NICE advice

PROPATEN heparin-bonded vascular graft for peripheral arterial disease

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Summary

The Gore PROPATEN heparin-bonded vascular graft is a synthetic graft used to treat peripheral arterial disease by bypassing damaged blood vessels. The graft is made from expanded polytetrafluoroethylene (ePTFE) that has a layer of heparin anticoagulant bonded to its inner surface, which is designed to reduce graft occlusion. Relevant evidence was limited and consisted of 1 randomised controlled trial and 5 cohort studies, with either artificial graft or autologous vein graft comparators. The reports indicate that the PROPATEN graft is either equivalent or inferior to autologous vein grafts in maintaining patency (that is, remaining open and functional over time). In scenarios where vein grafts could not be used, PROPATEN performed at least as well or better than other types of artificial graft. The manufacturer declined to provide the cost of a PROPATEN graft. Based on similar products, and expert advice, the likely cost of a PROPATEN graft is estimated to be between £600 and £1000, excluding VAT.

Product summary and likely place in therapy	Effectiveness and safety
• The Gore PROPATEN heparin-bonded vascular graft is a synthetic graft used to treat peripheral arterial disease. • It would be used as an alternative to currently available synthetic peripheral vascular grafts to maintain effective blood flow to the lower limbs. Current practice varies in the choice of artificial grafts, which are typically used only when an autologous graft is unavailable.	• The evidence is of limited quality and based on 6 studies, including approximately 1124 patients who had PROPATEN grafts. • Patency rates were used as a surrogate end point in all studies, with some studies also reporting more relevant clinical outcomes. In addition, patency rates are known to vary depending on whether the bypass extends beyond the knee, so study findings, which did not generally distinguish between above- and below-knee procedures, may not be directly comparable. • The PROPATEN graft was reported to have lower primary patency than autologous saphenous vein (ASV) grafts in 1 cohort study, and 2 cohort studies reported no statistically significant differences. • The PROPATEN graft showed a better primary patency rate than other prosthetic grafts in 1 randomised controlled trial, but 3 cohort studies found no differences. • Safety issues were not consistently reported.

Technical and patient factors	Cost and resource use
• The PROPATEN graft has a layer of heparin anticoagulant bonded to its inner surface, designed to reduce graft occlusion. • The PROPATEN graft would be used in secondary care by suitably qualified clinicians, experienced in peripheral vascular bypass graft procedures. • The PROPATEN graft is available in a range of configurations which vary in length, internal diameter and structural features such as wall thickness and presence or absence of reinforcing rings.	• The manufacturer declined to provide the cost of a PROPATEN graft. Based on similar products, and expert advice, the likely cost of a PROPATEN graft is estimated to be between £600 and £1000 excluding VAT. • One cohort study described longer procedure lengths using the PROPATEN graft with a distal vein patch when compared with a pre-cuffed prosthetic graft. The randomised trial reported no differences in procedure lengths between using the PROPATEN graft and a standard PTFE graft. • Two cohort studies reported that post-procedure hospital stays were longer with the PROPATEN graft compared with ASV grafts ($p<0.001$) and another artificial graft (no statistical comparison reported). • Any graft that reduces the need for repeated interventional procedures could reduce long-term treatment costs.

Introduction

Peripheral arterial disease (PAD) is a form of cardiovascular disease caused by a build-up of fatty deposits in the arterial walls of the leg. These fatty deposits, called atheroma, narrow the arteries in a process known as atherosclerosis. PAD is estimated to affect 1 in 5 people aged over 60 years in the UK and its incidence increases with age, according to NICE's quality standard on peripheral arterial disease. It is more common in people with diabetes, high blood pressure or high cholesterol, and in those who smoke. PAD is more common in men, with an overall incidence of 8.2% compared with 5.5% in women (Kroger et al. 2006).

Although some people with PAD may have no symptoms, it often causes muscle pain and

aching (known as claudication) in the affected leg. PAD can cause severe claudication, making walking painful and reducing quality of life. In approximately 1 in 5 people with PAD, the narrowing of the arteries leads to increasingly severe symptoms with the development of critical limb ischaemia. Symptoms of critical limb ischaemia include gangrene and ulcers (NHS Choices) and it is the most common cause of leg amputation in the UK.

PAD is also a risk factor for other cardiovascular events, such as heart attack and ischaemic stroke; people with PAD have a 3–4-fold increased risk of such an event.

Peripheral vascular grafts are used during vascular bypass procedures, which are done to restore blood flow to the lower limbs. This is achieved through bypass of the diseased (blocked) portion of the blood vessel with a portion of healthy vessel or, if no healthy vessels are available, with an artificial graft.

During bypass surgery, a healthy vein is taken from another part of the leg and joined, or grafted, above and below the blocked artery. This procedure, referred to as an autologous graft, allows the flow of blood to be rerouted to avoid the blockage and maintain an efficient blood supply. A vascular surgeon assesses whether a vein is available and suitable for the procedure. Autologous grafts have a lower failure rate than prosthetic grafts and are used wherever possible. However, when it is not feasible to use a healthy vein, an artificial graft may be used. PTFE is commonly used in the manufacture of artificial grafts.

Reduction in the patency of grafts can lead to graft failure. Early failure (within the first 30 days) is usually due to technical issues. A common cause of mid-term (1–18 months) graft failure is thrombosis resulting from neointimal hyperplasia (NIH), an accumulation of vascular smooth muscle cells at the furthest attachment of the graft (the distal anastomosis). NIH causes thickening of the graft walls and narrowing of the vessel, which reduces blood flow and can lead to graft failure. Late failure (after more than 18 months) is usually due to progression of atheroma above or below the graft.

Factors that could affect patency rates include the location of the distal anastomosis and run-off, severity of disease, use of adjuvant techniques and compliance with medications, previous intervention, sex and smoking status.

Further surgery may be needed to salvage or re-open the graft using techniques such as endovascular thrombolysis, angioplasty, stent placement or mechanical thrombectomy to restore blood flow. If this is unsuccessful, and if all other revascularisation options have

been exhausted, the affected limb may have to be amputated. Artificial grafts that are designed to reduce the risk of thrombosis may be less prone to failure than standard prosthetic grafts.

The anticoagulant drug heparin is widely used to prevent clot formation and to treat the symptoms associated with PAD and other thrombotic diseases. patients with PAD may have systemic (whole-body) anticoagulants to protect against cardiovascular events such as stroke or heart attack, although they carry some risk of causing excessive bleeding. In recent years, heparin has also been bonded directly to artificial grafts. The aim is to prolong graft patency by making use of heparin's antithrombogenic properties to reduce the risk of graft occlusion. It is also thought that heparin may reduce or delay the development of NIH (Daenens et al. 2009, Dorigo 2012).

A potential concern about the use of heparin to coat vascular grafts is the possible development of an adverse drug reaction called heparin-induced thrombocytopaenia (HIT). HIT type 1 is benign and not associated with an increased risk of thrombosis but HIT type 2 is caused by an immune response to heparin, leading to clumping and trapping of platelets. It is associated with significant morbidity and mortality if untreated. The incidence of HIT type 2 is rare.

Kasirajan (2012) evaluated 27 cases of suspected HIT following implantation of PROPATEN heparin-bonded grafts. He concluded that the graft does not appear to induce an immune response associated with the development of HIT, and that this complication was more likely attributable to the systemic administration of heparin.

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

CE marking

WL Gore & Associates first received a Class III CE mark for the Gore PROPATEN

heparin-coated vascular graft ('PROPATEN graft') in May 1999. The current certificate is effective from 16 November 2014, and is valid until 15 November 2017.

The associated Declaration of Conformity is dated 10 March 2011, and the Design Examination Certificate is effective from 3 May 2014 (valid until 2 May 2019).

Description

The PROPATEN graft is an artificial vascular graft made from ePTFE and coated on the inner (luminal) surface with low molecular weight heparin (CBAS 2-heparin). The graft incorporates stretch technology which is intended to improve anastomotic compatibility, length forgiveness and kink resistance.

