KCE REPORT 221S

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

REVASCULARILZATION FOR LOWER LIMB PERIPHERAL ARTERIAL DISEASE

APPENDIX





KCE REPORT 221S
GOOD CLINICAL PRACTICE

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APPENDICES

1. COMPOSITION OF THE GUIDELINE DEVELOPMENT GROUP

1.1. Composition of the Guideline Development Group

Clinicians	Field of expertise, affiliations
Olivier d'Archambeau	Interventional Radiology, UZA
Inge Fourneau	Vascular Surgery, UZ Leuven
Benedicte Heyndrickx	Cardiac Rehabilitation, UZ Brussel
Philippe Kolh	Cardiovascular Surgery, ULiège
Geert Maleux	Interventional Radiology, UZ Leuven
Serge Motte	Vascular pathology, Erasme ULB
Muriel Sprynger	Cardiology, ULiège
Frank Vermassen	Vascular Surgery, UGent

1.2. Composition of the KCE expert team

KCE member	Specific role
Kristel De Gauqier	Program Director
Joan Vlayen	Principal Investigator
Kirsten Holdt	Scientific research and methodological support

1.3. Researchers involved in the guideline

Subcontractor	Specific role
Katie Jones	NCGC; Project manager
Serena Carville	NCGC; Associate director – project lead
Carlos Sharpin	NCGC; Joint head of information science and research fellow
Maggie Westby	NCGC; Methodological lead
Julie Neilson	NCGC; Senior research fellow

2. SEARCH STRATEGIES

2.1. Search strategy for guidelines

Table 1 – Search results - Guidelines on management of lower limb PAD

Date	07-03-2013	
Search engine	Search terms	Number of hits
GIN database	Peripheral Vascular Diseases (C14.907.617)	21
National Guideline Clearinghouse	arterial occlusive disease*	23
OVID Medline	Arterial Occlusive Diseases/ and (recommendation*.m_titl. or standard*.m_titl. or guideline*.m_titl. or Guideline/ or Practice Guideline/)	110
National Institute for Health and Clinical Excellence (NICE) (www.nice.org.uk)		1
Scottish Intercollegiate Guideline Network (SIGN) (http://www.sign.ac.uk/)		1

After removal of duplicate guidelines, 12 guidelines were selected based on title and abstract and retained for full-text evaluation. Of these, 5 guidelines were excluded for the following reasons:

- Published before 2010 (N=3)
- Out of scope (N=2)

Finally, 7 guidelines were retained for an evaluation of the methodological quality

2.2. Search strategies for other publications (systematic reviews, meta-analyses, individual studies)

2.2.1. Assessment of PAD

2.2.1.1. Protocol

Diagnostic test accuracy

Protocol	
Review question	What is the most clinically effective method of assessment of PAD (intermittent claudication or critical limb ischemia)?
Population	Adults (≥ 18 years old) with PAD including intermittent claudication or Fontaine stage II and critical limb ischemia or Fontaine stage III, IV.
Intervention	Duplex ultrasound (DUS) Magnetic resonance angiography (MRA) Computed tomography angiography (CTA)
Reference standard	Digital subtraction angiography / arteriography (DSA).
Target condition	Lower limb peripheral arterial disease, separately by: Severity (as defined by degree of stenosis) Type of lesion (whole leg, above and below the knee).
Statistical measures	True positive (TP), false positive (FP), false negative (FN), true negative (TN) 2x2 tables Specificity Sensitivity Negative predictive value Positive predictive value Positive likelihood ratio Negative likelihood ratio. Adverse events of the tests will be noted if reported.
Study design	Cross sectional studies and prospective cohort studies.
Search strategy	**The electronic databases to be searched are**: • Medline (OVID interface), Embase, Library of the Cochrane Collaboration • All years
Other terms	
Notes	

Test and treat strategy

Protocol	
Review question	What is the most clinically effective method of assessment of PAD (intermittent claudication or critical limb ischemia)?
Population	Adults (≥ 18 years old) with PAD including intermittent claudication or Fontaine stage II and critical limb ischemia or Fontaine stage III, IV.
Intervention	Duplex ultrasound (DUS) Magnetic resonance angiography (MRA) Computed tomography angiography (CTA)
Comparisons	Interventions compared with each other.
Outcomes	Mortality Amputation rate / amputation free survival Quality of life (all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), HUI (Health Utilities Index), QWB (Quality of Well Being), AQol (Assessment of Quality of Life), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)) Walking distance (all measures) Adverse events Re-intervention rates.
Study design	Randomised trials.
Search strategy	**The electronic databases to be searched are**: • Medline (OVID interface), Embase, Library of the Cochrane Collaboration • All years
Other terms	
Notes	

2.2.1.2. Search strategies per database

Medline

Date	09-09-2013		
Database (name + access ; e.g.: Medline OVID)	Medline (Ovid) (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present)		
Search Strategy (attention, for PubMed, check « Details »)	1	exp Peripheral Vascular Diseases/	43689
	2	exp peripheral arterial disease/	1739
	3	intermittent claudication/	7029
	4	(pvd or pvod or paod or poad).ti,ab,hw.	2411
	5	(claudication or claudicant*).ti,ab,hw.	10984
	6	peripheral vascular disease.ti,ab,hw.	6948
	7	peripheral arter* disease.ti,ab,hw.	7898
	8	peripheral arter* occlusive disease.ti,ab,hw.	1647
	9	critical limb isch?emia.ti,ab.	1999
	10	fontaine stage.ti,ab.	279
	11	or/1-10	63932
	12	letter/	822503
	13	editorial/	346450
	14	news/	158490
	15	exp historical article/	320462
	16	Anecdotes as Topic/	4580
	17	comment/	569094
	18	case report/	1672970
	19	(letter or comment*).ti.	92577
	20	or/12-19	3298642
	21	randomized controlled trial/ or random*.ti,ab.	828112

	22	20 not 21	3281332
	23	animals/ not humans/	3937252
	24	exp Animals, Laboratory/	752968
	25	exp Animal Experimentation/	6365
	26	exp Models, Animal/	431342
	27	exp Rodentia/	2759483
	28	(rat or rats or mouse or mice).ti.	1129049
	29	or/22-28	7845542
	30	11 not 29	50003
	31	exp ultrasonography, doppler, duplex/	20506
	32	exp ultrasonography, doppler,color/	15872
	33	(duplex adj3 (utrasonograph* or ultrasound* or ecograph*)).tw.	3310
	34	exp magnetic resonance angiography/	16858
	35	exp tomography, x-ray computed/	297854
	36	(((comput* adj1 tomograph*) or ct or magnetic or MR*) adj3 (angiograph* or arteriograph*)).tw.	27572
	37	Angiography, Digital Subtraction/	7598
	38	(digital subtraction adj3 (angiograph* or arteriograph*)).tw.	6089
	39	or/31-38	345637
	40	30 and 39	2504
	41	(2012* or 2013*).ed,dc.	2307888
	42	40 and 41	304
	43	limit 40 to (dutch or french or german)	251
	44	42 or 43	544
Note			

Embase

Date	**09-09-2013**		
Database (name + access ; e.g.: Medline OVID)	Embase (Ovid) 1974 to 2013 September 09		
Search Strategy (attention, for PubMed, check « Details »)	1	*peripheral vascular disease/	9504
	2	*artery disease/	5226
	3	*intermittent claudication/	4818
	4	(pvd or pvod or paod or poad).ti,ab.	3310
	5	(claudication or claudicant*).ti,ab.	10122
	6	peripheral vascular disease.ti,ab.	9054
	7	peripheral arter* disease.ti,ab.	9712
	8	peripheral arter* occlusive disease.ti,ab.	2254
	9	critical limb isch?emia.ti,ab.	2912
	10	fontaine stage.ti,ab.	352
	11	or/1-10	42061
	12	letter.pt. or letter/	842185
	13	note.pt.	582797
	14	editorial.pt.	446547
	15	Case report/ or Case study/	1999727
	16	(letter or comment*).ti.	149979
	17	or/12-16	3724161
	18	randomized controlled trial/ or random*.ti,ab.	943783
	19	17 not 18	3695271
	20	animal/ not human/	1405081
	21	Nonhuman/	4123486
	22	exp Animal Experiment/	1715714
	23	exp Experimental animal/	464044

	24	Animal model/	713619
	25	exp Rodent/	2938458
	26	(rat or rats or mouse or mice).ti.	1288842
	27	or/19-26	9914418
	28	11 not 27	35198
	29	Doppler echography/	28996
	30	(duplex adj3 (utrasonograph* or ultrasound* or echograph*)).tw.	4701
	31	magnetic resonance angiography/	22989
	32	computed tomographic angiography/	19622
	33	(((comput* adj1 tomograph*) or ct or magnetic or MR*) adj3 (angiograph* or arteriograph*)).tw.	36985
	34	digital subtraction angiography/	13560
	35	(digital subtraction adj3 (angiograph* or arteriograph*)).tw.	7513
	36	or/29-35	97675
	37	28 and 36	2090
	38	(2012* or 2013*).dd.	2323922
	39	37 and 38	296
	40	limit 37 to (dutch or french or german)	201
	41	39 or 40	489
Note			

Cochrane Library

Date	**09-09-2013**		
Database (name + access ; e.g.: Medline OVID)	The Cochrane Library		
Search Strategy (attention, for PubMed, check « Details »)	#1	MeSH descriptor: [Peripheral Vascular Diseases] explode all trees	2195
	#2	MeSH descriptor: [Peripheral Arterial Disease] explode all trees	107
	#3	MeSH descriptor: [Intermittent Claudication] this term only	725
	#4	(pvd or pvod or paod or poad):ti,ab	215
	#5	(claudication or claudicant*):ti,ab	1123
	#6	peripheral vascular disease:ti,ab	1758
	#7	peripheral arter* disease:ti,ab	2124
	#8	peripheral arter* occlusive disease:ti,ab	648
	#9	(critical limb ischaemia or critical limb ischemia):ti,ab	224
	#10	fontaine stage:ti,ab	185
	#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	5353
	#12	MeSH descriptor: [Ultrasonography, Doppler, Duplex] explode all trees	753
	#13	(duplex near/3 (utrasonograph* or ultrasound* or ecograph*)):ti,ab	240
	#14	MeSH descriptor: [Magnetic Resonance Angiography] explode all trees	350
	#15	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees	3427
	#16	((comput* near/1 tomograph*) near/3 (angiograph* or arteriograph*)):ti,ab	226
	#17	((ct or magnetic or MR*) near/3 (angiograph* or arteriograph*)):ti,ab	501
	#18	MeSH descriptor: [Angiography, Digital Subtraction] this term only	190
	#19	(digital subtraction near/3 (angiograph* or arteriograph*)):ti,ab	183
	#20	#12 or #13 or #14 or #15 or #16 or #17 or #18 or #19	4921
	#21	#11 and #20	188
Note			

2.2.2. Selective versus primary stenting

2.2.2.1. Protocol

Protocol	
Review question	What is the clinical effectiveness of angioplasty with selective stent placement compared to angioplasty with primary stent placement for the treatment of PAD in adults with intermittent claudication or critical limb ischemia?
Population	Adult patients (≥18 years of age) with lower extremity PAD presenting with: (1) intermittent claudication (IC) (i.e. walking-induced pain in the lower limbs caused by diminished circulation) or (2) critical limb ischemia (CLI) (i.e. severely impaired circulation, at imminent risk of limb loss without undergoing revascularization), with a lesion of the following arterial segment: (a) aorto-iliac (b) femoro-popliteal (c) infra-geniculate. (stratified analysis)
Intervention	Angioplasty with selective stent placement (all types of stents). Studies should indicate that bailout stents were used in the selective stenting group in the event of angioplasty failure.
Comparison	Angioplasty with primary stent placement (all types of stent)
Outcomes	• Mortality • Amputation rate / amputation free survival • Quality of life (including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), HUI (Health Utilities Index), QWB (Quality of Well Being), AQol (Assessment of Quality of Life), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)) • Walking distance (all measures, n.b. Specify if pain free walking distance) • Peri-procedural complications • Pain (if reported on a pain scale (e.g. VAS) or as a QOL subscale separate from overall score (e.g. SF-36) • Wound healing (defined as proportion of people with complete wound healing or time to complete healing) • Adverse events • Re-intervention rates.

Study design	• High quality systematic reviews of RCTs and/or RCTs only. • Cochrane reviews will be included if they match our inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions)
Exclusion	• Studies with another population, intervention, comparison or outcome. • Quasi-randomized and non-randomized studies • Non-English, non-French, non-Dutch, non-German language papers
Search strategy	**The electronic databases to be searched are**: • Medline (OVID interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	**How will individual PICO characteristics be combined across studies in a meta-analysis (for intervention reviews)** • Minimum duration of treatment = no minimum. • Minimum follow up = no minimum. • Minimum total sample size = no minimum. Use available case analysis for dealing with missing data if there is a 10% differential or higher between the groups or if the missing data is higher than the event rate, if cannot work out the available case analysis will take the author's data.
Analysis	**The following groups will be considered separately if data are present:** • Unit of analysis – patients and limb/lesion • Intermittent claudication and critical limb ischemia will be analysed separately, Mixed populations will be analysed with the intermittent claudication group as the majority of patients are likely to fall into this category. • The following arterial segments will be analysed separately: aorta-illiac, femoro-popliteal and infra-geniculate

2.2.2.2. Search strategies per database

Medline

Date	**11-09-2013**		
Database (name + access ; e.g.: Medline OVID)	Medline (Ovid) (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present)		
Search Strategy (attention, for PubMed, check « Details »)	1	exp Peripheral Vascular Diseases/	43713
	2	exp peripheral arterial disease/	1752
	3	intermittent claudication/	7032
	4	(pvd or pvod or paod or poad).ti,ab,hw.	2413
	5	(claudication or claudicant*).ti,ab,hw.	10987
	6	peripheral vascular disease.ti,ab,hw.	6948
	7	peripheral arter* disease.ti,ab,hw.	7915
	8	peripheral arter* occlusive disease.ti,ab,hw.	1647
	9	critical limb isch?emia.ti,ab.	2003
	10	fontaine stage.ti,ab.	279
	11	or/1-10	63962
	12	letter/	822698
	13	editorial/	346597
	14	news/	158568
	15	exp historical article/	320548
	16	Anecdotes as Topic/	4580
	17	comment/	569309
	18	case report/	1673661
	19	(letter or comment*).ti.	92594
	20	or/12-19	3299835
	21	randomized controlled trial/ or random*.ti,ab.	828536
	22	20 not 21	3282519
	23	animals/ not humans/	3938854
	24	exp Animals, Laboratory/	753350

25 exp Animal Experimentation/ 6373
26 exp Models, Animal/ 431718
27 exp Rodentia/ 2760829
28 (rat or rats or mouse or mice).ti. 1129205
29 or/22-28 7848509
30 11 not 29 50025
31 Meta-Analysis/ 50547
32 Meta-Analysis as Topic/14012
33 (meta analy* or metanaly* or metaanaly*).ti,ab. 63883
34 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. 73859
35 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. 29430
36 (search strategy or search criteria or systematic search or study selection or data extraction).ab. 34202
37 (search* adj4 literature).ab. 27269
38 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. 96139
39 cochrane.jw. 18135
40 or/31-39 206989
41 randomized controlled trial.pt. 385636
42 controlled clinical trial.pt. 89192
43 randomi#ed.ab. 365924
44 placebo.ab. 161877
45 drug therapy.fs. 1751469
46 randomly.ab. 212829
47 trial.ab. 316698
48 groups.ab. 1353924
49 or/41-48 3396167
50 Clinical Trials as topic.sh. 174368
51 trial.ti. 129799
52 or/41-44,46,50-51 946503
53 40 or 52 1089729
54 exp angioplasty/ or exp angioplasty, balloon/ or exp angioplasty, laser/ or exp atherectomy/ or exp angioplasty, balloon, laser-assisted/ or exp catheterization, peripheral/ 63634

	55	(Angioplast* or atherectom*).ti,ab.	37849		
	56	(Endoluminal adj1 repair*).ti,ab.	210		
	57	(Balloon adj1 (catheter* or dilatation*)).ti,ab.	9127		
	58	(Dilatation* adj2 (transluminal or arter*)).ti,ab.	1378		
	59	(Catheter* adj2 peripheral).ti,ab.	973		
	60	or/54-59	84063		
	61	30 and 60 and 53	617		
	62	limit 61 to (dutch or english or french or german)	604		
Note	The same search was used to cover 2 questions: • What is the clinical effectiveness of angioplasty with selective stent placement compared to angioplasty with primary stent placement for the treatment of PAD in adults with intermittent claudication or critical limb ischemia? • What is the clinical effectiveness of drug-coated balloon angioplasty for the treatment of PAD in adults with critical limb ischemia?				
Embase					
Date	**11-09-2013**				
Database (name + access ; e.g.: Medline OVID)	Embase (Ovid) 1974 to 2013 September 11				
Search Strategy (attention, for PubMed, check « Details »)	1	*peripheral vascular disease/	9506		
	2	*artery disease/	5231		
	3	*intermittent claudication/	4818		
	4	(pvd or pvod or paod or poad).ti,ab.	3314		
	5	(claudication or claudicant*).ti,ab.	10128		
	6	peripheral vascular disease.ti,ab.	9064		
	7	peripheral arter* disease.ti,ab.	9733		
	8	peripheral arter* occlusive disease.ti,ab.	2256		
	9	critical limb isch?emia.ti,ab.	2916		
	10	fontaine stage.ti,ab.	352		
	11	or/1-10	42105		
	12	letter.pt. or letter/	842997		

13 note.pt. 583401
14 editorial.pt. 446953
15 Case report/ or Case study/ 2001078
16 (letter or comment*).ti. 150078
17 or/12-16 3727098
18 randomized controlled trial/ or random*.ti,ab. 945100
19 17 not 18 3698182
20 animal/ not human/ 1405283
21 Nonhuman/ 4128297
22 exp Animal Experiment/ 1717423
23 exp Experimental animal/ 465006
24 Animal model/ 715092
25 exp Rodent/ 2942926
26 (rat or rats or mouse or mice).ti. 1290496
27 or/19-26 9924812
28 11 not 27 35227
29 systematic review/ 64024
30 meta-analysis/ 75607
31 (meta analy* or metanaly* or metaanaly*).ti,ab. 74382
32 ((systematic or evidence) adj2 (review* or overview*)).ti,ab. 79342
33 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. 29827
34 (search strategy or search criteria or systematic search or study selection or data extraction).ab. 30680
35 (search* adj4 literature).ab. 31654
36 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. 98690
37 ((pool* or combined) adj2 (data or trials or studies or results)).ab. 38151
38 cochrane.jw. 12633
39 or/29-38 277759
40 random*.ti,ab. 856059
41 factorial*.ti,ab. 22209
42 (crossover* or cross over*).ti,ab. 70187
43 ((doubl* or singl*) adj blind*).ti,ab. 159291

	44	(assign* or allocat* or volunteer* or placebo*).ti,ab. 647821
	45	crossover procedure/ 38413
	46	single blind procedure/ 18230
	47	randomized controlled trial/ 358223
	48	double blind procedure/ 120036
	49	or/40-48 1398109
	50	39 or 49 1593429
	51	exp percuteneous transluminal angioplasty/ or exp angioplasty/ or exp laser angioplasty/ 66394
	52	(Angioplast* or atherectom*).ti,ab. 48530
	53	(Endoluminal adj1 repair).ti,ab. 247
	54	(Balloon adj1 (catheter* or dilatation*)).ti,ab. 12133
	55	(Catheter* adj2 peripheral).ti,ab. 1250
	56	(Dilatation* adj2 (transluminal or arter*)).ti,ab. 1745
	57	or/51-56 90632
	58	28 and 57 and 50 607
	59	limit 58 to (dutch or english or french or german) 590
Note	The same search was used to cover 2 questions: • What is the clinical effectiveness of angioplasty with selective stent placement compared to angioplasty with primary stent placement for the treatment of PAD in adults with intermittent claudication or critical limb ischemia? • What is the clinical effectiveness of drug-coated balloon angioplasty for the treatment of PAD in adults with critical limb ischemia?	

Cochrane Library

Date	**11-09-2013**		
Database (name + access ; e.g.: Medline OVID)	The Cochrane Library		
Search Strategy (attention, for PubMed, check « Details »)	#1	MeSH descriptor: [Peripheral Vascular Diseases] explode all trees	2195
	#2	MeSH descriptor: [Peripheral Arterial Disease] explode all trees	107
	#3	MeSH descriptor: [Intermittent Claudication] this term only	725
	#4	(pvd or pvod or paod or poad):ti,ab	215
	#5	(claudication or claudicant*):ti,ab	1123
	#6	peripheral vascular disease:ti,ab	1759
	#7	peripheral arter* disease:ti,ab	2125
	#8	peripheral arter* occlusive disease:ti,ab	649
	#9	(critical limb ischaemia or critical limb ischemia):ti,ab	224
	#10	fontaine stage:ti,ab	185
	#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	5354
	#12	[mh angioplasty]	4239
	#13	MeSH descriptor: [Catheterization, Peripheral] explode all trees	654
	#14	(Angioplast* or atherectom*):ti,ab	3281
	#15	(Endoluminal near repair*):ti,ab	6
	#16	(Balloon near (catheter* or dilatation*)):ti,ab	416
	#17	(Dilatation* near/2 (transluminal or arter*)):ti,ab	93
	#18	(Catheter* near/2 peripheral):ti,ab	137
	#19	{or #12-#18}	6638
	#20	#11 and #19	386
Note	The same search was used to cover 2 questions: • What is the clinical effectiveness of angioplasty with selective stent placement compared to angioplasty with primary stent placement for the treatment of PAD in adults with intermittent claudication or critical limb ischemia? • What is the clinical effectiveness of drug-coated balloon angioplasty for the treatment of PAD in adults with critical limb ischemia?		

2.2.3. Bare metal versus drug eluting stents

2.2.3.1. Protocol

Protocol	
Review question	What is the clinical effectiveness of bare metal stents compared to drug eluting stents for the treatment of peripheral arterial disease (PAD) in adults with intermittent claudication or critical limb ischemia?
Population	Adult patients (≥18 years of age) with lower extremity PAD presenting with: (1) Intermittent claudication (IC) (i.e. walking-induced pain in the lower limbs caused by diminished circulation) or (2) Critical limb ischemia (CLI) (i.e. severely impaired circulation, at imminent risk of limb loss without undergoing revascularisation), With a lesion of the following arterial segment: (a) Aorto-iliac (b) Femoro-popliteal (c) Infra-geniculate (stratified analysis).
Intervention	Bare metal stents
Comparison	Drug eluting stents
Outcomes	• Mortality • Amputation rate / amputation free survival • Quality of life (including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)) • Walking distance (all measures n.b. specify if pain free wlaking distance) • Peri-procedural complications • Pain (if reported on a pain scale (e.g. VAS) or as a QOL subscale sparate from overall score (e.g. SF-36) • Wound healing (defined as proportion of people with complete wound healing or time to complete healing) • Adverse events • Re-intervention rates
Study design	• RCT excluding quasi-randomized trials.
Exclusion	• Studies with another population, intervention, comparison or outcome.

	• Quasi-randomized and non-randomized studies • Non-English, non-French, non-Dutch, non-German language papers
Search strategy	**The electronic databases to be searched are**: • Medline (OVID interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	• Minimum duration of treatment = no minimum. • Minimum follow up = no minimum. • Minimum total sample size = no minimum.
Analysis	**The following groups will be considered separately if data are present:** • Unit of analysis – patients, limb/lesion • Intermittent claudication and critical limb ischemia will be analyzed separately, Mixed populations will be analyzed with the intermittent claudication group as the majority of patients are likely to fall into this category. • The following arterial segments will be analyzed separately: aorta-illiac, femoro-popliteal and infra-geniculate

2.2.3.2. Search strategies per database

Medline

Date	**11-09-2013**		
Database (name + access ; e.g.: Medline OVID)	Medline (Ovid) (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present)		
Search Strategy (attention, for PubMed, check « Details »)	1	exp Peripheral Vascular Diseases/	43713
	2	exp peripheral arterial disease/	1752
	3	intermittent claudication/	7032
	4	(pvd or pvod or paod or poad).ti,ab,hw.	2413
	5	(claudication or claudicant*).ti,ab,hw.	10987
	6	peripheral vascular disease.ti,ab,hw.	6948
	7	peripheral arter* disease.ti,ab,hw.	7915
	8	peripheral arter* occlusive disease.ti,ab,hw.	1647
	9	critical limb isch?emia.ti,ab.	2003
	10	fontaine stage.ti,ab.	279

11	or/1-10	63962
12	letter/	822698
13	editorial/	346597
14	news/	158568
15	exp historical article/	320548
16	Anecdotes as Topic/	4580
17	comment/	569309
18	case report/	1673661
19	(letter or comment*).ti.	92594
20	or/12-19	3299835
21	randomized controlled trial/ or random*.ti,ab.	828536
22	20 not 21	3282519
23	animals/ not humans/	3938854
24	exp Animals, Laboratory/	753350
25	exp Animal Experimentation/	6373
26	exp Models, Animal/	431718
27	exp Rodentia/	2760829
28	(rat or rats or mouse or mice).ti.	1129205
29	or/22-28	7848509
30	11 not 29	50025
31	randomized controlled trial.pt.	385636
32	controlled clinical trial.pt.	89192
33	randomi#ed.ab.	365924
34	placebo.ab.	161877
35	drug therapy.fs.	1751469
36	randomly.ab.	212829
37	trial.ab.	316698
38	groups.ab.	1353924
39	or/31-38	3396167
40	Clinical Trials as topic.sh.	174368
41	trial.ti.	129799
42	or/31-34,36,40-41	946503

43	Meta-Analysis/ 50547
44	Meta-Analysis as Topic/14012
45	(meta analy* or metanaly* or metaanaly*).ti,ab. 63883
46	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. 73859
47	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. 29430
48	(search strategy or search criteria or systematic search or study selection or data extraction).ab. 34202
49	(search* adj4 literature).ab. 27269
50	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. 96139
51	cochrane.jw. 18135
52	or/43-51 206989
53	42 or 52 1089729
54	Stent*.ti,ab,hw. 72373
55	Restenosis.ti,ab. 17288
56	Stenos*.ti,ab. 117029
57	(Pathologic * adj constriction*).ti,ab. 19765
58	Stricture*.ti,ab. 20459
59	Pathologic constriction/ 19190
60	or/54-59 222906
61	30 and 60 and 53 617
62	limit 61 to (dutch or english or french or german) 605

Note

Embase

Date	**11-09-2013**		
Database (name + access ; e.g.: Medline OVID)	Embase (Ovid) 1974 to 2013 September 11		
Search Strategy (attention, for PubMed, check « Details »)	1	*peripheral vascular disease/	9506
	2	*artery disease/	5231
	3	*intermittent claudication/	4818
	4	(pvd or pvod or paod or poad).ti,ab.	3314
	5	(claudication or claudicant*).ti,ab.	10128
	6	peripheral vascular disease.ti,ab.	9064
	7	peripheral arter* disease.ti,ab.	9733
	8	peripheral arter* occlusive disease.ti,ab.	2256
	9	critical limb isch?emia.ti,ab.	2916
	10	fontaine stage.ti,ab.	352
	11	or/1-10	42105
	12	letter.pt. or letter/	842997
	13	note.pt.	583401
	14	editorial.pt.	446953
	15	Case report/ or Case study/	2001078
	16	(letter or comment*).ti.	150078
	17	or/12-16	3727098
	18	randomized controlled trial/ or random*.ti,ab.	945100
	19	17 not 18	3698182
	20	animal/ not human/	1405283
	21	Nonhuman/	4128297
	22	exp Animal Experiment/	1717423
	23	exp Experimental animal/	465006
	24	Animal model/	715092
	25	exp Rodent/	2942926
	26	(rat or rats or mouse or mice).ti.	1290496

27	or/19-26	9924812
28	11 not 27	35227
29	random*.ti,ab.	856059
30	factorial*.ti,ab.	22209
31	(crossover* or cross over*).ti,ab.	70187
32	((doubl* or singl*) adj blind*).ti,ab.	159291
33	(assign* or allocat* or volunteer* or placebo*).ti,ab.	647821
34	crossover procedure/	38413
35	single blind procedure/	18230
36	randomized controlled trial/	358223
37	double blind procedure/	120036
38	or/29-37	1398109
39	systematic review/	64024
40	meta-analysis/	75607
41	(meta analy* or metanaly* or metaanaly*).ti,ab.	74382
42	((systematic or evidence) adj2 (review* or overview*)).ti,ab.	79342
43	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	29827
44	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	30680
45	(search* adj4 literature).ab.	31654
46	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	98690
47	((pool* or combined) adj2 (data or trials or studies or results)).ab.	38151
48	cochrane.jw.	12633
49	or/39-48	277759
50	38 or 49	1593429
51	Stent*.ti,ab,hw.	112303
52	exp "Stenosis, Occlusion and obstruction"/ or exp stenosis/	340561
53	(Restenosis or stenos?s).ti,ab.	169117
54	(Pathologic * adj constriction*).ti,ab.	23229
55	Stricture*.ti,ab.	28287
56	or/51-55	498816
57	28 and 56 and 50	986

	58	limit 57 to (dutch or english or french or german)	964
Note			
Cochrane Library			
Date	**11-09-2013**		
Database (name + access ; e.g.: Medline OVID)	The Cochrane Library		
Search Strategy (attention, for PubMed, check « Details »)	#1	MeSH descriptor: [Peripheral Vascular Diseases] explode all trees	2195
	#2	MeSH descriptor: [Peripheral Arterial Disease] explode all trees	107
	#3	MeSH descriptor: [Intermittent Claudication] this term only	725
	#4	(pvd or pvod or paod or poad):ti,ab	214
	#5	(claudication or claudicant*):ti,ab	1123
	#6	peripheral vascular disease:ti,ab	1759
	#7	peripheral arter* disease:ti,ab	2125
	#8	peripheral arter* occlusive disease:ti,ab	649
	#9	(critical limb ischaemia or critical limb ischemia):ti,ab	224
	#10	fontaine stage:ti,ab	185
	#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	5354
	#12	Stent*:ti,ab,kw	4626
	#13	Restenosis:ti,ab	1600
	#14	Stenos*:ti,ab	3684
	#15	(Pathologic * next constriction*):ti,ab	1
	#16	Stricture*:ti,ab	533
	#17	[mh ^"Pathologic constriction"]	320
	#18	{or #12-#17}	8448
	#19	#11 and #18	326
Note			

2.2.4. Autologous vein versus prosthetic bypass

2.2.4.1. Protocol

Protocol	
Review question	What is the clinical effectiveness of autologous vein versus prosthetic bypass for the treatment of PAD in adults with intermittent claudication?
Population	Adult patients (≥ 18 years of age) with lower extremity PAD presenting with intermittent claudication (i.e. walking-induced pain in the lower limbs caused by diminished circulation) with a femoro-popliteal lesion.
Intervention	Autologous vein
Comparison	Prosthetic bypass
Outcomes	• Mortality • Amputation rate / amputation free survival • Quality of life (including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)) • Walking distance (all measures n.b. specify if pain free walking distance) • Peri-procedural complications • Pain (if reported on a pain scale (e.g. VAS) or as a QOL subscale separate from overall score (e.g. SF-36) • Wound healing (defined as proportion of people with complete wound healing or time to complete healing) • Adverse events • Re-intervention rates.
Study design	• RCT excluding quasi-randomized trials.
Exclusion	• Studies with another population, intervention, comparison or outcome. • Quasi-randomized and non-randomized studies • Non-English, non-French, non-Dutch, non-German language papers
Search strategy	**The electronic databases to be searched are**: • Medline (OVID interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	• Minimum duration of treatment = no minimum.

	• Minimum follow up = no minimum. • Minimum total sample size = no minimum.
Analysis	**The following groups will be considered separately if data are present:** • Unit of analysis – patients, limb/lesion • Mixed populations of intermittent claudication and critical limb ischemia will be analyzed with the intermittent claudication group as the majority of patients are likely to fall into this category.

2.2.4.2. Search strategies per database

Medline

Date	**12-09-2013**
Database **(name + access ; e.g.: Medline OVID)**	Medline (Ovid) (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present)
Search Strategy **(attention, for PubMed, check « Details »)**	1. exp Peripheral Vascular Diseases/ 2. exp peripheral arterial disease/ 3. intermittent claudication/ 4. (pvd or pvod or paod or poad).ti,ab,hw. 5. (claudication or claudicant*).ti,ab,hw. 6. peripheral vascular disease.ti,ab,hw. 7. peripheral arter* disease.ti,ab,hw. 8. peripheral arter* occlusive disease.ti,ab,hw. 9. critical limb isch?emia.ti,ab. 10. fontaine stage.ti,ab. 11. or/1-10 12. letter/ 13. editorial/ 14. news/ 15. exp historical article/ 16. Anecdotes as Topic/

17. comment/
18. case report/
19. (letter or comment*).ti.
20. or/12-19
21. randomized controlled trial/ or random*.ti,ab.
22. 20 not 21
23. animals/ not humans/
24. exp Animals, Laboratory/
25. exp Animal Experimentation/
26. exp Models, Animal/
27. exp Rodentia/
28. (rat or rats or mouse or mice).ti.
29. or/22-28
30. 11 not 29
31. exp angioplasty/ or exp angioplasty, balloon/ or exp angioplasty, laser/ or exp atherectomy/ or exp angioplasty, balloon, laser-assisted/ or exp catheterization, peripheral/
32. (Angioplast* or atherectom*).ti,ab.
33. (Endoluminal adj1 repair*).ti,ab.
34. (Balloon adj1 (catheter* or dilatation*)).ti,ab.
35. (Dilatation* adj2 (transluminal or arter*)).ti,ab.
36. (Catheter* adj2 peripheral).ti,ab.
37. Stent*.ti,ab,hw.
38. or/31-37
39. Vascular surgical procedures/
40. exp surgical procedures, operative/
41. Su.fs.
42. Surg*.ti,ab,hw.
43. Graft*.ti,ab,hw.
44. Bypass*.ti,ab,hw.
45. or/39-44
46. 38 or 45
47. randomized controlled trial.pt.

48. controlled clinical trial.pt.
49. randomi#ed.ab.
50. placebo.ab.
51. randomly.ab.
52. Clinical Trials as topic.sh.
53. trial.ti.
54. or/47-53
55. Meta-Analysis/
56. Meta-Analysis as Topic/
57. (meta analy* or metanaly* or metaanaly*).ti,ab.
58. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
59. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
60. (search strategy or search criteria or systematic search or study selection or data extraction).ab.
61. (search* adj4 literature).ab.
62. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
63. cochrane.jw.
64. or/55-63
65. 54 or 64
66. 30 and 46 and 64
67. limit 66 to (dutch or english or french or german)

Note

Embase

Date	**12-09-2013**
Database (name + access ; e.g.: Medline OVID)	Embase (Ovid) Embase 1980 to 2013 Week 36
Search Strategy (attention, for PubMed, check « Details »)	1. *peripheral vascular disease/ 2. *artery disease/ 3. *intermittent claudication/ 4. (pvd or pvod or paod or poad).ti,ab. 5. (claudication or claudicant*).ti,ab. 6. peripheral vascular disease.ti,ab. 7. peripheral arter* disease.ti,ab. 8. peripheral arter* occlusive disease.ti,ab. 9. critical limb isch?emia.ti,ab. 10. fontaine stage.ti,ab. 11. or/1-10 12. letter.pt. or letter/ 13. note.pt. 14. editorial.pt. 15. Case report/ or Case study/ 16. (letter or comment*).ti. 17. or/12-16 18. randomized controlled trial/ or random*.ti,ab. 19. 17 not 18 20. animal/ not human/ 21. Nonhuman/ 22. exp Animal Experiment/ 23. exp Experimental animal/ 24. Animal model/ 25. exp Rodent/ 26. (rat or rats or mouse or mice).ti.

27.	or/19-26
28.	11 not 27
29.	exp percuteneous transluminal angioplasty/ or exp angioplasty/ or exp laser angioplasty/
30.	(Angioplast* or atherectom*).ti,ab.
31.	(Endoluminal adj1 repair).ti,ab.
32.	(Balloon adj1 (catheter* or dilatation*)).ti,ab.
33.	(Catheter* adj2 peripheral).ti,ab.
34.	(Dilatation* adj2 (transluminal or arter*)).ti,ab.
35.	Stent*.ti,ab,hw.
36.	or/29-35
37.	exp vascular surgery/
38.	Su.fs.
39.	exp surgery/
40.	Surg*.ti,ab,hw.
41.	Graft*.ti,ab,hw.
42.	Bypass*.ti,ab,hw.
43.	or/37-42
44.	36 or 43
45.	random*.ti,ab.
46.	factorial*.ti,ab.
47.	(crossover* or cross over*).ti,ab.
48.	((doubl* or singl*) adj blind*).ti,ab.
49.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
50.	crossover procedure/
51.	single blind procedure/
52.	randomized controlled trial/
53.	double blind procedure/
54.	or/45-53
55.	systematic review/
56.	meta-analysis/
57.	(meta analy* or metanaly* or metaanaly*).ti,ab.
58.	((systematic or evidence) adj2 (review* or overview*)).ti,ab.

	59. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. 60. (search strategy or search criteria or systematic search or study selection or data extraction).ab. 61. (search* adj4 literature).ab. 62. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. 63. ((pool* or combined) adj2 (data or trials or studies or results)).ab. 64. cochrane.jw. 65. or/55-64 66. 54 or 65 67. 28 and 44 and 66 68. limit 67 to (dutch or english or french or german)
Note	
Cochrane Library	
Date	**12-09-2013**
Database (name + access ; e.g.: Medline OVID)	Cochrane Library (Wiley)
Search Strategy (attention, for PubMed, check « Details »)	#1 MeSH descriptor: [Peripheral Vascular Diseases] explode all trees #2 MeSH descriptor: [Peripheral Arterial Disease] explode all trees #3 MeSH descriptor: [Intermittent Claudication] this term only #4 (pvd or pvod or paod or poad):ti,ab #5 (claudication or claudicant*):ti,ab #6 peripheral vascular disease:ti,ab #7 peripheral arter* disease:ti,ab #8 peripheral arter* occlusive disease:ti,ab #9 (critical limb ischaemia or critical limb ischemia):ti,ab #10 fontaine stage:ti,ab #11 {or #1-#10} #12 (angioplast* or atherectom* or endoluminal repair*):ti,ab #13 (balloon near (catheter* or dilatation*)):ti,ab

	#14 (dilatation* near/2 (transluminal or arter*)):ti,ab #15 (catheter* near/2 peripheral):ti,ab #16 (surg* or graft* or bypass* or stent*):ti,ab,kw #17 Any MeSH descriptor with qualifier(s): [Surgery - SU] #18 [mh angioplasty] #19 [mh "angioplasty, balloon"] #20 [mh "angioplasty, laser"] #21 [mh atherectomy] #22 [mh "angioplasty, balloon, laser-assisted"] #23 [mh "catheterization, peripheral"] #24 [mh "surgical procedures, operative"] #25 [mh "vascular surgical procedures"] #26 {or #12-#25} #27 #11 and #26
Note	

2.2.5. Drug-coated balloon angioplasty

2.2.5.1. Protocol

Protocol	
Review question	What is the clinical effectiveness of drug-coated balloon angioplasty for the treatment of PAD in adults with peripheral arterial disease?
Population	Adult patients (≥18 years of age) with lower extremity PAD presenting with: (1) intermittent claudication (IC) (i.e. walking-induced pain in the lower limbs caused by diminished circulation) or (2) critical limb ischemia (CLI) (i.e. severely impaired circulation, at imminent risk of limb loss without undergoing revascularization), with a lesion of the following arterial segment: (a) aorto-iliac (b) femoro-popliteal (c) infra-geniculate. (stratified analysis)
Intervention	Drug coated balloons

Comparison	Any other endovascular revascularization intervention
Outcomes	Critical: • All-cause mortality • Amputation rate / amputation free survival • Quality of life (including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)) • Re-intervention rate • Adverse events • Peri-procedural complications • Pain (if reported on a pain scale (e.g. VAS) or as a QOL subscale separate from overall score (e.g. SF-36) and pain-free walking distance). • Wound healing (defined as proportion of people with complete wound healing or time to complete healing).
Study design	• RCT excluding quasi-randomized trials.
Exclusion	• Studies with another population, intervention, comparison or outcome. • Quasi-randomized and non-randomized studies • Non-English, non-French, non-Dutch, non-German language papers
Search strategy	**The electronic databases to be searched are**: • Medline (OVID interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	• Minimum duration of treatment = no minimum. • Minimum follow up = no minimum. • Minimum total sample size = no minimum.
Analysis	**The following groups will be considered separately if data are present:** • Unit of analysis – patients, limb/lesion • Mixed populations of intermittent claudication and critical limb ischemia will be analyzed with the intermittent claudication group as the majority of patients are likely to fall into this category.

2.2.5.2. Search strategies per database

Medline

Date	**11-09-2013**
Database (name + access ; e.g.: Medline OVID)	Medline (Ovid) (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present)
Search Strategy (attention, for PubMed, check « Details »)	1 exp Peripheral Vascular Diseases/ 43713 2 exp peripheral arterial disease/ 1752 3 intermittent claudication/ 7032 4 (pvd or pvod or paod or poad).ti,ab,hw. 2413 5 (claudication or claudicant*).ti,ab,hw. 10987 6 peripheral vascular disease.ti,ab,hw. 6948 7 peripheral arter* disease.ti,ab,hw. 7915 8 peripheral arter* occlusive disease.ti,ab,hw. 1647 9 critical limb isch?emia.ti,ab. 2003 10 fontaine stage.ti,ab. 279 11 or/1-10 63962 12 letter/ 822698 13 editorial/ 346597 14 news/ 158568 15 exp historical article/ 320548 16 Anecdotes as Topic/ 4580 17 comment/ 569309 18 case report/ 1673661 19 (letter or comment*).ti. 92594 20 or/12-19 3299835 21 randomized controlled trial/ or random*.ti,ab. 828536 22 20 not 21 3282519

23	animals/ not humans/	3938854
24	exp Animals, Laboratory/	753350
25	exp Animal Experimentation/	6373
26	exp Models, Animal/	431718
27	exp Rodentia/	2760829
28	(rat or rats or mouse or mice).ti.	1129205
29	or/22-28	7848509
30	11 not 29	50025
31	Meta-Analysis/	50547
32	Meta-Analysis as Topic/	14012
33	(meta analy* or metanaly* or metaanaly*).ti,ab.	63883
34	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.	73859
35	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	29430
36	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	34202
37	(search* adj4 literature).ab.	27269
38	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	96139
39	cochrane.jw.	18135
40	or/31-39	206989
41	randomized controlled trial.pt.	385636
42	controlled clinical trial.pt.	89192
43	randomi#ed.ab.	365924
44	placebo.ab.	161877
45	drug therapy.fs.	1751469
46	randomly.ab.	212829
47	trial.ab.	316698
48	groups.ab.	1353924
49	or/41-48	3396167
50	Clinical Trials as topic.sh.	174368
51	trial.ti.	129799

	52 or/41-44,46,50-51 946503 53 40 or 52 1089729 54 exp angioplasty/ or exp angioplasty, balloon/ or exp angioplasty, laser/ or exp atherectomy/ or exp angioplasty, balloon, laser-assisted/ or exp catheterization, peripheral/ 63634 55 (Angioplast* or atherectom*).ti,ab. 37849 56 (Endoluminal adj1 repair*).ti,ab. 210 57 (Balloon adj1 (catheter* or dilatation*)).ti,ab. 9127 58 (Dilatation* adj2 (transluminal or arter*)).ti,ab. 1378 59 (Catheter* adj2 peripheral).ti,ab. 973 60 or/54-59 84063 61 30 and 60 and 53 617 62 limit 61 to (dutch or english or french or german) 604
Note	The same search was used to cover 2 questions: • What is the clinical effectiveness of angioplasty with selective stent placement compared to angioplasty with primary stent placement for the treatment of PAD in adults with intermittent claudication or critical limb ischemia? • What is the clinical effectiveness of drug-coated balloon angioplasty for the treatment of PAD in adults with critical limb ischemia?

Embase

Date	**11-09-2013**
Database (name + access ; e.g.: Medline OVID)	Embase (Ovid) 1974 to 2013 September 11
Search Strategy (attention, for PubMed, check « Details »)	1 *peripheral vascular disease/ 9506 2 *artery disease/ 5231 3 *intermittent claudication/ 4818 4 (pvd or pvod or paod or poad).ti,ab. 3314 5 (claudication or claudicant*).ti,ab. 10128 6 peripheral vascular disease.ti,ab. 9064 7 peripheral arter* disease.ti,ab. 9733

8	peripheral arter* occlusive disease.ti,ab.	2256
9	critical limb isch?emia.ti,ab.	2916
10	fontaine stage.ti,ab.	352
11	or/1-10	42105
12	letter.pt. or letter/	842997
13	note.pt.	583401
14	editorial.pt.	446953
15	Case report/ or Case study/	2001078
16	(letter or comment*).ti.	150078
17	or/12-16	3727098
18	randomized controlled trial/ or random*.ti,ab.	945100
19	17 not 18	3698182
20	animal/ not human/	1405283
21	Nonhuman/	4128297
22	exp Animal Experiment/	1717423
23	exp Experimental animal/	465006
24	Animal model/	715092
25	exp Rodent/	2942926
26	(rat or rats or mouse or mice).ti.	1290496
27	or/19-26	9924812
28	11 not 27	35227
29	systematic review/	64024
30	meta-analysis/	75607
31	(meta analy* or metanaly* or metaanaly*).ti,ab.	74382
32	((systematic or evidence) adj2 (review* or overview*)).ti,ab.	79342
33	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	29827
34	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	30680
35	(search* adj4 literature).ab.	31654
36	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	98690

	37	((pool* or combined) adj2 (data or trials or studies or results)).ab.	38151
	38	cochrane.jw.	12633
	39	or/29-38	277759
	40	random*.ti,ab.	856059
	41	factorial*.ti,ab.	22209
	42	(crossover* or cross over*).ti,ab.	70187
	43	((doubl* or singl*) adj blind*).ti,ab.	159291
	44	(assign* or allocat* or volunteer* or placebo*).ti,ab.	647821
	45	crossover procedure/	38413
	46	single blind procedure/	18230
	47	randomized controlled trial/	358223
	48	double blind procedure/	120036
	49	or/40-48	1398109
	50	39 or 49	1593429
	51	exp percuteneous transluminal angioplasty/ or exp angioplasty/ or exp laser angioplasty/	66394
	52	(Angioplast* or atherectom*).ti,ab.	48530
	53	(Endoluminal adj1 repair).ti,ab.	247
	54	(Balloon adj1 (catheter* or dilatation*)).ti,ab.	12133
	55	(Catheter* adj2 peripheral).ti,ab.	1250
	56	(Dilatation* adj2 (transluminal or arter*)).ti,ab.	1745
	57	or/51-56	90632
	58	28 and 57 and 50	607
	59	limit 58 to (dutch or english or french or german)	590
Note	The same search was used to cover 2 questions: • What is the clinical effectiveness of angioplasty with selective stent placement compared to angioplasty with primary stent placement for the treatment of PAD in adults with intermittent claudication or critical limb ischemia? • What is the clinical effectiveness of drug-coated balloon angioplasty for the treatment of PAD in adults with critical limb ischemia?		
Cochrane Library			

Date	11-09-2013		
Database (name + access ; e.g.: Medline OVID)	The Cochrane Library		
Search Strategy (attention, for PubMed, check « Details »)	#1	MeSH descriptor: [Peripheral Vascular Diseases] explode all trees	2195
	#2	MeSH descriptor: [Peripheral Arterial Disease] explode all trees	107
	#3	MeSH descriptor: [Intermittent Claudication] this term only	725
	#4	(pvd or pvod or paod or poad):ti,ab	215
	#5	(claudication or claudicant*):ti,ab	1123
	#6	peripheral vascular disease:ti,ab	1759
	#7	peripheral arter* disease:ti,ab	2125
	#8	peripheral arter* occlusive disease:ti,ab	649
	#9	(critical limb ischaemia or critical limb ischemia):ti,ab	224
	#10	fontaine stage:ti,ab	185
	#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	5354
	#12	[mh angioplasty]	4239
	#13	MeSH descriptor: [Catheterization, Peripheral] explode all trees	654
	#14	(Angioplast* or atherectom*):ti,ab	3281
	#15	(Endoluminal near repair*):ti,ab	6
	#16	(Balloon near (catheter* or dilatation*)):ti,ab	416
	#17	(Dilatation* near/2 (transluminal or arter*)):ti,ab	93
	#18	(Catheter* near/2 peripheral):ti,ab	137
	#19	{or #12-#18}	6638
	#20	#11 and #19	386
Note	The same search was used to cover 2 questions: • What is the clinical effectiveness of angioplasty with selective stent placement compared to angioplasty with primary stent placement for the treatment of PAD in adults with intermittent claudication or critical limb ischemia? • What is the clinical effectiveness of drug-coated balloon angioplasty for the treatment of PAD in adults with critical limb ischemia?		

