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[Intervention Review]

Atherectomy for peripheral arterial disease

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ABSTRACT

Background

Symptomatic peripheral arterial disease (PAD) has several treatment options, including angioplasty, stenting, exercise therapy, and bypass surgery. Atherectomy is an alternative procedure, in which atheroma is cut or ground away within the artery. This is the first update of a Cochrane Review published in 2014.

Objectives

To evaluate the effectiveness of atherectomy for peripheral arterial disease compared to other established treatments.

Search methods

The Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Allied and Complementary Medicine (AMED) databases, and the World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov trials registers to 12 August 2019.

Selection criteria

We included all randomised controlled trials that compared atherectomy with other established treatments. All participants had symptomatic PAD with either claudication or critical limb ischaemia and evidence of lower limb arterial disease.

Data collection and analysis

Two review authors screened studies for inclusion, extracted data, assessed risk of bias and used GRADE criteria to assess the certainty of the evidence. We resolved any disagreements through discussion. Outcomes of interest were: primary patency (at six and 12 months), all-cause mortality, fatal and non-fatal cardiovascular events, initial technical failure rates, target vessel revascularisation rates (TVR; at six and 12 months); and complications.

Main results

We included seven studies, with a total of 527 participants and 581 treated lesions. We found two comparisons: atherectomy versus balloon angioplasty (BA) and atherectomy versus BA with primary stenting. No studies compared atherectomy with bypass surgery. Overall, the evidence from this review was of very low certainty, due to a high risk of bias, imprecision and inconsistency.

Six studies (372 participants, 427 treated lesions) compared atherectomy versus BA. We found no clear difference between atherectomy and BA for the primary outcomes: six-month primary patency rates (risk ratio (RR) 1.06, 95% confidence interval (CI) 0.94 to 1.20; 3 studies, 186 participants; very low-certainty evidence); 12-month primary patency rates (RR 1.20, 95% CI 0.78 to 1.84; 2 studies, 149 participants; very low-certainty evidence) or mortality rates (RR 0.50, 95% CI 0.10 to 2.66, 3 studies, 210 participants, very low-certainty evidence). One

study reported cardiac failure and acute coronary syndrome as causes of death at 24 months but it was unclear which arm the participants belonged to, and one study reported no cardiovascular events.

There was no clear difference when examining: initial technical failure rates (RR 0.48, 95% CI 0.22 to 1.08; 6 studies, 425 treated vessels; very low-certainty evidence), six-month TVR (RR 0.51, 95% CI 0.06 to 4.42; 2 studies, 136 treated vessels; very low-certainty evidence) or 12-month TVR (RR 0.59, 95% CI 0.25 to 1.42; 3 studies, 176 treated vessels; very low-certainty evidence). All six studies reported complication rates (RR 0.69, 95% CI 0.28 to 1.68; 6 studies, 387 participants; very low-certainty evidence) and embolisation events (RR 2.51, 95% CI 0.64 to 9.80; 6 studies, 387 participants; very low-certainty evidence). Atherectomy may be less likely to cause dissection (RR 0.28, 95% CI 0.14 to 0.54; 4 studies, 290 participants; very low-certainty evidence) and may be associated with a reduction in bailout stenting (RR 0.26, 95% CI 0.09 to 0.74; 4 studies, 315 treated vessels; very low-certainty evidence). Four studies reported amputation rates, with only one amputation event recorded in a BA participant. We used subgroup analysis to compare the effect of plain balloons/stents and drug-eluting balloons/stents, but did not detect any differences between the subgroups.

One study (155 participants, 155 treated lesions) compared atherectomy versus BA and primary stenting, so comparison was extremely limited and subject to imprecision. This study did not report primary patency. The study reported one death (RR 0.38, 95% CI 0.04 to 3.23; 155 participants; very low-certainty evidence) and three complication events (RR 7.04, 95% CI 0.80 to 62.23; 155 participants; very low-certainty evidence) in a very small data set, making conclusions unreliable. We found no clear difference between the treatment arms in cardiovascular events (RR 0.38, 95% CI 0.04 to 3.23; 155 participants; very low-certainty evidence). This study found no initial technical failure events, and TVR rates at six and 24 months showed little difference between treatment arms (RR 2.27, 95% CI 0.95 to 5.46; 155 participants; very low-certainty evidence and RR 2.05, 95% CI 0.96 to 4.37; 155 participants; very low-certainty evidence, respectively).

Authors' conclusions

This review update shows that the evidence is very uncertain about the effect of atherectomy on patency, mortality and cardiovascular event rates compared to plain balloon angioplasty, with or without stenting. We detected no clear differences in initial technical failure rates or TVR, but there may be reduced dissection and bailout stenting after atherectomy although this is uncertain. Included studies were small, heterogenous and at high risk of bias. Larger studies powered to detect clinically meaningful, patient-centred outcomes are required.

PLAIN LANGUAGE SUMMARY

Atherectomy for peripheral arterial disease

Background

Peripheral arterial disease is a narrowing or blockage of the arteries in the legs. People with this condition can experience pain on walking, pain at rest, or leg ulceration due to poor blood supply. Treatment options are: surgery, using a blood vessel or graft to bypass the narrowed or blocked section of the artery; balloon angioplasty, when a deflated balloon is passed into the narrowing at the end of a wire, then blown up to stretch the artery; and stenting (used in addition to balloon angioplasty), which holds open the balloon-stretched section for extra support. A final option, less commonly used, is a technique called atherectomy. This treatment cuts or grinds away the fatty deposition (atheroma) within the artery that is causing the narrowing or occlusion.

Key results

In this review, we compared atherectomy with the other treatment options described above. We also looked within the two groups to assess whether using drug-releasing balloons or stents impacted on participants' outcomes. We identified seven studies with a total of 527 participants.

Six trials compared atherectomy against balloon angioplasty (372 participants, 427 treated lesions). We found no clear difference between the procedures when examining artery patency at six and 12 months, risk of death, initial procedure failure rates, need to re-treat the artery, risk of forming clots (embolisation), complication rates or risk of amputation. We found that atherectomy was associated with lower rates of emergency stenting during the procedure and lower balloon inflation pressures when compared with balloon angioplasty alone. We found no difference in results depending on whether the balloons were drug-releasing or not.

One study compared atherectomy against balloon angioplasty and primary stenting (155 participants and 155 treated lesions). This study did not report primary patency. We found no clear difference between the treatment arms in risk of death, complication rates, cardiovascular events and the need to re-treat the artery. This study found no initial procedure failure events,

We did not find any studies that compared bypass surgery against atherectomy.

Certainty of the evidence

Overall, our certainty in the evidence is very low, which means we do not have confidence that our results show the true effect of the treatments. We downgraded our certainty in the evidence because the studies were at high risk of bias (lack of blinding of participants or assessors, several outcomes were not reported and a number of the participants did not complete the studies); the trials were all small; and their results were inconsistent.

Conclusions

In conclusion, we have found no clear difference in effect on patency, mortality or cardiovascular event rates when comparing atherectomy against balloon angioplasty with or without stenting. The limited evidence available does not support a significant advantage of atherectomy over conventional balloon angioplasty or stenting.

Summary of findings 1. Atherectomy compared to balloon angioplasty for peripheral arterial disease

Atherectomy compared to BA for PAD

Patient or population: people with PAD
Setting: hospital
Intervention: atherectomy
Comparison: BA

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with BA	Risk with atherectomy
Primary patency (follow-up: 6 months)	186 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[a]	RR 1.06 (0.94 to 1.20)	Study population	
				575 per 1000	609 per 1000 (540 to 690)
Primary patency (follow-up: 12 months)	149 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[a]	RR 1.20 (0.78 to 1.84)	Study population	
				671 per 1000	805 per 1000 (524 to 1000)
Mortality (follow-up: 12 months)	210 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[a]	RR 0.50 (0.10 to 2.66)	Study population	
				102 per 1000	51 per 1000 (10 to 271)
Fatal and non-fatal cardiovascular events (follow-up: 24 months)	160 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[a]	—	Zeller 2017 reported cardiac failure and acute coronary syndrome as causes of death at 24 months, but it was unclear for which participants in which arms this was accountable for. Shammas 2011 declared embolic stroke and myocardial infarction to be secondary outcomes, but no events were recorded in either arm	
TVR (follow-up: 6 months)	136 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[a]	RR 0.51 (0.06 to 4.42)	Study population	
				70 per 1000	36 per 1000 (4 to 311)
TVR (follow-up: 12 months)	176 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[a]	RR 0.59 (0.25 to 1.42)	Study population	
				140 per 1000	82 per 1000 (35 to 198)
Complication rates (follow-up: 12 months)	387 (6 RCTs)	⊕⊖⊖⊖ VERY LOW[a]	RR 0.69 (0.28 to 1.68)	Study population	

				219 per 1000	151 per 1000 (61 to 367)

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

BA: balloon angioplasty; **CI:** confidence interval; **PAD**: peripheral arterial disease; **RR:** risk ratio; **TVR**: target vessel revascularisation

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a] We downgraded by three steps due to risk of bias (lack of blinding and high rates of attrition); imprecision (small trials with few participants and events); and inconsistency (heterogeneity).

Summary of findings 2. Atherectomy compared to balloon angioplasty with primary stenting for peripheral arterial disease

Atherectomy compared to BA and primary stenting for PAD

Patient or population: people with PAD
Setting: hospital
Intervention: atherectomy
Comparison: BA with primary stenting

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with BA with primary stenting	Risk with atherectomy
Primary patency (follow-up 6 months)	Not reported for this comparison				
Primary patency (follow-up 12 months)	Not reported for this comparison				
Mortality (follow-up: 24 months)	155 (1 RCT)	⊕⊖⊖⊖ VERY LOW[a]	RR 0.38 (0.04 to 3.23)	Study population	
				40 per 1000	15 per 1000 (2 to 129)

Fatal and non-fatal cardiovascular events (follow-up: 24 months)	155 (1 RCT)	⊕⊖⊖⊖ VERY LOW[a]	RR 0.38 (0.04, 3.23)	Ott 2017 reported 4 deaths at 24 months (3 deaths in the drug-eluting balloon and stent arm and 1 death in the plain balloon and stent arm) which they attributed to underlying cardiovascular disease, but no specific causes were stated.	
TVR (follow-up: 6 months)	155 (1 RCT)	⊕⊖⊖⊖ VERY LOW[a]	RR 2.27 (0.95 to 5.46)	Study population	
				80 per 1000	182 per 1000 (76 to 437)
TVR (follow-up: 24 months)	155 (1 RCT)	⊕⊖⊖⊖ VERY LOW[a]	RR 2.05 (0.96 to 4.37)	Study population	
				240 per 1000	492 per 1000 (230 to 1000)
Complication rates (follow-up: 24 months)	155 (1 RCT)	⊕⊖⊖⊖ VERY LOW[a]	RR 7.04 (0.80 to 62.23)	Ott 2017 reported 3 complications, all 3 of which were in the atherectomy arm: 2 vessel perforations and 1 flow-limiting dissection.	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

BA: balloon angioplasty **CI:** confidence interval; **PAD**: peripheral arterial disease; **RR**: risk ratio; **TVR**: target vessel revascularisation

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a] We downgraded by three steps due to risk of bias (inadequate blinding and high rates of attrition); and imprecision (small trial size, few participants and events, and wide confidence intervals).

BACKGROUND

Description of the condition

Symptomatic peripheral arterial disease (PAD) may be treated by a number of options, including exercise therapy, angioplasty, stenting and bypass surgery (Fowkes 1998; Fowkes 2008; Watson 2008). Atherectomy is a competing technique that uses a rotating cutting blade to excise the atheroma (Garcia 2009). Due to the risk of vessel perforation, atherectomy tends to be performed only in the superficial femoral and popliteal arteries, though it may be used in infrapopliteal vessels. While established treatments have a strong evidence base and guidelines for their use (TASC II 2007), the outcomes for atherectomy are less well understood. The National Institute for Health and Care Excellence (NICE) in the UK published guidelines in 2011, stating that there was inadequate evidence, especially given the risk of embolisation, and therefore they would not support the use of atherectomy outside of clinical trials (NICE 2011). This guideline is still in place.

Description of the intervention

Atherectomy is an endovascular procedure for revascularisation. Pieces of atherosclerotic plaque are removed in order to increase the luminal diameter of the vessel (Schwarzwälder 2010). The procedure is normally performed percutaneously through a 7-French (F) or 8-F sheath, unless vessel access is difficult, in which case an arterial cut-down is required. The mechanism used to remove pieces of plaque can involve a variety of techniques, but usually involves some kind of rotating cutting blade, often with a chamber to store the cut pieces.

Why it is important to do this review

This is an update of a Cochrane Review first published in 2014, which included four trials with small numbers of participants (Ambler 2014). The low number of included studies and participants made it difficult for the review authors to draw conclusions. This update is important to ensure that all current evidence from randomised trials that compare atherectomy with any established treatment for PAD is identified, in order to aid decision making.

OBJECTIVES

To evaluate the effectiveness of atherectomy for peripheral arterial disease compared to other established treatments.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) that compared atherectomy with other established treatments, including angioplasty, stenting and bypass surgery.

Types of participants

We included participants with symptomatic peripheral arterial disease (PAD) with either claudication or critical limb ischaemia and evidence of lower limb arterial disease. We considered arterial disease in any peripheral territory. We excluded studies with participants who had previously had bypass, percutaneous transluminal angioplasty (PTA) or stents in the target lesion, as these treatments might affect the primary patency rates.

Types of interventions

We included RCTs that compared atherectomy against any established treatment for PAD, in order to evaluate the effectiveness of atherectomy. We identified the following comparisons for the inclusion criteria:

- atherectomy versus balloon angioplasty, with or without stenting;
- atherectomy plus adjunctive balloon angioplasty versus balloon angioplasty; and
- atherectomy versus surgical bypass procedures.

Types of outcome measures

Primary outcomes

- Primary vessel patency, as assessed by ankle brachial index (ABI), arterial doppler ultrasound or angiography at six months and one year, and as data available in the studies
- All-cause mortality at six months and one year, and as data available in the studies
- Fatal and non-fatal cardiovascular events at six months and one year, and as data available in the studies

Secondary outcomes

- Immediate procedural and angiographic outcomes (technical failure rates)
- Target vessel revascularisation rates (TVR)
- Complication rates, including thrombus, embolus, perforation and aneurysm
- Morbidity assessment, including:
  - tissue healing;
  - avoidance of any amputation; and
  - performance of less extensive amputation
- Quality of life (QoL) outcomes, as measured in the included studies
- Clinical and symptomatic outcomes, e.g. improved walking distance, symptom relief

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Information Specialist conducted systematic searches of the following databases for randomised controlled trials and controlled clinical trials without language, publication year or publication status restrictions:

- Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web) (searched on 12 August 2019);
- Cochrane Central Register of Controlled Trials (CENTRAL; 2019, Issue 8) via the Cochrane Register of Studies Online (CRSO)
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE) 1946 to Present (searched from 1 January 2017 to 12 August 2019);
- Embase Ovid (searched from 1 January 2017 to 12 August 2019);

- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; searched from 1 January 2017 to 12 August 2019);
- AMED Ovid (Allied and Complementary Medicine Database; searched from 1 January 2017 to 12 August 2019).

The Information Specialist modelled search strategies for other databases on the search strategy designed for MEDLINE or CENTRAL. Where appropriate, the Information Specialist combined these with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6, Lefebvre 2011). Search strategies for major databases are provided in Appendix 1.

The Information Specialist searched the following trials registries on 12 August 2019:

- the World Health Organization International Clinical Trials Registry Platform (who.int/trialsearch);
- ClinicalTrials.gov (clinicaltrials.gov).

Searching other resources

We did not search any other resources.

Data collection and analysis

Selection of studies

Two review authors (BW and GA) independently selected trials for inclusion in the review. They resolved any disagreements through discussion. The section 'Criteria for considering studies for this review' details the inclusion criteria used for the selection process.

Data extraction and management

BW extracted the data, and GA cross-checked them. They resolved any disagreements through discussion. BW extracted the following information for each trial.

- Trial methods: method of randomisation, method of allocation
- Participants: country of origin, age, sex distribution, severity of disease, as measured by the ABI and using the European Consensus definition of critical ischaemia (European Consensus Document 1989), inclusion and exclusion criteria
- Interventions: type of procedure (atherectomy, angioplasty or bypass)
- Outcomes: primary and secondary outcomes, as listed in ''Types of outcome measures'

We extracted data directly from the published papers using data extraction forms, and did not make any attempt to obtain additional unpublished data. We based all analyses on endpoint data from the individual clinical trials, which all provided intention-to-treat results. We synthesised the data by comparing group results and did not amalgamate individual participant data from different trials.

Assessment of risk of bias in included studies

Two review authors (BW, GA) assessed the included studies' risk of bias independently, using Cochrane's 'Risk of bias' tool, according to the guidelines given in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1 (Higgins 2011).

The review authors assessed the following domains as 'low risk of bias', 'unclear risk of bias' or 'high risk of bias':

- sequence generation;
- allocation concealment;
- blinding of personnel and participants;
- blinding of outcome assessors;
- incomplete outcome data;
- selective outcome reporting; and
- other risk of bias.

The Characteristics of included studies table reports the assessments for each individual study.

Measures of treatment effect

We measured the treatment effects for dichotomous outcomes using risk ratios (RR) with 95% confidence intervals (CI). For continuous outcomes, we measured treatment effects as the mean difference (MD) with 95% CI.

Unit of analysis issues

For the outcomes of mortality, fatal and non-fatal cardiovascular events, complications, quality of life, and clinical and symptomatic outcomes, the unit of analysis was the individual participant rather than the treated vessel. Three trials included multiple treated vessels per participant in some cases (Dattilo 2014; Shammas 2011; Shammas 2012). This means that the observations from these trials will not be totally independent, and therefore should have less emphasis placed on them in the meta-analysis. However, as the majority of participants in these trials had only one treated vessel, and very few (16%) had more than one treated vessel, it is not likely that this will have a large impact on the results presented below. We therefore did not feel it was necessary to introduce more sophisticated statistical methods such as meta-regression to take account of these differences. We could not re-examine the data at an individual participant level.

Dealing with missing data

We performed analysis on a complete case basis, and it was not necessary to contact authors for additional data.

Assessment of heterogeneity

We looked for clinical heterogeneity by examination of the study details, and used Chi^2 tests to assess heterogeneity between trials, using P values less than 0.1 to indicate the possible presence of significant heterogeneity. Since trials contained low participant numbers, the power of this test is likely to be low if a small P value is used (Higgins 2011).

Assessment of reporting biases

We planned to assess the likelihood of potential publication bias using funnel plots, but we identified insufficient studies to create a funnel plot (Higgins 2011).

Data synthesis

We intended to pool data from all studies when the clinical procedures followed were comparable. Where possible, we used inverse-variance random-effects models for data synthesis because the included studies used different devices for atherectomy

(clinical heterogeneity) (DerSimonian 1986). We used Review Manager 5.3 software to synthesise the data (Review Manager 2014).

Subgroup analysis and investigation of heterogeneity

We had planned to carry out subgroup analyses where the studies reported the presence or absence of concomitant illness such as diabetes, hypertension, hyperlipidaemia, or chronic kidney disease. We had also planned to conduct subgroup analyses if the studies reported data on smoking, gender of participants, lesion location, length and percentage of stenosis, including whether any studies classified lesion length and percentage of stenosis according to the Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC II) (TASC II 2007). However, the included studies did not report data on these subgroups.

We performed subgroup analysis to investigate the differences between:

- atherectomy versus plain balloon angioplasty or drug-eluting angioplasty;
- atherectomy versus drug-eluting stent plus angioplasty or plain stenting plus angioplasty.

We performed this subgroup analysis given the recent concerns regarding paclitaxel-eluting devices and their potential correlation with increased risk of mortality, which arose from a systematic review and meta-analysis by Katsanos 2018. There was significant heterogeneity between the subgroups for plain balloon angioplasty/stenting versus drug-eluting balloon angioplasty/stenting in both groups, so we used random-effect models to calculate the risk ratios.

Sensitivity analysis

Many participants in the atherectomy arm of the included studies underwent additional angioplasty. Not all studies specified details of this exactly, so we were unable to analyse these participants separately. The result of atherectomy is still considered successful even with additional angioplasty, so we included these participants in the atherectomy arm for analysis. Only one trial did not perform routine angioplasty with atherectomy (Vroegindeweij 1995). We performed sensitivity analysis to assess the effect of including this study in the overall meta-analyses of the primary outcomes.

Summary of findings and assessment of the certainty of the evidence

We included 'Summary of findings' tables in this update to present the most important findings and the certainty of the evidence for the most clinically relevant outcomes. The seven outcomes in the 'Summary of findings' tables are: primary patency (six and 12 months); mortality; fatal and non-fatal cardiovascular events; TVR (six and 12 months); and complications.

We included one 'Summary of findings' table for the comparison 'Atherectomy compared to balloon angioplasty for peripheral arterial disease' (Summary of findings 1) and one for 'Atherectomy compared to balloon angioplasty with primary stenting for peripheral arterial disease' (Summary of findings 2). We determined the certainty of the evidence for each outcome using the GRADE approach, which considers the overall risk of bias of the included studies, the directness of the evidence, inconsistency within the results, precision of the estimate and risk of publication bias (Guyatt 2008). We created the 'Summary of findings' tables using GRADEpro GDT 2015 software.

