lot easier/easier	63.6 (14/22)	Referent	NR
	Easier	85.7 (12/14)	Referent	NR
	A lot less tired/less energy (%) (vs. NMPK)	95.4 (21/22)	Referent	NR
	Gait pattern (%) (vs. NMPK)		Referent	NR
	Walking more normal	95.4 (21/22)	Referent	NR
	Comments by others (very favorable/ positive)	86.3 (19/22)	Referent	NR
	More mechanically reliable (%) (vs. NMPK)	63.6 (14/22)	Referent	NR
	Learning to walk was easy and quick (%) (vs. NMPK)	81.8 (18/22)	Referent	NR
	Overall improvement (vs. NMPK)		Referent	NR
	Improved/much improved	100 (22/22)	Referent	NR
	Much improved	72.7 (16/22)	Referent	NR
	Prefer to continue with MPK prosthesis (vs. NMPK)	95.4 (21/22)	Referent	NR
Gerzeli (2009)	**EuroQol (EQ-5D), %**			
	Physical Mobility			.045

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	I have no problems walking about	64	44	
	I have some problems walking about	36	56	
	I am confined to bed	0	0	
	Self-care			ns (.068)
	I have no problems with self-care	82	66	
	I have some problems washing or dressing myself	18	34	
	I am unable to was or dress myself	0	0	
	Usual activities			ns (.070)
	I have no problems performing my usual activities	64	44	
	I have some problems performing my usual activities	36	52	
	I am unable to perform my usual activities	0	4	
	Pain or discomfort			ns
	I have no pain or discomfort	16	14	
	I have moderate pain or discomfort	84	84	
	I have extreme pain or discomfort	0	2	
	Anxiety or depression			
	I am not anxious or depressed	78	60	ns
	I am moderately anxious or depressed	22	38	
	I am extremely anxious or depressed	0	2	
	HRQoL weight - mean Utility score scale 0 to 1 (±SD)	0.753 ± 0.119	0.663 ± 0.197	.007
Hafner (2009)†	**Satisfaction, VAS 0-100 (mean ± SD)**			
	MFCL-2	76.1 ± 15.5	63.1 ± 12.1	ns
	MFCL-3	79.1 ± 23.6	57.4 ± 21.7	.002
	Satisfaction, VAS 0-100 (mean change, 95% CI)‡			
	Combined population	17.6 (8–27)		.001
	Prosthesis Evaluation Questionnaire, by MFCL (mean ± SD), 4 weeks			
	Ambulation			
	MFCL-2	72.7 ± 12.3	67.9 ± 11.2	ns
	MFCL-3	78.4 ± 20.7	61.3 ± 23.8	.01
	Appearance			
	MFCL-2	77.6 ± 14.7	76.1 ± 17.7	ns
	MFCL-3	74.5 ± 18.0	72.1 ± 15.5	ns
	Frustration			
	MFCL-2	71.6 ± 15.8	71.0 ± 15.7	ns
	MFCL-3	85.5 ± 24.3	65.2 ± 26.5	ns
	Perceived Response			
	MFCL-2	95.1 ± 4.7	92.0 ± 9.0	ns

