NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction

Erectile dysfunction (impotence) is the inability to get or maintain an erection. Sometimes this is caused by poor blood flow to the penis, because a blood vessel in the pelvis has narrowed. In this procedure, a balloon is inflated, or a small tube made of metal mesh (a stent) is placed across the narrowing. This opens the blood vessel, improving blood flow to the penis, with the aim of making an erection possible.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in June 2015 and updated in November 2015.

Procedure name

- Angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction

Specialist societies

- British Association of Urological Surgeons
- British Society for Sexual Medicine
- British Society of Interventional Radiology.

Description

Indications and current treatment

There are many causes of erectile dysfunction (ED). It is often multifactorial and precise identification of a cause may be complex. One cause of arteriogenic ED is atherosclerosis causing narrowing or blocking of the arteries in the pelvis or the penis and reducing blood flow to the penis. This guidance is limited to treatment of atherosclerosis in arteries distal to the internal iliacs. It does not include angioplasty or stenting of the iliac arteries done for intermittent claudication, with ED as an accompanying symptom.

Treatment of ED secondary to atherosclerosis includes management of cardiovascular risk factors (stopping smoking, antithrombotic medication and statin treatment) and oral phosphodiesterase-5 inhibitors. In ED that has not responded to conservative treatments or phosphodiesterase-5 inhibitors, other options (including vacuum erection devices, intracavernosal or intraurethral prostaglandin, and penile prostheses) or surgical revascularisation may be considered.

What the procedure involves

Angioplasty and stenting of atherosclerosis in the small arteries distal to the internal iliac arteries aim to offer a less invasive alternative to open surgical revascularisation to patients with arteriogenic ED that is refractory to standard treatments.

Under local anaesthesia and using fluoroscopic guidance, a catheter is introduced percutaneously through the femoral artery and guided into the narrowed target artery (usually the internal pudendal or common penile artery). Balloon angioplasty of the narrowed artery may be done to dilate the narrowing, or a stent may be placed across the narrowing with or without prior angioplasty.

Outcome measures

International index for erectile function (IIEF) questionnaire

The IIEF questionnaire includes 15 questions divided into 5 domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. The total score range is from 1 to 75, from worst to best.

The IIEF-5 and the IIEF-6 questionnaires are subsets of 5 or 6 questions specific to erectile function (score ranges from 1 to 25 [IIEF-5] or from 1 to 30 [IIEF-6], from worst to best). A score of 21 or less indicates ED.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction. The following databases were searched, covering the period from their start to 4 November 2015: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with peripheral arterial disease causing refractory erectile dysfunction.
Intervention/test	Angioplasty and/or stenting.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 50 patients from 2 case series[1, 2].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction

Study 1 Rogers JH (2012)

