NICE advice

LARS for reconstructing damaged intra-articular cruciate knee ligaments

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Summary

The LARS (ligament augmentation and reconstruction system) is a synthetic scaffold indicated for the repair and reconstruction of damaged ligaments. Comparative studies show no statistically significant differences in the majority of outcomes for people undergoing LARS procedures compared with people treated with an autograft at a follow-up of 4 years. One study reported statistically significantly less laxity for LARs procedures. Each LARS costs £1391.

Product summary and likely place in therapy	Effectiveness and safety
• The LARS is a synthetic ligament for use as scaffolding in the reconstruction of damaged anterior or posterior cruciate knee ligaments. • The LARS would only be used in ligament repair procedures when the clinician and patient have decided that non-synthetic alternatives (autograft and allografts) have been considered as possible treatment options. The LARS can be used instead of autograft or allograft procedures, if sufficient native tissue remains, or alongside these grafts to protect the joint.	• Five comparative studies (1 randomised controlled trial and 4 cohort comparative studies) investigated the effectiveness of the LARS in cruciate knee ligament reconstructions. These studies reported measures of knee stability and patient-reported outcomes. No statistically significant differences were reported in the majority of outcomes for people having LARS procedures compared with people having autograft treatment at a follow-up of 4 years. One study reported statistically less laxity for LARS procedures. • One systematic review provided safety information on synthetic ligament scaffolds including the LARS. LARS had the lowest failure rate at 2.4% of procedures, with the highest reported failure rate being 33.6%. Revision rates ranged from 2.2% with the LARS to 11.8%. No corresponding rates for autograft or allograft were reported.

Technical factors	Cost and resource use
• The LARS is made of polyethylene terephthalate (PET). • Each LARS is composed of 2 sections (intra- and extra-articular). The design aims to mimic normal ligament anatomy and overcome fibre breakdown, which can lead to synovitis. • The LARS is available in different sizes. It is generally fixed into place using 2 screws.	• The cost of the LARS, excluding fixings, is £1391, excluding VAT. Fixing screws, which are also needed for other ACL reconstruction techniques, cost £153 each. • It has been suggested that the LARS reduces rehabilitation time and has a lower failure rate than autografts or allografts, which could lead to resource savings. However, there is currently little evidence to support these claims.

Introduction

The knee joint is 1 of the most complex joints in the body, comprising several bones and muscles connected by tendons and ligaments. Tendons join muscle to bone and allow movement in the knee joint, whereas ligaments connect bone to bone and provide stability of the joint. There are 2 types of ligament in the knee joint: the extra-articular ligaments that run down the side of the knee on the outside of the joint and the intra-articular cruciate ligaments that are within the knee joint and bathed in synovial fluid (eOrthopod 2015).

Injuries to the knee joint are common. The estimated incidence in the USA is 2.29 injuries per 1000 people (Gage et al. 2012). Damage to the ligaments is the most common type of injury, causing about 40% of all knee injuries. Of these ligament-specific injuries, approximately 50% involve individual intra-articular ligaments (Bollen 2000).

There are 2 main intra-articular ligaments in the knee joint: the anterior cruciate ligament (ACL) and the posterior cruciate ligament (PCL). Both ligaments connect the femur to the tibia. The ACL prevents too much forward movement of the leg (that is, the tibia sliding in front of the femur) and resists rotation of the tibia. The PCL prevents too much backward movement of the leg. Of the 2 ligaments, the PCL is the stronger and is less susceptible to

injury. Only 8% of intra-articular ligament injuries involve the PCL, whereas 92% involve the ACL (Bollen 2000). Generally, injury to the PCL is caused by blunt force trauma to the knee (OrthoInfo 2015). ACL injury can occur in several ways, such as suddenly changing direction, landing incorrectly after jumping, or suddenly stopping moving (OrthoInfo 2015). Injury to the ACL is particularly common in people who play high-energy sport, such as football or basketball. There is some evidence to suggest that in many of these sports, women have a significantly higher risk than men of ACL injury (Prodromos et al. 2007). However, more men than women play high-energy sports, and so ACL injury presents more often in men (Allan et al. 2013).

If any ligament in the knee is damaged, the knee loses structural integrity resulting in instability that can reduce mobility in the joint. Inflammation caused by the injury can also cause pain. Extra-articular ligaments generally respond well to conservative treatment, such as physiotherapy aimed at regaining muscle strength and restoring motion in the joint (NOC 2015). In comparison, the intra-articular cruciate ligaments (ACL and PCL) tend to heal poorly because they are in synovial fluid, which limits the blood supply and potential for revascularisation (Laurencin and Freeman 2005). Further, this position within the synovial fluid prohibits clot formation, which in turn stops the bridging of tissue between ligament remnants (Murray et al. 2000). As a result of these limitations, cruciate ligaments are commonly repaired by surgical reconstruction (Mascarenhas and MacDonald 2008).

Surgical reconstruction of the intra-articular cruciate ligaments can involve autograft or allograft transplants. In the UK, most procedures use autograft transplants, in which a healthy tendon from another joint in the person's body (often the hamstring tendon) is surgically implanted into the joint. In allograft surgery, healthy ligaments or tendons are taken from 1 person and implanted into another (NHS Choices 2015). The donor tissue can come from either a living or dead donor, the latter being common in UK practice, with tendons supplied by NHS Blood and Transplant (NHS Blood and Transplant 2015).

Popular techniques for reconstruction of the ACL used within the NHS are hamstring tendon autograft and bone-patellar tendon-bone autograft (Shaerf et al. 2014). Hamstring, patellar tendon and quadriceps tendon autografts are favoured in PCL reconstruction (Robertson et al. 2006).

The Hospital Episode Statistics for England for 2013–14 reported 13,015 procedures in England involving the reconstruction of intra-articular ligaments (Health & Social Care Information Centre 2015). The mean age of people having these procedures was 30 years, and 76% were men. These data did not include the rates of reconstruction surgery for

different sites in the body, but the knee is the most common site of intra-articular ligament reconstruction.

Various adverse events related to tendon autograft and allograft procedures have been reported. In particular, autografts are often associated with donor-site morbidity, anterior knee pain and reduced knee flexor strength (Gao et al. 2010). Allografts can lead to immune rejection and infection (Huang et al. 2010; Legnani et al. 2010).

The risks associated with autograft and allograft procedures prompted the development of synthetic materials for ligament reconstruction. The first synthetic ligaments were developed in the 1970s and were seen as an attractive alternative to autograft, in part because their application was less complex. They either acted as prostheses, directly replacing the damaged ligament, or they could be used as scaffolding alongside the healing or donated ligament or tendon (Legnani et al. 2010). These first generation artificial ligaments have largely been withdrawn from the market because of high failure rates (Smith et al. 2014). Further developments since the 1980s have resulted in a variety of second and third generation synthetic ligaments becoming available for ligament reconstruction. These newer materials generally act as scaffolding to allow the damaged ligament or donated tendon to grow into the joint and to protect the healing ligament.