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	MFCL-3	96.5 ± 6.2	91.7 ± 16.2	ns
	Residual Limb			
	MFCL-2	79.5 ± 13.1	80.9 ± 11.7	ns
	MFCL-3	79.5 ± 16.2	81.4 ± 18.2	ns
	Social Burden			
	MFCL-2	88.6 ± 13.2	87.2 ± 14.9	ns
	MFCL-3	91.1 ± 13.1	89.7 ± 11.6	ns
	Sounds			
	MFCL-2	68.9 ± 21.6	65.6 ± 26.6	ns
	MFCL-3	80.1 ± 16.2	61.2 ± 23.8	.046
	Utility			
	MFCL-2	72.7 ± 14.5	71.9 ± 17.5	ns
	MFCL-3	79.2 ± 21.3	66.2 ± 22.7	.01
	Well-being			
	MFCL-2	82.8 ± 7.7	77.7 ± 12.8	ns
	MFCL-3	80.6 ± 18.7	74.4 ± 22.2	ns
	Prosthesis Evaluation Questionnaire, combined population, 4 weeks (mean change, 95% CI)‡			
	Ambulation	11.3 (3–19)		.008
	Appearance	2.0 (-3 to 8)		ns
	Frustration	11.0 (-2 to 25)		ns
	Perceived response	4.0 (0–9)		ns
	Residual limb	-1.7 (-6 to 3)		ns
	Social burden	1.4 (-4 to 7)		ns
	Sounds	11.6 (-1 to 24)		ns
	Utility	7.3 (0–15)		ns
	Well-being	5.6 (1–10)		.016
	Prosthesis Evaluation Questionnaire -A (mean)			
	Mental energy expenditure			
	MFCL-2	60.1±9.6	51.1±23.6	ns
	MFCL-3	74.9±28.8	55.2±24.4	0.046
	Frequency of stumbling			
	MFCL-2	85.6±9.1	74.0±14.7	0.05
	MFCL-3	79.1±12.1	60.4±22.9	0.03
	Number of stumbles			
	MFCL-2	2.7±2.2	4.0±2.7	ns
	MFCL-3	3.7±1.7	7.3±6.0	ns
	Frequency of semi-controlled falling			

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	MFCL-2	93.1±6.5	83.8±16.8	ns
	MFCL-3	94.3±5.5	86.0±12.2	ns
	Number of semi-controlled falls			
	MFCL-2	0.6±0.3	1.6±1.5	ns
	MFCL-3	0.7±0.9	2.9±4.7	ns
	Frequency of uncontrolled falling			
	MFCL-2	98.1±1.9	93.9±3.3	0.01
	MFCL-3	97.8±2.1	93.1±6.8	ns
	Number of uncontrolled falls			
	MFCL-2	0.0±0.1	0.5±0.5	0.01
	MFCL-3	0.4±0.5	0.5±0.3	ns
	Confidence while walking			
	MFCL-2	86.1±4.3	76.2±12.5	ns
	MFCL-3	82.6±24.1	67.2±27.4	0.004
	Difficulty multitasking while walking			
	MFCL-2	85.8±7.0	70.8±18.9	0.04
	MFCL-3	85.0±16.4	67.4±26.9	0.03
	Frustration with falling			
	MFCL-2	94.5±6.3	76.6±21.9	ns (0.06)
	MFCL-3	94.8±5.2	79.9±20.7	0.05
	Embarrassment with falling			
	MFCL-2	82.9±14.3	78.0±20.7	ns
	MFCL-3	93.8±7.6	90.9±12.5	ns
	Difficulty with concentration			
	MFCL-2	82.3±10.0	74.1±25.0	ns
	MFCL-3	88.5±17.7	79.9±17.4	ns
Hafner (2007)	**Prosthesis Evaluation Questionnaire (mean), previous 4 weeks**			
	Satisfaction	82.2	67.9	< .001
	Ambulation	78	62	ns
	Appearance	78	74	ns
	Frustration	81	62	ns
	Perceived response	96	94	ns
	Residual limb	77	79	ns
	Social burden	88	90	ns
	Sounds	71	64	ns
	Utility	78	64	ns
	Well-being	85	78	ns