Details

Study type	**Case series**
Country	USA
Recruitment period	Not reported
Study population and number	n=**30** patients (45 lesions treated) with atherosclerotic ED and a suboptimal response to phosphodiesterase-5 inhibitors
Age and sex	Mean 60 years; 100% (30/30) male
Patient selection criteria	Inclusion criteria: Men 18 years or older in an active sexual relationship with 1 partner for 6 months or more; suboptimal response to PDE5i therapy, as documented by a 4-week run-in phase; reduced cavernosal arterial penile flow with duplex ultrasound peak systolic velocity of the right and left cavernosal arteries of less than 30 cm/s; cavernosal artery anteroposterior and transverse diameter at mid-shaft ≥0.3 mm; and angiographic stenosis of 1 or both internal pudendal artery(ies) with target vessel reference diameter(s) ≥2.25 mm and ≤4.20 mm by visual estimation and primary lesion length(s) ≤27 mm. Exclusion criteria: Any nonvascular cause of ED; untreated hypogonadism; diabetes mellitus with glycosylated haemoglobin levels ≥8%; chemotherapy in the previous12 months or life expectancy of fewer than 12 months; myocardial infarction, cardiovascular accident, life threatening arrhythmia, or unstable angina requiring hospitalisation within 3 months before enrolment, or any subject actively receiving nitrate therapy; bleeding diathesis or known hypercoagulable state; penile veno-occlusive dysfunction (venous leak) by duplex ultrasound with right or left cavernosal artery end-diastolic velocity greater than 5 cm/s; serum creatinine levels greater than 2.5 mg/dl; and non-target lesions of the common iliac artery, internal iliac artery, or common penile artery ≥70%.
Technique	The Resolute zotarolimus-eluting stent system (Medtronic) was used. Zotarolimus is eluted over 180 days. On confirmation of angiographic eligibility, patients received heparin to achieve an activated clotting time ≥250 s before and during stent placement. All patients received 325 mg aspirin within 24 h of the procedure and daily thereafter for at least 6 months. A loading dose of clopidogrel ≥300 mg (or ticlopidine if allergic) was given peri-procedurally, and clopidogrel 75 mg daily was prescribed for 6 months. Use of any PDE5i within 36 h of the procedure was prohibited, and PDE5i use was resumed in follow-up at investigator discretion as clinically required. Pre-dilatation with a balloon catheter less than or equal to the reference diameter of the artery was performed, and direct stenting was not allowed. Target lesions were treated with a single stent whenever possible, but up to 2 stents could be placed in an overlapping manner to cover longer lesions up to 27 mm or multiple lesions (provided the primary lesion met angiographic eligibility) or to cover any stent-edge dissections. The total number of stents per patient was limited to 4. Post-dilation was performed at operator discretion.
Follow-up	**6 months**
Conflict of interest/source of funding	The trial was funded by Medtronic Cardiovascular. Most of the authors are consultants for Medtronic.

Analysis

Follow-up issues:

- Patients had follow-up at 30 days, 3 months and 6 months. A follow-up of 5 years has been planned for all patients.
- The per-protocol analysis excluded 5 patients who had lesions in pelvic arteries other than the internal pudendal artery resulting in a per-protocol cohort of 25 patients. In the intention-to-treat (ITT) group, 3 patients were unavailable for follow-up at 3 and 6 months. In the per-protocol group, 3 patients were unavailable for follow-up at 3 months and 2 were unavailable at 6 months.

Study design issues:

- Patients were screened at 16 centres by a urologist with expertise in sexual medicine and a vascular interventional specialist.
- 383 patients were originally screened and 353 patients were excluded from the study.
- Quantitative angiographies were performed by observers who were unaware of the clinical outcomes in an angiographic core laboratory.
- 63% (19/30) of patients received 27 unilateral stents (12 patients received 1 stent, 6 received 2 stents and 1 received 3 stents) and 37% (11/30) of patients received 29 bilateral stents (4 received 2 stents, 7 received 3 stents).

Study population issues: Many patients had known cardiovascular risk factors but most patients had no history of ischemic heart disease.

Other issues: Some examinations were not interpretable formally because of the learning curve related to the required Doppler angle of insonation.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **30 (45 lesions were treated)**

Mean hospital stay: 0.5±0.5 days

Procedural success (stent could cross the target lesion after adequate pre-dilation): 100%

Post-stent balloon dilatation was performed in 50% of lesions.

Angiographic lesion characteristics (45 lesions in 30 patients)

Angiographic quantitative analysis	Before the procedure	Immediately after the procedure	6 months after the procedure
Reference vessel diameter (mm)	2.63 ± 0.43	--	2.48 ± 0.35
Lesion length (mm)	17.55 ± 9.94	--	--
Lesion minimum luminal diameter (mm)	0.96 ± 0.41	2.08 ± 0.51	1.49 ± 0.56
Lesion percent stenosis (%)	63 ± 15	23 ± 11	40 ± 20
Acute gain (mm)	--	1.13 ± 0.54	--
Late lumen loss	--	--	0.56 ± 0.57

- The proximal and distal reference vessel diameter and the minimal lumen diameter were used to determine the percent diameter stenosis before and after the procedures and at 6 months of follow-up.
- Acute gain was defined as the increase in the minimal lumen diameter from baseline to the post-procedure angiogram; late lumen loss was defined as the loss in minimal lumen diameter from the post-procedural to the follow-up angiogram.