PROPATEN grafts are available in a range of configurations and sizes:

- Standard-walled or thin-walled – Thin-walled PROPATEN grafts are approximately 40% thinner than standard walled grafts and may be used because of their similarity to the host vessel.
- Fixed rings, removable rings, or without rings – Integrated rings provide low-profile radial support. Removable rings are attached to thin film so that they can be removed without damaging the graft.
- Internal diameters ranging from 5–8 mm or tapered (from 6–4 mm or 7–4 mm).
- Ringed section lengths of 5, 30, 40, 60 or 70 cm.
- Standard lengths of 10, 20, 40, 45, 50, 60, 70, 80 or 90 cm.

The grafts can be cut to the appropriate length at an anastomotic angle to suit the procedure being performed.

Setting and intended use

The PROPATEN vascular grafts are intended for use as vascular prostheses for replacing or bypassing diseased vessels in patients with occlusive diseases. The scope of this briefing is the PROPATEN graft for treating PAD.

The grafts are designed to be used in the secondary care inpatient setting. They are intended only to be used by suitably qualified clinicians who are experienced in peripheral

vascular bypass procedures. Their use is contraindicated in patients with known sensitivity to heparin, including patients who have had a previous (or existing) incident of HIT type 2.

Current NHS options

Lifestyle changes for people with PAD are described in the NICE guideline on prevention of cardiovascular disease and drug interventions are described in the NICE technology appraisal guidance on cilostazol, naftidrofuryl oxalate, pentoxifylline and inositol nicotinate for the treatment of intermittent claudication in people with peripheral arterial disease.

Surgical procedures, including angioplasty and bypass grafts, are additional treatment options for PAD. These aim to restore the flow of blood through the arteries of the legs, known as revascularisation. Angioplasty is a method where the narrowed area of the artery is widened by a small balloon which is inflated inside the vessel. Sometimes a 'stent' or small mesh tube may be left in place to keep the artery open.

Bypass surgery may be offered to people with severe lifestyle-limiting intermittent claudication when angioplasty has been unsuccessful or is unsuitable, and where imaging has confirmed that it is appropriate. It may also be used in people with critical limb ischaemia needing revascularisation. NICE's guideline on lower limb peripheral arterial disease recommends that an autologous vein should be used whenever possible. A range of synthetic grafts is currently available to the NHS and current practice varies in the choice of graft.

NICE has also issued interventional procedures guidance on percutaneous laser atherectomy as an adjunct to balloon angioplasty (with or without stenting) for peripheral arterial disease.

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

- Hybrid vascular graft (Gore), featuring a nitinol reinforced section and heparin bonding (Carmeda BioActive Surface)
- Flowline BIPORE HEPARIN ePTFE vascular graft (Jotec)
- FUSION BIOLINE vascular grafts (Maquet), made of ePTFE and polyethylene terephalate (PET) with a heparin coating

- INTERGARD heparin vascular graft (Atrium), made of PET
- Vascutek Gelsoft Plus (Terumo) gelatin-sealed knitted polyester vascular graft, with temporary heparin activity of up to 4 days.

Costs and use of the technology

The manufacturer declined to provide the cost of a PROPATEN graft. Based on similar products, and expert advice, the likely cost of a PROPATEN graft is estimated to be between £600 and £1000 excluding VAT. For similar products, the cost varies depending on the size, shape and length.

According to the manufacturer, no additional or special training, equipment or support is needed in order to use the device. Optional educational programmes are available.

The lifespan of the technology is dependent on the functionality of the graft. Grafts with higher patency rates are less likely to need repeated interventional procedures and will therefore reduce overall costs to the NHS.

In England in 2013–14, 4285 bypass procedures of the femoral artery were done, including 330 emergency procedures. Of these, 2542 used autologous vein grafts and 810 used prosthetic grafts (HSCIC 2015).

The payment by results tariff for 2013–14 (Department of Health 2013) has been provided below for information. The NHS tariffs for outpatient attendance relating to consultant-led vascular surgery services (service code 107) are:

- first attendance: £156 (WF01B/WF02B)
- follow-up attendance: £93 (WF01A/WF02A).

The NHS costs for combined day case or ordinary elective spells (Payment by Results 2013–14) are:

- bypasses to tibial arteries: £8266 (HRG code, QZ03Z)
- amputations without complications and co-morbidities: £7625 (HRG code, QZ11B)
- amputations with complications and co-morbidities: £14,724 (HRG code, QZ11A).

The costing report for the NICE guideline on lower limb peripheral arterial disease suggests that amputation may be offered when revascularisation options such as bypass cannot control critical limb ischaemia. It estimates that in addition to the procedure itself, the cost of care to the NHS is approximately £20,000 per patient in the year following an amputation.

Likely place in therapy

The PROPATEN graft could be used for patients with PAD needing a synthetic bypass graft. Use of the device is not expected to change the current clinical pathway.

Specialist commentator comments

One specialist commentator noted that there was a wide range of study designs and outcomes. No individual study was thought to be sufficiently powerful to be considered definitive. Two specialist commentators emphasised the importance of differentiating between results for above- and below-knee femoropopliteal bypasses. It was suggested that the device should be evaluated in the context of historical data relating to other types of heparin-bonded graft.

Three specialist commentators concluded that the overall performance of the PROPATEN graft was not as good as ASV grafts, but in most clinical scenarios it provided an outcome that was similar to that of standard (that is, non-heparin-bonded) ePTFE grafts. One specialist commentator suggested that there may be a higher long-term risk of amputation with PTFE compared with heparin-bonded PET, but that this has not yet been established.

One specialist commentator observed that in patients with an unsuitable or absent vein because of previous peripheral vascular surgery, the PROPATEN graft appears to be inferior to a Distaflo with vein patch in tibial bypasses. One specialist commentator advised that use of any prosthetic graft to bypass the arteries of the calf may rarely, if ever, be justified.

One specialist commentator suggested that the use of heparin-bonded grafts might reduce the number of subsequent revisions needed, which could ultimately reduce pressure on the healthcare system. One specialist commentator noted that information about the relative costs of the PROPATEN grafts and other comparator grafts would help to inform decision-making.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. In producing guidance, NICE aims 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 (these are protected characteristics under the Equality Act 2010).

PAD is more common in people over the age of 60 years and affects more men than women. people with diabetes have an increased risk of developing PAD, and diabetes is recognised as a long-term health condition that may cause disability.

The heparin that is used in the PROPATEN graft is of porcine origin. A number of religious groups are prohibited from contact with the flesh of pigs, and some patients may be opposed to the use of a heparin-coated product.

Age, sex, disability and religion (or belief) are protected characteristics under the Equality Act 2010.

Evidence review

Clinical and technical evidence

Regulatory bodies

The manufacturer was not able to locate any records of a Field Safety Notice having been submitted to the Medicines and Healthcare Products Regulatory Agency (MHRA). A search of the MHRA website between 12 January 2015 and 31 July 2015 revealed no manufacturer Field Safety Notices for this device (MHRA 2015).

A search of the US Food and Drug Administration (FDA) database: Manufacturer and User Device Facility Experience (MAUDE) identified 307 medical device reports relating to

PROPATEN grafts. There were 57 reports determined to be relevant to the scope of this briefing, based on the clinical indication and the anatomical location of the graft (see appendix for details of the analysis). The following adverse events were noted.

Table 1 Adverse events relating to PROPATEN grafts

Adverse event	N	Outcome	n
Occlusion/thrombosis	6 + 35*	Amputation	4
		Stent insertion	1
		Not reported	1 + 35*
Infection	4	Graft removed or replaced	2
		Debridement and irrigation	1
		Death (resulting from sepsis)	1
Infection/'allergic reaction'/graft rupture	1	Graft partially removed and replaced	1
Bleeding and graft infection	1	Amputation	1
Occlusion and infection	1	Not reported	1
Pain and erythema	1	Graft removed	1
Heparin-induced thrombocytopaenia**	1	Graft replaced	1
Compartment syndrome	1	Not reported	1
Seroma/fluid accumulation	3	Amputation	1
		Graft removed	1
		Drainage	1
Complex history involving occlusion of other grafts (not PROPATEN)	1	PROPATEN graft replaced	1
Not reported	2	Amputation	2

Total	**57**
* These 35 patients were reported in Dorigo et al. (2012), which has been reviewed in this briefing. ** This patient had a history of HIT, and received systemic heparin at the time of graft insertion.	

It should be noted that the MAUDE database is a passive surveillance system and potentially includes incomplete, inaccurate, untimely, unverified or biased data. The incidence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about frequency of device use (FDA, 2015).