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

The Ligament Augmentation and Reconstruction System (LARS) is a synthetically-produced ligament scaffold that is constructed from polyethylene terephthalate (PET) fibres. The LARS is manufactured by the LARS Company and distributed in the UK by the Corin Group.

Occasionally LARS is referred to as Ligament Advanced Reinforcement System, although this name is less common.

The LARS is available in different forms for use in soft-tissue reconstruction applications for the knee, shoulder, foot and ankle, hip joint and in reconstructive surgery following treatment for soft-tissue tumours. This briefing focuses on the LARS as a scaffold for treating damaged anterior cruciate ligaments (ACLs) and posterior cruciate ligaments (PCLs). Other applications for the LARS are beyond the scope of this briefing.

CE marking

The LARS was first CE-marked to the LARS Company as a Class IIb medical device in August 1997. The certificate was extended in August 2014, and is valid until August 2017. This certificate includes all ligament types, as well as auxiliary clips and screws. A coterminous certificate applies to instrument kits that include ligament pins, a drill bit, a drill bit guide, a cannulated drill bit and a K-wire.

Description

The LARS is formed from an intra- and an extra-articular section. The intra-articular section of the LARS is placed within the knee joint and is made of parallel longitudinal fibres that are twisted into a spiral. The fibres of the extra-articular section are also arranged longitudinally, and are additionally knitted together by a transverse structure made of the same polyethylene terephthalate (PET) fibres (Mascarenhas and MacDonald 2008). This design aims to mimic the natural anatomy of cruciate ligaments and overcome fibre breakdown, which was a problem in the early generations of artificial ligaments. Fibre breakdown can result in accumulation of synthetic material in the knee, causing inflammation of the joint — known as synovitis. High rates of synovitis were associated with older-generation artificial ligaments (Machotka et al. 2010). Depending on the severity of the synovitis, this can cause some people to need revision surgery (Batty et al. 2015).

The LARS is intended to act as scaffolding to the damaged ligament. Its main role is to allow tissue ingrowth and provide structural support to the repairing ligament, which can be an autograft, allograft or the native ligament, if sufficient tissue remains. It also protects the repairing ligament during healing (Newman et al. 2013). The LARS remains in the joint once the ligament has repaired.

LARS scaffolds are sold individually, and are available in different sizes based on the total number of fibres in the scaffold. Cruciate ligament procedures use LARS with between 80 and 160 fibres. The surgeon chooses the size of the ligament, depending on various

factors including: joint size; quality of the bone for ligament attachment; type of lesion; and the volume and vascularisation status of remaining tissue (Dericks 1995).

In most cruciate ligament procedures, 2 screws fix the LARS in place and sometimes staples may also be needed. Pins may be used to create bone tunnels for effective fixation of the LARS. All of the components needed to fix the LARS must be bought separately from Corin Group, or in exceptional circumstances from other manufacturers.

Reusable instrument kits are also available from Corin Group. These kits are procedure-specific and so separate ACL and PCL kits are available. Each kit contains the equipment needed for a LARS procedure, including the appropriate drills and drill guides. For hospitals performing infrequent LARS procedures the instrument kits can be loaned from Corin Group. In these cases Corin Group send an implant kit that contains a range of components used to fix the LARS in place.

Intended use

The LARS can be used for orthopaedic procedures involving the reconstruction of missing or damaged ligaments. Uses beyond the reconstruction of knee ligaments are outside of the scope of this briefing.

The LARS should only be used in cruciate ligament procedures after non-synthetic alternatives (autograft and allografts) have been considered as possible treatment options by the clinician and the patient. The success of the LARS procedure in ACL and PCL reconstruction depends on various factors. These include the experience of the surgeon, especially their ability to correctly place the bone tunnels and fix LARS in place, and the quality of the post-operative rehabilitation.

Setting and intended user

The LARS is intended for use in secondary or tertiary care for non-emergency patients. Depending on the nature of the reconstruction, the procedure may be carried out in a day-case, inpatient or outpatient setting. The procedure should be done by surgeons who have experience of cruciate ligament reconstruction and who have had relevant training in the LARS procedure.

Current NHS options

There are currently 2 treatment options for cruciate ligament injuries available on the NHS. The first line of therapy is conservative treatment, which focuses on physiotherapy to restore motion in the knee joint and strength in the muscle. However, conservative treatment does not always restore complete function of the injured knee, and this can result in persistent joint pain. The second-line option is surgical reconstruction. This option is particularly common for people with active lifestyles (NOC 2015).

Surgical reconstruction is usually done arthroscopically and uses a graft to reconstruct the ruptured ligament. Autograft procedures are most commonly used for ligament reconstruction, with allografts also an option in certain circumstances, such as when there are concerns regarding morbidity associated with autograft harvest (Robertson et al. 2006). Treatment decisions are made through discussions between the surgeon and the patient. Following surgical reconstruction, patients have a structured rehabilitation programme that includes physiotherapy appointments and recovery exercises (NHS Choices 2015).

Surgeons and patients involved in ACL reconstruction procedures can also register their reconstruction surgeries on the UK National Ligament Registry (NLR). The NLR aims to improve the management of, and outcomes from, ACL surgery.

NICE is aware of the following CE marked devices that appear to fulfil a similar function to LARS:

- Ligastic (Orthomed)
- Leeds-Keio (Neoligaments)
- JewelACL (Neoligaments).

Costs and use of the technology

The cost, excluding VAT, of the LARS and associated consumables are:

- the LARS scaffold: £1391
- the LARS screw (4.7×15 mm, 5.2×15 mm, 5.2×20 mm or 5.2×30 mm): each £153

- staple (8×20 mm): £171
- pin (2x250 mm): £30
- ligament screw (6×30 mm, 7×25 mm, 7×30 mm, 8×25 mm, 8×30 mm, 9×25 mm, 9×30 mm): each £171.

All consumables are single-use and can be purchased individually in sterile packaging from the distributor, Corin Group.

The distributor sells reusable instrument kits to hospitals that frequently do LARS procedures. Alternatively, the distributor will loan the instrument kits on a short-term basis to hospitals where procedures are carried out infrequently. When the instrument kits are loaned, an implant kit, containing a range of fixings, is provided. The surgeon is charged for the fixings used (according to the prices listed above), and the remaining fixings in the kit are returned to Corin Group:

- purchase cost of instrument kit for ACL procedure: £3600
- purchase cost of instrument kit for PCL procedure: £5500
- loan cost of instrument kit (ACL or PCL procedures): £450.