Binary restenosis at 6 months

ITT group: 34% (95% CI 19% to 53%), number of lesions = 32

PP group: 31% (95% CI 14% to 52%), number of lesions = 26

- Binary restenosis was defined as ≥50% diameter stenosis on follow-up angiography.
- Binary restenosis was observed at 6 months in 33% (10/30) subjects in the ITT group and 34% (11) of 32 reported lesions; 2 of these 11 cases of binary restenosis were observed on non-target lesions (left obturator artery and middle rectal artery), the latter of which occurred after stent migration. Binary restenosis was seen in 8 of 26 lesions treated in the PP group.

Stent integrity (absence of stent fracture or deformation)

ITT group: 100% (95% CI: 89% to 100%), number of lesions = 31.

Erectile function

	Pre-procedure	1 month	3 months	6 months
Total IIEF score	40.4 ± 9.0, n=30	47.9 ± 15.3, n=30	51.9 ± 16.6, n=27	52.9 ± 15.8, n=28
Peak Systolic velocity (cm/s)	16.4 ± 8.1, n=14	28.8 ± 10.0, n=25	Duplex ultrasound not performed	42.0 ± 26.9, n=23

Values are reported as mean ± SD.

Total change in IIEF from pre-procedure to 6 months= 12.5 (95% CI 6.1 to 19.0)

IIEF-6 improvement ≥4 points

	3 months	6 months
ITT group	59% (95% CI 39% to 78%), n=27	59% (95% CI 39% to 78%), n=27
PP group	68% (95% CI 45% to 86%), n=22	70% (95% CI 47% to 87%), n=23

Safety

There were no deaths reported.

No major safety events were reported within the follow-up of 6 months.

Abbreviations used: CI, confidence interval; ED, erectile dysfunction; IIEF, international index of erectile function; ITT, intention-to-treat; PDE5i, phosphodiesterase-5 inhibitors; PP, per-protocol; SD, standard deviation.

Study 2 Wang T-D (2014)

Details

Study type	**Case series**
Country	Taiwan
Recruitment period	2012-2013
Study population and number	n=**20** patients with ED and isolated penile artery stenoses
Age and sex	Mean 61 years; 100% (20/20) male
Patient selection criteria	Inclusion criteria: Men 20 years or older with "consistent" erectile dysfunction defined as 2 IIEF-5 scores, taken at least 4 weeks apart, being in the range of 5 to 21 points and with a difference of ≤2 points; unilateral luminal diameter stenosis ≥70% or bilateral diameter stenoses ≥50% in the common penile artery, cavernosal artery, or dorsal penile artery proximal to the first cavernosal artery, a target lesion reference vessel diameter ≥1 mm, and a target lesion length ≤30 mm. Exclusion criteria: Arterial inflow to the penis entirely from the accessory pudendal arteries; presence of focal diameter stenosis ≥50% in the common iliac artery, internal iliac artery, anterior division of internal iliac artery, or internal pudendal artery; previous radical prostatectomy, pelvic radiation, or Peyronie's disease; untreated hypogonadism; acute coronary syndrome, stroke, or life-threatening arrhythmia within 3 months before enrolment; poorly controlled diabetes mellitus with glycosylated haemoglobin levels >9%; serum creatinine levels >2.5 mg/dL; bleeding diathesis or known hypercoagulopathy; life expectancy of less than 12 months; and known intolerance to contrast agents.
Technique	After confirmation of angiographic eligibility, patients received 8000 U of heparin to maintain an activated clotting time ≥250 s. All patients received aspirin (100 mg daily) and clopidogrel (75 mg daily and 300 mg loading 1 day before intervention) before balloon angioplasty of the penile artery. After the intervention, 2 doses of subcutaneous enoxaparin (1 mg/kg) were administered. Post-procedural antiplatelet therapy included aspirin (100 mg daily) indefinitely and clopidogrel (75 mg daily) for 3 months.
Follow-up	**6 months**
Conflict of interest/source of funding	The authors reported no conflict of interest.