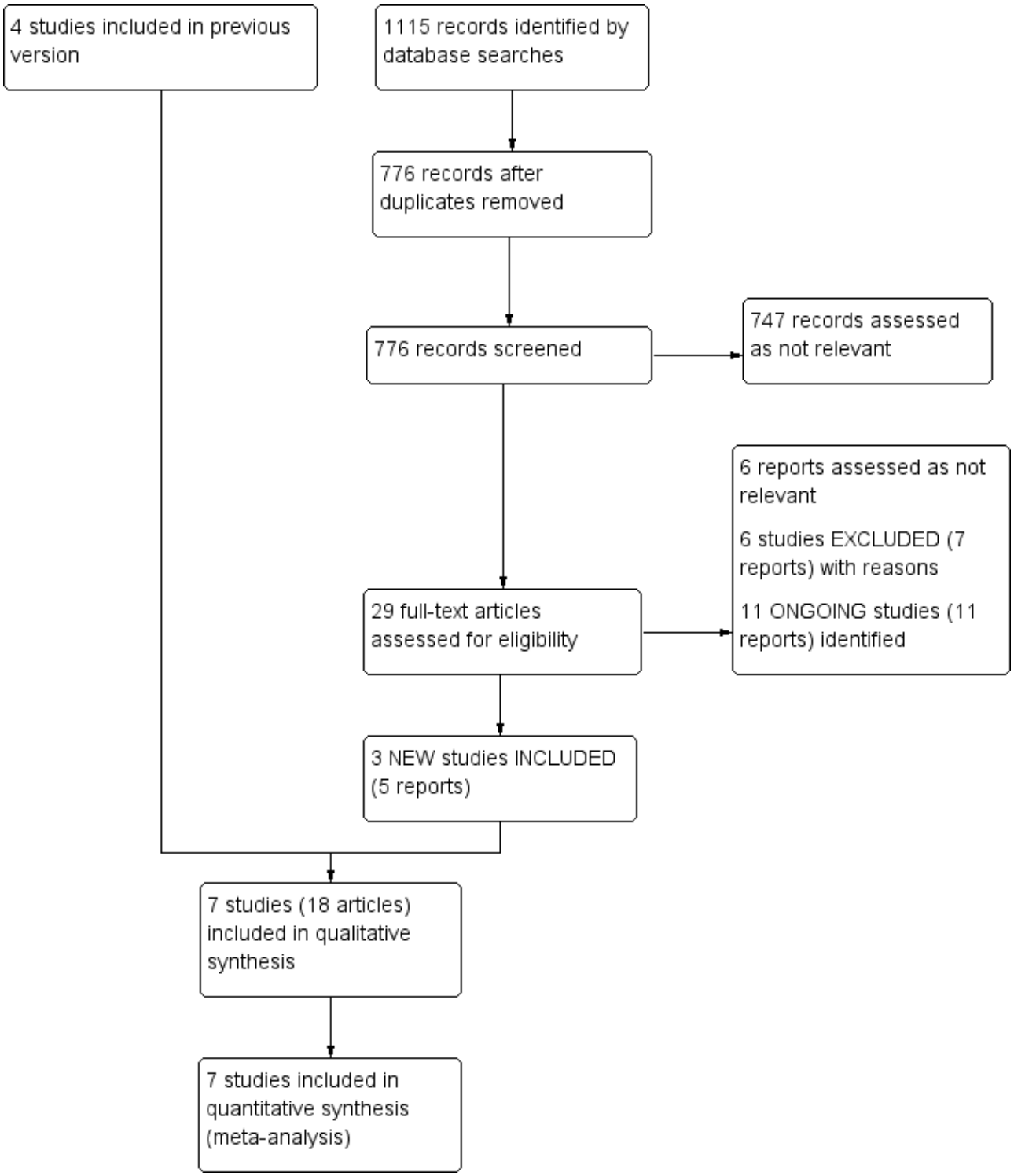
RESULTS

Description of studies

Results of the search

See Figure 1.

Figure 1. Study flow diagram.



Included studies

The 'Characteristics of included studies' table summarises the details of the included studies.

We identified three new studies for this update (Dattilo 2014; Ott 2017; Zeller 2017). Overall, seven studies involving 527 participants and 581 treated lesions met the selection criteria (Dattilo 2014; Nakamura 1995; Ott 2017; Shammas 2011; Shammas 2012; Vroegindeweij 1995; Zeller 2017). Six studies compared atherectomy to balloon angioplasty (BA) (Dattilo 2014; Nakamura 1995; Shammas 2011; Shammas 2012; Vroegindeweij 1995; Zeller 2017), and one study compared atherectomy to BA and primary stenting (Ott 2017). None of the studies used atherectomy followed

by stenting as a primary intervention; they only used bailout stenting.

Four of the six BA studies reported on primary patency (Dattilo 2014; Nakamura 1995; Vroegindeweij 1995; Zeller 2017). Vroegindeweij 1995 reported follow-up at three-month intervals for two years. The study defined loss of patency as increased flow velocities (peak systolic velocity ratio (PSVR) ≥ 2.5) or absence of flow in occluded arterial segments on duplex ultrasound scan. Nakamura 1995 reported patencies at six months' follow-up only, and assessed patency via arterial duplex. Zeller 2017 reported follow-up patencies at six months and 12 months using duplex ultrasound (defined as PSVR ≤ 2.4). Dattilo 2014 reported clinical follow-up along with ABIs and Rutherford classifications at 30 days, six months and 12 months. This trial also reported duplex ultrasound at six and 12 months, with primary patency defined as freedom from target lesion revascularisation or restenosis (PSV ≥ 2.5). Ott 2017, the primary stenting trial, did not report primary patency as one of their outcomes. Instead, the study reported target vessel revascularisation data. Shammas 2011 reported follow-up target lesion revascularisation and target vessel revascularisation at 12 months. Shammas 2012 reported follow-up target lesion revascularisation/target vessel revascularisation at three, six and 12 months.

There were also differences in modality of follow-up between studies: Ott 2017 used angiogram, Dattilo 2014 and Vroegindeweij 1995 used duplex ultrasound, Zeller 2017 used duplex ultrasound at six months and plain ultrasound at 12 months, and Nakamura 1995 used doppler pressures. Neither Shammas 2011 nor Shammas 2012 used imaging at follow-up, instead using ABI and clinical correlation.

Overall, there were a lot of differences in the clinical design and atherectomy devices used in each study.

Nakamura 1995 compared balloon angioplasty to transluminal extraction catheter (TEC) atherectomy (Stack 1988), followed by adjunctive balloon angioplasty in 39 participants with intermittent claudication (IC). TEC atherectomy utilises an over-the-wire device with a conical motorised cutting head with triangular blades, which rotate at 700 rpm, with a proximal suction apparatus that removes excised plaque. The study did not specify a medication protocol.

Vroegindeweij 1995 compared balloon angioplasty to Simpson atherectomy (Simpson 1988), in 73 participants with IC. The Simpson atherectomy device consists of cylindrical housing with a longitudinal opening down one side and a balloon on the other side. The balloon is inflated in order to both fix the device in place and press the longitudinal opening up against the wall of the vessel. A rotating cutting blade (2000 rpm) is then advanced through the cylinder so that any part of the vessel wall projecting through the longitudinal window will be cut away. The day before the procedure, all participants commenced low-dose aspirin therapy.

Shammas 2011 compared balloon angioplasty to Silverhawk atherectomy followed by adjunctive balloon angioplasty in 58 participants with claudication, rest pain or minor tissue loss. The Silverhawk atherectomy device is similar to the Simpson device, described above, except the cylindrical housing is hinged in the region of the window, with the device flexing away from the window causing the tip and tail of the device to press up against one side of the vessel wall while the window is pressed up against the other side. In this trial, a distal embolism filter was used in approximately half of the participants. If participants were not already established on dual antiplatelet therapy (aspirin and clopidogrel), they were given loading doses of aspirin and clopidogrel immediately prior to the procedure. Participants on established therapy continued on their regular doses.

Both Shammas 2012 and Dattilo 2014 compared balloon angioplasty to Diamondback atherectomy (Heuser 2008), followed by adjunctive balloon angioplasty. The Diamondback atherectomy device files away plaque, as opposed to cutting it away, via an eccentrically mounted abrasive crown on a catheter that rotates at high speed (100,000 rpm). This results in extremely small pieces of plaque, so no system for removing resulting debris is required. The Shammas 2012 trial included 50 participants with rest pain or tissue loss and stenosed, calcified vessels. The trial did not specify a medication protocol. The Dattilo 2014 trial included 50 participants (with 65 lesions) with symptomatic femoropopliteal (FP) disease. The participants had to have Rutherford class 2 to 4 symptoms (moderate claudication/Ischaemic rest pain), and de novo FP stenosis > 70% with fluoroscopically visible calcium. Participants were recommended to be on an antiplatelet agent preprocedure (preferably clopidogrel), and then aspirin and clopidogrel for a minimum of four to six weeks postprocedure.

Zeller 2017 compared paclitaxel-eluting balloon angioplasty and SilverHawk (described above) or TurboHawk atherectomy devices. The TurboHawk device is a cutting or grinding rotational atherectomy device, with the different attachments to be chosen depending upon how calcified the lesions are. It is recommended to be used in conjunction with the SpiderFX embolic protection device if using the larger cutter. This study included 102 participants with claudication or rest pain with a target lesion of ≥ 70% stenosis in the superficial femoral or popliteal artery. A uniform antiplatelet protocol was in place for both arms, requiring dual antiplatelets preprocedure, clopidogrel for four weeks postprocedure, and aspirin indefinitely.

Ott 2017 compared paclitaxel-eluting balloon angioplasty and stenting, balloon angioplasty and stenting, and SilverHawk atherectomy (described above) with distal protection (spider filter) and bailout stenting. The SpiderFX embolic protection device captures debris from the atherectomy procedure using a braided nitinol basket, and is placed downstream to stop distal trashing or embolisation. This study included 155 participants with symptomatic peripheral vascular disease and angiographic de novo stenosis > 70% or occlusion of the superficial femoral artery. Participants were given 500 mg aspirin intravenously immediately after the procedure, then 100 mg aspirin once daily indefinitely, with 75 mg clopidogrel once daily for six months or more.

Excluded studies

See Characteristics of excluded studies.

We excluded six studies following the most recent search (Del Giudice 2014; Dippel 2015; Gandini 2013; NCT02730234; NCT02832024; Schwindt 2017), bringing the total number of excluded studies to nine (Brodmann 2013; Del Giudice 2014; Dippel 2015; Gabrielli 2012; Gandini 2013; Gisbertz 2009; NCT02730234; NCT02832024; Schwindt 2017). Gabrielli 2012 and Gisbertz 2009 performed remote endarterectomy rather than atherectomy. Brodmann 2013, Del Giudice 2014, Dippel 2015,

Gandini 2013 and NCT02832024 included participants with an in-stent restenosis. We excluded NCT02730234 and Schwindt 2017 as they were non-randomised single arm trials. We reassessed one previously excluded study as ongoing (NCT01579123).

Ongoing studies

See Characteristics of ongoing studies.

We identified 11 new studies that compared drug-coated balloon angioplasty with atherectomy, and listed these as ongoing (ChiCTR-IOR-17012486; Martinsen 2015; NCT01579123; NCT01763476; NCT02514460; NCT02517827; NCT02561299; NCT02840786; NCT03206762; NCT03380650; NCT03495453). Two studies previously assessed as ongoing are now included studies (Ott 2017; Zeller 2017).

Risk of bias in included studies

The 'Risk of bias' assessments are presented in the 'Characteristics of included studies' table and summarised in Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

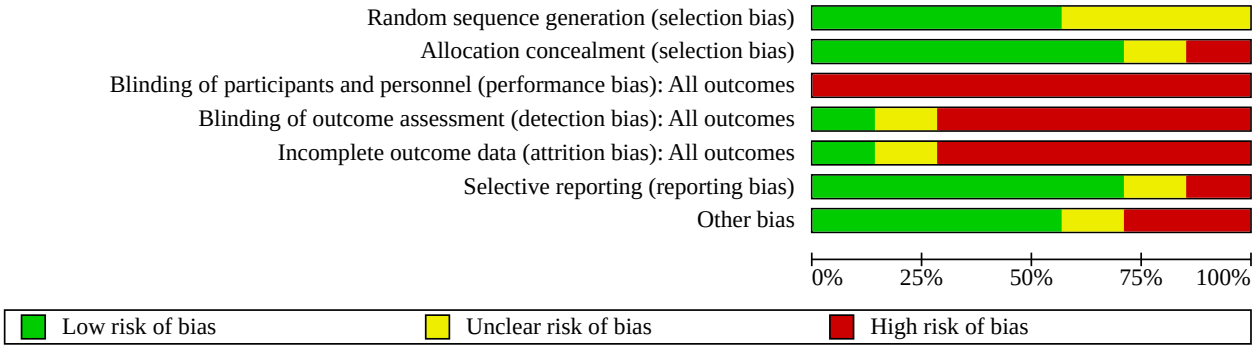
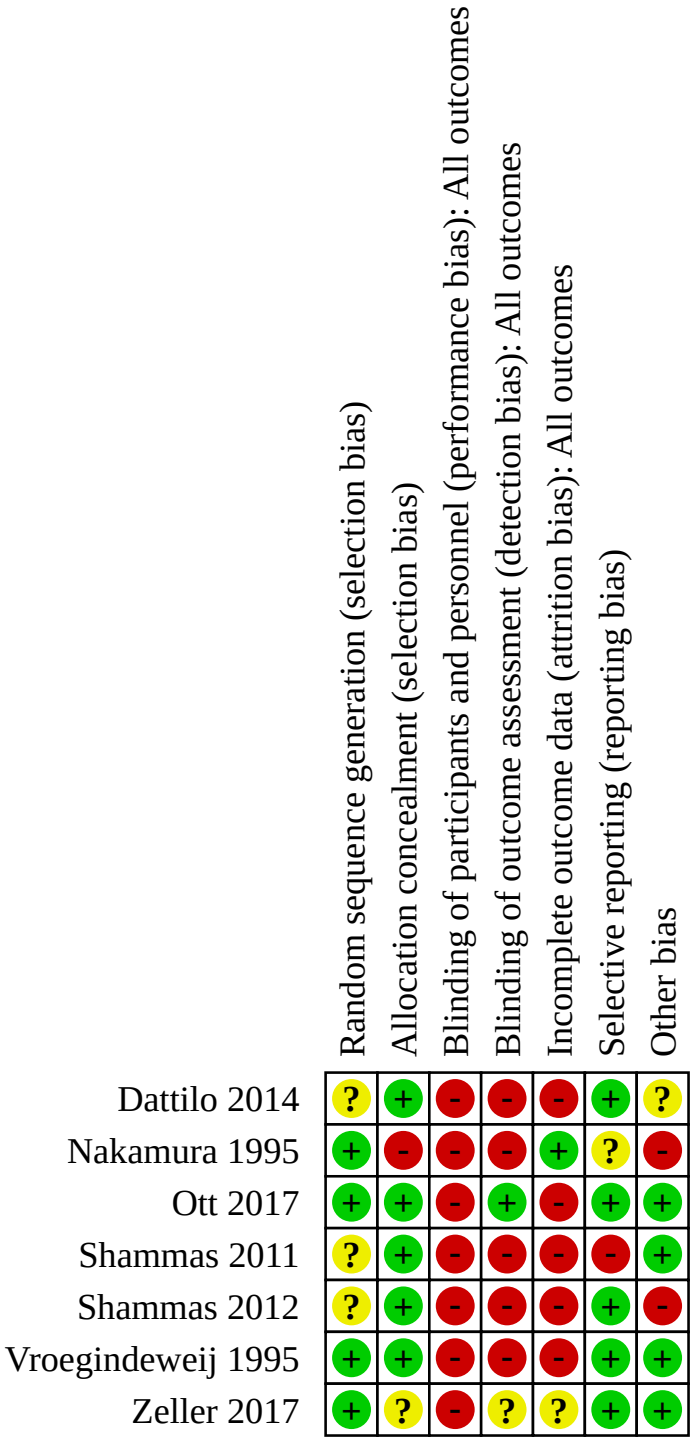


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

We judged four of the studies to be at low risk for randomisation methods: Nakamura 1995 used a random numbers table; Ott 2017 used a computer-generated sequence; Vroegindeweij 1995 used numbered envelopes opened sequentially and Zeller 2017 used block randomisation by centre. Three studies were of unclear risk for randomisation methods: Dattilo 2014 did not state the method of randomisation; Shammas 2011 performed simple randomisation on a 1:1 basis, but did not describe the method of sequence generation; and Shammas 2012 stated that sealed envelopes were provided to all centres for randomisation, but did not report the randomisation method.

We deemed five studies to be at low risk for allocation bias. Dattilo 2014, Shammas 2012, Vroegindeweij 1995 and Ott 2017 performed randomisation only after passing the guidewire and assessing inclusion and exclusion criteria, and used sealed envelopes to conceal allocation. Shammas 2011 used sealed envelopes for allocation concealment. Zeller 2017 assigned participants to treatment groups after successful passage of the guidewire across the target lesion, so we judged this to be at unclear risk. Nakamura 1995 did not report any method of allocation concealment, so we judged this to be at high risk.

Blinding

It is not possible to blind operators for this procedure, so we assessed all trials to be at high risk for performance bias (Dattilo 2014; Nakamura 1995; Ott 2017; Shammas 2011; Shammas 2012; Vroegindeweij 1995; Zeller 2017). We also deemed bailout stenting to be at high risk of bias, given that the decision is made at the time of intervention by non-blinded technicians, who could therefore influence results. Blinding for postprocedure follow-up is possible, but Ott 2017 appears to have been the only study to implement this fully, as the independent core laboratory was blinded to the treatment assignment, We therefore considered Ott 2017 to be at low risk of detection bias. Zeller 2017 blinded the duplex ultrasound core laboratory staff and clinical events committee, but none of the other outcome assessors, giving an unclear risk of detection bias. We judged all of the remaining studies to be at high risk of detection bias (Dattilo 2014; Nakamura 1995; Shammas 2011; Shammas 2012; Vroegindeweij 1995). There was, therefore, an overall risk of both performance and detection bias in all seven trials.

Incomplete outcome data

Five of the seven studies had high risk of attrition bias due to significant numbers of participants not being followed up to both six and 12 months (Dattilo 2014; Ott 2017; Shammas 2011; Shammas 2012; Vroegindeweij 1995). We judged Zeller 2017 to be at unclear risk of bias. Although participants in the study were lost to follow-up, only 15/102 failed to provide primary outcome data. We deemed Nakamura 1995 to be at low risk because there was a complete data set up to six months. Overall, we had serious concerns about the presence of attrition bias.

Selective reporting

All studies reported the primary outcomes fully, but two studies failed to completely report all secondary outcomes. Nakamura 1995 reported initial and six-month patencies, but only reported ABIs for participants whose vessels remained patent. We therefore judged this study to be at unclear risk of selection bias. Shammas 2011 also failed to completely report follow-up ABIs and did not fully report major adverse events, so we considered this to be at high risk of selection bias. The remaining studies reported all outcomes fully, so we rated them to be at low risk of selective reporting (Dattilo 2014; Ott 2017; Shammas 2012; Vroegindeweij 1995; Zeller 2017) .

Other potential sources of bias

Antiplatelet protocols were clear and uniform in four studies, reducing the risk of confounding by medication differences and so were at low risk of other bias (Ott 2017; Shammas 2011; Vroegindeweij 1995; Zeller 2017). Shammas 2012 and Nakamura 1995 did not address antiplatelet protocols, which may have impacted outcomes between participant groups. We judged these to be at high risk as no antiplatelet protocol was in place. We considered Dattilo 2014 to be 'unclear' for risk of other bias, as the trial randomised vessels rather than participants, meaning a participant could be enrolled more than once and therefore could confound results.

Effects of interventions

See: **Summary of findings 1** Atherectomy compared to balloon angioplasty for peripheral arterial disease; **Summary of findings 2** Atherectomy compared to balloon angioplasty with primary stenting for peripheral arterial disease

See Summary of findings 1 for the comparison 'Atherectomy compared to balloon angioplasty for peripheral arterial disease'.

See Summary of findings 2 for the comparison 'Atherectomy compared to balloon angioplasty with primary stenting for peripheral arterial disease'.

We performed meta-analyses using a random-effects model as there was clinical heterogeneity between the studies due to the different devices used.

Primary outcomes

Primary vessel patency

Three of the six atherectomy versus BA studies reported primary patency at six months (Nakamura 1995; Vroegindeweij 1995; Zeller 2017). Pooled analysis did not show any clear benefit of atherectomy primary patency at six months (RR 1.06, 95% CI 0.94 to 1.20; 3 studies, 186 participants; very low-certainty evidence Analysis 1.1) or at 12 months (RR 1.20, 95% CI 0.78 to 1.84; 2 studies, 149 participants; very low-certainty evidence; Analysis 1.2). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

In the atherectomy versus primary stenting study, Ott 2017 did not report primary patency.

All-cause mortality

In the atherectomy versus BA comparison, three studies reported mortality rates at one year (Shammas 2011; Shammas 2012; Zeller 2017). In Shammas 2012, there were an unexpectedly high number of deaths in the BA arm (6/25 (24%) participants), with no deaths in the atherectomy arm, though the trialists could find no good explanation for this. Shammas 2011 reported 4/29 (14%) deaths

in the BA arm and 2/29 (7%) deaths in the atherectomy arm. Zeller 2017 reported one-year mortality as 2/48 (4%) deaths in the atherectomy arm compared to 1/54 (2%) deaths in the BA arm. These deaths were not attributed to the procedure, however, with the causes listed as heart failure/stroke, acute coronary syndrome, respiratory failure and neoplastic disorder. Meta-analysis of this endpoint showed no difference in mortality between the two arms (RR 0.50, 95% CI 0.10 to 2.66; 3 studies; 210 participants; very low-certainty evidence; Analysis 1.3). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

In the atherectomy versus primary stenting comparison, Ott 2017 reported mortality at six and 24 months as a secondary outcome. Ott 2017 reported one postprocedural death caused by haemorrhagic shock secondary to retroperitoneal bleeding in the stenting and drug-eluting balloon arm. At 24 months, they reported three deaths in the drug-eluting balloon and stent arm, one death in the plain balloon and stent arm and no deaths in the atherectomy arm. All of these deaths were attributed to underlying cardiovascular disease (RR 0.38, 95% CI 0.04 to 3.23; 1 study, 155 participants; very low-certainty evidence; Analysis 2.1). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition) and imprecision (small trial size).