The surgical procedure for ligament reconstruction using the LARS is different from autograft or allograft reconstruction without the LARS. Therefore, surgeons must complete training for this procedure. Training can be in the form of a 1-hour online session run by experienced surgeons or a workshop at the surgeon's own hospital. Surgeons with no experience of doing LARS procedures may also observe an experienced surgeon. All training is organised by Corin Group, the distributor, and provided free-of-charge.

The costs of autograft and allograft procedures were not available from the NHS Reference Costs database.

Likely place in therapy

Following cruciate ligament surgery, patients have a structured rehabilitation programme that is coordinated by the surgeon and/or a physiotherapist. This programme includes exercises to strengthen the joint and surrounding muscles. A full recovery can be expected within 6 months of the procedure (NHS Choices, 2015). The use of the LARS is unlikely to impact on the pre-operative care pathway, and it is unclear whether it will impact on the

post-surgical care pathway.

Specialist commentator comments

All 3 specialist commentators felt that the main role of the LARS could be to provide an alternative treatment, where there are barriers to using autografts. The possible roles include allograft revision surgery procedures, multi-ligament reconstructions, or where there is not enough material for an autograft procedure. One commentator noted that there is an unmet need for surgical procedures when there is no native ligament tissue available, such as in revision surgery.

One specialist commentator observed there was no long-term evidence, such as 10-year follow-up data, to support the use of the LARS in cruciate ligament indications. This commentator noted that, in their experience, none of the synthetic ligament scaffolds worked in the long term. They added that there was no evidence that any PET synthetic ligament scaffold has been associated with intra-articular ingrowth in the knee. Another commentator noted that the LARS has not demonstrated superiority over the well-established autograft surgery for ligament reconstruction.

All 3 specialist commentators remarked that there is no evidence to support the claims that the LARS can lead to faster rehabilitation or allow people to return to sport sooner. One of the commentators reflected that a more important factor for the post-surgical recovery time is the use of appropriate surgical technique. A second commentator agreed that the success of the surgery was more likely to relate to the surgical procedure, noting that the positioning of bone tunnels, tensioning of the ligament scaffold and adequacy of its fixation were important factors.

One commentator stated that there is a general opinion that using synthetic ligament augmentation devices, such as the LARS and other synthetic scaffolds, shields the repairing native ligament or autograft ligament from physical stress. This stress on the ligament is thought to be needed to allow the ligament to re-grow normally and for the collagen to be correctly orientated. As a consequence, the use of synthetic scaffolds could cause the ligament to have sub-optimal mechanical characteristics. They felt that the LARS might be more useful in the reconstruction of lateral collateral ligaments, medial collateral ligaments and medial patellofemoral ligaments.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance (these are protected characteristics under the Equality Act 2010).

Most intra-articular ligament reconstruction procedures in England are performed on men, with a mean age of 30 years, indicating that younger men in particular could benefit from the LARS scaffold. Sex and age are protected characteristics under the 2010 Equality Act.

Evidence review

Clinical and technical evidence

Regulatory bodies

A search of the Medicines and Healthcare Products Regulatory Agency website revealed no manufacturer Field Safety Notices or Medical Device Alerts for this device.

The LARS is not licensed for use in the US, so no search of Food and Drug Administration (FDA) database: Manufacturer and User Device Facility Experience (MAUDE) was undertaken.

Clinical evidence

A literature search revealed 659 studies on the LARS: 649 of these studies were excluded for failing to meet the inclusion and exclusion criteria, mainly because the studies did not use the LARS device. The remaining 10 papers were assessed for quality. The 5 comparative papers, of which 1 is a randomised trial and 4 are cohort studies, represent the best-quality evidence and are described in this briefing and summarised in tables 2–7.

The safety profile of the LARS was most comprehensively addressed in the systematic review conducted by Batty et al. (2015). This review included 20 studies of knee surgery using the LARS, 3 of which were comparative studies that are also discussed individually in this briefing (Nau et al. 2002; Liu et al. 2010, Pan et al. 2013). The other 17 studies were non-comparative case series. A total of 1102 knee surgeries were reported in the Batty et al. (2015) review: 13 anterior cruciate ligament (ACL) patient cohorts (843 knees, of which 50 were revisions); 4 posterior cruciate ligament (PCL) cohorts (120 knees, 0 revisions); and 5 combined ACL and PCL cohorts (139 knees, 0 revisions).

In this study the authors reported that the incidence of complications in each category (failure, revision and non-infective effusion and synovitis) ranged from 0% to 3% for ACL and PCL surgeries.

In addition to the LARS, theBatty et al. study also reported on other synthetic ligaments, namely Kennedy LAD, Leeds-Kieo I, Leeds-Kieo II, Dacron, Gore-Tex and Trevira-Hochfest. The LARS had the lowest overall failure rate at 2.4% (20/862) with other synthetic ligaments having failure rates that ranged from 7.7% (Leeds-Kieo, 1/13) to 33.6% (Dracon, 168/499). LARS had the lowest overall revision rate, at 2.2% (21/945) with the Kennedy LAD having the second lowest, 3.5% (13/368), and the Dacron the highest at 11.7% (48/409). There were no observed incidences of non-infective effusion and synovitis for the Leeds-Keio II (0/13). A rate of 0.4% (2/562) was reported for the LARS, with the highest reported rate being 26.6% (103/387) for the Gore-Tex. A summary is provided in table 1.

Table 1 Summary of the Batty et al. (2015) study

Study component	Description
Objectives/ hypotheses	To assess safety and efficacy of LARS and other synthetic devices for cruciate ligament surgery.
Study design	Systematic review.
Inclusion/ exclusion criteria	Included studies: Controlled and uncontrolled trials, n>10, that assessed safety and efficacy of synthetic devices used for ACL and PCL. Excluded studies: in vivo, animal studies, not reported in English, non-peer reviewed, abstract only, cruciate reconstruction in conjunction with high tibial or distal femoral osteotomy.