Analysis
Follow-up issues: Complete follow-up data were obtained for all 20 patients at 1, 3 and 6 months.
Study design issues:
- 150 consecutive patients with ED were initially screened; 25 patients were enrolled in the study but only 20 patients were treated by balloon angioplasty because of insufficient penile artery disease following intra-arterial nitroglycerine administration during invasive pelvic angiography.
- Single-centre study.

Study population issues:
- Comorbidities and risk factors: previous myocardial infarction (1/20), coronary heart disease 65% (13/20), peripheral artery disease (1/20), hypertension 75% (15/20), diabetes mellitus 55% (11/20), hyperlipidaemia 90% (18/20), family history 35% (7/20) and smoking 20% (4/20).
- Baseline IIEF-5 scores: mild ED (score17–21), 15% (3/20) of patients; mild to moderate ED (score 12–16), 25% (5/20); moderate ED (score 8–11), 15% (3/20); severe ED (score of 7 or less).
- 15% (3/20) of patients had bilateral penile artery stenoses.
- 29 segments were treated: 59% (17/29) from the common penile artery, 38% (11/29) from the dorsal penile artery and 1 from the cavernosal artery.

Other issues:
- Patients with concomitant venogenic erectile dysfunction may have been included in the study because objective penile blood flow assessments such as duplex ultrasonography were not routinely performed before the procedure, although pelvic CT angiography was performed.
- No CT angiography was performed at follow-up.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 20 patients (23 vessels)

Technical success (residual diameter stenosis ≤30% and adequate distal run-off)
100% (23/23) of vessels

Clinical success (change in the IIEF-5 score from baseline by ≥4 points or IIEF-5 ≥22)
• At 1 month: 75% (15/20)
• At 3 months: 65% (13/20)
• At 6 months: 60% (12/20)

Erectile function
<table>
<tr><th></th><th>Baseline</th><th>After 1 month</th><th>After 3 months</th><th>After 6 months</th></tr>
<tr><td>IIEF-5 score (mean ± SD)</td><td>10.0±5.2</td><td>15.2±6.7</td><td>15.4±6.9</td><td>15.2±6.3</td></tr>
<tr><td>p value (versus baseline)</td><td></td><td><0.001</td><td><0.001</td><td><0.001</td></tr>
<tr><td>IIEF-5 ≥ 22</td><td>0</td><td>20% (4/20)</td><td>20% (4/20)</td><td>15% (3/20)</td></tr>
</table>
• Change of IIEF-5 score from baseline to 6 months after the procedure: +5.2 points (95% CI 3.0 to 7.4)
• Gradual decrease in IIEF-5 scores were reported in 27% (4/15) of patients who achieved clinical success at 1 month whereas gradual increases in IIEF-5 scores were reported in another 4 responders.

There was no case of clinical worsening or need for re-intervention during the follow-up of 6 months.
No significant changes in IIEF-5 scores from baseline to 6 months were reported among the 5 patients who were enrolled in the study but not treated by angioplasty.
</td><td>
No major adverse events were reported.

Flow-limiting dissection was reported in 1 patient. It occurred after dilating the stenotic common penile artery lesion with a 1.2 mm balloon catheter. After prolonged dilatation with the same balloon catheter, adequate distal run-off was established.
</td></tr>
<tr><td colspan="2">Abbreviations used: CT, computed tomography; ED, erectile dysfunction; IIEF, international index of erectile function; SD, standard deviation.</td></tr>
</table>

Efficacy

Erectile function

A case series of 30 patients with atherosclerotic erectile dysfunction (ED) treated by zotarolimus-eluting stents (45 lesions stented) reported international index of erectile function (IIEF; total scores range from 1 to 75, from worst to best) mean scores (±standard deviation [SD]) of 40.4 (±9.0, n=30) before the procedure and 52.9 (±15.8, n=28) 6 months after the procedure. At 6 months, 59% (16/27) of patients (95% confidence interval [CI] 39% to 78%) reported an improvement of 4 or more points on the IIEF-6 questionnaire (scores range from 1 to 30, from worst to best)[1].