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	Prosthesis Evaluation Questionnaire -A (mean), 4 weeks			
	Mental energy expenditure	61	54	ns
	Frequency of stumbling	83	66	< .05
	Number of stumbles	3.3	5.7	ns
	Frequency of semi-controlled falling	95	81	< .05
	Number of semi-controlled falls	0.4	3.2	ns
	Frequency of uncontrolled falling	98	89	< .05
	Number of uncontrolled falls	0.3	0.7	ns
	Confidence while walking	88	66	ns
	Difficulty multitasking while walking	87	68	< .05
	Fear of falling	91	77	ns
	Frustration with falling	97	68	< .01
	Embarrassment with falling	95	86	ns
	Fearful of falling without prosthesis	83	80	ns
	Difficulty with concentration	89	74	ns
	Preference between prostheses (%)	82.4 (14/17)§	5.9 (1/17)§	< .001
Jepson (2008)	**Questionnaire (n = 5)****			
	Flat walking 500 m††	-1		
	Flat walking 1000 m††	-2		
	Walking up slopes/hills††	2		
	Walking down slopes/hills††	1		
	Walking up a flight of stairs††	No change		
	Walking down a flight of stairs††	-4		
	Stumble while walking‡‡	-2		
	Fall because the knee has given away‡‡	3		
	Number of falls in the last 8 weeks	-3		
	Opinion about the weight of the leg§§	No change		
	Comfort score***	-13		
	Would not revert back to NMPK (%)	60 (3/5)		
	Still using MPK 6 months post-fitting (%)	40 (2/5)		
Kahle (2008)	**Prosthesis Evaluation Questionnaire (overall mean ± SD), 4 weeks**	1184.1 ± 243.1	942.3 ± 269.3	.007
	Preference between prostheses (%)	73.7 (14/19)	26.3 (5/19)	NR
	Stumbles (mean ± SD), 60 days	3 ± 4	7 ± 6	.006
	Falls (mean ± SD), 60 days	1 ± 2	3 ± 3	.03
Kaufman (2008)	**Prosthesis Evaluation Questionnaire (mean)†††, 4 weeks**			
	Ambulation	75	61	.02

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	Appearance	69	60	.02
	Frustration	60	56	.02
	Perceived response	89	90	ns
	Residual limb	69	65	.02
	Social burden	88	76	.02
	Sounds	70	56	.02
	Utility	71	66	.02
	Well-being	81	70	.02
	Total Daily Energy Expenditure (MJ/d)‡‡‡	14.1	13.0	.04
	Physical activity-related energy expenditure	5.5	4.4	.04
Kirker (1996)	**Questionnaire (VAS 100 mm scale)§§§**			
	Effort walking at normal speed	28	47	< .05
	Effort walking at fast speed	31	76	< .01
	Effort walking at slow speed	35	46	ns
	Effort walking outdoors, at work	31	64	< .01
	Effort walking down slope	47	69	< .05
	Effort walking up slope	55	67	ns
	Effort walking up steps	61	68	ns
	Effort walking down steps	47	54	ns
	Confidence when walking	86	70	ns
	Confidence when standing	92	88	ns
	Preference for IP or NMPC prosthesis	86		< .001
Seelen (2009)	**SF-36 scores, mean ± SD**			
	Physical functioning	91.5 ± 9.9	68.2 ± 23.3	.004
	Social functioning	78.7 ± 35.1	58.8 ± 37.7	ns (.059)
	Role limitations due to physical health problems	65.4 ± 33.1	40.4 ± 37.6	.045
	Role limitations due to emotional problems	97.5 ± 9.2	61.5 ± 46.9	.011
	Mental health	92.3 ± 11.0	62.2 ± 29.3	.003
	Vitality	86.2 ± 12.6	57.7 ± 22.2	.001
	Bodily pain	87.6 ± 20.0	70.5 ± 23.4	.028
	General health	70.0 ± 16.3	55.4 ± 26.6	ns (.071)
	Health transition/improvement	53.9 ± 13.9	34.6 ± 24.0	.014
	SF-36 scores (mean ± SD) for patients wearing their first prosthesis— MPK, n = 5; NMPK, n = 6			
	Physical functioning	84.0 ± 11.4	65.0 ± 27.2	ns
	Social functioning	82.0 ± 40.2	73.0 ± 32.0	ns
	Role limitations due to physical health problems	65.0 ± 28.5	54.2 ± 36.8	ns
	Role limitations due to emotional problems	100.0 ± 0	66.7 ± 42.2	.041