2.3. Search for patient issues

Date	29-11-2013
Database (name + access ; e.g.: Medline OVID)	OVID Medline
Search Strategy (attention, for PubMed, check « Details »)	1 exp Patients/ (67462) 2 patient$.tw. (4391121) 3 inpatient$.tw. (60079) 4 outpatient$.tw. (106059) 5 client$.tw. (37340) 6 survivor$.tw. (61586) 7 user$.tw. (106745) 8 consumer$.tw. (38074) 9 exp persons/ (7718641) 10 person$.tw. (435398) 11 people$.tw. (245235) 12 individual$.tw. (950174) 13 victim$.tw. (34096) 14 amputee$.tw. (3621) 15 personal$.tw. (180660) 16 adult$.tw. (789473) 17 caregiver$.tw. (29555) 18 (care adj giver$).tw. (1818) 19 carer$.tw. (7385) 20 guardian$.tw. (4219) 21 exp family/ (239218) 22 family.tw. (545735) 23 families.tw. (162821) 24 relative$.tw. (926995)

25	relation$.tw. (1170562)
26	spouse$.tw. (12036)
27	partner$.tw. (103835)
28	parent$.tw. (278141)
29	stepparent$.tw. (90)
30	step-parent$.tw. (57)
31	husband$.tw. (11882)
32	wife.tw. (4281)
33	wives.tw. (4128)
34	chld$.tw. (110)
35	offspring.tw. (45986)
36	daughter$.tw. (19030)
37	father$.tw. (28404)
38	stepfather$.tw. (170)
39	step-father$.tw. (22)
40	mother$.tw. (147983)
41	brother$.tw. (11039)
42	sister$.tw. (28431)
43	sibling$.tw. (37445)
44	"next of kin".tw. (917)
45	woman$.tw. (153347)
46	women$.tw. (653953)
47	friend.tw. (9804)
48	friends.tw. (15598)
49	exp focus groups/ (17337)
50	stepmother$.tw. (72)
51	step-mother$.tw. (10)
52	(focus adj group$).tw. (20402)
53	exp Self-Help Groups/ (8930)
54	"self-help group$".tw. (1296)

55	"support group$".tw. (4527)
56	exp Community Networks/ (5634)
57	"community network$".tw. (311)
58	exp social support/ (52277)
59	"social support".tw. (20696)
60	"social network$".tw. (7348)
61	"terminally ill".tw. (4011)
62	sufferer.tw. (533)
63	sufferers.tw. (4958)
64	or/1-63 (11213878)
65	view$.tw. (312455)
66	experience$.tw. (658723)
67	perspective$.tw. (163277)
68	perception/ (21325)
69	social perception/ (17396)
70	perception$.tw. (139190)
71	narrative$.tw. (13593)
72	discourse$.tw. (8161)
73	story.tw. (14109)
74	stories.tw. (6738)
75	satisfaction.tw. (71407)
76	perceived.tw. (102993)
77	concern$.tw. (371598)
78	issue$.tw. (317788)
79	exp attitude/ (269678)
80	attitude$.tw. (91262)
81	exp emotions/ (168113)
82	emotion$.tw. (106968)
83	anger$.tw. (9461)

84	fear$.tw. (48551)
85	disappoint$.tw. (11078)
86	angry.tw. (2620)
87	afraid.tw. (1596)
88	sadness.tw. (2899)
89	distress$.tw. (74250)
90	nervous$.tw. (220204)
91	anxiety.tw. (104585)
92	anxieties.tw. (1635)
93	anxious$.tw. (10784)
94	euphoria.tw. (1350)
95	euphoric.tw. (562)
96	frustat$.tw. (27)
97	guilt$.tw. (6251)
98	hate$.tw. (740)
99	hatred.tw. (214)
100	hostility.tw. (5106)
101	jealous$.tw. (680)
102	loneliness.tw. (2789)
103	lonely.tw. (834)
104	grief.tw. (4108)
105	grieving.tw. (1017)
106	bereavement$.tw. (3385)
107	mourn$.tw. (1357)
108	mood$.tw. (46322)
109	feeling$.tw. (35246)
110	happiness.tw. (3254)
111	happy.tw. (5361)
112	joy$.tw. (2837)
113	laugh$.tw. (2002)

114	love.tw. (5280)
115	loving.tw. (834)
116	honest$.tw. (3303)
117	despair$.tw. (1588)
118	hope$.tw. (54126)
119	hoping.tw. (945)
120	exp empathy/ (12517)
121	empathy.tw. (5451)
122	compassion$.tw. (4540)
123	exp Negativism/ (934)
124	faith$.tw. (9922)
125	ethics/ (9591)
126	morale.tw. (2236)
127	exp morale/ (2683)
128	"unmet need$".tw. (4608)
129	exp human rights/ (117797)
130	exp stress/ (0)
131	exp stress, psychological/ (93427)
132	exp adaptation, psychological/ (102619)
133	((psycho$ or social) adj adjust$).tw. (5269)
134	cope.tw. (18854)
135	coping.tw. (31716)
136	exp psychology, social/ (683398)
137	"social values".tw. (512)
138	worry$.tw. (7142)
139	worries.tw. (2416)
140	exp quality of life/ (120720)
141	"quality of life".tw. (140148)
142	qol.tw. (18183)

143	"quality of recovery".tw. (437)
144	dignity.tw. (4068)
145	dignif$.tw. (427)
146	"right to die".tw. (874)
147	"patient advocacy".tw. (605)
148	exp suicide/ (48230)
149	suicid$.tw. (49642)
150	exp euthanasia/ (13904)
151	euthanasia.tw. (7627)
152	"right to live".tw. (175)
153	"right to choose".tw. (338)
154	(choice$ or empower$).tw. (219529)
155	"self esteem".tw. (12784)
156	exp decision making/ (122846)
157	(decision adj making).tw. (62172)
158	exp communication/ (369188)
159	"access to information".tw. (2155)
160	exp confidentiality/ (44135)
161	confidentiality.tw. (7791)
162	privacy.tw. (8361)
163	(truth adj3 disclosure$).tw. (51)
164	((psycho$ or cultural) adj depriv$).tw. (97)
165	social isolation/ (11024)
166	"social isolation".tw. (3746)
167	"access to services".tw. (1724)
168	exp information services/ (927126)
169	exp counseling/ (33883)
170	counsel$.tw. (66665)
171	(pastoral adj (care or psychology)).tw. (571)
172	spiritual$.tw. (9956)

173	exp religion/ (47789)
174	(beliefs or prayer$ or customs).tw. (34084)
175	exp sexuality/ (28715)
176	sexuality.tw. (10310)
177	exp culture/ (113626)
178	((psycho$ or social) adj support).tw. (24378)
179	exp social support/ (52277)
180	exp self-help groups/ (8930)
181	"self-help group$".tw. (1296)
182	"support group$".tw. (4527)
183	exp community networks/ (5634)
184	"community network$".tw. (311)
185	"social network$".tw. (7348)
186	misperception$.tw. (1584)
187	suffer$.tw. (198466)
188	exp pain/ (310090)
189	pain.tw. (377816)
190	comfort$.tw. (26403)
191	comfortable.tw. (9655)
192	190 not 191 (16748)
193	or/65-189,192 (5018186)
194	64 and 193 (3389101)
195	exp Patients/ed, px [Education, Psychology] (20009)
196	exp persons/ed, px (284037)
197	exp family/ed, px [Education, Psychology] (67794)
198	exp Interpersonal Relations/ (260256)
199	exp Family Relations/ (73187)
200	exp Professional-Patient Relations/ (119782)
201	Consumer Satisfaction/ (17617)

202	exp Consumer Participation/ (32440)
203	exp Patient Education/ (71515)
204	exp personal satisfaction/ (10933)
205	"patient information".tw. (4693)
206	(patient adj (leaflet$ or booklet$ or pamphlet$)).tw. (59)
207	or/195-206 (652838)
208	194 or 207 (3539508)
209	exp peripheral arterial disease/ or peripheral vascular diseases/ (13160)
210	Intermittent claudication/ (7076)
211	(Pvd or pvod or paod or poad).ti,ab,hw. (2298)
212	(Claudication or claudicant*).ti,ab,hw. (10763)
213	Peripheral vascular disease.ti,ab,hw. (6747)
214	Peripheral arter* disease.ti,ab,hw. (7639)
215	Peripheral arter* occlusive disease.ti,ab,hw. (1618)
216	Critical limb isch?emia.ti,ab. (1904)
217	Fontaine stage.ti,ab. (276)
218	or/209-217 (32653)
219	Arterial Occlusive Diseases/ (24804)
220	Femoral Artery/ (24385)
221	Popliteal Artery/ (7946)
222	aortoiliac.mp. (2215)
223	aorto-iliac.mp. (1200)
224	femoropopliteal.mp. (2497)
225	femoro-popliteal.mp. (909)
226	infrageniculate.mp. (98)
227	infra-geniculate.mp. (1)
228	or/220-227 (31054)
229	219 and 228 (5532)
230	218 or 229 (36572)
231	208 and 230 (9957)

232	limit 231 to yr="2009 -Current" (2527)

Note

3. QUALITY APPRAISAL

3.1. Quality appraisal tools

3.1.1. Guidelines

The AGREE II evaluation score was used to critically appraise guidelines retrieved (Table 2).

Table 2 – AGREE II instrument

Critical appraisal of clinical practice guidelines - AGREE II
Domain 1. Scope and Purpose
1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.
Domain 2. Stakeholder Involvement
4. The guideline development group includes individuals from all the relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.
Domain 3. Rigour of Development
7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.
Domain 4. Clarity of Presentation

Critical appraisal of clinical practice guidelines - AGREE II
15. The recommendations are specific and unambiguous.
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.
Domain 5. Applicability
18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.
20. The potential resource implications of applying the recommendations have been considered.
21. The guideline presents monitoring and/ or auditing criteria.
Domain 6. Editorial Independence
22. The views of the funding body have not influenced the content of the guideline.
23. Competing interests of guideline development group members have been recorded and addressed.

3.1.2. Systematic reviews

AMSTAR criteria were used to assess systematic reviews (Table 3).

Table 3 – AMSTAR checklist

Question	Answer
1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration,	☐ Yes ☐ No

severity, or other diseases should be reported.	☐ Can't answer ☐ Not applicable
7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
11. Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable

3.1.3. Primary studies for diagnosis

The quality assessment tool for diagnostic test accuracy in use at the time of the HTA report appeared to be an early version of QUADAS 1, and the NICE guideline also used a later version of QUADAS 1. However, in recent years the authors of QUADAS 1 have considerably revised the tool, forming QUADAS 2, and its focus is on risk of bias and applicability, rather than quality assessment with aspects of reporting. For this review, we planned to use QUADAS 2 and therefore it became necessary to map from the HTA and the NICE guideline tools to QUADAS 2.

After Whiting et al: http://www.bris.ac.uk/quadas/resources/quadas2reportv4.pdf , we removed aspects of QUADAS 1 that were more connected to reporting than quality assessment. These included questions about whether the particular aspect was 'clearly described'.

Secondly, QUADAS 2 usefully maps from QUADAS 1 by separating items from the latter into risk of bias and applicability sections.

Finally, some items of QUADAS 1 have been split and renamed using the headers of bias for each of the test accuracy components.

We note that QUADAS 1 expects the answer to be 'yes', 'no', 'unclear', but QUADAS 2 assigns values of 'low', 'high' and 'unclear' risk of bias. The response 'yes' then maps onto 'low' risk of bias.

We produced a map to go from QUADAS 1 (as used in the HTA report) to QUADAS 2, and the items are shown in Table 4. This was then used for the review to map the HTA studies and to add in the new studies and those from the NICE guideline.

Table 4 – QUADAS 1 mapped onto QUADAS 2

QUADAS 1 item	Transfer action	Maps onto QUADAS 2 section	QUADAS 2 question
Spectrum of patients representative of those who would receive the test in practice?	Split and convert	Domain 1 selection of patients: risk of bias	Consecutive or random sample? (NEW)
		Domain 1 selection of patients: risk of bias	Case control avoided? (NEW)
		Domain 1 selection of patients: risk of bias	Inappropriate exclusions avoided? (NEW)
		Domain 1 selection of patients: applicability	Patients and settings do not match review question (NEW)
No corresponding item	NA	Domain 1 overall risk of selection bias Does not map	Could the selection of patients have introduced bias? (NEW)
Selection criteria clearly described?	Delete item	Does not map	-----
Index test results interpreted without knowledge of the results of the	Moved across	Domain 2 index test: risk of bias	Index test results interpreted without knowledge of results of reference standard?

QUADAS 1 item	Transfer action	Maps onto QUADAS 2 section	QUADAS 2 question
reference standard?			(SAME)
No corresponding item	NA	Domain 2 index test: risk of bias Does not map	If a threshold was used, was it prespecified? (NEW)
No corresponding item	NA	Domain 2 overall risk of index test bias Does not map	Could the index test have introduced bias? (NEW)
No corresponding item	NA	Domain 2 index test: applicability Does not map	Index test does not match review question (NEW)
Was reference standard likely to classify target condition successfully?	Moved across Not in earlier QUADAS I (such as HTA)	Domain 3 reference standard: risk of bias and applicability	Was reference standard likely to classify target condition successfully? (SAME)
Reference standard independent of the index test (and not part of it)? AND Execution of reference standard described in sufficient detail to permit replication?	Mapped for earlier QUADAS I (such as HTA) or deleted for later QUADAS I	Domain 3 reference standard risk of bias and applicability	Was reference standard likely to classify target condition successfully? (MAPPED)
Reference standard results interpreted without knowledge of the results of the index test?	Moved across	Domain 3 reference standard: risk of bias	Reference standard results interpreted without knowledge of the results of the index test? (SAME)
No corresponding item	NA	Domain 2 overall risk of reference standard bias Does not map	Could the reference standard have introduced bias? (NEW)
No corresponding item	NA	Domain 3 reference standard: applicability Does not map	Target condition as defined by reference standard does not match review question (NEW)

QUADAS 1 item	Transfer action	Maps onto QUADAS 2 section	QUADAS 2 question
Period between reference standard and index test short enough to ensure target condition did not change between the two tests?	Moved across	Domain 4 flow: risk of bias	Period between reference standard and index test short enough to ensure target condition did not change between the two tests? (SAME)
Did whole sample or random selection of sample receive verification using the reference standard?	Map	Domain 4 flow: risk of bias	Did all patients receive a reference standard? (SIMILAR)
Same reference standard regardless of index test result?	Map	Domain 4 flow: risk of bias	Did patients receive same reference standard? (SIMILAR)
Withdrawal explained?	Map	Domain 4 flow: risk of bias	Were all patients included in the analysis? (SIMILAR)
No corresponding item	NA	Domain 4 overall patient flow bias Does not map	Could the patient flow have introduced bias? (NEW)
No corresponding item	NA	Comparative tests Does not map	Was there more than one index test? If so do the comparative test risk of bias
Execution of index test described in sufficient detail to permit replication?	Delete	Does not map	-----
Same clinical data available when test results interpreted as would be available when test is used in practice?	Delete	Does not map	-----
Uninterpretable, indeterminate or intermediate test results reported?	Delete	Does not map	-----
NO CORRESPONDING ITEM	NEW FOR NCGC	All domain risk of bias	Across all domains, what is the risk of bias? LOW /

3.1.4. Primary studies for treatment

To assess risk of bias from primary studies, we used the Cochrane Collaboration's Risk of Bias tool (Table 5).

Table 5 – Cochrane Collaboration's tool for assessing risk of bias

Domain	Support for judgement	Review authors' judgement
Selection bias		
Random sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence
Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment
Performance bias		
Blinding of participants and personnel Assessments should be made for each main outcome (or class of outcomes)	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Detection bias		
Blinding of outcome assessment Assessments should be made for each main outcome (or class of outcomes)	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Detection bias due to knowledge of the allocated interventions by outcome assessors
Attrition bias		
Incomplete outcome data Assessments should be made for each main outcome (or class of outcomes)	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any reinclusions in analyses performed by the review authors	Attrition bias due to amount, nature or handling of incomplete outcome data

Domain	Support for judgement	Review authors' judgement
Reporting bias		
Selective reporting	State how the possibility of selective outcome reporting was examined by the review authors, and what was found	Reporting bias due to selective outcome reporting
Other bias		
Other sources of bias	State any important concerns about bias not addressed in the other domains in the tool If particular questions/entries were prespecified in the review's protocol, responses should be provided for each question/entry	Bias due to problems not covered elsewhere in the table

3.2. Guideline quality appraisal results

The appraisal of the 7 included **guidelines** was performed by two researchers (KHH and JV) independently (Table 6).

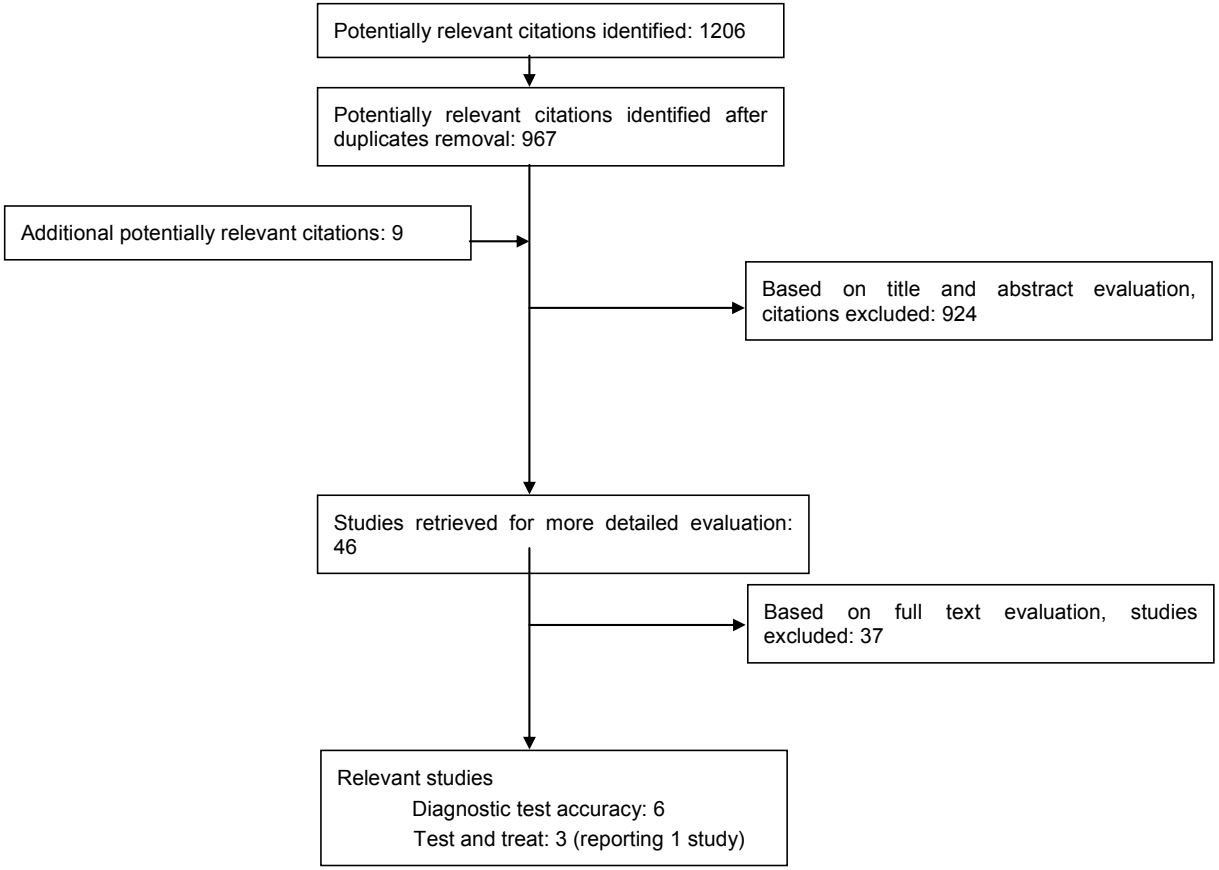
Table 6 – AGREE scores of identified guidelines

Source	Title	Standardized Score						Final Appraisal
		Scope	Stakeholder involvement	Rigour of development	Clarity	Applicability	Editorial Independence	
NICE	Lower limb peripheral arterial disease. Diagnosis and management	100%	75%	94%	100%	73%	83%	Included
ACR	Claudication – suspected vascular etiology	47%	0%	29%	61%	0%	13%	Excluded
ACR	Recurrent symptoms following lower extremity angioplasty	64%	14%	29%	67%	17%	13%	Excluded
ACR	ACR–AIUM–SRU practice guideline for the performance of peripheral arterial ultrasound using color and spectral Doppler	58%	22%	14%	22%	6%	13%	Excluded
ACCP	Antithrombotic therapy in peripheral artery disease	86%	67%	84%	92%	38%	96%	High quality, but out of scope
ACCF/AHA	2011 ACCF/AHA Focused Update of the Guideline for the Management of Patients With Peripheral Artery Disease	72%	22%	44%	83%	2%	75%	Excluded
ESC	ESC Guidelines on the diagnosis and treatment of peripheral artery diseases	56%	22%	19%	78%	4%	50%	Excluded

3.3. Study selection and quality appraisal

3.3.1. Assessment of PAD

3.3.1.1. Clinical article selection



3.3.1.2. List of excluded studies

Diagnostic test accuracy

Reference	Reason of exclusion
Abd-elgawad 2013[5]	Data reported insufficient to calculate 2x2 table. Conflicting data made the data unusable
Douek 1998[54]	Narrative review
Gornik 2008[74]	Incorrect index test. Not imaging technique (ankle brachial index testing)
Healy 2013[78]	Systematic review of 3 studies, one of which is included separately, and the other two studies were added to the review
Hendrickx 1985[79]	Incorrect index test. Conventional angiography versus digital subtraction angiography
Koshy 2011[90]	Data reported insufficient to calculate 2x2 table. Only kappa statistics reported, no test accuracy data
Lackner 1985[93]	Examination of digital subtraction angiography alone (i.e. not test accuracy of index test)
Partovi 2013[108]	Data reported insufficient to calculate 2x2 table
Ubbink 2002[158]	Population was patients who had uncertain diagnosis on duplex scanning. Only 14 vessels. No subtraction component for DSA reference standard

Test and treat strategy

Reference	Reason of exclusion
Adriaensen 2004[8]	Not comparison of two index tests: CT angiography versus digital subtraction angiography
Kock 2005[89]	Not comparison of two index tests: CT angiography versus digital subtraction angiography
Vahl 2008[159]	Not comparison of two index tests: magnetic resonance angiography versus digital subtraction angiography

3.3.1.3. List of included studies that had more than one index test

Study	Index tests	Comment
Andreisek 2007[15]	Contrast enhanced MRA Time resolved CE MRA	Different numbers of lesions were examined using the two types of MRA, so comparison was unreliable
Bueno 2010[37]	Contrast Enhanced MRA Duplex ultrasound	The study only reported sensitivity and specificity (although the 2x2 tables could be estimated). See figure 19 for the calculated data shown on forest plots. The study showed small differences between the CE MRA and DUS assessments, with the former consistently having the larger sensitivities; specificities were very similar. Differences were more pronounced for assessments of 50-100% stenosis compared with measuring occlusion. It did not appear to make much difference which part of the leg was being studied.
Currie 1995[47]	2D time-of-flight MRA Duplex ultrasound	Thresholds were different, so this comparison was not reported further: 2D TOF MRA was 50-99% and DUS was occlusion.
Gjonnaess 2006[71]	Contrast Enhanced MRA Duplex ultrasound	See Figure 18 for the forest plot comparison. The study gave a much higher sensitivity (94%) for the CE MRA compared with DUS (70%) for measuring stenosis of 50-100% above the knee
Lundin 2000[101]	2D time-of-flight MRA Contrast Enhanced MRA Duplex ultrasound	See Figure 18 for the forest plot comparison. The study showed no difference in sensitivity (81%) between the two types of MRA, but the DUS gave slightly lower values (71%) for measuring stenosis of 50-100% above the knee

3.3.1.4. Quality appraisal

Quadas 2

Table 7 – QUADAS 1 mapped onto QUADAS 2 for studies from the HTA

QUADAS I and new	Appropriate spectrum	DOMAIN RISK OF SELECTION BIAS	Index test blind to reference std results	DOMAIN RISK OF BIAS FOR INDEX TEST	Reference standard details well reported	Reference standard independent	Reference standard likely to classify target condition	Reference standard blind to test results	DOMAIN RISK OF BIAS FOR REFERENCE STD	<1 month between tests	All received reference standard	Same reference standard?	Withdrawals explained? / all included in analysis?	DOMAIN RISK OF BIAS FOR FLOW AND TIMING	More than one index test?	ALL DOMAIN RISK OF BIAS
QUADAS 2					Combine		Into this									
Aly, 1998	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Low		High
Ashleigh, 1993	Unclear	Unclear	Unclear	Unclear	No	Yes	Unclear	Unclear	High	No	Yes	Yes	Yes	High		Very high
Baxter 1993	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low		High
Bergamini 1995	Unclear	Unclear	Unclear	Unclear	No	Yes	Unclear	Yes	Low	No	Yes	Yes	Yes	High		High
Bostrom, 2001	No	High	Yes	Low	No	Yes	Unclear	Yes	Low	No	Yes	Yes	Yes	High		Very high
Currie, 1995	Yes	Low	Yes	Low	No	Yes	Unclear	Yes	Low	No	Yes	Yes	Yes	High	Y	High
Davies, 1992	Unclear	Unclear	Unclear	Unclear	No	Yes	Unclear	Unclear	High	Yes	Unclear	Yes	No	High		Very high
Eiberg, 2001	Yes	Low	Yes	Low	No	Yes	Unclear	Yes	High	Yes	Yes	Yes	Yes	Low		Low
El Kayali 2004	Unclear	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low		Unclear
Fletcher 1990	Unclear	Unclear	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low		Unclear /Low
Grasbaugh 2003	No	High	Yes	Low	No	Yes	Unclear	Yes	Low	Unclear	Yes	Yes	Yes	Low		High
Hatsukami 1992	No	High	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low		High
Hirai, 1998	Unclear	Unclear	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Unclear	Low		Unclear /low
Hofmann 2004	No	High	Unclear	Unclear	Yes	Yes	Yes	Yes	Low	Unclear	Yes	Yes	No	High		Very high
Karacagil 1996	Unclear	Unclear	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	No	High		High
Koelemay, 1998	Yes	Low	Yes	Low	Yes	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low		Low

QUADAS I and new	Appropriate spectrum	DOMAIN RISK OF SELECTION BIAS	Index test blind to reference std results	DOMAIN RISK OF BIAS FOR INDEX TEST	Reference standard details well reported	Reference standard independent	Reference standard likely to classify target condition	Reference standard blind to test results	DOMAIN RISK OF BIAS FOR REFERENCE STD	<1 month between tests	All received reference standard	Same reference standard?	Withdrawals explained? / all included in analysis?	DOMAIN RISK OF BIAS FOR FLOW AND TIMING	More than one index test?	ALL DOMAIN RISK OF BIAS
Koelemay, 1997	No	High	Yes	Low	Yes	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low		High
Lai, 1995	Yes	Low	Yes	Low	No	Yes	Unclear	Yes	Low	Unclear	Yes	Yes	No	high		High
Lai, 1996	Unclear	Unclear	Yes	Low	No	Yes	Unclear	Yes	Low	No	Yes	Yes	No	high		High
Legemate, 1991	Unclear	Unclear	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low		Unclear
Linke 1994	Yes	Low	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low		Unclear
Lundin 2000	Unclear	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low	Y	Unclear /Low
Mergelsberg 1986	Unclear	Unclear	Unclear	Unclear	No	Unclear	No	Unclear	High	Yes	Yes	Yes	Yes	Low		High/very high
Sensier, 1996	Yes	Low	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low		Low
Shaalan, 2006	No	High	Yes	Low	No	Yes	Unclear	Unclear	High	Unclear	Yes	Yes	Yes	Unclear		Very high
Wilson 1997	Yes	Low	Yes	Low	No	Yes	Unclear	Yes	Low	Unclear	Yes	Yes	Yes	Unclear		Low
Whyman 1992	Unclear	Unclear	Unclear	Unclear	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low		High
Zeuchner, 1994	Yes	Low	Yes	Low	No	Yes	Unclear	Yes	Low	Yes	Yes	Yes	Yes	Low		Low

Table 8 – QUADAS 2 for studies from the NICE guideline

	Consecutive / random	Not case control	No inappropriate exclusions	DOMAIN 1 RISK OF BIAS	DOMAIN 1 APPLICABILITY	Index test blinded to reference standard	Pre-specified threshold	DOMAIN 2 RISK OF BIAS	DOMAIN 2 APPLICABILITY	Ref standard likely to classify target condition	Reference standard blinded to index test	DOMAIN 3 RISK OF BIAS	DOMAIN 3 APPLICABILITY	Time between tests < 1mo	All received reference std	Same reference standard	All included in the analysis	DOMAIN 4 RISK OF BIAS	More than one index test	ALL DOMAIN RISK OF BIAS	COMMENTS
Bueno 2010 (ID 16105)	Yes	Yes	Yes	Low	Applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Yes	Yes	Yes	No	Low	Yes	**Low**	8.5% missing segments for analysis for DUS, and 4.01% for MRA
Eiberg 2010 (ID 16106)	Unclear	Yes	Not stated	Unclear	Applicable	Yes	NA	Low	Applicable	Yes	Yes (DUS on day before)	Low	Applicable	Yes (1 day)	Yes	Yes	Yes 9% segments missing	Low	No	**Unclear / high**	Only 32% of those eligible enrolled (limited by availability of DUS equipment and examiners, and patient consent); if 2 or more eligible on the same day, the one with the lowest ankle pressure chosen (i.e. not random) and reasons for not participating in study not systematically recorded
Gjønnæss 2006 (ID 16138)	Yes	Yes	Yes	Low	Applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Not stated	Yes	Yes	Yes	Unclear	Yes	**Unclear**	Up to 13% segments not visualised for DUS)
Kos 2009 (ID 16119)	Yes	Yes	Yes	Low	Applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Yes	Yes	Yes	Yes	Low	No	**Low**	People excluded with contraindications to MRI. 6% segments not usable for MRA analysis

	Consecutive / random	Not case control	No inappropriate exclusions	DOMAIN 1 RISK OF BIAS	DOMAIN 1 APPLICABILITY	Index test blinded to reference standard	Pre-specified threshold	DOMAIN 2 RISK OF BIAS	DOMAIN 2 APPLICABILITY	Ref standard likely to classify target condition	Reference standard blinded to index test	DOMAIN 3 RISK OF BIAS	DOMAIN 3 APPLICABILITY	Time between tests < 1mo	All received reference std	Same reference standard	All included in the analysis	DOMAIN 4 RISK OF BIAS	More than one index test	ALL DOMAIN RISK OF BIAS	COMMENTS
Kreitner 2008 (ID 206)	Yes	Yes	Yes	Low	Applicable	Yes	Unclear	Unclear	Applicable	Yes	Unclear	Unclear	Applicable	Yes	Yes	Yes	Yes	Low	No	**Unclear**	Unclear what was analysed (occlusion or stenosis)
Napoli et al 2011 (ID 16355)	Yes	Yes	Yes	Low	Applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Yes	Yes	Yes	Yes	Low	No	**Low**	Excluded 41/253 people with contraindications to DSA.
Scherntha ner et al 2008	Yes	Yes	Unclear	Unclear	Applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Yes	Yes	Yes	Unclear	Unclear	No	**Unclear**	Time between tests: mean 12 days (1-30days range)

Table 9 – QUADAS 2 for studies from the update review

	Consecutive / random	Not case control	No inappropriate exclusions	DOMAIN 1 RISK OF BIAS	DOMAIN 1 APPLICABILITY	Index test blinded to reference standard	Pre-specified threshold	DOMAIN 2 RISK OF BIAS	DOMAIN 2 APPLICABILITY	Ref standard likely to classify target condition	Reference standard blinded to index test	DOMAIN 3 RISK OF BIAS	DOMAIN 3 APPLICABILITY	Time between tests < 1mo	All received reference std	Same reference standard	All included in the analysis	DOMAIN 4 RISK OF BIAS	More than one index test	ALL DOMAIN RISK OF BIAS	COMMENTS
Andreisek 2007	Yes	Yes	Yes	Low	Part applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Yes	Yes	Yes	No	Unclear	No	**Low**	Funded by GE. Non-diagnostic: 6% - DSA (21% in foot); 24% MRA; 12% calf and 20% foot for TRICKS. Diabetes population.
Balzer 2005	No	Yes	No	High	Applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Yes	Yes	Yes	Yes	Low	No	**High**	100/615 patients who had MRA met the inclusion criteria; retrospective analysis of selected patients. 6% segments not evaluated
Burbelko 2013	Yes	Yes	No	Very high	Not applicable	Yes	NA	Low	Applicable	Yes	No	High	Applicable	Yes	Yes	Yes	Not stated	Unclear	No	**Very high**	Population was patients who did not require additional imaging after MRA excluded 209/437. Patients excluded if >30 days between tests. Reference standard assessor was aware of "other diagnostic findings". Many exclusions may have made the study less applicable.
Iezzi 2013	Yes	Yes	No	High	Applicable	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Not stated	No	Yes	No	High	No	**High/very high**	Patients who did not have DSA were not included in analysis, and CTA results used to include patients for DSA. Therefore not all received the reference standard.

	Consecutive / random	Not case control	No inappropriate exclusions	DOMAIN 1 RISK OF BIAS	DOMAIN 1 APPLICABILITY	Index test blinded to reference standard	Pre-specified threshold	DOMAIN 2 RISK OF BIAS	DOMAIN 2 APPLICABILITY	Ref standard likely to classify target condition	Reference standard blinded to index test	DOMAIN 3 RISK OF BIAS	DOMAIN 3 APPLICABILITY	Time between tests < 1mo	All received reference std	Same reference standard	All included in the analysis	DOMAIN 4 RISK OF BIAS	More than one index test	ALL DOMAIN RISK OF BIAS	COMMENTS
Lapeyre 2005	Yes	Yes	Yes	Low	Yes	Yes	NA	Low	Applicable	Yes	Yes	Low	Applicable	Yes	Yes	Yes	Yes	Low	No	**Low**	All patients had stage IV CLI
Wang 2012	Yes	Yes	Yes	Low	Applicable	Unclear	NA	Low	Applicable	Yes	Unclear	Unclear	Applicable	Not stated	Yes	Yes	Yes	Unclear	No	**High**	5/35 DSA failed to catheterise but surgery was used instead as the reference standard,

3.3.1.5. Risk of Bias tool

DiPAD 2008 – QUALITY OF LIFE (EQ 5D) AT 3 months and 6 months

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Computer generated block design
Allocation concealment (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Central randomization through a central co-ordinating center by phone. Statement that patients, referring surgeons and research assistants were all unaware of randomization sequence
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded; outcome assessors were the patients
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	At both 3 and 6 months, the response to the QoL questionnaire was 89%; it is unclear if this level would affect the outcome
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable for this outcome (times appeared to be pre-specified)
Other bias	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Baseline levels taken into account in the analysis for MRA versus CTA, using an adjusted analysis, although large baseline difference (0.18) Not adjusted for MRA versus DUS and baseline difference of 0.03 is comparable with the effect estimate.

DiPAD 2008 – WALKING DISTANCE AT 6 MONTHS; additional imaging within 6 months; AND number of procedures AT 6 months

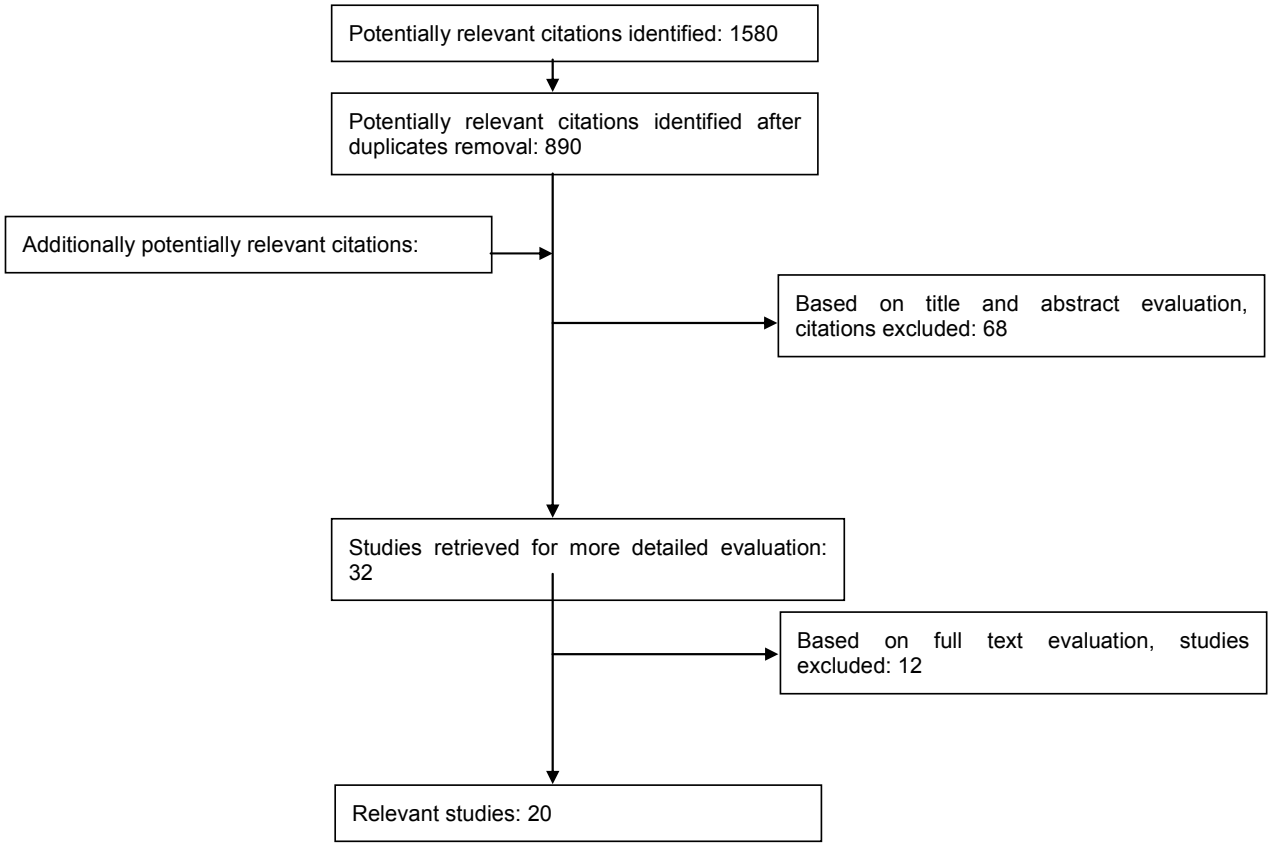
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Computer generated block design
Allocation concealment (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Central randomization through a co-ordinating center by phone. Statement that patients, referring surgeons and research assistants were all unaware of randomization sequence
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded; outcome assessors were the patients for walking and the surgeons for additional imaging
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Low level of missing data for walking distance: 1/77 for MRA, 0/79 for CTA (MRA versus CTA) 2/180 for MRA, 3/177 for DUS (MRA versus DUS) Unlikely to affect this outcome
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable for this outcome (times appeared to be pre-specified)
Other bias	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Analysis not adjusted for baseline for MRA versus DUS, and baseline difference of 11m is larger than the effect estimate (2m).

DiPAD 2008 – number of Amputations

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Computer generated block design
Allocation concealment (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Central randomization through a central co-ordinating center by phone. Statement that patients, referring surgeons and research assistants were all unaware of randomization sequence
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded, but objective outcome
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded; but objective outcome
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Low level of missing data: 1/77 for MRA, 0/79 for CTA (MRA versus CTA) Number of amputations: 5 and 2; unlikely to give high risk of bias
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable for this outcome
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

3.3.2. Selective versus primary stenting

3.3.2.1. Clinical article selection



3.3.2.2. List of excluded studies

Reference	Reason of exclusion
Cejna 1999[42]	Not selective stenting
Greenacher 2004[76]	Not selective stenting
Grimm 2001[77]	Not selective stenting
Katsanos 2012[83]	Abstract of Scheinert 2012 (included study)
Katzen 2012[84]	Abstract of Laird 2010 (included study
Randon 2010[114]	Not selective stenting
Van der Zaag 1996[160]	Letter, not primary study
Vroegindeweij 1997[167]	Not selective stenting
Zdansowski 1999[175]	Not selective stenting

3.3.2.3. List of included studies

Study	Intervention/comparator	Population	Outcome	Length of study
Brodman 2011[35]	Balloon expandable stent with silicon carbon coating Angioplasty with secondary stenting if angioplasty failed. . Predefined criteria for failure.	CLI (Rutherford classification 4 to 6) Infrapopliteal arteries	Mortality (not reported by group) Complications	12 months follow up
Cejna 2001[43]	Palmaz Stent Angioplasty with secondary stenting if angioplasty failed. . Predefined criteria for failure.	Society of Vascular Surgery/International Cardiovascular Surgery categories 1 to 5 Femorapopliteal arteries	Mortality Amputations Re-intervention Complications	30 days and 12 months follow up
Dake 2011[50]	Angioplasty self-expanding drug-eluting (paclixatel) nitinol stent Angioplasty with secondary stenting after PTA repeated once.	Rutherford category ≥2 Femorapopliteal arteries	Mortality Amputations Target lesion	12 months follow up Patients recruited between 2005 and 2008

Study	Intervention/comparator	Population	Outcome	Length of study
	Patient requiring bailout stent randomized to bare metal stent or sirolimus-eluting stent. . Predefined criteria for failure.		revascularisation	
Dick 2009[52]	Self expandable nitinol stents Angioplasty with secondary stenting after PTA repeated once. Predefined criteria for failure.	Severe intermittent claudication (Rutherford 3), chronic CLI (Rutherford 4) or ischaemic ulcers (Rutherford 5) Superficial femoral arteries	Mortality Complications Walking distance	6, 12 & 24 months follow up
Goode 2013[72]	Stents not described Angioplasty with secondary stenting if no flow following angioplasty or complications that could be resolved by use of a stent.	Illiac arteries *No further information reported*	Mortality Major complications Re-intervention	2 years follow up Patients recruited between 1995 and 2002
Greenberg 2004[75]	InterCoil self expanding Stent Angioplasty with bailout stent. Predefined criteria for failure.	Symptomatic limb ischemia Superficial femoral/popliteal arteries	Mortality Amputations Complications	12 months follow up Patients recruited between 1997 and 1999
Krakenberg 2007[91]	Self expanding open-cell nitinol stent Angioplasty with selective stenting. Predefined criteria for failure.	Rutherford category ≥2 Superficial femoral arteries	Mortality TLR Major adverse events Walking distance (for subset of patients only)	Discharge, 1, 6 & 12 months follow up Patients recruited between 2004 and 2005
Laird 2010[94]**, Laird 2012**[95]	Self-expanding nitinol stent PTA with bailout stent after multiple suboptimal angioplasty attempts. Predefined criteria for failure.	Intermittent claudication (Rutherford categories 1 to 3) Superficial femoral or proximal popliteal arteries	Mortality Amputations TLR Quality of life	12 and 36 months follow up Patients recruited between 2004 and 2006
Rand 2006[112]	Carbostents PTA with bailout stent for	Chronic CLI (Fontaine III or IV)	Mortality Amputations	6 months follow up

Study	Intervention/comparator	Population	Outcome	Length of study
	unsatisfactory angioplasty	Infrapopliteal arteries	Complications Re-intervention	
Rand 2011[113]	Inperia stent PTA with bailout stent. Predefined criteria for failure.	CLI (Rutherford-Becker 4 or 5) Infrapopliteal arteries	Mortality Amputations TLR	3 & 9 months follow up Patients recruited between 2006 and 2008
Rastan 2013[116]	Self expanding nitinol stent PTA with bailout stent after repeated angioplasty failure. Predefined criteria for failure.	Rutherford-Becker 2 to 5 (intermittent claudication 79.3%, CLI 20.7%) Popliteal arteries	Mortality Amputations TLR Perioperative complications	6 & 12 months follow up Patients recruited between 2007 and 2010
Scheinert 2012[128]	Sirolimus-eluting stent (SES) PTA with bailout stent after repeated angioplasty failure. Predefined criteria for failure.	Symptomatic CLI (Rutherford 3 to 5) Infrapopliteal arteries	Mortality Amputations TLR	6 weeks, 6 & 12 months follow up Patients recruited between 2008 and 2010
Schillinger 2006[131], **Schillinger 2007**[130], **Sabeti 2007**[123]	Self expanding open-cell nitinol stent PTA with bailout stent after repeated angioplasty failure. Predefined criteria for failure.	Rutherford categories 3 to 5 Superficial femoral artery	Mortality Amputations Re-intervention Complications Quality of life	6, 12 and 24 months follow up Patients recruited between 2003 and 2004
Tetteroo 1998[152], **Bosch 1999**[25], **Klein 2004**[86], **Klein 2006**[87]	Palmaz Stent PTA with bailout stent after repeated angioplasty failure. Predefined criteria for failure.	Society of Vascular Surgery/International Cardiovascular Surgery categories 1 to 5.	Mortality Amputations Re-intervention Complications Quality of life Pain Walking distance	3 months and 1, 2, 5 and 6-8 years follow up Patients recruited between 1993 and 1997

3.3.2.4. Quality appraisal

Goode 2013 – MORTALITY at 2 years

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Unlikely to be blinded but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Unlikely to be blinded but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	6 patients dropped out of PTA group. Potentially there could have been deaths in this group. Trial stopped early but all patients up to that point accounted for.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

Goode 2013 – Major complications and reinterventions at 2 years

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Unlikely to be blinded. Key personal also likely to be involved in outcome assessment. Not reported what criteria were used to determine the diagnosis of embolisations and thrombosis and how they decided intervention was required.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Unlikely to be blinded. Not reported what criteria were used to determine the diagnosis of embolisations and thrombosis and how they decided intervention was required.
Incomplete outcome data (attrition bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	6 patients dropped out of PTA group. Potentially there could have been more complications in this group so the result could be an underestimate. Trial stopped early but all patients up to that point accounted for.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

RASTAN 2013 – MORTALITY AND AMPUTATIONS at 1 year

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Very low event rate for both outcomes so the number of missing patients could affect the results. Reports those died during follow up but does not state if the study investigators tried to find the patients who did not visit at one year or looked at death certificates. More patients lost to follow up in PTA group.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

RASTAN 2013 – Peri-operative complications

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded. Key personnel involved in assessment could have affected the outcome.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded and no clear description of how this outcome was determined.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	All patients appear to be accounted for.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

RASTAN 2013 – re-interventions: target lesion or vessel revascularisation, by pass surgery

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded. Participants unlikely to influence results. All patients had duplex scanning and radiographic imaging at I year. Independent analysis of results by core laboratories. Core personnel would not have the
Blinding of outcome assessment (detection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Not blinded and no clear description of how it was decided to reintervene. However, study reports that core laboratories provided independent analysis for duplex ultrasound and radiographic imaging.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	More patients lost to follow up in PTA group.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

SCHEINERT 2012 – MORTALITY at 1 year

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Appears to account for all patients
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

SCHEINERT 2012 –AMPUTATIONS at 1 year

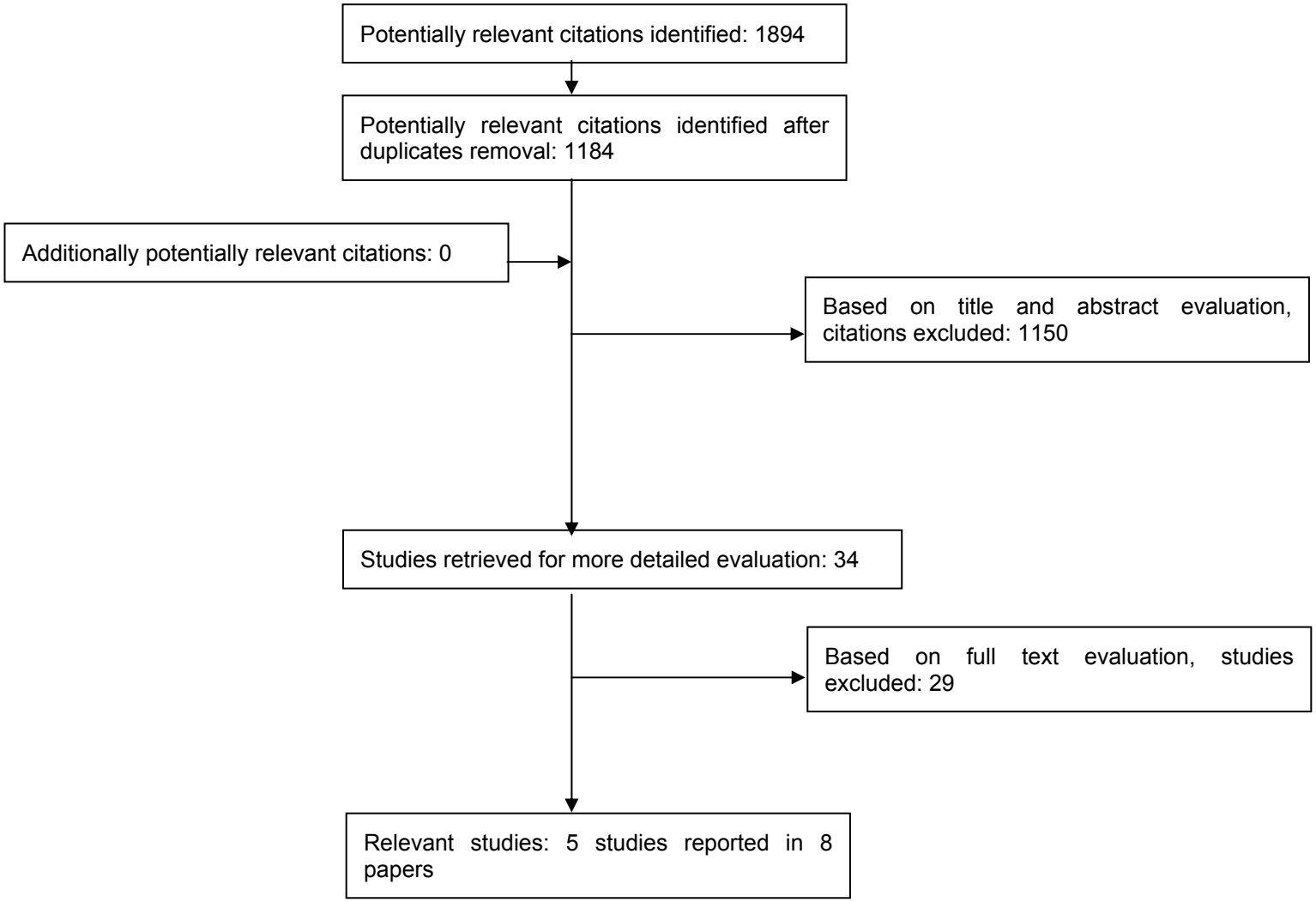
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Not all patients appear to be included in the analysis and it is not clear who the missing patients are.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

SCHEINERT 2012 – re-interventions: target lesion or vessel revascularisation

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study only states it is a prospective randomized trial and provides no other information.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No information on allocation concealment reported
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded. Study reports ultrasound results were not analysed by core laboratory suggesting the personel may have been involved in the decisions for these outcomes. Participants unlikely to influence results.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Not blinded and no clear description of how it was decided to reintervene. Study reports ultrasound results were not analysed by core laboratory suggesting the outcome assesors were not blinded and there was no adjucation of results.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Not all patients appear to be included in the analysis and it is not clear who the missing patients are. The event rates are similar to the numbers of patients not available at 12 months.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable

3.3.3. Bare metal versus drug eluting stents

3.3.3.1. Clinical article selection



3.3.3.2. List of excluded studies

Reference	Reason of exclusion
Abbate 2009[4]	Conference abstract
Acin 2012[7]	Systematic review - checked for extra studies
Albajara 1996[10]	Spanish HTA report
Anon 2003[1]	Evidence summary only
Anon 2010a	Systematic review - checked for extra studies
Benjo 2012[21]	Systematic review - abstract only
Biondizoccai 2009[23]	Systematic review of non-randomized studies
Bosiers 2008d[27]	Conference abstract
Bosiers 2008b[26]	Review of types of stents
Chan 2011[44]	Literature review - checked for extra studies
Dake 2012[48]	Conference abstract
Duda 2004[58]	Conference abstract
Fischer2012[64]	Intervention more applicable to other question
Katsanos2012[83]	Literature review
Katsanos2013[82]	Systematic review - checked for extra studies
Lejay2009[96]	Literature review
Lim2013[100]	Review of Scheinert et al 2012
Muradin2001[106]	Systematic review - checked for extra studies
Rastan 2012a[118]	Systematic review - checked for extra studies
Sabeti2004[124]	non-randomized study
Sheth2013[137]	Conference abstract of systematic review

Reference	Reason of exclusion
Siablis2005[138]	Non-randomized study
Siablis2007[140]	Non-randomized study
Siablis2009[139]	Non-randomized study
Siebert2009[141]	Incorrect study ordered
Simpson2013[142]	Systematic review - checked for extra studies
Tsetis2011[156]	Conference teaching session
Varcoe2013[163]	Literature review
Yaneza2012[174]	Conference abstract of systematic review

3.3.3.3. List of included studies

Study	Intervention/comparator	Population	Outcome	Length of study
Bosiers, 2012[28]	Bare-metal stent versus everolimus drug- eluting stent	Patients with critical limb ischemia (Rutherford-Becker categories 4 to 5) and infrapopliteal arterial occlusive disease.	Mortality; Target Lesion Revascularisation; Amputation.	12 months
Dake, 2013[49]**, 2011**[50]	Bare-metal stent versus self-expanding nitinol drug eluting stent	Patients with Rutherford category 2-4 (critical limb ischemia and intermittent claudication) and femoropopliteal lesions	Mortality; Procedure/device-related deaths; Target Lesion Revascularisation.	24 months
Duda, 2006[55]**, 2005**[56]**, 2002**[57]	Bare- metal (nitinol) stent versus sirolimus drug-eluting stent	Patients with Rutherford categories 1 to 4 (critical limb ischemia and intermittent claudication) and superficial femoral artery lesions	Mortality; Amputation; Target Lesion Revascularisation; Target Vessel Revascularisation; Major adverse events.	24 months

Study	Intervention/comparator	Population	Outcome	Length of study
Geraghty, 2013[69]	Bare-metal (nitinol) stent versus drug-eluting stent	Patients with Rutherford categories 1 to 5 (critical limb ischemia and intermittent claudication) and superficial femoral artery occlusive disease	Mortality; Target Lesion Revascularisation; Peri-procedural complications; quality of life (SF-36)	36 months
Rastan, 2012[115]**, 2011**[117]	Bare-metal stent (ethanol-coated) versus sirolimus-containing drug-eluting stent	Patients with Rutherford categories infra-geniculate disease and critical limb ischemia and intermittent claudication (results for CLI and IC reported separately)	Mortality; Amputation; Total Lesion Revascularisation; Major adverse events.	1200 days

3.3.3.4. Quality appraisal

Bosiers2012 – Mortality (Hazard Ratio)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Randomized 1:1 using pre-provided sealed envelopes; block randomization and stratification per centre using block sizes of 8.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Preprovided sealed envelopes
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Patients were blinded. Personnel were not but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No information on outcome assessment blinding reported but the outcome is objective and unlikely to be affected by this.

Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	The attrition and exclusions were reported, with reasons but the reasons were not given by group. The drop-out was similar in both arms.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Bosiers2012 – TarGET LESION REVASCULARISATION (HAZARD RATIO)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Randomized 1:1 using pre-provided sealed envelopes; block randomization and stratification per centre using block sizes of 8.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Preprovided sealed envelopes
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Patients were blinded. Personnel were not but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	No information on outcome assessment blinding reported. The outcome was not pre-defined.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	The attrition and exclusions were reported, with reasons but the reasons were not given by group. The drop-out was similar in both arms.

Selective reporting (reporting bias)	• Low risk of bias • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Results were given in percentages and it was unclear what the denominator was.

Bosiers2012 – AMPUTATION (AT 1 year)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Randomized 1:1 using pre-provided sealed envelopes; block randomization and stratification per centre using block sizes of 8.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Preprovided sealed envelopes
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Patients were blinded. Personnel were not but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No information on outcome assessment blinding reported but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	The attrition and exclusions were reported, with reasons but the reasons were not given by group. The drop-out was similar in both arms. The loss to follow-up was higher than the event rate.
Selective reporting (reporting bias)	• Low risk of bias • High risk of bias • Unclear risk of bias	Not applicable.

Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

GERAGHTY2013 – TARGET LESION REVASCULARISATION (RE-INTERVENTION) - PATIENTS

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details except saying it was randomized.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No details but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Outcome assessors were blinded.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Attritions and exclusions and reasons were given by group. The drop-out rate was similar in both arms.
Selective reporting (reporting bias)	• Low risk of bias • High risk of bias • Unclear risk of bias	Not applicable
Other bias	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Patients receiving VIABAHN device were significantly older than those receiving bare nitinol stents.

GERAGHTY2013 – TARGET LESION REVASCULARISATION (RE-INTERVENTION) - LESIONS

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details except saying it was randomized.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No details but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Outcome assessors were blinded.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Attritions and exclusions and reasons were given by group. The drop-out rate was similar in both arms.
Selective reporting (reporting bias)	• Low risk of bias • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Patients receiving VIABAHN device were significantly older than those receiving bare nitinol stents.

GERAGHTY2013 – MORTALITY

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details except saying it was randomized.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No details but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Outcome assessors were blinded.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Attritions and exclusions and reasons were given by group. The drop-out rate was similar in both arms. Loss to follow-up was higher than the event rate.
Selective reporting (reporting bias)	• Low risk of bias • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Patients receiving VIABAHN device were significantly older than those receiving bare nitinol stents.

GERAGHTY2013 – Peri-procedural complications

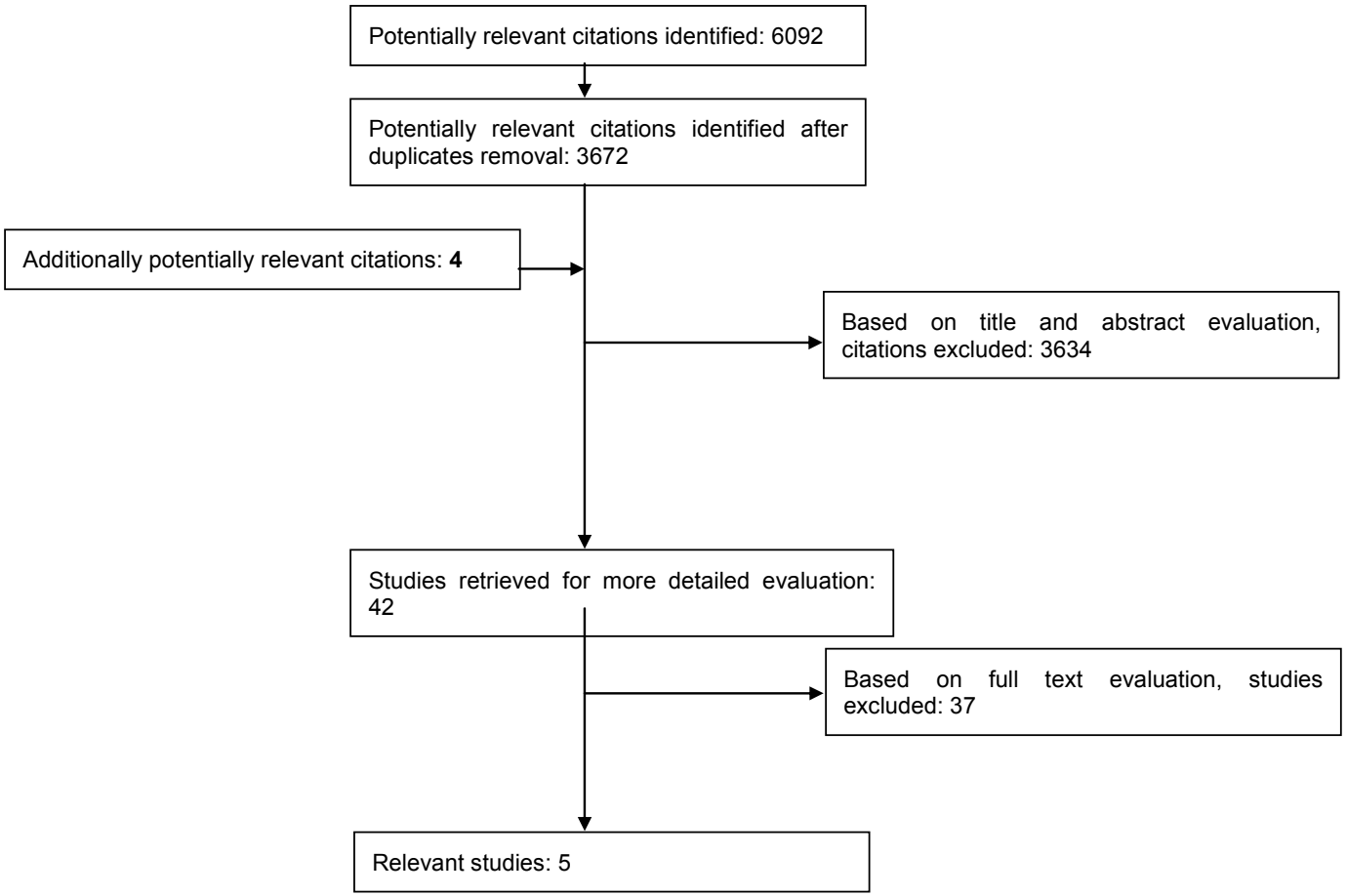
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details except saying it was randomized.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No details but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Outcome assessors were blinded.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Attritions and exclusions and reasons were given by group. The drop-out rate was similar in both arms. Loss to follow-up was higher than the event rate.
Selective reporting (reporting bias)	• Low risk of bias • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Patients receiving VIABAHN device were significantly older than those receiving bare nitinol stents.

GERAGHTY2013 – QUALITY OF LIFE (SF-36) (AT 1 month, 6 months, 12 months, 24 months, 36 months

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details except saying it was randomized.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details.
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	No details and subjective outcome
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Outcome assessors were blinded.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Attritions and exclusions and reasons were given by group. The drop-out rate was similar in both arms.
Selective reporting (reporting bias)	• Low risk of bias • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Patients receiving VIABAHN device were significantly older than those receiving bare nitinol stents.

3.3.4. Autologous vein versus prosthetic bypass

3.3.4.1. Clinical article selection



3.3.4.2. List of excluded studies

Reference	Reason of exclusion
Aalders 1992[3]	Wrong comparison
Aburahma 1999[6]	Wrong study design - not randomized, sequentially assigned
Ahmed 2013[9]	Cochrane protocol, wrong comparison, wrong disease
Albers 2003[12]	Meta-analysis of non-RCTs
Albers2004[11]	Meta-analysis of non-RCTs
Albers 2005[13]	Meta-analysis of non-RCTs
Anon 2009A[2]	Not an RCT
Antoniou 2013[16]	Meta-analysis, wrong comparison
Benoit 2013[22]	Review of RCTs and non-RCTs
Capoccia 2010[40]	Review of non-RCTs
Chikiar 2003[45]	Foreign language
Eickhoff 1983[60]	Outcome data not reported by group but for the whole trial, unable to distinguish data
Fowkes 2008[66]	Review - cross-checked for studies which match the review protocol
Gisbertz 2010[70]	Wrong comparison
Hunink 1994[80]	Review, wrong comparison
Khalilahmed 2012[85]	Wrong comparison - vein cuff
Kruidenier 2012[92]	Review of RCTs and non-RCTs
Leng 2000[97]	Review - cross-checked for studies which match the review protocol
Moody 1992[105]	Wrong comparison - reversed vs insitu procedures
Pereira 2006[109]	Metal-analysis of RCTs and non-RCTs

Reference	Reason of exclusion
Pfaff 2011[110]	Abstract
Ricco 2008[120]	Wrong comparison considers types of bypass
Rollins 2012[121]	Review, wrong comparison
Schanzer 2007[126]	Wrong comparison
Scharn 2008[127]	Wrong comparison
Schulman 1987[133]	Wrong study design - quasi-randomized
Slovut 2012[143]	Review, wrong comparison
Svensson 1989[150]	Not relevant, arteriosclerosis
Tilanus 1985[154]	Critical Limb Ischemia in majority of patients
Twine 2010[157]	Outcomes did not fit our protocol
Vanderzaag 1996[160]	Letter not a primary study
Veith 1986[164]	Wrong study design - quasi-randomized
Vemulapalli 2013[165]	Abstract of a review
Watelet 1997[169]	Wrong comparison - considers reversed vs in situ procedures
Wengerter 1991[170]	Wrong comparison - considers reversed vs in situ procedures
Wilson 1996[173]	Wrong comparison - considers full angioscopic vs in situ procedures
Zilla 1994[176]	Wrong comparison

3.3.4.3. List of included studies

Study	Intervention/comparator	Population	Outcome	Length of study
Klinkert, 2003[88]; Burger, 2000[39]	Reversed saphenous vein versus polytetrafluoroethylene prothesis	Patients with above-knee femoropopliteal bypass graft operation with indication for severe claudication, rest pain and ulceration	Mortality; amputation; re-intervention; peri-operative complications	5 year follow-up
Solakovic, 2008[145]	Reversed saphenous vein versus polytetrafluoroethylene/dacron prosthesis	Patients with above-knee femoropopliteal bypass graft operation with indication for severe claudication, rest pain and ulceration	Mortality; amputation; re-intervention	5 year follow-up
Tofigh, 2007[155]	Reversed saphenous vein graft versus impregnated woven polyester prosthesis	Patients with above-knee femoropopliteal bypass graft operation with indication for severe claudication, rest pain and ulceration.	Mortality; amputation; re-intervention	5 year follow-up
Balotta, 2003[17]	Reversed saphenous vein graft versus polytetraluoroethylene prosthesis	Patients with above-knee femoropopliteal bypass graft with indication for bilateral disabling claudication due to superficial femoral artery occlusion	Mortality, amputation, re-intervention; peri-operative complications	5 year follow-up

3.3.4.4. Quality appraisal

SOLAKOVIC 2008 - MORTALITY

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study says randomization took place with a closed envelope allocation and no further details are given.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Closed envelope allocation, no further details given.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	9 patients lost to follow-up, but does not say from which group.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

SOLAKOVIC 2008 - AMPUTATION

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study says randomization took place with a closed envelope allocation and no further details are given.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Closed envelope allocation, no further details given.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	9 patients lost to follow-up, but does not say from which group.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

SOLAKOVIC 2008 – RE-INTERVENTIONS

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Study says randomization took place with a closed envelope allocation and no further details are given.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Closed envelope allocation, no further details given.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	9 patients lost to follow-up, but does not say from which group.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

TOFIGH 2007 - MORTALITY

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	The author says there was randomization but no further details are given about randomization.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details of allocation concealment.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	6 patients were lost to follow up, details given for each group.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

TOFIGH 2007 - AMPUTATION

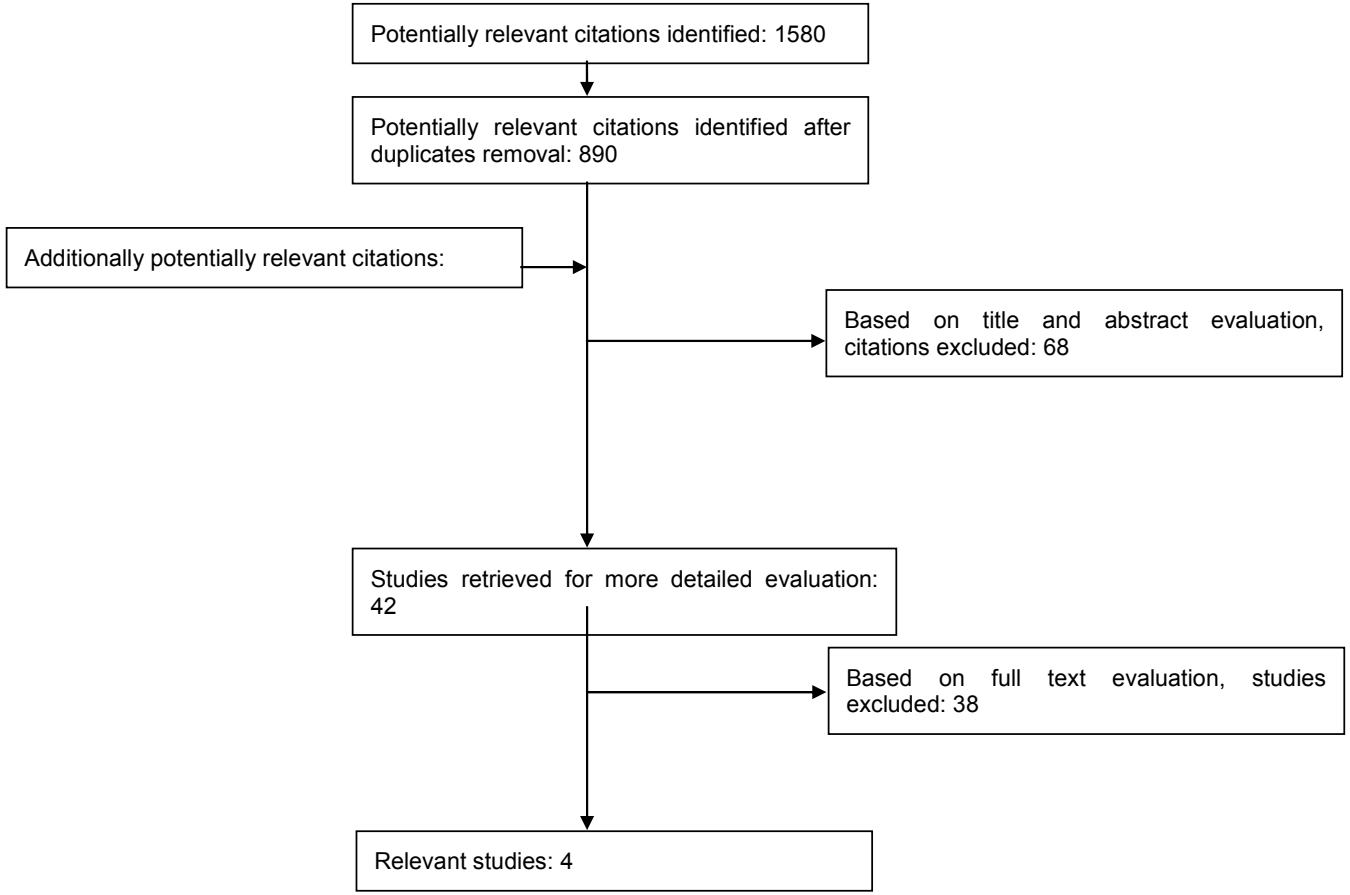
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	The author says there was randomization but no further details are given about randomization.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details of allocation concealment.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	6 patients were lost to follow up, details given for each group
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

TOFIGH 2007 – re-intervention

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	The author says there was randomization but no further details are given about randomization.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details of allocation concealment.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No blinding reported but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	6 patients were lost to follow up, details given for each group
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

3.3.5. Drug-coated balloon angioplasty

3.3.5.1. Clinical article selection



3.3.5.2. List of excluded studies

Reference	Reason of exclusion
Amighi 2008[14]	Not a study about drug coated angioplasty
Banerjee 2012[18]	RCT of cryoplasty
Baumann 2012[19]	Narrative review of drug eluting devices
Bekken 2012[20]	Protocol for a study still ongoing
Biondizoccai 2009[23]	Systematic review of non-randomised studies
Bischoff 2008[24]	Conference abstract
Bosiers 2009[29]	Not a study about drug coated angioplasty
Bradbury 2010[32]	Not a study about drug coated angioplasty
Bradbury 2010a[31]	Not a study about drug coated angioplasty
Bradbury 2010b[34]	Not a study about drug coated angioplasty
Bradbury 2010c[33]	Not a study about drug coated angioplasty
Bradbury 2010d[30]	Not a study about drug coated angioplasty
Brodmann 2013[36]	Not a study about drug coated angioplasty
Cassese 2012[41]	Systematic review - checked for included studies
Conte 2010a[46]	Narrative review of RCT
Das 2009[51]	Not a study about drug coated angioplasty
Diehin 2011[53]	Abstract of protocol of a trial
Dux 2012[59]	Conference session on drug coated balloons
Eskelinen 2007[61]	Review article
Fanelli 2012b[63]	Conference abstract
Fischer 2012[64]	Not a comparison of interest?

Reference	Reason of exclusion
Forbes 2010[65]	Not a study about drug coated angioplasty
Franke 2007[67]	Conference abstract
Gabrielli 2012[68]	Not a study about drug coated angioplasty
Gorenoi 2009[73]	Systematic review of intravascular brachytherapy
Kruidenier 2012[92]	Review article
Liistro 2012[98]	Conference abstract. Full text publication (Liistro 2013) included in review.
Martens 2009[102]	Update of trial still recruiting
Matsagas 2003[103]	Case series of angioplasty
Mccaslin 2013[104]	Systematic review of cryoplasty
Popusoi 2012[111]	Abstract of a case series
Romiti 2008[122]	Systematic review with mixed study designs included
Saxon 2008[125]	Not a study about drug coated angioplasty
Scheinert 2010a[129]	Conference abstract
Schnorr 2013[132]	Narrative review
Shammas 2011[134]	Not a study about drug coated angioplasty
Shammas 2011a[135]	Not a study about drug coated angioplasty
Shammas 2012a[136]	Not a study about drug coated angioplasty
Simpson 2013[142]	Systematic review - checked for included studies
Soder 2000[144]	Not a study about drug coated angioplasty
Spiliopoulos 2010[146]	Not a study about drug coated angioplasty
Sultan 2009[149]	Not a study about drug coated angioplasty
Sultan 2011[147]	Not a study about drug coated angioplasty

Reference	Reason of exclusion
Sultan 2013[148]	Not a study about drug coated angioplasty
Tielbeek 1996[153]	Not a study about drug coated angioplasty
Vanderzaag 1996[160]	Letter not primary study
Vroegindeweij 1992[166]	Not a study about drug coated angioplasty
Werk 2011[171]	Conference abstract

3.3.5.3. List of included studies

Study	Intervention/comparator	Population	Outcome	Length of study
Fanelli et al, 2012[62] **DEBELLUM Study**	Paclitaxel coated balloons Conventional balloon angioplasty	Peripheral arterial disease Fontaine classification IIB, III & IV Superficial femoral, popliteal or below the knee arterial lesions	Mortality Target lesion revascularization per limb Amputation per limb Total major adverse events	6 months follow-up
Liistro et al, 2013[99] **DEBATE-BTK Study**	Paclitaxel coated balloons Standard PTA	Diabetic patients with critical limb ischaemia Rutherford classes 4 to 6 (5 out of 132 class 4) Below the knee arterial lesions	Mortality Major amputation Major adverse events Complete index ulcer healing Time to complete index ulcer healing	12 months follow-up
Tepe et al, 2008[151] **THUNDER Trial**	Paclitaxel coated balloons Uncoated balloons with paclitaxel in contrast medium Standard balloon catheters without paclitaxel	Symptomatic peripheral arterial disease Rutherford classes 1 to 5 Superficial femoral and/or popliteal arterial lesions	Mortality Target lesion revascularization Amputation of target leg above the foot Serious adverse events	6, 12 and 24 months follow up

Study	Intervention/comparator	Population	Outcome	Length of study
Werk et al, 2008[172] **FemPac Trial**	Paclitaxel coated balloons Uncoated balloons	Peripheral arterial disease Rutherford classes 1 to 4 Femoropopliteal arterial lesions	Mortality Target lesion revascularisation Amputation	6 and 18 to 24 months follow-up

3.3.5.4. Quality appraisal

Fanelli 2012 – mortality and amputations

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Computer generated assignments as patients entered angiographic suite.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details on allocation concealment reported
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Single blinded study, only patients blinded to treatment. Operators not blinded but this is unlikely to influence these outcomes.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Outcome assessors not blinded to treatment but this is unlikely to influence these outcomes.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No missing data
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias**	Not applicable.

	• High risk of bias • Unclear risk of bias	

Fanelli 2012 – target lesion revascularization

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Computer generated assignments as patients entered angiographic suite.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details on allocation concealment reported
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Single blinded study, only patients blinded to treatment. Operators not blinded and target lesion revascularization is not defined in the paper.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Outcome assessors not blinded to treatment and target lesion revascularization is not defined in the paper.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No missing data
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Fanelli 2012 – Major adverse events (death, amputation, target lesion revascularization and thrombosis

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Computer generated assignments as patients entered angiographic suite.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details on allocation concealment reported
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Single blinded study, only patients blinded to treatment. Operators not blinded to treatment. Assessment of thrombosis and target lesion revascularization is not defined in the paper.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Outcome assessors not blinded to treatment. Assessment of thrombosis and target lesion revascularization is not defined in the paper.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No missing data
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Unclear if the total number of major adverse events includes double counting of limbs.

Liistero 2013 – mortality and major amputations

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Randomization performed in blocks of 10 with the use of computer generated random digits and the assignments were placed in sealed envelopes
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Unclear if envelopes were opaque. No central allocation of numbers, all done at the study site. No other details reported.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not blinded but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No incomplete data
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Liistero 2013 – minor amputations

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Randomization performed in blocks of 10 with the use of computer generated random digits and the assignments were placed in sealed envelopes
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Unclear if envelopes were opaque. No central allocation of numbers, all done at the study site. No other details reported.
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Study personnel not blinded to the outcome. 'Minor amputations' are not defined within the study.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Outcome assessors not blinded to the outcome. 'Minor amputations' are not defined within the study.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No incomplete data
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Liistero 2013 – major adverse events

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Randomization performed in blocks of 10 with the use of computer generated random digits and the assignments were placed in sealed envelopes
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Unclear if envelopes were opaque. No central allocation of numbers, all done at the study site. No other details reported.
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Study personnel not blinded to the outcome. Outcome defined as post hoc analysis.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Outcome assessors not blinded to the outcome. Outcome defined as post hoc analysis.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No incomplete data
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Liistero 2013 – Complete index ulcer healing

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Randomization performed in blocks of 10 with the use of computer generated random digits and the assignments were placed in sealed envelopes
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Unclear if envelopes were opaque. No central allocation of numbers, all done at the study site. No other details reported.
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Study personnel not blinded to the outcome. Outcome defined as post hoc analysis. No indication how outcome was assessed.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Outcome assessors not blinded to the outcome. Outcome defined as post hoc analysis. No indication how outcome was assessed.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	No incomplete data
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Tepe 2008 – mortality and amputations

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Allocated to treatments according to a 'lot-generated random list'.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Patients and investigators not informed of the assigned intervention however study reports the drug coated balloons had a distinctive appearance that could be recognized by investigators who performed some post-study evaluations.
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Patients and investigators not completely blinded to the interventions but the outcome is objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Unclear if outcome assessors were adequately blinded to the interventions but the outcome is objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	None reported
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Tepe 2008 – target lesion revascularisation and serious adverse events

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Allocated to treatments according to a 'lot-generated andom list'.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	Patients and investigators not informed of the assigned intervention however study reports the drug coated balloons had a distinctive appearance that could be recognized by investigators who performed some post-study evaluations.
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Investigators not informed of the assigned intervention however study reports the drug coated balloons had a distinctive appearance that could be recognized by investigators who performed some post-study evaluations. Outcomes not clearly defined.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Unclear if outcome assessors were adequately blinded to the interventions study reports the drug coated balloons had a distinctive appearance that could be recognized by investigators who performed some post-study evaluations. Outcomes not clearly defined. Assessment of outcomes at 12 and 24 months involved a visit by patient or a telephone call. Not reported how many patients had their assessment by telephone.
Incomplete outcome data (attrition bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	None reported
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Werk 2008 – mortality and amputations

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Centrally done. Portions of the random list were assigned to centres.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details on allocation concealment reported
Blinding of participants and personnel (performance bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Blinding attempted but not guaranteed as of differences in appearance of coated and uncoated balloons. The outcomes are objective and unlikely to be affected by this.
Blinding of outcome assessment (detection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Blinding attempted but not guaranteed as of differences in appearance of coated and uncoated balloons. The outcomes are objective and unlikely to be affected by this.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No missing data reported. Study reports one centre was unable to enroll assigned number of patients. Unclear if the patients enrolled were included in the analysis.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

Werk 2008 - target lesion revascularization

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Centrally done. Portions of the random list were assigned to centres.
Allocation concealment (selection bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No details on allocation concealment reported
Blinding of participants and personnel (performance bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Blinding attempted but not guaranteed as of differences in appearance of coated and uncoated balloons. Target lesion revascularization not defined in study.
Blinding of outcome assessment (detection bias)	• Low risk of bias • **High risk of bias** • Unclear risk of bias	Blinding attempted but not guaranteed as of differences in appearance of coated and uncoated balloons. Target lesion revascularization not defined in study.
Incomplete outcome data (attrition bias)	• Low risk of bias • High risk of bias • **Unclear risk of bias**	No missing data reported. Study reports one centre was unable to enroll assigned number of patients. Unclear if the patients enrolled were included in the analysis.
Selective reporting (reporting bias)	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.
Other bias	• **Low risk of bias** • High risk of bias • Unclear risk of bias	Not applicable.

4. EVIDENCE TABLES BY CLINICAL QUESTION

4.1. Assessment of PAD

4.1.1. Diagnostic test accuracy studies

Reference	Study type and comments on quality	Number of patients	Prevalence	Patient characteristics	Index test	Reference standard	Se and Sp	PPV and NPV	Source of funding
Bueno A, 2010; (Guideline Ref ID 16105)	Prospective study High quality	40 patients (43 segments per patient for a total of 1720 segments; grouped as aorto-iliac (abdominal aorta; common and external iliac aorta), femoro-popliteal (common, deep and superficial femoral; upper popliteal) and infra-popliteal (lower popliteal, TPT, anterior and posterior tibial,	clinical situation: Fontaine stage III 15% and IV 50%	Inclusion: Scheduled for DSA because of lower extremity arterial disease Exclusion: Patients with metal implants Baseline characteristics: 90% men; 60% smokers; 62.5% hypertension; 57.5% diabetes; 15% hyperlipidaemia; 25% ischaemic cardiopathy; 15% renal insufficiency	(1) Duplex ultrasound (abdominal aorta and pelvic iliac arteries scanned and lower limbs to pedal vessels; significant lesions: PSV ratio 2.5 or more, stenosis >50% or no Doppler signal=occlusion) (2) hybrid 3D-contrast-enhanced magnetic resonance angiography (1.5 T). Assessed unaware of patients'	Digital subtraction angiography from abdominal aorta to pedal vessels; angiographers unaware of patients' identity and clinical situation. Maximum time between investigations 15 days.	see below	see below	no financial support

	including retromaleolar ; peroneal; pedal (i.e. foot included))			identity and clinical situation or other tests.	
Effect Size **Stenosis graded for each segment: normal; stenosis <50%; stenosis >50% or occlusion**					
Duplex ultrasound vs. DSA as gold standard (95% CI)					
	Sensitivity	Specificity	Positive predictive value	Negative predictive value	TP, FP, FN, TN
Aorto-iliac: >50% stenosis (280 segments; 10.7% missing)	100% (67.8-100)	99.5% (97-99)	91.6% (59-99)	100% (97-100)	
Aorto-iliac: Occlusion (280 segments; 10.7% missing)	100% (56-100)	100% (67-100)	100% (56-100)	100% (67-100)	10.7%
Femoro-popliteal: >50% stenosis **Occlusion (480 segments)**	87% (78-92) 93.6% (83-98)	98% (96-99) 100% (94-100)	95.2% (87-98) 100% (92-100)	96% (93-97) 95.2% (87-98)	4.58%
Infra-popliteal: >50% stenosis **Occlusion (**	77% (70-83) 88% (83-92)	99% (97-99) 96.4% (91-98)	97% (92-99) 97.6% (94-99)	91.5% (88-93) 84% (77-89)	9.79%
Total: >50% stenosis **Occlusion**	81.4% (76-85) 90% (85-93)	99% (98-99.5) 97% (94-99)	96.2% (92-98) 98.1% (95-99)	94.8% (93-96) 88.4% (83-91)	8.5%
Contrast-enhanced MRA vs. DSA as gold standard (95% CI)					
	Sensitivity	Specificity	Positive predictive value	Negative predictive value	% missing segments
Aorto-iliac: Occlusion **280 segments, 5.7% missing**	100% (69-100)	99% (96-99)	85% (56-97)	100% (98-100)	5.7%
Aorto-iliac: Occlusion **280 segments, 5.7% missing**	100% (56-100)	100% (69-100)	100% (56-100)	100% (69-100)	

Femoro-popliteal: stenosis	**>50%**	97.8% (91-99)	98.3% (96-99)	95% (87-98)	99% (97-99)	1.45%
Occlusion		97% (88-99)	100% (95-100)	100% (93-100)	97.8% (91-99)	
Infra-popliteal: >50% stenosis		88% (82-92)	99% (98-99)	98.8% (95-99)	95.3% (92-97)	4.8%
Occlusion		94.8% (91-97)	97% (93-98)	97.9% (95-99)	92.7% (87-95)	
Total: >50% stenosis		91% (87-94)	99% (98-99)	96.7% (93-98)	97.6% (96-98)	4.01%
Occlusion		95.4% (92-97)	98% (95-99)	98.4% (96-99)	94.7% (91-96)	

Kappa value for interobserver agreement 0.93 (0.91-0.95) for MRA (0.95 [0.93-0.97] aorto-iliac; 0.97 [0.95-0.99] femoro-popliteal; 0.91 [0.88-0.93] infra-popliteal) and 0.72(0.68-0.74) for DSA (0.78 [0.66-0.90] aorto-iliac; 0.69 [0.62-0.75] femoro-popliteal; 0.66 [0.62-0.70] infra-popliteal).

Complete agreement between MRA, DSA and DU in 83.6% of segments; 7.8% different categories in 1 of the 3 tests, and 8.5% missing data.

	Aorto-iliac	Femoro-popliteal	Infra-popliteal	Total
Same results	247	425	766	1438
Different results	2	33	100	135
Missing	31	22	94	147
Total	280	480	960	1720

2x2 tables calculated (from sensitivity, specificity, PPV and NPV and number of patients (excluding the missing data); only calculated for occlusion because >50% stenosis appeared to exclude occluded vessels). Calculation did not reproduce confidence intervals for sensitivity and specificity, so some lack of confidence in 2x2.

		DSA	
CE MRA (whole leg)	100%	<100%	
100%	857	14	871
<100%	41	739	780
	898	753	1651

		DSA	
DUS (whole leg)	100%	<100%	
100%	796	15	813
<100%	88	674	762

		886	689	1575				
Collins R, 2007; (Guideline Ref ID 2434)	Systematic review: to assess stenosis/occlusion. Studies were identified through searches of MEDLINE, EMBASE, BIOSIS Previews, Science Citation Index, LILACS and Pascal from 1996 to April 2004, with update searches in May 2005, handsearching of journals, scanning reference lists of included studies and consultation with experts in the field	A total of 58 studies provided diagnostic accuracy results: Aly, 1998 Ashleigh, 1993 Baum, 1995 Baxter, 1993 Bergamini, 1995 Bostrom, 2001 Catalano, 2004 Cortell, 1996 Cronberg, 2003 Currie, 1995 Davies, 1992 Eiberg, 2001 Eklof, 1998 El-Kayali, 2004 Fletcher, 1990 Grassbaugh,2003 Hany, 1997 Hatsukami, 1992 Heuschmid, 2003 Hirai, 1998 Hoch, 1996	RCTs comparing diagnostic accuracy of different tests to evaluate stenosis and occlusion in patients with peripheral arterial disease	Angiography (with DSA in most studies)	2D PC MRA 2D TOF MRA CE MRA CTA DUS	Dependent on each study	Diagnostic accuracy of tests to diagnose stenosis/occlusion	HTA programme

	Hoch, 1999
	Hofmann, 2004
	Karacagil, 1996
	Koelemay, 1997
	Koelemay, 1998
	Kreitner, 2008
	Lai, 1995
	Lai, 1996
	Laissy, 1998
	Legemate, 1991
	Lenhart, 2000
	Linke, 1994
	Lundin, 2000
	Martin, 2003
	McDermott, 1995
	Meaney, 1999
	Mergelsberg,1986
	Portugaller, 2004
	Puls, 2002
	Rieker, 1996
	Rieker, 1997
	Schafer, 2003
	Sensier, 1996
	Shaalan, 2003
	Snidow, 1995
	Snidow, 1996
	Steffens, 1997
	Steffens, 2003

		Sueyoshi, 1999 Timonina, 1999 Vavrik, 2004 Whyman, 1992 Wilson, 1997 Winterer, 1999 Yucel, 1993 Zeuchner, 1994 Zhang, 2005				
Effect size						
2D PC or 2d TOF MRA						
Study	Stenosis threshold	Results reported by	TP	FP	FN	TN
2D PC MRA; whole leg						
Steffens 1997	50-100%	area of stenosis / occlusion	229	5	5	14
2D TOF MRA; whole leg ≥50% stenosis						
Baum, 1995	50-100%	Segment	527	101	100	460
Houch 1999	50-100%	Segment	161	37	44	302
Houch 1996	50-100%	Segment	172	13	12	155
Snidow 1995	50-100%	Segment	80	76	7	215
Yucel 1993	50-100%	Segment	65	16	6	119
2D TOF MRA: whole leg, ≥70% stenosis						
Yucel 1993	70-100%	Segment	53	5	6	142
2D TOF MRA; whole leg, occlusion						
Baum, 1995	100%	Segment	322	118	76	672
Hoch 1999	100%	Segment	103	17	31	393
Hoch 1996	100%	Segment	101	4	11	236
Yucel 1993	100%	Segment	40	4	0	162

2D TOF MRA; above knee,						
Currie, 1995	50-99%	Segment	25	7	10	38
Lundin 2000	50-100%	Segment	35	20	8	197
Lundin 2000	100%	Segment	13	7	2	238
Timonina 1999	100%	Artery	36	0	1	163
2D TOF MRA: below the knee, 50-100%						
Cortell 1996	50-100%	Segment	172	10	3	208
Eklof 1998	50-100%	Artery	59	2	14	31
Cortell 1996	75-100%	Segment	155	10	3	225
McDermott 1995	diseased or occluded	Segment	124	7	15	70
2D TOF MRA: below the knee, occlusion						
Cortell 1996	100%	Segment	125	7	3	258
McDermott 1995	100%	Segment	95	1	21	99
Eklof 1998	100%	Artery	40	10	7	49
2D TOF MRA: foot						
Eklof 1998	100%	Artery	19	8	3	3
CE MRA						
Study	Stenosis threshold	Results reported by	TP	FP	FN	TN
Whole leg, ≥50% stenosis						
Cronberg, 2003	50-100%	Segment	227	62	20	109
Laissy 1998	50-100%	Segment	104	14	9	393

Lenhart 2000	50-100%	Segment	79	8	4	129
Schafer 2003	50-100%	Segment	138	13	9	416
Steffens, 2003	51-100%	Segment	185	8	1	706
Sueyoshi 1999	50-100%	Segment	67	3	2	351
Winterer, 1999	51-100%	Segment	362	43	14	1361
Whole leg, ≥70% stenosis						
Schafer 2003	76-100%	Segment	110	3	4	459
Steffens, 2003	76-100%	Segment	147	11	4	738
Sueyoshi 1999	75-100%	Segment	53	4	0	366
Vavrik 2004	70-100%	Segment	170	26	17	661
Whole leg; occlusion						
Lenhart 2000	100%	Segment	54	2	4	160
Meaney 1999	100%	Segment	83	16	15	516
Schafer 2003	100%	Segment	72	1	5	498
Steffens, 2003	100%	Segment	85	7	4	804
Sueyoshi 1999	100%	Segment	39	1	0	383
Winterer, 1999	100%	Segment	255	11	13	1502
Above knee, ≥50% stenosis						
Lenhart 2000	50-100%	Segment	24	6	2	83
Lundin 2000	50-100%	Segment	35	18	8	204
Hany 1997	50-100%	Artery	62	7	2	163
Snidow 1996	50-100%	Artery	26	6	0	96
Above knee, ≥70% stenosis						
Vavrik 2004	70-100%	Segment	86	13	9	468
Above knee, occlusion						
Lenhart 2000	100%	Segment	14	0	2	99

Lundin 2000	100%	Segment	13	0	2	250
Hany 1997	100%	Segment	19	1	0	214
Snidow 1996	100%	Segment	18	0	0	110
Below knee ≥50% stenosis						
Kreitner 2008	50-100%	Segment	27	3	11	33
Lenhart 2000	50-100%	Segment	55	2	2	46
Zhang, 2005	51-100%	Segment	252	31	52	207
Below knee ≥70% stenosis						
Vavrik 2004	70-100%	Segment	84	13	8	193
Below knee; occlusion						
Lenhart 2000	100%	Segment	40	2	2	61
Zhang, 2005	100%	Segment	200	22	32	288
Foot						
Zhang, 2005	51-100%	Segment	59	20	16	48
	100%	Segment	50	11	13	69

CTA						
Study	Stenosis threshold	Results reported by	TP	FP	FN	TN
Whole leg; ≥50% stenosis						
Heuschmid 2003	51-100%	Segment	133	40	16	379
Martin 2003	50-100%	Segment	327	61	38	886
Puls 1996	51-100%	Segment	56	17	7	106
Rieker, 1996	50-100%	Segment	111	20	3	193
Catalano, 2004	51-100%	Segment	251	23	3	860
Portugaller, 2004	50-100%	Segment	240	80	21	399
Whole leg; ≥70% stenosis						

Heuschmid 2003	76-100%	Segment	88	7	12	461
Martin 2003	75-100%	Segment	236	20	34	1022
Rieker, 1996	75-100%	Segment	91	6	6	224
Whole leg, occlusion						
Heuschmid 2003	100%	Segment	49	6	5	508
Martin 2003	100%	Segment	202	2	26	1082
Puls 1996	100%	Segment	13	0	0	173
Rieker, 1996	100%	Segment	61	1	1	264
Catalano, 2004	100%	Segment	170	5	5	957
Above knee; ≥50% stenosis						
Rieker 1997	50-100%	Segment	49	2	3	101
Rieker 1997	50-100%	Segment	63	4	2	114
Portugaller, 2004	50-100%	Segment	86	23	3	238
Above knee ≥70% stenosis						
Rieker 1997	75-100%	Segment	28	0	0	127
Rieker 1997	75-100%	Segment	30	0	0	153
Above knee, occlusion						
Rieker 1997	100%	Segment	39	0	2	114
Rieker 1997	100%	Segment	48	1	2	132
Below knee; ≥50% stenosis						
Portugaller, 2004	50-100%	Segment	154	57	18	161

DUS						
Study	Stenosis threshold	Results reported by	TP	FP	FN	TN
Whole leg; ≥50% stenosis						
Aly, 1998	50-100%	Segment	404	27	34	2643

Beramini 1995	50-100%	Segment	94	13	24	273
Hatsukami 1992	50-100%	Segment	73	6	12	152
Linke 1994	50-100%	Segment	41	4	2	87
Sensier, 1996	50-100%	Segment	214	26	28	201
El-Kayali 2004	50-100%	Segment	123	15	3	216
Legemate, 1991	50-100%	Segment	179	30	33	676
Ashleigh, 1993	50-100%	Limb	69	2	0	5
Baxter 1993	50-100%	Limb	32	1	3	4
Whole leg; occlusion						
Aly, 1998	100%	Segment	272	18	25	2793
Beramini 1995	100%	Segment	76	10	13	305
Hatsukami 1992	100%	Segment	51	3	6	173
Linke 1994	100%	Segment	14	0	5	115
Sensier, 1996	100%	Segment	166	11	21	271
Zeuchner, 1994	100%	Segment	50	3	3	266
Legemate, 1991	100%	Segment	103	6	9	800
Ashleigh, 1993	100%	Limb	36	7	6	27
Whole leg; other stenosis thresholds						
Zeuchner, 1994	50-99%	Segment	12	1	4	305
Ashleigh, 1993	Suitability for angioplasty	Limb	25	7	4	42
Lai, 1995	Selection for angioplasty	Limb	14	9	9	54
Above knee; ≥50% stenosis						
Bergamini 1995	50-100%	Segment	83	12	8	194
Fletcher 1990	50-100%	Segment	59	12	8	89

Hatsukami 1992	50-100%	Segment	34	2	6	73
Lai, 1996	50-100%	Segment	124	12	42	354
Lundin 2000	50-100%	Segment	27	7	11	207
El-Kayali 2004	50-100%	Segment	74	9	1	171
Whyman 1992	51-100%	Segment	41	1	0	1
Eiberg, 2001	50-100%	Limb	50	8	1	35
Shaalan, 2003	50-100%	Limb	97	12	5	100
Above knee; ≥70% stenosis						
Fletcher 1990	75-100%	Segment	14	2	0	40
Lai, 1996	76-100%	Segment	83	8	44	397
Above knee; occlusion						
Currie, 1995	100%	Segment	25	4	5	146
Fletcher 1990	100%	Segment	45	7	5	111
Hatcukami 1992	100%	Segment	29	0	1	85
Hirai, 1998	100%	Segment	64	0	1	454
Lai, 1996	100%	Segment	50	0	12	470
Lundin 2000	100%	Segment	13	1	1	237
Whyman 1992	100%	Segment	26	1	0	16
Davies 1992	100%	Limb	27	1	1	36
Mergelsberg	100%	Limb	25	6	1	17
Above knee; other stenosis thresholds						
Bostrom, 2001	Suitable for endovascular intervention	Segment	93	11	6	53
Hirai, 1998	50-99%	Segment	43	3	9	399
Davies 1992	50-99%	Limb	16	1	1	47
Below knee, ≥50% stenosis						

Bergamini 1995	50-100%	Segment	11	1	16	79
Hatsukami 1992	50-100%	Segment	27	1	6	44
Karacagil 1996	51-100%	Segment	211	47	36	186
El-Kayali 2004	50-100%	Segment	49	6	2	45
Below knee; occlusion						
Hatsukami 1992	100%	Segment	25	0	5	48
Karacagil 1996	100%	Segment	199	44	34	203
Koelemay, 1998	100%	Segment	457	77	324	655
Koelemay, 1997	100%	Segment	84	21	33	121
Wilson 1997	100%	Segment	80	1	5	36
Grassbaugh 2003	100%	Artery	36	6	12	56
Below knee; other stenosis thresholds						
Koelemay, 1998	Severe stenosis	Segment	813	99	257	344
Koelemay, 1997	Severe and occluded	Segment	136	23	52	48
Foot						
Hofmann 2004	Target vessels suitable for surgery	Segment	54	11	30	45

Reference	Study type and comments on quality	Number of patients	Prevalence	Patient characteristics	Index test	Reference standard	Se and Sp	PPV and NPV	Source of funding
Eiberg JP, 2010; Guideline Ref ID 16106)	Prospective study Moderate (sample may not be representative)	169 patients (15 segments per patient, including foot; grouped as supragenicular (common femoral, deep femoral, proximal femoral, distal femoral and above-the-knee popliteal) and infragenicular (popliteal below the knee, TPT, anterior and posterior tibial and peroneal artery, dorsalis pedis and medial and lateral plantar) total 2535 segments). Only 169/530 eligible (32%) enrolled, limited by availability of DUS equipment and examiners, and patient consent	Intermittent claudication 25%; critical limb ischaemia 75%	Inclusion: Patients admitted with lower limb ischaemia scheduled for arteriography as part of treatment Exclusion: Patients with previous infra-inguinal reconstructions Baseline characteristics: median age 71 (interquartile range 62-77) years; 63% male; ankle BP 60 (IQ range 44-80)mmHg; ankle-brachial index 0.38 (IQ range 0.30-0.53);	Duplex ultrasound (the day before DSA) from common femoral artery to pedal arteries after 15 minutes rest (femoral and anterior tibial, patient supine; popliteal, peroneal and posterior tibial patients in lateral decubitus position); <50% stenosis if peak systolic velocity <2;	Digital subtraction angiography from distal aorta to pedal arteries; classified as <50% stenosis or ≥50% stenosis (including occlusions), or non-diagnostic if neither genuine vessel nor unnamed collaterals could be visualised due to inadequate amount of contrast.	see below	see below	Danish Medical Research Council, Frode V. Nyegaard and Wife's Foundation and the Kathrine and Vigo Skovgaards Foundation

			symptoms: claudication <300m: 25%, rest pain 31%, tissue loss 44%; type I or type II diabetes 31%; renal insufficiency (creatinine >150mmol/L) 6%.	≥50% stenosis if PSV ≥2.	

Effect Size

Overall agreement "good": kappa 0.67 (0.64-0.70)

Agreement according to level or severity of disease (1st p value compares supra- and infra-genicular segments; 2nd p value compares intermittent claudication and critical limb ischaemia) ≥50% including occlusions. 2x2 tables calculated from the sensitivity, specificity, PPV and NPV and the number of segments; confidence intervals reproduced closely, so we have confidence in the calculations.