A case series of 20 patients with ED and isolated penile artery stenosis treated by balloon angioplasty of the penile artery reported significant improvement in mean IIEF-5 scores (scores range from 1 to 25, from worst to best) from 10.0 (±5.2) before the procedure to 15.2 (±6.3) after 6 months (change of +5.2 points, 95% CI 3.0 to 7.4, p<0.001). IIEF-5 scores of 22 or higher were reported in none of the patients at baseline, in 20% (4/20) at 1 and 3 months, and in 15% (3/20) after 6 months. Clinical success (change in the IIEF-5 score from baseline by 4 or more points or IIEF-5 score of 22 or greater) was reported in 75% (15/20) of patients after 1 month, in 65% (13/20) after 3 months and in 60% (12/20) after 6 months[2].

Measured blood flow

The case series of 30 patients reported mean peak systolic velocities of the cavernosal arteries (±SD) of 16.4 (±8.1) cm/s before the procedure (n=14) and 42.0 (±26.9) cm/s after 6 months (n=23)[1].

Restenosis

The case series of 30 patients reported restenosis (defined as more than 50% diameter stenosis on follow-up angiography) 6 months after the procedure in 33% (10/30) of patients (34% [11/32] of lesions, 95% CI 19% to 53%). Two of these 11 cases of restenosis were observed on non-target lesions (left obturator artery and middle rectal artery, the latter of which occurred after stent migration)[1].

Technical success

The case series of 20 patients reported technical success (defined as residual diameter stenosis of 30% or less and adequate distal run-off) for all vessels treated (23/23)[2].

Safety

Arterial dissection

Flow-limiting dissection was reported in 1 patient in a case series of 20 patients with erectile dysfunction and isolated penile artery stenosis treated by balloon angioplasty of the penile artery. It occurred after dilating the stenotic common penile artery lesion with a balloon catheter. After prolonged dilatation with the same balloon catheter, adequate distal run-off was established[2].

Validity and generalisability of the studies

- In this overview, 1 study involved angioplasty with stenting (using drug-eluting stents[1]) and 1 study involved angioplasty without stenting[2].
- No controlled studies were included in table 2 and there is a lack of long-term data.
- Difficulty in selecting patients for inclusion in studies (such as evaluating the influence of psychological factors over functional causes of ED and absence of venous leak) led to small numbers of patients included.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

NICE guidelines

- Type 2 diabetes in adults: management. NICE guideline 28 (2015). Available from https://www.nice.org.uk/guidance/ng28
- Type 1 diabetes in adults: diagnosis and management. NICE guideline 17 (2015). Available from https://www.nice.org.uk/guidance/ng17
- Myocardial infarction: cardiac rehabilitation and prevention of further MI. NICE clinical guideline 172 (2013). Available from https://www.nice.org.uk/guidance/cg172

- Chronic heart failure: management. NICE clinical guideline 108 (2010). Available from https://www.nice.org.uk/guidance/cg108

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Six Specialist Advisor Questionnaires for angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 2 questionnaires to 1 NHS trust for distribution to patients who had the procedure (or their carers). NICE received 2 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Issues for consideration by IPAC

- Ongoing studies:
  - NCT01643200 Safety and Feasibility of the Zotarolimus Stent in Treating Males With Erectile Dysfunction (ED) (ZEN). Ongoing. Enrolment: 30 patients. Estimated completion date: June 2016.
  - NCT02178761 Imaging and Interventional Study for Erectile Dysfunction and Lower Urinary Tract Symptoms (PERFECT). Ongoing. Enrolment: 300 8patients. Estimated completion date: June 2016.