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	Mental health	93.6 ± 8.3	68.7 ± 18.1	.007
	Vitality	83.0 ± 17.2	60.8 ± 20.1	.049
	Bodily pain	83.0 ± 21.7	67.8 ± 25.6	ns
	General health	72.0 ± 22.5	57.5 ± 30.9	ns
	Health transition/improvement	55.0 ± 20.9	29.2 ± 29.2	ns (.066)
Seymour (2007)	**SF-36 (mean ± SD), mean 16 ± 15 months**			
	Physical Component Score	50 ± 7	NR	n/a
	Mental Component Score	59 ± 4	NR	n/a
	General Health	57 ± 10	NR	n/a
	Bodily Pain	59 ± 14	NR	n/a
	Role Physical	53 ± 16	NR	n/a
	Physical Functioning	50 ± 13	NR	n/a
	Vitality	60 ± 10	NR	n/a
	Social Functioning	60 ± 12	NR	n/a
	Role Emotional	57 ± 14	NR	n/a
	Mental Health	60 ± 11	NR	n/a

HRQoL: health-related quality of life; MFCL: Medicare Functional Classification Level; MPK: microprocessor; NMPK: no microprocessor; NR: not reported; ns: not statistically significant; SD: standard deviation; VAS: visual analog scale.
*Answers to the questions are related to patients MPK prosthesis compared to their previously used NMPK prosthesis.
†MFCL-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. MFCL-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.
‡Mean change in PEQ scores – with use of the MPK vs. NMPK prosthesis - for the MFCL-2 and MFCL-3 groups combined. Confidence intervals estimated from graph.
§2/17 had no preference.
**Lower score reflects worse outcome with the MPK prosthesis.
††Do you find the following activity: very easy, easy, a little difficult, difficult, extremely difficult.
‡‡How often does the event occur: Often, Sometimes, Occasionally, Never.
§§What is your opinion about the weight of your prosthesis?: Extremely heavy, very heavy, heavy, average, light.
***How comfortable is your artificial limb (0 to 10): 1 = extremely uncomfortable; 10 = extremely comfortable.
†††Means estimated from figures provided in the articles.
‡‡‡Estimated using the doubly labeled water (DLW) method. Participants consumed water containing isotopes of oxygen and hydrogen; three urine samples were collected before dosing, and then 3 timed urine samples were collected a day for 10 days. Measurement of the difference in clearance of the 2 isotopes from the body represented carbon dioxide production which in turn reflected energy expenditure.
§§§Higher score indicates greater effort, greater confidence or preference for IP.

Table 32: Controlled setting assessment comparing MCP with NMCP (detailed results)

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
Hafner (2009)	**By MFCL (mean ± SD)**			
	Stair Assessment Index			
	MFCL-2	9.0 ± 3.7	3.3 ± 1.6	.008
	MFCL-3	10.1 ± 2.9	4.4 ± 2.9	.004
	Hill Assessment Index			
	MFCL-2	7.5 ± 2.6	5.4 ± 3.9	.008
	MFCL-3	8.6 ± 3.3	7.2 ± 3.2	ns
	Hill speed, m/s			
	MFCL-2	2.16 ± 0.41	1.70 ± 0.29	.002
	MFCL-3	3.04 ± 0.95	2.17 ± 0.81	.017
	Obstacle course speed, m/s			
	MFCL-2	0.89 ± 0.26	0.80 ± 0.26	.02
	MFCL-3	1.12 ± 0.22	1.05 ± 0.21	.007
	Attention speed, m/s			
	MFCL-2	0.93 ± 0.18	0.83 ± 0.17	.02
	MFCL-3	1.11 ± 0.22	1.08 ± 0.20	ns
	Attention accuracy (% correct)			
	MFCL-2	77.2 ± 20.6	73.3 ± 19.8	ns
	MFCL-3	68.7 ± 25.3	65.0 ± 19.4	ns
	Combined Population (mean change, 95% CI)			
	Stair Assessment Index	5.7 (4.0–7.5)		< .001
	Hill Assessment Index	1.7 (0.8–2.8)		< .001
	Hill speed, m/s	0.68 (0.33–1.03)		.001
	Obstacle course speed, m/s	0.08 (0.04–0.12)		< .001
	Attention speed, m/s	0.06 (0.02–0.10)		.01
Hafner (2007)	Side-step length affected (cm, mean)	64	57	ns
	Side-step length sound (cm, mean)	59	59	ns
	Stair Assessment Index descent (mean)	9.6	3.7	< .001
	Stair Assessment ascent (mean)	4.7	4.9	ns
	Hill Activity score (mean)	7.6	6.7	ns
	Hill time (s) (mean)	39	55	< .01
	Side-step length descending Hill affected (cm, mean)	49	33	< .001
	Side-step length descending Hill sound (cm, mean)	51	45	ns
	Concentration – walking speed (m/s, mean)	1.03	0.96	ns
	Concentration – test accuracy (% correct)	73	65	ns
Jepson (2008)	**Gait analysis (mean change NMPK to MPK)**			