Fatal and non-fatal cardiovascular events

Three studies reported cardiovascular outcomes (Ott 2017; Shammas 2011; Zeller 2017).

In the atherectomy versus BA comparison, Zeller 2017 reported cardiac failure and acute coronary syndrome as causes of death at 24 months, but it was unclear which participants in which arms this related to. Shammas 2011 declared embolic stroke and myocardial infarction to be secondary outcomes, but recorded no events in either arm. We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

In the atherectomy versus primary stenting comparison, Ott 2017 reported four deaths at 24 months (three deaths in the drug-eluting balloon and stent arm and one death in the plain balloon and stent arm). The trialists attributed these to underlying cardiovascular disease, but did not state any specific causes (RR 0.38, 95% CI 0.04 to 3.23; 1 study, 155 participants; very low-certainty evidence; Analysis 2.2).

Secondary outcomes

Immediate procedural and angiographic outcomes

All seven trials reported on initial technical failure rates (Dattilo 2014; Nakamura 1995; Ott 2017; Shammas 2011; Shammas 2012; Vroegindeweij 1995; Zeller 2017). We were able to pool the six trials that compared atherectomy to BA. There was no clear improved technical success when using atherectomy compared to BA alone (RR 0.48, 95% CI 0.22 to 1.08; 6 studies; 425 treated vessels; very low-certainty evidence; Analysis 1.4). In the drug-eluting balloon angioplasty subgroup, there was an apparent benefit from atherectomy (RR 0.29, 9% CI 0.12 to 0.72, 1 study; 101 treated vessels; very low-certainty evidence). However, the test for subgroup differences did not demonstrate a difference between the balloon angioplasty and drug-eluting balloon angioplasty groups (P = 0.32).

In the atherectomy versus primary stenting trial (Ott 2017), there were no initial technical failures in either arm (Analysis 2.3).

We downgraded the certainty of the evidence from high to very low across both comparisons due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

Four studies that compared atherectomy with BA reported rates of bailout stenting, with similar indications (presence of severe dissection or > 30% residual stenosis) in both arms (Dattilo 2014; Shammas 2011; Shammas 2012; Zeller 2017). Shammas 2012 also reported perforation or significant vessel recoil as a reason for bailout stenting. There were higher incidences of bailout stenting in the BA participants (RR 0.26, 95% CI 0.09 to 0.74; 4 studies, 315 treated vessels; very low-certainty evidence; Analysis 1.5). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

The atherectomy versus primary stenting trial by Ott 2017 reported that 14/55 (25%) participants in the atherectomy group received bailout stenting due to flow-limiting dissections, one of whom developed thrombus requiring thrombus aspiration. Two participants had perforations, one treated with a covered stent, the other by prolonged balloon inflation and protamine administration. We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

Three studies that compared atherectomy with BA reported balloon inflation pressures (Dattilo 2014; Shammas 2011; Shammas 2012). Meta-analysis showed a reduction in balloon pressures needed to inflate the angioplasty balloons (MD -3.68 mmHg, 95% CI -5.36 to -2.01; 3 studies, 213 treated vessels; very low-certainty evidence; Analysis 1.6). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity). The atherectomy versus primary stenting trial did not report balloon inflation pressures (Ott 2017).

Target vessel revascularisation rates

There was some variation between trials as to whether they collected target lesion revascularisation data or target vessel revascularisation data, or both. Upon discussion, we made the decision to collect target vessel revascularisation data, as we felt this allowed us to perform the fairest comparison between all studies, as only a small minority of participants had more than one lesion treated and only Dattilo 2014 reported target lesion revascularisation rates. For this reason, we have not included Dattilo 2014 in the meta-analysis.

Three atherectomy versus BA studies reported TVR as one of their outcomes (Shammas 2011; Shammas 2012; Zeller 2017). Two of the studies reported six-month TVR. Shammas 2012 reported 0/22 (0%) in the atherectomy arm and 3/20 (15%) in the angioplasty arm;

and Zeller 2017 reported 2/43 (5%) in the atherectomy arm and 2/51 (4%) in the angioplasty arm. On pooling the study data, we found no clear differences between the two arms at six months (RR 0.51, 95% CI 0.06 to 4.42; 2 studies, 136 treated vessels; very low-certainty evidence; Analysis 1.7). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity). Dattilo 2014 reported that 6/35 (17%) participants in the atherectomy arm and 2/26 (8%) participants in the angioplasty arm required revascularisation by six months.

Shammas 2011, Shammas 2012 and Zeller 2017 all reported 12-month TVR outcomes. The pooled analysis showed no clear benefit when using atherectomy (RR 0.59, 95% CI 0.25 to 1.42; 3 studies, 176 treated vessels; very low-certainty evidence; Analysis 1.8). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

For the comparison of atherectomy versus primary stenting with or without drug eluting balloon, Ott 2017 reported TVR at six months and 24 months. Results did not show a clear difference between the treatment arms for either six-month TVR (RR 2.27, 95% CI 0.95 to 5.46; 1 study, 155 participants; very low-certainty evidence; Analysis 2.4) or 24-month TVR (RR 2.05, 95% CI 0.96 to 4.37; 1 study, 155 participants; very low-certainty evidence; Analysis 2.5). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); and imprecision (small trial size and wide confidence intervals).

Complication rates

All six studies in the atherectomy versus BA comparison reported complication events, with no clear difference detected (RR 0.69, 95% CI 0.28 to 1.68; 6 studies, 387 participants; very low-certainty evidence; Analysis 1.9) (Dattilo 2014; Nakamura 1995; Shammas 2011; Shammas 2012; Vroegindeweij 1995; Zeller 2017). Atherectomy showed no clear difference in the incidence of embolisation (RR 2.51, 95% CI 0.64 to 9.80; 6 studies, 387 participants; very low-certainty evidence; Analysis 1.10). We detected lower incidences of dissection following atherectomy (RR 0.28, 95% CI 0.14 to 0.54; 4 studies, 290 participants; very low-certainty evidence; Analysis 1.11). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

Dattilo 2014 reported that 0/25 (0%) participants in the atherectomy arm and 1/25 (4%) participants in the angioplasty arm had a perforation during the procedures. Six participants in the atherectomy arm and 13 participants in the angioplasty arm had a dissection, but the trialists did not report whether any of these participants required further intervention as a result. They did not report any other complications.

Nakamura 1995 reported that 3/13 (23%) participants in the balloon angioplasty group had perforations due to guidewire manipulation, all of which were treated conservatively. In the atherectomy group, 1/26 (4%) participants had a perforation, 4/26 (15%) participants had distal embolisation and two of the atherectomy devices broke intraprocedure. They also reported that one participant had an acute myocardial infarction during the operation, but did not state which intervention arm the participant belonged to.

Shammas 2012 reported that 1/25 (4%) participants in the atherectomy arm and 6/25 (24%) participants in the angioplasty arm experienced vessel dissection. Five of these were treated by stent placement, and two (both in the angioplasty arm) were treated with dilatation. One of the 25 participants (4%) in the atherectomy arm received a stent for slow flow, and 1/25 (4%) participants in the angioplasty arm received a stent for vessel recoil. One of the 25 participants (4%) in the angioplasty arm experienced vessel perforation (treated by balloon dilatation), and 1/25 (4%) participants in the angioplasty arm experienced distal embolisation.

Shammas 2011 reported that one of the 29 participants (3%) in the atherectomy arm, who was not treated with a distal embolisation filter, had a clinically significant distal embolisation that required mechanical and pharmacological therapy. In the atherectomy arm, 17/29 (58%) participants were treated with a distal embolisation filter, of whom 11/17 (65%) had macroembolisation with debris larger than 2 mm captured in the filter. None of the 10 participants in the angioplasty group who were treated with a filter had significant debris caught in it. No participants treated with a filter had clinically significant embolisation distal to the filter, and all filters were removed without further complications.

Vroegindeweij 1995 reported one large dissection that caused superficial femoral occlusion after three months, and one small dissection in the atherectomy arm (38 participants). The study also reported one thrombosis event in the atherectomy arm during the procedure, which was treated with streptokinase, and one case of failure to pass the guidewire. In the balloon angioplasty arm, the trialists reported that there were five small dissections among the 35 participants.

Zeller 2017 reported that there were two clinically significant distal embolisation events that required endovascular intervention, and one distal embolisation event that was not clinically significant in the atherectomy cohort (48 participants). Additionally, two perforations occurred in this group, which were successfully treated with prolonged percutaneous transluminal angioplasty. No embolisations and no perforations occurred in the angioplasty group (54 participants). In the angioplasty arm, 10 grade C or higher dissections occurred, with only one in the atherectomy arm.

Ott 2017 (atherectomy versus primary stenting) reported three complications, all of which were in the atherectomy arm (55 participants): two vessel perforations and one flow-limiting dissection (Analysis 2.6).

Morbidity assessment

Four studies reported rates of amputation, three of which compared atherectomy versus BA (Shammas 2011; Shammas 2012; Zeller 2017), with only one event across all trials (in the angioplasty arm of Shammas 2011) (RR 0.33, 95% CI 0.01 to 7.80; 3 studies, 178 participants; very low-certainty evidence; Analysis 1.12). We downgraded the certainty of the evidence from high to very low due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

There were no amputation events in the study that compared atherectomy versus BA and primary stenting (Analysis 2.7; Ott 2017).

Quality of life outcomes

None of the included studies reported on quality of life outcomes.

Clinical and symptomatic outcomes

Two atherectomy versus BA trials reported clinical and symptomatic outcomes. Zeller 2017 reported functional outcomes in their study, including pain score, walking distance score, walking speed score and stair climbing score for baseline, six months and one year. However, they did not report any benefit for any of the outcomes at either time period. None of the other studies reported clinical or symptomatic outcomes. Shammas 2011 reported 30-day and 12-month ABI and Rutherford class, and stated that there was no difference between any of these outcomes in the two treatment arms.

The atherectomy versus primary stenting trial did not report clinical and symptomatic outcomes (Ott 2017).

Sensitivity analysis

Three studies treated more than one vessel per participant or limb (Dattilo 2014; Shammas 2011; Shammas 2012). It is possible, therefore, that the outcomes of these trials received greater weight in the meta-analysis than is appropriate in the analysis of six-month and 12-month patency and TVR. Ideally, we would have carried out sensitivity analysis to assess the impact this had upon the results. However, given the low number of studies, this was not possible.

Only Vroegindeweij 1995 did not perform routine angioplasty with atherectomy. We performed sensitivity analysis to assess the effect of including this study in the overall meta-analyses of the primary outcomes (primary vessel patency and all-cause mortality), and did not observe any difference between including or excluding this study in the analysis.

DISCUSSION

Summary of main results

The main findings from this update involving seven RCTs (527 participants and 581 treated lesions) show that the evidence is very uncertain about the effect of atherectomy on primary patency compared to balloon angioplasty (BA) or primary stenting at either six or 12 months (Analysis 1.1; Analysis 1.2). There was also no clear difference in mortality between atherectomy and BA or primary stenting (very low-certainty evidence; Analysis 1.3; Analysis 2.1). Although cardiac events were reported in two of the atherectomy versus BA trials, in one study it was unclear which arm the participants belonged to and the second study reported no events. Cardiac event rates showed no clear difference between atherectomy and primary stenting (very low-certainty evidence; Analysis 2.2).

Initial technical failure rates showed no clear difference when using atherectomy compared with BA (very low-certainty evidence; Analysis 1.4), and there were no events available for comparison between atherectomy and BA with primary stenting (very low-certainty evidence; Analysis 2.3).

There was a reduction in the need for bailout stenting associated with a reduction in the inflation pressure necessary to achieve an optimal balloon inflation in the atherectomy arm compared to BA (very low-certainty evidence; Analysis 1.5 and Analysis 1.6, respectively).

When comparing atherectomy with BA, TVR was not reduced at either six or 12 months (very low-certainty evidence; Analysis 1.7 and Analysis 1.8). In the atherectomy versus primary stenting arms, analysis did not show any clear benefit of primary stenting on TVR at either six or 24 months (very low-certainty evidence; Analysis 2.4; Analysis 2.5).

This review showed there was no overall reduction in complications when using atherectomy compared with BA (very low-certainty evidence; Analysis 1.9). The atherectomy versus BA trials reported embolisation and dissection events. Embolisation events were fewer in the BA arm, although results are subject to very low certainty; Analysis 1.10). Dissection events were fewer in the atherectomy arm (very low-certainty evidence; Analysis 1.11).

There was only one amputation event in the three trials (178 participants) which compared atherectomy with angioplasty (very low-certainty evidence; Analysis 1.12), and there were no events in the atherectomy versus primary stenting trial.

Zeller 2017 was the only trial to report clinical and symptomatic outcomes, such as walking distance or symptom relief, with no reported benefit. Similarily, Shammas 2011 reported no differences between groups in terms of ABI and Rutherford classification; outcomes reported only by Shammas 2011.

We performed subgroup analysis in this review because the included trials used both drug-eluting and plain balloon angioplasty devices as control arms. However, we found no clear difference between these two groups for any outcome in either comparison.

One concern with atherectomy devices is the risk of distal embolisation, as the devices physically cut or grind plaques (Briguori 2003). One of the included studies found this to be a particular issue, and deployed a distal embolic filter in 17/29 (59%) of participants, which caught macroembolic debris (defined as debris greater than 2 mm in the longest axis) in 11/17 (65%) cases (Shammas 2011). The filter was deployed in 10/29 (34%) of the participants in the BA arm, but did not catch macroemboli in any cases. In addition, one participant in the atherectomy arm who was treated without a filter had a clinically significant distal embolic event. In Shammas 2012, one participant out of 20 (5%) in the BA arm had a clinically significant embolic event. Zeller 2017 reported two clinically significant distal embolic events that required endovascular intervention in the atherectomy cohort. However, the device used comes with a recommendation to use a SpiderFX embolic filter if using the larger atherectomy device.

Overall completeness and applicability of evidence

This update includes all information from RCTs identified by the searches, and we have presented an up-to-date meta-analysis of atherectomy versus any other therapy for peripheral arterial disease (PAD). We found comparisons for atherectomy versus BA and atherectomy versus primary stenting plus angioplasty; but not for atherectomy versus bypass surgery.

The indication for intervention was claudication in two studies (Nakamura 1995; Vroegindeweij 1995); claudication or rest pain in Dattilo 2014; and claudication, rest pain or tissue loss in three studies (Ott 2017; Shammas 2011; Shammas 2012). Results of angioplasty and bypass surgery are known to vary between people with these indications (TASC II 2007), so may bias the results from the different studies. Some of the included studies did not state the severity of claudication, which may mean that the participants would have been managed conservatively in many centres (Frans 2012), so the results should be interpreted with a degree of caution. Unfortunately, we were not able to separate results by symptoms (claudication or critical ischaemia) because of the way the studies reported results. In addition, the majority of included studies did not report on all of this review's prespecified outcomes. Therefore, the findings of this review are based in most cases on results from only one or two studies.

Amputation-free survival is an important endpoint in trials for chronic limb threatening ischaemia, but the included trials did not report this. One reason may be the reliance on including participants with less severe form of peripheral arterial disease (claudication) into the trials.

Mortality is commonly reported in trials of lower limb revascularisation, which is why we considered it a primary outcome measure. However, mortality rates from angioplasty are much lower than primary patency or limb loss rates (Laird 2010; Schillinger 2006), so trials would not be expected to show a difference if powered to detect primary patency. The results presented may be a consequence of random error due to few events in small sample sizes. There was little difference in all-cause mortality rates between interventions, but mortality was only reported in four of the seven included trials, and rates of death were low (16 deaths out of 365 participants (4%)).

In addition, there were differences in modality of follow-up between studies, which could introduce potential bias: Ott 2017 used angiogram; Dattilo 2014 and Vroegindeweij 1995 used duplex ultrasound; Zeller 2017 used duplex ultrasound at six months and plain ultrasound at 12 months; and Nakamura 1995 used doppler pressures. Neither Shammas 2011 nor Shammas 2012 used imaging at follow-up; instead they used ABI and clinical correlation. These differences in outcome collection should be considered when interpreting the results.

Quality of the evidence

All seven included studies were of poor methodological quality, with a high risk of overall bias due to a lack of blinding and high attrition, meaning the conclusions that can be drawn from the analyses are severely limited. There was significant statistical heterogeneity between studies, due to the small participant numbers. In addition, there was heterogeneity due to clinical differences in participant groups, trial protocols and target vessels. Only one included trial compared stenting versus atherectomy (Ott 2017). We interpreted the results for any outcome with only one study with caution, given the small trial sizes and lack of information. Using the GRADE approach, which considers the overall risk of bias of the included studies, the directness of the evidence, inconsistency within the results, precision of the estimate and risk of publication bias (Guyatt 2008), we judged all outcomes to have very low-certainty evidence. Summary of findings 1 and Summary of findings 2 show that there is currently no clear evidence to support the use of atherectomy as a treatment for peripheral vascular disease. We downgraded all the outcomes from high to very low-certainty due to risk of bias (inadequate blinding and high rates of attrition); imprecision (small trial sizes); and inconsistency (from heterogeneity).

Only Ott 2017 and Shammas 2011 utilised power calculations to assess the required number of participants. Overall study numbers were very low, and meta-analysis of very low participant numbers in randomised trials can be unreliable (Rerkasem 2010). As a result, the observed lack of difference in primary patency could easily be a type II error. Two of the trials did not state medication protocols (Nakamura 1995; Shammas 2012). This may be important as it is known that the use of antiplatelet agents, cilostazol, and heparin are all associated with lower restenosis rates after angioplasty (Robertson 2012). The included trials did not include important clinical endpoints such as secondary patency, limb survival, and complication rates between techniques in sufficient detail.

One included study compared atherectomy alone with BA (Vroegindeweij 1995), whereas five trials compared atherectomy plus adjunctive BA with BA alone (Dattilo 2014; Nakamura 1995; Shammas 2011; Shammas 2012; Zeller 2017), creating concerns about heterogeneity. Three participants in the atherectomy arm of Vroegindeweij 1995 crossed over and had subsequent BA after failure of atherectomy alone.

Potential biases in the review process

Despite carrying out a thorough unrestricted search, our review process identified only seven trials of varying size, so it is difficult to assess the impact of reporting bias.

Three trials treated more than one vessel per participant or limb (Dattilo 2014; Shammas 2011; Shammas 2012). Failure of patency of any of the treated vessels increases the chances that other treated vessels will cease to be patent, so these observations will be correlated. It is possible, therefore, that the outcomes of these trials are given greater weight in the meta-analysis than is appropriate in the analysis of six-month and 12-month patency. As both the angioplasty and atherectomy arms of these trials included multiple vessels per participant, it is unlikely that the magnitude of the observed effect has been affected significantly, though our degree of confidence in this effect may be overstated.

There was some variation in whether trials collected target lesion revascularisation data or target vessel revascularisation data, or both. Upon discussion, we made the decision to collect target vessel revascularisation, as we felt this allowed us to perform the fairest comparison between all studies. Similarly, there was variation between trials in outcome definitions, with studies collecting primary patency rates or occlusion rates. Given the inter-trial variation for the definitions between the two, we only included studies that collected 'primary patency' in the meta-analysis.

Agreements and disagreements with other studies or reviews

This is an update of a previous Cochrane Review of atherectomy for PAD (Ambler 2014). Very little further evidence exists in the literature for the use of atherectomy in peripheral vascular disease since the last review. This may in part be due to NICE guidelines recommending against the use of atherectomy devices unless in clinical trials (NICE 2011).

Akkus 2014 performed a review of atherectomy devices, and argued that different types of atherectomy devices should be chosen to treat the most appropriate types of lesion in order to get the best possible clinical outcomes. The review looked at several studies, including the TALON Registry 2006, ERBAC 1997, and McKinsey 2008. Kim 2018 examined dissection rates in atherectomy after BA, and similarly found dissection rates were reduced compared to angioplasty alone. However, this benefit alone does not justify the use of atherectomy over BA. Ramkumar 2019 studied five-year clinical outcomes of atherectomy compared to other endovascular interventions using the Medicare-linked VQI (Vascular Quality Initiative) registry for endovascular interventions from 2010 to 2015. They found an increased risk of any amputation in people treated with atherectomy compared to BA, and found that people who had atherectomy had a higher risk of major amputation, any amputation and major adverse limb event compared to stenting.

Atherectomy has been more thoroughly investigated in the coronary arteries. The ORBIT II trial looked at the three-year outcomes of de novo, severely calcified coronary lesions treated with a coronary orbital atherectomy system prior to stenting (Lee 2017). This study found a lower rate of adverse ischaemic events compared to historical controls. However the ROTAXUS trial, which examined paclitaxel-eluting stents with or without atherectomy, found no difference in primary patency at nine months between the two arms (Abdel-Wahab 2013).