Primary outcomes	Rates of failure, revision, and non-infective effusion and synovitis.
Statistical methods	Summative data were used for categorical variables, with means and standard deviations for continuous variables. Meta-analysis was not possible because of heterogeneity and inconsistent outcome reporting.
Studies	20 studies on LARS involving ACL, PCL and combined. Total of 1102 knees included (ACL, 843; PCL, 120; and combined, 139). Mean follow-up ranged from 22–95 months for ACL cohorts; 26–44 months for PCL and 27–44 months for combined cohorts.
Results: Failure	LARS: ACL: 2.6% (19/736) PCL: 1.0% (1/99) A combined ACL and PCL procedure: 0.0% (0/27) Kennedy LAD: ACL: 13.9% (180/1,364) Leeds-Keio I: ACL: 16.8% (60/365) Leeds-Keio II: ACL: 7.7% (1/13) Dacron: ACL: 33.6%(168/499) Gore-Tex: ACL:12.9%(59/475) Trevira-Hochfest: ACL: 9.8% (26/265) PCL: 16.7% (2/12)
Results: Revision	ACL: 2.6% (19/728) PCL: 0.0% (0/120) Combined ACL and PCL: 2.2% (2/89) Range for all devices: 2.2% LARS to 11.7% (Dacron, 48/409)

Results: Non-infective effusion/ synovitis	ACL: 0.2% (1/438) PCL: 1.2% (1/79) Combined ACL and PCL: NR Range for all devices: 0% (Leeds-Keio II, 0/13) to 26.6% (Gore-Tex, 103/387) The authors noted that half of the LARS studies did not report synovitis and effusion and so the reported low incidence should be interpreted with caution.
Conclusions	Authors concluded that the LARS studies reported acceptably low rates of failure and complications for ACL and PCL, including revision surgery.
Abbreviations: ACL, anterior cruciate ligament; n, number of patients; NR, not reported; PCL, posterior cruciate ligament.	

The clinical evidence on the use of the LARS in knee reconstruction has been divided into 2 groups relating to either ACL or PCL reconstruction. The studies used a variety of measures of knee stability and function as outcome measures.

Measures of knee stability:

- KT-1000 evaluation is a clinical test of anterior tibial motion relative to the femur. The test measures the extent of this motion in millimetres compared with the uninjured knee. Higher scores represent greater knee laxity (Arneja and Leith 2009).
- The posterior drawer test measures the integrity and laxity of the PCL. The clinician stabilises the patient's foot using 1 of a variety of positions then pushes the proximal tibia posteriorly. The translation or movement is estimated in millimetres, relative to the opposite, uninjured knee (Feltham and Albright 2001). Objective and subjective knee functioning is independent of the degree of PCL laxity (Shelbourne et al. 1999), but this laxity does lead to a change in knee mechanics (Logan et al. 2004).

Patient-reported measures of knee function:

- The Lysholm score is a questionnaire measuring knee function within 8 domains: limp, locking, pain, stair climbing, support, instability, swelling and squatting. The overall score ranges from 0-100, with a score of 95–100 considered excellent, 84–94 good, 65–83 fair and 65 or lower, poor (Briggs et al. 2009).

- The Tegner score is a self-assigned score. Patients assign themselves a score from 0–10, with 0 representing 'sick leave or disability pension because of knee problems' and 10 representing 'competitive sports — soccer, football, rugby (national elite)' (Briggs et al. 2009).
- The International Knee Documentation Committee (IKDC) score is a questionnaire assessing 4 areas: subjective assessment, symptoms, range of motion and ligament examination. People are categorised within each domain and overall as normal, nearly normal, abnormal and severely abnormal (Hefti et al. 1993).
- The Knee Injury and Osteoarthritis Outcome Score (KOOS) allows knee function to be assessed across 5 domains: pain, symptoms, daily living, sports and recreation, and knee-related quality of life. A score is decided by the patient for each of the 5 domains, ranging from 0 (extreme symptoms) to 100 (no symptoms; KOOS website).

Anterior cruciate ligament

The use of the LARS for ACL reconstruction was investigated in 3 studies that are summarised in this briefing. Of these, 1 reported a randomised controlled trial conducted in Canada (Nau et al. 2002) and 2 were retrospective cohort studies conducted in China (Liu et al. 2010; Pan et al. 2013).

All 3 studies report clinical measures of knee stability as well as patient-reported measures of knee function. Statistically significant differences between autograft and the LARS were rarely observed, and were fewest at later assessment time points. Only the study by Liu et al. (2010) reported a statistically significant difference at the final time point, where the LARS patients had statistically greater stability at 49 months than autograft, as measured by KT-1000.

Rates of complications were reported in less than 10% of autograft patients and less than 5% of the LARS patients within each of these ACL studies. No reports of infection or synovitis were observed in Nau et al. (2002) or Liu et al. (2010) or reported to have been observed in Pan et al. (2013). The 3 studies involved a total of 83 people having the LARS, 2 of whom reported complications. There was 1 case of excess laxity in the study by Nau et al. (1/83, 1.2%), which required surgical intervention to retighten the graft and the other was a report of pain caused by a tibial screw in the trial by Liu et al. (1/83, 1.2%). No statistical analysis was reported to have been conducted on rates of complications in these studies.

These studies are summarised within tables 2, 3, 4 and 5.

Table 2 Summary of the Nau et al. (2002) study

Study component	Description
Objectives/ hypotheses	To compare clinical outcomes and patient satisfaction between BPTB autografts and LARS.
Study design	Prospective randomised controlled trial.
Setting	Patients recruited December 1996–August 1998. Follow-up at 2, 6, 12 and 24 months.
Inclusion/ exclusion criteria	Inclusion criteria were adults with closed growth plates and chronic symptomatic rupture of ACL. People with a history of previous surgery on the ACL, infection or septic arthritis in either knee, or additional ligamentous instability in the affected knee were excluded.
Primary outcomes	Tegner score, IKDC evaluation, Instrumented laxity testing[a], KOOS evaluation.
Statistical methods	Pre-operative treatment group characteristics and post-operative outcomes were compared. Student's unpaired t-test was used for parametric data, chi-square test for categorical data and Mann–Whitney U test for non-parametric data. Statistically significant differences at $p<0.05$.
Participants	n=27 in BPTB group; n=26 in the LARS group. 1 patient from each group was lost to follow-up.

Results	No significant differences between the groups in Tegner score and IKDC evaluation. The LARS patients reported statistically significant higher laxity than BPTB, at 6 months; thereafter differences were not significant. No significant difference between KOOS subscales pre-operatively and at 24 months. The LARS group recorded significantly higher scores in some subdomains at intermediate time points. Excess laxity was shown by one BPTB and 1 LARS patient, the latter requiring further surgery. The 2 people who were lost to follow-up were assumed to have experienced failure.
Conclusions	Authors concluded that the use of the LARS in ACL reconstruction provided high patient satisfaction in first 24 months but longer-term results were required.
Abbreviations: ACL, anterior cruciate ligament; BPTB, bone-patellar tendon-bone; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; n, number of patients. [a]Instrumented laxity testing — This test may refer to the KT-1000 measure, although the specific details of the test were not provided.	