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	Stride length (m)			
	Slow speed	0.03		ns
	Preferred speed	-0.02		ns
	Fast speed	-0.02		ns
	Cadence (steps/min)			
	Slow speed	0.80		ns
	Preferred speed	-0.20		ns
	Fast speed	1.10		ns
	Temporal symmetry (%)			
	Slow speed	-1.16		ns
	Preferred speed	-5.00		ns
	Fast speed	-1.35		ns
	Spatial symmetry (%)			
	Slow speed	2.18		ns
	Preferred speed	8.38		ns
	Fast speed	9.07		.043
	Prosthetic step length (m)			
	Slow speed	0.05		NR
	Preferred speed	0.02		NR
	Fast speed	0.01		NR
	Physiological cost index (beats/min)			
	Patient 1	0.60	0.56	NR
	Patient 2	0.79	0.79	NR
	Patient 4	0.42	0.39	NR
	Patient 5	0.67	0.56	NR
	Total/Mean (n = 4)	0.62	0.58	NR
Kahle (2008)	SSWS 75 m (s) (mean ± SD)	86.4 ± 32.8	101.3 ± 47.8	.03
	FPWS 75 m (s) (mean ± SD)	71.2 ± 26.1	81.4 ± 33.6	.005
	FPWS 38 m uneven terrain (s) (mean ± SD)	44.2 ± 16.4	55.9 ± 22.0	< .001
	FPWS 6 m (s) (mean ± SD)	5.4 ± 2.2	6.5 ± 2.6	.001
	MRPP, improved PCS (%)	63.2 (12/19)*	10.5 (2/19)*	NR
Kaufman (2008)†	**Borg RPE (mean)**			
	Speed 0.45 m/s	8.5	9.5	.002
	Speed 0.90 m/s	10	11	.002
	Speed 1.35 m/s	14	13	.002
	Energy efficiency/O_2 expenditure (ml/kg/m, mean)			
	Speed 0.45 m/s	0.29	0.31	ns
	Speed 0.90 m/s	0.21	0.21	ns

Author (year)	Outcome	MPC knee	NMPC knee	*P*-value
	Speed 1.35 m/s	0.19	0.20	ns
Kirker (1996)	**SSWS in 100 m corridor (m/min), mean**			
	Slow	60	62	ns
	Normal	75	74	ns
	Fast	88	86	ns
	Gait symmetry (% of stride length)			< .017 overall
	Slow	1	5	
	Normal	2	2	
	Fast	1	3	
	Oxygen consumption (ml/min/kg)			
	Slow	15	15	ns
	Normal	18	17	ns
	Fast	23	23	ns
Seymour (2007)	**Obstacle course – hands free (mean ± SD)‡**			
	Steps	15.6 ± 2.9	17.0 ± 3.1	.004
	Time (s)	11.5 ± 2.4	12.7 ± 2.4	.004
	Step-offs	0.2 ± 0.3	05 ± 0.4	.03
	Stumbles	0	0	n/a
	Obstacle course – carrying 10 lb basket (mean ±SD)‡			
	Steps	15.6 ± 2.9	18.2 ± 4.6	ns
	Time (s)	11.5 ± 2.4	15.6 ± 3.7	.007
	Step-offs	0.3 ± 0.4	0.4 ± 0.5	ns
	Stumbles	0	0	n/a
	Typical pace (49 ± 15 m/min, mean ± SD)			
	Heart rate (bpm)	102 ± 14	102 ± 12	ns
	O2 consumption (ml/kg/min)	12.6 ± 1	13.5 ± 2	.04
	O2 consumption (ml/kg/m)	0.29 ± 0.09	0.30 ± 0.09	.05
	Fast pace (70 ± 20 m/min, mean ± SD)			
	Heart rate (bpm)	103 ± 16	104 ± 15	ns
	O2 consumption (ml/kg/min)	16.0 ± 2	17.2 ± 2	.03
	O2 consumption (ml/kg/m)	0.23 ± 0.06	0.25 ± 0.05	.04