Clinical evidence

A literature search identified 98 studies of potential relevance to the PROPATEN graft, of which 59 were excluded from further assessment because they did not meet the inclusion criteria. The full text of 39 studies was requested. The manufacturer identified 6 other studies which were considered for inclusion.

Six studies were included in the final selection for this briefing, based on the following criteria:

- Study design – Due to the large number of relevant studies, only randomised controlled trials and other comparative studies were considered for inclusion.
- Comparator – Of the comparative studies, all those comparing PROPATEN grafts with other types of prosthetic grafts were included. Of those comparing PROPATEN grafts with ASV grafts, all multisite studies and studies with more than 200 patients were included.
- Multiple comparators – One additional study identified by the manufacturer was included. This was the only 3-arm study identified (comparing PROPATEN grafts with standard ePTFE and ASV grafts).

Details of the 6 included studies and results can be found in tables 1–12 in the appendix.

Study outcome definitions and results

All of the studies describe outcomes in terms of patency, which is used as a surrogate outcome. Patency describes whether a graft remains open and functional over time. Primary patency refers to grafts or vessels that remain patent over time, or that have limited re-stenosis that has not needed further intervention. Secondary patency describes grafts or vessels that are currently patent, including those which have previously occluded and had an intervention to restore patency. Some studies also reported more relevant clinical outcomes such as limb salvage and survival.

The randomised controlled trial reported by Lindholt et al. (2011) enrolled patients with intermittent claudication or critical lower limb ischaemia from 11 Scandinavian vascular centres between 2006 and 2009. Randomisation of patients at a ratio of 1:1 was stratified by the centres. Included patients had a clinical indication for a femoral-femoral crossover or femoropopliteal bypass (above or below the knee) with an artificial graft. Informed consent was obtained from each patient before implantation.

The authors compared the patency of 272 PROPATEN grafts with that of 274 standard PTFE grafts (without heparin bonding). There was a significant difference in primary patency rates, with 86% (235/272) of PROPATEN grafts and 80% (219/274) of standard PTFE grafts remaining patent at 1-year follow-up (odds ratio [OR] 0.627, 95% confidence interval [CI] 0.398 to 0.989, p=0.04). Secondary patency rates after 1 year were not significantly different, at 88% (240/272) for PROPATEN grafts and 81% (222/274) for standard PTFE grafts (odds ratio 0.569, 95% confidence interval 0.353 to 0.917, p=0.020).

The retrospective cohort study by Bellosta et al. (2013) compared the PROPATEN graft (used with a distal vein patch, n=40) with a pre-cuffed PTFE graft (Distaflo, n=39) at a single site. At 24 months' follow-up, primary patency rates were not significantly different (p=0.793), with rates of 33% (95% CI 21 to 53) for the PROPATEN group and 47% (95% CI 32 to 70) for the comparator group. Similarly, secondary patency rates at 24 months were not significantly different (p=0.855) between the PROPATEN group (36%, 95% CI 23 to 57) and the comparator (49%, 95% CI 33 to 72).

Bechara (2014) reported primary and secondary patency rates of the PROPATEN graft (n=39) compared with a Spiral Laminar Flow graft (SLFG; n=20). Results were reported separately depending on bypass location (femoropopliteal or femorotibial) at regular intervals of 6, 12, 18 and 24 months. Primary patency rates for femoropopliteal bypasses at 24 months were 54% for PROPATEN and 50% for SLFG; at 18 months, the rates were

37% for PROPATEN and 17% for SLFG. Secondary patency rates for femoropopliteal bypasses at 24 months were 66% (PROPATEN) and 57% (SLFG); at 18 months, the rates were 34% (PROPATEN) and 20% (SLFG). Details of statistical significance were not provided, but the author reported that the groups were not significantly different at each of the intervals, regardless of the distal target artery.

Dorigo et al. (2012) conducted a non-randomised retrospective review of records from 7 vascular centres in Italy, comparing PROPATEN grafts (n=556) with ASV grafts (n=394). There were significant differences in primary patency at 48 months, with PROPATEN rates of 45% and ASV rates of 61% (p=0.004). Secondary patency rates at 48 months were not significantly different (p=0.1), with rates of 57% for PROPATEN grafts and 68% for ASV grafts.

The non-randomised retrospective cohort study by Daenens et al. (2009) compared heparin-bonded ePTFE grafts (n=240) with ASV grafts (n=110) in femoropopliteal and femorocrural bypasses after 1 and 2 years at a single hospital site. patients in the 2 groups followed a similar postoperative regimen. Although PROPATEN grafts were not specifically named in the methods, they were referred to in the introductory paragraph. The same authors also contributed to the multicentre non-comparative PEPE II study (including PROPATEN grafts) in the same period (Hugl et al. 2009).

Daenens et al. (2009) reported results separately according to subgroup (above-knee femoropopliteal, below-knee femoropopliteal, and femorocrural bypasses). For all subgroups, primary patency after 2 years was not significantly different between the 2 types of graft (p>0.05). The patency rates for PROPATEN grafts were 83% for above-knee femoropopliteal, 83% for below-knee femoropopliteal and 69% for femorocrural; for the ASV grafts, the corresponding rates were 80%, 72% and 69%.

Secondary patency rates were not reported. There were no significant differences in disease severity (critical ischaemia or claudication) in any of the subgroups (p>0.4), with 1 exception. In below-knee femoropopliteal bypasses for critical ischaemia, primary patency rates at 1 and 2 years were significantly better (p=0.02) with PROPATEN grafts (90% and 61%) than ASV grafts (76% and 55%).

In some cases an adjuvant technique (such as vein patch or arteriovenous fistula) was used during PROPATEN insertion; the authors demonstrated that this did not significantly affect patency in the below-knee subgroups (p>0.5). There were more secondary interventions at the femorocrural site in the PROPATEN group (61%, 59/97) than in the ASV

group (24%, 12/50), but this did not influence patency at 1 and 2 years (p=0.5).

Results from 49 of the patients in the Dorigo et al. (2005) paper may have also been included in the larger (n=950) Italian multicentre study previously described (Dorigo et al. 2012). However, the Dorigo et al. (2005) study was the only report that included multiple comparators, and therefore was also considered to be of interest. In this study, PROPATEN grafts (n=24) were compared with both ASV (n=25) and standard ePTFE grafts (n=21).

In terms of early graft thrombosis (at 30 days), there were no significant differences (p=0.4) between PROPATEN (21%, 5/24) and ASV (12%, 3/25), but both performed significantly better than standard ePTFE grafts (48%, p<0.01).

Estimated primary patency at 18 months was significantly better in the ASV group (75%) than in the ePTFE group (40%, p=0.01). The difference between ASV and PROPATEN (53%) is of borderline statistical significance (p=0.05), although the authors reported this difference as significant. The estimated primary patency rates for PROPATEN and the ePTFE group were not significantly different (p=0.07).

Recent and ongoing studies

No ongoing or in-development trials on PROPATEN heparin-bonded vascular graft for PAD were identified.

A comparison of primary patency between PROPATEN vascular grafts and thin-walled GORE-TEX Stretch vascular grafts is listed on ClinicalTrials.gov as having been completed in August 2007, but no study results were posted (trial identifier: NCT00205790).

A study comparing the primary patency between PROPATEN vascular grafts and disadvantaged autologous vein grafts for below-knee arterial bypass (PRODIGY) was terminated in January 2011 by the manufacturer (Gore), due to low enrolment (trial identifier: NCT00617279).

Costs and resource consequences

PROPATEN grafts are currently used in the NHS. No published UK evidence on resource consequences was identified from literature searches.

The graft can be used as an alternative to standard ePTFE grafts and no additional

resources would be needed before or during the bypass procedure.

There is some evidence that the duration of the bypass procedure may vary depending on the type of graft used. The Bellosta et al. (2013) study reported significantly longer operating times with PROPATEN grafts (with a distal vein patch) than with a pre-cuffed ePTFE graft (215 minutes compared with 138 minutes; 95% CI 45 to 118 minutes, $p<0.001$). However, the Lindholt et al. (2011) trial observed no differences in operation time between PROPATEN grafts and standard PTFE grafts, though no supporting data were provided.

In their discussion, Daenens et al. (2009) note that ASV graft procedures are more complex than synthetic graft procedures, with more incisions (of larger size) and longer operating times. However, in the absence of references or supporting data, these observations should be considered with the same caution that applies to any anecdotal evidence.