Table 3 Results from Nau et al. (2002) study

	BPTB	LARS	Analysis
Randomised	n=27	n=26	
Efficacy	n=26	n=25	2 lost to follow-up.
Primary outcome: IKDC score[a]			

Subjective domain: (median)	Pre-op: C 2 months: C 6 months: B 12 months: B 24 months: A	Pre-op: C 2 months: B 6 months: B 12 months: B 24 months: A	No statistically significant differences across the groups (p>0.05) at all time points.
Stability domain: (median)	Pre-op: C 2 months: A 6 months: B 12 months: B 24 months: B	Pre-op: C 2 months: B 6 months: B 12 months: B 24 months: B	No statistically significant differences across the groups (p>0.05) at all time points.
Range of movement domain: (median)	Pre-op: A 2 months: B 6 months: A 12 months: A 24 months: A	Pre-op: A 2 months: B 6 months: A 12 months: A 24 months: A	No statistically significant differences across the groups (p>0.05) at all time points.

Symptoms domain: (median)	Pre-op: D 2 months: D 6 months: C 12 months: C 24 months: A	Pre-op: D 2 months: D 6 months: C 12 months: C 24 months: B	No statistically significant differences across the groups (p>0.05) at all time points.
Selected secondary outcomes:			
Instrumented laxity testing[b] (mm) (mean±SD)	24 months: 2.38±1.8	24 months: 4.86±3.8	6 months: p=0.01 (BPTB<LARS) Results not reported at other time points but p>0.05.
KOOS evaluation	NR	NR	No statistically significant differences (p>0.05) between groups pre-operatively and at 24 months. The LARS group recorded statistically significant higher scores in some subdomains at intermediate time points.
Tegner score	NR	NR	No statistically significant differences (p>0.05) between the groups at all-time points.
Safety	n=26	n=25	2 lost to follow-up.
Excessive laxity	3.8% (1/26)	4.0% (1/25)	The LARS patient needed surgery.

Abbreviations: BPTB, bone-patellar tendon-bone graft; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; n, number of patients.

[a]IKDC score key:

A = Normal, B = Nearly normal, C = Abnormal, D = Severely abnormal.

[b]Instrumented laxity testing — This test may refer to the KT-1000 measure, although the specific details of the test were not provided.

Table 4 Summary of the Liu et al. (2010) study

Study component	Description
Objectives/ hypotheses	To compare the outcomes after ACL reconstruction using either a 4SHG or a LARS and assess the effectiveness of the 2 grafts.
Study design	Retrospective cohort study.
Setting	Patients having ACL reconstruction surgery January 2003–July 2004. All procedures were performed by the same surgeon. Mean follow-up 49 months.
Inclusion/ exclusion criteria	All patients who had surgery for an ACL rupture during the recruitment period were considered for inclusion. Exclusion criteria were a combined ligament injury, radiographically visible degenerative changes, previous knee surgery history, contralateral knee ligament injury and less than 4 years' follow-up.
Primary outcomes	Lysholm score, Tegner score, IKDC score and KT-1000 evaluation.
Statistical methods	Pre-operative treatment group characteristics and post-operative outcomes compared statistically. Continuous variables analysed by the unpaired Student's t-test, nominal data analysed by chi-square test and categorical variables analysed by Wilcoxon test. Statistically significant differences at $p<0.05$.
Participants	n=32 in 4SHG group and n=28 in the LARS group, with no statistical differences across gender, age, cause of injury, mean time to surgery, Lysholm score and Tegner score.

Results: Lysholm score, (mean±SD)	4SHG group: • pre-operatively: 43.8±6 • post-operatively: 92.1±7.9 LARS group: • pre-operatively: 44.9±7.6 • post-operatively: 94.6±9.2 This difference was not statistically significant across the 2 groups (p>0.05).
Results: Tegner score, (mean±SD)	4SHG group: • pre-operatively: 3.2±0.4 • post-operatively: 6.2±1.6 LARS group: • pre-operatively: 3.7±0.6 • post-operatively: 6.6±1.8 This difference was not statistically significant across the 2 groups (p>0.05).
Results: IKDC score[a] (post-operative only)	4SHG group: A=22, B=6, C=4, D=0 LARS group: A=21, B=5, C=2, D=0 This difference was not statistically significant across the 2 groups (p>0.05).
Results: KT-1000, (mean mm±SD)	4SHG group: 2.4±0.5 mm LARS group: 1.2±0.3 mm LARS group had statistically significantly less anterior displacement than 4SHG group (p=0.013).
Results: Adverse events	2 patients (6.2%) in the 4SHG group lost 5° of full flexion and a third (3.1%) developed arthrofibrosis; 1 patient (3.6%) in the LARS group needed removal of a tibial screw because of pain.

Conclusions	Authors concluded functional outcomes were improved with both LARS and 4SHG. Patients in the LARS group displayed higher knee stability than those in the 4SHG group.
Abbreviations: 4SHG, 4-strand hamstring tendon graft; ACL, anterior cruciate ligament; IKDC, International Knee Documentation Committee; n, number of patients; SD, standard deviation. [a]IKDC score key: A = Normal, B = Nearly normal, C = Abnormal, D = Severely abnormal.	

Table 5 Summary of the Pan et al. (2013) study

Study componen	Description
Objectives/ hypotheses	To compare 4-year outcomes of ACL reconstruction using arthroscopic surgery and BPTB autografts or LARS.
Study design	Retrospective cohort study.
Setting	Patients treated for a ruptured ACL July 2004–March 2006. All procedures were performed by the same surgeon. Mean follow-up was 50 months.
Inclusion/ exclusion criteria	Included patients had an ACL rupture, possibly with meniscal and/or cartilaginous injury. Patients with previous knee surgery, contralateral knee ligament injury, osteoarthritis or infection were excluded. 62 patients met the inclusion criteria and were allocated to groups based on patient preference.
Primary outcomes	Lysholm knee scoring scale, Tegner score, IKDC score and KT-1000 evaluation.
Statistical methods	Continuous variables were analysed by the unpaired Student's t-test, nominal data were analysed by the chi-square test and categorical variables were analysed by the Wilcoxon-signed rank test. Statistically significant differences at $p<0.05$.

Participants	n=30 in the BPTB group and n=30 in the LARS group, with no statistical differences across gender, age, time to operation, Lysholm score, Tegner score and IKDC score.
Results: Lysholm score, (mean±SD)	BPTB group: • pre-operatively: 46.30±11.53 • post-operatively: 93.13±9.03 LARS group: • pre-operatively: 44.66±11.89 • post-operatively: 94.09±6.75 This difference was not statistically significant across the 2 groups (p>0.05).
Results: Tegner score, (mean±SD)	BPTB group: • pre-operatively: 3.30±0.99 • post-operatively: 5.83±1.18 LARS group: • pre-operatively: 3.00±0.98 • post-operatively: 6.16±1.17 This difference was not statistically significant across the 2 groups (p>0.05).

