What is an evidence note

Evidence notes are rapid reviews of published secondary clinical and cost-effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They are intended to provide information quickly to support time-sensitive decisions and are produced in an approximately 3 month period. Evidence notes are not comprehensive systematic reviews. They are based on the best evidence that Healthcare Improvement Scotland could identify and retrieve within the time available. The reports are subject to peer review but do not undergo external consultation. Evidence notes do not make recommendations for NHSScotland.

Introduction

This evidence note summarises the literature relating to the clinical effectiveness and cost effectiveness of microprocessor-controlled knees, compared with mechanically-controlled knees, in people who have had unilateral, above the knee (transfemoral) amputations.

Health technology description

People who have had a transfemoral amputation may use a prosthetic knee for ambulation. Prosthetic knees can be mechanically controlled or microprocessor-controlled\(^1\). Mechanically controlled knees have been in use for many years, and can be further classified based on the complexity of their stance stability and swing-phase control capabilities\(^1\). The swing phase can be controlled using mechanical, pneumatic or hydraulic devices.

In the early 1990s, the Intelligent Prosthesis™ (Blatchford and Sons, Basingstoke) became available. This utilises microprocessor technology to improve the swing phase of the gait cycle\(^2\). In 1999, Otto Bock introduced the C-Leg®, a microprocessor-controlled prosthetic knee that controls stance and swing phase and adjusts to the requirements of the prosthesis wearer at the rate of fifty times per second\(^3\). In 2004, Otto Bock introduced the new ‘C-Leg Compact®’ with additional features (standing mode, handheld remote to switch between modes, adaptable swing-phase dynamics for slight adjustments)\(^1\). Finally the RHEO KNEE® (Össur, Reykjavik) is a swing and stance phase system which uses a microprocessor as well as artificial intelligence to ‘learn’ about the wearer’s walking characteristics over time\(^2\).

Epidemiology

Transfemoral amputations can be the result of trauma, malignancy or congenital limb deficiencies. However, most commonly (up to 95%) they are attributable to vascular disease\(^3\). There is a higher incidence of vascular-related amputation with advancing age\(^3\).

Key points

- The available evidence suggests that in certain patient groups (ie healthy and active younger people who have had a transfemoral amputation), the C-Leg® (Otto Bock, Duderstadt) may improve health outcomes (eg body image, safety, energy efficiency, gait and functionality) compared with mechanically controlled knees. There is little evidence relating to older people with chronic illness or reduced function.
- There is insufficient evidence to determine whether or not microprocessor controlled prosthetic knees are cost effective compared with mechanically controlled knees.
In Scotland in 2009, there were 773 lower-limb amputations. Of these, 321 (41.53%) were transfemoral amputations. The mean age was 67.5 years and peripheral arterial disease, with or without diabetes, accounted for 83.3% of all amputations. In 2009, 41% of lower-limb amputees were fitted with a prosthesis. When examined by level, 68% of transtibial (which retains the knee joint) and 24% of transfemoral amputees were fitted with a prosthesis. Figures from the last 5 years in Scotland show that more transfemoral amputees abandon use of their prosthesis within the rehabilitation period compared with transtibial amputees (in 2009; unilateral transtibial 2.9%; unilateral transfemoral 17.1%). The NHS currently routinely uses mechanically controlled knees.

The C-Leg® is routinely provided to military amputees within the Ministry of Defence Medical Rehabilitation Centre at Headley Court, where a commercial company fits the prostheses. The C-Leg® is more expensive than hydraulic prostheses (approximately £16,000 versus £2,000). The resource impact is magnified as prosthetic limbs are typically replaced every 5 years. The C-leg® is not routinely used in Scotland (D Gow, SMART Centre. Personal Communication, 5 April 2011).

Clinical effectiveness

The evidence for this section comes from three systematic literature reviews, a randomised crossover trial and two non-randomised crossover trials.

The most recent review (2010) evaluated the evidence on patient safety, gait energy efficiency, and cost effectiveness of the C-Leg®. The authors identified 17 studies: six (in seven publications) related to safety, eight to energy efficiency and three to cost effectiveness. Most of the included patients were amputees due to trauma, and mean patient age ranged between 30–55 years.