	Supragenicular segments (n=845)	Infragenicular segments (n=1690)	All segments (n=2535)
Kappa	0.75 (0.70-0.80)	0.63 (0.59-0.67) p<0.0001	0.67 (0.64-0.70)
Sensitivity	0.88 (0.85-0.91)	0.88 (0.85-0.90) NS	0.88 (0.86-0.89)
Specificity	0.88 (0.84-0.91)	0.75 (0.71-0.78) p<0.0001	0.79 (0.77-0.82)
PPV	0.93 (0.90-0.95)	0.83 (0.81-0.86) p<0.01	0.87 (0.85-0.88)
NPV	0.81 (0.77-0.85)	0.81 (0.77-0.84) NS	0.81 (0.78-0.84)
Technical success rate:			
DUS	100% (844)	93% (1569) p<0.001	95% (2413)
DSA	99% (839)	93% (1573) p<0.001	95% (2412)
2x2	DSA Positiv Negative	DSA Positive Negative	DSA Positive Negative

		e										
TP, FP, FN, TN (calculated)	DUS +ve	471	35	506	DUS +ve	879	180	1059	DUS +ve	1358	203	1561
	negative	64	274	338	negative	120	511	631	negative	185	789	974
		535	309	845		999	691	1690		1543	992	2535
	Intermittent claudication (n=615)				Critical limb ischaemia (n=1860)				All segments (n=2535)			
Kappa	0.63 (0.56-0.70)				0.70 (0.66-0.73) NS				0.67 (0.64-0.70)			
Sensitivity	0.88 (0.85-0.91)				0.87 (0.85-0.89) NS				0.88 (0.86-0.89)			
Specificity	0.75 (0.68-0.80)				0.82 (0.79-0.85) p<0.01				0.79 (0.77-0.82)			
PPV	0.87 (0.83-0.90)				0.86 (0.84-0.88) NS				0.87 (0.85-0.88)			
NPV	0.77 (0.70-0.82)				0.84 (0.81-0.86) p<0.01				0.81 (0.78-0.84)			
Technical success rate:												
DUS	96% (589)				95% (1765) NS				95% (2413)			
DSA	91% (562)				96% (1790) p<0.001				95% (2412)			
2x2	DSA	Positive	Negative		DSA	Positive	Negative		DSA	Positive	Negative	
TP, FP, FN, TN (calculated)	DUS +ve	353	53	406	DUS +ve	887	144	1031	DUS +ve	1358	203	1561
	negative	48	161	209	negative	133	696	829	negative	185	789	974
		401	214	615		1020	840	1860		1543	992	2535

Reference	Study type and comments on quality	Number of patients	Prevalence	Patient characteristics	Index tests	Reference standard	Se and Sp	PPV and NPV	Source of funding
Gjonnaess E, 2006; (Guideline Ref ID 16138)	Prospective Moderate quality (time between investigations not stated)	58 patients (15 segments each for total of 870 segments; segments pooled into supra-inguinal [Aorta+ Common iliac artery+ External iliac artery]; thigh [Common femoral artery + Deep femoral artery + Superficial femoral artery] and knee regions [Popliteal artery+ Tibio-peroneal trunk	Significant stenoses: ≥50% 61/870 and occlusions 61/870 segments	Inclusion: Patients with intermittent claudication (Fontaine stage IIa/IIb) referred for angiography of the lower extremities Exclusion: previous vascular or endovascular treatment Baseline characteristics: 36 men and 22 women; median age 66.5 years (range 47-80); previous cardiac infarction 4 patients; angina 5; heart failure 0; hypertension 24; hypercholesterolaemia 19; chronic obstructive pulmonary disease	(1) Gadolinium-enhanced magnetic resonance angiography and (2) colour duplex ultrasound (stenosis defined as significant [>50%] when 100% rise in Doppler peak velocity compared to velocities in normal adjacent [proximal or distal] segment; occluded if Doppler signals absent)	Digital subtraction angiography	see below	see below	Pfizer AS, Norway

	artery])		5;diabetes 7; renal failure 0					
Stenosis >50% or occlusion combined to "positive" category.								
Segments (classified as 'above the knee')		Stenosis ≥50% (50-99%)			Occlusion (100%)			
Aorta		4			0			
Common iliac artery		10			5			
External iliac artery		4			3			
Common femoral artery		3			5			
Deep femoral artery		5			1			
Superficial femoral artery		18			34			
Popliteal artery		9			4			
Tibio-peroneal trunk artery		8			9			
Total		61			61			
Effect Size (for combined stenosis 50-99% and occlusion)								
	Sensitivity	Specificity	PPV	NPV	Kappa	2 x 2 calculated		
Magnetic resonance angiography	94% (89-98)	95% (93-97)	76% (69-83)	99% (98-100)	0.81 (0.74-0.87)	115	37	152
						7	711	718
						122	748	870
Duplex ultrasound	70% (61-78)	98% (96-99)	82% (74-90)	95% (94-97)	0.72 (0.65-0.79)	85	15	100
						37	733	770
						122	748	870
Suprainguinal region (intrarenal aorta, CIA, EIA):	96% (90-100)	94% (91-97) 96% (93-98)	64% (50-79) 67% (50-83)	100% (99-100) 99% (98-100)	0.74 (0.63-0.85) 0.74 (0.62-0.86)			

MRA **DU**	91%	(79-100)				
Thigh region (CFA, DFA, SFA): **MRA** **DU**	92% 76%	(86-99) (66-87)	95% (92-97) 99% (98-100)	80% (71-89) 94% (88-100)	98% (97-100) 95% (92-97)	0.82 (0.72-0.93) 0.81 (0.71-0.92)
Knee region (popliteal artery and TPT: **MRA** **DU**	93% 33%	(84-100) (14-52)	96% (94-99) 98% (96-100)	80% (67-93) 67% (40-93)	99% (97-100) 91% (87-95)	0.84 (0.71-0.97) 0.40 (0.27-0.52)

Both duplex ultrasound and magnetic resonance angiography had a tendency to overestimate the length of the lesion.

	Too short	Correct (within 2cm of DSA measurement)	Too long
Magnetic resonance angiography	9%	70%	21%
Duplex ultrasound	7%	65%	28%

All 870 segments were successfully visualised with magnetic resonance angiography, but duplex ultrasound failed to visualise 10% segments in the suprainguinal region; 2% in the thigh region and 13% in the knee region.

Reference	Study type and comments on quality	Number of patients	Prevalence	Patient characteristics	Index test	Reference standard	Se and Sp	PPV and NPV	Source of funding
Kos S, 2009; (Guideline Ref ID 16119)	Prospective High quality	20 patients (14 segments per foot (distal anterior and posterior tibial arteries; distal peroneal:communicating and perforating branches; dorsal; common, medial and lateral plantar;medial and lateral tarsal; arcuate; pedal arch; deep perforating) [60% of patients had left foot measured and 40% right foot] for a total of 280 segments)	All patients had peripheral arterial occlusive disease diagnosed by an experienced angiologist; Fontaine stage I (complicated by e.g. acral lesions) 5 patients (25%); stage II with claudication limiting quality of life 13 patients (65%); stage III 1 patient (5%); stage IV 1 patient (5%)	Inclusion: Patients with confirmed PAOD referred for percutaneous transluminal angiography Exclusion: contraindications to MRI; estimated glomerular filtration rate <30mL/min/1.73 m2 body surface area Baseline characteristics: 9 women and 11 men; mean age 71.8 (range 58-83) years; smoker 60%; diabetes 40%; arterial hypertension 80%; dyslipidaemia 50%; mean ankle-brachial index 0.91 (range 0.59-1.26)	Contrast-enhanced magnetic resonance angiography (mean of 1.5 days [range 1-7 days] after DSA); 2 readers performed consensus reading in random manner; readers blinded to patient name, clinical history and results of other	Digital subtraction angiography with selective imaging of pedal vessels; 2 readers performed consensus readings	see below	see below	none stated

					examination.	
Stenosis graded for each segment: grade 0 = no stenosis; grade 1 = 1-49% stenosis; grade 2 = 51-99% stenosis; grade 3 = occlusion <50% of segment; grade 4 = occlusion >50% of segment; arterial visualisation grade 1=excellent; 2=good; 3=moderate; 4=poor; 5=none. Mean score for arterial visibility DSA 2.89 (SEM 0.11) and MRA 2.70 (0.10), NS.						
235/280 (83.9%) segments usable; 39 (13.9%) suboptimal and 6 (2.2%) unusable						
Effect Size						
156/280 segments had any grade of stenosis or occlusion on DSA (128 [82%] rated as clinically significant i.e. ≥50% stenosis or occlusion).						
MRA overestimated lesions in 26/280 (9.3%) segments and underestimated 21/280 (7.5%, including 17 [13.3%] with clinically significant stenosis or occlusion).						
MRA:	DSA					
	Occlusion ≥50% of segment	Occlusion <50% of segment	Stenosis ≥50%	Stenosis <50%	Normal	
Occlusion ≥50% of segment	90	0	0	0	0	90
Occlusion <50% of segment	4	12	2	0	0	18
Stenosis 50-99%	2	0	7	4	2	15
Stenosis <50%	2	0	4	20	18	44
Normal	3	2	0	4	104	113
	101	14	13	28	124	280
MRA vs. DSA in detecting clinically significant lesions i.e. ≥50% stenosis or occlusion						
	Sensitivity	Specificity	PPV	NPV	Accuracy	
All segments (≥50% including occlusion)	91.4%	96.1%	95.1%	93.0%	93.9%	

Reference	Study type and comments on quality	Number of patients	Prevalence	Patient characteristics	Index test	Reference standard	Se and Sp	PPV and NPV	Source of funding
Kreitner KF, 2008; (Guideline Ref ID 206)	Prospective High quality	22 patients (7 vascular segments per patient: distal anterior tibial; distal posterior tibial; distal peroneal; dorsalis pedis; lateral plantar; medial plantar; pedal arch; total 154 segments)	10 moderate and 10 severe claudication; 1 ischaemic gangrene and 1 minor tissue loss with non-healing ulcer	Inclusion: patients with peripheral arterial occlusive disease Exclusion: Baseline characteristics: 14 men and 8 women; mean age 64 years (range 43-83 years); ankle-brachial index ranged from 0.2 to 1.64 (mean 0.71)	Contrast-enhanced magnetic resonance angiography of the calf and entire foot; image analysis performed by 2 readers in random order after interval of 6 weeks, blinded to result of DSA, patient identity and clinical history	Digital subtraction angiography of the ankle and pedal stations within 7 days of MRA; read after 4-week interval by 2 readers	not stated and insufficient data to calculate	not stated and insufficient data to calculate	not stated

Segments classified as patent or occluded; patent divided into stenosis ≤50% (including no stenosis) or >50%.

Image quality scored 1=excellent; 2=good; 3=moderate; 4=non-diagnostic. Motion artefacts scored 1=none, 2=slight, 3=moderate, 4=severe.

Higher image quality and fewer motion artefacts for MRA (1.32 [0.84] for MRA vs. 1.77 [0.61] for DSA, p=0.021 and 1.32 [0.84] vs. 1.95 [0.72], p=0.008 respectively). Intraobserver agreement good (kappa = 0.78) for image quality and moderate (kappa = 0.46) for motion artefacts.

Effect Size

	No. of arterial segments seen							
	MRA and	Neither	MRA only	DSA only	Total	Kappa	95% CI	p value

	DSA							
Anterior tibial	18	3	1	0	22	0.83	0.68-1.32	1.00
Posterior tibial	22	0	0	0	22	1.00	1.00-1.00	1.00
Peroneal	17	4	1	0	22	0.86	0.60-1.12	1.00
Dorsalis pedis	20	2	0	0	22	1.00	1.00-1.00	1.00
Lateral plantar	21	1	0	0	22	1.00	1.00-1.00	1.00
Medial plantar	18	3	1	0	22	0.83	0.51-1.15	1.00
Pedal arch	21	1	0	0	22	1.00	1.00-1.00	1.00
Overall	137	14	3	0	154	0.89	0.77-1.00	0.25

Overall agreement “very good”; but on DSA, significantly more patent vessel segments assessed as partially occluded than on MRA (p=0.004)
Of the 137 patent vessels visualised by both techniques:

	Characterised by DSA:		
Characterised by MRA:	With segmental occlusion	Without segmental occlusion	Total
With segmental occlusion	23	5	28
Without segmental occlusion	20	89	109
Total	43	94	137

Reference	Study type and comments on quality	Number of patients	Prevalence	Patient characteristics	Index test	Reference standard	Se and Sp	PPV and NPV	Source of funding
Napoli A, 2011; (Guideline Ref ID 16355)	Prospective study High quality	212 patients; 7392 segments; 1060 regions Pelvic and leg arteries were imaged (intrarenal aorta, common iliac, external iliac, internal iliac, common femoral, deep femoral, superficial femoral, polipteal, tibiofibular trunks, anterior tibial, peroneal, posterior tibial, including dorsalis pedis and	By DSA: atherosclerotic lesions detected in 6126 / 7420 (82.6%) arterial segments; 657 (62%) vascular regions; 210 (99.1% patients). Atherosclerotic lesions classified as: grade 1 – 1961 (32%) segments; grade 2 – 1041 (17%) segments; grade 3 – 2994 (48.9% segments) and grade 4 occlusion in 130 (2.1%) segments.	Patients with symptomatic PAD (Fontaine stage IIa-IV), positive ABI index test results, and referred for imaging of the abdominal aorta and in-flow and run-off arteries after duplex US. Baseline characteristics: 168 men + 44 women; mean age 62 years (men), 68 years (women) – range 41-88; current smokers 123 (SD 58), previous smokers 34 (SD 16); diabetes 176 (83); BMI 28 (5.0); Fontaine IIa – 97 (45.8); Fontaine IIb – 55 (25.9); Fontaine III – 34 (16); Fontaine IV – 26	Multidetector CT angiography using 64 section scanner and Visual Station for visualisation (MD-CTA blinded to DSA)	Digital subtraction angiography (DSA blinded to CTA)	see below	see below	None mentioned

	plantar arteries (i.e. including foot)	(12).

Stenosis graded visually for each segment: grade 1 = no / mild stenosis (≤49% luminal narrowing); grade 2 = moderate stenosis (50-69% luminal narrowing); grade 3 severe stenosis (70-99% luminal narrowing); grade 4 = occlusion (100% luminal blockage)

Effect Size (≥70% stenosis)

Segments

	DSA (positive)	DSA (negative)	Total
CT (positive)	307241	138	3210
CT (negative)		4141	4182
Total	3113	4279	7392

Diagnostic accuracy of CTA vs DSA fro detecting clinically relevant steno-occlusive disease at segmental level.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Whole leg + 70% stenosis	99% (3072/3113)	97% (4141/4279)	96% (3072/3187)	99% (4141/4180)

Adverse events: 4 patients experienced 6 adverse events following DSA (2 femoral false aneurysms, 4 large groin haematomas) and 2 patients developed a mild skin reaction 1-6 hours after iv administration of the contrast agent during CT angiography.

Reference	Study type and comments on quality	Number of patients	Prevalence	Patient characteristics	Index test	Reference standard	Se and Sp	PPV and NPV	Source of funding
Scherntha ner R, 2008; (Guideline Ref ID 197)	Prospective study Moderate quality (not all vessel segments visualised during DSA due to ethical considerations concerning exposure of patient to more radiation than required for clinical purposes.)	50 patients; 1351 vessels	358/1351 significant stenoses by DSA; 247 occluded by DSA	Patients referred for DSA of the lower legs due to known or suspected peripheral arterial occlusive disease. 27 men + 23 women; mean age 68 years (range 43-90 years)	Multidetect or CT angiograph y using 16-row scanner and MulitPathC PR for visualisatio n (MD-CTA blinded to DSA) of aorta and run-off vessels at least 1 day prior to DSA (mean 12 days, range 1-30 days). From the level of the renal arteries to the mid-foot	Digital subtraction angiograph y (DSA blinded to CTA); not all vessel segments visualised during DSA due to ethical considerati ons concerning exposure of patient to more radiation than required for clinical purposes.	see below	see below	Fonds zur Förderung der wissen-schaftlichen Forschung (FWF Austria)

Stenosis graded visually for each segment: grade 0 = healthy; grade 1 = 1-49% stenosis (i.e. patent); grade 2 = 51-69% stenosis (no haemodynamic significance); grade 3 = 70-99% stenosis (haemodynamically significant); grade 4 = 100% stenosis (occlusion); grades 3 and 4 combined to "positive" category.

Stenosis length graded as: short (<1cm); 1-3cm; 3-5cm; 5-10cm; entire segment.

Number of lesions within each segment graded as: single or multiple lesions per segment.					
Effect Size **Segments (same table as above but divided as above and below knee)**					
Iliac plus femoropopliteal arteries (above knee)			DSA		
CTA	100%	70-99%	50-69%	<50%	
100%	**107**	**0**	**0**	**0**	**107**
70-99%	**2**	**83**	**4**	**0**	**89**
50-69%	**0**	**2**	**81**	**6**	**89**
<50%	**0**	**0**	**6**	**521**	**527**
	109	**85**	**91**	**527**	**812**
Intrapopliteal arteries (below knee)					
CTA	100%	70-99%	50-69%	<50%	
100%	**138**	**0**	**0**	**0**	**138**
70-99%	**0**	**23**	**1**	**0**	**24**
50-69%	**0**	**3**	**35**	**2**	**40**
<50%	**0**	**0**	**0**	**337**	**337**
	138	26	36	339	539
Above knee ≥ 70% stenosis: sensitivity = 99%; specificity = 99.4% **Below knee ≥ 70% stenosis: sensitivity = 98.2; specificity = 99.7%**					

Study ID	Method	Patient characteristics	Index test and reference standard	Outcomes	Critical appraisal of study quality
Ref Andreisek 2007	• **Design**: Diagnostic cohort study • **Source of funding**: Other author(s) funded by industry (One author is employee of GE Healthcare Systems (MRA manufacturer)) • **Setting**: Conducted in Switzerland; Setting: Diagnostic radiology institute • **Sample size**: 31 patients (465 segments examined with DSA; 620 on MRA bolus chase)	• **Eligibility criteria:** Diabetes and peripheral arterial disease • **Exclusion criteria:** None stated • **Patient characteristics**: • Consecutive patients with diabetes and PAD referred to Institute of Diagnostic Radiology for elective DSA between July 2004 and December 2004 • Age - Mean (range): 67 years (43 to 81). Gender (M:F): 23:8. Ethnicity: Not stated • **Disease characteristics:** Method of	**Index test**: Magnetic resonance angiography - Contrast enhanced MRA. Standard 3-station bolus-chase MRA (20 segments). Gadobutrol contrast agent 12ml as 6ml at 1.0ml/s, then 6ml at 0.6 ml/s, followed by saline 25ml at 1.0ml/s, then 30ml saline at 1.0 ml/s. Mask data images subtracted from the contrast enhanced images and maximum intensity projection used. Images evaluated by 2 radiologists. Only diseased leg images analysed. Further details: Field strength for MRA: 1.5 Tesla. Foot not included in scan (Calf arteries (tibiofibular trunk, anterior and posterior tibial arteries, peroneal arteries); Thigh (Common and superficial femoral arteries, popliteal artery)). Type of coil for MRA: Phased-array (12-element quadrature phased-array coil). **Index test 2**: Magnetic resonance angiography - Contrast enhanced MRA. Time Resolved Imaging of Contrast Kinetics (TRICKS) MRA performed (segments 10-20); eleven 3D data sets acquired, 121 s after	Whole leg, ≥ 50% stenosis per segment DSA / MRA: 84 / 13 / 97; 21 / 182 / 203; 105 / 195 / 300 Above knee, >50% stenosis DSA / MRA: 20 / 3 / 23; 4 / 96 / 100; 24 / 99 / 123 Below knee ≥50% stenosis DSA / MRA: 64 / 10 / 74; 17 / 86 / 103; 81 / 96 / 177	**See QUADAS**

	assessment /diagnosis not stated • Overall: Most patients (26/31) had intermittent claudication (Fontaine IIa or Rutherford 1 or 2 (n=10); Fontaine IIb or Rutherford 3 (n=16)); rest pain (Fontaine III or Rutherford 4; n=1); chronic trophic foot lesions, with non-healing ulceration or focal gangrene (Fontaine IV or Rutherford 5 or 6, n=4) • Diabetes (16% patients with type I diabetes mellitus, 84% type II).	contrast agent Gadobutrol (6 ml at 1.0ml/s). Mask data images subtracted from the contrast enhanced images and maximum intensity projection used. Images evaluated by 2 radiologists, with 3 weeks between bolus chase and TRICKS. Only diseased leg images analysed. Test conducted after standard 3-station bolus-chase MRA in the same session Further details: Field strength for MRA: 1.5 Tesla. Foot included in scan (Calf arteries (tibiofibular trunk, anterior and posterior tibial arteries, peroneal arteries); Foot arteries (dorsal pedal artery, medial and lateral plantar arteries, pedal arch)). Type of coil for MRA: Phased-array (12-element quadrature phased-array coil). **Reference standard**: Digital subtraction angiography. Intra-arterial fine needle DSA performed by experienced angiographer (15 years). Multiple manual injections of 40-60 ml non-ionic iodinated iso-osmolar contrast material (32 mg iodine per	CE MRA time resolved sequence, below knee (calf only) ≥ 50% stenosis MRA DSA: 77 / 9 / 86 17 / 88 / 105 94 / 97 / 191 CE MRA time resolved sequence, below knee (calf and foot) ≥ 50% stenosis MRA DSA: 100 / 15 / 115 34 / 141 / 175 134 / 156 / 290 CE MRA foot ≥50% MRA DSA: 23 / 6 / 29 17 / 53 / 70 40 / 59 / 99

		100 ml iodixanol per kg body weight); anterior and lateral projections for calf and pedal vessels. Concurrent medication/care: None Further details: Foot included in scan (Calf arteries (tibiofibular trunk, anterior and posterior tibial arteries, peroneal arteries); Thigh (Common and superficial femoral arteries, popliteal artery); Foot arteries (dorsal pedal artery, medial and lateral plantar arteries, pedal arch)).	

Study ID	Method	Patient characteristics	Intervention(s)
Ref **Balzer 2005**	**Design**: Retrospective analysis **Source of funding**: No funding (Authors declared no conflict of interest) **Sample size**: 100 patients; 2200 vessels examined	**Eligibility criteria:** Retrospective analysis of patients receiving tests for treatment planning between January 2003 and December 2003. 615 patients but only 100 selected for analysis **Patient characteristics**:61 men (mean age 63 years, SD 11) + 39 women (mean age 67 years, SD 11)	**Index test:** Magnetic resonance angiography - Contrast enhanced MRA. Moving table technique. Patient in supine position, feet first. Care bolus method for contrast agent: iv bolus of single body weight adjusted dose of contrast agent - Gadobutrol 20ml if >70kg or 15ml if <70kg; 0.7ml/s, then saline 10ml at 0.5ml/s, then 30ml saline at 1.0 ml/s. Plain images subtracted from the contrast enhanced images and maximum intensity projection used. Images evaluated by 2 experienced radiologists. Field strength 1.5 Tesla. Peripheral angiography array surface coil (lower leg) and body array surface coil

Study ID	Method	Patient characteristics	Intervention(s)
			(pelvis). **Reference standard:** Digital subtraction angiography. 5F pigtail catheter via the common femoral artery, using a step translation technique. Care bolus method for contrast agent: iv bolus of iodixanol 320 mg/ml via an automatic power injector and flow rates according to region - abdominal aorta: 30 ml at flow rate 15 ml/s; pelvic and peripheral arteries: 80 ml, flow rate 10 ml/s. Images evaluated by 2 experienced radiologists. Local anaesthesia to right or left groin using 10ml Scandicain 1%.
Stenosis graded visually for each segment: normal; <50% stenosis; 50-70% stenosis; >70% stenosis; 100% stenosis (occlusion).			
Effect sizes			
All arteries occlusions (observer 1)	**DSA**		
MRA	100%	<100%	
100%	**331**	**38**	**369**
<100%	**3**	**1691**	**1694**
	334	**1729**	**2063**
Note: quoted sensitivity and specificity in the table do not agree with those calculated using figures in the text: for observer 1 (observer 2) Sensitivity 100% (100%) , Specificity 98.1% (99.8%), PPV 90.5% (99.0%), NPV 100% (100%); no confidence intervals reported			

Study ID	Method	Patient characteristics	Index test and reference standard	Outcomes	Critical appraisal of study quality
Ref Burbelko 2013[38]	• **Design**: Diagnostic cohort study • **Source of funding**: Funding not stated (University hospitals) • **Setting**: Conducted in Switzerland; Setting: Hospital • **Sample size**: 152 patients (406 lesions)) • **Duration**: Up to 30 days between tests	• **Eligibility criteria:** All patients who underwent peripheral MRA for chronic symptomatic peripheral arterial occlusive disease between August 2006 to July 2008 (437 patients); 209 patients excluded because did not require DSA in the course of endovascular treatment or as additional imaging before bypass surgery because of suboptimal imaging quality; 88 patients excluded from analysis because delay between MRA and DSA >30 days; 36 patients with renal failure excluded from the analysis • **Patient characteristics**: • Age - Mean (range): 71.6 years (43 to 94).	**Index test** (n=152): Magnetic resonance angiography - Contrast enhanced MRA. Patients in supine position; bolus triggering technique. 3D gradient echo. Contrast enhancement: gadolinium-chelate at 0.1 mmol/kg body weight at 2ml/s, followed by 20ml saline. The series obtained before contrast enhancement was subtracted and angiograms created using maximum-intensity-projection algorithm. Images evaluated by 2 blinded radiologists with more than 10 years' experience. Field strength for MRA: 1.5T. Foot not included in scan (Arteries scanned: distal aorta; common, internal and external iliac arteries; Common, deep and superficial femoral arteries; popliteal (thigh); tibiofibular trunk; anterior and posterior tibial and fibular artery.). Type of coil for MRA: Phased-array (Specialised circular polarised array coil). **Reference standard**: (n=152) Digital subtraction angiography. Access depended on examination goal and level of lesions: most had retrograde contralateral femoral access. Radiologist with 14 years experience read the images with full knowledge of	Whole leg >50% stenosis (occlusion implied too) DSA / MRA: 255 / 22 / 277; 47 / 82 / 129; 302 / 104 / 406 Above knee, >50% stenosis DSA / MRA: 147 / 14 / 161; 22 / 68 / 90; 169 / 82 / 251 Below knee, >50% stenosis DSA / MRA: 109 / 7 / 116; 24 / 15 / 39; 133 / 22 / 155	**See QUADAS**

		Ethnicity: Not stated **Disease characteristics:** • Fontaine stages IIb and higher • Patients only had DSA if needed for further imaging following MRA • **Extra comments**: Vessels investigated: iliac, common femoral artery, superficial femoral artery, popliteal artery, lower leg (including foot by implication). Entire peripheral tree investigated in 86/152 patients and in 66 patients only in the thigh and calf stations. • **Indirectness of population:** Serious indirectness: Selected patients: those who were diagnosed on MRA and went on to treatment without further imaging excluded from the analysis	the patient's history and other diagnostic findings. All patients anaesthetised locally in the groin with 10ml Mepiracain. Patients (28/152) with moderate renal insufficiency (GFR 30-60 ml/mim/1.73m2) received pre- and post-procedure hydration with 0.9% saline solution (100ml/h for 12h) Foot not included in scan		

Study ID	Method	Patient characteristics	Index test and reference standard	Outcomes	Critical appraisal of study quality
Ref Iezzi 2013[81]	• **Design**: Diagnostic cohort study • **Source of funding**: No funding (Explicit statement that no financial conflict of interest) • **Setting**: Conducted in Italy; Setting: Single centre hospital • **Sample size**: 1 (n=40 (64 segments)) • **Duration**: Not clear:	• **Eligibility criteria:** Patients who underwent DSA after CTA before an endovascular procedure • **Exclusion criteria:** History of congestive heart failure, previous myocardial infarction, severe rhythm disturbances, severe renal impairment or serum creatinine levels greater than 2 mg/dl. Patients with any medical conditions or circumstances that would significantly decrease chances of getting reliable data or achieving study objectives (e.g. psychiatric disorders, drug dependency and	**Index test 1**: Computed tomography angiography. 64 detector row unit; patients in supine position with their feet first. Unenhanced CT scans obtained first, then CT angiography from suprarenal abdominal aorta to the foot, with iv injection of 100ml non-ionic iodinated contrast medium (iodine 400mg/ml) and 40ml saline: flow rate 4 ml/s. Collimation 0.625 x 64 mm, rotation 0.7, pitch 0.9. Technically adequate images selected by experienced radiologist, then inexperienced radiologist (4 years experience) assessed them using semi-automated software. Foot not included in scan **Index test 2**: Computed tomography angiography. 64 detector row unit; patients in supine position with their feet first. Unenhanced CT scans obtained first, then CT angiography from suprarenal abdominal aorta to the foot, with iv injection of 100ml non-ionic iodinated contrast medium (iodine 400mg/ml) and 40ml saline: flow rate 4 ml/s. Collimation 0.625 x 64 mm, rotation 0.7, pitch 0.9. Technically adequate images selected by experienced radiologist, then 2 other experienced radiologists assessed them blinded. Further details: Foot not included in scan (Aortoiliac, iliacfemoral,	Above knee, 70-100% stenosis CTA MRA: 33 / 5 / 38 1 / 25 / 26 34 / 30 / 64	**See QUADAS**

	dementia) • **Patient characteristics**: • Only patients who underwent DSA after CTA (some patients excluded – number not stated). • Age - Mean (SD): 67.2 years (10.6), range 40-93. Gender (M:F): 29:11. Ethnicity: Not stated • **Disease characteristics:** Adequate method of assessment/diagnosis: Colour duplex ultrasound • Prior tests for this assessment: Diagnosis of PAD with duplex ultrasound • **Indirectness:** Possible indirectness - patients only included if they had DSA	femoropopliteal - 6 segments per person (i.e. above knee)). **Index test 3**: Computed tomography angiography. 64 detector row unit; patients in supine position with their feet first. Unenhanced CT scans obtained first, then CT angiography from suprarenal abdominal aorta to the foot, with iv injection of 100ml non-ionic iodinated contrast medium (iodine 400mg/ml) and 40ml saline: flow rate 4 ml/s. Collimation 0.625 x 64 mm, rotation 0.7, pitch 0.9. Technically adequate images selected by experienced radiologist, then 1 other experienced radiologist assessed them, using semi-automated software. **Index test 4**: Computed tomography angiography. 64 detector row unit; patients in supine position with their feet first. Unenhanced CT scans obtained first, then CT angiography from suprarenal abdominal aorta to the foot, with iv injection of 100ml non-ionic iodinated contrast medium (iodine 400mg/ml) and 40ml saline: flow rate 4 ml/s. Collimation 0.625 x 64 mm, rotation 0.7, pitch 0.9. Technically adequate images selected by experienced radiologist, then inexperienced radiologist (4 years experience) assessed them visually. **Reference standard:** Digital subtraction angiography. Via antegrade femoral approach in 29/40 patients. Arterial segments not visualised in DSA were not included in the evaluation. Foot not included in scan

Study ID	Method	Patient characteristics	Intervention(s)	Outcomes	Critical appraisal of study quality
Ref Lapeyre 2005	• **Design**: Diagnostic cohort study • **Source of funding**: Study funded by industry (Supported in part by grant from O.P.A.L. foundation, Sanofi-Synthelabo) • **Setting**: Conducted in France; Setting: Department of vascular surgery • **Sample size**: n=31 (310 segments)	• **Eligibility criteria:** Non-healing ulceration or focal gangrene consistent with PAD • **Exclusion criteria:** Trophic changes related to neuropathy or infection (n=21). Prior below knee amputation on the same side (n=6). Contraindication MRA (n=10). Previous arterial stenting (n=5). Non-availability of MRA within 10 days after physical examination (n=16). Allergy to iodinated contrast agents. • **Patient characteristics**: • Patients with long term diabetes referred to department of vascular surgery. Age - Mean (range): 65 years (35 to 85). Gender (M:F): 22:9. Ethnicity: Not stated • Diabetes: Diabetes (Type 2: 74% (23/31)). • **Disease characteristics:** Adequate method of assessment/diagnosis:	**Index test**: Magnetic resonance angiography - Phase contrast MRA. Infragenicular MRA: patient in supine position, feet first; surface phase array body coil. Contrast agent - gadoterate dimeglumine 0.01 mmol/kg at 3 ml/s then 20ml saline at same rate. Aortic and lower limb MRA: 60-90 min later, 3 stations pelvis, thigh and calf, body and phased array coils, moving table. Contrast agent: 0.015 mmol/kg at 2 ml/s, then 0.005 mmol/kg at 0.8ml/s; then saline 30ml at 0.8ml/s. Assessors: interventional radiologist (13 years experience) and vascular surgeon (14 years) reviewed MRA and DSA angiograms. Field strength for MRA: 1.5 Tesla. Foot included in scan Type of coil for MRA: Phased-array **Reference standard**: Digital subtraction angiography. 4F introducer sheath in the common femoral artery. Contrast agent: iodixanol 320 via a power injector and flow rates according to region - abdominal aorta: 30 ml at flow rate 15 ml/s; pelvic and peripheral arteries: 80 ml, flow rate 10 ml/s. Unenhanced mask image subtracted. Assessors: interventional radiologist (13	Whole leg ≥50% stenosis DSA / MRA: 160, 4, 164; 8, 138, 146; 168, 142, 310 Whole leg, occlusion DSA / MRA: 102, 2, 104; 9, 197, 206; 111, 199, 310 Above knee ≥50% stenosis DSA / MRA: 36, 1, 37; 1, 54, 55; 37, 55, 92	**See QUADAS**

	Physical examination by a vascular surgeon • Fontaine stage IV: Non-healing ulceration (n=16), focal gangrene (n=15) • **Extra comments:** Results reported as sum of 2 reviewers, so we divided by 2 (i.e. average of two reviewers)	years experience) and vascular surgeon (14 years) reviewed MRA and DSA angiograms. Duration DSA performed within 72 hours after MRA. Foot included in scan (Superficial femoral artery, above knee popliteal artery, below knee popliteal artery, anterior and posterior tibial arteries, tibioperoneal trunk, peroneal artery, dorsal and plantar arteries of the foot).	Above knee, occlusion MRA / DSA 13 0 13 0 79 79 13 79 92 Below knee 50-100% stenosis MRA / DSA 124 3 127 7 84 91 131 87 218 Below knee occlusion MRA / DSA 89 2 91 9 118 127 98 120 218	

Study ID	Method	Patient characteristics	Index test and reference standard	Outcomes	Critical appraisal of study quality
Ref Wang 2012[168]	• **Design**: Diagnostic cohort study • **Source of funding**: Funding not stated • **Setting**: Conducted in China; Setting: Research institute • **Sample size**: 1 (n=35 (805 segments)) • **Duration**: Time between tests not stated	• **Eligibility criteria:** Not stated. • **Exclusion criteria:** Not stated. • **Patient characteristics**: • Patients randomly selected from those who had 3D CE-MRA from June 2007 to March 2010 • Age - Mean (range): 56.1 years (36 to 78). Gender (M:F): 23:12. Ethnicity: Not stated • If more than one segment, classification was of the one at the highest level. **Disease characteristics:** • Unclear method of assessment/diagnosis • Overall: Mild intermittent claudication (Grade O; n=5); moderate-severe IC (Grade I, n=11); rest pain (Grade II, n=12); foot or leg ulcers (Grade III, n=7)	**Index test**: Magnetic resonance angiography - Contrast enhanced MRA. 3D-contrast enhanced; spoiled gradient recall acquisition in steady state; automatic bed movement; mask scan done prior to contrast agent. Contrast agent not stated, but volume 20ml at flow rates of 2ml/s then 0.5ml/s, followed by saline 20 ml at 2ml/s. Maximum intensity projection, multi-planar reformation and volume rendering. Magnetic field: 3 Tesla. Foot included in scan (arteries scanned: abdominal aorta; common, internal and external iliac; femoral, deep and superficial femoral; popliteal; anterior and posterior tibial; peroneal; dorsal pedal). Type of coil for MRA: body coils dedicated to lower limbs. **Reference standard**: Digital subtraction angiography. DSA and/or surgery. Foot included in scan Comments: 30/35 successful examinations	Whole leg occlusion | | MRA | | | |---|---|---|---| | DSA | 115 | 4 | 119 | | | 2 | 684 | 686 | | | 117 | 688 | 805 | Whole leg 50-100% stenosis | | MRA | | | |---|---|---|---| | DSA | 256 | 5 | 261 | | | 2 | 542 | 544 | | | 258 | 547 | 805 |	**See QUADAS**

4.1.2. Test and treat studies

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Ouwendijk R, de Vries M, Stijnen T et al,Multicenter randomized controlled trial of the costs and effects of noninvasive diagnostic imaging in patients with peripheral arterial disease: The DIPAD trial. AJR 190: 1349-1357. 2008. RCT – Multi-centre - Netherlands; Setting: Tertiary care radiology/vascular surgery departments in four Dutch hospitals **Randomisation:** patients randomised in two comparisons – in 3 hospitals to CE MRA and DUS and in another hospital to CE MRA and CTA, all three with treatment. Computer generated randomisation. **Allocation concealment:** Central randomisation by	Total N = 514 Inclusion criteria: Adults at least 18 years with symptomatic PAD, referred from the department of vascular surgery for diagnosis to evaluate feasibility of revascularisation. Exclusion criteria: Contraindications for MRA (e.g. pacemaker, cerebral vessel clipping, claustrophobia) or for CTA (severe renal insufficiency or adverse reaction to iodinated contrast material). If patients needed an acute intervention at the time of randomisation Previous imaging workup indicating that revascularisation was needed. Mean age MRA group 64 (SD 11); DUS group 64(11); CTA group 64(12) years	1. Contrast enhanced MRA + treatment (N=258):. **Imaging technique**: 1.5T imager; body coil/dedicated phase-array coil. In 3 hospitals, bolus-chase MRA with single biphasic contrast material injection, automated table movement and real-time bolus monitoring. In 1 hospital (37 patients), a multi-injection protocol was used. All patients received 40 ml contrast agent (gadopentetate dimeglumine). All hospitals used subtraction technique before generating maximum intensity projections (MIPs). **Treatment**: 97/258 received	2. Usual imaging (according to hospital): 2a: Duplex Ultrasound plus treatment (n=177) – **Imaging technique**: Duplex equipment using 5 and 7.5MHz transducers. Peak systolic velocity (PSV) recorded.Qualified experienced vascular technologists under supervision of a radiologist or vascular surgeon. **Treatment**: 68/177 received	• Quality of life (EQ-5D,SF36, VascuQol, Rating scale at 2 weeks and 3 and 6 months) • Change in Walking distance from baseline • Amputation • Number of interventional procedures • Number of further imaging Group 1: 2/258 had additional MRA, 28 additional DUS, 27 additional DSA (total 57/258 = 22%) Group 2a:	Funding source: Academic or government funding (ZonMW (Netherlands Organisation for Health R&D) and from NWO (Netherlands Organisation for Scientific Research))

Baseline (n)	MRA + Tmt	DUS + tmt	CTA + tmt
Lesions	Not stated		-
CLI	15%	12%	18%
Diabetes	26	17	22
Smoking	Not stated		
Cardiac disease	40%	36%	25%

Study details	Patients				Intervention	Comparison	Outcome measures	Other comments
phone, **Blinding:** Outcome assessors not blinded (patients for quality of life) **Sample size calculation:** No details **Drop outs:** 0 for CTA, 3 each for MRA and DUS Follow up duration: 6 months					conservative treatment, 129 had percutaneous intervention, 79 had surgical intervention (some patients had several interventional procedures). Concurrent medication/care: Interpreted by radiologists with extensive experience. All images were assessed in a vascular conference and the need for further testing and treatment determined.	conservative treatment, 85 had percutaneous intervention, 39 had surgical intervention (some patients had several interventional procedures). These treatments followed review in a vascular conference. 2b: Computed tomography angiography plus treatment (n=79). **Imaging technique**: 16-MDCT scanner; bolus tracking technique with automated table	20/177 had additional MRA, 17 additional DUS, 38 additional DSA (total 75/177 = 42%) Group 2b: 0/79 had additional MRA, 4 additional DUS, 8 additional DSA (total 12/79 = 15%)	

Study details	Patients				Intervention	Comparison	Outcome measures	Other comments
						movement and automated bolus detection. Before generating maximum intensity projections, segmentation technique used to remove bone structures and vessel wall calcification. **Treatment**: 26/79 received conservative treatment, 38 had percutaneous intervention, 27 had surgical intervention (some patients had several interventional procedures). These		

Study details	Patients				Intervention	Comparison	Outcome measures	Other comments
						treatments followed review in a vascular conference.		

	Effect Size			
Outcome		DUS + treatment (n=174)	MRA + treatment (n=178) and (n=78)	CTA + treatment (n=79)
Quality of life, EQ-5D (unadjusted , 3 months) Change from baseline; scale 0 to 1 Baseline difference for MRA minus DUS is -0.03		0.03 (SE 0.02)	0.04 (SE 0.02) (n=178)	---
Quality of life, EQ-5D (unadjusted , 6 months) Change from baseline; scale 0 to 1		0.03 (SE 0.03)	0.05 (SE 0.03) (n=178)	----
Quality of life, EQ-5D (adjusted*), Change from baseline; scale 0 to 1 Note baseline difference is -0.14 for MRA minus CTA *adjusted for outcome at baseline, severity of disease (CLI vs IC), diabetes, renal disease, cerebrovascular disease, cardiac disease and rank order of tests		----	Mean difference -0.06 (95%CI -0.15 to 0.04) for MRA minus CTA (3 months) Mean difference -0.02 (95% CI -0,12 to 0.07) at 6 months	
Walking distance (m) 6 months, unadjusted Note baseline difference of -11m for MRA minus DUS; change scores		23 (SE 7) (n=174)	25 (7) (n=178)	-----
Maximum walking distance (m), change from baseline, adjusted as above. Baseline		-----	Mean difference -14m (95%CI -41 to 14) at 6 months for MRA minus CTA	

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
difference not reported					
Amputation, number of procedures not number of people – 6 months Above knee Below knee	Not reported	 0 5 (n=77)	 2 0 (n=79)		
Number of surgical procedures (6 months) Number of PCIs (6 months)	---- ---	53/77 47/77	31/79 38/79		
Number of surgical procedures (6 months) Number of PCIs (6 months)	39/174 93/174	39/180 96/180	-----		
Additional imaging within 60 days of initial imaging Additional imaging within 6 months Additional imaging before therapy Additional imaging total	---- ---- 47/174 69/174	8/78 13/78 19/180 40/180	7/79 10/79 --- ---		

4.2. Selective versus primary stenting

4.2.1. New evidence published since NICE guideline

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Ref Goode, S. D., Cleveland, T. J., Gaines, P. A., and STAG, trial collaborators. Randomized clinical trial of stents versus angioplasty for the treatment of iliac artery occlusions (STAG trial). British Journal of Surgery 100(9), 1148-1153. 2013	• **Design**: multicentre RCT • **Source of funding**: Trent regional health authority • **Setting**: 6 centres in the UK • **Sample size**: 118 • **Duration**: May 1995 to February 2002 • **Follow-up**: discharge, 1 month, 6 months, 1 year and 2 years	• **Eligibility criteria:** Patients with **iliac artery** occlusion 8 cm or less • **Exclusion criteria:** not reported • **Patient characteristics**: • Group 1: Mean (SD) age: 60.2 (8.9) Male/female: 35/20 • Group 2: Mean (SD) age: 60.6 (10.5) Male/female: 41/16 • **Disease characteristics:** • Group 1: mild claudication: 9 moderate claudication: 16 severe claudication: 25 Group 2: mild claudication: 3	**Group 1**: n=61 Percutaneous transluminal angioplasty (PTA) with bailout stenting. If there was either no flow following angioplasty or complications that could be resolved by stents, secondary stenting was allowed 9 patients required a bailout stent versus **Group 2** : n=57 Iliac stents **Pharmacological regimen** All patients:	**Trial halted early after 118 patients had been recruited due to an increase in major complications in PTA group. Intention was to recruit 144 patients** **Outcome 1:** mortality at 2 years - Group 1: n=3/55; Group 2: n=5/57 **Outcome 2:** major complications* at 2 years – Group 1: n=11/55; Group 2: n=3/57 * (Group 1 – re-intervention for 9 distal embolisations and 2 episodes of acute thrombosis; Group 2 – re-intervention for 1 rupture in stent graft and 2 distal embolisations) **Outcome 3:** minor complications at 2 years – Group 1: n=2/55; Group 2: n=1/57 **Outcome 4:** secondary non-stenting procedure ¬ at 2 years – Group 1: n=9/55; Group 2: n =3/57 ¬ (i.e not related to rescue stenting during procedure. Used this outcome to indicate re-interventions in the analyses).	**Results critical appraisal**: Low quality **Dropouts: (at 2 year follow up)** Group 1: n=6 due to major protocol violations Group 2: n=0

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		moderate claudication: 24 severe claudication: 23	Aspirin before intervention, or dipyridamole if aspirin intolerant. 5000 units of unfractionated heparin once percutaneous arterial access achieved.		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Ref Rastan, A., Krankenberg, H., Baumgartner, I., Blessing, E., Muller-Hulsbeck, S., Pilger, E., Scheinert, D., Lammer, J., Gisler, M., Noory, E., Neumann, F. J., Zeller, T., and Zeller, T. Stent placement versus balloon angioplasty for the treatment of obstructive lesions of the popliteal artery: a prospective, multicenter, randomized trial. Circulation 127(25), 2535-2541. 2013. ETAP Study (Endovascular Treatment of Artherosclerotic Popliteal Artery	• **Design**: multicentre RCT • **Source of funding**: investigator initiated and secondarily supported by Bard Peripheral Vascular Corp in terms of study monitoring, data collection and data evaluation, with direct financial support. • **Setting**: 9 medical centres in Germany, Austria and Switzerland. • **Sample size**: 246 patients • **Duration**: February 2007 to October 2010 • **Follow-up** : 6 & 12 months	• **Eligibility criteria:** ≥ 21 years old; not pregnant; had peripheral arterial disease with a Rutherford-Becker classification (RC) of 2 to 5. Angiographic eligibility required a single primary de novo target lesion (occlusion or stenosis) in the **popliteal artery** (4-7mm in diameter) with a stenosis ≥70%, estimated by angiography. Lesion not allowed to involve the superficial femoral artery (SFA) or to extend into the infrapopliteal arteries. • **Exclusion criteria:** subintimal recanalization of the target lesion; restenosis of the popliteal artery;	**Group 1**: n=127 Percutaneous transluminal angioplasty (PTA) with provisional stenting. If there was residual stenosis of >30% or a flow-limiting dissection an additional, prolonged (5 minutes) PTA had to be performed. If there was persistent stenosis of >30% after repeated and prolonged PTA or a flow limiting dissection a study stent was placed at the target lesion. 32 patients (25.2%) received a stent in the target limb. versus **Group 2** : n=119 Self expanding nitinol	**Outcome 1:** mortality at 1 year - Group 1: n=4/98; Group 2: n=2/99 **Outcome 2:** lower limb amputations of target limb at 1 year – Group 1: n=3/98; Group 2: n=3/99 **Outcome 3:** perioperative complications (e.g. postprocedural access site bleeding, abdominal wall haemorrhage, closure device related stenosis) – Group 1: 2.4% (3/127); Group 2: 1.7% (2/119). Numbers calculated by NCGC, appear to relate to numbers randomized. **Outcome 4:** target lesion revascularisation (includes the need for surgical re-intervention) at 1 year (excluding stent placement in PTA group) – Group 1: n=22; Group 2: n=15 **Outcome 5:** target vessel revascularisation at 1 year – Group 1: n=4/98; Group 2: n=3/99	**Results critical appraisal**: Moderate Allocation concealment and sequence generation not reported **Dropouts: (at 1 year follow up)** Group 1: n=29 (3 withdrew consent; 11 lost to follow up; 2 died; 13 did not visit at 1 year meeting) Group 2: n=20 (3 withdrew consent; 6 lost to follow up; 4 died; 7 did not visit at 1 year meeting)

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Lesions-Balloon Angioplasty Versus Primary Stenting)		known systemic coagulopathy; renal failure requiring dialysis, life expectancy <2 years or other factors that made follow up impossible; intolerance to aspirin, clopidogrel or heparin. • **Patient characteristics**: • Group 1: Mean (range) age: 73 (41-89) Male: 64.6% BMI: 26±4 kg/m^2 Diabetes mellitus: 37.8% Dyslipidemia: 81.9% Hypertension: 88.2% Current smoker: 24.4% Coronary heart disease: 43.3% Carotid artery disease: 13.4% • Group 2: Mean (range) age: 72 (42-89)	stent (LifeStent Vascular Stent, Bard Peripheral Vascular, Tempe, AZ). Intent was to treat isolated artherosclerotic lesion with a single stent. Placement of ≥2 stents was allowed if the target lesion was longer than the longest available stent, the stent did not completely cover the target lesion, or if a flow-limiting dissection required treatment proximal or distal to the primary stent. A strict definition of primary stent placement was followed with the goal of not predilating the lesion before the placement. **All patients** Arterial access site left to discretion of investigator. After arterial puncture and placement of a 6F introducer sheath an	**Outcome 6:** bypass surgery at 1 year – Group 1: n=1/98; Group 2: n=1/99	

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		Male: 63.9% BMI: 27±4 kg/m^2 Diabetes mellitus: 36.1% Dyslipidemia: 75.6% Hypertension: 82.4% Current smoker: 21.8% Coronary heart disease: 42.9% Carotid artery disease: 17.6% • **Disease characteristics:** • <u>All patients:</u> Intermittent claudication: 195 (79.3%) Critical limb ischemia: 51 (20.7%)	initial dose of 5000 IU of heparin was administered. All patients given 100mg of acetylsalicylic acid daily. If the patients was not taking acetylsalicylic acid before the procedure a 500-mg loading dose was administered before the intervention. Loading dose of clopidogrel (1x300mg PO) was administered on the day of intervention, followed by a daily dose of 75mg for a minimum of 4 weeks.		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Ref Scheinert, D., Katsanos, K., Zeller, T., Koppensteiner, R., Commeau, P., Bosiers, M., Krankenberg, H., Baumgartner, I., Siablis, D., Lammer, J., Van Ransbeeck, M., Qureshi, A. C., Stoll, H. P., and ACHILLES, Investigators. A prospective randomized multicenter comparison of balloon angioplasty and infrapopliteal stenting with the sirolimus-eluting stent in patients with ischemic peripheral arterial disease: 1-year results from the ACHILLES trial. Journal of the American College of Cardiology	• **Design**: multicentre RCT • **Source of funding**: Cordis, Johnson and Johnson • **Setting**: 16 centres in 9 countries • **Sample size**: 200 • **Duration**: March 2008 to January 2010 • **Follow-up**: 6 weeks, 6 months and 12 months	• **Eligibility criteria:** Patients with **infrapopliteal** PAD; between 18 and 85 years old; negative pregnancy test within 10 days of index test and using reliable birth control if female of childbearing potential; clinical diagnosis of symptomatic **critical limb ischemia** (Rutherford 3, 4 or 5); single treatment of de novo or restenotic (after PTA only) lesion(s) in the tibioperoneal trunk, anterior and/or posterior tibial and or peroneal artery; target lesion stenosis is >70% diameter stenosis (visual estimate); guidewire must be across the first (if applicable) target lesion and located	**Group 1**: n=101 (115 lesions) Percutaneous transluminal angioplasty (PTA) with bailout stenting. Not reported how it was decided to introduce a bailout stent. Further balloon dilation encouraged in case of unsatisfying immediate PTA to minimize crossover to stents. 8 patients received a stent in the target limb. versus **Group 2** : n=99 (113 lesions) Sirolimus-eluting stent (Cordis, Johnson & Johnson, Bridgewater, New	**Outcome 1:** mortality at 1 year - Group 1: n=12/101; Group 2: n=11/99 (disrcepency in paper: Table 4 in paper reports 12 and 10 deaths but ITT diagram and text in report imply 12 and 11 deaths) **Outcome 2:** index limb amputation of at 1 year – Group 1: n=17/85; Group 2: n=11/80 **Outcome 3:** target lesion revascularisation at 1 year (clinically driven) – Group 1: n=14/85; Group 2: n=8/80 **Outcome 4:** target vessel revascularisation at 1 year (non-TLR count) – Group 1: n=2/84; Group 2: n=5/78	**Results critical appraisal**: Moderate **Dropouts: (at 1 year follow up)** Group 1: n=21 (7 withdrew consent; 6 lost to follow up; 12 died) Angiograms available for 74/115 lesions Group 2: n=25 (4 withdrew consent; 10 lost to follow up; 11 died) Angiograms available for 67/113 lesions

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
60(22), 2290-2295. 2012.		intraluminally within the distal vessel before the study randomization; willing to comply with follow up evaluation; written informed consent before any study procedure. • **Exclusion criteria:** significant stenosis (>50%) distal to the target lesion that might require revascularization or impede runoff; angiographical evidence of thrombus or history of thrombolysis within 72 hours; lesions not suitable for stenting; untreated lesions (>75% stenosis) in the common or external iliac; common or superficial femoral and popliteal artery; infrapopliteal tricfurcation lesions	Jersey). Maximum of 2 vessels in 1 limb may be treated in the study, each vessel for only 1 target lesion, resulting in at single risk target lesion; in case 1 target lesion is located in the tibioperoneal trunk – the 2nd target lesion can only be locate in the anterior tibial artery. Additional non-target lesion(s) in remaining non-target vessel(s) can be treated at physician's discretion by means of balloon dilation +/- bailout stent; sum of the total length of both target lesions can be maximum of 120mm; maximum of 4 stents implanted to cover the maximum of 2		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		requiring 2- or 3-branch treatment; stent placement across or within 1 cm of knee joint or in the an artery subject to external compression; prior stenting within the target vessel(s) or aneurysm in the superficial femoral or popliteal artery; history of thrombophlebitis, deep vein thrombosis, or impaired renal function (Cr >2.5mg/dl); MI, stroke or coronary intervention <30 days before index procedure); life expectancy <12 months; known intolerance to antiplatet medication; current prescription to warfarin or any significant medical condition which in investigator's	target lesions per subject; target vessel is ≥2.5 & ≤3.5mm in diameter (visual estimate); **Pharmacological regimen** All patients: Aspirin and a loading dose of 300mg of clopidogrel (or 2 x 250mg ticlopidine) was administered pre-procedure. Intraprocedural heparin was used to maintain activated clotting time levels ≥250 s, and low-dose aspirin. Stent patients only: 75mg clopigodrel (or 2 x 250mg ticlopidine) maintained for 6 months.		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		opinion may interfere with the patient's participation; participation in another investigational drug/device study that has not completed its primary endpoint or clinically interferes with endpoints of this study. • **Patient characteristics**: • <u>All patients</u>: n=200 Mean (SD) age: 73.4 (8.8) Male: 71.5% Diabetes: 64.5% History of PAD: 65% History of coronary artery disease: 45% Hypertension: 90.5% Hyperlipidemia: 72.9% Smoker: 32.3% • **Disease characteristics:**			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		• <u>All patients:</u> Claudication: 15.2% in PTA group, 15.1% in stent group			

4.2.2. Evidence tables for angioplasty with selective stents vs angioplasty with primary stents from NICE guideline CG147

4.2.2.1. Management of intermittent claudication

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Krankenberg H, Schluter M, Steinkamp HJ, Burgelin K, Scheinert D, Schulte KL, Minar E, Peeters P, Bosiers M, Tepe G, Reimers B, Mahler F, Tubler T, Zeller T. Nitinol Stent Implantation Versus Percutaneo	RCT Multicentre (n=11 sites,Germany) FAST trial Randomisation: 4 block randomisation Allocation concealment: Envelopes provided by independent management	Total N = 244	Inclusion criteria: ≥ 21 years of age and had a de novo SFA lesion located at least 1 cm from the SFA origin with a length between 1 and 10 cm. Target lesion diameter stenosis had to be ≥ 70% by visual estimate. The popliteal artery as well as 1 of the infrapopliteal (below-the-knee) vessels had to be continuously patent for sustained distal runoff. Clinically, the patients had to suffer	N = 123 Self expanding open-cell nitinol stent (BARD Luminex)	N= 121 Balloon angioplasty +/- stent if required 13 patients required a stent insertion Patients who had received a stent were given 300 mg of clopidogrel within 1 hour of the final digital subtraction angiography	Evaluated at baseline, before discharge and 1, 6 and 12 months. Follow up consisted of ABPI at rest, treadmill test if possible, duplex ultrasound, and biplane xray for stents at 12mnths.	1o outcome: Target lesion revascularization ABPI Absolute walking distance Rutherford category of peripheral arterial	C.R. Bard Inc, Murray Hill, NJ.

us Transluminal Angioplasty in Superficial Femoral Artery Lesions Up to 10 Cm in Length: the Femoral Artery Stenting Trial (FAST). Circulation. 2007; 116(3):285-292.	organisation Blinding: Outcome assessors were blinded Sample size calculation: Yes based on 12 month binary stenosis ITT analysis: Yes Drop outs: 9 in the stent group and 6 in the PTA group dropped out of clinical follow- up at 12 months	from chronic limb ischemia of at least Rutherford category 2 (moderate claudication). Exclusion criteria: A target lesion that required pretreatment with adjunctive devices such as lasers or debulking catheters; a target lesion that extended into the popliteal artery; previous stent implantation in the targeted SFA; multiple lesions exceeding a total length of 10 cm; acute or subacute (≤4 weeks) thrombotic occlusion; an untreated ipsilateral iliac artery stenosis; ongoing dialysis treatment; and treatment with oral anticoagulants other than antiplatelet agents.			disease. Major adverse events Mortality
		Baseline	Stent N=123	PTA N = 121	All patients had to be premedicated

Mean age (years) SD	67±9	66±10	with acetylsalicylic acid (aspirin, 100 mg/d) for at least 10 days. Patients not on this regimen were given an intravenous bolus of 500 mg of aspirin immediately before the intervention NOTE: All patients were discharged the day after the intervention on a regimen of aspirin (100 mg/d indefinitely). Patients who had undergone stent implantation were additionally prescribed clopidogrel (75 mg/d) for at least 4 weeks.
Male (%)	62.6	75.2	
BMI SD	26.6±4.3	27.3±4.5	
Smoking history (%)	68.3	72.7	
Diabetes Mellitus (%)	35.8	30.6	
Hypertension (%)	82.9	82.6	
Stroke (%)	10.6	5.8	
Hyperlipidaemia (%)	60.2	61.2	
History of CAD	42.3	31.4	
Clinical grade Rutherford category %			
0 asymptomatic	1/119 (0.8)	1/114 (0.9)	
2 mild/moderate claudication	35/119 (29.4)	26/114 (31.6)	
3 Severe claudication	80/119 (67.2)	73/114 (64)	
4 Ischaemic pain at rest	1/119 (0.8)	3/114 (2.6)	
5 Minor tissue loss	2/119 (1.7)	1/114 (0.9)	
ABPI rest	0.68±0.16 n=105	0.72±0.15 n = 102	
Median (IQR) Walking distance (m)	110 (68-163) n = 97	100(60-150) n = 99	

Baseline characteristics

Patients well matched expect for a lower baseline line ABPI in the stent group (unknown if statistically significant).