Results: IKDC score[a]	BPTB group: • pre-operatively: A=0, B=0, C=23, D=7 • post-operatively: A=14, B=12, C=4, D=0 LARS group: • pre-operatively: A=0, B=0, C=22, D=10 • post-operatively: A=19, B=9, C=4, D=0 This difference was not statistically significant across the 2 groups (p>0.05).
Results: KT-1000, (mean mm±SD)	BPTB group: 2.62±2.12 mm LARS group: 2.29±2.03 mm Results not statistically significant across the 2 groups (p>0.05).
Results: Adverse events	There were no reported cases of synovitis or infection in either group. Anterior knee pain occurred in 2 patients (6.7%) from the BPTB group which lasted for around 18 months after surgery.
Conclusions	Authors concluded BPTP and the LARS had similar clinical outcomes at 4 years follow-up and were satisfactory treatment options for ACL rupture.
Abbreviations: ACL, anterior cruciate ligament; BPTB, bone-patellar tendon-bone; IKDC, International Knee Documentation Committee; n, number of patients; SD, standard deviation. [a]IKDC score key: A = Normal, B = Nearly normal, C = Abnormal, D = Severely abnormal.	

Posterior cruciate ligament

Two retrospective cohort studies, both conducted in China, assessed the use of the LARS in posterior cruciate ligament (PCL) reconstruction (Li et al. 2009; Xu 2014). These papers are summarised in tables 5 and 6.

The study by Li et al. (2009) reported that 2-years post-operatively, the Lysholm score,

KT-1000 test and posterior drawer test results for the LARS patients were statistically significantly better than those for autograft patients. The study by Xu et al. (2014), found no statistically significant differences in any of the outcomes measured 51 months post-operatively.

One LARS patient (n=19; 5.3%) in the study by Xu et al. (2014) experienced synovitis and recovered after having an arthroscopic synovectomy. No other complications with the LARS were reported.

Table 6 Summary of the Li et al. (2009) study

Study component	Description
Objectives/ hypotheses	To compare the outcomes of PCL reconstruction using either 4SHG or LARS.
Study design	Retrospective cohort study.
Setting	Patients presented August 2002–March 2006 with chronic PCL rupture. All procedures were performed by the same surgeon. Mean length of follow-up was slightly longer for 4SHG than the LARS at 2.4 and 2.2 years respectively.
Inclusion/ exclusion criteria	All consecutive chronic PCL rupture patients were assessed against inclusion and exclusion criteria. Inclusion required patients to have a symptomatic isolated PCL rupture. Exclusion criteria were combined ligament injury, radiographically visible degenerative changes, contralateral knee ligament injury and follow-up of less than 2 years. 36 of 54 identified patients were included.
Primary outcomes	Lysholm score, Tegner score, IKDC rating, KT-1000 evaluation and posterior drawer test.
Statistical methods	Results from the primary outcomes were tested across the 2 groups using the Wilcoxon signed rank test. Statistical significance was set at $p<0.05$.
Participants	n=15 in 4SHG group; n=21 in the LARS group.

Results: Lysholm score, median (range)	4SHG group: • pre-operatively: 71 (28–99) • post-operatively: 85 (33–100) LARS group: • pre-operatively: 70 (29–95) • post-operatively: 93 (43–100) This difference was statistically significant across the 2 groups ($p<0.05$).
Results: Tegner score, median (range)	4SHG group: • pre-operatively: 2 (1–5) • post-operatively: 6 (1–9) LARS group: • pre-operatively: 2 (1–6) • post-operatively: 7 (2–10) This difference was statistically significant across the 2 groups ($p<0.05$).
Results: IKDC score[a]	4SHG group: • pre-operatively: A=0, B=0, C=6, D=9 • post-operatively: A=8, B=3, C=3, D=1 LARS group: • pre-operatively: A=0, B=0, C=11, D=10 • post-operatively: A=14, B=5, C=2, D=0 This difference was not statistically significant across the 2 groups ($p=0.285$).

Results: KT-1000	4SHG group: • pre-operatively: 0–2 mm, 0; 3–5 mm, 0; 6–10 mm. 0; >10 mm,15 • post-operatively: 0–2 mm, 4; 3–5 mm, 3; 6–10 mm, 6; >10 mm, 2 LARS group: • pre-operatively: 0–2 mm, 0; 3–5 mm, 0; 6–10 mm, 0; >10 mm, 21 • post-operatively: 0–2 mm,10; 3–5 mm, 8; 6–10 mm, 3; >10 mm, 0 This difference was statistically significant across the 2 groups ($p<0.05$).
Results: Posterior drawer test	4SHG group: • pre-operatively: 0–2 mm, 0; 3–5 mm, 0; 6–10 mm, 11; >10 mm, 4 • post-operatively: 0–2 mm, 6; 3–5 mm, 5; 6–10 mm, 4; >10 mm, 0 LARS group: • pre-operatively: 0–2 mm, 0; 3–5 mm, 0; 6–10 mm, 15; >10 mm, 6 • post-operatively: 0–2 mm,16; 3–5 mm, 5; 6–10 mm, 0; >10 mm, 0 This difference was statistically significant across the 2 groups ($p<0.05$).
Results: Adverse events	No patient had immediate post-operative complications. 1 member of each group (6.7% and 4.8%) experienced anterior knee pain. 2 patients (13.3%) in the 4SHG group felt paraesthesia on the medial side of the knee, but recovered within 6 months. 1 knee (6.7%) in the 4SHG group developed arthrofibrosis requiring arthroscopic lysis and manipulation with satisfactory results.
Conclusions	Authors concluded that the LARS was clinically more useful than 4SHG in treating PCL, restoring better knee stability and knee function, with no complications at 2 years. However, longer term follow-up is needed as problems with the LARS graft may occur later.

Abbreviations: 4SHG, 4-strand hamstring graft; IKDC, International Knee Documentation Committee; n, number of patients; PCL, posterior cruciate ligament.

[a]IKDC score key:

A = Normal, B = Nearly normal, C = Abnormal, D = Severely abnormal.

Table 7 Summary of the Xu et al. (2014) study

Study component	Description
Objectives/ hypotheses	To follow patients receiving PCL reconstruction using 4SHG or LARS and compare their clinical results in a long-term follow-up.
Study design	Retrospective cohort study.
Setting	Patients undergoing surgery December 2006–September 2008 by a single surgeon. Mean follow-up of 51 months.
Inclusion/ exclusion criteria	56 patients with PCL reconstruction were eligible for inclusion, of which 21 patients were excluded because of posteromedial or posterolateral corner injuries (11), multi-ligament injuries (8) and bilateral PCL rupture (2). Patients self-selected into treatment groups.
Primary outcomes	Lysholm score, Tegner score, IKDC rating, KT-1000 score and reported complications.
Statistical methods	Treatment groups and outcomes tested for statistical differences. Unpaired Student's t–test was used to analyse continuous variables, chi square test to analyse nominal data and Wilcoxon signed rank test to analyse categorical variables. Statistical significance was set at $p<0.05$.
Participants	n=16 in 4SHG group and n=19 in the LARS group, with no statistically significant differences across age, gender, side of injury and time from injury to surgery.