With regards to safety, five of the six studies (three crossover trials in four publications, two case reports and one pre/post test study) reported statistically significant reductions in self-reported stumble and fall events with the C-Leg® compared with mechanical knees. Of the crossover trials, the first (Kahle et al., 2008) reported a statistically significant reduction in the number of stumble (59%; p<0.006) and fall (64%; p<0.03) events in 19 subjects with heterogeneous function and aetiology. The second (Kaufman et al., 2007; n=15) directly evaluated balance using dynamic posturography and reported that the C-Leg® significantly improved balance performance (p<0.01). The third (Hafner and Smith 2009; n=17) reported that Medicare Functional Classification Level 2 (MFCL-2) users (people with limited ambulation who can manage stairs, kerbs and uneven surfaces) had a 15.8% (p=0.05) reduction in the frequency of stumbles, and an 80% reduction (p=0.01) in the number of uncontrolled falls; whereas MFCL-3 users (people who require sophisticated prostheses for more vigorous activity) reported a 31% reduction (p=0.03) in the frequency of stumbles.

For energy efficiency, the authors state that seven out of eight studies (two case reports, three pre/post test studies, two crossover studies and one repeated measures study) reported increased energy efficiency while walking with the C-Leg® compared with other knees. However, the only two that presented statistically significant improvements were small pre/post test studies (Seymour et al., 2007 (n=13) and Schmalz et al., 2002 (n=6)). These reported increased energy efficiency with the C-Leg® compared with non-microprocessor knees at two different walking speeds: typical (6.4%; p=0.05) and fast (7%; p=0.04) pace (Seymour et al.), and medium (6–7%; p<0.05) and slow (6–7%; p<0.05) (Schmalz et al., 2002). The authors of the review also refer to two very small studies (Johansson et al., 2005 (n=8) and Chin et al., 2006 (n=4)) which compared the C-Leg® with other microprocessor knees: Intelligent Prosthesis™ and the RHEO KNEE®. Neither reported statistically significant differences in energy efficiency.

All the studies relating to safety and energy were of low methodological quality. They included case series, pre/post test studies, and crossover trials. They were generally small, and heterogeneity prevented any meta-analyses. Only two of the crossover trials were randomised (though for both the sample size was <10) and none were blinded. Patients who had lost limbs due to vascular disease were not represented at levels proportionate with estimates from epidemiologic studies, limiting the generalisability of the results.
Finally, the authors of the review appear to have only extracted the positive findings from the studies.

Two further reviews were identified, one of which was published in 2009\(^1\) (number of included studies=58; 37 of which were taken from the Otto Bock website) and one in 2007\(^2\) (number of included studies=13). Most of the evidence they include comes from crossover studies, but there were also case series and case reports. There was considerable overlap with the review by Highsmith et al.\(^3\). Both reviews reported improvement in outcomes such as body image, energy expenditure, gait biomechanics, balance and speed, with microprocessor-controlled prosthetic knees compared with mechanical knees. However, the authors of both also highlighted that the included studies were methodologically weak; and that the majority of the patient populations were healthy and active adults, and so generalisability to other patient groups is limited.

A randomised crossover trial from the Netherlands, published in 2011\(^6\), compared functional performance of the C-Leg\(^\circledR\) and C-Leg compact\(^\circledR\) with a mechanically controlled knee in people with transfemoral amputation. The authors evaluated patients classified as MFCL-2, who were able to walk at least 500 metres and had no previous experience of using a microprocessor-controlled knee (n=41). People with severe orthopaedic, rheumatological, neurological or cardiovascular disease were excluded. The authors argued that while the MFCL-2 population tends to be older and have lower activity levels than people classified MFCL-3 and MFCL-4, they are a heterogeneous population and some of them may benefit from a microprocessor-controlled knee. Therefore, the authors further split the participants into ‘low’, ‘intermediate’ and ‘high’ functional mobility subgroups. Functional performance was assessed for each of the prosthetic knees using a test in which participants performed 17 simulated activities of daily living (eg hanging out laundry, stairs descent and climb). The authors reported that for some activities, those in the ‘high’ and ‘intermediate’ subgroups performed significantly faster with both the microprocessor knees compared with the mechanical knees. However, the performance times of the participants in the ‘low’ subgroup did not differ for any of the activities between prostheses. Based on these findings, the authors concluded that people classified as MFCL-2 with higher functional abilities may benefit from using microprocessor knees to perform activities of daily living.