Dorigo et al. (2012) noted significant differences in the mean post-operative length of stay for patients who had PROPATEN grafts (13.1 days) compared with patients who had ASV grafts (10.2 days, $p<0.001$). A comparison of the PROPATEN graft (with a distal vein patch) and a pre-cuffed ePTFE graft reported lengths of stay as 11.8 days and 11 days respectively (Bellosta et al. 2013). A statistical calculation was not reported. PROPATEN grafts are used in the same way as other prosthetic grafts so additional training is not essential, although the manufacturer does offer optional training if desired.

Strengths and limitations of the evidence

The quality of the included studies was generally weak. The evidence consisted of 1 randomised controlled trial (which was both conducted and reported poorly), and retrospective cohort studies (which are subject to selection bias). Three of the studies are limited by relatively small sample sizes at single sites, with the number of patients totalling less than 100 in each study. Three other studies, 2 of which were multicentre studies, had stronger sample sizes (total numbers of 350 to 950 patients).

The primary outcome was not specified by the authors of the cohort studies, and primary patency was evaluated as the primary effect in the clinical trial. Patency as a surrogate endpoint may not be as relevant as direct clinical outcomes such as limb salvage or survival. These clinical outcomes were inconsistently reported.

The literature search only identified 1 randomised controlled trial (Lindholt et al. 2011),

which compared PROPATEN grafts with standard PTFE grafts. Neither the conduct nor the reporting of this study was robust. Randomisation was not done correctly at some sites; it is not clear how many patients were affected. patients were not stratified by disease severity (critical ischaemia or claudication) or type of bypass (femoral-femoral crossover or femoropopliteal), which the authors acknowledged as a limitation of the design. Similarly the authors did not differentiate between those bypasses that terminated above or below the knee. This is of relevance, because it is widely recognised that patency rates for below-knee grafts are considerably worse than those for below-knee grafts (Twine and McLain 2010). No differences were found between baseline variables, but it is not clear whether unknown confounders could have resulted in a selection bias.

Although the authors report application of an intention-to-treat methodology, some patients were excluded. It is not clear how many patients from each group were lost after randomisation. The data presented by the authors are inconsistent and there are some miscalculations. After having treatment, it is reported that 7 patients were lost to follow-up and 4 died before follow-up, but there is no indication of which study arm they were in. A further 14 patients had been excluded, for reasons such as 'use of wrong graft' and 'technical errors', again with no record of the treatment arm. A flow diagram suggested that these exclusions were made after randomisation and before the operation, but it would seem more likely that these were post-surgery effects.

There were slight differences in the appearance of the 2 grafts, meaning that the attempted blinding of surgeons was ineffective in at least some of the cases, although assessors of outcomes were blinded. It is not known if all vascular grafts of the 'standard PTFE' type were the same, because the device and manufacturer is not reported.

The described lengths of follow-up add further confusion. Average lengths of follow-up were reported as 9.75±3.79 months (PROPATEN) and 10.30±3.35 months (standard PTFE), but the authors also assert that all 546 included patients had follow-up data for the assessment of 1-year primary patency. This suggests there may have been some additional attrition bias that has not been acknowledged. The authors also note that 1 year may not be a sufficient length of follow-up to determine whether the heparin-bonding maintains its effects over time.

The authors noted that a 'surprisingly high' number of silent occlusions were detected at the 1-year follow-up appointment. Because of this, planned Cox regression analyses were changed to logistical regression analyses, and supplemental analyses were introduced to adjust for differences in indication and bypass type (though not above-/below-knee

results). The reported significant difference in primary patency between the 2 graft types was lost once these adjustments had been made.

Not all outcomes were adequately reported. Perioperative bleeding was only mentioned in the abstract. There was a reference to the influence of 'prosthetic infections' on statistical analyses, but no details of how many there were or which patients were affected. It is not known whether other adverse events occurred. Finally, throughout the text and the tables there were many reporting errors and inconsistencies. It is probable that these problems will have affected the validity of the results, which should be interpreted with a high level of caution.

All retrospective studies may, by their nature, have been affected by performance bias and detection bias due to the lack of blinding. Selection bias is another common flaw of these non-randomised studies. This is less of a risk in those instances where the analyses have taken all important confounders into account, but there remains some potential for unknown confounders to have influenced results.

Bellosta et al. (2013) compared the PROPATEN graft (with a distal vein patch, n=40) with a pre-cuffed PTFE graft (Distaflo, n=39) in a retrospective cohort analysis at a single site. With a total of 79 patients included, this was a relatively small sample compared with the studies with an autologous graft comparator. The use of a distal vein patch may have influenced the results and may not be directly comparable to other outcomes where adjunctive techniques were not performed, affecting external validity.

Treatment decisions depended upon the surgeon's preference, so there may have been some selection or performance bias. In the methods, the authors describe how they used propensity scoring to adjust for baseline differences between groups. However, it is not clear that this was applied and the authors suggest that age differences are the most likely explanation for a discrepancy in survival between groups.

Attrition bias may have been present. Mean follow-up for all patients was 17 months, but ranged from 3 to 82 months, and was not reported by intervention group. Results are reported up to 24 months, so there must have been some degree of extrapolation/ estimation in the time-to-event analyses. Safety outcomes were not reported separately for the 2 treatment groups.

Bechara (2014) did not distinguish between above- and below-knee results for the patients who had femoropopliteal bypasses in this single-site study. Sample sizes

were relatively small (PROPATEN n=39, SLFG n=20). Methods and inclusion criteria were not explicitly stated, and there is a high risk of selection bias in this retrospective review. There was no reporting of any baseline measures or attempts to account for potential confounders, except that results for femoropopliteal and femorotibial bypasses were reported separately. No explanation is given for the absence of 24-month results for the femorotibial bypasses. The apparent increase in primary patency between 12 and 18 months for the PROPATEN group suggests that comparisons did not take into account loss to follow-up. Safety outcomes were not reported. Given the paucity of information reported, caution is advised in interpretation of the results.

One strength of the multicentre study by Dorigo et al. (2012) was the large sample sizes for both PROPATEN grafts (n=556) and ASV grafts (n=394). However, there is a high risk of selection bias. Data were obtained from a register that did not have specific inclusion or exclusion criteria, and treatment choices were made by each participating surgeon. The influence of some confounders was determined to be significant following univariate and multivariate analyses, but these findings were not used to statistically adjust key outcome measures. The study only included results for below-knee bypasses, and so would not have been affected by any above-knee results.

The average length of follow-up was not reported by graft type, and full data were not available for all patients. Of the 950 patients, 97% (921) had at least 1 post-operative clinical and duplex ultrasound investigation, but only 50% had at least 2 years of follow-up data available. Some of the longer-term (2 -ear) follow-up results did not differentiate between treatment groups. It is not clear how many patients were lost to follow-up from each of the 2 treatment groups, possibly resulting in attrition bias.

The single-site study by Daenens et al. (2009) included 240 heparin-bonded ePTFE grafts (presumed to be PROPATEN) and 110 ASV grafts. The PROPATEN graft was named in the introduction and in another study by the same authors, but because it was not specifically described in the methods there is a small chance that a different graft was used. Results were analysed separately depending on bypass type, which is a strength of the study. The authors recognised that patients who had the heparin-bonded ePTFE grafts were more likely to have had a secondary intervention, and that a lower proportion of these patients was represented in the below-knee femoropopliteal group. Other potential confounders were similarly taken into account in the analyses, and supported by data. The risk of selection bias was therefore relatively low for a non-randomised study.

Data were available from all patients after the same length of follow-up, although 4%

of patients (15/350) may not have had duplex ultrasonography at the end of the study period to confirm patency, leading to a slight risk of attrition bias.

The study by Dorigo et al. (2005) was the only study to report comparisons of PROPATEN grafts with both other (non-heparin-bonded) PTFE grafts and ASV grafts. Another strength was that it focused on below-knee bypasses only.

Small sample sizes (21–25 patients in each group) were a limitation, and it appears that the study was done at a single vascular centre. There may also have been some performance bias, because the results of the PROPATEN group were prospectively collected and the surgeons may have been aware that outcomes for this group would be scrutinised. There is a high likelihood of selection bias, particularly with the retrospective choice of comparators. The authors state that these control groups were 'randomly selected', but provide no further detail about how this was achieved.