Results: Lysholm score (mean±SD)	4SHG group: • pre-operatively: 56.2±7.7 • post-operatively: 87.9±7.7 LARS group: • pre-operatively: 58.4±9.8 • post-operatively: 87.0±6.8 The estimated treatment effect was not statistically significant across the 2 groups (p>0.05).
Results: Tegner score (mean±SD)	4SHG group: • pre-operatively: 3.38±0.89 • post-operatively: 6.31±0.79 LARS group: • pre-operatively: 3.21±0.63 • post-operatively: 6.42±0.84 The estimated treatment effect was not statistically significant across the 2 groups (p>0.05).
Results: IKDC score[a]	4SHG group: • pre-operatively: A=0, B=0, C=13, D=3 • post-operatively: A=9, B=6, C=1, D=0 LARS group: • pre-operatively: A=0, B=0, C=12, D=7 • post-operatively: A=10, B=7, C=2, D=0 The estimated treatment effect was not statistically significant across the 2 groups (p>0.05).

Results: KT-1000 (mean mm±SD)	4SHG group: • pre-operatively: 14.03±1.82 • post-operatively: 3.28±1.95 LARS group: • pre-operatively: 13.68±1.49 • post-operatively: 3.27±2.13 The estimated treatment effect was not statistically significant across the 2 groups (p>0.05).
Results: Adverse events	2 patients (12.5%) reported anteromedial knee pain after hamstring autografts, but recovered in a few months. 1 LARS patient (5.3%) developed synovitis post-operatively and received an arthroscopic synovectomy.
Conclusions	Authors concluded that there was no statistically significant difference in clinical endpoints between use of 4SHG or LARS in PCL reconstruction.
Abbreviations: 4SHG, 4-strand hamstring tendon autograft; IKDC, International Knee Document Committee; n, number of patients; PCL, posterior cruciate ligament; SD, standard deviation. [a]IKDC score key: A = Normal, B = Nearly normal, C = Abnormal, D = Severely abnormal.	

Recent and ongoing studies

A search of clinicaltrials.gov and the Australian New Zealand Clinical Trial Registry (ANZCTR) identified no ongoing LARS studies.

The distributor provided details of 2 Australian trials using the LARS for ACL reconstruction:

- An evaluation of outcome measures across rehabilitation of 2 different ACL reconstruction techniques. Aim: to quantitatively measure recovery of function following ACL reconstruction using hamstring reconstruction or the LARS. Patient numbers: hamstring reconstruction, 32; LARS, 32; healthy control, 50. Outcome measures: isokinetic testing, quadriceps strength, hamstring strength, step-down test, physical activity (measured by global positioning system with accelerometer). Status: Recruitment started in February 2012. Data collection is complete with the final report expected in 2015.
- Comparison of hamstring and the LARS hamstring augmentation double-bundle ACL reconstruction: 2, 5 and 10-year follow-up. Aim: to provide mid- to long-term results for patients following ACL repair using double-bundle hamstring reconstruction or double-bundle hamstring reconstruction augmented by the LARS. Patient numbers: double-bundle hamstring reconstruction, 56; double-bundle hamstring reconstruction augmented by the LARS, 56. Outcome measures: International Knee Documentation Committee score; Tegner score; Cincinnati rating system; Lysholm score; Lachman's test; ACL quality-of-life score; ACL recovery score; VAS pain rating; and KT-1000 score. Status: Recruitment started April 2012. Data collection is ongoing, with publication of results expected from 2, 5 and 10-year follow-up points.

Costs and resource consequences

No published evidence on resource consequences was identified.

The distributor, Corin Group, states that the LARS is used widely across NHS trusts, with a total of 1142 LARS synthetic ligaments sold in the UK in 2014. The distributor also estimated that 25% of these ligaments were used in cruciate ligament procedures. Of these, approximately 3% were ACL and 97% were PCL.

One factor that could affect resource use is recovery time following surgery. It has been suggested that people having ligament replacement procedures with the LARS have a shorter rehabilitation and a faster return to pre-injury function (Li et al. 2009; Gao et al. 2010). According to Li et al. (2009) this is because autografts and allografts must go through a process of remodelling, called ligamentisation (Scheffler et al. 2008). The LARS does not undergo this process (Liu et al. 2010) so people who have LARS surgery require less conservative treatment post-operatively. However, current evidence to support this theory is based on small patient numbers in non-comparative studies (Machotka 2010). It is not clear from the available evidence how the claimed faster rehabilitation would impact

on resource use.

Using the LARS in ligament replacement may reduce resource use if it lowers the number of revision procedures needed as a result of graft failure. The Batty et al. (2015) study suggested that revision rates are lower for LARS surgery compared with other synthetic ligaments, although it is not clear if the difference was statistically significant (Batty et al. 2015). There is no clear evidence that revision rates are better for LARS surgeries compared to autografts and allografts. Smith et al. (2014) noted a failure rate of 0.78% for the LARS, which was lower than the rates recorded for autologous hamstring graft reconstruction (1.8–10.1%). However, the follow-up length for the hamstring graft procedures was significantly longer, preventing a direct comparison of these figures.

Strengths and limitations of the evidence

The review by Batty et al. (2015) was a well-conducted systematic review that synthesised the safety and efficacy data for synthetic ligament procedures on more than 1100 knees, reported in published, peer-reviewed studies that were comparative, cohort, and case series of more than 10 patients. The scope was limited to synthetic devices in surgery of ACL or PCL, excluding studies of autograft or allograft procedures. This meant that complication figures were not compiled for autograft and allograft procedures, which are routinely used in current NHS practice, making it difficult to compare between the LARS and standard care. Limitations of the evidence included a paucity of well-conducted, long-term clinical trials and variability and heterogeneity in outcome reporting.

The quality of the efficacy evidence was evaluated using appropriate checklists. Potential sources of bias are summarised in table 8.

Table 8 Assessed sources of potential bias within included studies

Study	Selection bias	Performance bias	Attrition bias	Detection bias
Nau et al. (2002)	Yes	No	No	Yes
Liu et al. (2010)	No	Yes	N/A	Yes
Pan et al. (2013)	Yes	Yes	N/A	Yes
Li et al. (2009)	Yes	Yes	N/A	Yes
Xu et al. (2014)	Yes	Yes	N/A	Yes

The study by Nau et al. (2002), the only randomised trial summarised in this briefing, used a weak randomisation process (sealed envelopes) that could have resulted in selection bias. The distribution of sexes in the groups was also unbalanced; 19% women in the LARS group compared with 44% women in the autograft group. However, this was the only study with the same post-operative rehabilitation protocol for both treatment groups and the same surgeon conducted all the procedures. Together, these factors eliminated major sources of performance bias.