Two studies (both non-randomised crossover trials) were identified that considered the Intelligent Prosthesis\(^\circledR\). The first included 10 people (mean age 38 years, range 23–46 years) who used a conventional pneumatic swing-phase control knee\(^7\). The authors reported that at lower walking speeds, oxygen cost was lower (suggesting reduced physical effort) with the Intelligent Prosthesis\(^\circledR\). At 0.69 metres per second (m/s) oxygen cost was 0.33 ml/kg.m with the conventional limb and 0.30 ml/kg.m with the Intelligent Prosthesis\(^\circledR\) (p=0.01). At 1.25 m/s the mean oxygen cost for the conventional limb was 0.24 ml/kg.m and for the Intelligent Prosthesis\(^\circledR\) was 0.22 ml/kg.m (difference not statistically significant)\(^7\). At normal walking speeds, there was no significant difference in oxygen cost. Gait analysis detected no significant changes between the two legs.

The second study also included 10 ‘generally fit and reasonably active participants’ (mean age 38 years), who normally wore a pneumatic swing-phase control prosthesis\(^8\). The authors examined the cognitive demand of walking when participants used their conventional prosthesis compared with the Intelligent Prosthesis\(^\circledR\), and reported that there was no significant difference. As both these studies are small and non-randomised, they cannot support robust recommendations.

Safety

A 2009 study was identified that performed biomechanical tests in an instrumented gait laboratory to evaluate the safety of the C-Leg\(^\circledR\) and two non-microprocessor controlled knees\(^5\). Only three participants were included (all relatively active, with their amputation being the result of trauma). Tests included level ground walking at self-selected velocity, sudden stopping, sidestepping, stepping on an object and tripping by disrupting swing extension. The C-Leg\(^\circledR\) did not collapse in any of the tests. Both the non-microprocessor knees collapsed in the majority of the tests.
Cost effectiveness

Three economic evaluations were identified by Highsmith et al.3: two cost-utility studies and one cost-consequence evaluation.

The first cost-utility analysis, from Italy (manufacturer funded)9 compared the C-Leg® with mechanical alternatives in transfemoral amputees, and estimated both healthcare and societal costs for the lifecycle of the technologies (5 years). Data for a 12-month period were obtained retrospectively from an observational study of people aged from 18–65 years, who had a unilateral amputation due to trauma (mostly a work or traffic accident). To extrapolate to 5 years, the differences in utility and costs were assumed to be constant over time. Fifty C-Leg® users were included, and case-matched to 50 mechanical knee users. Outcomes were measured in terms of quality of life, evaluated with the EuroQol questionnaire (EQ-5D). From the Italian healthcare system perspective, costs included the acquisition cost of the prosthesis (which included the cost of the technology and its fitting, but excluded the cost of the socket and foot components since these were said to be common to both interventions) maintenance and repair, hospitalisations, drugs, general practitioners, specialist visits and diagnostic services and laboratory examinations. Both costs and effectiveness values were discounted at an annual rate of 3%9. Estimates of resource use were based on Italian charges and tariffs set in the national fee-schedules, therefore limiting generalisability. Total healthcare costs were €22,744 (approximately £19,300) for the C-Leg® and €7,449 (approximately £6,321) for the mechanical prosthesis. C-Leg® users accumulated 3.55 quality-adjusted life years (QALYs) compared with 3.13 for those with mechanical knees (mean difference 0.42; 95% confidence interval 0.12–0.73). The incremental cost-effectiveness ratio (ICER) of the C-Leg® was €35,971 (approximately £30,755) per QALY. Varying the discount rate within the 0–5% range did not substantially alter this value. The authors noted that bias might have been introduced because of the retrospective nature of the data and the matched case-control design. In addition, they could not exclude the possibility that the C-Leg® might have been fitted to patients with more opportunities to improve quality of life.

The second cost-utility analysis was based in an outpatient setting in Sweden, and evaluated whether the C-Leg® was cost effective compared with non-microprocessor controlled knees10. Data on costs, rates and duration of problems, knee survival and health-related quality of life were obtained from interviews with patients and prosthetists. These data were used in a decision-analytic Markov model to estimate cost effectiveness from a healthcare perspective.

Five prosthetists and 20 C-Leg® users (mean age 41 years) were interviewed10. The 20 patients had been using the C-Leg® for 6 months, having previously used a non-microprocessor knee recommended for active patients. The main reason that they had been given a C-Leg® was that the prior knee had not fully met their needs, in relation to safety, durability and negotiation of stairs. The time horizon for the analysis was 8 years from the delivery of the first prosthesis, as this is the functional time of a C-Leg® guaranteed by the manufacturer.