References

1. Rogers JH, Goldstein I, Kandzari DE et al. (2012) Zotarolimus-eluting peripheral stents for the treatment of erectile dysfunction in subjects with suboptimal response to phosphodiesterase-5 inhibitors. Journal of the American College of Cardiology 60:2618-2627.

2. Wang TD, Lee WJ, Yang SC et al. (2014) Safety and six-month durability of angioplasty for isolated penile artery stenoses in patients with erectile dysfunction: a first-in-man study. Eurointervention 10:147-156.

Appendix A: Additional papers on angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Angelini P and Fighali S. (1987) Early experience with balloon angioplasty of internal iliac arteries for vasculogenic impotence. Catheterization & Cardiovascular Diagnosis 13:107-110.	Case series n=5 FU=2 to 18 months	Balloon angioplasty is an adequate, expeditious, and relatively inexpensive method for treating subtotal obstruction of the internal iliac and/or internal pudendal arteries in patients with vasculogenic impotence	Study including patients with stenoses of the internal iliac as well as internal pudendal arteries.
Babaev A and Jhaveri RR. (2012) Angiography and endovascular revascularization of pudendal artery atherosclerotic disease in patients with medically refractory erectile dysfunction. Journal of Invasive Cardiology 24:236-240.	Case reports n=3 FU=not reported	Three men with known peripheral arterial disease and erectile dysfunction that was non-responsive to treatment with phosphodiesterase inhibitors underwent angiography and stent placement of the pudendal artery. Stent placement was performed using standard endovascular techniques. All 3 patients reported significant improvement in erectile function following revascularization.	Studies with more patients or longer follow-up are included.
Valji K and Bookstein JJ. (1988) Transluminal angioplasty in the treatment of arteriogenic impotence. Cardiovasc.Intervent.Radiol. 11:245-252.	Case reports n=3 FU= Maximum 3 months	Unilateral transluminal angioplasty, when technically successful, should prove clinically successful when patients have been properly selected. Transluminal angioplasty can reduce the cost and morbidity of penile revascularization and may assume a modest role in the treatment of arteriogenic impotence.	Case reports including patients with stenoses of the common iliac as well as internal pudendal and common penile arteries.

Appendix B: Related NICE guidance for angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction

Guidance	Recommendations
NICE guidelines	**Type 2 diabetes in adults: management. NICE guideline 28 (2015).** **1.7 Managing complications** **Erectile dysfunction** 1.7.13 Offer men with type 2 diabetes the opportunity to discuss erectile dysfunction as part of their annual review. [2015] 1.7.14 Assess, educate and support men with type 2 diabetes who have problematic erectile dysfunction, addressing contributory factors such as cardiovascular disease as well as possible treatment options. [2015] 1.7.15 Consider a phosphodiesterase-5 inhibitor to treat problematic erectile dysfunction in men with type 2 diabetes, initially choosing the drug with the lowest acquisition cost and taking into account any contraindications. [new 2015] 1.7.16 Following discussion, refer men with type 2 diabetes to a service offering other medical, surgical or psychological management of erectile dysfunction if treatment (including a phosphodiesterase-5 inhibitor, as appropriate) has been unsuccessful. [2015] **Type 1 diabetes in adults: diagnosis and management. NICE guideline 17 (2015).** **1.15 Managing complications** **Erectile dysfunction** 1.15.37 Offer men with type 1 diabetes the opportunity to discuss erectile dysfunction as part of their regular review. [new 2015] 1.15.38 Offer a phosphodiesterase-5 inhibitor to men with type 1 diabetes with isolated erectile dysfunction unless contraindicated. Choose the phosphodiesterase-5 inhibitor with the lowest acquisition cost. [new 2015] 1.15.39 Consider referring men with type 1 diabetes to a service offering further assessment and other medical, surgical or psychological management of erectile dysfunction if phosphodiesterase-5 inhibitor treatment is unsuccessful or contraindicated. [new 2015]