As with all the studies, failure to blind participants may have resulted in detection bias. This is of particular concern for patient-reported measures, such as IKDC and Tegner scores. The correlation between patient-reported satisfaction and clinical measures of knee laxity can be poor (Lavoie et al. 2000; Hyder et al. 1997). This suggests patient-reported measures may be prone to influence, although measures of laxity may also be poor surrogate outcomes. The methods used to collect patient-reported measures in any of the studies were insufficiently detailed in any of the studies included to establish whether there was a risk of detection bias. The small sample size of the Nau et al. (2002) study (n=53) limited the likelihood of detecting statistically significant differences across the groups and pre- and post-operatively.

The study by Liu et al. (2010) was at lower risk of selection bias because it used a temporal cut-off to separate patients. However, this may have introduced procedural confounders, such as change in ward or physiotherapy practice over time. The study was retrospective and patients with incomplete follow-up were excluded prior to analysis, which could have resulted in bias and limited external validity. Performance bias was possible because different post-operative rehabilitation protocols were adopted for the 2 groups, although the same surgeon conducted all procedures. Li et al. (2009) noted that differences arising from alternative rehabilitation programmes should diminish over time, although at what point the effect would be negligible is unknown. Detection bias was also a risk because patients and clinicians were unblinded to the intervention being used. The small sample size in this study made detection of statistically significant differences difficult. Only univariate analysis was used, which did not control for confounding influences.

In the study by Pan et al. (2013) patients chose their preferred treatment regimen, which may have introduced selection bias. The study had a similar potential for performance and detection bias to Liu et al. (2010). No confounding factors were controlled for in the statistical analysis. This was the largest study (n=62) but no power calculations were provided to inform effect size. Incomplete follow-up data was an exclusion criterion, which

limited the generalisability of results.

Li et al. (2009) did not report the allocation method or test for statistically significant differences in the characteristics of treatment groups pre-operatively, introducing a risk of selection bias. The study may also have performance bias, as a result of differing post-operative rehabilitation regimes, and detection bias, because the patients and clinicians were not blinded to the intervention being used. The sample size in this study was small, the follow-up was the shortest of the 5 studies, and only univariate analysis was conducted.

The study by Xu et al. (2014) used a similar methodology to that of Pan et al. (2013), creating risks of selection, performance and detection bias by the same mechanisms. Again, the sample size was small, confounders were not controlled and the external validity may have been limited by the patient recruitment method.

None of the included studies followed patients beyond 5 years. Longer-term outcomes and rates of complications cannot be evaluated on the basis of these included studies.

Relevance to NICE guidance programmes

NICE has issued interventional procedure guidance on partial replacement of the meniscus of the knee using a biodegradable scaffold.

NICE guidance on knee cartilage defects – autologous chondrocyte implantation is in development and is expected to be published in 2015. Guidance on cutting blocks for total knee arthroplasty has been announced, but currently has no anticipated publishing date.

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Search strategy and evidence selection

Search strategy

The search strategy was designed to identify evidence on the clinical and cost effectiveness of the LARS ligaments in patients undergoing reconstruction of knee ligaments.

The strategy was developed for MEDLINE (Ovid interface). The strategy was devised using a combination of subject indexing terms and free text search terms in the title, abstract, and keyword heading word fields. The search terms were identified through discussion within the research team, scanning background literature, browsing database thesauri and use of the PubMed PubReminer tool. The strategy reflected the nature of the MIB assessments as rapid evidence reviews.

The search comprised 2 concepts:

1) Population: patients undergoing reconstruction of knee ligaments

2) Intervention: Ligament Augmentation & Reconstruction System (LARS).

The search concepts were combined as follows: Population AND Intervention.

Additional search lines focusing on brand name, and manufacturer name combined with ligament terms, were also used. These lines were designed to capture any records that

may have been missed by the 2 concept approach.

The strategy excluded non-English language publications. Animal studies were also excluded using a standard algorithm. No additional filters for study design were applied. Results were limited to studies published from 1990 (according to the Corin Group website, the LARS was first introduced in 1992).

The final MEDLINE strategy was peer-reviewed by an independent information specialist. The MEDLINE strategy was translated appropriately for the other databases searched. The PubMed search was limited to records which were not fully indexed on MEDLINE. Conference-related papers were excluded from the Embase search.

The following databases were searched:

- Cochrane Central Register of Controlled Trials (Cochrane Library, Wiley)
- Cochrane Database of Systematic Reviews (Cochrane Library, Wiley)
- Database of Abstracts of Reviews of Effects (Cochrane Library, Wiley)
- Embase (Ovid SP)
- Health Technology Assessment Database (Cochrane Library, Wiley)
- MEDLINE and MEDLINE in Process (Ovid SP)
- NHS Economic Evaluation Database (Cochrane Library, Wiley)
- PubMed.

Evidence selection

A total of 976 studies were retrieved from the literature search. After de-duplication, 659 records remained. Two reviewers independently evaluated titles and abstracts against the exclusion criteria. Disagreement was solved through discussion between the reviewers and, if necessary, discussion with a third reviewer. In total 649 papers were removed, after evaluation against the following inclusion and exclusion criteria:

Inclusion criteria:

- Use of the LARS in knee ligament reconstruction in an acute care setting.
- Comparative studies which include autogenous and/or allogenous ligament reconstruction.
- Paper reports some form of outcome.

Exclusion criteria:

- Non-English-language studies.
- Conference abstracts.
- Review protocols (for example, Cochrane review protocols).
- Articles if neither the abstract not the full text is available online.

Full records were retrieved for the remaining 10 papers, and a second sift was undertaken by the same reviewers. No papers were excluded at this stage.

All papers were assessed for methodological quality using the checklists provided within the NICE guidelines manual: appendices B-I. Three systematic reviews were included in the selected papers (Machotka et al. 2010; Mulford et al. 2011; Newman et al. 2013), but these only provided narrative synthesis of the available evidence and included single-arm case studies. Given the quality of clinical evidence is higher with comparative studies, it was decided to include only the higher quality comparative studies, thereby excluding these systematic reviews. After the assessment of quality, 1 paper (Patrascu et al. 2014) was not included in the clinical evidence section, because of poor reporting of methods and outcomes.

One additional paper (Batty et al. 2015) was submitted by the distributor and judged appropriate for inclusion in this review. This was a well-conducted systematic review of safety outcomes that included 20 papers on 1102 knees. Several included papers compared the LARS to autograft or allograft procedures.

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Development of this briefing

This briefing was developed for NICE by Newcastle and York External Assessment Centre. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

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Specialist commentators

The following specialist commentators provided comments on a draft of this briefing:

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