The mean follow-up was 19±11 months, indicating that there was a high degree of variation between patients; differences between groups were not reported. Primary patency at 18 months was estimated, and results may have been affected by differential attrition. There also appeared to be a few errors in the reported data.

Relevance to NICE programmes

NICE has issued the following guidance or advice:

- Cilostazol, naftidrofuryl oxalate, pentoxifylline and inositol nicotinate for the treatment of intermittent claudication in people with peripheral arterial disease (2011) NICE technology appraisal guidance 223
- Endovascular stent-grafting of popliteal aneurysms (2011) NICE interventional procedure guidance 390
- Lower limb peripheral arterial disease: diagnosis and management (2012) NICE guideline CG147
- Percutaneous atherectomy of femoropopliteal arterial lesions with plaque excision devices (2011) NICE interventional procedure guidance 380

- Percutaneous laser atherectomy as an adjunct to balloon angioplasty (with or without stenting) for peripheral arterial disease (2012) NICE interventional procedure guidance 433

- Spiral Flow peripheral vascular graft for treating peripheral arterial disease (2015) NICE Medtech innovation briefing 34

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Search strategy and evidence selection

Search strategy

A search was conducted to identify evidence on the clinical and cost effectiveness of the Gore PROPATEN heparin-bonded vascular graft.

The strategy was developed in MEDLINE (Ovid). The strategy was devised using a combination of subject indexing terms and free text search terms that described the indication and free text search terms that specifically described the device. No limits were applied to the search.

The strategy was adapted for the following databases: Medline in Process, Embase, Cochrane Library (CENTRAL, CDSR, DARE, HTA, NHS EED), EconLit, Pubmed ('epub ahead of press' search only of key terms), Scopus and Web of Science (Web of Science – Science Citation Index and Conference Proceedings Citation Index- Science). Citation tracking in Google Scholar of included studies was also performed. The searches returned a total of 98 references after duplicate removal.

Information supplied by the manufacturer and also the manufacturer's website were checked for relevant studies.

ClinicalTrials.gov and the International Clinical Trials Registry Platform (ICTRP) were searched to identify ongoing or in-development trials.

Evidence selection

Retrieved results were independently sifted by two researchers using the selection criteria below, and disagreements discussed and resolved.

- Population: patients with symptomatic peripheral arterial disease in whom a peripheral vascular bypass procedure using a prosthetic graft is clinically indicated
- Intervention: PROPATEN heparin-bonded vascular graft (Gore)
- Comparators: Autologous lower extremity bypass, standard (non-heparin bonded) prosthetic graft, and other types of heparin-bonded prosthetic graft

- Outcomes:
  - procedural complications
  - primary patency rate
  - secondary patency rate
  - amputation rates
  - graft failure
  - graft occlusion
  - infection
  - re-intervention rates
  - limb salvage rate
  - death
  - heparin-induced thrombocytopaenia (HIT)
  - perioperative or postoperative bleeding.

Following the first sift, 59 records were removed based on the following criteria:

- not relevant to selection criteria
- review articles and conference abstracts.

Full articles were requested for the remaining 36 studies, one of which was not available. Additional studies were provided by the manufacturer.

Due to the abundance of data, it was necessary to further refine the remit. The following criteria were applied:

- Study design. Due to the large number of relevant studies, only randomised controlled trials and comparative studies were considered for inclusion.
- Comparator. Of the comparative studies, all those comparing PROPATEN to other types of prosthetic grafts were included. Of those comparing PROPATEN to ASV, multisite studies and studies with more than 200 patients were included.

- Multiple comparators. One further study was identified by the manufacturer. This was the only 3-arm study identified (comparing PROPATEN with standard ePTFE graft and ASV).

Ultimately six studies were selected for inclusion in this briefing.

Summary of medical device reports

Selection criteria and categorisation

A search of the FDA MAUDE database identified 307 MDRs relating to use of the PROPATEN vascular graft in 332 procedures.

Initially, records of 140 procedures were excluded for the following reasons:

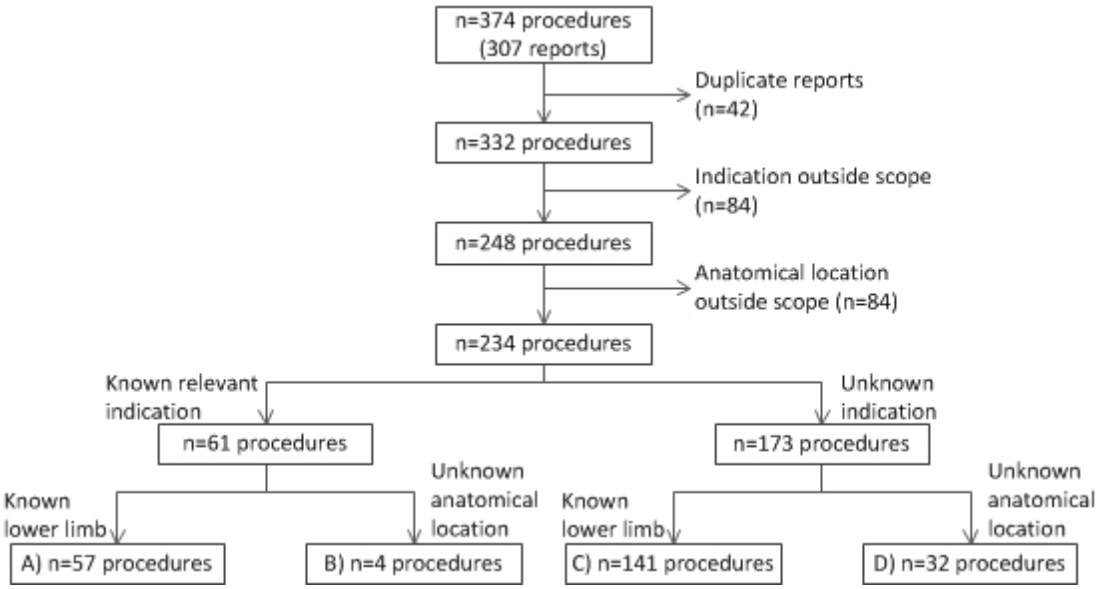
- 42 suspected duplicates
- 84 procedures with clinical indications that were outside of the scope (such as paediatric shunt or arteriovenous access for dialysis)
- 14 procedures carried out in an anatomical location not typically associated with peripheral arterial disease.

The remaining 234 procedures were allocated into these 4 categories:

- Known clinical indication associated with peripheral arterial disease (such as claudication), in the lower limb (n=57)
- Relevant clinical indication but unreported anatomical location (n=4)
- No indication reported (other than "bypass" in some cases) but known lower limb procedure (n=141)
- Neither indication nor anatomical location reported (n=32)

Figure 1 illustrates the above MDR selection process.

Figure 1 Schematic diagram illustrating the breakdown of medical device reports



Appendix

Contents

Data tables

Table 2 Overview of the Lindholt et al. (2011) study

Study component	Description
Objectives/ hypotheses	To compare 1–year patencies of PROPATEN grafts with those of standard PTFE grafts.
Study design	Blinded, multicentre randomised control trial.
Setting	Eleven vascular centres at Scandinavian hospitals from 2006 to 2009. All patients included in analyses were followed up for 1 year. Patency was assessed by detecting pulse and measuring blood pressure at follow-up appointments up to 12 months. There is no indication of the frequency of these appointments or whether they were at set intervals. At 1 year, duplex ultrasound scanning was used to confirm patency.
Inclusion/ exclusion criteria	Inclusion criteria: Clinical indication for femoral-femoral cross-over or femoropopliteal bypass above or below the knee with an artificial graft, as determined by angiography. Exclusion criteria: Acute patients, patients not likely to attend follow-up, and those with heparin allergies.
Primary outcomes	Primary and secondary patency after 1 year.