AD: sensor arrays placed anterior and distally towards the end of the stump; AP: sensor arrays placed anteriorly and proximally at the patella tendon; FPWS: fastest possible walking speed; n/a: not applicable; MFCL: Medicare Functional Classification Level; MPK: microprocessor; MRPP: Montreal Rehabilitation Performance Profile; NMPK: no microprocessor; NR: not reported; ns: not statistically significant; PAEE: physical activity-related energy expenditure; PCS: Performance Composite Score; PM: sensor arrays placed posteriorly and about half the height of the stump; RPE: rate of perceived exertion; SD: standard deviation; SSWS: self-selected walking speed; VAS: visual analog scale.
*5/19 subjects showed no change in their PCS.

†Numbers estimated from figures provided in the articles.
‡Mean of four trials.

Table 33: Other outcomes assessed in uncontrolled settings

Author (year)	Outcome	MPC	NMPC		*P*-value
Datta (2005)	**O_2 consumption (ml/kg/m)***				
	Speed 0.7 m/s (n = 10)	0.297	0.335		.01
	Speed 0.85 m/s (n = 10)	0.265	0.290		< .05
	Speed 1 m/s (n = 9)	0.240	0.260		ns
	Speed 1.1 m/s (n = 8)	0.230	0.250		ns
	Speed 1.25 m/s (n = 6)	0.220	0.237		ns
	SSWS (m/s)				
	Slow (n = 9)	1.03 ± 0.12	1.01 ± 0.18		ns
	Normal (n = 10)	1.29 ± 0.14	1.23 ± 0.17		ns
	Fast (n = 8)	1.55 ± 0.10	1.47 ± 0.16		ns
	Gait quality, VAS 0-100mm (mean ± SD)				
	Slow speed (n = 9)	66 ± 10	66 ± 8		ns
	Normal speed (n = 9)	64 ± 10	62 ± 8		ns
	Fast speed (n = 9)	64 ± 11	63 ± 9		ns
	Spatial symmetry (ratio of longer step distance to shorter step distance)				
	Slow speed (n = 9)	1.17 ± 0.12	1.17 ± 0.07		ns
	Normal speed (n = 10)	1.13 ± 0.06	1.14 ± 0.10		ns
	Fast speed (n = 8)	1.11 ± 0.07	1.13 ± 0.08		ns
	Temporal symmetry (ratio of longer stance time to shorter stance time)				
	Slow speed (n = 6)	1.06 ± 0.06	1.05 ± 0.04		ns
	Normal speed (n = 9)	1.05 ± 0.04	1.08 ± 0.09		ns
	Fast speed (n = 5)	1.08 ± 0.08	1.06 ± 0.04		ns
Heller (2000)	**Cognitive Demand (whole body sway)†**				
	Mean velocity (mm/s) – Counting (3 tasks)†	181	206	<. 05	<. 05
	Mean velocity (mm/s) – Stroop (3 tasks)†	189	219	< .05	< .05
	Mean velocity (mm/s) – Counting and Stroop†	185	212	.047	.047
	Ratio – Stroop/Counting‡	1.05	1.07	ns	ns
Klute	**Level of activity measured via the StepWatch (steps/day, mean ± SD)**				