Effect Size

Reintervention: A second stent was required in 4 patients. 13 PTA pts crossed over to receive a stent, therefore on treatment cohort of 108 (PTA) and 136 for stenting.

There was no statistical difference in the improvement in clinical category or change in ABPI between groups

OR of 12 months stenosis in diabetic patients was 0.48 (95%CI 0.17-1.34) and for non diabetics was OR 0.94 (0.46- 1.90). There was no significant effect.

Outcome	Stent N=123	PTA N = 121
Procedural complications (<30days)	8/123 (7%)	5/121 (4%)
Overall mortality 12 months	4	1
Lower limb amputations due to pre-existing gangrene	2	0
Cumulative reintervention (TLR) at 12 months	17	21
Median change in ABPI at rest 12 months (subset of pts; around half of all patients)	0.21 (n=61)	0.15 (n=75)
Median walking distance at 12 months, m (subset of pts, around half of all patients)	150 (n=61)	185 (n=75)
Median change in walking distance at 12 months, m (subset of pts, around half of all patients)	30 (n=61)	52 (n=75)
Procedural complications		
Total, n (%)	8 (7%)	5 (4%)
False aneurysm	2	2
Hematoma	3	0
Dissection	1	1
Distal embolisation	0	0

Reaction to contrast agent	1	0
Contract nephropathy	0	0
Residual thrombus	0	1
Arteriovenous fistula	0	1
Closure device failure	1	0

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bosch, J. L., Van Der Graaf, Y., and Hunink, M. G. Health-related quality of life after angioplasty and stent placement in patients with iliac artery occlusive disease: results of a randomized controlled clinical trial. The Dutch	RCT Multicentre (6 sites Netherlands) DIST trial Randomisation: Computer generated randomisation table Allocation concealment: Randomisation table kept at the trial office and unavailable	Total N = 279 patients	Inclusion criteria: Intermittent claudication consisting of pain localised in the buttock, upper leg, or calf; reduced pulsation of the femoral artery and reduced ankle-brachial index (ABI); reduction, evident by angiography, in arterial diameter greater than 50%; and stenosis ≤ 10 cm in length in the common or external iliac artery or occlusion of 5 cm or less that allowed passage with a guide wire. Exclusion criteria: Stenosis > 10 cm in length; arterial occlusion > 5 cm in length, or of ≤5 cm not allowing the passage of a guide wire; stenosis involving the distal aorta; severe comorbidity (eg, severe cardiac or cerebrovascular abnormality, malignant disease); and non-medical factors such as inability to understand Dutch, or expected poor compliance.	N = 143 patients (187 lesions) Palmaz Stent Stent placement was not possible in 1 patient - - - - - - - - All patients received anticoagulant medication (aspirin or oral anticoagulants) in accordance	N = 136 patients (169 lesions) Primary balloon angioplasty + selective stent placement if required Nine patients were not treated according to protocol - - - - - - - - - 59 patients (43%) had selective	1, 3, 12, 24 months. Mean follow-up was 14.7 months (range 3 – 24 months). Also long-term follow-up of 6-8 years (mean 6.3 years, SD 1.8, range 0.7 to 8.6 years).	1o outcome: Quality of life: RAND 36 Time tradeoff Health Utilities Index EuroQol-5D Standard gamble 2 o outcomes: ABPI Walking	This study was supported by grant (OG-93/001) from the Commission of Investigative Medicine of the Dutch National Health Insurance Council and a Pionier award from the Netherland

Iliac Stent Trial Study Group. Circulation 99(24), 3155-3160. 22-6-1999. **Tetteroo, E., Van Der Graaf, Y., Van Engelen, A. D., Hunink, M. G. M., Eikelboom, B. C., and Mali, W. P. T. No difference in effect on intermittent claudication between primary stent placement and primary percutaneous translumina l angio plasty followed by selective**	to the treating physicians Blinding: Open study but outcome assessors were blinded Sample size calculation: Yes based on 12 month patency ITT analysis: Yes Drop outs: 25 due to the time between enrollment in the study and the procedure being too short to perform the interview or patients could not be reached by telephone). 2 year follow-	The majority of patients had intermittent claudication Baseline / Stent N=143 / Primary angioplasty N = 136 Mean age (years) SD: 59±11 / 60±10 M/F: 102/41 / 99/37 Tobacco use (%): 87% / 94% Diabetes Mellitus (%): 9% / 11% Hypertension (%): 28% / 27% Stroke (%): 14% / 7% Hyperlipidaemia (%): 24% / 26% Clinical grade (SVS/ISCVS) % 1: 24% / 27% 2: 54% / 51% 3: 16% / 13% 4: 5% / 8% 5: 1% / 1%	with local guidelines or the individual preference of the physician who initially referred the patient for treatment. Medication was independent of the type of intervention.	stent placement	distance	s Organisation for Scientific Research.

stent placement: A prospective randomized trial. Nederlands Tijdschrift Voor Geneeskunde 144(4), 167-171. 2000. **Klein, W. M., Van Der Graaf, Y., Seegers, J., Spithoven, J. H., Buskens, E., Van Baal, J. G., Buth, J., Moll, F. L., Overtoom, T. T., Van Sambeek, M. R. H. M., and Mali, W. P. Dutch Iliac Stent Trial: Long-term results in patients randomized for primary**	up was available in 101 of the 108 eligible patients At 6-8 year follow-up: (Numerators indicate number of pts attending follow-up session. Denominators decreased from number at inclusion because some patients died) Symptom assessment results – 95/118 (81%), ABI mmts – 101/118 (86%) Duplex US results for iliac arteries	ABPI rest	0.74±0.20	0.73±0.20
		Walking distance (m)	190±109	204±106

or selective stent placement. Radiology 238(2), 734-744. 2006.	109/118 (92%)
Klein, W. M., Van Der Graaf, Y., Seegers, J., Moll, F. L., and Mali, W. P. Long-term cardiovascular morbidity, mortality, and reintervention after endovascular treatment in patients with iliac artery disease: The Dutch Iliac Stent Trial Study. Radiology 232(2), 491-498. 2004.	
Effect size	

Results from Tettroo 1998		
Overall there were no differences identified between the two groups		
No difference in clinical success at 2 years between groups for improvement in clinical category (SVS/ISCVS).		
No difference in quality of life between groups although there was an improvement within groups compared with baseline		
No between group differences at 2 years in cumulative patency or reintervention.		
Primary angioplasty followed by selective stent placement seems to be the strategy of choice for treatment of lifestyle-limiting intermittent claudication-particularly since the strategy also seems the most cost-effective, requiring only a fraction of the stents needed in a strategy of primary stent placement (65 [38%] of 169 in this study).		
Outcome	Stent N=143	Primary angioplasty N = 136
Complication rates (% patients)*	6 (4%)	10 (7%)
Reintervention at treated site 3 months	2	2
Reintervention at treated site 1 year	4	2
Reintervention at treated site 2 years	4	2
Cumulative reintervention at treated site rate after 2 years	10/143 (7%)	6/136 (4%)
Mortality at 3 months	0	0
Mortality at 1 year	1	2
Mortality at 2 years	0	0
Cumulative mortality rate after 2 years	1	2
***puncture site haematoma, arterial-wall perforation, acute occlusion of treated arterial segment, embolism, vasovagal collapse**		
Results from Bosch, 1999		
Quality of Life results		
91% (254 patients) undertook QoL assessment. This was assessed at baseline, 1, 3, 12, and 24 months after treatment. 1 year follow up		
Both groups showed significant improvements in the RAND 36 after treatment but there were no significant differences between groups.		
Values for the Health Utilities Index and the EuroQol 5D did not differ between groups.		
Outcome	Stent N=143	Primary angioplasty N = 136

ABPI (mean±SD)		
ABPI rest before treatment	0.74±0.20	0.73±0.21
ABPI rest 3 months	0.92±0.25	0.93±0.22
ABPI rest 12 months	0.92±0.22	0.94±0.19
ABPI rest 24 months	0.88 ±0.24	0.96±0.20
Walking distance, m (mean±SD)		
Walking distance before treatment	190±109	204±106
Walking distance 3 months	263±57	255±64
Walking distance 12 months	261±58	263±65
Walking distance 24 months	258±68	255±68
Immediate post-procedure complications (% patients)	6 (4%)	10 (7%)
RAND 36 Median (95%CI)		
Physical functioning before treatment	40 (5-79)	45 (10-85)
Physical functioning 1 month	85 (10-100)	80 (15-100)
Physical functioning 3 months	85 (10-100)	85 (10-100)
Physical functioning 1 year	70 (7-100)	85 (20-100)
Physical functioning 2 years	75 (5-100)	85 (5-100)
Physical role functioning before treatment	0 (0-100)	0 (0-100)
Physical role functioning 1 month	0 (0-100)	0 (0-100)
Physical role functioning 3 months	100 (0-100)	100 (0-100)
Physical role functioning 1 year	100 (0-100)	100 (0-100)
Physical role functioning 2 years	75 (0-100)	100 (0-100)
Bodily pain before treatment	45 (3-100)	45 (0-99)

Bodily pain 1 month	80 (4-100)	67 (0-100)
Bodily pain 3 months	90 (20-100)	78 (10-100)
Bodily pain 1 year	78 (4-100)	80 (22-100)
Bodily pain 2 years	78 (2-100)	90 (20-98)
General health perception before treatment	55 (15-94)	55 (10-90)
General health perception 1 month	65 (16-100)	60 (15-95)
General health perception 3 months	65 (15-100)	60 (10-95)
General health perception 1 year	63 (15-100)	65 (15-95)
General health perception 2 years	55 (2-99)	60 (15-100)
Vitality before treatment	50 (6-95)	50 (5-90)
Vitality 1 month	65 (15-100)	65 (10-100)
Vitality 3 months	70 (15-100)	70 (20-100)
Vitality 1 year	65 (12-100)	65 (16-100)
Vitality 2 years	70 (15-100)	60 (15-100)
Social functioning before treatment	60 (0-100)	75 (13-100)
Social functioning 1 month	88 (13-100)	88 (13-100)
Social functioning 3 months	100 (14-100)	88 (13-100)
Social functioning 1 year	100 (0-100)	88 (25-100)
Social functioning 2 years	88 (0-100)	94 (0-100)
Emotional role functioning before treatment	100 (0-100)	67 (0-100)
Emotional role functioning 1 month	100 (0-100)	100 (0-100)
Emotional role functioning 3 months	100 (0-100)	100 (0-100)
Emotional role functioning 1 year	100 (0-100)	100 (0-100)

Emotional role functioning 2 years	100 (0-100)	100 (0-100)	
Mental health before treatment	76 (13-100)	74 (20-100)	
Mental health 1 month	80 (28-100)	80 (24-100)	
Mental health 3 months	84 (28-100)	80 (28-100)	
Mental health 1 year	80 (6-100)	76 (30-100)	
Mental health 2 years	80 (30-100)	80 (24-100)	
Health utilities index, Median (95% CI)			
Health utilities index before treatment	0.68 (0.35-0.87)	0.69 (0.28-0.80)	
Health utilities index 1 month	0.70 (0.37-1.00)	0.70 (0.24-1.00)	
Health utilities index 3 months	0.76 (0.04-1.00)	0.77 (0.28-1.00)	
Health utilities index Median	0.70 (0.28-1.0)	0.77 (0.28-1.0)	
Health utilities index Median	0.70 (0.22-1.0)	0.70 (0.16-1.0)	
EuroQoL-5D, Median (95% CI)			
EuroQoL-5D before treatment	0.46 (0.20-0.75)	0.46 (0.15-0.75)	
EuroQoL-5D 1 month	0.70 (0.15-1.00)	0.70 (0.20-1.00)	
EuroQoL-5D 3 months	0.75 (0.15-1.00)	0.70 (0.20-1.00)	
EuroQol-5D Median (95%CI) 1 year	0.59 (0.19-1.0)	0.70 (0.15-1.0)	
EuroQol-5D Median (95%CI) 2 years	0.70 (0.09 -1.0)	0.66 (0.15-1.0)	
Results from Klein 2004			
	Stent	Angioplasty	Log rank p value
Mortality at 5 years	21 out of 143 people	22 out of 136 people	
Re-intervention at 5 years	33 out of 187 limbs	33 out of 169 people	0.7

Amputation at 5 years	3 out of 143 people	8 out of 136 people
Results from Klein, 2005		
6-8 years (RESULTS PER LESION)	Stent N=????	Primary angioplasty N = ????
ABI measurement, mean (SD)	0.90 (0.20)	0.96 (0.22)
Reinterventions, n (%)	12/118 (10)	21/110 (19)
RAND-36 Scores, Mean (SD) at baseline	Stent N=????	Primary angioplasty N = ????
Physical functioning	39.6 (18.9)	42.1 (20.4)
Physical role functioning	27.1 (36.1)	32.0 (40.5)
Emotional role functioning	59.9 (44.5)	54.8 (44.7)
Social functioning	63.8 (27.0)	68.5 (28.2)
Bodily pain	50.3 (22.2)	49.3 (24.6)
General health perception	56.7 (21.0)	53.5 (22.8)
Mental health	70.4 (21.4)	69.1 (21.9)
Vitality	50.9 (23.3)	52.6 (21.5)
Health change	30.9 (22.5)	31.2 (21.0)
RAND-36 Scores, Mean (SD) at 1 month	Stent N=????	Primary angioplasty N = ????
Physical functioning	73.0 (25.2)	72.9 (25.4)
Physical role functioning	58.5 (44.3)	55.9 (45.2)
Emotional role functioning	72.2 (40.6)	66.4 (41.3)
Social functioning	77.8 (25.9)	76.4 (26.0)
Bodily pain	75.8 (24.6)	67.5 (27.8)

General health perception	63.2 (22.4)	57.2 (21.5)
Mental health	75.3 (20.2)	74.2 (19.2)
Vitality	62.2 (23.5)	61.3 (21.9)
Health change	71.2 (27.4)	62.4 (30.0)
RAND-36 Scores, Mean (SD) at 5 years	Stent N=????	Primary angioplasty N = ????
Physical functioning	61.0 (27.3)	71.2 (26.1)
Physical role functioning	61.2 (41.2)	70.0 (39.2)
Emotional role functioning	80.7 (35.3)	86.4 (28.2)
Social functioning	80.4 (25.1)	80.2 (23.6)
Bodily pain	67.8 (25.8)	77.5 (24.2)
General health perception	53.7 (21.1)	59.7 (24.4)
Mental health	75.2 (17.9)	76.7 (17.3)
Vitality	61.1 (20.6)	64.3 (20.6)
Health change	47.9 (22.1)	47.5 (18.9)

Reference	Study type	No pts	Patient characteristics	Intervention	Comparison	Follow-up	Outcome measures	Funding
Dake MD, Ansel GM, Jaff MR, Ohki T, Saxon RR, Smouse HB, Zeller T, Roubin GS, Burket MW,	RCT Multinational Randomisation: Block randomisation by interactive voice	479	Inclusion criteria: Rutherford category ≥2 and resting ankle brachial index (ABI) <0.9, lesion length ≤14 cm, ≥50% DS, reference vessel diameter 4-9 mm, and at least one patent runoff vessel (<50% DS throughout its course).	Angioplasty n = 238 Performed according to institutional standard procedure. 50% of these patients had	Angioplasty self-expanding drug-eluting (paclixatel) nitinol stent n = 241 self-expanding	6 and 12 months (only 12 months reported)	All cause mortality Procedure or device related mortality	Cook Medical

Khatib Y, Snyder SA, Ragheb AO, White JK, Machan LS, Zilver PTX Investigators. Paclitaxel-Eluting Stents Show Superiority to Balloon Angioplasty and Bare Metal Stents in Femoropopliteal Disease: Twelve-Month Zilver PTX Randomized Study Results. Circulation: Cardiovascular Interventions. 2011	response system Allocation concealment: Not reported Blinding: Not reported Sample size calculation: Calculated for primary outcome ITT analysis: ITT Drop outs: Angio group: 0 dropped out Stents group: 10 dropped out (5 withdrew and 5 loss to follow up	Exclusion criteria: criteria included: untreated >50% diameter stenosis (DS) of the inflow tract, lesion pre-treatment with adjunctive devices, and previous target vessel stenting			successful PTA. The other 50% had acute PTA failure, which required one repeat balloon inflation for 2-3 minutes prior to being considered an acute PTA failure. These 'failure' patients then underwent a secondary randomisation and received provisional stent placement with either BMS (50% of patients) or DES (50% of patients).	drug-eluting (paclixatel) nitinol stent n = 241	Amputation TLR ABPI

Baseline	Angio	Stent
Mean age	67.7 ± 10.6	67.9 ± 9.6
Male sex	152	155
BMI	28.2 ± 5.6	28.4 ± 5.3
Claudication	90.7%	90.2%
CLI	8.5%	8.9%
Diabetes	100	116
Type 1	13	19
Type 2	87	97
Hypertension	194	210
Hypercholesterolemia	166	180
History of smoking	200	204

Renal disease	25	34
Pulmonary disease	38	45
History of MI	41	50
SFA	232	229
SFA/popliteal	6	9
Popliteal	13	9
Previous intervention prior to study	14	13
ABPI	0.68 ± 0.2	0.67 ± 0.2

Effect size		
	PTA (n = 238)	Stents (n = 241)
All cause mortality at 12 months	4	9
All cause mortality at 24 months	8	18
Procedure or device related mortality at 12 & 24 months	0	0
Amputation (toe at 12 months)	0	1
Amputation at 24 months. Numbers not reported. States event rate <1%.		
TLR at 12 months	39	21
ABPI	0.89 ± 0.2	0.91 ± 0.23

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dick P, Wallner H, Sabeti S, Loewe C, Mlekusch W, Lammer J, Koppensteiner R, Minar E, Schillinger M. Balloon Angioplasty Versus Stenting With Nitinol Stents in Intermediate Length Superficial Femoral Artery Lesions. Catheterization and Cardiovascular Interventions. 2009; 74(7):1090-1095.	RCT ASTRON trial Multicentre (3 sites, Austria) Randomisation: Random number generator. Stratified by claudication versus critical limb ischemia, and length of the target lesion (≤ vs. >60 mm) Allocation concealment: Sealed envelopes Blinding: Not for primary researcher or patient but outcome assessors	Total N = 73	Inclusion criteria: Symptomatic peripheral artery disease (PAD) with either severe intermittent claudication (Rutherford class 3) or chronic critical limb ischemia with rest pain (Rutherford class 4) or ischemic ulcers (Rutherford class 5). >50% stenosis or occlusion of the SFA with a target lesion length between 30 mm and 200 mm, and at least one patent (<50% stenosis) tibioperoneal run-off vessel. Exclusion criteria: Acute critical limb ischemia, previous bypass surgery or stenting of the SFA, untreated inflow disease of the ipsilateral pelvic arteries (>50% stenosis or occlusion), and known intolerance of study medications or contrast agent. 95% of patients had intermittent claudication	N= 34 Primary stent implantation. Predilation with undersized balloons was performed restrictively in patients with very tight stenosis or heavily calcified lesions that did not allow primary passage with the stent introducer device. Stents were implanted to extend 10 mm proximal and distal to the margins of the target	N =39 PTA with optional secondary stenting. Minimal time for each balloon inflation was 2 minutes at 10–12 atm. After dilation control angiograms were obtained. In cases with a suboptimal primary result, a second prolonged balloon dilation (>2 minutes) of was performed. In patients	12 months (3, 6, and 12 months)	Complications Maximum walking distance ABPI Mortality	No details

were blinded.

Sample size calculation: Yes based on restenosis rate.

ITT analysis: Yes

Dropouts:

Complete follow-up data could be obtained 97% at 3 months, and in 93% at 6 and 12 months, Follow-up data were not available in two patients at 3 months (one died and one refused reevaluation) and in five patients at 6 and 12 months (three died, two refused reevaluation).

Baseline	Stent N = 34	PTA N = 39
Age (years) SD	69±9	69±10
Male %	74	64
BMI (SD)	27.9±3.6	27.7±3.8
Co-morbidity		
Hypertension %	79	85
Hyperlipidaemia %	91	92
Symptomatic coronary artery Disease %	35	31
History of myocardial infarction %	15	15
History of stroke %	6	5
Diabetes mellitus %	29	31
Current smoker	35	44

lesion. Multiple stents were overlapped for 10 mm. Postdilation after stenting was performed strictly within the stented segment with up to 10% oversizing of the postdilation balloon.

- - - - - - - - -

All interventions performed percutaneously

- - - - - - - - - - - -

All patients received aspirin 100 mg/day

with a persistent suboptimal result after the second balloon dilation, secondary stenting was performed.

- - - - - - - - -

For stent implantation in both groups, self-expandable nitinol stents with a nominal diameter of 6 mm were used.

Clinical stage of PAD (Rutherford)			indefinitely and clopidogrel 75 mg/day for 3 months postintervention. Aspirin and clopidogrel were initiated at least 2 days before the intervention in most patients; otherwise a loading dose of 300 mg clopidogrel was given during the intervention. Additionally patients received statins, antihypertensive medication, and oral antidiabetic therapy according to
Class 3 (intermittent claudication) %	91	97	
Class 4 (ischemic rest pain) %	3	0	
Class 5 (ischemic ulcers) %	6	3	
Maximum walking distance (m)	131±188	103±92	
ABPI	0.64±0.	0.63±0.	

		their cardiovascular risk profile.	
Effect Size			
In the PTA group, 10 of 39 patients (26%) underwent secondary stenting after two attempts of balloon dilation, due to a flow limiting dissection in six cases and a residual stenosis >30% in four cases. **Significantly higher rates of restenosis in angioplasty group.** **Significanlty higher mean walking capacity in stent group compared with angioplasty group at 6 months and 12 months.** **No significant differences between groups in ABPI**			
Outcome	Stent N = 34	PTA N = 39	P Value
Complications	0	1 (pseudoaneurysm)	
Baseline maximum walking capacity, m (mean ± SD)	131 ±188	103 ± 92	0.86
Maximum walking capacity, m at 6 months (mean)	800 ±265.33 ^	600 ±265.33 ^	0.002
Maximum walking capacity, m at (12 months (mean)	800 ±514.49 ^	550 ±514.49 ^	0.042
ABPI baseline (mean ± SD)	0.64 ± 0.33	0.63 ± 0.24	0.70
ABPI 6 months (mean)	1.20	1.06	0.84
ABPI 12 months (mean)	0.93	0.89	0.40
Minor complications at 30 days	0	1	
Major complications at 30 days	0	0	
1 death at 3 months, 3 deaths at 12 months (group unkown) **No ABPI/walking capacity data at 1 or 3 months** **^ standard deviations calculated by NCGC using p values**			

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Laird JR. Nitinol Stent Implantation Versus Balloon Angioplasty for Lesions in the Superficial Femoral Artery and Proximal Popliteal Artery: Twelve-Month Results From the RESILIENT Randomized Trial. Circulation: Cardiovascular Interventions. 2010; 3(3):267-276. **Laird, J. R., Katzen, B. T., Scheinert, D., Lammer, J., Carpenter, J., Buchbinder, M., Dave, R., Ansel, G., Lansky, A., Cristea, E., Collins, T. J., Goldsmith, J., Cao, Annie Y., Jaff, M. R., and RESILIENT, Investigators. Nitinol stent implantation vs.**	RCT RESILIENT: Randomized Study C omparing the Edwards Self-Expanding Lifestent versus Angioplasty Alone in LEsions INvolving The SFA and/or Proximal Popliteal Artery 24 centres in Europe and US Dec 2004 – Aug 2006 Randomized: Computer-generated randomisation (by patient) in blocks of 6 on 2:1 (2 stent : 1 angio) ratio Allocation concealment: Not mentioned Blinding:	Total N = 206	Inclusion criteria: Patients aged ≥18 years with symptoms of intermittent claudication (Rutherford 1 – 3) who were candidates for angioplasty or stenting, had de novo stenotic, occlusive or restenotic lesions in SFA, proximal popliteal art or both and had at least 1 patent infrapopliteal run-off vessel to the foot. Stenosis/restenosis of ≥50% and total lesion length of ≤150 mm. Exclusion criteria: Patients with critical limb ischemia (Rutherford 4 – 6), sensitivity to contrast media that was not amenable to	Angio N = 72 Percutaneous transluminal angioplasty Provisional (bailout) stent used if after multiple balloon inflations suboptimal angioplasty with flow-limiting dissection or residual stenosis >30% 40% (n=29) underwent bailout stenting	Stent N = 134 Self-expanding nitinol stent with predilatation and optional postdilatation	12 & 36 months	Mortality Amputation Target lesion revascularisation QoL	Not reported

balloon angioplasty for lesions in the superficial femoral and proximal popliteal arteries of patients with claudication: three-year follow-up from the RESILIENT randomized trial. Journal of endovascular therapy 19(1), 1-9. 2012.	Open Sample size calculation: Yes, for primary outcome ITT Analysis: Yes, all endpoints Drop outs: 12 (6%)	pretreatment with steroids, antihistamines, or both known allergies to study medications or materials, renal failure (Cr > 2.0 mg/dL) or hepatic insufficiency, previous bypass surgery of the target limb, extensive peripheral vascular disease that precluded safe insertion of introducer sheath, aneurysmal disease in the vessel segment to be treated, thrombus in the area to be treated that could not be resolved, angiographic evidence of poor inflow that was inadequate to support vascular bypass patients who were receiving dialysis or immunosuppressive

	therapy Baseline characteristics of randomized patients: Age, sex, race and pre-procedure classification of symptoms not significantly different between treatment groups (p>0.05). CV risk factors not significantly different between groups (p≥0.09) except slightly higher reported prevalence of hypertension in angio group compared with stent group (p=0.03)		
Effect size			
	Angio n=72	Stent n=134	P-value
Freedom from target lesion revascularisation (6 months) – bailout stent considered as revascularisation ¬	52.6%	98.5%	P<0.0001
Freedom from target lesion revascularisation (12 months) – bailout stent considered as revascularisation ¬	45.1%	87.3%	P<0.0001
Freedom from target lesion revascularisation (24 months) – bailout stent considered as revascularisation ¬	41.8%	77.8%	

Freedom from target lesion revascularisation (36 months) – bailout stent considered as revascularisation ¬	41.8%	75.5%	
Freedom from target lesion revascularisation (6 months) – bailout stent not considered as revascularisation ^	91.2% n=66 *	98.5% n=132 *	P<0.04
Freedom from target lesion revascularisation (12 months) – bailout stent not considered as revascularisation ^	77.3% n=56 *	87.3% n=117 *	P<0.09
Freedom from target lesion revascularisation (36 months) – bailout stent not considered as revascularisation ^	70.1% n=50 *	75.5% n=104 *	
Freedom from major adverse clinical events (MACE) at 6 months £	92.8% n=67 *	93.1% n=125*	
Freedom from major adverse clinical events (MACE) at 12 months £	86.6% n=64 *	85.8% n=115 *	
Death within 30 days of procedure	0	0	
Probability of survival at 36 months	91.7%	90.0%	P=0.71
Amputations at 12 months	2†	0	
Quality of Life			
SF-8 baseline	41.0±10.5	41.4±9.2	
Change in SF-8 at 12 months	5.9±11.2	5.7±11.2	P<0.0001 versus baseline
Change in SF-8 at 36 months	6.9±12.2	5.4±11.3	P<0.0001 versus baseline
Baseline walking distance score	20.3±20.8	26.1±25.4	
Walking distance score at 12 months	22.3±23.2	22.8±24.2	
Change at 12 months in walking distance score from baseline	29.4±37.4	25.6±34.6	P<0.0001 versus baseline

Change at 36 months in walking distance score from baseline	21.9±36.1	19.4±32.9	P<0.0001 versus baseline

†Single toe amputations

¬ a bailout stent in the PTA group was classified as TLR in the study's analysis for primary patency.

^ Study also reports a post hoc analysis classified as secondary patency where a bailout stent in the PTA group was not classified as TLR. (29 patients underwent bailout stents).

*** numbers calculated by NCGC. Study reports all end points analysed on an intention to treat (as randomized) basis. Numbers calculated as a percentage of numbers randomized for each and rounded up or down.**

£ defined as death within 30 days, stroke, myocardial infarction, significant distal embolization, emergent surgical revascularisation of target limb, thrombosis and worsening of Rutherford category).

Patients in the angioplasty group reported more claudication pain at 12 months than patients in the stent group (Walking Improvement Questionnaire evaluation, P=0.009); no further details given

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Greenberg D, Rosenfield K, Garcia LA, Berezin RH, Lavelle T, Fogleman S, Cohen DJ. In-Hospital Costs of Self-Expanding Nitinol Stent Implantation Versus Balloon Angioplasty in the Femoropopliteal Artery (The VascuCoil Trial).	RCT Multicenter prospective randomized trial (20 sites) – USA May 1997-Dec 1999 Randomized: Patients randomized – method not	Total N = 266	Inclusion criteria: Candidates for angioplasty with symptomatic leg ischaemia requiring treatment of the superficial femoral/popliteal vessel with an occluded lesion length ≤12 cm or a stenotic lesion length ≤15 cm and located proximal to the bifurcation of the tibial artery Exclusion criteria:	Angio N=131 patients, 177 lesions Percutaneous transluminal angioplasty (angio) Pts in angio arm allowed to	Stent N=135, 175 lesions Intracoil fermoropoplitteal stent	Clinical follow- up visits were conducted at 6 months, 9 months and 1 year, with continuing annual follow- up for safety.	Mortality Amputation Adverse events ABPI	Supported in part by a grant from IntraTherapeutics. Trail stopped early due to slow patient enrolment. Slow patient enrolment attributed to physician

Journal of Vascular and Interventional Radiology. 2004; 15:1065-1069. **US Food and Drug Administration. IntraCoil® Self-Expanding Peripheral Stent: Summary of Safety and Effectiveness Data. Silver Spring, MD: US Food and Drug Administration, 2002.**	stated Allocation concealment: Not stated Blinding: Open Sample size calculation: Not stated, however study originally designed to enroll 500 patients, but was stopped early due to slow patient enrollment. ITT Analysis: Yes Drop outs: not stated	Baseline characteristics of randomized patients: P-value non-significant for all comparisons: Baseline characteristics: Stent / Angioplasty Age: 66.8± 10.6 / 68.1±0.2 Male %: 67.4 / 63.4 DM %: 38.0 / 37.4 Smoking hx %: 81.9 / 80.0 Prior MI %: 37.2 / 29.1 Ref vessel diameter (mm): 4.2±0.96 / 4.2±1.0 Lesion length (cm): 3.6±3.0 / 3.3±3.0 Total occlusion: 22.7% / 16.8%	crossover to Stent if i) actue results indicated abrupt closure or impending closure due to severe recoil or extensive dissection, not correctable despite repeated balloon inflation or larger balloon size (if appropriate) or ii) during follow-up there was angiographically defined restenosis or dissection that was limb threatening		reluctance to include all eligible lesions in a randomized study of balloon angioplasty. Originally aimed to recruit 500 people. Very high risk of selection bias.
Effect size					

	Angioplasty (n=131 patients)	Stent (n=135 patients)
All-Cause Mortality	1	0
Amputation	1	0
Change in ABI (from baseline to 9 months) range (min, max)	0.08 ± 0.19 (n=64) (-0.25,0.52)	0.19 ± 0.20 (n=83) (-0.43,0.56)
Distal embolisation (major)	1	0
Major bleeding complications (major)	1	1
Major vascular complications (major)	6	5
Renal failure (major)	3	0
Major adverse cardiac events (MACE) at 9 months ¬	21	22

¬ defined as death within 30 days, prei-procedural Q wave MI, and clinical driven target lesion revascularisation. 21`(calculated by NCGC by adding in hospital MACE and out of hospital MACE together)

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Cejna M, Thurnher S, Illiasch H, Horvath W, Waldenberger P, Hornik K, Lammer J. PTA Versus Palmaz Stent Placement in Femoropopliteal Artery Obstructions: a Multicenter Prospective Randomized Study. Journal of Vascular and Interventional Radiology. 2001; 12(1):23-31.	RCT Multicentre (n = 4 sites Austria) Randomisation: Randomized by limb. Unclear method Allocation concealment: Closed envelopes Blinding: Open labelled Sample size calculation: Yes based on patency in lesions ITT analysis: Yes Drop outs:	Total N = One hundred fifty-four limbs in 141 patients	Inclusion criteria: chronic CLI (rest pain category 4 or minor tissue loss category 5) or IC (categories 1-3). Society of Vascular Surgery/International Cardiovascular Survery categories; up to three lesions (stenosis and/or occlusions), up to 5 cm in length, located in the superficial femoral artery or in the aboveknee segment of the popliteal artery. At least one run-off vessel had to be patent at angiography. Exclusion criteria: Pregnant women, or patients with an acute onset of symptoms (with an angiographic appearance resembling an acute thromboembolism). Patients who had previous vascular surgery in the treated segments, with an untreated obstruction of the inflow vessels (eg, iliac and common femoral arteries), or patients who were unable or unwilling to participate in follow-up examinations and drug therapy	N = 77 limbs PTA alone In case of failed PTA (residual stenosis >30% with impaired flow and/or massive dissections) stent implantation performed. 10 limbs required stent placement - - - - - - - - All patients received acetylsalicylic acid (100 mg/d) orally beginning the day before treatment. After successful	N = 77 limbs' PTA + stent - - - - - - - - - - Two patients underwent bilateral PTA, one patient underwent bilateral stent placement. Randomized groups not clear	3, 6, 12 months after intervention. Mean 352 days (range 1-1,252 days) for PTA and 353 days (range 1-1,215 days for stent group)	Mortality ABPI Amputation Re-intervention Complications	

	Angiographic follow-up within 12 months was available in 45 limbs in the PTA group and 46 limbs in the Stent group). No angiographic follow-up was available in 33 limbs (13 PTA, 20 stent) No clinical follow up was available for 20 limbs (6 PTA, 14 stent)	Inadvertently, two patients (39 and 87 years old, respectively) were randomized and included in the study. Six patients who had mild (walking distances between 250 and 500 m) but severely life-style inhibiting claudication were included (PTA, n = 4 versus stent, n= 2), as well as a patient who was 87 years old (stent, n = 1)	PTA or stent placement, patients received intravenous heparin at 750–1000 units per hour for 2 days. Acetylsalicylic acid (100 mg/d) was prescribed as a continuous life-long medication.	

Baseline	PTA N = 77 limbs	PTA +stent N = 77 limbs
Age (years) Range	65.5 (39.2-83)	68.6 (39.2-87)
Male %	59.8	63.6
Co-morbidities		
Hyperlipidemia (%)	46.8	35.0

Diabetes mellitus (%)	40.2	39.0
Smoking history (%)	61	62.4
SVS-ISCVS categories		
Mild and moderate(%)	16.9	14.3
Severe claudication(%)	58.4	50.6
Ischaemic rest pain (%)	9.0	14.2
Minor tissue loss	15.6	20.8
Location on lesion		
Proximal SFA	14.2	22.0
Distal SFA and hiatus adductoris	75.4	72.8
Above knee popliteal artery	10.4	5.2

Effect Size		
ABPI significantly increased following each procedure but there were no between group differences. **IN the stent group initial technical success was significantly greater than PTA alone (P=0.009)** **There was no significant difference between groups for major or minor complications.** **There were no differences between groups in primary or secondary patency rates** **There were no significant differences between groups in clinical stage of disease.**		
Outcome	PTA N = 77 limbs	PTA +stent N = 77 limbs

Mortality		
Mortality <30 d (n) patients	2 (MI; Sepsis)	0
Mortality >30 d (n)	5	12
Total mortality (n)	7	12
Outcome	PTA N = 77 limbs	PTA +stent N = 77 limbs
Reintervention at 12 months follow-up (n)	12	21
Bypass at 12 monthsfollow-up (n)	4	7
Total reintervention at 12 months follow-up	16	28
Complications		
Major complication Large groin haematoma (n)	2	0
Early thrombosis <30d (n)	1	3
Peripheral embolisation (treated) (n)	3	4
Amputations <30d (n)	4 (digits)	2 (crural)

ABPI		
ABPI pre-treatment (mean±SD)	0.62±0.22	0.63±0.20
ABPI post-treatment at unspecified timepoint (mean±SD)	0.97±0.20	0.99±0.18

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schillinger, M., Sabeti, S., Loewe, C., Dick, P., Amighi, J., Mlekusch, W., Schlager, O., Cejna, M., Lammer, J., and Minar, E. Balloon angioplasty versus implantation of nitinol stents in the superficial femoral artery. New England Journal of Medicine 354(18), 1879-1888. 2006. **Schillinger, M., Sabeti, S., Dick, P., Amighi, J., Mlekusch,**	RCT Austria Randomisation: Blocks of four with the use of computer-generated random digits. Patients were stratified according to the reason for revascularization (claudication vs. critical limb ischemia) and the length of the target lesion (≤60 mm vs. >60 mm). Allocation concealment: Sealed	Total N = 104	Patients referred for endovascular treatment of the superficial femoral artery owing to intermittent claudication or chronic critical limb ischemia. Inclusion criteria: Symptomatic peripheral-artery disease with severe intermittent claudication (Rutherford stage 3), chronic critical limb ischemia with pain while at rest (Rutherford stage 4), or chronic critical limb ischemia with ischemic ulcers (Rutherford stage 5). Stenosis of more than 50 percent or occlusion of the ipsilateral superficial femoral artery, a target-lesion length of more than 30 mm, and at least one patent (less than 50 percent stenosed) tibioperoneal runoff vessel. Exclusion criteria: Acute critical limb ischemia, previous bypass surgery or stenting of the superficial femoral artery, untreated inflow disease of the ipsilateral pelvic arteries (more than 50 percent stenosis or	N = 51 Self-expanding nitinol stent. Percutaneous approach See Dick 2009 Ref ID 32 for details - - - - - - - - - All patients received aspirin (100 mg daily) indefinitely and clopidogrel (75 mg daily) for three months after the intervention. Most patients started taking	N = 53 Angioplasty with optional secondary stenting. Percutaneous approach See Dick 2009 Ref ID 32 for details - - - - - - - - - 17 (32 %) underwent secondary stenting	24 hours, 3, 6 and 12 months	Complications Maximum walking distance ABPI Mortality Reintervention Amputation SF-36	Medical University of Vienna and the Vienna General Hospital.

W., Schlager, O., Loewe, C., Cejna, M., Lammer, J., and Minar, E. Sustained benefit at 2 years of primary femoropopliteal stenting compared with balloon angioplasty with optional stenting. Circulation 115(21), 2745-2749. 2007. **Sabeti, S., Czerwenka-Wenkstetten, A., Dick, P., Schlager, O., Amighi, J., Mlekusch, I., Mlekusch, W., Loewe, C., Cejna, M., Lammer, J., Minar, E., and Schillinger, M. Quality of life after**	envelopes Blinding: Not for patient or investigator but outcome assessors were blinded Sample size calculation: Yes based on restenosis rate ITT analysis: Yes Drop outs: Data were not available for three patients at 12 months 2 from stent group and 1 from angioplasty group(one died and two declined to be reevaluated). Groups not reported.	occlusion), and known intolerance to study medications or contrast agents. 88% of patients had intermittent claudication			clopidogrel at least two days before the intervention; for those who did not, a loading dose of 300 mg of clopidogrel was given during the intervention. 17 patients underwent secondary stenting

Baseline	Stent N = 51	Angioplasty +/- stent N = 53
Age (years) SD	65±10	68±10
Male %	59	47
BMI (SD)	27.5±3.8	27.4±4.0
Co-morbidities		
Hypertension (%)	94	89
Hyperlipidemia (%)	92	87
Diabetes mellitus (%)	43	32
Smoking at baseline (%)	53	36

balloon angioplasty versus stent implantation in the superficial femoral artery: Findings from a randomized controlled trial. Journal of endovascular therapy 14(4), 431-437. 2007.	Coronary artery disease (%)	67	75
	History of myocardial infarction (%)	20	8
	History of stroke (%)	4	9
	Rutherford stage of peripheral-artery disease		
	3 (%)	88	87
	4 (%)	2	4
	5 (%)	10	9
	Maximal distance walked on a treadmill (median, IQR)	92 (45–113)	87 (44–118)
	ABPI (SD)	0.57±0.19	0.54±0.20

Effect Size - Results from Schillinger, 2006		
Outcome	Stent N = 51	Angioplasty +/- stent N = 53
Complications during operation		
Major complication	0	0
Minor complications	1	1

Maximal walking distance, m (median, 95% CI)		
Maximal walking distance (Metres) 6 months	363 (260, 450)	270 (180, 340)
Maximal walking distance (Metres) 12 months	387 (310, 480)	267(170, 340)
ABPI (mean, 95% CI)		
ABPI 6 months	0.81 (0.75, 0.9)	0.73 (0.71, 0.80)
ABPI 12 months	0.87 (0.82, 0.91)	0.75 (0.7, 0.81)
Ipsilateral re-intervention within 12 months		
Balloon angioplasty	10/49	15/52
Stent implantation	1/49	1/52
Bypass surgery (supragenicular)	3/49	0/52
Total ipsilateral re-intervention rate within 12 months	14/49	16/52
Amputation		
Within 6 mo	0/51	0/53
Within 12 mo	0/51	0/53
Death		
Within 6 mo	0/51	0/53
Within 12 mo	1/51	0/53
Results from Schillinger, 2007 **There had been no major complications at baseline.**		
Outcome	Stent N = 46	Angioplasty +/- stent N = 52
Walking capacity treadmill Median	302 (99-700)	196 (77 – 355)

(IQR) at 2 years			
ABPI mean SD at 2 years	0.88 ± 0.18	0.78±0.17	
Reinterventions at 2 years	17	28	
Minor amputation at 2 years	0	1	
Results from Sabeti, 2007			
Up to 12 months follow-up all parameters of QoL significantly improved in the entire population (P<0.01) except for social functioning and role emotional perception. Patients without stenosis at 6 (physical and mental component score) and 12 months (physical component score) had significantly better quality of life compared with patients with restenosis			
There were no significant difference for any parameter of QoL at any time interval between stent and balloon angioplasty groups.			
Outcome	Stent N = 51	Angioplasty +/- stent N = 53	
SF-36 Median (IQR)			
Physical functioning baseline	50 (32-60)	45 (30-55)	NS
Physical functioning 6 months	60 (35-85)	62 (35-85)	NS
Physical functioning 12 months	65 (45-82)	67 (38-45)	NS
Role physical functioning baseline	0 (0-75)	0 (0-50)	NS
Role physical functioning 6 months	0 (0-100)	0 (0-100)	NS
Role physical functioning 12 months	25 (0-100)	0 (0-100)	NS
Bodily pain baseline	30 (12-41)	22 (10-40)	NS
Bodily pain 6 months	51 (22-100)	52 (30-74)	NS
Bodily pain 12 months	52 (22-100)	46 (22-76)	NS
General health baseline	52 (35-62)	45 (35-63)	NS
General health 6 months	47 (35-67)	47 (32-70)	NS

General health 12 months	52 (35-64)	50 (30-71)	NS
Vitality baseline	45 (30-55)	40 (27-50)	NS
Vitality 6 months	50 (36-60)	47 (33-66)	NS
Vitality 12 months	50 (37-67)	45 (30-66)	NS
Social functioning baseline	88 (50-100)	75 (50-100)	NS
Social functioning 6 months	88 (63-100)	88 (59-100)	NS
Social functioning 12 months	100 (75-100)	88 (59-100)	NS
Role emotional baseline	67 (0-100)	100 (0-100)	NS
Role emotional 6 months	100 (33-100)	100 (0-100)	NS
Role emotional 12 months	100 (67-100)	67 (0-100)	0.04
Mental health baseline	64 (46-80)	64 (52-78)	NS
Mental health 6 months	72 (48-84)	66 (48-80)	NS
Mental health 12 months	72 (58-84)	60 (48-84)	NS
Physical component summary baseline	31 (26-37)	27 (22-35)	0.07
Physical component summary 6 months	33 (29-49)	37 (30-47)	NS
Physical component summary 12 months	35 (30-48)	37 (27-49)	NS
Mental component summary baseline	48 (41-59)	49 (38-60)	NS
Mental component summary 6 months	53 (42-58)	50 (35-58)	NS
Mental component summary 12 months	54 (45-49)	51 (35-58)	NS

QoL outcome data not reported at 3 months

4.2.2.2. Management of critical limb ischemia

Study details	Patient	Intervention	Comparison	Outcome measures	Other comments
Brodmann, M., Froehlich, H., Dorr, A., Gary, T., Portugaller, R. H., Deutschmann, H., and Pilger, E. Percutaneous transluminal angioplasty versus primary stenting in infrapopliteal arteries in critical limb ischemia. VASA.Zeitschrift fur Gefasskrankheiten 40(6), 482-490. 2011. **RCT - Austria** **Randomisation:** **Computer generated block randomisation** **Allocation concealment:** **Sealed envelopes** **Blinding: Not reported** **Sample size calculation:**	Total N=54 Inclusion criteria: CLI (Rutherford Classification 4-6) Femoropopliteal Lesion characterized by either isolated stenoses greater than 70%; sequential stenoses up to cumulative length of 12 cm or total occusion of the curual arteries with a maximum length of 12 cm the target vessel must be a distal run-off vessel written informed consent life expectancy of at least 12 months Exclusion criteria: endovascular procedure in last 3 months refused informed consent known allergy to clopidogrel or aspirin, indication for oral anticoagulation concomitant participation in another clinical trial Baseline: Angio / Stent Age: 74.9 ± 1.3 / 68.9 ± 2.9	Angioplasty n = 33 Performed with Amphirion Deep catheter In the case of unsuccessful PTA (high grade restenosis through a high calcified plaque or vast dissection after PTA considered flow limitation) a secondary bailout stent was implanted. Two patients required bailout stents.	Stent n = 21 Balloon expandable stent with a silicon carbide coating the Motion Explorer Stent	Complications Mortality	Funding source: Not reported Study reports it was originally planned as multicentre trial but only 1 centre succeeded in recruiting patients. Study reports this accounts for difference between groups in numbers randomized.