Statistical methods	Baseline variables were compared using chi-squared and Student's t-test. No significant differences were detected. A comparison of primary and secondary patencies after 1 year between the two groups was carried out using logistic regression analysis[a], with and without adjusting for bypass type and critical ischaemia. Post hoc subgroup analyses were also conducted according to bypass type and indication for treatment[b]. The analyses used ITT, excluding those after randomisation who did not undergo the planned bypass but including early (technical) failures and prosthetic infections.
Patients included	Population: patients with intermittent claudication (n=348) or chronically critical ischaemia (n=198). Mean age 65 years; 53% male; 54% smokers. Randomised n=569, Operated n=555, Included n=546 Intervention (PROPATEN) group: n=272. Comparator (standard PTFE) group: n=274. 14 patients did not undergo the planned procedure due to technical failures (n=5), use of the wrong graft (n=5) or change of indication (n=4). 4 patients died postoperatively before follow-up. 7 patients were lost to follow-up after the procedure. Details and treatment groups for 11 patients were not reported.
Results (Primary patency at 1 year)	PROPATEN: 86.4% (235/272). Standard PTFE: 79.9% (219/274). OR 0.627, 95% CI 0.398 to 0.989, p=0.043[a]. Adjusted for bypass type: OR 0.629, 95% CI 0.393 to 1.001, p=0.051[a].
Conclusions	The authors report that PROPATEN significantly reduced the overall risk of primary graft failure by 37%. There was a reduction in risk when PROPATEN was used in both femoropopliteal bypasses (OR=0.515, p=0.030) and in patients with critical ischaemia (OR=0.490, p=0.036).

Abbreviations: CI, confidence interval; ITT, intention to treat; n, number of patients; OR, odds ratio; PTFE, polytetrafluoroethylene.

[a]These tests were pre-specified to be Cox regression analyses, but were changed post hoc due to the observation of a substantial number of silent occlusions.

[b]The study was not sufficiently powered to detect differences in subgroup analyses.

Table 3 Summary of results from the Lindholt et al. (2011) study

	PROPATEN group	Standard PTFE group	Analysis
Randomised	n=not clear	n=not clear	–
Efficacy	n=272	n=274	–
Primary patency at 1 year	86.4% (235/272)	79.9% (219/274)	OR 0.627 95% CI 0.398 to 0.989 p=0.043[a] Adjusted for bypass type: OR 0.629 95% CI 0.393 to 1.001 p=0.051[a]
Secondary patency at 1 year	88.2% (240/272)	81.0% (222/274)	OR 0.569 95% CI 0.353 to 0.917 p=0.020[a] Adjusted for bypass type and critical ischaemia: OR 0.565 95% CI 0.346 to 0.923 p=0.023[a]

Primary patency in FP subgroup	81.3% (91/112)	69.0% (87/126)	OR 0.515 95% CI 0.281 to 0.944 p=0.030[b]
Primary patency in critical ischaemia subgroup	82.7% (81/98)	70.0% (70/100)	OR 0.490 95% CI 0.249 to 0.962 p=0.036[b] Adjusted for bypass type: OR 0.47 95% CI 0.26 to 0.86 p=0.036[b]
Safety	n=not reported	n=not reported	There is some evidence that postoperative infections occurred, but no details were given.
Serious adverse events	The authors reported that there were 4 deaths in the postoperative period before follow-up took place. Treatment groups were not specified. The authors did not report any other SAEs; it is not known whether no other SAEs occurred, or whether they were simply not published.		
'Average' perioperative bleeding (millilitres)	399	370	p=0.32
Abbreviations: CI, confidence interval; FP, femoropopliteal; ITT, intention to treat; n, number of patients; OR, odds ratio; PTFE, polytetrafluoroethylene. [a]These tests were pre-specified to be Cox regression analyses, but were changed post hoc due to the observation of a substantial number of silent occlusions. [b]The study was not sufficiently powered to detect differences in subgroup analyses.			

Table 4 Overview of the Bellosta et al. (2013) study

Study component	Description

Objectives/ hypotheses	To evaluate early and midterm results of tibial bypasses comparing a precuffed ePTFE graft (Distaflo) to PROPATEN with a distal vein patch.
Study design	Retrospective cohort study.
Setting	Single hospital in Italy from April 2004 to December 2010. Doppler ultrasonography was carried out at the time of discharge; after 1, 3, 6 and 12 months; and thereafter every 6 months. The mean follow-up was 17 months (range 3–82). Follow-up outcomes were checked through direct contact with patients or the family.
Inclusion/ exclusion criteria	Records of patients undergoing femorotibial revascularisation for critical limb ischemia were obtained retrospectively from a single centre. The 2 groups were selected from the same period of time. None of the patients had a suitable autologous vein available. Intervention (PROPATEN with distal vein patch) group: n=40. Comparator (Distaflo ePTFE graft) group: n=39. The intervention group were treated using a 6 mm thin-walled PROPATEN graft without external rings. The distal anastomosis was performed using a Linton vein patch. The comparator group were treated with a premanufactured expanded anastomosis (Distaflo) with a small cuff and externally supported with rings.
Outcomes	Primary and secondary patency and limb salvage determined at regular intervals until 24 months. Estimated survival at 36 months. The primary outcome was not specified by the authors.
Statistical methods	Baseline characteristics were compared using chi-squared, t test, or Wilcoxon test. Primary and secondary patency, limb salvage and survival were analysed using univariate (Kaplan–Meier curves and log rank test) and multivariate (Cox regression) analyses. The association between groups was evaluated by OR (with CI). Propensity scoring was used to adjust for baseline differences.

Patients included	Population: patients with critical limb ischaemia who underwent femorotibial bypass using a PTFE graft. Total sample size n=79. After the operation all patients were given low-molecular weight heparin. patients underwent oral anticoagulant (warfarin) therapy or treatment with anti-platelet drugs.
Results	Baseline measures were comparable with the exception of age; the Distaflo group were on average 5 years older (95% CI 0.5 to 9, p=0.03). Though not statistically significant, there were also differences between groups in Rutherford classifications and number of simultaneous adjunctive procedures. After 2 years neither primary nor secondary patency, nor limb salvage, were significantly different between PROPATEN with vein patch and Distaflo. A significant difference was observed for survival at 36 months (PROPATEN: 84%; Distaflo: 21%, p<0.001). Factors associated with poorer long-term primary patency rates were age of >80 years, peroneal artery distal anastomosis, adjunctive procedures, and secondary interventions (all p<0.05).
Conclusions	The authors report that pre-cuffed Distaflo and PROPATEN with a distal vein patch have similar patency and limb salvage results. Differences in survival rates between groups were attributed to age.
Abbreviations: CI, confidence interval; ePTFE, expanded polytetrafluoroethylene; n, number of patients; OR, odds ratio; PTFE, polytetrafluoroethylene.	

Table 5 Summary of results from the Bellosta et al. (2013) study

	PROPATEN + vein patch group (n=40)	**Distaflo ePTFE group (n=39)**	**Analysis**
Primary patency at 2 years (95% CI)	33% (21–53)	47% (32–70)	p=0.793

Secondary patency at 2 years	36% (23–57)	49% (33–72)	p=0.855
Limb salvage	65% (51–84)	57% (41–79)	p=0.18
Survival at 36 months (95% CI)	84% (69–100)	21% (7–63)	OR 0.21, 95% CI 0.07 to 0.63, p<0.001
Deaths within 30 days	2.5% (2/79)		Not reported by intervention type.
Non-fatal perioperative MI	1.3% (1/79)		Not reported by intervention type.
Wound dehiscence	3.8% (3/79)		Not reported by intervention type. All resulted in protracted hospital stay.
Infection	Within 30 days=2.5% (2/79) Other infections during follow-up=3.8% (3/79) Total infections=6.3% (5/79)		Not reported by intervention type. Those patients with infections that occurred within 30 days died within 6 months. Others were candidates for major amputation.
Operation length (min)	215 (198 to 238)	138 (120 to 162)	Difference 76 (95% CI 45 to 118), p<0.001.
Mean length of stay (days)	11.8	11	No statistical analysis reported.
Abbreviations: CI, confidence interval; ePTFE, expanded polytetrafluoroethylene; MI, myocardial infarction; n, number of patients; OR, odds ratio.			

Table 6 Overview of the Bechara (2014) study

Study component	Description
Objectives/ hypotheses	To compare short and midterm infra-inguinal bypass patency rates between two ePTFE prosthetic grafts: PROPATEN and Spiral Laminar Flow Graft (SLFG).
Study design	Retrospective cohort study.
Setting	Single hospital in the USA from January 2010 to January 2012.
Inclusion/ exclusion criteria	Records of patients undergoing infra-inguinal bypass using prosthetic grafts were reviewed retrospectively for a single centre. The author implies that the indication was PAD. The two groups were selected from the same period of time. Intervention (PROPATEN) group: n=39. Comparator (SLFG) group: n=20.
Outcomes	Primary and secondary patency rates. It was not clear how patency was determined. The primary outcome was not specified by the authors.
Statistical methods	Kaplan–Meier analyses were performed to estimate primary and secondary patency rates.
Patients included	Population: patients undergoing infrainguinal bypass using prosthetic grafts.