Balloon angioplasty for peripheral vascular disease is widely practised, has a clear evidence base and is constantly evolving, with the use of covered stents and drug-eluting devices (Schroeder 2017; TASC II 2007). As the technique has evolved, so has the evidence base for its place compared to exercise therapy and bypass surgery (Fu 2015; Kayssi 2016). Fu 2015 demonstrated equivalent results to surgical bypass procedures for treating critical limb ischaemia at five-year follow-up for amputation-free survival, target vessel revascularisation, leg amputation and overall mortality. A cohort study examining subintimal angioplasty versus atherectomy for the treatment of occlusive lesions in lower limbs found that angioplasty appeared superior for both patency and limb salvage at 24 months (Indes 2010). Vroegindeweij 1995 performed a post hoc analysis to assess the effect of lesion length on patency. Using life-table analysis, they showed that atherectomy was equivalent to BA for short lesions (< 2 cm), but for longer lesions, long-term patency was significantly better following BA (P = 0.007).

Stenting in PAD has been the focus of significant attention. Several randomised trials have compared stenting to angioplasty alone, the majority favouring stenting (Dake 2011; Spreen 2017). Spreen 2017 found that drug-eluting stents were associated with significantly lower amputation and event-free rates at five years compared with percutaneous transluminal angioplasty. Murphy 2015 compared supervised exercise, primary stenting and optimal medical care, and found that stenting and exercise had either superior or equivalent outcomes for both walking distance and quality of life at 18 months.

AUTHORS' CONCLUSIONS

Implications for practice

This review update shows that the evidence is very uncertain about the effect of atherectomy on patency, mortality and cardiovascular event rates compared to plain balloon angioplasty, with or without stenting. We did not detect any clear differences in initial technical failure rates or target vessel revascularisation rates, but there may be reduced dissection and bailout stenting after atherectomy (very low-certainty evidence). Included studies were small, heterogenous and at high risk of bias. Larger studies powered to detect clinically meaningful, patient-centred outcomes are required. With the exception of bailout stenting, dissection and lower inflation pressures, there was no clear difference between atherectomy and angioplasty for any outcome. There was no evidence for atherectomy versus bypass surgery. The findings of this review agree with current widespread practice and established guidelines for balloon angioplasty in the routine treatment of people with peripheral arterial disease who are amenable to standard angioplasty.

Implications for research

Current evidence in this area is still limited. Larger and better designed trials in selected subgroups of participants are needed to increase our confidence in the evidence. However, performing a larger trial of atherectomy versus balloon angioplasty with greater power to detect differences in primary patency or limb survival may be inappropriate, considering the lack of difference in this analysis, increased technical difficulty, complication rates and the existing 'gold standard' practice of angioplasty. The exception to this may be in people with Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC) C or D lesions who are not fit for bypass surgery.

Future trials should address the following factors.

- Larger studies to detect smaller differences
- Studies examining surgery versus atherectomy, as we found no randomised controlled trials for this comparison. Participants should be stratified according to whether they suffer from intermittent claudication or critical ischaemia.
- More rigorous follow-up. It is important that future studies have both longer follow-up and blinded outcome assessment. The procedures are sometimes performed by interventional radiologists, but followed up by vascular surgeons, so this aim is achievable.
- Study designs should include outcomes which are more participant-centred, for example: quality of life; pain score; and psychosocial measures.

We could not include cost in this Cochrane review, but this is a significant factor when considering results from atherectomy as it is more expensive than BA angioplasty. Future research should explore this.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Dattilo 2014

Study characteristics	
Methods	Randomisation method: details of sequence generation not stated Allocation: sealed envelopes - not stated if opaque Intervention model: parallel Blinding: not stated
Participants	Country: United States of America No. of participants: 50 OA + BA: 25 BA alone: 25 Age (mean (years) ± SD): OA + BA: 68.0 ± 11.0 BA alone: 71.3 ± 10.5 Inclusion criteria: eligible participants were 18 years or older; PAD with Rutherford class 2 to 4 symptoms and de novo FP lesions of ≥ 70% stenosis with fluoroscopically visible calcium; gave informed consent; all participants had to have at least 1 patent run-off vessel Exclusion criteria: anticipated life span of less than 1 year; known allergy to heparin, aspirin, and clopidogrel, or sensitivity to contrast media; chronic renal failure; cardiac arrhythmias; congestive heart failure exacerbation; myocardial infarction
Interventions	OA + BA vs BA alone
Outcomes	Primary: freedom from TLR, including the need for adjunctive stenting or restenosis (PSVR ≥ 2.5 on duplex ultrasound) per lesion at 6 months. Secondary: changes in ABI and Rutherford Class from baseline to 30 days and 6 and 12 months

Dattilo 2014 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details given about method of random sequence generation.
Allocation concealment (selection bias)	Low risk	Randomisation performed only after guidewire passed and inclusion and exclusion criteria assessed. Sealed envelopes, not stated if opaque.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not stated, but impractical in trials of this type.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No mention of blinding of outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	High risk	Incomplete data set at 6 and 12 months, reasons for attrition not stated. Data only published for 45/50 (90%) at 6 months and 37/50 (74%) at 12 months.
Selective reporting (reporting bias)	Low risk	All primary and secondary outcomes reported.
Other bias	Unclear risk	Clear antiplatelet protocol specified, but unit of analysis issue as the trial randomised treated vessels

Nakamura 1995

Study characteristics

Methods	Randomisation method: random number table Allocation: not stated Intervention model: parallel Blinding: none
Participants	Country: United States of America No. of participants: 39: 2.7 mm TEC atherectomy plus BA: 13 4.0 mm TEC atherectomy plus BA: 13 BA: 13 Age (mean (years) ± SD): 2.7 mm TEC: 64 ± 6 4.0 mm TEC: 70 ± 6

Nakamura 1995 *(Continued)*

	BA: 61 ± 4.1 Inclusion criteria: occluded SFA with 1 to 2 block claudication Exclusion criteria: those with previous femoropopliteal graft or "insufficient run-off vessels"
Interventions	BA versus 2.7 mm TEC atherectomy plus BA versus 4.0 mm TEC atherectomy plus BA
Outcomes	Initial and 6-month vessel patency Preprocedure and 6-month ABI
Notes	6-month ABI only reported for participants with primary patency at 6 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table used for randomisation.
Allocation concealment (selection bias)	High risk	Not specifically stated.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Neither participants nor personnel were blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No mention of blinding of outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete data available to 6 months.
Selective reporting (reporting bias)	Unclear risk	Initial and 6 month patencies reported. ABI only reported for participants whose vessels remained patent at 6 months.
Other bias	High risk	No mention of antiplatelet protocol pre- or postprocedure.

Ott 2017

Study characteristics

Methods	Randomisation method: computer-generated sequence Allocation: sealed, opaque envelopes Intervention model: parallel assignment Blinding: single (outcomes assessor)
Participants	Country: Germany No. of participants: 155 Plain BA followed by PEB angioplasty and stenting: 48 BA and stenting: 52

Ott 2017 *(Continued)*

	Atherectomy with distal protection and bailout stenting: 55 Age (mean (years) ± SD): PEB + stent: 69.7 ± 9.4 BA + stent: 69.2 ± 8 Atherectomy: 68.8 ± 10 Inclusion criteria: de novo stenosis > 70% or occlusion of the SFA Exclusion criteria: acute ischaemia or acute thrombosis of the SFA; untreated ipsilateral iliac artery stenosis > 70%; previous stenting of the SFA; popliteal stenosis > 70%; severe renal insufficiency (estimated glomerular filtration rate < 30 mL/minute/1.73m^2); life expectancy of < 1 year; and contraindication to required medications.
Interventions	Plain BA followed by PEB angioplasty and stenting versus BA and stenting versus atherectomy with distal protection and bailout stenting.
Outcomes	Primary outcome: percentage diameter stenosis after 6 months, measured by angiography. Secondary outcomes: TLR; thrombosis; ipsilateral amputation; binary restenosis; and all-cause mortality at 6 and 24 months.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated sequence.
Allocation concealment (selection bias)	Low risk	Sealed, opaque envelopes opened after decision to proceed with the intervention. Randomisation performed only after guidewire passed and inclusion and exclusion criteria assessed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants or personnel.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Independent core laboratory was blinded to the treatment assignment.
Incomplete outcome data (attrition bias) All outcomes	High risk	39/155 (25%) participants did not provide primary outcome data.
Selective reporting (reporting bias)	Low risk	All primary and secondary outcomes addressed.
Other bias	Low risk	Clear antiplatelet protocol was the same in all arms.

Shammas 2011

Study characteristics	
Methods	Randomisation method: simple randomisation was performed on a 1:1 basis, no method of sequence generation described Allocation: sealed envelopes, not stated if opaque Intervention model: parallel assignment Blinding: not stated
Participants	Country: United States of America No. of participants: participants: 58; vessels: 84 Silverhawk atherectomy plus BA: participants: 29; vessels: 36 BA: participants: 29; vessels: 48 Age (mean (years) ± SD): atherectomy: 67.4 ± 9.1 BA: 70.9 ± 13.9 Inclusion criteria: adults with claudication, rest pain or minor tissue loss Exclusion criteria: 1. heavily calcified vessels; 2. total occlusions longer than 10 cm or any total occlusion with suspicion of subintimal wire recanalisation; 3. inability to take aspirin or adenosine diphosphate receptor antagonists; 4. bleeding disorder or platelet count less than 100,000/L; 5. creatinine level greater than 2.5 mg/dL; 6. unwillingness to give consent or return for future follow-up visits; 7. ongoing active infection; 8. decompensated congestive heart failure or acute coronary syndrome; or 9. a staged vascular procedure during the same hospital stay or 1 week after the index procedure.
Interventions	BA versus Silverhawk atherectomy with adjunctive BA
Outcomes	Primary: TLR at 1 year Secondary 1. The rate of "bailout" stent implantation because of suboptimal acute angiographic results, defined as a residual stenosis of more than 30% or the presence of type C–F dissection. 2. Final acute angiographic results in each arm at the end of the procedure 3. TLR at 1 year 4. Major adverse events including major amputation, death, distal embolisation, vascular complications (arteriovenous fistula, pseudoaneurysm, or perforation), major bleeding (loss of 3 U of packed red blood cells with a source of bleeding, or intracranial or retroperitoneal bleeding), unplanned urgent revascularisation of the treated vessel in the same hospital stay, myocardial infarction, embolic stroke, and renal failure (i.e. increase in creatinine clearance by 25% versus preprocedure baseline). 5. Change in the ABI at 1 month, 6 months, and 1 year after the procedure versus baseline
Notes	
Risk of bias	

Shammas 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Simple randomisation was performed on a 1:1 basis, no method of sequence generation described.
Allocation concealment (selection bias)	Low risk	Sealed envelopes, not stated if opaque.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not stated, but impractical in trials of this type.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated, probably not done.
Incomplete outcome data (attrition bias) All outcomes	High risk	Primary outcome only reported for 51/84 (61%) vessels.
Selective reporting (reporting bias)	High risk	Secondary outcomes major adverse events and change in ABI incompletely reported.
Other bias	Low risk	Clear antiplatelet protocol.

Shammas 2012

Study characteristics	
Methods	Randomisation method: sealed envelopes provided to all centres for randomisation, randomisation method for distribution not stated. Randomisation performed only after inclusion and exclusion criteria assessed. Allocation: sealed envelopes, not stated if opaque Intervention model: parallel assignment Blinding: not stated, probably not done
Participants	Country: United States of America No. of participants: participants: 50; vessels: 64 Diamondback atherectomy plus BA: participants: 25; vessels: 29 BA: participants: 25; vessels: 35 Age (mean (years) ± SD): atherectomy: 70.7 ± 13.4 BA: 71.8 ± 10.9 Inclusion criteria: adults with rest pain or tissue loss (Rutherford class 4 to 6); angiographic stenosis > 50%; fluoroscopically-visible calcium > 25% of the treated segment; atherectomy wire must cross all lesions with no subintimal wire passage; main target vessel reference diameter > 1.5 mm; more than one patent distal runoff vessel with brisk flow for any treated popliteal segment; distal portion of anterior tibial or posterior tibial target vessel must reconstitute to the ankle or foot and only proximal one third of the peroneal artery to be treated; distal two thirds must reconstitute.

Shammas 2012 *(Continued)*

	Exclusion criteria: 1. inability to understand study or history of non-compliance with medical advice; 2. unwilling or unable to sign informed consent form; 3. currently enrolled in another study that may interfere with study endpoints; 4. unsuccessful treatment of target leg superficial femoral artery or proximal vessel on procedure day; 5. pregnant or planning to become pregnant within study period; 6. known sensitivity to contrast media that cannot be adequately premedicated; 7. chronic renal failure/creatinine level > 2.0 mg/dL unless on chronic dialysis; 8. one or more of the popliteal or below-knee lesions to be treated are within a stent; 9. known allergy to heparin, aspirin, or clopidogrel; 10. history of bleeding disorders or platelet count < 80,000 cells/mL; 11. ongoing cardiac problems that would interfere with study procedures; 12. stroke or transient ischaemic attack within 4 weeks prior to procedure; 13. anticipated lifespan < 1 year; 14. known or suspected active systemic infection; 15. thrombus present or suspected in the target vessel; 16. concomitant thrombectomy/other atherectomy device treatment in target vessel; 17. investigator's medical judgment excludes person from the study.
Interventions	BA versus Diamondback atherectomy with adjunctive BA
Outcomes	Primary: ability to achieve adequate lumen diameter, defined as < 30% residual stenosis with no bailout stenting or dissection Secondary: 1. rate of bailout stenting; 2. limb salvage at 30 days, 6 months and 12 months; 3. TLR and TVR at 6 and 12 months; and 4. major adverse events (a composite of above-knee amputation, mortality from all causes, and TLR/TVR
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sealed envelopes provided to all centres for randomisation, randomisation method for distribution not stated. Randomisation performed only after inclusion and exclusion criteria assessed.
Allocation concealment (selection bias)	Low risk	Sealed envelopes, not stated if opaque.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not stated, but impractical in trials of this type.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated, probably not done.
Incomplete outcome data (attrition bias)	High risk	Secondary outcomes reported for only 33/50 (66%) participants.

Shammas 2012 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Low risk	All outcomes reported, though significant attrition present.
Other bias	High risk	No antiplatelet protocol

Vroegindeweij 1995

Study characteristics

Methods	Randomisation method: numbered envelopes opened sequentially Allocation: sealed envelopes, not stated if opaque Intervention model: parallel assignment Blinding: not stated, probably not done
Participants	Country: Netherlands No. of participants: 73 Simpson atherectomy: 38 BA: 35 Age (mean (years) range): Atherectomy: 64 (range 49 - 77) BA: 64 (range 46 - 80) Inclusion criteria: intermittent claudication of at least 3 months duration and obstructive lesions of the femoropopliteal arteries with a maximum length of 5 cm or complete occlusions shorter than 2 cm. Exclusion criteria: any previous ipsilateral femoropopliteal endovascular or operative intervention; participant unable to comply with the frequent follow-up visits required by the protocol.
Interventions	BA versus Simpson atherectomy
Outcomes	Primary patency during follow-up Restenosis as determined by duplex ultrasound
Notes	Four participants crossed over to the other treatment group: three participants had angioplasty following atherectomy, one participant had atherectomy in addition to angioplasty. Results were presented in an intention-to-treat format

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Numbered envelopes opened sequentially. Randomisation not performed until after inclusion and exclusion criteria evaluated.
Allocation concealment (selection bias)	Low risk	Sealed envelopes, not stated if opaque.
Blinding of participants and personnel (performance bias)	High risk	Not stated, but impractical in trials of this type.

Vroegindeweij 1995 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated, probably not done.
Incomplete outcome data (attrition bias) All outcomes	High risk	Three participants in the BA group were not followed up to 6 months. One participant in the atherectomy group and 10 in the BA group were not followed up to one year.
Selective reporting (reporting bias)	Low risk	Primary patency reported fully in life-table format; restenosis presented graphically.
Other bias	Low risk	Clear antiplatelet protocol.

Zeller 2017

Study characteristics	
Methods	Randomisation method: block randomisation by centre Allocation: assigned to treatment groups after successful passage of the guidewire across the target lesion Intervention model: parallel assignment Blinding: duplex outcomes assessor blinded
Participants	Country: Belgium, Germany, Poland, and Switzerland No. of participants: 102 DA + DCB (n = 48) DCB alone (n = 54) non-randomised DA + DCB (n = 19) Age (mean (years) ± SD): DA + DCB: 70.1 ± 9.7 DCB alone: 69.0 ± 8.2 non-randomised DA + DCB: 69.7 ± 8.9 Inclusion criteria: Rutherford Clinical Category 2 to 4; at least 18 years of age; is able and willing to provide written informed consent prior to study specific procedures. Exclusion criteria: Has a life expectancy of less than 24 months; is pregnant, of childbearing potential not taking adequate contraceptive measures, or nursing; has one or more of the contraindications listed in the SilverHawk/TurboHawk or Cotavance IFUs; surgical or endovascular procedure of the target vessel within 14 days before the index procedure; planned intervention within 30 days of the index procedure; had ≥ 2 lesions that required treatment in the target limb (not including the iliac arteries); had a target lesion with an occluded segment ≥ 5cm in length; had in-stent restenosis of target lesion or restenosis of the target lesion after previous treatment with DCB; had an acute intraluminal thrombus in the target lesion; had an aneurysmal target vessel; participants with severe calcification in the target lesion, defined as fluoroscopic dense circumferential calcification extending > 5 continuous centimetres, were

Zeller 2017 *(Continued)*

	excluded from the randomisation but were eligible for the non-randomised (NR) treatment arm after meeting all other inclusion criteria and no other exclusion criteria.
Interventions	Arm 1: randomised - drug-eluting balloon. Arm 2. randomised - TurboHawk/SilverHawk Device followed by a Cotavance drug-eluting balloon Arm 3: non-randomised - TurboHawk/SilverHawk Device followed by a Cotavance drug-eluting balloon
Outcomes	Primary outcome: target lesion percentage diameter stenosis at 1 year postprocedure, defined as the narrowest point of the target lesion divided by the estimated native vessel diameter at that location as determined by the angiographic core laboratory. Secondary outcomes: 1. technical success (defined as ≤ 30% residual stenosis following the protocol-defined treatment, before adjunctive treatments, at the target lesion as determined by the angiographic core laboratory); 2. MAE rate at 30 days and 1 year, defined as major unplanned amputation of the treated limb, all-cause mortality, or clinically driven TLR. Clinically driven TLR was defined as any reintervention or surgical revascularisation involving the target lesion in which the participant had ≥ 70% diameter stenosis and at least 2 of the following: worsening Rutherford Clinical Category, worsening WIQ score, or an ABI drop > 0.15 from baseline and was assessed at 6 months and 1 year.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation by centre.
Allocation concealment (selection bias)	Unclear risk	Assigned to treatment groups after successful passage of the guidewire across the target lesion, concealment not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible to blind investigators, participants, and the angiographic core laboratory to the treatment assignment, however the duplex ultrasound core laboratory staff and the clinical events committee were blinded to the treatment assignment.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not possible to blind investigators, participants, and the angiographic core laboratory to the treatment assignment, however the duplex ultrasound core laboratory staff and the clinical events committee were blinded to the treatment assignment.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	15/102 (15%) failed to provide primary outcome data.
Selective reporting (reporting bias)	Low risk	All outcomes reported. Primary outcomes reported in table format.
Other bias	Low risk	Antiplatelet protocol clear and uniform for both arms.