Author (year)	Outcome	MPC	NMPC		*P*-value
(2006)	**over 7 days (n = 5)**				
	Weekdays only	2708 ± 704	2710 ± 947		ns
	Weekends only	2527 ± 840	2587 ± 1093		ns
	All days	2657 ± 737	2675 ± 976		ns
	Duration of activity measured via the StepWatch (min/day, mean ± SD) over 7 days (n = 5)				
	Weekdays only	272 ± 5 6	253 ± 95		ns
	Weekends only	273 ± 89	280 ±115		ns
	All days	273 ± 65	260 ±100		ns
Orendurff (2006)	**Net O_2 cost (mL/kg/m, mean)**				
	Speed 0.8 m/s	0.25 ± 0.02	0.24 ± 0.02	ns	ns
	Speed 1.0 m/s	0.21 ± 0.02	0.22 ± 0.03	ns	ns
	Speed 1.3 m/s	0.21 ± 0.02	0.23 ± 0.03	ns	ns
	SSWS	0.21 ± 0.02	0.22 ± 0.02	ns	ns
	Mean SSWS	1.31 ± 0.12	1.21 ± 0.10	.04§	.04§
Williams (2006)**	Prosthetic Cognitive Burden Scale (mean ± SD)	2.12 ± 0.37	3.19 ± 0.37		< .001
	Attention to cognitive task (mean ± SD)	7.83 ± 0.49	7.40 ± 0.49		ns
	Attention to walking (mean ± SD)	2.12 ± 0.71	3.54 ± 0.71		< .001
	SSWS (m/s) (mean ± SD)	1.06 ± 0.06	1.03 ± 0.06		ns
	Semantic verbal fluency (mean ± SD)	22.9 ± 0.67	23.1 ± 0.67		ns
	Phonemic verbal fluency (mean ± SD)	40.6 ± 3.0	40.4 ± 3.0		ns
	Working memory (serial subtraction errors, mean ± SD)	0.88 ± 0.54	1.63 ± 0.54		ns
MPK vs. Able-bodied patients					
Author (year)	**Outcome**	**MPK (n = 8)**	**Able-bodied (n = 14)**		***P*-value**
Chin (2003)	**O_2 Cost (ml/kg/m), mean ± SD**				
	Walking speed 30 m/min	0.388 ± 0.070	0.290 ± 0.066		NR
	Walking speed 50 m/min	0.274 ± 0.053	0.209 ± 0.051		NR
	Walking speed 70 m/min	0.235 ± 0.034	0.190 ± 0.045		NR
	Walking speed 90 m/min	0.239 ± 0.028	0.193 ± 0.036		NR
	Walking speed 110 m/min	0.246 ± 0.030	0.205 ± 0.049		NR
	O_2 Uptake (ml/kg/min), mean ± SD				
	Walking speed 30 m/min	11.6 ± 2.1	8.7 ± 1.9		< .05
	Walking speed 50 m/min	13.7 ± 2.6	10.4 ± 2.5		< .05
	Walking speed 70 m/min	16.5 ± 2.4	13.3 ± 3.1		< .05
	Walking speed 90 m/min	21.5 ± 2.5	17.3 ± 3.2		< .05