Results	70% (14/20) of SLFG cases were FP bypasses, and 30% (6/20) were FT bypasses. The author reported that "similar percentages were seen" in the PROPATEN group, but it is not reported how many of the FP bypasses were above or below the knee. Primary patency rates for FP bypasses at 24 months were 54% (PROPATEN) and 50% (SLFG); the rates for FT bypasses at 18 months were 37% (PROPATEN) and 17% (SLFG). Secondary patency rates for FP bypasses at 24 months were 66% (PROPATEN) and 57% (SLFG); the rates for FT bypasses at 18 months were 34% (PROPATEN) and 20% (SLFG). The author stated: "Statistically, the 6-, 12-, 18-, and 24-month primary and secondary patency rates for both grafts were the same regardless of the distal target artery". Details of statistical results were not reported.
Conclusions	The author reported 'similar' primary and secondary patency rates between the two groups, and suggested that there should be different graft configurations for tibial targets and popliteal artery targets.
Abbreviations: FP, femoropopliteal; FT, femorotibial; n, number of patients; PAD, peripheral arterial disease; SLFG, spiral laminar flow graft.	

Table 7 Summary of results from the Bechara (2014) study

	PROPATEN group (n=39)	SLFG group (n=20)	Analysis

Primary patency	FP: 6 m: 94% 12 m: 61% 18 m: 61% 24 m: 54% FT: 6 m: 51% 12 m: 36% 18 m: 37%	FP: 6 m: 79% 12 m: 50% 18 m: 50% 24 m: 50% FT: 6 m: 50% 12 m: 33% 18 m: 17%	Details of statistical results were not reported. The author states: "Statistically, the 6-, 12-, 18-, and 24-month primary and secondary patency rates for both grafts were the same regardless of the distal target artery".
Secondary patency	FP: 6 m: 94% 12 m: 66% 18 m: 66% 24 m: 66% FT: 6 m: 54% 12 m: 34% 18 m: 34%	FP: 6 m: 86% 12 m: 57% 18 m: 57% 24 m: 57% FT: 6 m: 60% 12 m: 40% 18 m: 20%	Details of statistical results were not reported. The author states: "Statistically, the 6-, 12-, 18-, and 24-month primary and secondary patency rates for both grafts were the same regardless of the distal target artery".

Safety (adverse events)	Not reported	–
Abbreviations: FP, femoropopliteal; FT, femorotibial; m, months; n, number of patients; SLFG, spiral laminar flow graft.		

Table 8 Overview of the Dorigo et al. (2012) study

Study component	Description
Objectives/ hypotheses	To compare early and follow-up results of below-knee bypasses performed in patients with peripheral arterial obstructive disease using PROPATEN and ASV.
Study design	Retrospective cohort study.
Setting	Seven vascular centres in Italy from 2001 to 2010. Follow-up examinations were carried out within the third postoperative month, at 12 months and then annually. These included Duplex scans. Mean duration of follow-up was 28.5±22.1 months. Early results refer to the first 30 days after surgery.
Inclusion/ exclusion criteria	Data from patients undergoing below-knee revascularisation for PAD were obtained retrospectively from a multicentre registry. The two groups were selected from the same centres in the same period of time. Intervention (PROPATEN) group: n=556. Comparator (ASV) group: n=394. The procedure for the ASV group used in situ vein bypass (54%, 212/394) or inverted vein bypass (46%, 182/394).
Outcomes	Primary and secondary graft patency, limb salvage (in patients with critical limb ischaemia), and survival. The primary outcome was not specified by the authors.

Statistical methods	Early (safety) results were compared using chi-squared and Fisher's exact test. Follow-up results were compared using a log rank test. Survival was estimated using Kaplan–Meier curves. Univariate and Cox Regression analyses were used to investigate factors related to primary and secondary patency rates.
Patients included	Patients with critical limb ischaemia (n=745) or severe claudication (n=205). Total sample size n=950.
Results	Baseline measures showed some significant differences. patients in the PROPATEN group were more likely to have a history of smoking, hyperlipidaemia and coronary artery disease. The indication for surgery was more often critical limb ischaemia in the ASV group than in the PROPATEN group. Run-off status also differed. Secondary interventions accounted for a greater proportion of the procedures in the PROPATEN group (25%, 141/556) than in the ASV group (19%, 73/394, p=0.001). Primary patency at 48 months: PROPATEN=45%, ASV=61% (p=0.004). Multivariate analyses demonstrated that both secondary interventions and use of adjunctive distal procedures were associated with poorer primary and secondary patency rates. Male patients had better primary and secondary patency outcomes than females.
Conclusions	The authors report that PROPATEN provides satisfactory early and mid-term results in patients undergoing surgical below-knee revascularisation. While ASV maintains its superiority in terms of primary patency, secondary patency and limb salvage rates are comparable. It was observed that the wide discrepancy in primary patency rates may be explained by the fact that more of the PROPATEN patients were undergoing secondary interventions. Higher perioperative death rates for the PROPATEN group were attributed to a higher proportion of patients with coronary artery disease. They authors conclude that PROPATEN can represent a safe alternative to ASV, mainly when it is unusable or of poor quality.

Abbreviations: ASV, autologous saphenous vein; n, number of patients; PAD, peripheral arterial disease.

Table 9 Summary of results from the Dorigo et al. (2012) study

	PROPATEN group (n=556)	**ASV group (n=394)**	**Analysis**
Primary patency at 48 months	44.5%	61%	p=0.004 Log rank 8.1
Secondary patency at 48 months	57% (SE 0.03)	67.5% (SE 0.03)	p=0.1 Log rank 1.9
Limb salvage in patients with critical limb ischaemia at 48 months	77.2% (SE 0.02)	79.5% (SE 0.03)	p=0.3 Log rank 0.9
Survival (48 month estimate)	81%	74%	p=0.7 Log rank 0.1
Deaths (30 days)	2.0% (11/556)	0.5% (2/394)	p=0.07
Thromboses (30 days)	6.3% (35/556)	5.1% (20/394)	p=0.3
Major amputations (30 days)	3.4% (19/556)	1.8% (7/394)	p=0.1
Mean post-operative hospital stay (days)	13.1	10.2	95% CI 1.5 to 4.6, p<0.001
Abbreviations: ASV, autologous saphenous vein; n, number of patients; SE, standard error.			

Table 10 Overview of the Daenens et al. (2009) study

Study component	Description
Objectives/ hypotheses	To compare 1- and 2-year results in patients given heparin-bonded ePTFE grafts with those patients given ASV grafts during the study period.
Study design	Retrospective cohort study
Setting	Single hospital in Belgium from August 2002 to March 2006. Follow-up visits were scheduled for 1 and 6 months post-operatively and yearly thereafter. Duplex ultrasonography scan was performed in case of clinical problems, if pulses were absent, and routinely during the appointments at 1 and 2 years. Observations terminated in February 2007. Some patients without sufficient follow-up data in medical notes were asked to attend an additional visit. Other data were obtained by telephone or from primary care records.
Inclusion/ exclusion criteria	Records of patients undergoing above- and below-knee revascularisation for PAD (Rutherford disease stage class ≥3) in whom a PROPATEN or ASV graft was used were obtained retrospectively from a single centre. The two groups were selected from the same period of time. Intervention (PROPATEN) group: n=240; 8 mm thin-walled for AK FP, 6 mm ringed for BK FP and FC. Comparator (ASV) group: n=110; vein diameter ≥ 3 mm.
Outcomes	Primary patency at 1 and 2 years, limb salvage rates, infections. The primary outcome was not specified by the authors.
Statistical methods	Kaplan–Meier was used to assess primary patency and limb salvage for each bypass subgroup separately, with log rank testing used to compare results between treatment groups.