ABI: ankle brachial index
BA: balloon angioplasty
DA: directional atherectomy
DCB: drug coated balloon
FP: femoropopliteal

MAE: major adverse event
OA: orbital atherectomy
PAD: peripheral arterial disease
PEB: paclitaxel-eluting balloon
PSVR: peak systolic velocity ratio
SD: standard deviation
SFA: superficial femoral artery
TEC: transluminal extraction catheter
TLR: target lesion revascularisation
TVR: target vessel revascularisation
WIQ: Walking Impairment Questionnaire

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Brodmann 2013	Participants with a first in-stent reobstruction
Del Giudice 2014	In-stent restenosis
Dippel 2015	In-stent restenosis
Gabrielli 2012	Remote endarterectomy rather than atherectomy
Gandini 2013	In-stent occlusion
Gisbertz 2009	Remote endarterectomy rather than atherectomy
NCT02730234	Single group assignment
NCT02832024	In-stent restenosis
Schwindt 2017	Non-randomised single arm trial

Characteristics of ongoing studies *[ordered by study ID]*

ChiCTR-IOR-17012486

Study name	Drug-coated balloon versus drug-coated balloon with atherectomy for the treatment of femoral-popliteal calcified occlusive disease: a randomized, controlled and prospective study
Methods	Randomised, parallel controlled trial
Participants	100 participants Inclusion criteria: 1. participant aged ≥ 18 years, and younger than 80 years, male or female; 2. diagnosed with femoral-popliteal calcified occlusive disease; 3. ultrasound or CTA confirm that calcification exists at least one plane; 4. possess operation indication; 5. no operation contraindication; 6. participate in clinical trial, accept interference and be followed voluntarily. Exclusion criteria: 1. allergy to paclitaxel;

ChiCTR-IOR-17012486 *(Continued)*

	2. symptomatic myocardial infarction occurred in the past 3 months, or unstable angina occurred 3 times or more in the past one month, or severe heart failure that can not be well controlled by medicine; 3. suffer from severe respiratory insufficiency; 4. suffer from severe renal insufficiency; 5. suffer from severe hepatic disease; 6. suffer from therioma or other severe disease, and expectation of life is less than 6 months.
Interventions	Arm 1: drug-coated balloon combined with atherectomy Arm 2: drug-coated balloon
Outcomes	Primary: 1. rate of primary patency 2. rate of TLR Secondary: 1. intermittent claudication 2. critical lower-extremity ischaemia 3. amputation rate 4. all-cause mortality
Starting date	28 August 2017
Contact information	Applicant: Jia Senhao Study leader: Guo Wei
Notes	

Martinsen 2015

Study name	Economic study design for the optimise study on orbital atherectomy and drug-coated balloon devices for the treatment of below-the-knee peripheral arterial disease
Methods	Prospective, multicentre, randomised, postmarket pilot study
Participants	Country: Germany, Switzerland and Austria No of participants: 50
Interventions	1. OAS with adjunctive DCB angioplasty 2. DCB angioplasty alone
Outcomes	Health economic outcomes will be measured at the index procedure, at 30 days, three months, six months, 12 months, and 24 months postprocedure for the treatment of PAD and its complications (repeat procedures, amputations, etc.). Health-related quality of life will be measured using the EQ-5D instrument. Resource utilization will be collected from case report forms and hospital accounting systems, using site-specific procedure code information of relevant German, Swiss, and Austrian sites. Analyses from the third-party payer perspective will be informed by country-specific reimbursement amounts, using Germany as the initial reference case. Resulting cost difference and incremental cost-effectiveness are the main economic outcomes targeted in this analysis
Starting date	Unknown

Martinsen 2015 *(Continued)*

Contact information	Unknown
Notes	Published need for paper but no results available

NCT01579123

Study name	Laser atherectomy versus angioplasty for the treatment of critical limb ischaemia
Methods	Randomised, single blind (participant), parallel controlled trial
Participants	200 participants Inclusion criteria: 18 years of age and older; male or female (non-pregnant women); participants with PAD that has progressed to CLI; participants undergoing angiography with possible intervention for Rutherford Class 4 to 6 limb ischaemia that may benefit from revascularisation.
Interventions	Angioplasty versus laser atherectomy
Outcomes	Primary outcome measure: difference in patency rates (one year)
Starting date	February 2012
Contact information	William Shutze, MD Baylor Jack and Jane Hamilton Heart Hospital
Notes	

NCT01763476

Study name	Atherectomy and drug-coated balloon angioplasty in treatment of long infrapopliteal lesions (AD-CAT)
Methods	Prospective, open, randomised, parallel assignment, single-centre clinical trial
Participants	Estimated enrolment: 80 participants Ages eligible for study: 50 years to 85 years Inclusion criteria: 1. participant must be between 50 and 85 years old; 2. women of childbearing potential must have a negative pregnancy test within 10 days prior to index procedure and utilize reliable birth control until completion of the 12-month angiographic evaluation; 3. clinical diagnosis of symptomatic critical limb ischaemia as defined by Rutherford 3, 4, or 5; 4. single treatment of de novo lesion(s) in the tibioperoneal trunk, anterior, posterior or peroneal artery with a lesion length ≥ 6 cm; 5. one vessel in one limb may be treated in the study. Additional non-target lesion(s) in remaining non-target vessel(s) can be treated at the physician's discretion by means of balloon dilation or stent placement; 6. the total length of target lesion(s) can be a maximum of 250 mm; 7. in total, a maximum of four drug-coated balloons may be used to fully cover the target lesion; 8. target vessel is between 2.0 and 3.5 mm in diameter (visual estimate);

NCT01763476 *(Continued)*

	9. target lesion stenosis is > 70% diameter stenosis (visual estimate); 10. guidewire must be across the target lesion and located intraluminally within the distal outflow vessel before study randomisation; 11. interventions in TASC A and B lesions to restore adequate blood flow, in the same index procedure are allowed. This intervention must be prior to the treatment of the study lesion(s) and successful; 12. willing to comply with the specified follow-up evaluation; 13. written informed consent prior to any study procedures. Exclusion criteria: 1. significant (> 50%) stenoses distal to the target lesion (dorsalis pedis artery, plantar arch) that might require revascularisation, or impede runoff; 2. angiographic evidence of thrombus within target vessel; 3. thrombolysis within 72 hours prior to the index procedure; 4. in-stent restenosis or restenosis of a native artery; 5. aneurysm in the femoral artery or popliteal artery; 6. concomitant hepatic insufficiency, thrombophlebitis, DVT, coagulation disorder or receiving immunosuppressant therapy; 7. recent myocardial infarction or stroke < 30 days prior to the index procedure; 8. life expectancy less than 12 months; 9. known or suspected active infection at the time of the index procedure, excluding an infection of a lower extremity wound of the target limb; 10. known or suspected allergies or contraindications to aspirin, clopidogrel bisulphate (Plavix) and ticlopidine (Ticlid), heparin, or contrast agent; 11. any significant medical condition which, in the investigator's opinion, may interfere with the person's optimal participation in the study; 12. the person is currently participating in another investigational drug or device study that has not completed the primary endpoint or that clinically interferes with the endpoints of this study.
Interventions	Arm 1: paclitaxel-coated balloon angioplasty Arm 2: atherectomy + paclitaxel-balloon
Outcomes	Primary outcome measure: primary patency of the target lesion 6 months after index procedure measured by duplex ultrasound (PVR > 2.4) and angiography (core lab analysis). Secondary outcome measure: need for TLR from baseline to 6 months after index procedure. Other outcome measures: change in Rutherford-Becker Class from baseline to 6 and 12 months after index procedure.
Starting date	January 2013
Contact information	Aljoscha Rastan, M.D., Herz-Zentrums Bad Krozingen
Notes	

NCT02514460

Study name	Clinical study of stent versus direct atherectomy to treat lower limb ischemia
Methods	Randomised, single blind (participant), parallel controlled trial
Participants	Estimated enrolment: 120 participants Ages eligible for study: 18 years and older

NCT02514460 *(Continued)*

	Sexes eligible for study: all Inclusion criteria: provides written informed consent; willing to comply with follow-up evaluations at specified times; has claudication or rest pain due to PAD; disease located within the femoropopliteal artery; participant has a de novo or restenotic lesion(s) with > 50% stenosis documented angiographically and no prior stent in the target lesion; participant has symptoms of PAD classified as Rutherford Category 2 or more. Exclusion criteria: previously implanted stent(s) or stent graft(s) in target leg; life expectancy less than 12 months; has any planned surgical or endovascular intervention of target vessel 30 days before or after index procedure; thrombophlebitis, uremia, or deep venous thrombus, within past 30 days; receiving dialysis or immunosuppressant therapy; recent stroke within past 90 days; known allergies to the following: aspirin, clopidogrel bisulphate (Plavix) or ticlopidine (Ticlid), heparin, Nitinol (nickel titanium), contrast agent, that cannot be medically managed; tissue loss due to ischaemic disease (Rutherford/Becker category 5 or 6); serum creatinine level ≥ 2.5 mg/dL at time of screening visit; known or suspected active infection at the time of the procedure; bleeding diathesis; participant is unwilling or unable to comply with procedures specified in the protocol or has difficulty or inability to return for follow-up visits as specified by the protocol; participant is known to be pregnant, incarcerated, mentally incompetent, alcohol or drug abuser; participant is currently participating in any other investigational drug or medical device study that has not completed primary endpoint(s) evaluation or clinically interferes with the endpoints from this study or future participation in such studies prior to the completion of this study.
Interventions	Arm 1: stents Arm 2: direct atherectomy group
Outcomes	Primary outcome measures: 1. 12-month primary patency rate. Primary patency is defined as no significant reduction of flow detectable by Duplex ultrasound through the index lesion and no further clinically driven TVR performed in the interim. Significant reduction of flow is binary restenosis defined as the diameter stenosis > 50% with a peak systolic velocity ratio > 2.4 as measured by Duplex ultrasound 2. 12-month limb salvage rate. Limb salvage is defined as the freedom from secondary major amputation Secondary outcome measures: 1. Index limb ischaemia at 6-month follow-up. Index limb ischaemia is defined by Rutherford/Becker Classification categories 3 to 6 2. Index limb ischaemia at 12-month follow-up. Index limb ischaemia is defined as for 6 months 3. MAE at 12 months postprocedure. MAE including death, index limb ischaemia, index limb amputation, clinically driven TLR, and significant embolic events, which were defined as causing end-organ damage
Starting date	January 2014
Contact information	Xuanwu Hospital, Beijing
Notes	

NCT02517827

Study name	Percutaneous intervention versus surgery in the treatment of common femoral artery lesions (PESTO-AFC)
Methods	Prospective, open, randomised, parallel assignment, multi-centre clinical trial
Participants	Estimated enrolment; 306 participants

NCT02517827 *(Continued)*

	Inclusion criteria: 1. between 21 and 85 years old; 2. female of childbearing potential must have a negative pregnancy test within 10 days prior to index procedure and utilize reliable birth control until completion of the 12-month angiographic evaluation; 3. clinical diagnosis of symptomatic peripheral artery disease defined by Rutherford 2, 3, or 4; 4. CFA stenosis (including CFA bifurcation) > 70% (visual estimate) or occlusion; Additional non-target lesion(s) in remaining non-target vessel(s), except ipsilateral iliac arteries, can be treated at the physician´s discretion; 5. at least one vessel outflow (infrapopliteal arteries) to the foot (without stenosis > 50%). 6. endovascular procedure: successful target lesion crossing of the guidewire (guidewire located intraluminally); 7. non-target lesion interventions (TASC A and B) to restore adequate blood flow, in the same index procedure are allowed. This intervention must be prior to the treatment of the study lesion and successful; 8. willing to comply with the specified follow-up evaluation; 9. written informed consent prior to any study procedures. Exclusion criteria: 1. ipsilateral significant (> 50%) stenosis of the iliac arteries; 2. significant (> 50%) stenosis of all infrapopliteal arteries, no patent artery to the foot; 3. angiographic evidence of thrombus within target vessel; 4. thrombolysis within 72 hours prior to the index procedure; 5. in-stent restenosis or restenosis of the native common femoral artery; 6. aneurysm in the abdominal aorta or iliac arteries; 7. concomitant hepatic insufficiency, thrombophlebitis, deep venous thrombus, coagulation disorder or receiving immunosuppressant therapy; 8. recent MI or stroke < 30 days prior to the index procedure; 9. life expectancy less than 24 months; 10. known or suspected active infection at the time of the index procedure; 11. known or suspected allergies or contraindications to aspirin, clopidogrel bisulphate and ticlopidine, heparin, or contrast agent; 12. any significant medical condition which, in the investigator´s opinion, may interfere with the subject´s optimal participation in the study; 13. currently participating in another investigational drug or device study that has not completed the primary endpoint or that clinically interferes with the endpoints of this study.
Interventions	Arm Intervention/treatment Active comparator: endovascular procedure Common femoral artery (target lesion) to be treated with directional atherectomy and paclitaxel-coated balloon angioplasty. Optional: stent implantation. Device: Atherectomy and paclitaxel-coated balloon angioplasty Directional atherectomy and paclitaxel-coated balloon angioplasty (optional with stent implantation) of the CFA Active comparator: surgery CFA (target lesion) to be treated with open, surgical endarterectomy Procedure: open, surgical endarterectomy of the CFA
Outcomes	Primary outcome measure: Primary patency (12 months): primary patency of the CFA defined as freedom from target lesion restenosis (luminal narrowing of ≥ 50%) detected with duplex-ultrasound. The definition of a 50% restenosis is based on the peak systolic velocity ratio > 2.4. Secondary outcome measures: 1. Primary patency (24 months): defined as above

NCT02517827 *(Continued)*

	2. TLR (6, 12, and 24 month): need for TLR after index procedure Other outcome measures: Rutherford-Becker class (6, 12, and 24 months): change in Rutherford-Becker class
Starting date	1 August 2017
Contact information	Contact: Aljoscha Rastan, MD Contact: Thomas Zeller, MD
Notes	

NCT02561299

Study name	Orbital vessel preparation to maximIze DCB efficacy in calcified below the knee (BTK) lesions - a pilot study (OPTIMIZE BTK)
Methods	Prospective, open, randomised, parallel assignment clinical trial
Participants	Estimated enrolment: 66 participants Inclusion criteria: 1. ≥ 18 years old; 2. Rutherford clinical category 3 - 5; 3. lesions (except in-stent restenosis) of the distal popliteal (segment below the anatomical knee joint), anterior tibial, posterior tibial, tibial peroneal trunk, and peroneal arteries with ≥ 70 % diameter stenosis by angiography; 4. presence of clearly visible calcification in two views (both sides of vessel at the same location) evaluated angiographically- (CT angio images may substitute to confirm distribution of calcium, if available as standard of care); 5. length of calcium ≥ 25 % of total lesion length or ≥ 2 cm total length; 6. target lesion length up to 20 cm. Exclusion criteria: 1. not willing to sign an ethics committee approved informed consent form or comply with the study protocol requirements; 2. contraindicated by either device, per instructions for use; 3. presence of inflow lesion (≥ 50 % diameters stenosis) or inflow not successfully treated (≥ 50% diameter stenosis and/or unresolved significant angiographic complication); 4. compromised outflow distal to the target lesion (≥ 70% diameter stenosis) or presence of lesion(s) or occlusion(s) located from 5 cm above the ankle to below the ankle joint space 5. more than 2 target vessels requiring treatment; 6. guide wire cannot be passed across the target lesion(s) and/or guide wire position distal to target lesion(s) outside vessel lumen; 7. presence of significant (≥ 70% diameter stenosis) lesion(s) or occlusion(s) not meeting the study criteria which were not successfully treated during the index procedure (≥ 50% diameter stenosis and/or significant angiographic complication); 8. planned amputation (including minor) of the index limb or previous major amputation of the contralateral limb; 9. creatinine > 2.5 mg/dL, unless on dialysis; 10. any significant medical condition which, in the Investigator's opinion, may interfere with the subject's optimal participation in the study; 11. participating in an investigational drug or device study that has the potential to clinically interfere with the study outcome measures;

NCT02561299 *(Continued)*

	12.pregnant or planning to become pregnant within the study period; 13.unresolved severe systemic infection; 14.anticipated life span of less than one year; 15.known hypersensitivity to paclitaxel or paclitaxel related compounds; 16.cannot receive recommended anti-platelet and/or anticoagulant therapy; 17.pre-dilatation of the target lesion prior to randomisation and OA treatment.
Interventions	Arm 1: lesion preparation with peripheral orbital atherectomy system followed by drug-coated balloon angioplasty Arm 2: DCB angioplasty
Outcomes	Primary outcome measure: device success (per each DCB used during the index procedure), defined as the ability to achieve successful delivery and deployment of the DCB to the target lesion as described per IFU within 3 minutes of insertion without removal and use of an additional device Secondary outcome measures: 1. patency of the target lesion by DUS at 6 months and 12 months post-procedure 2. change in Rutherford Category at 6 months and 12 months, post-procedure from baseline 3. freedom from clinically driven target lesion revascularisation at 6 months, 12 months post-procedure 4. freedom from unplanned, unavoidable major amputation of the index limb at 6 months and 12 months post-procedure 5. freedom from MAEs at 6 months and 12 months post-procedure
Starting date	September 2015
Contact information	Cardiovascular Systems Inc
Notes	

NCT02840786

Study name	Clinical study of stent versus direct atherectomy to treat arteriosclerosis occlusive disease of lower extremity
Methods	Open, randomised, parallel assignment clinical trial
Participants	Estimated enrolment: 221 participants Inclusion criteria: Patients were included if they were de novo stenosis > 70% or occlusion of the femoropopliteal at least 18 years of age and referred for claudication (Rutherford-Becker class II-III) or critical limb ischaemia (Rutherford-Becker class IV-V). Exclusion criteria: 1. acute or subacute lower limb ischaemia; 2. severe calcification lesions; 3. total occlusions lesions more significant than 10 cm or total occlusion lesions with a suspicion of subintimal wire recanalisation; 4. untreated ipsilateral iliac artery stenosis > 70%, or the distal runoff artery < 1 root; 5. previously lower extremity intervention or surgical graft artery bypass;

NCT02840786 *(Continued)*

	6. severe renal insufficiency, creatinine level greater than 2.5 mg/dL; 7. platelet count is less than 100,000/uL, antiplatelet or anticoagulant contraindications to required medications; 8. immune system diseases or malignant tumours; 9. ongoing active infection; 10. decompensated congestive heart failure or acute coronary syndrome; 11. unwillingness to return for future follow-up visits.
Interventions	Arm 1: stent Arm 2: direct atherectomy
Outcomes	Primary outcome measure: 12-month primary patency rate (12 months) (systolic velocity ratio > 2.4 as measured by Duplex ultrasound) Secondary outcome measures: 1. technical success defined as residual stenosis less than 30% by final angiography and/or a flow-limiting dissection (1 day); 2. freedom from clinically-driven TLR defined as the freedom from clinically-driven TLR (12 months); 3. MAE at 12-months postprocedure. MAEs included death, index limb ischaemia, index limb amputation, clinically driven target lesion revascularisation, and significant embolic events, which were defined as causing end-organ damage; 4. 12-month limb salvage rate defined as the freedom from secondary major amputation.
Starting date	21 July 2016
Contact information	
Notes	

NCT03206762

Study name	JET-RANGER Trial - JETStream atherectomy with adjunctive paclitaxel-coated balloon angioplasty versus plain old balloon angioplasty followed by paclitaxel-coated balloon
Methods	Prospective, single blind (participant), randomised, parallel assignment, multi-centre study
Participants	Estimated enrolment: 255 participants Ages eligible for study: 18 years and older Sexes eligible for study: all General inclusion criteria: has a Rutherford Clinical Category of 2 to 4; is willing and capable of complying with all follow-up evaluations at the specified times (including an angiogram at the 1-year follow-up visit); is able and willing to provide written informed consent prior to study specific procedures Angiographic inclusion criteria: Participant must meet all of the following angiographic inclusion criteria. Unless otherwise specified, the Investigator performing the procedure bases all angiographic inclusion criteria on visual determination at the time of the procedure: 1. has evidence at the target lesion of ≥ 70% de novo stenosis of (a) ≥ 10 cm length, or (b) any chronic total occlusion (> 1 month by history or known by conventional or CT angiography or arterial duplex ultrasound) in the SFA (at least 1 cm from the bifurcation of the profunda) or popliteal artery,

NCT03206762 *(Continued)*

or (c) at least grade 2 or higher calcification as defined by the peripheral arterial calcium scoring system (PACCS) 26;

2. has evidence of at least one runoff vessel to the ankle/foot of the limb to be treated that does not have significant (< 70%) stenosis during the index procedure;
3. has a reference vessel diameter of 4 to 7 mm;
4. has a target lesion an exchangeable guidewire can cross via the true lumen (without using a re-entry device or a subintimal approach)

General exclusion criteria:

1. has one or more of the contraindications listed in the JetStream or Ranger IFUs;
2. has a contraindication or known untreated allergy to antiplatelet therapy, anticoagulants, thrombolytic drugs or any other drug anticipated to be used (that cannot be reasonably substituted);
3. is expected to require cilostazol (Pletal) during the one-year follow-up period;
4. has a hypersensitivity to contrast material that cannot be adequately pretreated;
5. has known hypersensitivity to treatment device materials including paclitaxel or nitinol;
6. has known uncontrollable hypercoagulable condition, or refuses blood transfusion;
7. has life expectancy of less than 24 months;
8. is pregnant, of childbearing potential not taking adequate contraceptive measures, or nursing;
9. has surgical or endovascular procedure of the target vessel within 30 days prior to the index procedure;
10. has any planned surgical intervention (requiring hospitalisation) or endovascular procedure within 30 days after the index procedure;
11. is currently participating in an investigational drug or another device study that may clinically interfere with the study outcomes;
12. has any comorbid condition that in the judgment of the physician precludes safe percutaneous intervention;
13. has had a previous peripheral bypass affecting the target vessel (allowable for physician to pass through bypass graft in aorta-iliac region to get to the target lesion);
14. has chronic renal insufficiency (eGFR < 30 ml/min or creatinine ≥ 2.5 including dialysis patients);
15. has planned laser, cryo, TurboHawk or any other treatment except study treatment within 30 days after the index procedure;
16. has had superficial thrombophlebitis or deep venous thrombus within 30 days prior to index procedure;
17. has had a stroke within 3 months prior to index procedure;
18. has had a myocardial infarction within 1 month prior to index hospitalisation;
19. has history of significant gastrointestinal bleeding in the past 2 months prior to index procedure, or any history of hemorrhagic diathesis;
20. has a known or suspected systemic infection at the time of the index procedure;
21. participants with ipsilateral Iliac and CFA disease are allowed in the study but these lesions have to be treated successfully first (< 30% residual) before participant can be enrolled; treatment as per investigator's preference;
22. aneurysm located in the target vessel or aneurysmal vessel

Angiographic exclusion criteria:
the Investigator performing the procedure bases all angiographic exclusion criteria on visual determination at the time of the procedure;

1. has < 70% stenosis prior to treatment of the target lesion;
2. has in-stent restenosis of the target lesion;
3. has an acute intraluminal thrombus within the target lesion;
4. has an aneurysmal target vessel;
5. participant has already been enrolled in the study or any other study that by the investigator judgment may interfere with the outcome of this trial;

NCT03206762 *(Continued)*

	6. has two or more lesions that require treatment in the target vessel; lesions have to be separated by > 5 cm in order to be considered different lesions; only one lesion per target vessel can be enrolled during the index procedure; 7. has disease that precludes safe advancement of the Jetstream device to the target lesion; 8. P3 segments of the popliteal vessel.
Interventions	Arm 1: Jetstream atherectomy used in conjunction with the Ranger DCB or Medtronic IN.PACT D Arm 2: POBA and then DCB treatment (Ranger or IN.PACT)
Outcomes	Primary outcome measures: 1. TLR at 1 year: TLR is defined as re-treatment of the index lesion (extended 1 cm proximal and distal to the lesion) at 1 year. For the primary endpoint, intraprocedural bail out stenting of the index lesion is considered meeting a TLR endpoint. (ITT analysis) 2. MAE at 30 day: unplanned amputation, total mortality or TLR at 30 days (TLR includes bail-out stenting)
Starting date	28 March 2018
Contact information	Midwest Cardiovascular Research Foundation
Notes	