Costs and QALYs were discounted by 3% per annum10. The utilities were based on the EQ-5D visual analogue scale. Estimates of resource use associated with different health states and transition probabilities were obtained from manufacturers of the prosthetic components, as well as prosthetists. The mean incremental cost (in 2006 Euros) and QALYs gained for the C-Leg® was €7,657 (approximately £6,399) and 2.38, respectively, yielding a cost per QALY gained of €3,218 (approximately £2,689). The authors concluded that the C-Leg® appeared to yield positive health outcomes at an acceptable cost, but caution that the results are to a large degree based on informed judgments rather than clinical trial evidence. The sensitivity analysis showed that the model results were sensitive to the utility values associated with each intervention, however remained cost effective.

The ICER reported by Gerzeli et al.9 (€35,971) is approximately eleven times greater than that reported by Brodtkorb et al.10 (€3,218). This could be partly explained by the way in which the utility scores were collected by Brodtkorb et al. The participants were C-Leg® users whose main
reason for using the C-Leg® was that a non-microprocessor knee had not met their needs. To obtain utility ratings for the non-microprocessor knee condition, users were asked to hypothesise what their life would be like without the C-Leg®. This approach is likely to introduce bias in favour of the C-Leg®. The difference in ICERs may also be partly due to differences in the assumed lifecycle of the C-Leg®: 5 years for Gerzeli et al. and 8 years for Brodtkorb et al.

The cost-consequence study was based in the Netherlands11. The aim was to assess from a societal point of view the costs and functional health of people using a C-Leg® (C-group) or a non-microprocessor controlled knee (N-group). A 1-year time horizon was used. This was a retrospective study of 26 people (13 C-Leg® users and 13 non-microprocessor knee users) with a unilateral knee/hip disarticulation or transfemoral amputation.

Intervention costs, healthcare costs, patients/family costs, productivity costs and total costs were calculated11. Costs were obtained from a cost questionnaire, a subset of the PROductivity and DISease Questionnaire and a Dutch database, and valued using a Dutch costing manual. Functional health was measured using the 36-Item Short Form Health Survey and patients medical records were also used for data on the daily functioning of patients at the start of rehabilitation. The results showed mean total costs of €39,350 (approximately £32,365) and €46,086 (approximately £37,908), for the C-group and N-group, respectively. Based on intervention and healthcare costs only, the results showed mean total costs of €29,860 (approximately £24,559) and €23,886 (approximately £19,644), for the C-group and N-group, respectively.

The authors concluded that while the C-Leg® was associated with higher purchasing costs, this may be counterbalanced with savings in other domains (eg patients/family costs, housekeeping assistance costs and productivity losses)11. The sensitivity analysis showed the results were sensitive to increasing the cost of the prosthesis by 10%, and average total costs were higher when oncological patients were included. The third sensitivity analysis examined only patients who were wearing their first prosthesis and showed that average total costs were higher in the C-group (€70,029; approximately £57,576) than the N-group (€64,584; approximately £53,085). (Note: all reported costs converted to pounds sterling using the exchange rate as at 16 April 2012).

**Conclusion**

The most robust evidence relating to the C-Leg® comes from crossover randomised trials. While this is a suitable study design, the studies were generally small and methodologically weak. Many received sponsorship from the manufacturer, and the patient groups were often fit and healthy adults, and so the generalisability of the results to other patient groups is questionable.

The available evidence suggests that in certain patient groups (ie healthy and active younger amputees), the C-Leg® may improve health outcomes (eg body image, safety, energy efficiency, gait and functionality). There is little evidence relating to older people with chronic illness or reduced function.

The two cost-utility analyses yielded ICERs broadly within acceptable cost per QALY thresholds. However methodological issues, limited clinical evidence and lack of generalisability to the Scottish setting means that it is not possible to conclude whether the C-Leg® would be cost effective for use in NHSScotland.

**Equality and diversity**

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The evidence note process has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on www.healthcareimprovementscotland.org
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To propose a topic for an evidence note, email evidencenotes.HCIS@nhs.net

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network http://knowledge.scot.nhs.uk, or by contacting your local library and information service.

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References continued