Patients included	Population: All patients who underwent an above- or below-knee bypass for PAD (Rutherford disease stage class ≥3) in whom a PROPATEN or ASV graft was used. All patients followed similar postoperative antiplatelet and anticoagulant regimen, including 160 mg of aspirin/day. Warfarin therapy continued for patients receiving if before surgery and started for those who underwent secondary interventions. Total sample size n=350. Secondary interventions accounted for a greater proportion of the procedures in the PROPATEN group than in the ASV group. There were significantly more above-knee and less below-knee femoropopliteal bypasses in the PROPATEN group. Because of this, results were analysed separately by subgroup. Median follow-up times in months (with range) for living patients in subgroups: AK FP (PROPATEN): 25.3 (<1–45) AK FP (ASV): 28.5 (<1–45) BK FP (PROPATEN): 24.6 (<1–47) BK FP (ASV): 20.6 (<1–46) FC (PROPATEN): 18.8 (<1–48) FC (ASV): 19.6 (<1–44)
Results	At baseline there were no significant differences between groups with respect to age, sex, Rutherford classification, or proportion of smokers. Primary patency after 2 years was not significantly different between treatments as analysed by subgroup (AK FP, p=0.804; BK FP, p=0.075; FC, p=0.391).
Conclusions	The authors report that PROPATEN had 1- and 2-year primary patency results that were not significantly different from those for ASV grafts. Results in below-knee applications were especially promising.
Abbreviations: AK FP, above-knee femoropopliteal; ASV, autologous saphenous vein; BK FP, below-knee femoropopliteal; CI, confidence interval; ePTFE, expanded polytetrafluoroethylene; FC, femorocrural; n, number of patients; PAD, peripheral arterial disease.	

Table 11 Summary of results from the Daenens et al. (2009) study

	PROPATEN group (n=240)	ASV group (n=110)	Analysis
Primary patency at 1 and 2 years (95% CI)	AK FP 1 yr: 92% (83–96) AK FP 2 yrs: 83% (72–90) BK FP 1 yr: 92% (81–97) BK FP 2 yrs: 83% (68–91) FC 1 year: 79% (69–86) FC 2 years: 69% (58–78)	AK FP 1 yr: 91% (51–99) AK FP 2 yrs: 80% (39–95) BK FP 1 yr: 72% (59–83) BK FP 2 yrs: 72% (59–83) FC 1 year: 69% (54–80) FC 2 years: 64% (48–76)	AK FP 1 year: p=not reported AK FP 2 years: p=0.804 BK FP 1 year: p=not reported BK FP 2 years: p=0.75 FC 1 year: p=not reported FC 2 years: p=0.391 For FC, primary bypasses performed better than secondary interventions (p=0.006).

Amputations/limb salvage at 2 years, patients with critical ischaemia	AK FP: 3/92% BK FP: 1/98% FC: 12/87%	AK FP: 0/100% BK FP: 3/91% FC: 2/96%	AK FP: p=0.697 BK FP: p=0.054 FC: p=0.157
Death from all causes	AK FP: 10% (9/86) BK FP: 11% (6/57) FC: 19% (18/97)	AK FP: 8% (1/12) BK FP: 10% (5/48) FC: 14% (7/50)	AK FP: p=0.912 BK FP: p=0.879 FC: p=0.075
In-hospital deaths	0.42% (1/240)	0.91% (1/110)	–
Deep infections	0.83% (2/240)	0% (0/110)	–
Seroma/ haematoma	0% (0/240)	0% (0/110)	–
HIT	0% (0/240)	0% (0/110)	–
Abbreviations: AK FP, above-knee femoropopliteal; ASV, autologous saphenous vein; BK FP, below-knee femoropopliteal; CI, confidence interval; FC, femorocrural; HIT, heparin-induced thrombocytopaenia; n, number of patients; yr/s, year/s.			

Table 12 Overview of the Dorigo et al. (2005) study

Study component	Description

Objectives/ hypotheses	To retrospectively evaluate immediate and mid-term results of below-knee bypasses performed with PROPATEN, compared with results obtained with autologous vein and standard ePTFE.
Study design	Retrospective cohort study.
Setting	Appears to have been conducted at a single hospital in Italy, from March 2002 to December 2004. Mean duration of follow-up was 19±11 months. Clinical and ultrasonographic follow-up was performed at 1, 6, and 12 months and then once a year.
Inclusion/ exclusion criteria	The study collected data for patients undergoing below-knee revascularisation for PAD that had resulted in critical limb ischaemia or severe intermittent claudication. Records for patients in the intervention (PROPATEN) group were prospectively collected, then compared retrospectively with randomly selected controls (ASV and standard ePTFE) from an existing database. patients in all three groups appear to have been treated at the same site during the same study period. Patients in the intervention (PROPATEN) group did not have a suitable autologous vein. Intervention (PROPATEN) group: n=24. Comparator 1 (ASV) group: n=25. Comparator 2 (standard ePTFE) group: n=21.
Outcomes	Early graft thrombosis (within 30 days), primary patency at 18 months, and limb salvage at 18 months. The primary outcome was not specified by the authors.
Statistical methods	Differences between groups in graft patency, amputation rate and mortality at 30 days were analysed using chi-squared and Fisher's exact tests. Follow-up data were analysed by Kaplan–Meier life table (survival) analysis and log rank tests.
Patients included	Population: patients undergoing below-knee revascularisation after critical limb ischaemia or severe intermittent claudication. Total sample size n=70.

Results	There were no significant differences in baseline measures between the three groups in terms of sex, age, preoperative clinical status, or run-off scores. Numbers of re-do (secondary) interventions were similar for PROPATEN (13%, 3/24), ASV (8%, 2/25) and ePTFE (5%, 1/21). Adjunctive procedures (such as patching of distal anastomosis) were performed in 50% (12/24) patients in the PROPATEN group, 16% (4/25) patients in the ASV group, and 48% (10/21) patients in the ePTFE group. Early graft thrombosis occurred in 5 (21%) patients in the PROPATEN group, 3 (12%) in the ASV group, and 10 (48%) in the ePTFE group. Both PROPATEN and ASV performed significantly better than ePTFE (p=0.002 and p=0.003); there were no differences between PROPATEN and ASV in early graft thrombosis. At 18 months follow-up, ASV grafts had higher primary patencies (75%) than ePTFE grafts (40%), but were not significantly higher than PROPATEN (53%). The difference between the two prosthetic grafts was not statistically significant (p=0.07).
Conclusions	The authors report that the use of a PROPATEN graft seems to significantly reduce the rate of early graft thrombosis compared with standard synthetic materials and provides also slightly better mid-term results, making it a possible graft of choice in the absence of suitable autologous veins.
Abbreviations: ASV, autologous saphenous vein; ePTFE, expanded polytetrafluoroethylene; n, number of patients; PAD, peripheral arterial disease.	

Table 13 Summary of results from the Dorigo et al. (2005) study

	PROPATEN group (n=24)	**ASV group (n=25)**	**ePTFE group (n=21)**	**Analysis**
Early graft thrombosis (within 30 days)	21% (5/24)	12% (3/25)	48% (10/21)	PROPATEN better than ePTFE (p=0.002). ASV better than ePTFE (p=0.003). PROPATEN not significantly different to ASV (p=0.4).

Estimated primary patency at 18 months	53%	75%	40%	ASV better than ePTFE (p=0.01, log rank 6.7), but not significantly better than PROPATEN (p=0.05, log rank 3.3). PROPATEN not significantly different to ePTFE (p=0.07, log rank 1.2).
Limb salvage at 18 months	68%	83%	64%	ASV better than PROPATEN (p=0.03, log rank 2.6), but reported as not significantly better than ePTFE (p=0.05, log rank 3.3). PROPATEN not significantly different than ePTFE (p=0.08, log rank 2.9).
Survival at 18 months	93% (65/70)			–
Perioperative deaths	0% (0/24)	0% (0/25)	0% (0/21)	–
Major amputations (perioperative)	8.3% (2/24)	4.0% (1/25)	9.5% (2/21)	No significant differences between all 3 groups.
Severe bleeding	0% (0/24)	0% (0/25)	0% (0/21)	–
Abbreviations: ASV, autologous saphenous vein; ePTFE, expanded polytetrafluoroethylene; n, number of patients.				

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 Cedar. The interim process & 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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Declarations of interest

- Mr Eric Chemla has organised workshops with W L Gore, but paid the honorarium into the hospital research fund.
- No other relevant conflicts of interest were declared.

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