Not reported **ITT analysis: ITT** **Drop outs: not reported** **Follow-up duration: 12 months**	Weight (kg)	72.3 ± 13.2	76.5 ± 15.2
	BMI	25.9 ± 3.7	26.9 ± 3.2
	Female	60.6%	42.9%
	Hypertension	27	19
	Hyperlipidaemia	6	14
	Diabetes mellitus Insulin dependat	24 36.4%	16 47.6%
	Smoking	8	7
	CVD	29	18
	CAD	29	18

Effect size		
	PTA (n = 33)	Stent (n = 21)
Mortality at 12 months: 9 out of 44 patients died but not reported which groups there were in.		
Complications at 12 months		
Acute re-obstruction	0	0
Peripheral embolisation	1	0
Local haematoma	3	0
Haemodynamically instability	0	0
Need of blood transfusion	0	0
Total minor complications at 12 months (as defined by GDG)	4	0
Complete ulcer healing at 12 months	16/20	5/13

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Rand, T., Basile, A., Cejna, M., Fleischmann, D., Funovics, M., Gschwendtner, M., Haumer, M., Von Katzler, I., Kettenbach, J., Lomoschitz, F., Luft, C., Minar, E., Schneider, B., Schoder, M., and Lammer, J. PTA versus carbofilm-coated stents in infrapopliteal arteries: pilot study. Cardiovascular and Interventional Radiology 29(1), 29-38. 2006. **RCT - Single centre - Austria** **Randomisation: one to one and performed per patient. Unclear method** **Randomisation performed after target lesion was passed by guidewire.** **Allocation concealment: Numbered envelopes**	Total N = 51 (95 lesions) Inclusion criteria: chronic critical limb ischemia stages III and IV of the Fontaine classification Isolated stenosis >70% or occlusion of the tibial arteries patients with up to three lesions; and lesions up to 3 cm with a cumulative lesion length of ≤9 cm, including the tibiofibular trunk, anterior and posterior tibial arteries, and peroneal artery. There was no further limitation regarding lesion position. Exclusion criteria: Patients with: a significant inflow obstruction at the pelvic or superficial femoral artery level; evidence of a systemic coagulopathy in whom anticoagulant and antiplatelet treatment was contraindicated, previously implanted stents in the target lesion, patients with total occlusion in the target vessel following the target lesion, patients without distal runoff, inflammatory vascular disease, peptic ulcer or gastric/intestinal bleeding in the previous 6 months, and patients with clinically assessed intolerance to contrast medium. Total occlusion through which the guidewire could not	N=27 patients (53 infra-popliteal lesions) PTA Balloon angioplasty Postinterventional anticoagulation therapy for the angioplasty group consisted of low molecular- weight heparin (Enoxaparin 2 · 40mg) for 3 days and acetylsalicylic acid (ASA; ThromboAss, 100 mg per day permanently). 1 failure resulted in secondary stenting	N=24 patients (42 infrapopliteal lesions) Stent (Carbostent) Adjunct therapy for the stent group consisted of clopidrogel (Plavix), administered as a bolus of 300 mg on the day of the procedure and 75 mg per day orally for 4 weeks, and ASA medication permanently. 1 failure	Minor and major amputations Complications Re-intervention Mortality	Funding source: Ludwig Boltzmann Institute for Radiologic Tumor Diagnosis and the Ludwig Boltzmann Institute of Interdisciplinary Vascular Research.

Blinding: Outcome assessors blinded

be passed. Claudication only.

Sample size calculation: No details

Mean age 72 (range 47 -80) years

Baseline (n)	Angioplasty N = 27	Stent N = 24
Lesions	53	42
Fontaine III	8	4
Fontaine IV	19	20
Diabetes	19	16
Smoking	17	14
Cardiac disease	11	9

ITT analysis: No

Drop outs: 14 patients (20 angioplasty and 17 stents) in total. By lesion, 21 lesions from angioplasty group and 17 lesions from stents

Follow up duration:

6 months

angioplasty (mean 5.6±1.97)

Stent (mean 6.0±3.21).

Consisted of clinical investigation and Doppler US within 2 days of procedure.

At 6 mnths – digital subtraction angiography or spiral CT angiography was performed.

Effect Size		
Outcome	Angioplasty N = 27	Stent N = 24

Amputation total – no time point given (assume 6 months)	1	2
Major	0	1
Minor	1	1
Re-intervention (6 months)	0	1

Reintervention: 1 stent patient underwent bypass procedure, which later failed and resulted in minor amputation. No further data presented on reintervention

Mortality: 2 deaths (of 51 patients) within 30days and 1 death at >30 days from sepsis (groups unknown).

Complications: rate of major complications within 30 days was 3.9% (2/51 patients). 1 major complication (haematoma) group unknown

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Rand, T., Lammer, J., Rabbia, C., Maynar, M., Zander, T., Jahnke, T., Muller-Hulsbeck, S., Scheinert, D., and Manninen, H. I. Percutaneous transluminal angioplasty versus turbostatic carbon-coated stents in infrapopliteal arteries: InPeria II trial. Radiology 261(2), 634-642. 2011. **RCT - Multicente, Europe** **Randomisation: Not reported**	Total N = 88 Inclusion criteria: Critical limb ischaemia (Rutherford classification stage 4 or 5) Symptomatic PAD due to de novo lesion of an infrapopliteral artery Stenosis of at least 50% Substantial inflow stenosis if stenosis had been successfully treated without complication In-line circulation to the foot distal to the lesion present Exclusion criteria: Previous treatment Total occlusion located in the target vessel No distal run off	Angioplasty n = 44 (69 lesions) 1 patient required a stent bailout	Stent n= 44 (62 lesions)	Mortality Amputation TLR ABPI	Funding source: Sorin Biomedica Cardio supplied devices for the trial

Allocation concealment: Not reported

Blinding: Not reported

Sample size calculation: Not reported

ITT analysis: Available case analysis

Drop outs:

Angio group: 24 dropped out

Stents group: 19 dropped out

Follow-up duration: 3 and 9 months

Underlying disease		
Baseline	Angio (n = 44)	Stent (n = 44)
Number of limbs	45	44
Male sex	28/45	30/44
Age	72.1 ± 9.5	71.4 ± 8
Diabetes	34/45	35/44
Rest pain	10/45	1/44
Ulcer and or gangrene	35/45	43/44
Number of lesions	69/45	62
De nono	69/69	61/62
Concentric	32/69	28/62
Calcification	54/69	49/62
Total occlusion	19/69	12/62

Effect size

	Angio	Stent
Mortality at 3 months	3 out of 32	5 out of 33
Mortality at 9 months	5 out of 24	5 out of 19
Amputation at 3 months	4 out of 32	6 out of 33
Amputation at 9 months	7 out of 24	10 out of 19
TLR at 3 months	0 out of 32	1 out of 33
TLR at 9 months	6 out of 24	7 out of 19

ABPI at 3 months	0.7 ± 0.3 (n = 32)	0.9 ± 0.1 (n = 33)
ABPI at 9 months	0.8 ± 0.3 (n = 24)	0.8 ± 0.1 (n = 19)

4.3. Bare metal versus drug eluting stents

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Duda, S. H., Bosiers, M., Lammer, J., Scheinert, D., Zeller, T., Oliva, V. L., Tielbeek, A., Anderson, J., Wiesinger, B., Tepe, G., Lansky, A., Jaff, M., Mudde, C., Tielemans, H., and Beregi, J. P. Drug-eluting and bare nitinol stents for the treatment of atherosclerotic lesions in the superficial femoral artery: long-term results from the SIROCCO trial. Journal of endovascular therapy 13(6), 701-710. 2006. **Duda, S. H., Pusich, B., Richter, G., Landwehr, P., Oliva, V. L., Tielbeek, A., Wiesinger, B., Hak, J. B., Tielemans, H., Ziemer, G., Cristea, E., Lansky, A., and Beregi, J. P. Sirolimus-eluting stents for the treatment of obstructive superficial femoral artery disease: six-month results. Circulation 106(12), 1505-1509. 17-9-2002.** **Duda, S. H., Bosiers, M., Lammer, J., Scheinert, D., Zeller, T., Tielbeek, A., Anderson, J.,**	Total N = 93 Inclusion criteria: • aged over 30 years old, symptomatic PAD (Rutherford scale 1 to 4) • obstructive (≥70 %) de novo or restenotic lesions in the native SFA. • The reference vessel diameter was 4 to 6 mm, stenotic lesions varied in length from 7 cm to 20 cm in the first phase of the study and 7 to 14.5 cm in the second phase of the study. The occlusions varied from 4 to 20 cm in the first phase of the study and 4 to 14.5 in the second phase. • All lesions were classified as TASC type C Exclusion criteria: • poor aorto-iliac or common femoral inflow, • uremia, • aneurism in target vessels, tandem lesions, previously stented lesions, • ischemic tissue loss, • deep venous thrombosis, pregnancy, hepatic insufficiency, end stage renal failure requiring dialysis, immunosuppressant therapy, • recent hemorrhagic stroke within past 3 months,	N = 47 Sirolimus-eluting SMART stent For both types of sent: SIROCCO I: a maximum of 3 stents implanted SIROCCO II: maximum of 2 stents implanted Patients not already on aspirin received a loading dose of 300 mg 1 day before the procedure; all received intra-arterial heparin boluses (3000-5000 units) at the time of the	N = 46 Bare SMART nitinol stent	Restenosis ABPI Adverse events Amputation	Funding source: Cordis Corporation, a Johnson and Johnson company, Miami lakes, Florida, USA

Wiesinger, B., Tepe, G., Lansky, A., Mudde, C., Tielemans, H., and Beregi, J. P. Sirolimus-eluting versus bare nitinol stent for obstructive superficial femoral artery disease: the SIROCCO II trial. Journal of Vascular and Interventional Radiology 16(3), 331-338. 2005.

RCT- Multicentre (Europe and Canada)

Trial conducted in two phases

Randomized: yes but method not stated

Allocation concealment: not reported

Blinding: double blinded

Sample size calculation: not reported

ITT analysis: ITT performed.

Drop outs: In the sirolimus stent group 7 patients died (1 due to stroke, 1 due to lung emboli, 1 due to cancer, 2 due to cardiac disease and 2 due to natural causes). In the bare stent group 2 patients died (1

- severe calcification that was deemed resistant to stenting, vessel tortuosity, revascularisation involving the same limb within 30 days, total occlusions of the iliac artery on the same side, requirement for stent in the popliteal artery,
- allergies to aspirin, heparin, sirolimus, nitinol, anticoagulants, antiplatelet therapy or contrast media, known or suspected active infection, presence of a aortic, iliac or femoral vascular prosthesis,
- life expectancy < 2 years,
- female patients of child bearing potential had a documented negative pregnancy test within 3 days prior to randomisation

Baseline	DES N=47	BMS N = 46
Age (years) SD	66.3 ±9.1	65.9 ± 10.8
Men %	66	78
Rutherford (n)		
1+2	20	26
3+4	27	20
ASA		
1	15	17
2	24	22
3	8	7
Cardiomyopathy (n)	23	18
Diabetes (n)	20	16
Hyperlipidemia (n)	30	29
Hypertension (n)	32	32
Current smoker (n)	22	14

procedure, followed by a 750-1000-U/h infusion as necessary.

After the procedure either ticlopidine or clopidogrel was recommended for 4 weeks in addition to aspirin for 12 months.

due to complications of coronary bypass surgery and 1 due to progressive cardiac failure). **In addition to those lost from the study due to death, at 24 months there are no outcome data for an extra 5 in the sirolimus stent group and 6 (for restenosis)/7 (for ABI) in the bare stent group.** **Follow-up duration: 2 years**	Reference vessel diameter, mm	4.9 ± 0.7	4.7 ± 0.6		
	Lesion length mm	85 ± 44	81 52		
	Calcification (n) (moderate and severe)	27	16		
	Types of lesion				
	De novo (n)	42	44		
	Restenotic (n)	5	2		
	Total occlusion (n)	31	26		
	Total stents (n)				
	1	15	10		
	2	25	28		
	3	6	8		
	4	1	0		
Effect size					
At 24 months the cumulative in-stent restenosis rates did not differ significantly between the treatment groups; following the procedure the ABI increased in both groups and remained elevated 24 months after stent implantation and there was no significant difference between the treatment groups at 24 months.					
Outcome	Sirolimus stent N = 47		Bare stent N = 46	p-value	P value from kaplin meier
ABPI at 24 months (mean±SD/median)	0.90±0.17/0.96 (n = 35)		0.84±0.20/0.87 (n = 37)	0.127*	
Adverse event rates at 24 months					
Target vessel revascularisation	6 (13%)		10 (22%)		0.33 Calculated variance 3.75; OE 1.89)
Target lesion revascularisation	3 (6%)		6 (13%)		0.3 Calculated variance 2.00; OE 1.47)

Total occlusion (minor adverse event)	0 (0%)	3 (6%)	
Amputation as a complication of the stent procedure	0 (0%)	0 (0%)	
Death	7 (15%)	2 (4%)	
Data extracted from Duda, 2002 (ref ID 15986) SIROCCO I			
Outcome	Sirolimus stent N = 18	Bare stent N = 18	p-value
Adverse events at 6 months			
Suspected cellulites (minor adverse event)	1	0	
Occlusion (minor adverse event)	0	1	
Data extracted from Duda, 2005 (ref ID 15987) SIROCCO II			
Outcome	Sirolimus stent N = 29	Bare stent N = 28	p-value
ABPI			
ABPI before procedure (mean±SD)	0.67 ± 0.2 n=23	0.61 ± 0.16 n=27	0.227
ABPI after procedure (mean±SD)	0.87 ± 0.11 n=26	0.86 ± 0.15 n=26	0.940
ABPI at 1 month (mean±SD)	0.96 ± 0.13 n=27	095 ± 0.16 n=23	0.935
ABPI at 6 months (mean±SD)	0.92 ± 0.15 n=23	0.88 ± 0.15 n=24	0.356
Patency at 6 months	n= 19/20	n= 22/22	Not reported
Adverse events at 6 months			
During procedure – stent thrombosis (minor adverse event)	1*	1*	
During procedure – pseudoaneurysm (minor adverse event)	1*	0	
During procedure – bleeding	0	1*	

(minor adverse event)		
Before discharge – revascularisation procedure on contralateral leg	2	2
Out of hospital events		
Death	2	1
Target lesion revascularization	0	0
Target vessel revascularization	1	3
Atypical chest pain (minor adverse event)	1	0
Hematoma at puncture site (minor adverse event)	0	1*
Severe internal bleeding (major adverse event)	1	0
Revascularisation procedure on contralateral leg	3	2
Total number (%)	13 (44.8)	13 (46.4)
*** Highly probably related to study procedure**		

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Rastan, A., Tepe, G., Krankenberg, H., Zahorsky, R., Beschorner, U., Noory, E., Sixt, S., Schwarz, T., Brechtel, K., Bohme, C., Neumann, F. J., and Zeller, T. Sirolimus-eluting stents vs. bare-metal stents for treatment of focal lesions in infrapopliteal arteries: a double-blind, multi-centre, randomized	Total N=161 Recruited between April 2006 and April 2008 N=82 polymer-free SES; N=79 received BMS NOTE: patients had infra-geniculate disease All patients (n=161 Sirolimus stent (n=82) Bare-metal stent (n=79	Polymer free SES (Yukon, Translumina, Hecklingen, Germany), coated in 2% sirolimus-containing solution All patients	Bare metal stent coated with ethanol	Mortality Target lesion revascularisation Amputation	Funding source: Not reported

clinical trial. European Heart Journal 32(18), 2274-2281. 2011. **Rastan, A., Brechtel, K., Krankenberg, H., Zahorsky, R., Tepe, G., Noory, E., Schwarzwalder, U., Macharzina, R., Schwarz, T., Burgelin, K., Sixt, S., Tubler, T., Neumann, F.-J., and Zeller, T. Sirolimus-eluting stents for treatment of infrapopliteal arteries reduce clinical event rate compared to bare-metal stents: long-term results from a randomized trial. Journal of the American College of Cardiology 60(7), 587-591. 2012.** **RCT - Multi-centre (4)** **Randomisation: Double-blind (physicians and patient), Computer generated random sequence, set in blocks** **Intention to treat analysis** **Follow-up duration: 6 and 12 month including clinical examination, calculation of the ankle brachial index (ABI), and DI (3-9 MHz linear transducer, IU 22 Philips, Bothell, WA, USA). Angiography performed in case of any conditioning limiting DU**		)		)	received oral aspirin (100mg daily) and oral clopidogrel (a loading does of 600mg 24 hr before the procedure follower by 75mg daily for 6 months)	ABI
	Age (years)	72.9 ± 9	73.4 ± 8	72.3 ± 9		
	Male sex (%)	66.5	67.9	64.9		
	Body mass index	27 ± 4	28 ± 5	27 ± 4		
	Diabetes mellitus (%)	53.8	56.8	50.6		
	Dyslipidaemia %	76.6	76.5	76.6		
	Hypertension (%)	89.9	91.4	88.3		
	Current smoker (%)	28.5	28.4	28.6		
	Renal insufficiency*	35.4	35.8	35.1		
	Critical limb ischemia %	46.6	51.2	41.8		
	Target lesion Anterior tibial artery (%)	27	22	31		
	Tibioperoneal trunk	37	42	33		
	Peroneal artery	21	19	23		
	Posterior tibial artery	15	17	13		
	ABI pre-intervention	0.48 ± 0.16	0.47 ± 0.18	0.49 ± 0.14		
	ABI post-intervention	0.84 ± 0.17	0.86 ± 0.`5	0.83 ± 0.19		
	* defined by creatinine ≥ 1.5mg/dL					

Effect size:		
Results at 6 and 12 months		
Both CLI and IC	Sirolimus stent	Bare-metal stent
Mean change in ABPI		
Baseline	0.49 ± 0.15	0.51 ± 0.15 (P=0.72)
After 12 months	0.72 ± (0.16	0.65 ± 0.13 (P=0.14)
Adverse events		
Total	22 (27.1%)	29 (36.7%)
Death (major cardiac event – 8 [5%]; gastrointestinal and pulmonary infections – 5 [3.1%]; lung cancer – 1 [0.6%]; uncertain – 11 [6.8%])	14 (17.1%)	11 (13.9%, P=0.66)
TLR during follow-up	6 (9.7%)	11 (17.5%, P=0.29)
Target limb reintervention (inflow lesion)	8 (12.9%)	7 (11.1, P=0.84)
Amputation due to insufficiently controlled wound infection despite adequate antiobiotic treatment	Lower leg major amputation – 1 Minor toe amputation of target limb - 1	Lower-leg major amputation – 2 Minor toe amputation – 2
Limb salvage rates after 12 months	98.4%	96.8% (P=0.61)
Results at 12 months in patients with CLI at baseline		
	Sirolimus stent (n=42)	Bare-metal stent (n=33)
Mean change in ABPI		
Baseline	0.35 ± 0.18	0.45 ± 0.15 (P=0.33)
After 12 months	0.71 ± 0.13	0.64 ± 0.14 (P=0.23)
Major adverse events		
Death	9 (21.4%)	8 (24.3%)
Minor amputation	1 (3.4%)	1 (4.3%)
Major amputation	1 (3.4%)	1 (4.3%)
Target Lesion Revascularisation	4 (13.8%)	3 (13%)
Wound healing	19 (86.4%)	14 (66.6%)

Results at 1200 days in patients with CLI and IC		
Death	17 (22.6%)	18 (24%)
Minor amputation	1 (1.32%)	5 (6.67%)
Major amputation	1 (1.32%)	4 (5.33%)
All amputation	2 (2.65%)	7 (12.2%)
Target Vessel Revascularisation	7 (9.2%)	15 (20%)
Results at 1200 days in patients with CLI at baseline		
Death	10 (26.3%)	10 (32.3%)
Minor amputation	3 (9.7%)	1 (2.6%)
Major amputation	4 (10.5%)	1 (2.6%)
All amputation	7 (22.6%)	2 (5.3%)
Target Vessel Revascularisation	4 (12.9%)	4 (10.5%)
Results at 1200 days in patients with IC at baseline		
Death	7 (18.4%)	8 (18.2%)
Minor amputation	0 (0%)	2 (4.5%)
Major amputation	0 (0%)	0 (0%)
All amputation	0 (0%)	2 (6.4%)
Target Vessel Revascularisation	3 (7.9%)	11 (25%)

Study details	Patients	Intervention	Comparison	Outcomes	Other comments
Dake, M. D., Ansel, G. M., Jaff, M. R., Ohki, T., Saxon, R. R., Smouse, H. B., Zeller, T., Roubin, G. S., Burket, M. W., Khatib, Y., Snyder, S. A., Ragheb, A. O., White, J. K., Machan, L. S., and Zilver,	Total N = 120 The inclusion / exclusion criterion below is for the study as a whole which first randomisation for PTA to DES. This data extraction is for the secondary randomisation for patients who failed PTA and were therefore randomized to DES or BMS. Patients who failed PTA were those who had ≥ 30% DS noted on arteriography after 1	N = 61 Drug eluting stent – self expanding nitinol drug eluting stent	N = 59 Bare metal stent – 3µg/mm= polymer-free paclitaxel	Procedure / device related deaths All cause morality	Funding source: Cook Medical

P. T. X., I. Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. Circulation: Cardiovascular Interventions 4(5), 495-504. 2011. **Dake, M. D. Drug-eluting stents-Zilver PTX. Cardiovascular and Interventional Radiology 35, S110-S111. 2012.** **RCT** **Multicentre RCT** **Randomized: not reported** **Allocation concealment: not reported** **Blinding: not reported** **Sample size calculation: not reported** **ITT analysis: ITT performed.**	repeat 2-3 minute balloon inflation **Inclusion criteria:** • Rutherford category ≥2 and ABP <0.9, • lesion length ≤14 cm, ≥50% DS, • reference vessel diameter 4-9 mm, and at least one patent runoff vessel (<50% DS throughout its course). **Exclusion criteria:** • untreated >50% diameter stenosis (DS) of the inflow tract, • lesion pre-treatment with adjunctive devices, • previous target vessel stenting The study did not report baseline characteristics for those who failed PTA and went on to have DES or BMS Baseline characteristics for all patients randomized to PTA (including those who had successful PTA) Mean age, years - 67.7 ± 10.6 Male sex, n 152 (63.9%) Claudication (Rutherford class 2-4) - 95.4% Critical Limb Ischemia - (Rutherford class 2-4) - 3.8% Diabetes, n - 100 (42.0%) Type I diabetes, n - 13 (13.0%) Type II diabetes, n - 87 (87.0%) Hypertension, n - 194 (81.5%) Hypercholesterolemia, n - 166 (69.7%) History of smoking, n - 200 (84.0%)	coating

Drop outs: 7 in total, 4 withdrew and 1 was lost from the BMS group, 2 withdrew from the DES group. **Follow-up duration: 2 years**	Renal disease, n - 25 (10.5%) Pulmonary disease, n - 38 (16.0%) History of myocardial infarction, n - 41 (17.2%) Lesion Characteristics Lesions, n - 251 247 Lesion location: SFA - 232 (92.4%) SFA/Popliteal - 6 (2.4%) Popliteal - 13 (5.2%)	
Effect size		
Outcome	BMS N = 59	DES N = 61
12 month results		
Procedure / device related deaths	0	0
All cause mortality	1	0
Patency	73%	89% (P-value for BMS vs DES = 0.01)
24 month results		
Target lesion revascularisation	10.8%	23.1% (P-value for 'freedom from TLR for BMS vs DES = 0.05)
Patency	81.2%	62.7% (P-value for BMS vs DES = <0.01)
All cause mortality	2	1

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Bosiers, M., Scheinert, M.D., Peeters, P., Torsello, G., Zeller, T., Deloose, K., Schmidt, A., Tessarek, J., Vinch, E., Schwartz, M.D. Randomized comparison of everolimus-eluting versus bare-metal stents in patients with critical limb ischemia and infrapopliteal arterial occlusive disease. Journal of Vascular Surgery 55, 390-399. 2012. **The DESTINY trial.**	• **Design**: multicentre RCT • **Source of funding**: Abbott laboratories • **Setting**: 5 European investigative centres • **Sample size**: 140 • **Duration**: 12 months • **Follow-up** : 1, 6 and 12 months • **Statistical analysis**: not reported.	• **Eligibility criteria:** symptomatic PAD due to a maximum of two focal de novo atherosclerotic target lesions in one or more infrapopliteal vessels; lesions with ≥50% diameter stenosis were considered for the trial when their length was ≤40mm and they arose in target vessels with diameters of 2.0 to 3.5mm. Lesions that arose in arteries located in the upper half of the lower leg were considered 'proximal' and those arising in the lower half of the lower leg were considered 'distal'; patients with significant inflow stenosis were eligible if the stenosis had been	**Group 1**: Bare-metal stent (Multi-Link Vision Stent). Made from L6015 cobalt chromium alloy with very thin strut architecture (81µm [0.0032 in]). Delivery balloons composed of a semi-compliant polyether block amide (PEBAX; Arkema, Colombes, France). The complete stent system crossing profile was ~1mm versus **Group 2**: Drug-eluting Stent (Xience V everolimus-eluting stent system, Abbott), which includes three components: the Multi-Link Vision Stent platform, the polymer coating (poly-vinylidene fluoride-co-hexafluoropropylen	**Outcome 1** *Mortality (hazard ratio):* *HR 0.88 (0.39 to 1.99)* *Survival %:* *Group 1 at 6 months: 90.7%* *Group 2 at 6 months: 91.8%* *Group 1 at 12 months: 84.2%* *Group 2 at 12 months: 81.9%* **Outcome 2** *Target Lesion Revascularisation by lesion at year 1* HR 3.50 (1.67 to 7.3) *Group 1 at 6 months: 85.5%* *Group 2 at 6 months: 96.1%* *Group 1 at 12 months: 66.4%* *Group 2 at 12 months: 91.3%* **Outcome 3:** *Amputation rate* *Group 1: 2/66* *Group 2: 1/74*	**Results critical appraisal**: moderate quality **Dropouts:** 33 patients were censored: 23 deaths, 3 major amputations (two for group 1 and one for group 2), 7 patients lost to follow-up during the first year.

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		successfully treated without complication; at least one patent tibial artery that provided in-line circulation to the foot; at least single-vessel outflow to the foot (distal to the target lesion). • **Exclusion criteria:** see above • **Patient characteristics**: Group 1: n=66 Dropouts at 1 year follow up: Mean (s.d, range) age: 76 (56-95) Male: 44 (67%) Prior tobacco abuse: 15 (22%) Current tobacco abuse: 12 (15%) Hypertension requiring medication:7 (11%) Non-insulin-dependent diabetes mellitus:	e) PVDF-HFP), and everolimus, an antiproliferative drug. The polymer coating of the Xience V consists of a primer layer and a drug polymer reservoir layer. The polymer of the thin primer layer is poly (n=butyl methacrylate). **All patients:** Before stenting procedure, patients received aspirin daily (75-300mg) and clopidogrel (75mg daily or by loading with 300 to 600mg). Arterial access, diagnostic arteriography, systemic anticoagulation, and lesion traversal were performed at the discretion of the operator. Activated clotting time was neither routinely		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		16 (24%) Insulin-dependent diabetes mellitus: 17 (26%) Chronic renal insufficientcy:22 (33%) Hypercholesterolemia: 25 (38%) Obesity: 23 (35%) Rutherford-Becker class 4: 26 (39%) 40 (61%) Rutherford-Becker class 5: 40 (61%) Group 2: n=74 Dropouts at 1 year follow up: Mean (range) age: 75 (52-89) Male: 45 (61%) Prior tobacco abuse: 15 (22%) Current tobacco abuse: 11 (16%) Hypertension requiring medication: 47 (64%) Non-insulin-dependent diabetes mellitus: 19 (26%) Insulin-dependent	checked nor captured. Successful trasversal was an entry criterion.		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		diabetes mellitus: 25 (34%) Chronic renal insufficiency: 22 (30%) Hypercholesterolemia: 28 (38%) Obesity: 26 (35%) Rutherford-Becker class 4: 26 (39%) 37 (50%) Rutherford-Becker class 5: 37 (50%) • **Disease characteristics:** patients with critical limb ischemia (Rutherford-Becker categories 4 to 5) and infrapopliteal arterial occlusive disease.			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Geraghty, P.J., Mewissen, M.W., Jaff, M.R., Ansel, G.M. Three-year results of the VIBRANT trial of VIABAHN endoprosthesis versus bare nitinol stent implantation for complex superficial femoral artery occlusive disease. Journal of vascular surgery, 58(2), 386-295 **The VIBRANT trial.**	• **Design**: multicentre RCT • **Source of funding**: W.L Gore and Associates. • **Setting**: 19 medical centres in the USA • **Sample size**: n=148 • **Duration**: 36 months • **Follow-up** : 1,6, 12, 24 and 36 months • **Statistical analysis**: Kaplan-Meier analysis used for patency rates/estimates. Log-rank test used to compare patency estimates when patency end points were stratified. SAS software v 9.2.	• **Eligibility criteria:** presence of de novo atherosclerosis or >6 months post-percutaneous transluminal angioplasty disease of the Superficial Femoral Artery (SFA) with stenosis and/or occlusion ≥8cm in length (consistent with The TransAtlantic Inter-Society Consensus (TISC) I class C and D lesions), with patency of the aortoiliac inflow arteries, the proximal 1cm of the SF, and the popliteal artery beginning 5cm above the radiographic knee joint line. Unobstructed runoff to the level of the ankle was documented,	**Group 1**: VIABAHN stent graft (GORE) versus **Group 2** : Bare nitinol stent Both groups: Daily aspirin therapy was initiated prior to intervention. After implantation and hemostatis, those not already on clopidogrel were given 600mg loading dose. Study participants received daily clopidogrel (75mg) for at least 6 months postprocedure and aspirin (81mg) until study completion.	**Outcome 1** *Mortality* *Group 1: 9/72 (12.5%)* *Group 2:3/76 (3.9%)* **Outcome 2** *Proportion of patients with Target Lesion Revascularisation(re-interventions)* *Group 1:25/72 (34.7%)* *Group 2:26/76 (34.2%)* **Outcome 3** *Proportion of lesions with Target Lesion Revascularisation (re-interventions)* *Group 1:38/72 (52.7%)* *Group 2:43/76 (56.5%)* **Outcome 4** Peri-procedural complications (non-study limb thrombosis that occurred 2 days after the index procedure and required surgical intervention) *Group 1: 1/72 (98.6%)* *Group 2: 0/76 (0%)* **Outcome 5** *Quality of life (SF-36) at 1 month, mean (standard deviation) median (range)* *Group 1: 45.2 (10.2) 43 (19-59) n=66* *Group 2: 41.4 (10.8) 42 (12-59)n=72*	**Results critical appraisal**: moderate quality **Dropouts:** Group 1: 29/72 (40%); Group 2: 29/76 (38%)

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		consisting of a patent popliteal artery and at least one tibial artery. Vessel reference diameters were appropriate to the use of 6-, 7-, or 8-mm diameter stents or stent grafts. Because of a lack of FDA approval at the time of the study, 5-mm diameter and heparin-bonded VIABAHN stent grafts were not used. • **Exclusion criteria:** See above. • **Patient characteristics**: Group 1: n=72 Dropouts at 1 year follow up: Mean (s.d, range) age: 69 (10, 45-90) Male: 45 (62.5%) Smoking status: Ever smoked: 59 (81.9%) Never smoked:13		**Outcome 6** *Quality of life (SF-36) at 6 months, mean (standard deviation) median (range)* *Group 1: 40.4 (11.1) 42 (22-56) n=57* *Group 2: 40.3 (10.4) 41 (18-58) n=66* **Outcome 7** *Quality of life (SF-36) at 12 months, mean (standard deviation) median (range)* *Group 1: 40.5 (11.7) 40 (17-60 n=52* *Group 2: 39.8 (10.7) 39 (19-59) n=62* **Outcome 8** *Quality of life (SF-36) at 24 months, mean (standard deviation) median (range)* *Group 1: 39.8 (11.5) 38 (15-61) n=43* *Group 2: 40.6 (10.9) 40 (19-62) n=48* **Outcome 9** *Quality of life (SF-36) at 36 months, mean (standard deviation) median (range)* *Group 1: 41.9 (11.7) 45 (21-61) n=39* *Group 2: 38.7 (10.5) 37 (16-59) n=45*	

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		(18.1%) Diabetes: Insulin-dependent diabetic:11 (15.3%) Noninsulin-dependent diabetic:20 (27.8%) General medical history: Myocardial infarction: 17 (23.6%) Hypertension: 63 (87.5%) Dyslipidemia: 52 (72.2%) Stroke:4 (5.6%) Chronic obstructive pulmonary disease:9 (12.5%) Current treatment for angina:2 (2.8%) Congestive heart failure:3 (4.2%) Previous PTA on study limb > 6 months ago: 5 (6.9%) Group 2: n=76 Dropouts at 1 year follow up:			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		Mean (s.d, range) age: 64 (11, 43-89) Male:49 (64.5%) Smoking status: Ever smoked:67 (88.2%) Never smoked:9 (11.8%) Diabetes: Insulin-dependent diabetic:12 (15.8%) Noninsulin-dependent diabetic:22 (28.9%) General medical history: Myocardial infarction: 19 (25%) Hypertension: 58 (76.3%) Dyslipidemia: 59 (77.6%) Stroke:7 (9.2%) Chronic obstructive pulmonary disease: Current treatment for angina: 6 (7.9%) Congestive heart			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		failure: 8 (10.5%) Previous PTA on study limb > 6 months ago: 4 (5.3%) • **Disease characteristics:** claudication symptoms and/or ischemic rest pain, with or without minor ischemic tissue loss (Rutherford categories 1-5), corroborated by demonstration of an ankle-brachial index of ≤0.9 in the symptomatic limb			

4.4. Autologous vein versus prosthetic bypass

4.4.1. New evidence published since NICE guideline

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Ref: Solakovic, E., Totic, D., Solakovic, S. Femoro-popliteal bypass above knee with saphenous vein vs synthetic graft. Bosnian journal of basic medical sciences, 2008, 8(4), 367-372.	• **Design**: prospective randomised trial • **Source of funding**: not reported • **Setting**: not reported. • **Sample size**: n=121 • **Duration**: operating time (mean 125 minutes in venous bypasses and 73 minutes in the PTFE group, p=0.002). • **Follow-up** : 6 weeks, 3 months, 6 mpnths 1 year, 2 years, 3 years, 4 years, 5 years • **Statistical analysis**: not reported	• **Eligibility criteria: people who** underwent a femoropopliteal bypass operation and had disabling claudication, rest pain or tissue-loss who underwent arterial reconstruction • **Exclusion criteria:** people with an earlier arterial bypass graft procedure in the same leg or with the greater saphenous vein removed earlier • **Patient characteristics**: **Group 1**: **Age, median (years)**: 70 **Gender (m)**: 33 **Risk factors**: - **Smoking**: 39 - **Diabetes mellitus**:12 - **Cardiac**	**Group 1**: reversed saphenous vein bypass graft versus stretched thin-walled 6-mm polytetrafluoroethylene or 6mm prosthesis (DACRON) bypass graft – depending on availability of the prosthetic material. **Group 2** : Before operation all people received 1g of cefasolin intravenously. Patients had general or regional anesthesia for the operation. 5000 international units of Heparin was given intravenously prior to clampging. During postoperative	**Outcome 1 Mortality at 30 days after operation** *Group 1: 0/60* *Group 2: 0/61* Total mortality: the study reported 45 deaths but the patency tables (where the data was divided by intervention and comparison) added up to 34 deaths. **Outcome 2** *Amputation* *Group 1:2/60* *Group 2:2/61* **Outcome 3** *Re-interventions* *Group 1:4/60* *Group 2:12/61*	**Results critical appraisal**: low quality **Dropouts: 45 patients died (37%) after 5 years, but the data in the patency tables only shows results for 34 patients who have died; 9 (7%) patients were lost to follow-up. Three of the amputations were in people with critical limb ischaemia.**

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		history:15 - **Cerebrovascular accident**:5 **Indication**: - **Claudication**: 49 - **Rest pain**:7 - **Necrosis**:3 **Open tibial arteries**: - **3:34** - **2:17** - **1:9** - **Group 2**: **Age, median (years)**: 68 **Gender (m)**: 37 **Risk factors**: - **Smoking**: 46 - **Diabetes mellitus**:21 - **Cardiac history**:16 - **Cerebrovascular accident**: 2 **Indication**: - **Claudication**: 47 - **Rest pain**:9 - **Necrosis**:6 **Open tibial arteries**: - **3:30** - **2:21**	hospitalization people were given Clexan 0.5mg/kg once per day. After discharge oral 150mg acetylsalicylic acid given daily.		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		- **1:10** • **Disease characteristics:** disabling claudication, rest pain or tissue-loss who underwent arterial reconstruction (the majority had claudication)			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Ref: Tofigh, A.M., De Wailly, G.W., Rhissassi, B. Internationa journal of surgery 2007, 5, 109-113.	• **Design**: prospective randomised trial • **Source of funding**: not reported • **Setting**: not reported • **Sample size**: n=85 patients, 103 bypass grafts. • **Duration**: operating time was 105 minutes for venous bypass grafts and 73 minutes for collagen impregnated woven polyester grafts • **Follow-up** : 6 weeks, 3 months, 6 months, 1 year , 2 years • **Statistical analysis**: not reported except for patency rates.	• **Eligibility criteria:** severe claudication, defined as claudication with a walking distance of less than 50m, rest pain, or tissue loss undergoing femoropopliteal reconstruction with the site of the distal anastomosis above the knee joint; the above knee grafting was performed when the above-knee popliteal artery was patent and suitable for anastomosis at operation. • **Exclusion criteria:** if an arterial bypass graft procedure had previously been performed in the same leg or if the greater saphenous vein had been removed earlier. • **Patient**	**Group 1**: reversed saphenous vein bypass graft versus **Group 2**: 6mm collagen impregnated woven polyester prosthesis (POLYTHESE IC, Perouse Labs). An intravenous dose of 1g Cefalotin was administered. The operation was performed after the administration of general or regional anesthesia. Before arterial occlusion, a bolus of 5000 IE of heparin was administered. Post-operative anticoagulation therapy consisted of coumarin during the first 6 month, followed by acetylsalicylic acid (38mg daily).	**Outcome 1** *Mortality at 104 weeks* *Group 1:6/47* *Group 2:6/49* **Outcome 2** *Amputation (because of ischemia)* *Group 1:1* *Group 2:0* *This data was not analysed as it was unclearly reported and it is uncertain if there were any amputations in group 2.* **Outcome 3** *Re-intervention* There was data on re-interventions but it was unclearly reported and it is uncertain if these were re-interventions, and for which group they were reporting.	**Results critical appraisal**: low quality **Dropouts:12 patients died (6 in each arm); 6 lost to follow-up, unsure which arm.** **Notes: patients could be included twice for primary option on the left or the right limb. Analysis of the primary end point was performed for each limb.**

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		characteristics: • **Age**: • **Gender (m)**: 49 (57%) • **Indication for surgery**: Severe claudication:74 Rest pain: 7 Necrosis: 4 • Preoperative risk factors for vascular occlusive disease: - diabetes: 20 (24%) - previous myocardial infarction: 19 (23%) Cigarette smoking: 63 (74%) **Group 1:** Number of bypass grafts: 51 **Group 2:** Number of bypass grafts: 52 • **Disease characteristics: severe claudication**			

4.4.2. Evidence tables for autologous vein compared to prosthetic bypass from NICE guideline CG147

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Ballotta 2003; (Guideline Ref ID 944) **RCT- Single centre (Italy)** **Randomisation: Computer generated randomisation schedule** **Allocation concealment: Sealed envelopes** **Blinding: No details** **Sample size calculation: No details** **ITT analysis: No details** **Drop outs: Unclear** **Follow up duration:** **59 months mean follow-up (range: 1-108 months)** **(1,3,6,12 months and every 6 months thereafter)**	51 patients (102 limbs) Inclusion criteria: • Disabling claudication after failure of a nonsurgical protocol (i.e. earlier risk modification and gradual exercise with or without pharmacologic therapy) • Angiographic evidence of a long superficial femoral artery occlusion and above-knee rehabilitation of the popliteal artery with 1-3 runoff vessels • Adequate segments of SV available for revascularisation on the basis of duplex scan venous mapping (compliant vein with diameter of ≥4 mm proximally and 3 mm distally) Exclusion criteria: Patients with uncompressible vessels ABI >0.9 SV already removed, or previously placed ipsilateral prosthetic or SV femoropopliteal above-knee or below-knee bypass graft Short life expectancy (<1 year) Popliteal aneurysm disease Serum creatinine >2.0 mg/dL Polycythemia (red blood cell count >7.5 x 106/mm3) Platelet count >106/mm2	Treatment consisted of reversed SV graft in one limb and PTFE graft in the contralateral limb for above-knee femoropopliteal revascularisation All bilateral procedures were generally performed 6-8 weeks apart All anastomoses were made end-to-side with continuous 5/0 polypropylene suture, proximal to the ipsilateral common femoral artery and distal to the above-knee popliteal artery Intravenous heparin (5000 IU) was administered before clamping Blood pressure was maintained at average preoperative level or slightly higher Heparinisation was not reversed with protamine Oral warfarin therapy was started the day before the operation and was continued for 6 months, aiming for a normalised ration between 2 and 4. After 6 months, 325 mg of aspirin was taken daily		Reintervention rates Amputation rates Mortality Perioperative complication rates	Funding source: Not detailed

Baseline	n	%
Patients	51	
Procedures	102	
Age (years)		
Median	62	
Range	47-82	
Male gender	33	65
Critical ischemia		87
Hypertension*	31	61
Coronary artery disease	13	25
Smoking	44	86
Diabetes mellitus	27	53
Hyperlipidemia	22	43
History of stroke	12	23.5
Previous ipsilateral inflow procedure	8	16
*Defined as elevated blood pressure treated with medication		
Mean preoperative ABI		
SV	0.53 ± 0.07	
PTFE	0.54 ± 0.07	

Effect size	
Perioperative complication rates	
SV	PTFE
14%	12%
	1 patient; perioperative pneumonia

3 patients; deep vein thrombosis	2 patients; deep vein thrombosis
2 patients; significant bleeding requiring surgical exploration	2 patients; significant bleeding requiring surgical exploration
2 patients; non-infectious wound complications	1 patient; non-infectious wound complications

- **No perioperative (30 day) limb loss or death**
- **5 late deaths (3 due to myocardial infarction; 2 due to cancer) – late survival rate 90%. Median observation time before death was 637 days. Unknown which interventions.**
- **Reintervention rates: PTFE: 5 patients (1, disabling claudication; 4, rest pain. All five required new bypass grafts); SV: 1 patient (onset of rest pain prompted creation of a new bypass graft)**
- **No major amputation was necessary during follow-up in the two groups**

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Burger DH, et al. 2000; (Guideline Ref ID 16040) **Klinkert P, et al. 2003; (Guideline Ref ID 739) Prospective randomised trial** **Randomisation: decided on operating table. If vein deemed suitable (ie diameter >4mm proximally and 3mm distally) then randomised. Closed envelope following surgeons inspection on popliteal artery and**	N= 151 operations in 136 patients. Inclusion criteria: patients with severe claudication, rest pain, or tissue loss undergoing femoropopliteal reconstruction with site of distal anastomosis above the knee joint. Exclusion criteria: • previous arterial bypass graft on same leg or if greater saphenous vein had been removed. • Patients where vein unsuitable for use as graft. _____ Patients could be included in study twice for primary operation on left or right limb. _____ New operations not considered in cases of mild claudication. Where there was necrosis or pain,	Autologous saphenous vein graft.	6mm Polytetrafluoro ethylene (PTFE) bypass graft If PTFE graft occluded and occlusion detected within 7 days, patient underwent thrombectomy.	Mortality Complications Reintervention Amputation	Funding source: Not stated

saphenous vein.

redo bypass grafts were performed.

Allocation concealment: Not stated

Blinding: Not stated

ITT: Not stated

Drop out:

11 lost to follow up at 5yrs

Follow-up duration:

5years, this study reports 2 year data.

Patients examined 6weeks, 3months, 6months and every year thereafter.

Baseline characteristics (table taken from Klinkert paper):

	Total (n)	Human vein (n)	PTFE (n)	p-value
Reconstructions (n)	151	75	76	-
Median age	69	70	68	0.10
Male Gender (n)	88	42	46	0.28
Indication for surgery (n)				
Claudication	120	62	58	-
Rest pain	20	9	11	-
Necrosis	11	4	7	-
Risk factors (n)				
Smoking	105	48	57	0.07
Diabetes	33	12	21	0.04
Cardiac history	31	15	16	0.44
Cerebrovascular accident	7	5	2	0.12

Effect size

Overall data (data same in both Burger and Klinkert papers):

- **No died in hospital or within 30 days of operation**
- **Superficial wound infection seen in 3 PTFE grafts and 4 venous grafts. None resulted in reoperation or bypass graft loss.**

Data at 2yrs (reported in Burger study)

- **Amputation – 1 case after 2 years. Does not state which intervention.**
- **Reintervention - 4 below knee graft (3 x PTFE and 1 with human umbilical vein graft) and 1 above knee PTFE**

Data at 5yrs (reported in Klinkert paper)

		Vein (n)	PFTE (n)	P value
Re-intervention		5	16	0.011
Amputation	Above knee	1	1	-
	Below knee	1	1	-
Death of patients with open bypass - data not analysed as this did not include occluded bypass patient mortality		24	18	-

Study details	Patients	Intervention	Comparison	Outcome measures	Other comments
Ballotta 2003; (Guideline Ref ID 944) **RCT- Single centre (Italy)** **Randomisation: Computer generated randomisation schedule** **Allocation concealment: Sealed envelopes** **Blinding: No details** **Sample size calculation: No details** **ITT analysis: No details** **Drop outs: Unclear** **Follow up duration:** **59 months mean follow-up (range: 1-108 months)** **(1,3,6,12 months and every 6 months thereafter)**	51 patients (102 limbs) Inclusion criteria: • Disabling claudication after failure of a nonsurgical protocol (i.e. earlier risk modification and gradual exercise with or without pharmacologic therapy) • Angiographic evidence of a long superficial femoral artery occlusion and above-knee rehabilitation of the popliteal artery with 1-3 runoff vessels • Adequate segments of SV available for revascularisation on the basis of duplex scan venous mapping (compliant vein with diameter of ≥4 mm proximally and 3 mm distally) Exclusion criteria: Patients with uncompressible vessels ABI >0.9 SV already removed, or previously placed ipsilateral prosthetic or SV femoropopliteal above-knee or below-knee bypass graft Short life expectancy (<1 year) Popliteal aneurysm disease Serum creatinine >2.0 mg/dL Polycythemia (red blood cell count >7.5 x 106/mm3) Platelet count >106/mm2 Baseline n %	• Treatment consisted of reversed SV graft in one limb and PTFE graft in the contralateral limb for above-knee femoropopliteal revascularisation • All bilateral procedures were generally performed 6-8 weeks apart • All anastomoses were made end-to-side with continuous 5/0 polypropylene suture, proximal to the ipsilateral common femoral artery and distal to the above-knee popliteal artery • Intravenous heparin (5000 IU) was administered before clamping • Blood pressure was maintained at average preoperative level or slightly higher • Heparinisation was not reversed with protamine • Oral warfarin therapy was started the day before the operation and was continued for 6 months, aiming for a normalised ration between 2 and 4. After 6 months, 325 mg of aspirin was taken daily		Reintervention rates Amputation rates Mortality Perioperative complication rates	Funding source: Not detailed

Patients	51		
Procedures	102		
Age (years)			
Median	62		
Range	47-82		
Male gender	33	65	
Critical ischemia		87	
Hypertension*	31	61	
Coronary artery disease	13	25	
Smoking	44	86	
Diabetes mellitus	27	53	
Hyperlipidemia	22	43	
History of stroke	12	23.5	
Previous ipsilateral inflow procedure	8	16	
*Defined as elevated blood pressure treated with medication			
Mean preoperative ABI			
SV	0.53 ± 0.07		
PTFE	0.54 ± 0.07		
Effect size			
Perioperative complication rates			
SV	PTFE		
14%	12%		
	1 patient; perioperative pneumonia		
3 patients; deep vein thrombosis	2 patients; deep vein thrombosis		

2 patients; significant bleeding requiring surgical exploration	2 patients; significant bleeding requiring surgical exploration
2 patients; non-infectious wound complications	1 patient; non-infectious wound complications

- **No perioperative (30 day) limb loss or death**
- **5 late deaths (3 due to myocardial infarction; 2 due to cancer) – late survival rate 90%. Median observation time before death was 637 days. Unknown which interventions.**
- **Reintervention rates: PTFE: 5 patients (1, disabling claudication; 4, rest pain. All five required new bypass grafts); SV: 1 patient (onset of rest pain prompted creation of a new bypass graft)**
- **No major amputation was necessary during follow-up in the two groups**

4.5. Drug-coated balloon angioplasty

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Fanelli, F., Cannavale, A., Boatta, E., Corona, M., Lucatelli, P., Wlderk, A., Cirelli, C., and Salvatori, F. M. Lower limb multilevel treatment with drug-eluting balloons: 6-month results from the DEBELLUM randomized trial. Journal of endovascular therapy 19(5), 571-580. 2012	• **Design**: prospective randomised single blinded trial • **Source of funding**: no manufuacturer funding • **Setting**: Italian study, not other details • **Sample size**: n= • **Duration**: Enrolment between September 2010 and March 2011 • **Follow-up** : 6 months reported in this study, 12 & 24 months follow up also planned • **Statistical analysis**:	• **Eligibility criteria:** Symptomatic peripheral arterial disease with single or multiple lesions (stenosis or occlusion between 3 and 30cm in length) in the native superficial femoral, popliteal or below the knee arteries, and/or concomitant multilevel disease. • **Exclusion criteria:** in-stent restenosis, aneurysms, acute thrombosis, pregnancy, life expectancy <1	**Group 1**: n=25 patients, 33 limbs Drug eluting balloons (DEB) coated with paclitaxel: In.Pact Admiral (Medtronic) for femorapopliteal arteries and In.Pact Amphirion (Medtronic) for below the knee arteries Balloons per lesion: 1.5±0.5 **Group 2** : n=25 patients, 38 limbs Conventional	**Outcome 1** Mortality at 6 months *Group 1: 0/25* *Group 2: 0/25* **Outcome 2** Amputations per limb at 6 months *Group 1:1/33* *Group 2:3/38* **Outcome 3** Target lesion revascularisation per limb at 6 months *Group 1: 2/33* *Group 2: 9/38* **Outcome 4** Aggregate major adverse events (death, TLR, amputation & thrombosis) at 6 months. Appears to total numbers, unclear if double	**Results critical appraisal**: Low quality Limitations of study: • Unclear allocation concealment • Only patients blinded to treatment • Some discrepancy in the numbers reported in the paper, possibly due to typos. • Study reports sample size sufficient to support primary endpoint of late lumen loss but not other time points.