NCT03380650

Study name	Study of combined use of directional atherectomy and local drug delivery with balloon catheter system in the treatment of femoropopliteal occlusive disease
Methods	Single blind (participant), randomised, parallel assignment clinical trial
Participants	Estimated enrolment: 40 participants Ages eligible for study: 18 years to 80 years (adult, older adult) Sexes eligible for study: all Inclusion criteria: 1. people with femoropopliteal occlusive disease (Rutherford 2 to 4); 2. length of lesion ≤ 20 cm; 3. have signed the informed consent; Exclusion criteria: 1. serum creatinine > 150 umol/L; 2. people with acute thrombosis; 3. received endovascular treatment for femoropopliteal disease in recent 6 months; 4. less than 1 run-off vessel; 5. allergic to aspirin, heparin, clopidogrel, paclitaxel, contrast medium; 6. pregnancy and lactation; 7. relatively easy bleeding; 8. malignancy or irreversible organ failure.
Interventions	Device: directional atherectomy and local drug delivery Device: drug-coated balloon dilation

NCT03380650 *(Continued)*

Outcomes	Primary outcome measures: 1. rate of late lumen loss of target vessel (12 months) 2. patency rate of target vessel (6 months and 12 months) Secondary outcome measures: 1. minimal lumen diameter of target vessel at 6 months. 2. clinical outcomes (12 months) (rate of reintervention of target vessel) 3. incidence of complications (12 months); incidence of treatment induced major complications 4. restenosis rate (12 months); the rate of restenosis (≥ 50) 5. adverse events (12 months); incidence of treatment related adverse events 6. Rutherford level (12 months); change of Rutherford level 7. ABI (12 months) 8. main amputation (12 months); rate of main amputation
Starting date	1 January 2018
Contact information	Shuofei Yang, MD, PhD
Notes	

NCT03495453

Study name	Directional versus orbital atherectomy plaque modification and luminal area assessment of the femoropopliteal artery via intravascular ultrasound
Methods	Prospective, open, randomised, parallel assignment, single-centre study
Participants	Estimated enrolment: 60 participants Inclusion criteria: 1. age ≥ 18 years; 2. willing and able to provide consent before any study-specific test or procedure is performed, signs the consent form, and agrees to attend all required follow-up visits; 3. chronic, symptomatic lower limb ischaemia defined as Rutherford categories 1-4; 4. target lesion(s) located in a superficial femoral or popliteal arteries; 5. degree of stenosis ≥70% via Qualitative Comparative Analysis (QCA); 6. total lesion length ≥ 80 mm and ≤ 150 mm; 7. reference vessel ≥ 3.0 mm and < 6.5 mm; 8. patent infrapopliteal artery, i.e., single vessel runoff or better with at least one of three vessels patent (< 50% stenosis) to the ankle or foot with no planned intervention; 9. acceptable candidate for percutaneous intervention using the OAS or DAS in accordance with their labeled indications and instructions for use. Exclusion criteria: People who have: 1. a previously stented target lesion/vessel; 2. undergone prior surgery of the SFA/PA in the target limb to treat atherosclerotic disease; 3. presence of aneurysm in the target vessel; 4. interventional treatment is intended for in-stent restenosis at the peripheral vascular site; 5. target vessel with moderate or severe angulation (e.g., > 30°) or tortuosity at the treatment segment, that precludes safe advancement of the atherectomy device;

NCT03495453 *(Continued)*

	6. pre-planned interventional treatment includes planned laser, brachytherapy or atherectomy procedure other than OAS or DAS; 7. known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated; 8. known hypersensitivity/allergy to antiplatelet, anticoagulant, thrombolytic medications; 9. platelet count < 80,000 mm^3 or > 600,000 mm^3 or history of bleeding diathesis; 10. any known coagulation disorder, including hypercoagulability; 11. receiving dialysis or immunosuppressant therapy; 12. evidence of intracranial or gastrointestinal bleeding within last 3 months; 13. history of severe trauma, fracture, major surgery or biopsy of a parenchymal organ within past 14 days; 14. female patient who is pregnant or nursing a child; 15. current participation in another investigational drug or device clinical study that has not completed the primary endpoint at the time of randomisation/enrolment or that clinically interferes with the current study endpoints.
Interventions	Arm Intervention/treatment Active comparator: CSI's DIAMONDBACK 360 Peripheral OAS OAS (using CSI device) followed by Inpact Admiral DCB Device: percutaneous revascularisation of the femoropopliteal arteries using an OAS device HawkOne DAS is a small catheter with cutting device. The doctor slowly and smoothly advances it across the blockage in the artery and shaves the plaque from the vessel wall and collects it in the reservoir. Active Comparator: Medtronic's Hawkone DAS DAS (using the Hawkone device) followed by DCB Device: percutaneous revascularisation of the femoropopliteal arteries using a DAS Diamondback 360 Peripheral OAS is a small catheter with a diamond crown. The doctor inserts it at the groin and advances into the leg.The OAS works by spinning around inside the artery to "sand down" the buildup of material along the artery walls while leaving the healthy vessel behind.
Outcomes	Primary outcome measure: Measure of luminal area measured via IVUS at pretreatment and postatherectomy (12 months). All participants will undergo IVUS at pretreatment run to assess the severity and morphology of the plaque composition and postatherectomy run to assess changes postatherectomy treatment. Secondary outcome measure: Plaque burden reduction (12 months): the amount of removed plaque will be analysed via IVUS pretreatment and postatherectomy.
Starting date	12 April 2018
Contact information	Zulfiya Bakirova
Notes	

ABI: ankle brachial index
CFA: common femoral artery
CT: computed tomography
CTA: computed tomography angiogram
CLI: critical limb ischaemia
DAS: directional atherectomy system
DCB: drug coated balloon
DUS: duplex ultrasound
DVT: deep vein thrombosis
EQ-5D: EuroQoL Quality of Life Questionnaire
IFU: instructions for use
IVUS: intravascular ultrasound
LLL: late lumen loss

MAE: major adverse event
OA: orbital atherectomy
OAS: orbital atherectomy system
PA: popliteal artery
PAD; peripheral arterial disease
POBA: plain old balloon angioplasty
PTA: percutaneous transluminal angioplasty
PVR: peak velocity ratio
QoL: quality of life
QVA: quantitative vascular angiography
RCT: randomised controlled trial
SFA: superficial femoral artery
TASC: Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease
TLR: target lesion revascularisation
TBI: toe brachial index

DATA AND ANALYSES

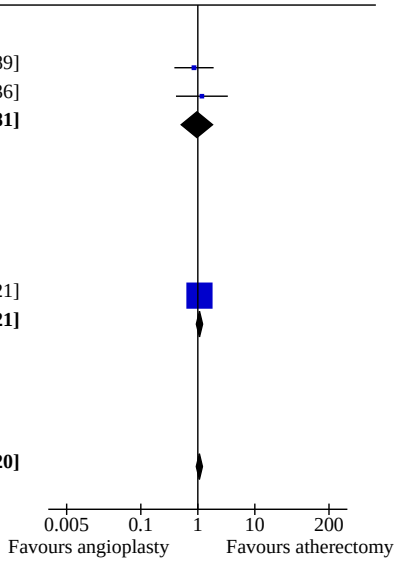
Comparison 1. Atherectomy versus balloon angioplasty

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 6-month primary patency	3	186	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.94, 1.20]
1.1.1 Balloon angioplasty	2	101	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.51, 1.81]
1.1.2 Drug-eluting balloon angioplasty	1	85	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.94, 1.21]
1.2 12-month primary patency	2	149	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.78, 1.84]
1.2.1 Balloon angioplasty	1	62	Risk Ratio (M-H, Random, 95% CI)	1.55 [0.90, 2.67]
1.2.2 Drug-eluting balloon angioplasty	1	87	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.86, 1.26]
1.3 Mortality	3	210	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.10, 2.66]
1.3.1 Balloon angioplasty	2	108	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.04, 1.68]
1.3.2 Drug-eluting balloon angioplasty	1	102	Risk Ratio (M-H, Random, 95% CI)	2.25 [0.21, 24.04]
1.4 Initial technical failure rates	6	425	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.22, 1.08]
1.4.1 Balloon angioplasty	5	324	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.20, 1.73]
1.4.2 Drug-eluting balloon angioplasty	1	101	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.12, 0.72]
1.5 Bailout stenting	4	315	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.09, 0.74]
1.5.1 Balloon angioplasty	3	213	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.07, 0.89]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.5.2 Drug-eluting balloon angioplasty	1	102	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.01, 4.56]
1.6 Balloon inflation pressure	3	213	Mean Difference (IV, Random, 95% CI)	-3.68 [-5.36, -2.01]
1.7 Target vessel revascularisation at 6 months	2	136	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.06, 4.42]
1.7.1 Balloon angioplasty	1	42	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.01, 2.38]
1.7.2 Drug-eluting balloon angioplasty	1	94	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.17, 8.07]
1.8 Target vessel revascularisation at 12 months	3	176	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.25, 1.42]
1.8.1 Balloon angioplasty	2	85	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.15, 1.39]
1.8.2 Drug-eluting balloon angioplasty	1	91	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.22, 3.86]
1.9 Complication rate	6	387	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.28, 1.68]
1.9.1 Balloon angioplasty	5	285	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.22, 2.42]
1.9.2 Drug-eluting balloon angioplasty	1	102	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.27, 1.72]
1.10 Embolisation	6	387	Risk Ratio (M-H, Random, 95% CI)	2.51 [0.64, 9.80]
1.10.1 Plain balloon angioplasty	5	285	Risk Ratio (M-H, Random, 95% CI)	1.84 [0.39, 8.55]
1.10.2 Drug-eluting balloon angioplasty	1	102	Risk Ratio (M-H, Random, 95% CI)	7.86 [0.42, 148.34]
1.11 Dissections	4	290	Risk Ratio (M-H, Random, 95% CI)	0.28 [0.14, 0.54]
1.11.1 Plain balloon angioplasty	3	188	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.16, 0.62]
1.11.2 Drug-eluting balloon angioplasty	1	102	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.01, 0.85]
1.12 Amputation	3	178	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.80]
1.12.1 Balloon angioplasty	2	76	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.80]
1.12.2 Drug-eluting balloon angioplasty	1	102	Risk Ratio (M-H, Random, 95% CI)	Not estimable

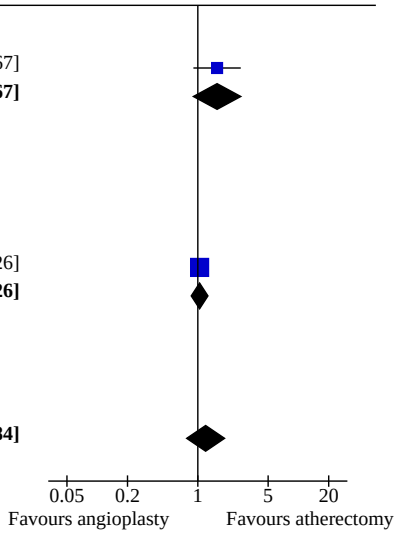
Analysis 1.1. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 1: 6-month primary patency

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Balloon angioplasty						
Nakamura 1995	9	21	5	10	2.4%	0.86 [0.39 , 1.89]
Vroegindeweij 1995	7	38	5	32	1.4%	1.18 [0.41 , 3.36]
Subtotal (95% CI)		**59**		**42**	**3.8%**	**0.96 [0.51 , 1.81]**
Total events:	16		10			
Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 0.12 (P = 0.91)						
1.1.2 Drug-eluting balloon angioplasty						
Zeller 2017	38	40	40	45	96.2%	1.07 [0.94 , 1.21]
Subtotal (95% CI)		**40**		**45**	**96.2%**	**1.07 [0.94 , 1.21]**
Total events:	38		40			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.04 (P = 0.30)						
Total (95% CI)		**99**		**87**	**100.0%**	**1.06 [0.94 , 1.20]**
Total events:	54		50			
Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 2 (P = 0.83); I² = 0%						
Test for overall effect: Z = 1.00 (P = 0.32)						
Test for subgroup differences: Chi² = 0.10, df = 1 (P = 0.75), I² = 0%						



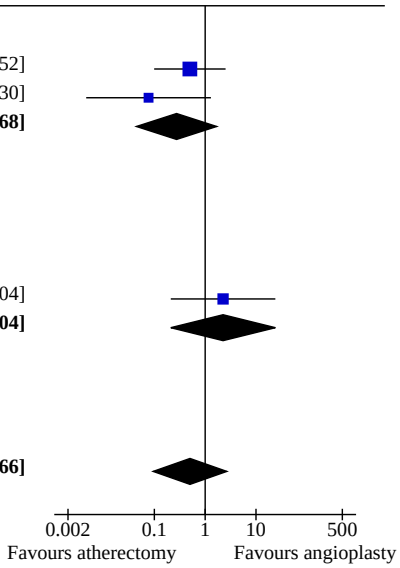
Analysis 1.2. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 2: 12-month primary patency

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Balloon angioplasty						
Vroegindeweij 1995	23	37	10	25	34.5%	1.55 [0.90 , 2.67]
Subtotal (95% CI)		**37**		**25**	**34.5%**	**1.55 [0.90 , 2.67]**
Total events:	23		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.59 (P = 0.11)						
1.2.2 Drug-eluting balloon angioplasty						
Zeller 2017	33	39	39	48	65.5%	1.04 [0.86 , 1.26]
Subtotal (95% CI)		**39**		**48**	**65.5%**	**1.04 [0.86 , 1.26]**
Total events:	33		39			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.42 (P = 0.68)						
Total (95% CI)		**76**		**73**	**100.0%**	**1.20 [0.78 , 1.84]**
Total events:	56		49			
Heterogeneity: Tau² = 0.06; Chi² = 2.51, df = 1 (P = 0.11); I² = 60%						
Test for overall effect: Z = 0.81 (P = 0.42)						
Test for subgroup differences: Chi² = 1.86, df = 1 (P = 0.17), I² = 46.4%						



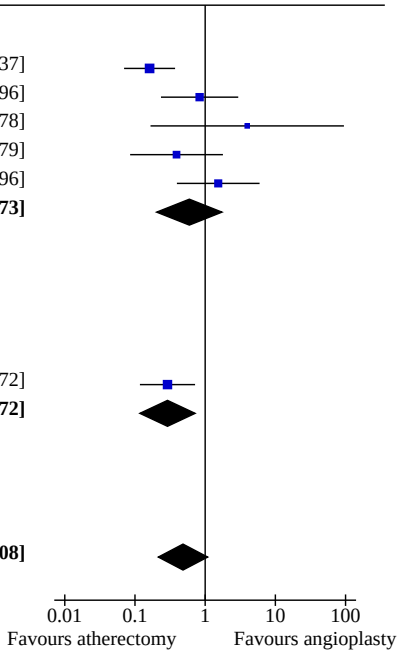
Analysis 1.3. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 3: Mortality

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Balloon angioplasty						
Shammas 2011	2	29	4	29	45.4%	0.50 [0.10 , 2.52]
Shammas 2012	0	25	6	25	24.2%	0.08 [0.00 , 1.30]
Subtotal (95% CI)		**54**		**54**	**69.5%**	**0.27 [0.04 , 1.68]**
Total events:	2		10			
Heterogeneity: Tau² = 0.58; Chi² = 1.42, df = 1 (P = 0.23); I² = 30%						
Test for overall effect: Z = 1.40 (P = 0.16)						
1.3.2 Drug-eluting balloon angioplasty						
Zeller 2017	2	48	1	54	30.5%	2.25 [0.21 , 24.04]
Subtotal (95% CI)		**48**		**54**	**30.5%**	**2.25 [0.21 , 24.04]**
Total events:	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.50)						
Total (95% CI)		**102**		**108**	**100.0%**	**0.50 [0.10 , 2.66]**
Total events:	4		11			
Heterogeneity: Tau² = 0.91; Chi² = 3.41, df = 2 (P = 0.18); I² = 41%						
Test for overall effect: Z = 0.81 (P = 0.42)						
Test for subgroup differences: Chi² = 1.92, df = 1 (P = 0.17), I² = 47.8%						



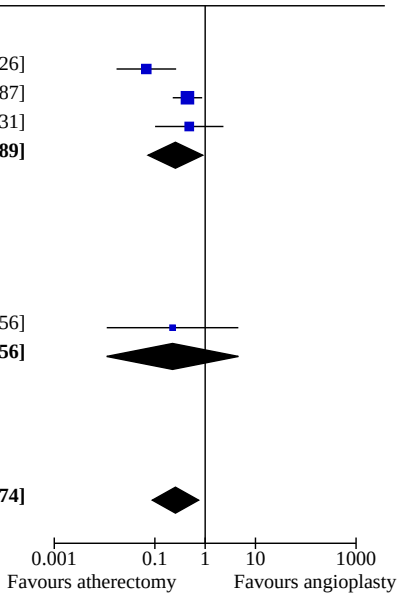
Analysis 1.4. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 4: Initial technical failure rates

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 Balloon angioplasty						
Dattilo 2014	5	38	22	27	23.3%	0.16 [0.07 , 0.37]
Nakamura 1995	5	26	3	13	17.6%	0.83 [0.23 , 2.96]
Shammas 2011	1	36	0	48	5.4%	3.97 [0.17 , 94.78]
Shammas 2012	2	29	6	34	14.8%	0.39 [0.09 , 1.79]
Vroegindeweij 1995	5	38	3	35	16.6%	1.54 [0.40 , 5.96]
Subtotal (95% CI)		**167**		**157**	**77.6%**	**0.59 [0.20 , 1.73]**
Total events:	18		34			
Heterogeneity: Tau² = 0.90; Chi² = 11.59, df = 4 (P = 0.02); I² = 65%						
Test for overall effect: Z = 0.95 (P = 0.34)						
1.4.2 Drug-eluting balloon angioplasty						
Zeller 2017	5	48	19	53	22.4%	0.29 [0.12 , 0.72]
Subtotal (95% CI)		**48**		**53**	**22.4%**	**0.29 [0.12 , 0.72]**
Total events:	5		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.68 (P = 0.007)						
Total (95% CI)		**215**		**210**	**100.0%**	**0.48 [0.22 , 1.08]**
Total events:	23		53			
Heterogeneity: Tau² = 0.55; Chi² = 12.01, df = 5 (P = 0.03); I² = 58%						
Test for overall effect: Z = 1.76 (P = 0.08)						
Test for subgroup differences: Chi² = 1.00, df = 1 (P = 0.32), I² = 0.4%						



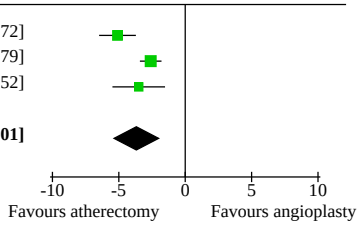
Analysis 1.5. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 5: Bailout stenting

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Balloon angioplasty						
Dattilo 2014	2	38	21	27	26.7%	0.07 [0.02 , 0.26]
Shammas 2011	8	36	24	48	40.2%	0.44 [0.23 , 0.87]
Shammas 2012	2	29	5	35	23.4%	0.48 [0.10 , 2.31]
Subtotal (95% CI)		**103**		**110**	**90.2%**	**0.26 [0.07 , 0.89]**
Total events:	12		50			
Heterogeneity: Tau² = 0.84; Chi² = 6.74, df = 2 (P = 0.03); I² = 70%						
Test for overall effect: Z = 2.14 (P = 0.03)						
1.5.2 Drug-eluting balloon angioplasty						
Zeller 2017	0	48	2	54	9.8%	0.22 [0.01 , 4.56]
Subtotal (95% CI)		**48**		**54**	**9.8%**	**0.22 [0.01 , 4.56]**
Total events:	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						
Total (95% CI)		**151**		**164**	**100.0%**	**0.26 [0.09 , 0.74]**
Total events:	12		52			
Heterogeneity: Tau² = 0.61; Chi² = 6.79, df = 3 (P = 0.08); I² = 56%						
Test for overall effect: Z = 2.52 (P = 0.01)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%						



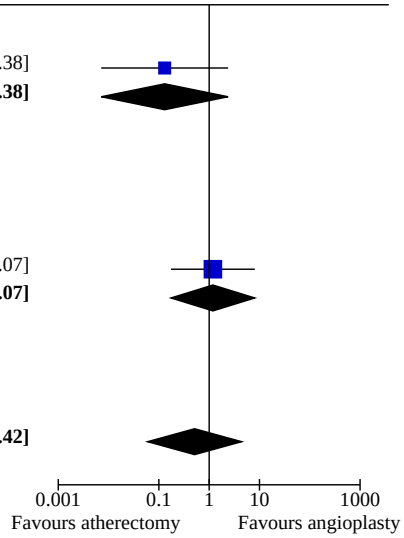
Analysis 1.6. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 6: Balloon inflation pressure

Study or Subgroup	Atherectomy Mean	Atherectomy SD	Atherectomy Total	Angioplasty Mean	Angioplasty SD	Angioplasty Total	Weight	Mean Difference IV, Random, 95% CI
Dattilo 2014	4	1.3	38	9.1	3.5	27	33.5%	-5.10 [-6.48 , -3.72]
Shammas 2011	7.9	1.7	36	10.5	2.1	48	39.4%	-2.60 [-3.41 , -1.79]
Shammas 2012	5.9	4.2	29	9.4	3.8	35	27.0%	-3.50 [-5.48 , -1.52]
Total (95% CI)			**103**			**110**	**100.0%**	**-3.68 [-5.36 , -2.01]**
Heterogeneity: Tau² = 1.68; Chi² = 9.38, df = 2 (P = 0.009); I² = 79%								
Test for overall effect: Z = 4.31 (P < 0.0001)								
Test for subgroup differences: Not applicable								