Author (year)	Outcome	MPC	NMPC		*P*-value
	Walking speed 110 m/min	27.1 ± 3.3	22.5 ± 5.4		< .05
	Rate of increase in energy expenditure (%), MPK vs. Able-bodied				
	Walking speed 30 m/min	33.7			< .05
	Walking speed 50 m/min	31.1			< .05
	Walking speed 70 m/min	24.1			< .05
	Walking speed 90 m/min	24.2			< .05
	Walking speed 110 m/min	20.1			< .05
MPK vs. MPK					
Author (year)	**Outcome**	**C-Leg MPK (n = 8)**	**Rheo MPK (n = 8)**	**Mauch NMPK (n = 8)**	***P*-value**
Johansson (2005)	**Walking speed (m/s)**	1.18	1.14	1.20	ns
	Affected side:				
	Step time (s)	0.65	0.69	0.66	ns†† .038‡‡ .007§§
	Step length (m)	0.74	0.75	0.76	ns
	Single support (s)	0.42	0.43	0.42	ns
	Double support (s)	0.29	0.32	0.30	ns
	Unaffected side:				
	Step time (s)	0.58	0.59	0.57	ns
	Step length (m)	0.71	0.69	0.71	ns
	Single support (s)	0.52	0.53	0.51	ns
	Double support (s)	0.31	0.33	0.31	ns
	Rate of O_2 consumption at SSWS (ml/kg/min)* **				
	Patient 1	12	11	11	ns
	Patient 2	15	15	16	.009††† ns‡‡‡
	Patient 3	13	12	14	.009††† ns‡‡‡
	Patient 4	20	19	21	.009††† ns‡‡‡
	Patient 5	13	12	13	.009††† ns‡‡‡
	Patient 6	23	22	25	.009††† ns‡‡‡
	Patient 7	20	18	19	.009††† ns‡‡‡
	Patient 8	13	13	13	ns

Author (year)	Outcome	MPC	NMPC			*P*-value
Author (year)	**Outcome**	**C-Leg MPK (n = 9)**	**Hybrid Knee MPK (n = 9)**	**Rheo MPK (n = 9)**	**Adaptive2 MPK (n = 9)**	***P*-value**
Bellmann (2010)	**O_2 Cost (ml/kg/m), mean ± SD**					
	2006					
	Speed 0.6–0.8 m/s	0.255 ± 0.018	0.256 ± 0.016			ns
	Speed 0.8–1.0 m/s	0.231 ± 0.025	0.232 ± 0.016			ns
	Speed 1.0–1.2 m/s	0.220 ± 0.027	0.226 ±0.010			ns
	2008					
	Speed 0.6–0.8 m/s	0.253 ± 0.027		0.253 ± 0.035		ns
	Speed 0.8–1.0 m/s	0.224 ± 0.022		0.236 ± 0.027		< .05
	Speed 1.0–1.2 m/s	0.214 ± 0.027		0.220 ±0.022		ns
	Hand rail use when descending (%)					
	Stairs	44	56	78	100	NR
	Ramp (10°)	22	44	78	100	NR
	Fall Prevention Potential					
	Stopping	w/o problems	w/o problems	Increased compensation movements	Incidental knee joint collapse	
	Sidestepping	w/o problems	w/o problems	Increased compensation movements	Incidental knee joint collapse	
	Stepping onto an obstacle	w/o problems	w/o problems	w/o problems	w/o problems	

MPC: microprocessor-controlled prosthesis; NMPC: non- microprocessor-controlled prostheses; NR: not reported; ns: not statistically significant; SD: standard deviation;
*Numbers estimated from figures provided in the articles.
†The performance measure used was whole body sway, assessed by measuring the 3-dimensional movements of a marker placed on the subjects' forehead at 20-ms intervals using a video-based motion analysis system. The magnitudes of the marker displacement in each 20-ms period were summed to give a total distance travelled by the marker; this was divided by the duration of the trial to give a mean velocity.
‡The mean velocities for all three Stroop tasks performed wearing the NMPK prosthesis and the MPK prosthesis were divided by the mean velocities for all three counting tasks wearing the same prosthesis. A value > 1 indicates that performance is degraded while performing the Stroop task (higher cognitive demand) relative to the simple counting task.
§Self-selected walking speed was significantly faster with C-leg without any increase in oxygen costs.
**Reflect performance during a combined cognitive and walking test.
††Comparison between Mauch and C-Leg.
‡‡Comparison between Mauch and Rheo.
§§Comparison between C-Leg and Rheo.
***Values estimated from graph provided in article.
†††Comparison between Rheo and Mauch; average decrease equal to 5% across the eight subjects.

‡‡‡Comparisons between C-Leg and Rheo (P = .092) and C-leg and Mauch (P = .250); average decrease equal to 3% and 2% across the eight subjects, respectively.