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		year and absence of a patent crural artery • **Patient characteristics**: **Group 1**: Age, mean (SD): 66 (6) Gender (m/f): 19/6 Diabetes: 13 Hypercholeterolemia: 12 Hypertension: 19 Past/current smoker: 17 **Group 2**: Age, mean (SD): 67 (6) Gender (m/f): 18/7 Diabetes: 9 Hypercholeterolemia: 17 Hypertension: 15 Past/current smoker: 14 • **Disease characteristics:** Fontaine class: o IIB: 31 o III: 14 o IV: 5 Lesion location: o SFA: 88	angioplasty balloons (AB): Admiral (Medtronic) for femorapopliteal arteries and Amphirion (Medtronic) for below the knee arteries. Balloons per lesion: 1.0±1.0 **Drug regimens common to both groups** Aspirin 100mg/d and clopidogrel 75mg/d for at least 3 days before angioplasty. Patients not on antiplatelet medication were given a 300mg loading dose of clopidogrel before the procedure. 5000-unit heparin bolus given after sheath insertion. **Procedures common to both groups**	counting lesions). *Group 1:4/33* *Group 2:14/38*	**Dropouts:** none

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		o popliteal: 4 o below the knee: 30 Lesion length: o <7cm: 38 o 7-15cm: 63 o >15cm: 21	Balloons used for dilation of new lesions at any level or post dilation after primary stenting in the SFA area only. The decision to implant a nitinol stent left to the judgment of the operator and typically driven by lesion length and presence of severe claudication. Patients requiring provisional or bailout stenting after angioplasty as a result of flow-limiting dissection or residual stenosis >50% were excluded from the study.		

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Liistro, F., Porto, I., Angioli, P., Grotti, S., Ricci, L., Ducci, K., Falsini, G., Ventoruzzo, G., Turini, F., Bellandi, G., and Bolognese, L. Drug-eluting balloon in peripheral intervention for below the knee angioplasty evaluation (DEBATE-BTK): A randomized trial in diabetic patients with critical limb ischemia. Circulation 128(6), 615-621. 2013	• **Design**: prospective randomised trial • **Source of funding**: paper reports "funded without any industry financial support" • **Setting**: Single centre study in Italy • **Sample size**: n=132 • **Duration**: Recruitment between November 2010 and October 2011 • **Follow-up** : 12 months • **Statistical analysis**:	• **Eligibility criteria:** Consecutive diabetic patients with CLI (≥Rutherford class 4); age>18 years; angiographic stenosis or occlusion ≥40mm of at least of one tibial vessel with distal running off to the foot; agreement to 12 month angiographic evaluation. • **Exclusion criteria:** life expectancy <1 year; allergy to paclitaxel; contraindication to antiplatelet treatment; planned major amputation before angiography. • **Patient characteristics**: **Group 1**: Age, mean (SD): 74 (9.4) Gender (m/f):	**Group 1**: n=80 lesions, 65 patients, 71 limbs Paclitaxel-eluting balloon angioplasty (IN.PACT Amphirion, Medtronic) **Group 2** : n=78 lesions, 67 patients, 72 limbs Uncoated balloon angioplasty (Amphirion Deep, Medtronic) **Drug regimens common to both groups** Aspirin 100mg/d. After sheath insertion 70IU/kg heparin. Postintervention aspirin 100mg/d and clopidogrel 75mg/d for at least 4 weeks; aspirin 100mg/d thereafter. **Procedures common to both**	**Outcome 1** Mortality at 12 months *Group 1: 5/65 patients* *Group 2: 3/67 patients* **Outcome 2** Major amputations at 12 months (unplanned amputation of the target limb in which a prosthesis was required for standing or walking) *Group 1: 0/71 limbs* *Group 2: 1/72 limbs* **Outcome 3** Minor amputations at 12 months (undefined) *Group 1: 17/71* *Group 2: 19/72* Assumed to be assessed as limbs with minor limitations. Unclear in paper whether this refers to limbs or people. **Outcome 4** Major adverse events at 12 months (death, major amputation, TLR and Rutherford class ≥4) *Group 1: 20 (34%) – 65 patients* *Group 2: 34 (51%) – 67 patients* **Outcome 5** Freedom from target lesion revascularisation at 12 months *Numbers not reported even though this was a prespecified secondary*	**Results critical appraisal**: Low quality Limitations of study: • Unclear allocation concealment • Unblinded study. Methods report study as a Prospective Randomized Open Blinded Endpoint trial and cites a paper that describes this as the outcome assessor being blinded. However, study limitations section reports this study as unblinded and that there was no external adjucator of outcomes. **Dropouts:** 0 dropouts Angiograms only available in 67/74 lesions in drug coated balloon group and 68/74 lesions in

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		54/65 Risk factors: - Hypertension: 46 - Smoking: 13 - Hypercholest-erolemia: 23 - Dialysis: 7 - Coronary artery disease: 12 - Cerebro-vascular disease: 5 **Group 2**: Age, mean (SD): 75 (9.6) Gender (m/f): 52/67 Risk factors: - Hypertension: 52 - Smoking: 7 - Hypercholest-erolemia: 16 - Dialysis: 7 - Coronary artery disease: 10 - Cerebro-vascular disease: 7	**groups** Drug eluting coronary stents used as bailout. 1 lesion in each group received a bailout stent.	*endpoint. Study only reports that freedom from TLR was significantly higher in the DEB group.* **Outcome 6** Complete index ulcer healing at 12 months ¬ *Group 1: 56/65 limbs* *Group 2: 43/64 limbs* **Outcome 7** Time to complete index ulcer healing at 12 months ¬ *Group 1: 4.4±1.5 months* *Group 2: 5.2±1.6 months* ¬ refers to limbs available at 12 month follow up with Rutherford class 5 or 6 at baseline. 69/71 and 69/72 limbs were Rutherford class 5 or 6 at baseline.	uncoated group.

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		• **Disease characteristics:** **Group 1**: Rutherford class: o 4: 2 o 5: 56 o 6: 13 Lesion length (mean±SD): 129±83 mm Dialysis (10% of patients) **Group 2**: Rutherford class: o 4: 3 o 5: 59 o 6: 10 Lesion length (mean±SD): 131±79 mm Dialysis (10% of patients)			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Tepe, G., Zeller, T., Albrecht, T., Heller, S., Schwarzwälder, U., Beregi, J. P., Claussen, C. D., Oldenburg, A., Scheller, B., and Speck, U. Local delivery of paclitaxel to inhibit restenosis during angioplasty of the leg. New England Journal of Medicine 358(7), 689-699. 2008	• **Design**: prospective randomised trial • **Source of funding**: Bavaria Medizintechnologie and Schering, Germany. Paper reports the sponsor had no involvement in the design of the trial, collection and analysis of the data, or writing of the report. • **Setting**: Multicentre German study • **Sample size**: n=154 • **Duration**: patients enrolled between June 2004 and June 2005 • **Follow-up**: 6 & 24 months • **Statistical analysis**:	• **Eligibility criteria:** 18 and 95 years; symptomatic peripheral-artery disease (Rutherford stages 1 to 5); one or more obstructive lesions, either new lesions or restenoses, at least 70% of vessel diameter and at least 2 cm in length, in the superficial femoral artery,the popliteal artery, or both. If more than one lesion required intervention, only one was treated as the study lesion. • **Exclusion criteria:** poor inflow, absence of a patent crural artery, acute onset of symptoms, pregnancy, life expectancy of less than 1 year, and contraindications to required	**Group 1**: n=48 Paclitaxel coated balloons **Group 2**: n=52 Uncoated balloons with paclitaxel in the contrast medium **Group 3**: n=54 Uncoated balloons without drug on contrast medium **Drug regimens common to both groups** Patients not already taking aspirin or clopidogrel were given 300mg of each before procedure. 3000 to 5000 U interarterial heparin at time of procedure. Postintervention aspirin 100mg/d and clopidogrel 75mg/d for at least	**Outcome 1** Mortality at 6 months *Group 1: 2/48* *Group 2: 2/52* *Group 3: 0/54* **Outcome 2** *Amputations of target leg above the foot at 6 months* *Group 1: 2/48* *Group 2: 2/52* *Group 3: 1/54* **Outcome 3** *Target lesion revascularisation at 12 months* *Group 1: 5/48* *Group 2: 18/52* *Group 3: 26/54* **Outcome 4** *Target lesion revascularisation at 24 months* *Group 1: 7/48* *Group 2: 21/52* *Group 3: 28/54* **Outcome 5** *Serious adverse events up to 2 weeks after procedure* *Group 1: 3/48* *Group 2: 4/52* *Group 3: 2/54*	**Results critical appraisal**: Low quality Limitations of study: • Unclear allocation concealment **Dropouts:** None reported

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		medication • **Patient characteristics**: **Group 1**: Age, mean (SD): 69 (8) Gender (m/f): 31/17 Risk factors: - Diabetes mellitus: 24 - Type 1 diabetes mellitus: 18 - Hyperlipidemia: 33 - Hypertension: 38 **Group 2**: Age, mean (SD): 68 (8) Gender (m/f): 36/16 Risk factors: - Diabetes mellitus: 27 - Type 1 diabetes mellitus: 14 - Hyperlipidemia: 33 - Hypertension: 45 **Group 3**: Age, mean (SD): 68 (9) Gender (m/f): 34/20 Risk factors:	4 weeks. **Procedures common to both groups** Nitinol stents used in lesions that had persistent residual stenosis or as clinically needed: • group 1 – 2 • group 2 – 3 • group 3 – 12	**Outcome 5** *Serious adverse events at 6 months* *Group 1: 25/48* *Group 2: 34/52* *Group 3: 30/54*	

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		- Diabetes mellitus: 25 - Type 1 diabetes mellitus: 14 - Hyperlipidemia: 34 - Hypertension: 45 • **Disease characteristics:** **Group 1**: Mean (SD) baseline Rutherford stage: 3.4 (0.8) Target vessel: • SFA only: 33 • PA +/- SFA: 15 Target lesion length (mean±SD): 7.5±6.2 cm No. of lesions treated: 1.8 (0.8) **Group 2**: Mean (SD) baseline Rutherford stage: 3.4 (1.0) Target vessel: • SFA only: 35 • PA +/- SFA: 17 Target lesion length (mean±SD): 7.4±6.5 cm No. of lesions			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		treated: 1.7 (0.9) **Group 3**: Mean (SD) baseline Rutherford stage: 3.1 (0.8) Target vessel: • SFA only: 35 • PA +/- SFA: 19 Target lesion length (mean±SD): 7.4±6.7 cm No. of lesions treated: 1.6 (0.7)			

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
Werk, M., Langer, S., Reinkensmeier, B., Boettcher, H. F., Tepe, G., Dietz, U., Hosten, N., Hamm, B., Speck, U., and Ricke, J. Inhibition of restenosis in femoropopliteal arteries: paclitaxel-coated versus uncoated balloon: femoral paclitaxel randomized pilot trial. Circulation 118(13), 1358-1365. 2008	• **Design**: prospective randomised trial • **Source of funding**: balloon catheters provided by Bavaria Medizin Technologie, financial support from Bayer-Schering-Pharma AG • **Setting**: multicentre study in Germany • **Sample size**: n=87 • **Duration**: patients enrolled between July 2004 and January 2006 • **Follow-up**: 6 months and 18 to 24 months • **Statistical analysis**:	• **Eligibility criteria:** occlusion or stenosis ≥70% diameter of the superficial femoral artery and/or popliteal artery; Rutherford stage 1 to 5; age 18 to 90 years • **Exclusion criteria:** acute symptoms with an indication for thrombolytic therapy or operation; leg-threatening ischemia; distal outflow over <1 vessel; manifest hyperthyroidism; renal insufficiency (creatinine >2.0 mg/dL); major gastrointestinal bleeding within the last 6 months; known intolerance to study medications or contrast agents; additional severe disease that might lead to noncompliance or was associated with reduced life expectancy <2 years; conditions requiring different treatment, serious safety concerns regarding the procedure, or doubtful willingness or capability of patients to undergo the 6-month follow-up. • **Patient characteristics**: **Group 1**: Age, median (interquartile range): 67.3 (63.5-76.4) Gender (m/f): 27/18 Risk factors: - Diabetes mellitus: 18	**Group 1**: n=45 Paclitaxel coated balloons **Group 2** : n=42 Uncoated balloons **Drug regimens common to both groups** Aspirin 100mg/d and clopidogrel 75mg/d started day of angioplasty. 2500 to 5000 U heparin bolus given after femoral sheath insertion. **Procedures common to both groups** Repeat dilation and stent placement allowed after acute failure of PTA in cases of dissection and	**Outcome 1** Mortality at 6 months *Group 1: 1/45* *Group 2: 0/42* **Outcome 2** Mortality at 18-24 months *Group 1: 6/45* *Group 2: 3/42* **Outcome 3** Major amputations of target leg excluding toes at 6 months *Group 1: 0/45* *Group 2: 1/42* **Outcome 4** Major amputations of target leg excluding toes at 18-24 months *Group 1: 0/45* *Group 2: 1/42* **Outcome 5** Target lesion revascularisation at 6 months *Group 1: 3/45* *Group 2: 14/42*	**Results critical appraisal**: Low quality Limitations of study: • Unclear allocation concealment • Study reports small number of patients as a limitation. **Dropouts:** none reported

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of study quality
		- Current smokers: 21 - Hypertension: 35 - Hypercholeterolemia: 26 - Family history of vascular disease: 24 **Group 2**: Age, median (interquartile range): 70.2 (66.2-77.6) Gender (m/f): 25/17 Risk factors: - Diabetes mellitus: 23 - Current smokers: 15 - Hypertension: 34 - Hypercholeterolemia: 24 - Family history of vascular disease: 15 • **Disease characteristics:** **Group 1**: Rutherford class: o 1: 2 o 2: 10 o 3: 31 o 4: 2 Lesion length (median): 4.0 (2.1-6.1) cm **Group 2**: Rutherford class: o 1: 1 o 2: 7 o 3: 31 o 4: 2 Lesion length (median): 4.7 (2.7-8.5) cm	recoil. Stents placed: • group 1 – 4/45 • group 2 – 6/42	**Outcome 6** Target lesion revascularisation at 18-24 months *Group 1: 6/45* *Group 2: 21/42*	

5. GRADE TABLES

5.1. Assessment of PAD

5.1.1. Whole leg, 50-100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	**Design**	**No. of Segments**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sensitivity (%)**	**Specificity (%)**	**Quality**
50-100% stenosis										
CTA (including 3 studies at very high risk of bias, to allow meta-analysis)										
7	Diagnostic cohort studies	5621	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision[4]	None	95.2 (95%CI 88.7 to 98.2)	93.7 (95% CI 85.3 to 97.5)	VERY LOW
DUS (sensitivity analysis)										
8	Diagnostic cohort studies	8168	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	Serious imprecision[4]	None	89.8 (95%CI 83.5 to 94.4)	94.8 (95%CI 89.1 to 97.7)	LOW
CE MRA (sensitivity analysis)										
9	Diagnostic cohort studies	5447	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	No serious imprecision	None	95.0 (95%CI 90.6 to 97.6)	96.2 (95% CI 91.1 to 98.5)	MODERATE
2D TOF MRA (including one study at very high risk of bias)										
5	Diagnostic cohort studies	2668	Serious risk of bias[2]	Serious inconsistency[3]	No serious indirectness	Very serious imprecision[5]	None	88.6 (95%CI 77.7 to 94.9)	85.9 (95%CI 73.8 to 93.1)	VERY LOW
3D CE MRA (3 Tesla)										
1	Diagnostic cohort study	805	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	No serious imprecision	None	99 (95%CI 97 to 100)	99 (95%CI 98 to 100)	MODERATE

[1] *Majority of the evidence from studies at very high risk of bias*
[2] *Majority of the evidence from studies at high risk of bias*
[3] *Variation in point estimates consistent with different decisions*
[4] *Sensitivity confidence interval consistent with more than one decision and/or confidence ellipse in the meta-analysis extensive.*
[5] *Sensitivity confidence interval consistent with more than two decisions*

5.1.2. Whole leg, 70-100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	**Design**	**No. of Segments**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sensitivity (%)**	**Specificity (%)**	**Quality**
70-100% stenosis										
CTA (sensitivity analysis)										
3	Diagnostic cohort, data taken from HTA	9070	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	Median study: 99 (95%CI 97 to 100); range 94 to 99	Corresponding median: 99 (95%CI 99 to 100); range 97 to 99	HIGH
DUS										
No studies reported at this threshold										
CE MRA										
4	Diagnostic cohort, data taken from HTA	3196	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	Median study: 96 (95%CI 91 to 99); range 91 to 100	Corresponding median: 99 (95%CI 98 to 100); range 96 to 99	MODERATE
2D TOF MRA										
1	Diagnostic cohort, data taken from HTA	206	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	Very serious imprecision[3]	None	90 (95%CI 79 to 96)	97 (95%CI 92 to 99)	VERY LOW

[1] *Majority of the evidence from studies at unclear risk of bias*
[2] *Majority of the evidence from studies at high risk of bias*
[3] *Sensitivity confidence interval consistent with more than two decisions*

5.1.3. Whole leg, 100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	**Design**	**No. of Segments**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sensitivity (%)**	**Specificity (%)**	**Quality**
Occlusion (100% stenosis)										
CTA										
6	Diagnostic cohort studies	4881	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision[4]	None	96.2 (95%CI 89.7 to 98.9)	99.7 (95% CI 99.1 to 99.9)	LOW
DUS (sensitivity analysis)										
7	Diagnostic cohort studies	5588	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	Serious imprecision[4]	None	89.6 (95%CI 83.0 to 93.9)	98.8 (95%CI 97.3 to 99.5)	LOW
CE MRA (sensitivity analysis)										
8	Diagnostic cohort studies	7398	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	No serious imprecision	None	96.3 (95%CI 92.1 to 98.6)	99.1 (95% CI 98.2 to 99.6)	MODERATE
2D TOF MRA (sensitivity analysis)										
3	Diagnostic cohort studies	1746	No serious risk of bias	Serious inconsistency[3]	No serious indirectness	Serious imprecision[5]	None	Median study: 90 (95%CI 83 to 95); range 81 to 100	Corresponding median: 98 (95%CI 96 to 100); range 85 to 98	LOW

[1] *Majority of the evidence from studies at high and unclear risk of bias*
[2] *Majority of the evidence from studies at high risk of bias*
[3] *Variation in point estimates consistent with different decisions*
[4] *Sensitivity confidence interval consistent with more than one decision and/or confidence ellipse in the meta-analysis extensive.*
[5] *Median sensitivity confidence interval was consistent with more than one decision*

5.1.4. Above the knee, 50-100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	Design	No. of Segments	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sensitivity (%)	Specificity (%)	Quality
50-100% stenosis										
CTA (sensitivity analysis)										
4	Diagnostic cohort studies	1500	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	Median study: 97 (95%CI 89 to 100); range 94 to 98	Corresponding median: 97 (95%CI 92 to 99); range 91 to 99	MODERATE
DUS (sensitivity analysis)										
9	Diagnostic cohort studies	3376	Serious risk of bias[1]	Very serious inconsistency[3]	No serious indirectness	Very serious imprecision[4]	None	85.6 (95%CI 74.5 to 92.8)	95.3 (95%CI 91.5 to 97.5)	VERY LOW
CE MRA (sensitivity analysis)										
5	Diagnostic cohort studies	1465	Serious risk of bias[2]	Serious inconsistency[3]	No serious indirectness	Very serious imprecision[4]	None	91.6 (95%CI 80.3 to 97.0)	95.2 (95% CI 90.2 to 98.1)	VERY LOW
2D TOF MRA										
1	Diagnostic cohort study	260	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious imprecision[4]	None	81 (95%CI 67 to 92)	91 (95%CI 86 to 94)	LOW

[1] *Majority of the evidence from studies at high and unclear risk of bias*
[2] *Majority of the evidence from studies at unclear risk of bias*
[3] *Variation in point estimates consistent with different decisions (downgrade one increment for serious variation and downgrade 2 for very serious)*
[4] *Sensitivity confidence interval was consistent with more than one decision and/or confidence ellipse in the meta-analysis extensive.*

5.1.5. Above the knee, 70-100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	Design	No. of Segments	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sensitivity (%)	Specificity (%)	Quality
70-100% stenosis										
CTA (sensitivity analysis)										
3	Diagnostic cohort studies	1150	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[5]	None	100 (95%CI 88 to 100) and 99 (95%CI 96 to 100)	100 (95%CI 97 to 100) and 99 (95%CI 98 to 100)	MODERATE
DUS										
2	Diagnostic cohort, data taken from HTA	588	Serious risk of bias[1]	Very serious inconsistency[2]	No serious indirectness	Serious imprecision[3]	None	100 (95%CI 77 to 100) and 65 (95%CI 56 to 74)	95 (95%CI 84 to 99) and 98 (95%CI 96 to 99)	VERY LOW
CE MRA										
1	Diagnostic cohort, data taken from HTA	576	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[3]	None	91 (95%CI 83 to 96)	97 (95%CI 95 to 99)	MODERATE

[1] *Majority of the evidence from studies at high risk of bias*
[2] *Wide variation in point estimates and lack of overlap of confidence intervals, consistent with different decisions and unexplained*
[3] *Sensitivity confidence interval consistent with two decisions and/or confidence ellipse in the meta-analysis very extensive*

5.1.6. Above the knee, 100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	**Design**	**No. of Segments**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sensitivity (%)**	**Specificity (%)**	**Quality**
Occlusion (100% stenosis)										
CTA										
3	Diagnostic cohort studies	1150	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[3]	None	Median study: 96 (95%CI 86 to 100); range 95 to 98	Corresponding median: 99 (95%CI 96 to 100); range 99 to 99	MODERATE
DUS (sensitivity analysis)										
7	Diagnostic cohort studies	1809	Serious risk of bias[1]	Serious inconsistency[2]	No serious indirectness	Serious imprecision[3]	None	92.7 (95%CI 84.4 to 97.3)	99.0 (95%CI 96.8 to 99.7)	VERY LOW
CE MRA										
5	Diagnostic cohort studies	834	No serious risk of bias	Serious inconsistency[2]	No serious indirectness	Serious imprecision[3]	None	92.7 (95%CI 81.5 to 97.8)	99.4 (95% CI 98.2 to 99.9)	LOW
2D TOF MRA										
1	Diagnostic cohort study	260	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious imprecision[4]	None	87 (95%CI 60 to 98)	97 (95%CI 94 to 99)	LOW

[1] *Majority of evidence at high risk of bias*
[2] *Variation in point estimates consistent with different decisions*
[3] *Sensitivity confidence interval consistent with more than one decision and/or confidence ellipse in the meta-analysis extensive.*
[4] *Sensitivity confidence interval consistent with more than two decisions*

5.1.7. Below the knee, 50-100% stenosis

Study characteristics			Quality Assessment					Summary of findings		Quality
No. of studies	**Design**	**No. of Segments**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sensitivity (%)**	**Specificity (%)**	
50-100% stenosis										
CTA										
2	Diagnostic cohort studies	390	Serious risk of bias[1]	Serious inconsistency[3]	No serious indirectness	No serious imprecision[7]	None	90 (95%CI 84 to 94) and 100 (95%CI 98 to 100)	74 (95%CI 67 to 80) and 99 (95%CI 98 to 100)	LOW
DUS (sensitivity analysis)										
5	Diagnostic cohort studies	2457	Serious risk of bias[1]	Very serious inconsistency[3]	No serious indirectness	Very serious imprecision[5]	None	82.4 (95%CI 55.8 to 94.6)	91.3 (95%CI 70.8 to 98.5)	VERY LOW
CE MRA (sensitivity analysis)										
5	Diagnostic cohort studies	1116	Serious risk of bias[2]	Very serious inconsistency[3]	No serious indirectness	Very serious imprecision[5]	None	87.7 (95%CI 70.7 to 96.0)	92.7 (95% CI 84.2 to 97.3)	VERY LOW
2D TOF MRA										
1	Diagnostic cohort study	393	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	No serious imprecision	None	98 (95%CI 95 to 100)	95 (95%CI 92 to 98)	MODERATE
CE MRA time resolved sequence (calf and foot)										
1	Diagnostic cohort study	290	No serious risk of bias	No serious inconsistency	Serious indirectness[6]	Serious imprecision[4]	None	75 (95%CI 66 to 82)	90 (95%CI 85 to 95)	LOW

[1] *Majority of evidence from studies at high or unclear risk of bias*
[2] *Majority of evidence from studies at high risk of bias*
[3] *Variation in point estimates consistent with different decisions*
[4] *Sensitivity confidence interval consistent with more than one decision*
[5] *Sensitivity confidence interval consistent with more than two decisions and/or confidence ellipse in the meta-analysis very extensive*
[6] *All patients had diabetes and MRA used is not widely used*
[7] *Not downgraded for imprecision because covered by inconsistency downgrading*

5.1.8. Below the knee, 70-100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	**Design**	**No. of Segments**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sensitivity (%)**	**Specificity (%)**	**Quality**
70-100% stenosis										
CTA										
1	Diagnostic cohort studies	539	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	98 (95%CI 95 to 100)	100 (95%CI 99 to 100)	MODERATE
DUS										
No studies reported this outcome										
CE MRA										
1	Diagnostic cohort, data taken from HTA	298	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[3]	None	91 (95%CI 84 to 96)	94 (95%CI 89 to 97)	MODERATE
2D TOF MRA										
1	Diagnostic cohort, data taken from HTA	393	Serious risk of bias[2]	No serious inconsistency	No serious indirectness	No serious imprecision	None	98 (95%CI 95 to 100)	96 (95%CI 92 to 98)	MODERATE

[1] *Unclear risk of bias*
[2] *High risk of bias*
[3] *Sensitivity confidence interval consistent with two decisions and/or confidence ellipse in the meta-analysis extensive*

5.1.9. Below the knee, 100% stenosis

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	**Design**	**No. of Segments**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sensitivity (%)**	**Specificity (%)**	**Quality**
Occlusion (100% stenosis)										
CTA										
1	Diagnostic cohort studies	539	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	100 (95%CI 97 to 100)	100 (95%CI 99 to 100)	MODERATE
DUS (sensitivity analysis)										
6	Diagnostic cohort studies	2562	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	Very serious imprecision[6]	None	80.2 (95%CI 63.4 to 91.0)	91.8 (95%CI 81.9 to 97.7)	VERY LOW
CE MRA (sensitivity analysis)										
3	Diagnostic cohort studies	804	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[4]	None	Median study: 91 (95%CI 83 to 96); range 86 to 95	Corresponding median: 98 (95%CI 94 to 100); range 93 to 98	MODERATE
2D TOF MRA										
2	Diagnostic cohort, data taken from HTA	609	Serious risk of bias[2]	Serious inconsistency[4]	No serious indirectness	No serious imprecision	None	98 (95%CI 93 to 100) and 82 (95%CI 74 to 88)	97 (95%CI 95 to 99) and 99 (95%CI 95 to 100)	LOW

[1] *Unclear risk of bias*
[2] *Majority of the evidence from studies at high risk of bias*
[3] *Wide variation in point estimates and lack of overlap of confidence intervals, consistent with different decisions and unexplained*
[4] *Sensitivity confidence interval consistent with more than one decision and/or confidence ellipse in the meta-analysis extensive.*
[5] *Median sensitivity confidence interval consistent with more than one decision*
[6] *Sensitivity confidence interval consistent with more than two decisions and/or confidence ellipse in the meta-analysis is very extensive*

5.1.10. Imaging of the foot

Study characteristics			Quality Assessment					Summary of findings		
No. of studies	Design	No. of Segments	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sensitivity (%)	Specificity (%)	Quality
DUS; degree of stenosis not stated										
1	Diagnostic cohort studies		Very serious risk of bias[1]	No serious inconsistency	Serious indirectness[2]	No serious imprecision	None	64 (95%CI 53 to 74)	100 (95%CI 99 to 100)	VERY LOW
CTA										
No studies reported this outcome										
CE MRA; 50-100% stenosis										
3	Diagnostic cohort studies	379	Serious risk of bias[3]	Serious inconsistency[4]	No serious indirectness	No serious imprecision	None	Median study: 57 (95%CI 41 to 73); range 53 to 79	Corresponding median: 90 (95%CI 79 to 96); range 71 to 95	LOW
CE MRA time resolved sequence; 50-100% stenosis										
1	Diagnostic cohort study	280	Serious risk of bias[3]	No serious inconsistency	No serious indirectness	Serious imprecision[5]	None	91 (95%CI 85 to 96)	96 (95%CI 92 to 99)	LOW
CE MRA; occlusion										
1	Diagnostic cohort study	143	Serious risk of bias[3]	No serious inconsistency	No serious indirectness	Serious imprecision[5]	None	79 (95%CI 67 to 89)	86 (95%CI 77 to 93)	LOW
CE MRA time resolved sequence; occlusion										
1	Diagnostic cohort study	280	Serious risk of bias[3]	No serious inconsistency	No serious indirectness	Serious imprecision[5]	None	92 (95%CI 86 to 96)	99 (95%CI 96 to 100)	LOW

[1] *Study at very high risk of bias*
[2] *Patients with diabetes; also threshold for stenosis not stated*
[3] *Majority of the evidence from studies at high risk of bias*
[4] *Variation in point estimates consistent with different decisions*
[5] *Sensitivity confidence interval consistent with two decisions and/or confidence ellipse in the meta-analysis extensive*

5.1.11. Test and treat, CE MRA versus CTA

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CE MRA	CTA	Relative (95% CI)	Absolute		
EQ 5D adjusted change from baseline (follow-up mean 3 months; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	77	79	-	MD 0.06 lower (0.15 lower to 0.03 higher)	⊕⊕OO LOW	CRITICAL
EQ 5D adjusted change from baseline (follow-up mean 6 months; measured with: EQ 5D by questionnaire; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	77	79	-	MD 0.02 lower (0.12 lower to 0.08 higher)	⊕⊕OO LOW	CRITICAL
Maximum walking distance (follow-up mean 6 months; measured with: Treadmill test set at 4.0km/h at 0%; patients walked until they had pain or 5 min; Better indicated by higher values)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious imprecision[8]	none	77	79	-	MD 14 lower (41 lower to 13 higher)	⊕⊕OO LOW	CRITICAL
Number of amputations (follow-up mean 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	5/77 (6.5%)	2/79 (2.5%)	RR 2.56 (0.51 to 12.83)	39 more per 1000 (from 12 fewer to 299 more)	⊕⊕OO LOW	CRITICAL
Additional imaging within 6 months												
1	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	13/78 (16.7%)	10/79 (12.7%)	RR 1.32 (0.61 to 2.82)	41 more per 1000 (from 49 fewer to 230 more)	⊕OOO VERY LOW	ADDITIONAL
Number of percutaneous intervention procedures (follow-up mean 6 months)												

1	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[6]	none	47/77 (61%)	38/79 (48.1%)	RR 1.27 (0.95 to 1.7)	130 more per 1000 (from 24 fewer to 337 more)	⊕⊕OO LOW	ADDITIONAL
Number of surgical procedures within 6 months												
1	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[7]	none	53/77 (68.8%)	31/79 (39.2%)	RR 1.75 (1.28 to 2.4)	294 more per 1000 (from 110 more to 549 more)	⊕⊕OO LOW	ADDITIONAL

[1] *Lack of blinding: high risk of performance/detection bias; adjusted analysis but large difference at baseline for EQ 5D; 11% unreturned questionnaires*
[2] *Assessment on the basis of MID of 0.5*
[3] *Lack of blinding*
[4] *High risk of bias*
[5] *Confidence interval crossed two MIDs*
[6] *Confidence interval crossed one MID*
[7] *Confidence interval precise, but Optimal Information Size not reached*
[8] *Confidence interval could not be assessed because no baseline values, but Optimal Information Size not reached*

5.1.12. Test and treat, CE MRA versus DUS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CE MRA**	**DUS**	**Relative (95% CI)**	**Absolute**		
EQ-5D change from baseline (not adjusted) (follow-up mean 3 months; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	178	174	-	MD 0.01 higher (0.05 lower to 0.07 higher)	⊕⊕OO LOW	CRITICAL
EQ-5D change from baseline (not adjusted) (follow-up mean 6 months; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	178	174	-	MD 0.02 higher (0.06 lower to 0.1 higher)	⊕⊕OO LOW	CRITICAL
Maximum walking distance (follow-up mean 6 months; measured with: Treadmill test set at 4.0km/h at 0%; patients walked until they had pain or 5 min; Better indicated by higher values)												
1	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	77	79	-	MD 4 lower (19 lower to 11 higher)	⊕⊕OO LOW	CRITICAL

Additional imaging before therapy												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Serious[6]	none	19/180 (10.6%)	47/174 (27%)	RR 0.39 (0.24 to 0.64)	165 fewer per 1000 (from 97 fewer to 205 fewer)	⊕⊕OO LOW	ADDITIONAL
Number of percutaneous intervention procedures (6 months)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[5]	none	96/180 (53.3%)	93/174 (53.4%)	RR 1.00 (0.82 to 1.21)	0 fewer per 1000 (from 96 fewer to 112 more)	⊕⊕OO LOW	ADDITIONAL
Number of surgical procedures within 6 months												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	39/180 (21.7%)	39/174 (22.4%)	RR 0.97 (0.65 to 1.43)	7 fewer per 1000 (from 78 fewer to 96 more)	⊕⊕OO LOW	ADDITIONAL

[1] *Lack of blinding: high risk of performance/detection bias; unadjusted and difference at baseline large for outcome compared to effect estimate; 11% unreturned questionnaires*
[2] *Very high risk of bias*
[3] *High risk of bias*
[4] *Confidence interval crosses two MIDs, but more precise around the absolute effect*
[5] *Confidence interval crosses one MID*
[6] *Optimal information size not reached*

5.2. Revascularization compared with or in combination with exercise or best medical treatment

5.2.1. Best medical treatment versus best medical treatment with angioplasty

5.2.1.1. Femoropopliteal or aortoiliac disease (mixed population)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Best medical treatment**	**Best medical treatment with angioplasty**	**Relative (95% CI)**	**Absolute**		
Max walking distance at 3 months (measured with: treadmill, mean (SD); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	MD 123.9 higher (16.69 to 231.11 higher)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Best medical treatment	Best medical treatment with angioplasty	Relative (95% CI)	Absolute		
Max walking distance at 1 year (measured with: treadmill, mean (SD); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	MD 197.10 higher (82.51 to 311.69 higher)	⊕OOO VERY LOW	CRITICAL
Max walking distance 2 years (measured with: treadmill, mean (SD); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	MD 219.70 higher (122.12 to 317.28 higher)	⊕OOO VERY LOW	CRITICAL
Pain free walking distance 3 months (measured with: treadmill, mean (SD); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	MD 219.90 higher (120.5 to 319.3 higher)	⊕OOO VERY LOW	CRITICAL
Pain free walking distance at 1 year (measured with: treadmill, mean (SD); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency[2]	serious[2]	serious[3]	none	28	28	-	MD 275.50 higher (172.61 to 378.39 higher)	⊕OOO VERY LOW	CRITICAL
Pain free walking distance at 2 years (measured with: treadmill, mean (SD); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	MD 260.10 higher (155.6 to 364.5 higher)	⊕OOO VERY	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Best medical treatment	Best medical treatment with angioplasty	Relative (95% CI)	Absolute		
											LOW	
Quality of life (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	See Appendix 2	⊕OOO VERY LOW	CRITICAL
Major complications at 1 year (Better indicated by lower values)												
1	observational studies	no serious risk of bias[4]	no serious inconsistency	serious[2]	no serious imprecision	none		28	-	0 out of 28 people in the angioplasty group had major complications	⊕OOO VERY LOW	CRITICAL
Re-interventions at 1 year (Better indicated by lower values)												
1	observational studies	no serious risk of bias[4]	no serious inconsistency	serious[2]	no serious imprecision	none		28	-	0 out of 28 people in the angioplasty group had re-intervention	⊕OOO VERY LOW	CRITICAL

[1] *no blinding*
[2] *population is mixed in terms of anatomical location*
[3] *sample size less than 400 (continuous outcome)*
[4] *data from an RCT, non-comparative outcome*

5.2.1.2. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Best medical treatment	Best medical treatment with angioplasty	Relative (95% CI)	Absolute		
Major complications at months (Better indicated by lower values)												
1	observational studies	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none		29	-	0 out of 29 in the angioplasty group had major complications	⊕⊕OO LOW	CRITICAL
Re-interventions at 6 months (Better indicated by lower values)												
1	observational studies	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none		29	-	0 out of 29 in the angioplasty group had re-interventions	⊕⊕OO LOW	CRITICAL
Re-interventions at 2 years (Better indicated by lower values)												
1	observational studies	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none		29	-	1 out of 29 in the angioplasty group had re-interventions	⊕⊕OO LOW	CRITICAL

[1] *data from an RCT, non comparative outcome*

5.2.2. Supervised exercise with best medical treatment and angioplasty versus supervised exercise with best medical treatment

5.2.2.1. Aortoiliac disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Supervised exercise with best medical treatment and angioplasty	Supervised exercise with best medical treatment	Relative (95% CI)	Absolute		
Maximum walking distance at 2 years (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	11	12	-	adjusted ratio 1.78 higher (1 to 3.16 higher)	⊕⊕OO LOW	CRITICAL
Pain free walking distance at 2 years												
1	randomised trials	serious[1,6]	no serious inconsistency	no serious indirectness	very serious[4,5]	none	7/11 (63.6%)	3/12 (25%)	RR 2.55 (0.87 to 7.47)	986 more per 1000 (from 83 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Quality of life at 6 months (Better indicated by lower values)												
1	randomised trials	serious[1,6]	no serious inconsistency	no serious indirectness	serious[7]	none	11	12	-	See comment	⊕⊕OO LOW	CRITICAL
Quality of life at 1 year (Better indicated by lower values)												
1	randomised trials	serious[1,6]	no serious inconsistency	no serious indirectness	serious[7]	none	11	12	-	See comment	⊕⊕OO LOW	CRITICAL
Complications following procedure (Better indicated by lower values)												
1	observational studies	serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	19	-	21 %	4 out of 19 people in the angioplasty group had complications	⊕⊕OO LOW	CRITICAL

[1] *Unclear allocation concealment*
[2] *low sample size (n=23)*
[4] *Large CI that includes appreciable benefit and no effect.*
[5] *low sample size and event rate*
[6] *unclear blinding.*
[7] *No information on variability (calculation of standard deviation, mean difference and CI was not possible)*
[8] *Data taken from RCT, non-comparable outcomes*

5.2.2.2. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Supervised exercise with best medical treatment and angioplasty**	**Supervised exercise with best medical treatment**	**Relative (95% CI)**	**Absolute**		
Quality of life at 6 months (Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	95	94	-	not pooled	⊕⊕OO LOW	CRITICAL
Quality of life 1 year (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	95	94	-	not pooled	⊕⊕OO LOW	CRITICAL
Maximum walking distance at 2 years (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	34	37	-	adjusted ratio 1.38 higher (1.01 to 1.9 higher)	⊕⊕OO LOW	CRITICAL
Pain free walking distance at 2 years												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7/34 (20.6%)	23/37 (62.2%)	RR 3.02 (1.49 to 6.12)	1000 more per 1000 (from 305 more to 1000 more)	⊕⊕⊕O MODERATE	CRITICAL
								0%		-		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Supervised exercise with best medical treatment and angioplasty	Supervised exercise with best medical treatment	Relative (95% CI)	Absolute		
Complications following procedure (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none		-	-	6 out of 48 people in the angioplasty group had complications	⊕⊕OO LOW	CRITICAL
Complications at 3 months (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none		-	-	0 out of 58 people in the angioplasty group had complications	⊕⊕OO LOW	CRITICAL
Re-intervention at 1 year (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none		-	-	0 out of 58 people in the angioplasty group had re-interventions	⊕⊕OO LOW	CRITICAL

[1] *Unclear allocation concealment*
[2] *no information on variability was given, calculation of SD, mean difference and CI was not possible*
[3] *Low sample size (n=71)*

5.2.3. Best medical treatment with supervised exercise and angioplasty versus best medical treatment and angioplasty

5.2.3.1. Aortoiliac or femoropopliteal disease (mixed population)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Best medical treatment with supervised exercise and angioplasty	Best medical treatment and angioplasty	Relative (95% CI)	Absolute		
Max walking distance at 3 months (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3,4]	none	32	29	-	MD 191.10 higher (35.1 lower to 417.3 higher)	⊕OOO VERY LOW	CRITICAL
Max walking distance at 6 months (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	34	27	-	MD 271.30 higher (68.43 to 474.17 higher)	⊕OOO VERY LOW	CRITICAL
Pain free walking distance at 3 months (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	32	28	-	MD 235.60 higher (15.77 to 455.43 higher)	⊕OOO VERY LOW	CRITICAL
Pain free walking distance at 6 months (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	34	27	-	MD 295.20 higher (106.19 to 484.21 higher)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Best medical treatment with supervised exercise and angioplasty	Best medical treatment and angioplasty	Relative (95% CI)	Absolute		
Quality of life at 6 months												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[5]	none	-	-	-	See remark	⊕OOO VERY LOW	CRITICAL
Major events at 6 months												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	3/35 (8.6 %)	0/35	RR 7 (0.37 -130.69)		⊕OOO VERY LOW	CRITICAL
										-		
Re-interventions at 12 months												
1	randomised trials	very serious[7]	no serious inconsistency	serious[2]	serious[3]	none	0/58 (0%)	9/60 (15%)	RR 0.05 (0 -0.91)	-	⊕OOO VERY LOW	CRITICAL
								0%		-		

[1] *unclear allocation concealment and no Blinding*
[2] *Population is mixed in terms of anatomical location*
[3] *Large confidence interval that includes both appreciable benefits and no effect*
[4] *small sample size (n=70)*
[5] *no information on variability was given in the study, SD, mean difference and CI cannot be estimated*
[6] *95 % CI crosses both MIDs*
[7] *unclear methodology*

5.2.3.2. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Best medical treatment with supervised exercise and angioplasty	Best medical treatment and angioplasty	Relative (95% CI)	Absolute		
Quality of life (Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	60	-	Cannot be estimated	⊕OOO VERY LOW	CRITICAL

[1] *Randomisation, blinding and allocation concealment not reported*
[2] *no information on variability, SD, mean difference and CI could not be estimated*

5.2.4. Angioplasty versus supervised exercise

5.2.4.1. Femoropopliteal or aortoiliac disease (mixed population)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Supervised exercise	Relative (95% CI)	Absolute		
Max walking distance from baseline at 6 months (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	75	75	-	MD 383.00 lower (537.62 to 228.38 lower)	⊕OOO VERY LOW	CRITICAL
Pain free walking distance from baseline at 6 months (Better indicated by lower values)												
1	randomised trials	serious[4]	no serious inconsistency	serious[2]	serious[3]	none	75	75	-	MD 220 lower (391.62 to 48.38 lower)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Supervised exercise	Relative (95% CI)	Absolute		
Max walking distance from baseline at 1 year (Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	75	75	-	MD 208.00 lower (359.79 to 56.21 lower)	⊕OOO VERY LOW	CRITICAL
Pain free walking distance from baseline at 1 year (Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[3]	none	75	75	-	MD 137.00 lower (305.66 lower to 31.66 higher)	⊕OOO VERY LOW	CRITICAL
Number of people who doubled their max walking distance at 3 months												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	very serious[6,7]	none	4/16 (25%)	7/15 (46.7%)	RR 0.54 (0.2 to 1.47)	215 fewer per 1000 (from 373 fewer to 219 more)	⊕OOO VERY LOW	CRITICAL
Number of people who doubled their max walking distance at 6 months												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[7]	none	9/12 (75%)	4/14 (28.6%)	RR 0.48 (0.22 to 1.03)	149 fewer per 1000 (from 223 fewer to 9 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
								0%		-		
Number of people who doubled their max walking distance at 9 months												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[7]	none	4/11 (36.4%)	9/12 (75%)	RR 0.48 (0.21 to 1.13)	390 fewer per 1000 (from 593 fewer to 97 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Number of people who doubled their max walking distance at 1 year												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Supervised exercise	Relative (95% CI)	Absolute		
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[7]	none	6/7 (85.7%)	2/5 (40%)	RR 0.47 (0.15 to 1.42)	212 fewer per 1000 (from 340 fewer to 168 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Quality of life at 3 months												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[8]	none	60	60	-	See comment	⊕OOO VERY LOW	CRITICAL
Quality of life at 6 months												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[8]	none	75	75	-	See comment	⊕OOO VERY LOW	CRITICAL
								0%		-		
Quality of life at 1 year												
1	randomised trials	serious[5]	no serious inconsistency	serious[2]	serious[8]	none	75	75	-	See comment	⊕OOO VERY LOW	CRITICAL
								0%		-		
Complications at 1 year (Better indicated by lower values)												
2	observational studies	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none		-	11/95 people in angioplasty group had complications	not pooled	⊕OOO VERY LOW	CRITICAL
Re-interventions at 6 months (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none		-	5/75 people in angioplasty group had re-interventions	not pooled	⊕OOO VERY LOW	CRITICAL
Re-interventions at 1 year (Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Supervised exercise	Relative (95% CI)	Absolute		
2	observational studies	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none		-	8/95 people in angioplasty group had re-interventions	not pooled	⊕OOO VERY LOW	CRITICAL
Re-interventions at 15 months (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none		-	3/30 people in angioplasty group had re-interventions	MD 0 higher (0 to 0 higher)	⊕OOO VERY LOW	CRITICAL

[1] *unclear allocation concealment*
[2] *population is mixed in terms of anatomical location*
[3] *total sample size less than 400 for continuous outcome*
[4] *Unclear allocation concealment, unclear or no blinding.*
[5] *unclear allocation concealment and no blinding.*
[6] *very small sample size (n=31)*
[7] *confidence interval crosses the line of no effect*
[8] *no information on variability given, no SD, mean and CI can be calculated*

5.2.4.2. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Supervised exercise	Relative (95% CI)	Absolute		
Re-interventions at 1 year (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none		-	-	9/60 people in angioplasty group had re-intervention	⊕⊕OO LOW	CRITICAL

5.2.5. Bypass surgery versus supervised exercise

5.2.5.1. Aortoiliac or femoropopliteal disease (mixed population)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bypass surgery	Supervised exercise	Relative (95% CI)	Absolute		
Max walking distance 12-15 months (Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	25	25	-	mean 0 higher (189 to 0 higher)	⊕OOO VERY LOW	CRITICAL
Symptom free walking distance 12-15 months (Better indicated by lower values)												
1	randomised trials	serious[4]	no serious inconsistency	serious[2]	serious[3]	none	25	25	-	MD 0 higher (0 to 0 higher)	⊕OOO VERY LOW	CRITICAL
Complications at 30 days												
1	observational	no serious	no serious	no serious	no serious	none	-	-	-	6/25 in the surgery group	⊕⊕OO	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bypass surgery	Supervised exercise	Relative (95% CI)	Absolute		
	studies	risk of bias	inconsistency	indirectness	imprecision					had complications	LOW	
								0%		-		
Re-interventions at 30 days												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	-	3/25 in the surgery group had re-interventions	⊕⊕OO LOW	CRITICAL
								0%		-		

[1] *no description of allocation concealment and no blinding of outcome assessment*
[2] *Population is mixed in terms of anatomical location*
[3] *Low sample size for continous outcome (n=50)*
[4] *no description of allocation concealment, no blinding of outcome assessment*

5.3. Angioplasty versus bypass surgery for intermittent claudication

5.3.1. Aortoiliac disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Bypass surgery	Relative (95% CI)	Absolute		
Amputation at 2 years												
1	randomised trials[1]	no serious risk of bias[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	8/130 (6.2%)	13/133 (9.8%)	RR 0.63 (0.27 to 1.47)	36 fewer per 1000 (from 71 fewer to 46 more)	⊕⊕OO LOW	IMPORTANT
Amputation at 4 years												
1	randomised trials[4]	no serious risk of bias[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/59 (10.2%)	3/59 (5.1%)	RR 2.00 (0.52 to 7.62)	51 more per 1000 (from 24 fewer to 337 more)	⊕⊕OO LOW	IMPORTANT
Post-procedure complications												

1	randomised trials[1]	serious[5]	no serious inconsistency	no serious indirectness	serious[6]	none	27/130 (20.8%)	10/133 (7.5%)	RR 2.76 (1.39 to 5.47)	132 more per 1000 (from 29 more to 336 more)	⊕⊕OO LOW	CRITICAL
Re-intervention at 2 years												
1	randomised trials[1]	serious[5]	no serious inconsistency	no serious indirectness	very serious[3]	none	26/130 (20%)	20/133 (15%)	RR 1.33 (0.78 to 2.26)	50 more per 1000 (from 33 fewer to 189 more)	⊕OOO VERY LOW	CRITICAL
Walking distance												
0	No evidence available					none	-	-	-	-		CRITICAL
Quality of life												
0	No evidence available					none	-	-	-	-		CRITICAL
Pain												
0	No evidence available					none	-	-	-	-		IMPORTANT

[1] *Wilson 1989*
[2] *Unclear blinding, but no impact on this outcome.*
[3] *Large CI that includes appreciable benefit and harm.*
[4] *Wolf 1993*
[5] *Unclear blinding.*
[6] *No MID crossed, but OIS not reached (865 for baseline risk of 20.8% and RRR of 25%).*

5.3.2. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Bypass surgery	Relative (95% CI)	Absolute		
Amputation at 1 year												
3	randomised trials[1,2,3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/103 (2.9%)	5/93 (5.4%)	RR 0.61 (0.17 to 2.18)	21 fewer per 1000 (from 45 fewer to 63 more)	⊕OOO VERY LOW	IMPORTANT
Amputation at 2 years												
1	randomised trials[6]	serious[7]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/50 (2%)	5/50 (10%)	RR 0.2 (0.02 to 1.65)	80 fewer per 1000 (from 98 fewer to 65 more)	⊕OOO VERY LOW	IMPORTANT
Amputation at 4 years												
2	randomised trials[8,9]	serious[10]	no serious inconsistency	no serious indirectness	serious[11]	none	4/88 (4.5%)	11/85 (12.9%)	RR 0.35 (0.11 to 1.05)	84 fewer per 1000 (from 115 fewer to 6 more)	⊕⊕OO LOW	IMPORTANT
Minor post-procedure complications												
2	randomised trials[1,6]	very serious[12]	no serious inconsistency	no serious indirectness	very serious[5]	none	7/73 (9.6%)	4/68 (5.9%)	RR 1.61 (0.49 to 5.32)	36 more per 1000 (from 30 fewer to 254 more)	⊕OOO VERY LOW	CRITICAL
Major adverse events at 1 year												
1	randomised trials[3]	very serious[13]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/30 (0%)	2/25 (8%)	RR 0.17 (0.01 to 3.34)	66 fewer per 1000 (from 79 fewer to 187 more)	⊕OOO VERY LOW	CRITICAL
Re-intervention at 1 year												
2	randomised trials[2,3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	14/80 (17.5%)	13/75 (17.3%)	RR 1.06 (0.55 to 2.06)	10 more per 1000 (from 78 fewer to 184 more)	⊕OOO VERY LOW	CRITICAL
Re-intervention at 2 years												