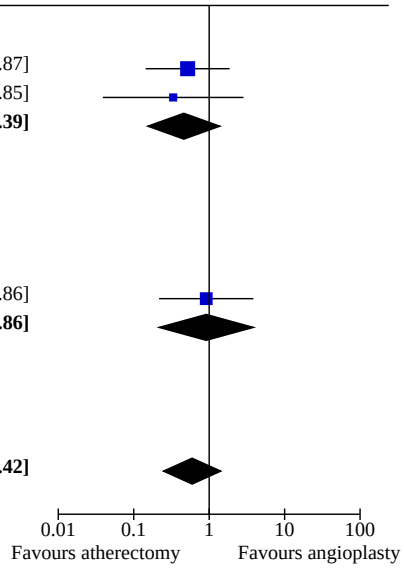
Analysis 1.7. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 7: Target vessel revascularisation at 6 months

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Balloon angioplasty						
Shammas 2012	0	22	3	20	37.9%	0.13 [0.01 , 2.38]
Subtotal (95% CI)		**22**		**20**	**37.9%**	**0.13 [0.01 , 2.38]**
Total events:	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.37 (P = 0.17)						
1.7.2 Drug-eluting balloon angioplasty						
Zeller 2017	2	43	2	51	62.1%	1.19 [0.17 , 8.07]
Subtotal (95% CI)		**43**		**51**	**62.1%**	**1.19 [0.17 , 8.07]**
Total events:	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.17 (P = 0.86)						
Total (95% CI)		**65**		**71**	**100.0%**	**0.51 [0.06 , 4.42]**
Total events:	2		5			
Heterogeneity: Tau² = 0.99; Chi² = 1.63, df = 1 (P = 0.20); I² = 38%						
Test for overall effect: Z = 0.61 (P = 0.54)						
Test for subgroup differences: Chi² = 1.55, df = 1 (P = 0.21), I² = 35.3%						



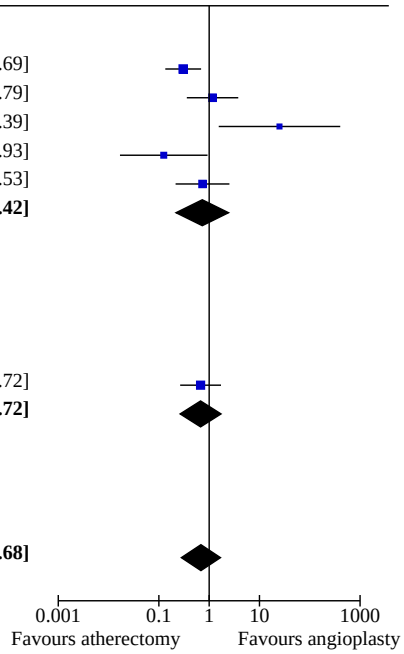
Analysis 1.8. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 8: Target vessel revascularisation at 12 months

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 Balloon angioplasty						
Shammas 2011	3	27	6	28	46.5%	0.52 [0.14 , 1.87]
Shammas 2012	1	15	3	15	16.6%	0.33 [0.04 , 2.85]
Subtotal (95% CI)		**42**		**43**	**63.1%**	**0.46 [0.15 , 1.39]**
Total events:	4		9			
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 1 (P = 0.73); I² = 0%						
Test for overall effect: Z = 1.38 (P = 0.17)						
1.8.2 Drug-eluting balloon angioplasty						
Zeller 2017	3	41	4	50	36.9%	0.91 [0.22 , 3.86]
Subtotal (95% CI)		**41**		**50**	**36.9%**	**0.91 [0.22 , 3.86]**
Total events:	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.90)						
Total (95% CI)		**83**		**93**	**100.0%**	**0.59 [0.25 , 1.42]**
Total events:	7		13			
Heterogeneity: Tau² = 0.00; Chi² = 0.67, df = 2 (P = 0.72); I² = 0%						
Test for overall effect: Z = 1.17 (P = 0.24)						
Test for subgroup differences: Chi² = 0.55, df = 1 (P = 0.46), I² = 0%						



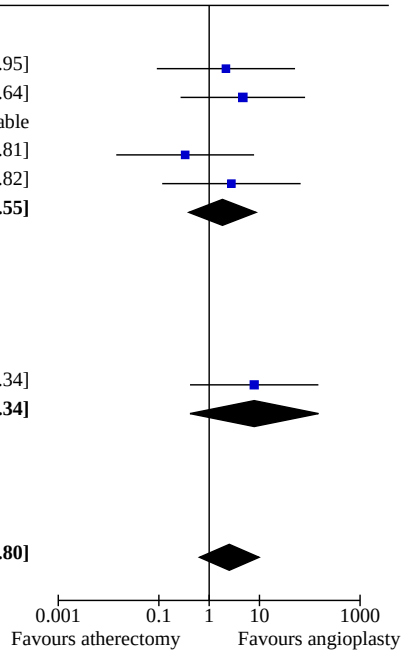
Analysis 1.9. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 9: Complication rate

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.9.1 Balloon angioplasty						
Dattilo 2014	6	38	14	27	22.6%	0.30 [0.13 , 0.69]
Nakamura 1995	7	26	3	13	18.8%	1.17 [0.36 , 3.79]
Shammas 2011	12	29	0	29	7.5%	25.00 [1.55 , 403.39]
Shammas 2012	1	25	8	25	11.6%	0.13 [0.02 , 0.93]
Vroegindeweij 1995	4	38	5	35	18.2%	0.74 [0.21 , 2.53]
Subtotal (95% CI)		**156**		**129**	**78.7%**	**0.73 [0.22 , 2.42]**
Total events:	30		30			
Heterogeneity: Tau² = 1.26; Chi² = 14.84, df = 4 (P = 0.005); I² = 73%						
Test for overall effect: Z = 0.51 (P = 0.61)						
1.9.2 Drug-eluting balloon angioplasty						
Zeller 2017	6	48	10	54	21.3%	0.68 [0.27 , 1.72]
Subtotal (95% CI)		**48**		**54**	**21.3%**	**0.68 [0.27 , 1.72]**
Total events:	6		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.82 (P = 0.41)						
Total (95% CI)		**204**		**183**	**100.0%**	**0.69 [0.28 , 1.68]**
Total events:	36		40			
Heterogeneity: Tau² = 0.75; Chi² = 14.62, df = 5 (P = 0.01); I² = 66%						
Test for overall effect: Z = 0.83 (P = 0.41)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%						



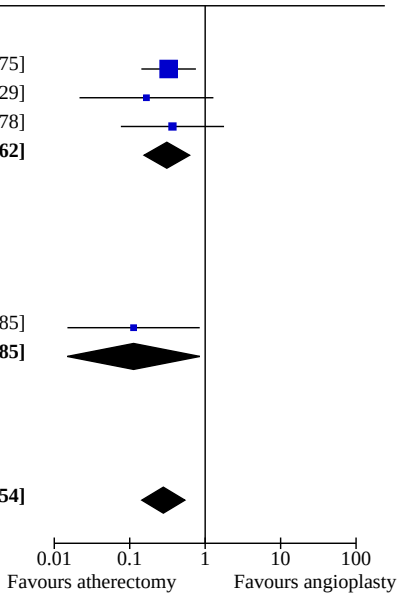
Analysis 1.10. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 10: Embolisation

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.10.1 Plain balloon angioplasty						
Dattilo 2014	1	38	0	27	18.5%	2.15 [0.09 , 50.95]
Nakamura 1995	4	26	0	13	22.8%	4.67 [0.27 , 80.64]
Shammas 2011	0	29	0	29		Not estimable
Shammas 2012	0	25	1	25	18.6%	0.33 [0.01 , 7.81]
Vroegindeweij 1995	1	38	0	35	18.5%	2.77 [0.12 , 65.82]
Subtotal (95% CI)		**156**		**129**	**78.5%**	**1.84 [0.39 , 8.55]**
Total events:	6		1			
Heterogeneity: Tau² = 0.00; Chi² = 1.61, df = 3 (P = 0.66); I² = 0%						
Test for overall effect: Z = 0.78 (P = 0.44)						
1.10.2 Drug-eluting balloon angioplasty						
Zeller 2017	3	48	0	54	21.5%	7.86 [0.42 , 148.34]
Subtotal (95% CI)		**48**		**54**	**21.5%**	**7.86 [0.42 , 148.34]**
Total events:	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						
Total (95% CI)		**204**		**183**	**100.0%**	**2.51 [0.64 , 9.80]**
Total events:	9		1			
Heterogeneity: Tau² = 0.00; Chi² = 2.36, df = 4 (P = 0.67); I² = 0%						
Test for overall effect: Z = 1.32 (P = 0.19)						
Test for subgroup differences: Chi² = 0.74, df = 1 (P = 0.39), I² = 0%						



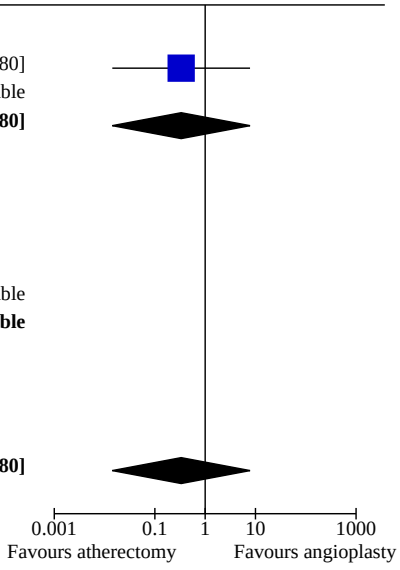
Analysis 1.11. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 11: Dissections

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.11.1 Plain balloon angioplasty						
Dattilo 2014	6	38	13	27	61.9%	0.33 [0.14 , 0.75]
Shammas 2012	1	25	6	25	10.3%	0.17 [0.02 , 1.29]
Vroegindeweij 1995	2	38	5	35	17.3%	0.37 [0.08 , 1.78]
Subtotal (95% CI)		**101**		**87**	**89.5%**	**0.31 [0.16 , 0.62]**
Total events:	9		24			
Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 2 (P = 0.81); I² = 0%						
Test for overall effect: Z = 3.31 (P = 0.0009)						
1.11.2 Drug-eluting balloon angioplasty						
Zeller 2017	1	48	10	54	10.5%	0.11 [0.01 , 0.85]
Subtotal (95% CI)		**48**		**54**	**10.5%**	**0.11 [0.01 , 0.85]**
Total events:	1		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.12 (P = 0.03)						
Total (95% CI)		**149**		**141**	**100.0%**	**0.28 [0.14 , 0.54]**
Total events:	10		34			
Heterogeneity: Tau² = 0.00; Chi² = 1.39, df = 3 (P = 0.71); I² = 0%						
Test for overall effect: Z = 3.82 (P = 0.0001)						
Test for subgroup differences: Chi² = 0.87, df = 1 (P = 0.35), I² = 0%						



Analysis 1.12. Comparison 1: Atherectomy versus balloon angioplasty, Outcome 12: Amputation

Study or Subgroup	Atherectomy Events	Atherectomy Total	Angioplasty Events	Angioplasty Total	Weight	Risk Ratio M-H, Random, 95% CI
1.12.1 Balloon angioplasty						
Shammas 2011	0	24	1	24	100.0%	0.33 [0.01 , 7.80]
Shammas 2012	0	14	0	14		Not estimable
Subtotal (95% CI)		**38**		**38**	**100.0%**	**0.33 [0.01 , 7.80]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
1.12.2 Drug-eluting balloon angioplasty						
Zeller 2017	0	48	0	54		Not estimable
Subtotal (95% CI)		**48**		**54**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**86**		**92**	**100.0%**	**0.33 [0.01 , 7.80]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
Test for subgroup differences: Not applicable						



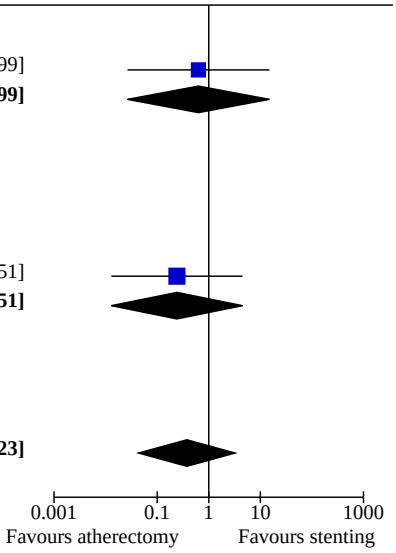
Comparison 2. Atherectomy +/- bailout stenting versus primary stenting

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Mortality	1	155	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.04, 3.23]
2.1.1 Plain balloon plus stent	1	79	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.03, 14.99]
2.1.2 Drug-eluting balloon plus stent	1	76	Risk Ratio (M-H, Random, 95% CI)	0.24 [0.01, 4.51]
2.2 Cardiovascular events	1	155	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.04, 3.23]
2.2.1 Plain balloon plus stent	1	79	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.03, 14.99]
2.2.2 Drug-eluting balloon plus stent	1	76	Risk Ratio (M-H, Random, 95% CI)	0.24 [0.01, 4.51]
2.3 Initial technical failure rates	1	155	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.3.1 Plain balloon plus stent	1	79	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.3.2 Drug-eluting balloon plus stent	1	76	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.4 Target vessel revascularisation at 6 months	1	155	Risk Ratio (M-H, Random, 95% CI)	2.27 [0.95, 5.46]
2.4.1 Plain balloon plus stent	1	79	Risk Ratio (M-H, Random, 95% CI)	1.93 [0.61, 6.08]
2.4.2 Drug-eluting balloon plus stent	1	76	Risk Ratio (M-H, Random, 95% CI)	2.86 [0.74, 11.06]
2.5 Target vessel revascularisation at 24 months	1	155	Risk Ratio (M-H, Random, 95% CI)	2.05 [0.96, 4.37]
2.5.1 Plain balloon plus stent	1	79	Risk Ratio (M-H, Random, 95% CI)	1.47 [0.85, 2.56]
2.5.2 Drug-eluting balloon plus stent	1	76	Risk Ratio (M-H, Random, 95% CI)	3.18 [1.44, 7.03]
2.6 Complication rate	1	155	Risk Ratio (M-H, Random, 95% CI)	7.04 [0.80, 62.23]
2.6.1 Plain balloon plus stent	1	79	Risk Ratio (M-H, Random, 95% CI)	9.46 [0.47, 190.41]
2.6.2 Drug-eluting balloon plus stent	1	76	Risk Ratio (M-H, Random, 95% CI)	5.07 [0.21, 120.38]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.7 Amputation	1	155	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.7.1 Plain balloon plus stent	1	79	Risk Ratio (M-H, Random, 95% CI)	Not estimable
2.7.2 Drug-eluting balloon plus stent	1	76	Risk Ratio (M-H, Random, 95% CI)	Not estimable

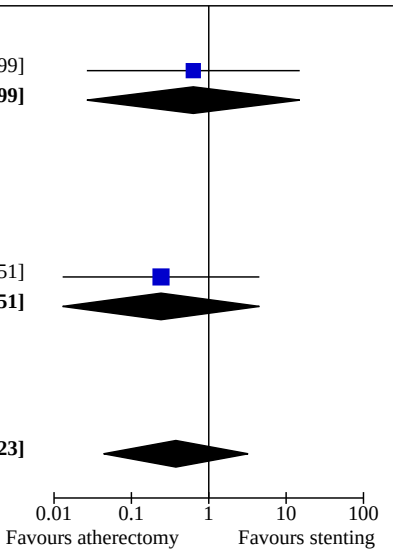
Analysis 2.1. Comparison 2: Atherectomy +/- bailout stenting versus primary stenting, Outcome 1: Mortality

Study or Subgroup	Atherectomy Events	Atherectomy Total	Stenting Events	Stenting Total	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 Plain balloon plus stent						
Ott 2017	0	27	1	52	46.1%	0.63 [0.03 , 14.99]
Subtotal (95% CI)		**27**		**52**	**46.1%**	**0.63 [0.03 , 14.99]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
2.1.2 Drug-eluting balloon plus stent						
Ott 2017	0	28	3	48	53.9%	0.24 [0.01 , 4.51]
Subtotal (95% CI)		**28**		**48**	**53.9%**	**0.24 [0.01 , 4.51]**
Total events:	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
Total (95% CI)		**55**		**100**	**100.0%**	**0.38 [0.04 , 3.23]**
Total events:	0		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.66); I² = 0%						
Test for overall effect: Z = 0.89 (P = 0.37)						
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.66), I² = 0%						



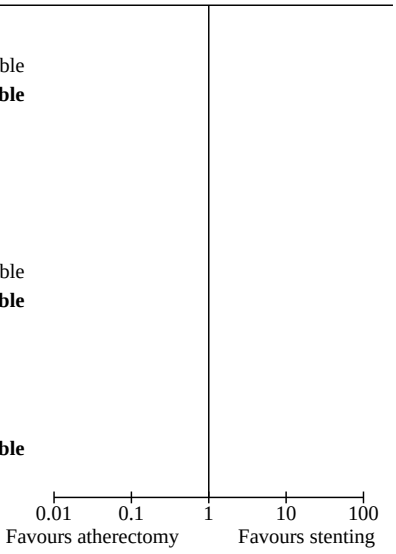
Analysis 2.2. Comparison 2: Atherectomy +/- bailout stenting versus primary stenting, Outcome 2: Cardiovascular events

Study or Subgroup	Atherectomy Events	Atherectomy Total	Stenting Events	Stenting Total	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 Plain balloon plus stent						
Ott 2017	0	27	1	52	46.1%	0.63 [0.03 , 14.99]
Subtotal (95% CI)		**27**		**52**	**46.1%**	**0.63 [0.03 , 14.99]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
2.2.2 Drug-eluting balloon plus stent						
Ott 2017	0	28	3	48	53.9%	0.24 [0.01 , 4.51]
Subtotal (95% CI)		**28**		**48**	**53.9%**	**0.24 [0.01 , 4.51]**
Total events:	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
Total (95% CI)		**55**		**100**	**100.0%**	**0.38 [0.04 , 3.23]**
Total events:	0		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.66); I² = 0%						
Test for overall effect: Z = 0.89 (P = 0.37)						
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.66), I² = 0%						



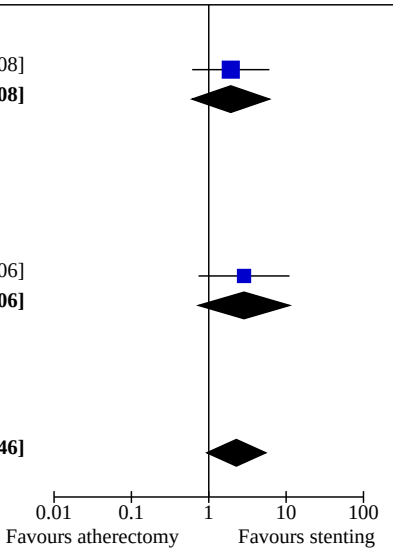
Analysis 2.3. Comparison 2: Atherectomy +/- bailout stenting versus primary stenting, Outcome 3: Initial technical failure rates

Study or Subgroup	Atherectomy Events	Atherectomy Total	Stenting Events	Stenting Total	Weight	Risk Ratio M-H, Random, 95% CI
2.3.1 Plain balloon plus stent						
Ott 2017	0	27	0	52		Not estimable
Subtotal (95% CI)		**27**		**52**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.3.2 Drug-eluting balloon plus stent						
Ott 2017	0	28	0	48		Not estimable
Subtotal (95% CI)		**28**		**48**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**55**		**100**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



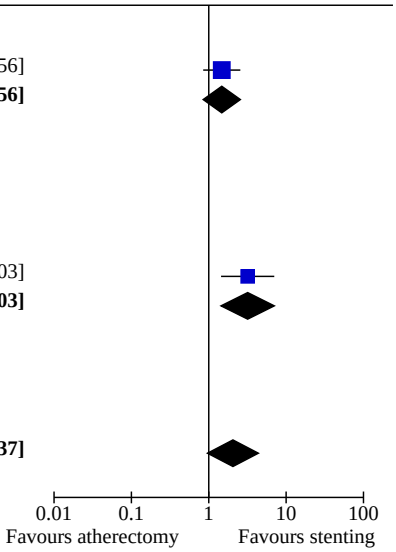
Analysis 2.4. Comparison 2: Atherectomy +/- bailout stenting versus primary stenting, Outcome 4: Target vessel revascularisation at 6 months

Study or Subgroup	Atherectomy Events	Atherectomy Total	Stenting Events	Stenting Total	Weight	Risk Ratio M-H, Random, 95% CI
2.4.1 Plain balloon plus stent						
Ott 2017	5	27	5	52	58.1%	1.93 [0.61 , 6.08]
Subtotal (95% CI)		**27**		**52**	**58.1%**	**1.93 [0.61 , 6.08]**
Total events:	5		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.12 (P = 0.26)						
2.4.2 Drug-eluting balloon plus stent						
Ott 2017	5	28	3	48	41.9%	2.86 [0.74 , 11.06]
Subtotal (95% CI)		**28**		**48**	**41.9%**	**2.86 [0.74 , 11.06]**
Total events:	5		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.52 (P = 0.13)						
Total (95% CI)		**55**		**100**	**100.0%**	**2.27 [0.95 , 5.46]**
Total events:	10		8			
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.66); I² = 0%						
Test for overall effect: Z = 1.84 (P = 0.07)						
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.66), I² = 0%						