	Myocardial infarction: cardiac rehabilitation and prevention of further MI. NICE clinical guideline 172 (2013). ***Sexual activity*** 1.1.32 Reassure patients that after recovery from an MI, sexual activity presents no greater risk of triggering a subsequent MI than if they had never had an MI. [2007] 1.1.33 Advise patients who have made an uncomplicated recovery after their MI that they can resume sexual activity when they feel comfortable to do so, usually after about 4 weeks.[2007] 1.1.34 Raise the subject of sexual activity with patients within the context of cardiac rehabilitation and aftercare. [2007] 1.1.35 When treating erectile dysfunction, treatment with a PDE5 (phosphodiesterase type 5) inhibitor may be considered in men who have had an MI more than 6 months earlier and who are now stable. [2007] 1.1.36 PDE5 inhibitors must be avoided in patients treated with nitrates or nicorandil because this can lead to dangerously low blood pressure. [2007] **Chronic heart failure: management. NICE clinical guideline 108 (2010).** ***Sexual activity*** 1.2.1.4 Healthcare professionals should be prepared to broach sensitive issues with patients, such as sexual activity, as these are unlikely to be raised by the patient. [2003]

Appendix C: Literature search for angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	04/11/2015	Issue 11 of 12, November 2015
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	04/11/2015	Issue 10 of 12, October 2015
HTA database (Cochrane Library)	04/11/2015	Issue 4 of 4, October 2015
MEDLINE (Ovid)	04/11/2015	1946 to October week 4 2015
MEDLINE In-Process (Ovid)	04/11/2015	November 03, 2015
EMBASE (Ovid)	04/11/2015	1974 to 2015 week 44
PubMed	04/11/2015	N/A
JournalTOCS	04/11/2015	N/A

Trial sources searched on 07/04/2015

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 07/04/2015

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) – MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Database: Ovid MEDLINE(R) <1946 to June Week 1 2015>
Search Strategy:
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1 Atherosclerosis/ (22611)
2 arteriosclerosis/ (54761)
3 Peripheral Arterial Disease/ (2711)
4 Arterial occlusive diseases/ (25061)
5 Iliac Artery/ (12472)
6 Peripheral Vascular Diseases/ (11173)
7 Intermittent claudication/ (7082)
8 (intermittent* adj4 claudicat*).ti,ab. (4108)
9 ((atherosclero* or arterisclero* or atherogenesis*) adj4 lesion*).ti,ab. (12341)
10 (peripher* adj4 (arter* or vascular*) adj4 disease*).ti,ab. (17851)
11 (PAD or PVD).ti,ab. (16586)
12 ((pudendal* or iliac* or peripher* or occlusi*) adj4 arter*).ti,ab. (67567)
13 or/1-12 (192951)
14 Drug-Eluting Stents/ (6590)
15 Angioplasty, Balloon, Coronary/ (33120)
16 Angioplasty/ (5856)
17 stents/ (51029)
18 Angioplast*.ti,ab. (35825)
19 (percutaneous adj1 coronary adj1 intervention*).ti,ab. (17086)
20 (pci or ptca).ti,ab. (19132)
21 (zotarolimus* or zotarolimus-elut* or "zotarolimus elut*" or sirolimus* or sirolimus-elut* or "sirolimus elut*" or bare-metal* or "bare metal*" or drug-elut* or "drug elut*").ti,ab. (12304)
22 (Stent* or tube* or balloon* or graft* or scaffold*).ti,ab. (681620)
23 (endeavour* or resolute* or liberte* or omega* or Promus element* or Promus-element* or Multilink 8xience prime or Vision xience v).ti,ab. (31483)
24 (balloon* adj4 (open* or narrow* or inflat* or broad* or thin*)).ti,ab. (4752)
25 or/14-24 (757872)
26 erectile dysfunction/ (15345)
27 penile erection/ (5847)
28 penis/ (15721)
29 impotence, vasculogenic/ (1014)
30 ((penis* or penile* or erect*) adj4 (dysfunct* or impoten*)).ti,ab. (11361)
31 or/26-30 (31849)
32 13 and 25 and 31 (94)
33 animals/ not humans/ (3963496)
34 32 not 33 (88)