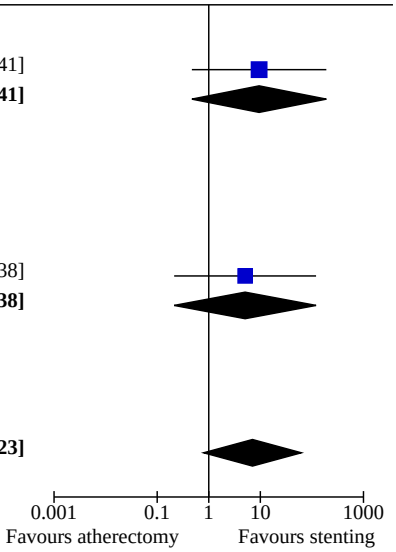
Analysis 2.5. Comparison 2: Atherectomy +/- bailout stenting versus primary stenting, Outcome 5: Target vessel revascularisation at 24 months

Study or Subgroup	Atherectomy Events	Atherectomy Total	Stenting Events	Stenting Total	Weight	Risk Ratio M-H, Random, 95% CI
2.5.1 Plain balloon plus stent						
Ott 2017	13	27	17	52	56.9%	1.47 [0.85 , 2.56]
Subtotal (95% CI)		**27**		**52**	**56.9%**	**1.47 [0.85 , 2.56]**
Total events:	13		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.37 (P = 0.17)						
2.5.2 Drug-eluting balloon plus stent						
Ott 2017	13	28	7	48	43.1%	3.18 [1.44 , 7.03]
Subtotal (95% CI)		**28**		**48**	**43.1%**	**3.18 [1.44 , 7.03]**
Total events:	13		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.87 (P = 0.004)						
Total (95% CI)		**55**		**100**	**100.0%**	**2.05 [0.96 , 4.37]**
Total events:	26		24			
Heterogeneity: Tau² = 0.18; Chi² = 2.50, df = 1 (P = 0.11); I² = 60%						
Test for overall effect: Z = 1.86 (P = 0.06)						
Test for subgroup differences: Chi² = 2.45, df = 1 (P = 0.12), I² = 59.2%						



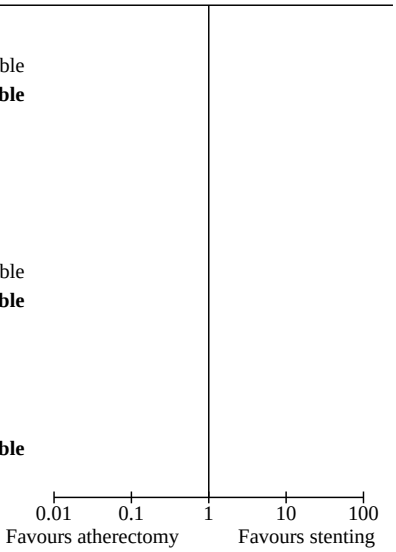
Analysis 2.6. Comparison 2: Atherectomy +/- bailout stenting versus primary stenting, Outcome 6: Complication rate

Study or Subgroup	Atherectomy Events	Atherectomy Total	Stenting Events	Stenting Total	Weight	Risk Ratio M-H, Random, 95% CI
2.6.1 Plain balloon plus stent						
Ott 2017	2	27	0	52	52.7%	9.46 [0.47 , 190.41]
Subtotal (95% CI)		**27**		**52**	**52.7%**	**9.46 [0.47 , 190.41]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						
2.6.2 Drug-eluting balloon plus stent						
Ott 2017	1	28	0	48	47.3%	5.07 [0.21 , 120.38]
Subtotal (95% CI)		**28**		**48**	**47.3%**	**5.07 [0.21 , 120.38]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						
Total (95% CI)		**55**		**100**	**100.0%**	**7.04 [0.80 , 62.23]**
Total events:	3		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%						
Test for overall effect: Z = 1.76 (P = 0.08)						
Test for subgroup differences: Chi² = 0.08, df = 1 (P = 0.78), I² = 0%						



Analysis 2.7. Comparison 2: Atherectomy +/- bailout stenting versus primary stenting, Outcome 7: Amputation

Study or Subgroup	Atherectomy Events	Atherectomy Total	Stenting Events	Stenting Total	Weight	Risk Ratio M-H, Random, 95% CI
2.7.1 Plain balloon plus stent						
Ott 2017	0	27	0	52		Not estimable
Subtotal (95% CI)		**27**		**52**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.7.2 Drug-eluting balloon plus stent						
Ott 2017	0	28	0	48		Not estimable
Subtotal (95% CI)		**28**		**48**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**55**		**100**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



APPENDICES

Appendix 1. Database search strategy

Source	Search strategy	Hits retrieved
CENTRAL via CRSO	#1 MESH DESCRIPTOR Arteriosclerosis 946	20 August 2018: 110
	#2 MESH DESCRIPTOR Arteriolosclerosis 0	12 August 2019: 57
	#3 MESH DESCRIPTOR Arteriosclerosis Obliterans 78	
	#4 MESH DESCRIPTOR Atherosclerosis 1061	
	#5 MESH DESCRIPTOR Arterial Occlusive Diseases 819	
	#6 MESH DESCRIPTOR Intermittent Claudication 825	
	#7 MESH DESCRIPTOR Ischemia 1542	
	#8 MESH DESCRIPTOR Peripheral Vascular Diseases EXPLODE ALL TREES 2783	
	#9 MESH DESCRIPTOR Vascular Diseases 645	
	#10 MESH DESCRIPTOR Leg EXPLODE ALL TREES 2801	
	#11 MESH DESCRIPTOR Femoral Artery EXPLODE ALL TREES 904	
	#12 MESH DESCRIPTOR Popliteal Artery EXPLODE ALL TREES 304	
	#13 MESH DESCRIPTOR Iliac Artery EXPLODE ALL TREES 159	
	#14 MESH DESCRIPTOR Tibial Arteries EXPLODE ALL TREES 38	
	#15 (atherosclero* or arteriosclero* or PVD or PAOD or PAD):TI,AB,KY 12285	
	#16 ((arter*) near (*occlus* or steno* or obstuct* or lesio* or block* or obliter*)):TI,AB,KY 6367	
	#17 ((vascular) near (*occlus* or steno* or obstuct* or lesio* or block* or obliter*)):TI,AB,KY 842	
	#18 ((veno*) near (*occlus* or steno* or obstuct* or lesio* or block* or obliter*)):TI,AB,KY 1151	
	#19 ((vein*) near (*occlus* or steno* or obstuct* or lesio* or block* or obliter*)):TI,AB,KY 1346	
	#20 ((peripher*) near (*occlus* or steno* or obstuct* or lesio* or block* or obliter*)):TI,AB,KY 2358	
	#21 (peripheral near/3 dis*):TI,AB,KY 0	
	#22 arteriopathic:TI,AB,KY 7	
	#23 (claudic* or hinken*):TI,AB,KY 1880	
	#24 (isch* or CLI):TI,AB,KY 32430	
	#25 dysvascular*:TI,AB,KY 23	
	#26 (leg near4 (obstruct* or occlus* or steno* or block* or obliter*)):TI,AB,KY 155	
	#27 (limb near4 (obstruct* or occlus* or steno* or block* or obliter*)):TI,AB,KY 239	
	#28 ((lower near3 extrem*) near4 (obstruct* or occlus* or steno* or block* or obliter*)):TI,AB,KY 103	

(Continued)

	#29 ((aort* or iliac or femoral or popliteal or femoro* or fempop* or crural) near3 (obstruct* or occlus*)):TI,AB,KY 454 #30 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 56041 #31 MESH DESCRIPTOR Atherectomy 24 #32 atherect*:TI,AB,KY 333 #33 (SilverHawk or "Silver Hawk"):TI,AB,KY 12 #34 Jetstream:TI,AB,KY 2 #35 (plaque near3 excis*):TI,AB,KY 12 #36 (atheroablation or rotational or orbital):TI,AB,KY 1514 #37 (angle near3 blade*):TI,AB,KY 10 #38 (cut near3 blade*):TI,AB,KY 1 #39 (blade near3 cathet*):TI,AB,KY 1 #40 EV3:TI,AB,KY 10 #41 #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 1735 #42 #30 AND #41 201 #43 01/11/2013 TO 20/08/2018:CD 584598 #44 #42 AND #43 110	
Clinicaltrials.gov	peripheral arterial disease OR artery OR vascular OR Arteriosclerosis OR Ischemia | Atherectomy OR atheroablation OR rotational OR orbital OR EV3 | Start date on or after 01/01/2013 | Last update posted on or before 08/08/2019	20 August 2018: 76 12 August 2019: 36
ICTRP Search Portal	peripheral arterial disease OR artery OR vascular OR Arteriosclerosis OR Ischemia | Atherectomy OR atheroablation OR rotational OR orbital OR EV3 | Start date on or after 01/01/2013 | Last update posted on or before 08/08/2019	20 August 2018: 41 12 August 2019: 14
Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®	1 ARTERIOSCLEROSIS/ 56458 2 ARTERIOLOSCLEROSIS/ 150 3 Arteriosclerosis Obliterans/ 3977 4 ATHEROSCLEROSIS/ 31372 5 Arterial Occlusive Diseases/ 26551 6 Intermittent Claudication/ 7623 7 ISCHEMIA/ 47700 8 exp Peripheral Vascular Diseases/ 50278 9 Vascular Diseases/ 35016 10 exp LEG/bs [Blood Supply] 25052 11 exp Femoral Artery/ 27179 12 exp Popliteal Artery/ 9025	20 August 2018: 59 12 August 2019: 59

(Continued)

13 exp Iliac Artery/ 13402

14 exp Tibial Arteries/ 1501

15 (atherosclero* or arteriosclero* or PVD or PAOD or PAD).ti,ab. 172197

16 (arter* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 63236

17 (vascular adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 15842

18 (vein* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 7223

19 (veno* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 7897

20 (peripher* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 1931

21 (peripheral adj3 dis*).ti,ab. 38014

22 arteriopathic.ti,ab. 162

23 (claudic* or hinken*).ti,ab. 9857

24 (isch* or CLI).ti,ab. 347912

25 (leg adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 591

26 (limb adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 1841

27 (lower adj3 extrem* adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 1541

28 ((aort* or iliac or femoral or popliteal or femoro* or fempop* or crural) adj3 (obstruct* or occlus*)).ti,ab. 8681

29 dysvascular*.ti,ab. 219

30 or/1-29 732181

31 ATHERECTOMY/ 667

32 atherect*.ti,ab. 2759

33 (SilverHawk or "Silver Hawk").ti,ab. 66

34 Jetstream.ti,ab. 31

35 (plaque adj3 excis*).ti,ab. 209

36 (atheroablation or rotational or orbital).ti,ab. 90480

37 (angle adj3 blade*).ti,ab. 112

38 (cut adj3 blade*).ti,ab. 80

39 (blade adj3 cathet*).ti,ab. 10

40 EV3.ti,ab. 238

41 or/31-40 93104

42 30 and 41 3188

(Continued)

	43 randomized controlled trial.pt. 467015	
	44 controlled clinical trial.pt. 92591	
	45 randomized.ab. 419437	
	46 placebo.ab. 191087	
	47 drug therapy.fs. 2041052	
	48 randomly.ab. 295632	
	49 trial.ab. 436703	
	50 groups.ab. 1824460	
	51 or/43-50 4263409	
	52 exp animals/ not humans.sh. 4488176	
	53 51 not 52 3685450	
	54 42 and 53 555	
	55 (2017* or 2018*).ed. 1598344	
	56 54 and 55 59	
	57 from 56 keep 1-59 59	
EMBASE	1 arteriosclerosis/ 23302	20 August 2018: 278
	2 arteriolosclerosis/ 539	12 August 2019: 361
	3 peripheral occlusive artery disease/ 29354	
	4 atherosclerosis/ 130224	
	5 peripheral occlusive artery disease/ 29354	
	6 intermittent claudication/ 8546	
	7 ischemia/ 70896	
	8 exp peripheral vascular disease/ 1521794	
	9 vascular disease/ 50928	
	10 exp femoral artery/ 28864	
	11 exp popliteal artery/ 7120	
	12 exp iliac artery/ 15142	
	13 exp tibial artery/ 2504	
	14 (atherosclero* or arteriosclero* or PVD or PAOD or PAD).ti,ab. 221645	
	15 (arter* adj (*occlus*/ or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 81145	
	16 (vascular adj (*occlus*/ or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 19845	
	17 (vein* adj (*occlus*/ or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 9432	

(Continued)

18 (veno* adj (*occlus*/ or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 10130

19 (peripher* adj (*occlus*/ or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 2816

20 (peripheral adj3 dis*).ti,ab. 51397

21 arteriopathic.ti,ab. 179

22 (claudic* or hinken*).ti,ab. 12594

23 (isch* or CLI).ti,ab. 478952

24 dysvascular*.ti,ab. 229

25 (leg adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 731

26 (limb adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 2595

27 (lower dj3 extrem* adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 0

28 ((aort* or iliac or femoral or popliteal or femoro* or fempop* or crural) adj3 (obstruct* or occlus*)).ti,ab. 10343

29 or/1-28 1820971

30 atherectomy/ 3475

31 atherect*.ti,ab. 3818

32 (SilverHawk or "Silver Hawk").ti,ab. 118

33 Jetstream.ti,ab. 65

34 (plaque adj3 excis*:).ti,ab. 355

35 (atheroablation or rotational or orbital).ti,ab. 82052

36 (angle adj3 blade*).ti,ab. 158

37 (cut adj3 blade*:).ti,ab. 97

38 (cut adj3 blade*).ti,ab. 97

39 (blade adj3 cathet*).ti,ab. 12

40 EV3.ti,ab. 443

41 or/30-40 86520

42 29 and 41 9677

43 randomized controlled trial/ 485173

44 controlled clinical trial/ 453439

45 random$.ti,ab. 1255139

46 randomization/ 78361

47 intermethod comparison/ 224177

48 placebo.ti,ab. 263135

49 (compare or compared or comparison).ti. 439907

(Continued)

	50 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 1683247 51 (open adj label).ti,ab. 61750 52 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 201070 53 double blind procedure/ 144969 54 parallel group$1.ti,ab. 20900 55 (crossover or cross over).ti,ab. 89795 56 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 271905 57 (assigned or allocated).ti,ab. 320231 58 (controlled adj7 (study or design or trial)).ti,ab. 281124 59 (volunteer or volunteers).ti,ab. 217649 60 trial.ti. 234748 61 or/43-60 3866425 62 42 and 61 1797 63 (2017* or 2018*).em. 2796615 64 62 and 63 278 65 from 64 keep 1-278 278	
CINAHL	S53 S51 AND S52 9 S52 EM 2016 OR EM 2017 334,593 S51 S40 AND S50 72 S50 S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 267,359 S49 MH "Single-Blind Studies" or MH "Double-Blind Studies" or MH "Triple-Blind Studies" 32,871 S48 MH "Factorial Design" 922 S47 MH "Placebos" 8,375 S46 MH "Clinical Trials" 93,030 S45 TX "multi-centre study" OR "multi-center study" OR "multicentre study" OR "multicenter study" OR "multi-site study" 4,542 S44 TX crossover OR "cross-over" 14,660 S43 AB placebo* 28,580 S42 TX trial* 252,485 S41 TX "latin square" 143 S40 S28 AND S39 293 S39 S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 4,240	20 August 2018: 9 12 August 2019: 31

(Continued)

S38 TX EV3 15

S37 TX blade N3 cathet* 0

S36 TX cut N3 blade* 0

S35 TX angle N3 blade* 0

S34 TX atheroablation or rotational or orbital 4,010

S33 TX plaque N3 excis* 0

S32 TX Jetstream 3

S31 TX SilverHawk or "Silver Hawk" 10

S30 TX atherect* 317

S29 (MH "Atherectomy") 82

S28 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 75,396

S27 TX dysvascular* 172

S26 TX aort* or iliac or femoral or popliteal or femoro* or fempop* or crural) N3 (obstruct* or occlus*) 583

S25 TX lower N3 extrem* N4 (obstruct* or occlus* or steno* or block* or obliter*) 82

S24 TX limb N4 (obstruct* or occlus* or steno* or block* or obliter*) 198

S23 TX leg N4 (obstruct* or occlus* or steno* or block* or obliter*) 92

S22 TX isch* or CLI 39,707

S21 TX claudic* or hinken* 1,389

S20 TX arteriopathic 10

S19 TX peripheral N3 dis* 9,270

S18 TX peripher* N (occlus* or steno* or obstuct* or lesio* or block* or obliter*) 10

S17 TX veno* N (occlus* or steno* or obstuct* or lesio* or block* or obliter*) 11

S16 TX vein* N (occlus* or steno* or obstuct* or lesio* or block* or obliter*) 7

S15 TX vascular N (occlus* or steno* or obstuct* or lesio* or block* or obliter*) 13

S14 TX arter* N (occlus* or steno* or obstuct* or lesio* or block* or obliter* 167

S13 TX atherosclero* or arteriosclero* or PVD or PAOD or PAD 26,503

S12 (MH "Tibial Arteries") 145

S11 (MH "Iliac Artery") 453

S10 (MH "Popliteal Artery") 359

S9 (MH "Femoral Artery") 1,188

S8 (MH "Leg/BS") 450

(Continued)

	S7 (MH "Vascular Diseases") 2,381	
	S6 (MH "Peripheral Vascular Diseases") 0	
	S5 (MH "Ischemia") 3,387	
	S4 (MH "Intermittent Claudication") 841	
	S3 (MH "Arterial Occlusive Diseases") 1,602	
	S2 (MH "Atherosclerosis") 3,372	
	S1 (MH "Arteriosclerosis") 4,820	
AMED	1 ARTERIOSCLEROSIS/ 78	20 August 2018: 0
	2 ATHEROSCLEROSIS/ 223	12 August 2019: 0
	3 Intermittent Claudication/ 75	
	4 ISCHEMIA/ 266	
	5 (atherosclero* or arteriosclero* or PVD or PAOD or PAD).ti,ab. 810	
	6 (arter* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 179	
	7 (vascular adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 44	
	8 (vein* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 4	
	9 (veno* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 29	
	10 (peripher* adj (occlus* or steno* or obstuct* or lesio* or block* or obliter*)).ti,ab. 11	
	11 (peripheral adj3 dis*).ti,ab. 439	
	12 arteriopathic.ti,ab. 1	
	13 (claudic* or hinken*).ti,ab. 150	
	14 (isch* or CLI).ti,ab. 1687	
	15 (leg adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 19	
	16 (limb adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 22	
	17 (lower adj3 extrem* adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. 12	
	18 ((aort* or iliac or femoral or popliteal or femoro* or fempop* or crural) adj3 (obstruct* or occlus*)).ti,ab. 11	
	19 dysvascular*.ti,ab. 58	
	20 or/1-19 3220	
	21 (atheroablation or rotational or orbital).ti,ab. 573	
	22 (angle adj3 blade*).ti,ab. 4	
	23 or/21-22 577	

(Continued)

24 20 and 23 4

25 exp CLINICAL TRIALS/ 3788

26 RANDOM ALLOCATION/ 314

27 DOUBLE BLIND METHOD/ 667

28 Clinical trial.pt. 1212

29 (clinic* adj trial*).tw. 5438

30 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw. 2866

31 PLACEBOS/ 591

32 placebo*.tw. 3132

33 random*.tw. 17749

34 PROSPECTIVE STUDIES/ 1119

35 or/25-34 22789

36 24 and 35 0

WHAT'S NEW

Date	Event	Description
1 October 2019	New search has been performed	New search run. Three new studies included. Six new studies were excluded and 11 new ongoing studies were identified.
1 October 2019	New citation required but conclusions have not changed	New search run. Three new studies included. Six new studies were excluded and 11 new ongoing studies were identified. Review text updated in keeping with current Cochrane standards including addition of 'Summary of findings' tables. No change to conclusions.

HISTORY

Protocol first published: Issue 3, 2007
Review first published: Issue 3, 2014

Date	Event	Description
29 October 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

BW: study selection, assessed trial quality, extracted data, updated the review text
GA: study selection, assessed trial quality, extracted data, updated the review text
RR: reviewed and edited update
RH: reviewed and edited update

CT: reviewed and edited update

DECLARATIONS OF INTEREST

BW: none known
GA: has declared that he has received money from NIHR for an academic clinical fellowship, but this does not cause any conflict of interest with this review.
RR: none known
RH: none known
CT: none known

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Internal sources

- No sources of support supplied

External sources

- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We assessed the quality of the trials using Cochrane's 'Risk of bias' tool (Higgins 2011). We have added 'Summary of findings' tables as part of this update, and used the GRADE approach to assess the certainty of the evidence, as recommended by Cochrane.

We have included additional subgroup analyses between drug-eluting and plain balloon angioplasty' as several RCTs have shown that paclitaxel-coated balloons and stents reduce the rates of TVR and vessel restenosis after lower extremity interventions. A systematic review and meta-analysis by Katsanos 2018 examining these studies has shown that the risk of death after a year was increased in participants treated with paclitaxel-eluting balloons and stents, so we performed subgroup analysis to see if this factor impacted on participants' outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

Acute Coronary Syndrome [mortality]; Angioplasty, Balloon [*methods] [mortality]; Atherectomy [*methods] [mortality]; Cause of Death; Heart Failure [mortality]; Peripheral Arterial Disease [mortality] [*therapy]; Randomized Controlled Trials as Topic; Stents

MeSH check words

Humans