1	randomised trials[6]	serious[7]	no serious inconsistency	no serious indirectness	very serious[5]	none	17/50 (34%)	17/50 (34%)	RR 1 (0.58 to 1.73)	0 fewer per 1000 (from 143 fewer to 248 more)	⊕OOO VERY LOW	CRITICAL
Re-intervention at 4 years												
1	randomised trials[9]	serious[7]	no serious inconsistency	no serious indirectness	very serious[5]	none	18/50 (36%)	15/50 (30%)	RR 1.2 (0.68 to 2.11)	60 more per 1000 (from 96 fewer to 333 more)	⊕OOO VERY LOW	CRITICAL
Walking distance												
0	No evidence available					none	-	-	-	-		CRITICAL
Quality of life												
0	No evidence available					none	-	-	-	-		CRITICAL
Pain												
0	No evidence available					none	-	-	-	-		IMPORTANT

[1] *Holm 1991*
[2] *Kendora 2007*
[3] *van der Zaag 2004*
[4] *All trials had unclear allocation concealment and no or unclear blinding. Only one trial with correct ITT analysis (Kendora 2007).*
[5] *Large CI that includes appraciable harm and benefit.*

5.4. Angioplasty with selective versus primary stent placement for intermittent claudication

5.4.1. Aortoiliac disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
Mortality at 3 months - Aortoiliac												
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	very serious[2]	none	0/136 (0%)	0/136 (0%)	-	0 fewer per 1000 (from 10 fewer to 10 more)[3]	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Mortality at 1 year - Aortoiliac												
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	very serious[2]	none	2/136 (1.5%)	1/143 (0.7%)	RR 2.1 (0.19 to 22.93)	8 more per 1000 (from 6 fewer to 153 more)	⊕OOO VERY LOW	IMPORTANT
								0.7%		8 more per 1000 (from 6 fewer to 154 more)		
Mortality at 2 years - Aortoiliac												
2	randomized trials	very serious[4]	no serious inconsistency	serious[1]	very serious[2]	none	5/191 (2.6%)	6/193 (3.1%)	RR 0.85 (0.27 to 2.72)	5 fewer per 1000 (from 23 fewer to 53 more)	⊕OOO VERY LOW	IMPORTANT
								4.8%		7 fewer per 1000 (from 35 fewer to 83 more)		
Mortality at 5 years - Aortoiliac												
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	very serious[2]	none	22/136 (16.2%)	21/143 (14.7%)	RR 1.1 (0.64 to 1.91)	15 more per 1000 (from 53 fewer to 134 more)	⊕OOO VERY LOW	IMPORTANT
								14.7%		15 more per 1000 (from 53 fewer to 134 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
Amputation at 5 years - Aortoiliac												
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	very serious[2]	none	8/136 (5.9%)	3/143 (2.1%)	RR 2.8 (0.76 to 10.35)	38 more per 1000 (from 5 fewer to 196 more)	⊕OOO VERY LOW	IMPORTANT
								2.1%		38 more per 1000 (from 5 fewer to 196 more)		
Re-intervention at 3 months - Aortoiliac												
1	randomized trials	serious[5,6]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/136 (1.5%)	2/143 (1.4%)	RR 1.05 (0.15 to 7.36)	1 more per 1000 (from 12 fewer to 89 more)	⊕OOO VERY LOW	CRITICAL
								1.4%		1 more per 1000 (from 12 fewer to 89 more)		
Re-intervention at 1 year - Aortoiliac												
1	randomized trials	serious[5,6]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/136 (2.9%)	6/143 (4.2%)	RR 0.7 (0.2 to 2.43)	13 fewer per 1000 (from 34 fewer to 60 more)	⊕OOO VERY LOW	CRITICAL
								4.2%		13 fewer per 1000 (from 34 fewer to 60 more)		
Re-intervention at 2 years - Aortoiliac												
2	randomized trials	serious[4,5,6]	serious[7]	no serious indirectness	very serious[2]	none	15/191 (7.9%)	13/200 (6.5%)	RR 1.21 (0.59 to 2.48)	14 more per 1000 (from 27 fewer to 96 more)	⊕OOO VERY LOW	CRITICAL
								6.1%		13 more per 1000 (from 25 fewer to 90 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
Re intervention (hazard ratio) at 5 years (for arterial segments treated)												
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[8]	very serious[2]	none	33/169 (19.5%)	33/187 (17.6%)	HR 1.18 (0.72 to 1.93)	28 more per 1000 (from 46 fewer to 136 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Re-intervention at 5 years (for arterial segments treated)												
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[8]	very serious[2]	none	33/169 (19.5%)	33/187 (17.6%)	RR 1.11 (0.72 to 1.71)	19 more per 1000 (from 49 fewer to 125 more)	⊕OOO VERY LOW	CRITICAL
								17.7%		19 more per 1000 (from 50 fewer to 126 more)		
Re-intervention at 6-8 years - Aortoiliac (for arterial segments treated)												
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[8]	serious[9]	none	21/118 (17.8%)	12/118 (10.2%)	RR 1.75 (0.9 to 3.39)	76 more per 1000 (from 10 fewer to 243 more)	⊕⊕OO LOW	CRITICAL
								10.2%		76 more per 1000 (from 10 fewer to 244 more)		
Complications/adverse events at 30 days - Aortoiliac												
1	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/136 (7.4%)	6/143 (4.2%)	RR 1.75 (0.65 to 4.69)	31 more per 1000 (from 15 fewer to 155 more)	⊕OOO VERY LOW	CRITICAL
								4.2%		32 more per 1000 (from 15 fewer to 155 more)		
Major complications/adverse events at 2 years - Aortoiliac												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
1	randomized trials	very serious[4,6]	no serious inconsistency	no serious indirectness	serious[10]	none	11/55 (20%)	3/57 (5.3%)	RR 3.8 (1.12 to 12.89)	147 more per 1000 (from 6 more to 626 more)	⊕OOO VERY LOW	CRITICAL
								5.3%		148 more per 1000 (from 6 more to 630 more)		
Walking distance at 3 months - Aortoiliac (Better indicated by higher values)												
1	randomized trials	serious[6,11]	no serious inconsistency	no serious indirectness	no serious imprecision	none	136	143	-	MD 8 lower (22.25 lower to 6.25 higher)	⊕⊕⊕O MODERATE	CRITICAL
Walking distance at 1 year - Aortoiliac (Better indicated by higher values)												
1	randomized trials	serious[6,11]	no serious inconsistency	no serious indirectness	no serious imprecision	none	136	143	-	MD 2 higher (12.48 lower to 16.48 higher)	⊕⊕⊕O MODERATE	CRITICAL
Walking distance at 2 years - Aortoiliac (Better indicated by higher values)												
1	randomized trials	serious[6,11]	no serious inconsistency	no serious indirectness	no serious imprecision	none	136	143	-	MD 3 lower (18.96 lower to 12.96 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain score - RAND-36 at 1 month (median) - Aortoiliac (Better indicated by higher values)												
1	randomized trials	serious[6,11]	no serious inconsistency	no serious indirectness	serious[12]	none	136 (median 67, 95%CI: 0-100)	143 (median 80, 95%CI: 4-100)	-	median 13 lower	⊕⊕OO LOW	IMPORTANT
Pain score - RAND-36 at 3 months (median) - Aortoiliac (Better indicated by higher values)												
1	randomized trials	serious[6,11]	no serious inconsistency	no serious indirectness	serious[12]	none	136 (median 78, 95%CI: 10-100)	143 (median 90, 95%CI: 20-100)	-	median 12 lower	⊕⊕OO LOW	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
Pain score - RAND-36 at 1 year (median) - Aortoiliac (Better indicated by higher values)												
1	randomized trials	serious[6,11]	no serious inconsistency	no serious indirectness	serious[12]	none	136 (median 80, 95%CI: 22-100)	143 (median 78, 95%CI: 4-100)	-	median 2 higher	⊕⊕OO LOW	IMPORTANT
Pain score - RAND-36 at 2 years (median) - Aortoiliac (Better indicated by higher values)												
1	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	serious[12]	none	136 (median 90, 95%CI: 20-98)	143 (median 78, 95%CI: 2-100)	-	median 12 higher	⊕⊕OO LOW	IMPORTANT

[1] *Outcome reported as dichotomous outcome and not time to event data*
[2] *95% CI crosses both MIDs*
[3] *Absolute effect calculated using the risk difference in Review Manager*
[4] *Method of randomized sequence generation and allocation concealment not reported. Blinding not possible. 6 patients dropped out of selective stenting group. Potentially there could have been deaths in this group. Trial stopped early.*
[5] *Not reported how decision to re-intervene was made.*
[6] *Unclear if outcome assessors were blinded to interventions.*
[7] *There is high statistical heterogeneity and studies show effect sizes in different directions.*
[8] *Results reported by arterial segment treated but study randomized by person not lesion.*
[9] *95% CI crosses one MID*
[10] *The event rate and sample size do not meet the optimal information size*
[11] *Patients not blinded to outcome*
[12] *Median data provided only. Assessing imprecision based on a cut off value not possible.*

5.4.2. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
Mortality at 30 days - femoropopliteal arteries												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/72 (0%)	0/134 (0%)	-	0 fewer per 1000 (from 20 fewer to 20 more)[3]	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Mortality at 30 days - femoropopliteal arteries (randomized by limb)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/77 (2.6%)	0%	OR 7.49 (0.46 to 120.79)	30 more per 1000 (from 20 fewer to 70 more)[4]	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Mortality at 6 months - femoropopliteal arteries												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/53 (0%)	0/51 (0%)	-	0 fewer per 1000 (from 40 fewer to 40 more)[3]	⊕⊕OO LOW	IMPORTANT
								0%		-		
Mortality at 1 year - femoropopliteal arteries												
5	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/641 (1.6%)	16/649 (2.5%)	RR 0.65 (0.31 to 1.38)	9 fewer per 1000 (from 17 fewer to 9 more)	⊕OOO VERY LOW	IMPORTANT
								2%		7 fewer per 1000 (from 14 fewer to 8 more)		
Mortality at 1 year - femoropopliteal arteries (randomized by limb)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/77 (9.1%)	12/77 (15.6%)	RR 0.58 (0.24 to 1.4)	65 fewer per 1000 (from 118	⊕OOO	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
										fewer to 62 more)	VERY LOW	
								15.6%		66 fewer per 1000 (from 119 fewer to 62 more)		
Amputations at 30 days - femoropopliteal arteries (randomized by limb)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/77 (5.2%)	2/77 (2.6%)	RR 2 (0.38 to 10.6)	26 more per 1000 (from 16 fewer to 249 more)	⊕OOO VERY LOW	IMPORTANT
								2.6%		26 more per 1000 (from 16 fewer to 250 more)		
Amputation at 6 months - femoropopliteal arteries												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/53 (0%)	0/51 (0%)	-	0 fewer per 1000 (from 40 fewer to 40 more)[3]	⊕⊕OO LOW	IMPORTANT
								0%		-		
Amputation at 1 year - femoropopliteal arteries												
6	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/713 (0.56%)	6/783 (0.77%)	RR 0.74 (0.25 to 2.21)	2 fewer per 1000 (from 6 fewer to 9 more)	⊕OOO VERY LOW	IMPORTANT
								0.2%		1 fewer per 1000 (from 2 fewer to 2 more)		
Amputation at 2 years - femoropopliteal arteries												
1	randomized	no serious	no serious	no serious	very serious[2]	none	1/52	0/46	Peto OR	20 more per	⊕⊕OO	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
	trials	risk of bias	inconsistency	indirectness			(1.9%)	(0%)	6.58 (0.12 to 334.26)	1000 (from 30 fewer to 70 more)	LOW	
								0%		-		
Target lesion revascularisation / re-intervention (hazard ratio)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	50/125 (40%)	47/185 (25.4%)	HR 1.29 (0.84 to 2)	61 more per 1000 (from 36 fewer to 190 more)	⊕⊕OO LOW	CRITICAL
								0%		-		
Target lesion revascularisation / re-intervention at 6 months - femoropopliteal arteries												
1	randomized trials	serious[5,6]	no serious inconsistency	no serious indirectness	serious[7]	none	6/72 (8.3%)	2/134 (1.5%)	RR 5.58 (1.16 to 26.96)	68 more per 1000 (from 2 more to 387 more)	⊕⊕OO LOW	CRITICAL
								1.5%		69 more per 1000 (from 2 more to 389 more)		
Target lesion revascularisation / re-intervention at 1 year - femoropopliteal arteries												
5	randomized trials	serious[5,6]	no serious inconsistency	no serious indirectness	serious[7]	none	114/581 (19.6%)	84/646 (13%)	RR 1.51 (1.16 to 1.95)	66 more per 1000 (from 21 more to 124 more)	⊕⊕OO LOW	CRITICAL
								13.8%		70 more per 1000 (from 22 more to 131 more)		
Re-intervention at 1 year - femoropopliteal arteries (randomized by limb)												
1	randomized	serious[1,6,8]	no serious	no serious	serious[9]	none	16/77	28/77	RR 0.57	156 fewer per	⊕⊕OO	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness			(20.8%)	(36.4%)	(0.34 to 0.97)	1000 (from 11 fewer to 240 fewer)	LOW	
								36.4%		157 fewer per 1000 (from 11 fewer to 240 fewer)		
Target lesion revascularisation / re-intervention at 2 years - femoropopliteal arteries												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[9]	none	28/52 (53.8%)	17/46 (37%)	RR 1.46 (0.93 to 2.29)	170 more per 1000 (from 26 fewer to 477 more)	⊕⊕⊕O MODERATE	CRITICAL
								37%		170 more per 1000 (from 26 fewer to 477 more)		
Target lesion revascularisation / re-intervention at 3 years - femoropopliteal arteries												
1	randomized trials	serious[5,10]	no serious inconsistency	no serious indirectness	very serious[2]	none	22/72 (30.6%)	30/134 (22.4%)	RR 1.36 (0.85 to 2.18)	81 more per 1000 (from 34 fewer to 264 more)	⊕OOO VERY LOW	CRITICAL
								22.4%		81 more per 1000 (from 34 fewer to 264 more)		
Perioperative complications - femoropopliteal arteries												
4	randomized trials	serious[1,10]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/337 (2.7%)	10/325 (3.1%)	RR 0.89 (0.37 to 2.11)	3 fewer per 1000 (from 19 fewer to 34 more)	⊕OOO VERY LOW	CRITICAL
								0.8%		1 fewer per 1000 (from 5 fewer		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
										to 9 more)		
Major complications/adverse events at 30 days - femoropopliteal arteries (randomized by limb)												
1	randomized trials	serious[1,6]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/77 (7.8%)	7/77 (9.1%)	RR 0.86 (0.3 to 2.43)	13 fewer per 1000 (from 64 fewer to 130 more)	⊕OOO VERY LOW	CRITICAL
								9.1%		13 fewer per 1000 (from 64 fewer to 130 more)		
Major complications/adverse event at 6 months												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/72 (6.9%)	9/134 (6.7%)	RR 1.03 (0.36 to 2.97)	2 more per 1000 (from 43 fewer to 132 more)	⊕OOO VERY LOW	CRITICAL
								6.7%		2 more per 1000 (from 43 fewer to 132 more)		
Major complications/adverse event at 9 months												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	very serious[2]	none	21/131 (16%)	22/135 (16.3%)	RR 0.98 (0.57 to 1.7)	3 fewer per 1000 (from 70 fewer to 114 more)	⊕OOO VERY LOW	CRITICAL
								16.3%		3 fewer per 1000 (from 70 fewer to 114 more)		
Major complications/adverse event at 1 year												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/72 (11.1%)	19/134 (14.2%)	RR 0.78 (0.36 to 1.7)	31 fewer per 1000 (from 91 fewer to 99	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
										more)		
								14.2%		31 fewer per 1000 (from 91 fewer to 99 more)		
Quality of life - change in Eq-5d at 6 months (median) - femoropopliteal (Better indicated by higher values)												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	serious[12]	none	53 (median 0.19)	51 (median 0.14)	-	median 0.0558 lower	⊕⊕OO LOW	CRITICAL
Quality of life - change in Eq-5d at 12 months (median) - femoropopliteal (Better indicated by higher values)												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	serious[12]	none	53 (median 0.16)	51 (median 0.16)	-	median 0.0041 lower	⊕⊕OO LOW	CRITICAL
Quality of life - change in SF8 at 12 months - femoropopliteal (Better indicated by higher values)												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	134	-	MD 0.2 higher (3.01 lower to 3.41 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life - change in SF8 at 3 years - femoropopliteal (Better indicated by higher values)												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	134	-	MD 1.5 higher (1.91 lower to 4.91 higher)	⊕⊕⊕O MODERATE	CRITICAL
Walking distance at 6 months - femoropopliteal arteries (Better indicated by higher values)												
1	randomized trials	serious[10,11]	no serious inconsistency	no serious indirectness	serious[9]	none	39	34	-	MD 200 lower (322.15 to 77.85 lower)	⊕⊕OO LOW	CRITICAL
Walking distance at 6 months (median) - femoropopliteal arteries (Better indicated by higher values)												
1	randomized trials	serious[11]	no serious inconsistency	no serious indirectness	serious[12]	none	53 (median 270,	51 (median 363,	-	median 93 lower	⊕⊕OO LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
							95% CI 180, 340)	95% CI 260, 450)				
Walking distance at 1 year - femoropopliteal arteries (Better indicated by higher values)												
1	randomized trials	serious[10,11]	no serious inconsistency	no serious indirectness	serious[9]	none	39	34	-	MD 250 lower (486.6 to 13.4 lower)	⊕⊕OO LOW	CRITICAL
Walking distance at 1 year (median) - femoropopliteal arteries (Better indicated by higher values)												
1	randomized trials	serious[11]	no serious inconsistency	no serious indirectness	serious[12]	none	53 (median 267, 95% CI 170, 340)	51 (median 387, 95% CI 340. 480)	-	median 120 lower	⊕⊕OO LOW	CRITICAL
Walking distance at 2 years (median) - femoropopliteal arteries (Better indicated by higher values)												
1	randomized trials	serious[11]	no serious inconsistency	no serious indirectness	serious[12]	none	52 (median 197, IQR 77, 355)	46 (median 302, IQR 99, 700)	-	median 106 lower	⊕⊕OO LOW	CRITICAL
Walking distance score at 1 year - femoropopliteal arteries (Better indicated by higher values)												
1	randomized trials	serious[5,10,11]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	134	-	MD 0.5 lower (7.25 lower to 6.25 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain score - SF36 at 6 months (median) - femoropopliteal (Better indicated by higher values)												
1	randomized trials	serious[11]	no serious inconsistency	no serious indirectness	serious[12]	none	53 (median 52, 95% CI 30, 70)	51 (median 51, 95% CI 22, 100)	-	median 1 higher	⊕⊕OO LOW	IMPORTANT
Pain score - SF36 at 12 months (median) - femoropopliteal (Better indicated by higher values)												
1	randomized trials	serious[11]	no serious inconsistency	no serious indirectness	serious[12]	none	53 (median 46, 95%	51 (median 52, 95%	-	median 6 lower	⊕⊕OO LOW	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
							CI 22, 76)	CI 22, 100)				

[1] *Method of randomized sequence generation not clearly reported*
[2] *95% CI crosses both MIDs*
[3] *Absolute effect calculated using the risk difference in Review Manager*
[4] *Absolute risk calculated by NCGC.*
[5] *Unclear allocation concealment*
[6] *Unclear if outcome assessors were blinded to interventions.*
[7] *The event rate and sample size do not meet the optimal information size*
[8] *Not reported how decision to re-intervene was made.*
[9] *95% CI crosses one MID*
[10] *Outcome assessors not blinded*
[11] *Patients not blinded to treatment*
[12] *Median data provided only. Assessing imprecision based on a cut off value not possible.*

5.4.3. Infrapopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
Mortality at 1 year - infrapopliteal arteries												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[3]	none	12/101 (11.9%)	11/99 (11.1%)	RR 1.07 (0.5 to 2.31)	8 more per 1000 (from 56 fewer to 146 more)	⊕OOO VERY LOW	IMPORTANT
								11.1%		8 more per 1000 (from 56 fewer to 145 more)		
Amputation at 1 year - infrapopliteal arteries												
1	randomized trials	serious[1,2,4]	no serious inconsistency	no serious indirectness	very serious[3]	none	17/85 (20%)	11/80 (13.8%)	RR 1.45 (0.73 to 2.91)	62 more per 1000 (from 37 fewer to 263 more)	⊕OOO VERY LOW	IMPORTANT
								13.8%		62 more per 1000 (from 37 fewer to 264 more)		
Target lesion revascularisation / re-intervention at 1 year												
1	randomized trials	serious[1,2,5]	no serious inconsistency	no serious indirectness	very serious[3]	none	14/85 (16.5%)	8/80 (10%)	RR 1.65 (0.73 to 3.71)	65 more per 1000 (from 27 fewer to 271 more)	⊕OOO VERY LOW	CRITICAL
								10%		65 more per 1000 (from 27 fewer to 271 more)		

[1] *Unclear allocation concealment*
[2] *Method of randomized sequence generation not clearly reported*
[3] *95% CI crosses both MIDs*
[4] *Not all patients appear to be included in the analysis and it is not clear who the missing patients are. The event rates are similar to the numbers of patients not available at 12 months.*
[5] *Unclear if outcome assessors were blinded to interventions.*

5.5. Bare metal versus drug eluting stents for intermittent claudication

5.5.1. Femoropopliteal disease (mixed intermittent claudication and critical limb ischemia)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS	DES	Relative (95% CI)	Absolute		
Mortality at 6 months												
1	randomized trials	serious[1,2]	no serious inconsistency	serious[3]	very serious[4]	none	1/28 (3.6%)	2/29 (6.9%)	RR 0.52 (0.05 to 5.4)	33 fewer per 1000 (from 66 fewer to 303 more)	⊕OOO VERY LOW	IMPORTANT
								6.9%		33 fewer per 1000 (from 66 fewer to 304 more)		
Mortality at 12 months												
1	randomized trials	serious[1,2]	no serious inconsistency	serious[3]	very serious[4]	none	1/59 (1.7%)	0/61 (0%)	Peto OR 7.64 (0.15 to 385.43)	20 more per 1000 (from 30 fewer to 60 more)[5]	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Mortality at 24 months												
2	randomized trials	serious[1,2]	serious[6]	serious[3]	very serious[4]	none	4/105 (3.8%)	8/108 (7.4%)	RR 0.51 (0.16 to 1.64)	36 fewer per 1000 (from 62 fewer to 47 more)	⊕OOO VERY LOW	IMPORTANT
								8.3%		41 fewer per 1000 (from 70 fewer to 53 more)		
Mortality at 36 months												
1	randomized trials	very serious[1,2]	no serious inconsistency	serious[3]	very serious[4]	none	9/72 (12.5%)	3/76 (3.9%)	RR 3.17 (0.89 to 11.23)	86 more per 1000 (from 4 fewer to 404 more)	⊕OOO VERY LOW	IMPORTANT
								4%		87 more per 1000 (from 4 fewer to 409 more)		
Procedure / device related deaths at 12 months												
1	randomized trials	serious[1,2]	no serious inconsistency	serious[3]	very serious[4]	none	0/59 (0%)	0/61 (0%)	-	0 fewer per 1000 (from 30 fewer to 30 more)[7]	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Amputation at 24 months												
1	randomized	serious[1,2]	no serious	serious[3]	very serious[4]	none	0/46	0/47	-	0 fewer per 1000 (from	⊕OOO	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS	DES	Relative (95% CI)	Absolute		
	trials		inconsistency				(0%)	(0%)		40 fewer to 40 more)[7]	VERY LOW	
								0%		-		
TLR at 6 months												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/28 (0%)	0/29 (0%)	-	0 fewer per 1000 (from 70 fewer to 70 more)[7]	⊕OOO VERY LOW	CRITICAL
								0%		-		
TLR at 24 months (HR)												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	6/46 (13%)	3/47 (6.4%)	HR 3.9 (0.77 to 19.75)	163 more per 1000 (from 14 fewer to 664 more)	⊕OOO VERY LOW	CRITICAL
								6.4%		163 more per 1000 (from 14 fewer to 665 more)		
TLR at 36 months in patients												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	25/72 (34.7%)	26/76 (34.2%)	RR 1.01 (0.65 to 1.58)	3 more per 1000 (from 120 fewer to 198 more)	⊕OOO VERY LOW	CRITICAL
								34.2%		3 more per 1000 (from 120 fewer to 198 more)		
TLR at 36 months by lesion												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[8]	none	38/72 (52.8%)	43/76 (56.6%)	RR 0.93 (0.7 to 1.25)	40 fewer per 1000 (from 170 fewer to 141 more)	⊕OOO VERY LOW	CRITICAL
								56.6%		40 fewer per 1000 (from 170 fewer to 141 more)		
TVR at 6 months												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/28 (10.7%)	1/29 (3.4%)	RR 3.11 (0.34 to 28.12)	73 more per 1000 (from 23 fewer to 935 more)	⊕OOO VERY LOW	CRITICAL
								3.5%		74 more per 1000 (from 23 fewer to 949 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS	DES	Relative (95% CI)	Absolute		
TVR at 24 months (HR)												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	serious[9]	none	10/46 (21.7%)	6/47 (12.8%)	HR 7.27 (1.75 to 30.2)	502 more per 1000 (from 85 more to 856 more)	⊕⊕OO LOW	CRITICAL
								12.8%		503 more per 1000 (from 85 more to 856 more)		
Revascularisation procedure on contralateral leg before discharge at 6 months												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/28 (7.1%)	2/29 (6.9%)	RR 1.04 (0.16 to 6.86)	3 more per 1000 (from 58 fewer to 404 more)	⊕OOO VERY LOW	CRITICAL
								6.9%		3 more per 1000 (from 58 fewer to 404 more)		
Revascularisation procedure on contralateral leg after discharge at 6 months												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/28 (7.1%)	3/29 (10.3%)	RR 0.69 (0.12 to 3.83)	32 fewer per 1000 (from 91 fewer to 293 more)	⊕OOO VERY LOW	CRITICAL
								10.3%		32 fewer per 1000 (from 91 fewer to 291 more)		
Peri-procedural complications												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/72 (1.4%)	0/76 (0%)	Peto OR 7.81 (0.15 to 394.22)	10 more per 1000 (from 20 fewer to 50 more)[5]	⊕OOO VERY LOW	CRITICAL
								0%		-		
Major adverse events at 6 months												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/29 (0%)	3.6%	Peto OR 0.13 (0 to 6.59)	31 fewer per 1000 (from 36 fewer to 201 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
Quality of life (SF-36 - physical domain) at 1 month (Better indicated by lower values)												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	serious[8]	none	66	72	-	MD 3.8 higher (0.3 to 7.3 higher)	⊕⊕OO LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS	DES	Relative (95% CI)	Absolute		
Quality of life (SF-36 - physical domain) at 6 months (Better indicated by lower values)												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	57	66	-	MD 0.1 higher (3.72 lower to 3.92 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life (SF-36 - physical domain) at 12 months (Better indicated by lower values)												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	52	62	-	MD 0.7 higher (3.45 lower to 4.85 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life (SF-36 - physical domain) at 24 months (Better indicated by lower values)												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	43	48	-	MD 0.8 lower (5.42 lower to 3.82 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life (SF-36 - physical domain) at 36 months (Better indicated by lower values)												
1	randomized trials	serious[1,2]	no serious inconsistency	no serious indirectness	serious[8]	none	39	45	-	MD 3.2 higher (1.58 lower to 7.98 higher)	⊕⊕OO LOW	CRITICAL

[1] *Unclear random sequence generation.*
[2] *Unclear allocation concealment.*
[3] *Incorrect assessment method.*
[4] *95% CI crossed both MIDs.*
[5] *Calculated by NCGC.*
[6] *Inconsistency in direction of estimate of effect.*
[7] *Absolute effect calculated using the risk difference in Review Manager*
[8] *95% CI crossed one MID.*
[9] *The event rate and sample size do not meet the optimal information size.*

5.5.2. Infrageniculate disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS	DES	Relative (95% CI)	Absolute		
All cause mortality at 12 months												
1	randomized trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	3/46 (6.5%)	5/40 (12.5%)	RR 0.52 (0.13 to 2.05)	60 fewer per 1000 (from 109 fewer to 131 more)	⊕OOO VERY LOW	IMPORTANT
								12.5%		60 fewer per 1000 (from 109 fewer to 131 more)		
Mortality at 1200 days												
1	randomized trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	8/44 (18.2%)	7/38 (18.4%)	RR 0.99 (0.39 to 2.47)	2 fewer per 1000 (from 112 fewer to 271 more)	⊕OOO VERY LOW	IMPORTANT
								18.4%		2 fewer per 1000 (from 112 fewer to 270 more)		
Amputation at 1 year												
1	randomized trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	2/79 (2.5%)	1/82 (1.2%)	RR 2.08 (0.19 to 22.44)	13 more per 1000 (from 10 fewer to 261 more)	⊕OOO VERY LOW	IMPORTANT
								1.2%		13 more per 1000 (from 10 fewer to 257 more)		
Amputation at 1200 days												
1	randomized trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	2/44 (4.5%)	0/38 (0%)	Peto OR 6.6 (0.4 to 108.15)	50 more per 1000 (from 30 fewer to 120 more)[4]	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Re-intervention at 1 year												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/79 (8.9%)	8/82 (9.8%)	RR 0.91 (0.35 to 2.39)	9 fewer per 1000 (from 63 fewer to 136 more)	⊕OOO VERY LOW	CRITICAL
								9.8%		9 fewer per 1000 (from 64 fewer to 136 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS	DES	Relative (95% CI)	Absolute		
TLR at 12 months in patients												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	8/46 (17.4%)	2/40 (5%)	RR 3.48 (0.78 to 15.44)	124 more per 1000 (from 11 fewer to 722 more)	⊕OOO VERY LOW	CRITICAL
								5%		124 more per 1000 (from 11 fewer to 722 more)		
TVR at 1200 days												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[5]	none	11/44 (25%)	3/38 (7.9%)	RR 3.17 (0.95 to 10.52)	171 more per 1000 (from 4 fewer to 752 more)	⊕⊕OO LOW	CRITICAL
								7.9%		171 more per 1000 (from 4 fewer to 752 more)		

[1] *Unclear allocation concealment.*
[2] *Incorrect assessment method.*
[3] *95% CI crossed both MIDs.*
[4] *Calculated by NCGC.*
[5] *95% CI crossed one MID.*

5.6. Autologous vein versus prostethic graft for intermittent claudication

5.6.1. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Autologous vein	Prosthetic bypass IC	Relative (95% CI)	Absolute		
Mortality at 30 days - femoropopliteal arteries												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/186 (0%)	0/188 (0%)	-	-	⊕⊕⊕O MODERATE	IMPORTANT
								0%		-		
Mortality at 2 years – femoropopliteal arteries.												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/47 (12.8%)	6/49 (12.2%)	RR 1.04 (0.36 to 3)	5 more per 1000 (from 78 fewer to 245 more)	⊕OOO VERY LOW	IMPORTANT
								12.2%		5 more per 1000 (from 78 fewer to 244 more)		
Amputation at 30 days - femoropopliteal arteries												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/51 (0%)	0/51 (0%)	-	-	⊕⊕⊕O MODERATE	IMPORTANT
								0%		-		
Amputation at 5 years - femoropopliteal arteries												
3	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/186 (2.2%)	4/188 (2.1%)	RR 1.01 (0.26 to 3.97)	0 more per 1000 (from 16 fewer to 63 more)	⊕OOO VERY LOW	IMPORTANT
								2.6%		0 more per 1000 (from 19 fewer to 77 more)		
Reintervention at 2 years - femoropopliteal arteries												

1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/75 (1.3%)	4/76 (5.3%)	RR 0.25 (0.03 to 2.21)	39 fewer per 1000 (from 51 fewer to 64 more)	⊕OOO VERY LOW	CRITICAL
								5.3%		40 fewer per 1000 (from 51 fewer to 64 more)		
Reintervention at 5 years - femoropopliteal arteries												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10/186 (5.4%)	33/188 (17.6%)	RR 0.31 (0.16 to 0.6)	121 fewer per 1000 (from 70 fewer to 147 fewer)	⊕⊕⊕O MODERATE	CRITICAL
								19.7%		136 fewer per 1000 (from 79 fewer to 165 fewer)		
Peri-operative complications at 30 days - femoropopliteal arteries												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/51 (13.7%)	6/51 (11.8%)	RR 1.17 (0.42 to 3.23)	20 more per 1000 (from 68 fewer to 262 more)	⊕OOO VERY LOW	CRITICAL
								11.8%		20 more per 1000 (from 68 fewer to 263 more)		
Perioperative minor adverse event - femoropopliteal arteries												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/75 (5.3%)	3/76 (3.9%)	RR 1.35 (0.31 to 5.83)	14 more per 1000 (from 27 fewer to 191 more)	⊕OOO VERY LOW	CRITICAL
								4%		14 more per 1000 (from 28 fewer to 193 more)		

[1] *Unclear randomisation and allocation concealment.*
[2] *Confidence interval crossed both MIDs.*
[3] *Confidence interval crossed one MID.*
[4] *Unclear allocation concealment.*

5.7. Angioplasty versus bypass surgery for critical limb ischemia

5.7.1. Aortoiliac disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Bypass surgery or amputation	Relative (95% CI)	Absolute		
Limb salvage at 4 years												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	16/22 (72.7%)	17/23 (73.9%)	RR 0.98 (0.69 to 1.4)	15 fewer per 1000 (from 229 fewer to 296 more)	⊕⊕OO LOW	CRITICAL
Quality of life												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		
Peri-procedural complications												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		
Re-intervention rate												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		
Wound healing												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		
Pain												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		

[1] *No information on blinding, but no impact on this outcome.*
[2] *Large CI that includes both appreciable harm and benefit.*

5.7.2. Femoropopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Bypass surgery or amputation	Relative (95% CI)	Absolute		
Amputation rate at 1 year												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/30 (6.7%)	8/31 (25.8%)	RR 0.26 (0.06 to 1.12)	191 fewer per 1000 (from 243 fewer to 31 more)	⊕OOO VERY LOW	CRITICAL
Amputation-free survival before 2 years												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/224 (0%)	0/228 (0%)	HR 1.03 (0.76 to 1.39)	-	⊕⊕OO LOW	CRITICAL
								0%		-		
Amputation-free survival after 2 years												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	0/224 (0%)	0/228 (0%)	HR 0.85 (0.5 to 1.07)	-	⊕⊕⊕O MODERATE	CRITICAL
								0%		-		
Amputation-free survival at 3 years												
1	randomised trials	no serious risk of bias[4]	no serious inconsistency	no serious indirectness	very serious[2]	none	82/224 (36.6%)	86/228 (37.7%)	RR 0.97 (0.76 to 1.23)	11 fewer per 1000 (from 91 fewer to 87 more)	⊕⊕OO LOW	CRITICAL
Limb salvage rate at 4 years												
1	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[6]	none	10/11 (90.9%)	10/16 (62.5%)	RR 1.45 (0.95 to 2.22)	281 more per 1000 (from 31 fewer to 763 more)	⊕⊕OO LOW	CRITICAL
								0%		-		
Major adverse events at 30 days												
1	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[3]	none	36/224 (16.1%)	51/228 (22.4%)	RR 0.72 (0.49 to	63 fewer per 1000 (from 114 fewer to	⊕⊕OO LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Bypass surgery or amputation	Relative (95% CI)	Absolute		
									1.06)	13 more)		
Minor adverse events at 30 days												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	70/224 (31.3%)	109/228 (47.8%)	RR 0.65 (0.52 to 0.83)	167 fewer per 1000 (from 81 fewer to 229 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
								0%		-		
Minor adverse events at 1 year												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[7]	none	3/30 (10%)	12/31 (38.7%)	RR 0.26 (0.08 to 0.83)	286 fewer per 1000 (from 66 fewer to 356 fewer)	⊕⊕OO LOW	CRITICAL
								0%		-		
Re-intervention at 30 days												
1	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[8]	none	67/224 (29.9%)	41/228 (18%)	RR 1.66 (1.18 to 2.34)	119 more per 1000 (from 32 more to 241 more)	⊕⊕OO LOW	CRITICAL
Re-intervention at 1 year												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/53 (18.9%)	4/49 (8.2%)	RR 2.31 (0.78 to 6.89)	107 more per 1000 (from 18 fewer to 481 more)	⊕OOO VERY LOW	CRITICAL
Quality of life (Better indicated by lower values)												
1	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[9]	none	133	119	-	MD 0 higher (0 to 0 higher)	⊕⊕OO LOW	CRITICAL
Wound healing												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Angioplasty	Bypass surgery or amputation	Relative (95% CI)	Absolute		
Pain												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		

[1] *Unclear allocation concealment and blinding.*
[2] *Large CI that includes appreciable benefit and harm.*
[3] *Large CI that includes appreciable benefit and no effect.*
[4] *Unclear blinding, but no impact on this outcome.*
[5] *Unclear blinding.*
[6] *Large CI that includes no effect and appreciable harm.*
[7] *OIS not reached.*
[8] *OIS not reached (for baseline risk of 18% and RRR of 25%).*
[9] *Mean difference and CI not estimable.*

5.8. Angioplasty with selective versus primary stent placement for critical limb ischemia

5.8.1. Infrapopliteal disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
Mortality at 3 months - infrapopliteal												
1	randomized trials	very serious[1,2,3]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/32 (9.4%)	5/33 (15.2%)	RR 0.62 (0.16 to 2.38)	58 fewer per 1000 (from 127 fewer to 209 more)	⊕OOO VERY LOW	IMPORTANT
								15.2%		58 fewer per 1000 (from 128 fewer to 210 more)		
Mortality at 9 months - infrapopliteal												
1	randomized trials	very serious[1,2]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/24 (20.8%)	5/19 (26.3%)	RR 0.79 (0.27 to 2.34)	55 fewer per 1000 (from 192 fewer to 353 more)	⊕OOO VERY LOW	IMPORTANT
								26.3%		55 fewer per 1000 (from 192 fewer to 352 more)		
Amputation at 3 months - infrapopliteal												
1	randomized trials	very serious[1,2,3]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/32 (12.5%)	6/33 (18.2%)	RR 0.69 (0.21 to 2.21)	56 fewer per 1000 (from 144 fewer to 220 more)	⊕OOO VERY LOW	CRITICAL
								18.2%		56 fewer per 1000 (from 144 fewer to 220 more)		
Amputation at 6 months - infrapopliteal												
1	randomized	serious[1,2]	no serious	no serious	very	none	1/27	2/24	RR 0.44	47 fewer per 1000 (from 80 fewer to	⊕OOO	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness	serious[4]		(3.7%)	(8.3%)	(0.04 to 4.6)	300 more)	VERY LOW	
								8.3%		46 fewer per 1000 (from 80 fewer to 299 more)		
Amputation at 9 months - infrapopliteal												
1	randomized trials	very serious[1,2,3]	no serious inconsistency	no serious indirectness	serious[5]	none	7/24 (29.2%)	10/19 (52.6%)	RR 0.55 (0.26 to 1.18)	237 fewer per 1000 (from 389 fewer to 95 more)	⊕OOO VERY LOW	CRITICAL
								52.6%		237 fewer per 1000 (from 389 fewer to 95 more)		
Target lesion revascularisation / re-intervention at 3 months - infrapopliteal												
1	randomized trials	serious[1,2,6]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/32 (0%)	1/33 (3%)	Peto OR 0.14 (0 to 7.03)	26 fewer per 1000 (from 30 fewer to 183 more)	⊕OOO VERY LOW	CRITICAL
								3%		26 fewer per 1000 (from 30 fewer to 181 more)		
Target lesion revascularisation / re-intervention at 6 months - infrapopliteal												
1	randomized trials	very serious[1,2,3,6,7,8]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/27 (0%)	1/24 (4.2%)	Peto OR 0.12 (0 to 6.06)	37 fewer per 1000 (from 42 fewer to 211 more)	⊕OOO VERY LOW	CRITICAL
								4.2%		37 fewer per 1000 (from 42 fewer to 213 more)		
Target lesion revascularisation / re-intervention at 9 months - infrapopliteal												
1	randomized trials	very serious[1,2,3,6]	no serious inconsistency	no serious indirectness	very serious[4]	none	6/24 (25%)	7/19 (36.8%)	RR 0.68 (0.27 to 1.68)	118 fewer per 1000 (from 269 fewer to 251 more)	⊕OOO VERY	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Selective stenting with angioplasty	Primary stenting with angioplasty	Relative (95% CI)	Absolute		
								36.8%		118 fewer per 1000 (from 269 fewer to 250 more)	LOW	
Complete ulcer healing at 12 months - infrapopliteal												
1	randomized trials	very serious[1,9,10,11]	no serious inconsistency	no serious indirectness	serious[5]	none	16/20 (80%)	5/13 (38.5%)	RR 2.08 (1.01 to 4.28)	415 more per 1000 (from 4 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
								38.5%		416 more per 1000 (from 4 more to 1000 more)		

[1] *Unclear allocation concealment*
[2] *Method of randomized sequence generation not clearly reported*
[3] *High dropout rate in both groups*
[4] *95% CI crosses both MIDs*
[5] *95% CI crosses one MID*
[6] *Unclear if outcome assessors were blinded to interventions.*
[7] *Outcome not redefined*
[8] *Not reported how decision to reintervene was made*
[9] *Unclear if patients were blinded*
[10] *Unclear if outcome assessors were blinded*
[11] *Around a third of patients in each group were not available for the assessment of this outcome.*

5.9. Bare metal versus drug eluting stents for critical limb ischemia

5.9.1. Infrageniculate disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS compared to DES: CLI, femoro-popliteal	Control	Relative (95% CI)	Absolute		
Mortality - HR												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/66 (15.2%)	13/74 (17.6%)	HR 0.88 (0.39 to 1.99)	19 fewer per 1000 (from 103 fewer to 143 more)	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Mortality at 12 months												
1	randomized trials	serious[1]	no serious inconsistency	serious[3]	very serious[2]	none	8/33 (24.2%)	9/42 (21.4%)	RR 1.13 (0.49 to 2.61)	28 more per 1000 (from 109 fewer to 345 more)	⊕OOO VERY LOW	IMPORTANT
								21.4%		28 more per 1000 (from 109 fewer to 345 more)		
Mortality at 1200 days												
1	randomized trials	serious	no serious inconsistency	serious[3]	very serious[2]	none	10/31 (32.3%)	10/38 (26.3%)	RR 1.23 (0.59 to 2.56)	61 more per 1000 (from 108 fewer to 411 more)	⊕OOO VERY LOW	IMPORTANT
								26.3%		60 more per 1000 (from 108 fewer to 410 more)		
Amputation at 12 months												
2	randomized trials	serious	no serious inconsistency	serious[3]	very serious[2]	none	4/107 (3.7%)	3/108 (2.8%)	RR 1.46 (0.33 to 6.46)	13 more per 1000 (from 19 fewer to 152 more)	⊕OOO VERY LOW	CRITICAL
								3.1%		14 more per 1000 (from 21 fewer to 169 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS compared to DES: CLI, femoro-popliteal	Control	Relative (95% CI)	Absolute		
Amputation at 1200 days												
1	randomized trials	serious	no serious inconsistency	serious[3]	very serious[2]	none	7/31 (22.6%)	2/38 (5.3%)	RR 4.29 (0.96 to 19.19)	173 more per 1000 (from 2 fewer to 957 more)	⊕OOO VERY LOW	CRITICAL
								5.3%		174 more per 1000 (from 2 fewer to 964 more)		
TLR - HR												
1	randomized trials	very serious[1,4]	no serious inconsistency	no serious indirectness	serious[5]	none	22/66 (33.3%)	6/74 (8.1%)	HR 3.5 (1.67 to 7.34)	175 more per 1000 (from 51 more to 381 more)	⊕OOO VERY LOW	CRITICAL
								0%		-		
TLR at 12 months by patient												
1	randomized trials	serious	no serious inconsistency	no serious indirectness	very serious[2]	none	3/33 (9.1%)	4/42 (9.5%)	RR 0.95 (0.23 to 3.97)	5 fewer per 1000 (from 73 fewer to 283 more)	⊕OOO VERY LOW	CRITICAL
								9.5%		5 fewer per 1000 (from 73 fewer to 282 more)		
Total vessel revascularisation at 1200 days												
1	randomized trials	serious	no serious inconsistency	no serious indirectness	very serious[2]	none	4/31 (12.9%)	4/38 (10.5%)	RR 1.23 (0.33 to 4.51)	24 more per 1000 (from 71 fewer to 369 more)	⊕OOO VERY LOW	CRITICAL
								10.5%		24 more per 1000 (from 70 fewer to 369 more)		
Wound healing at 12 months												
1	randomized trials	serious	no serious inconsistency	serious[3]	serious[5]	none	14/21 (66.7%)	19/24 (79.2%)	RR 0.84 (0.58 to 1.21)	127 fewer per 1000 (from 332 fewer to 166 more)	⊕OOO VERY	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMS compared to DES: CLI, femoro-popliteal	Control	Relative (95% CI)	Absolute		
								79.2%		127 fewer per 1000 (from 333 fewer to 166 more)	LOW	

[1] *Unclear allocation concealment*
[2] *95% CI crosses both MIDs.*
[3] *Incorrect assessment method.*
[4] *Outcome assessor was not blinded and the outcome was not pre-defined.*
[5] *95% CI crosses one MID.*

5.10. Drug-coated balloons for critical limb ischemia

5.10.1. Intermittent claudication or critical limb ischemia due to femoropopliteal lesions

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons	Relative (95% CI)	Absolute		
Mortality at 6 months - femoropopliteal (follow-up 6 months)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/93 (3.2%)	0/96 (0%)	OR 7.96 (0.82 to 77.36)	30 more per 1000 (from 10 fewer to 80 more)[3]	⊕OOO VERY LOW	IMPORTANT
								0%		-		
Mortality at 18 to 24 months - femoropopliteal (follow-up 18 to 24 months)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/45 (13.3%)	3/42 (7.1%)	RR 1.87 (0.5 to 6.99)	62 more per 1000 (from 36 fewer to 428 more)	⊕OOO VERY LOW	IMPORTANT
								7.1%		62 more per 1000 (from 36 fewer to 425 more)		
Amputation at 6 months - femoropopliteal (follow-up 6 months)												
2	randomised	serious[1]	no serious	no serious	very	none	2/93	2/96	RR 1.04 (0.19	1 more per 1000 (from 17	⊕OOO	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness	serious[2]		(2.2%)	(2.1%)	to 5.71)	fewer to 98 more)	VERY LOW	
								2.1%		1 more per 1000 (from 17 fewer to 99 more)		
Amputation at 18 to 24 months - femoropopliteal (follow-up 18 to 24 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/45 (0%)	1/42 (2.4%)	OR 0.13 (0 to 6.37)	20 fewer per 1000 (from 90 fewer to 40 more)[3]	⊕OOO VERY LOW	CRITICAL
								2.4%		21 fewer per 1000 (from 24 fewer to 111 more)		
Target lesion revascularization at 6 months - femoropopliteal (follow-up 6 months)												
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	serious[6]	none	3/45 (6.7%)	14/42 (33.3%)	RR 0.2 (0.06 to 0.65)	267 fewer per 1000 (from 117 fewer to 313 fewer)	⊕⊕OO LOW	CRITICAL
								33.3%		266 fewer per 1000 (from 117 fewer to 313 fewer)		
Target lesion revascularization at 12 months - femoropopliteal (follow-up 12 months)												
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	serious[6]	none	5/48 (10.4%)	18/52 (34.6%)	RR 0.3 (0.12 to 0.75)	242 fewer per 1000 (from 87 fewer to 305 fewer)	⊕⊕OO LOW	CRITICAL
								34.6%		242 fewer per 1000 (from 86 fewer to 304 fewer)		
Target lesion revascularization at 18 to 24 months - femoropopliteal (follow-up 18 to 24 months)												
2	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	serious[6]	none	13/93 (14%)	42/94 (44.7%)	RR 0.31 (0.18 to 0.54)	308 fewer per 1000 (from 206 fewer to 366 fewer)	⊕⊕OO LOW	CRITICAL
								45.2%		312 fewer per 1000 (from 208 fewer to 371 fewer)		
Serious adverse events up to 2 weeks after procedure - femoropopliteal (follow-up 2 weeks)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons	Relative (95% CI)	Absolute		
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/48 (6.3%)	4/52 (7.7%)	RR 0.81 (0.19 to 3.45)	15 fewer per 1000 (from 62 fewer to 188 more)	⊕OOO VERY LOW	CRITICAL
								7.7%		15 fewer per 1000 (from 62 fewer to 189 more)		
Serious adverse events at 6 months - femoropopliteal (follow-up 6 months)												
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	very serious[2]	none	25/48 (52.1%)	34/52 (65.4%)	RR 0.8 (0.57 to 1.11)	131 fewer per 1000 (from 281 fewer to 72 more)	⊕OOO VERY LOW	CRITICAL
								65.4%		131 fewer per 1000 (from 281 fewer to 72 more)		

[1] *Unclear allocation concealment*
[2] *95% CI crosses both MIDs*
[3] *Absolute effect calculated by NCGC*
[4] *Outcome assessors not blinded*
[5] *Outcome assessors not blinded*
[6] *The event rate and sample size do not meet the optimal information size*

5.10.2. Intermittent claudication or critical limb ischemia due to femoropopliteal lesions: drug in contrast medium

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons with the drug in a contrast medium	Relative (95% CI)	Absolute		
Mortality at 6 months - femoropopliteal (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/48 (4.2%)	2/52 (3.8%)	RR 1.08 (0.16 to 7.39)	3 more per 1000 (from 32 fewer to 246 more)	⊕OOO VERY LOW	IMPORTANT
								3.9%		3 more per 1000 (from 33 fewer to		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons with the drug in a contrast medium	Relative (95% CI)	Absolute		
										249 more)		
Amputation at 6 months - femoropopliteal (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/48 (4.2%)	2/52 (3.8%)	RR 1.08 (0.16 to 7.39)	3 more per 1000 (from 32 fewer to 246 more)	⊕OOO VERY LOW	CRITICAL
								3.9%		3 more per 1000 (from 33 fewer to 249 more)		
Target lesion revascularization at 12 months - femoropopliteal (follow-up 12 months)												
1	randomised trials	very serious[1,3,4]	no serious inconsistency	no serious indirectness	serious[5]	none	5/48 (10.4%)	26/54 (48.1%)	RR 0.22 (0.09 to 0.52)	376 fewer per 1000 (from 231 fewer to 438 fewer)	⊕⊕OO LOW	CRITICAL
								48.2%		376 fewer per 1000 (from 231 fewer to 439 fewer)		
Target lesion revascularization at 18 to 24 months - femoropopliteal (follow-up 18 to 24 months)												
1	randomised trials	very serious[1,3,4]	no serious inconsistency	no serious indirectness	serious[5]	none	7/48 (14.6%)	28/54 (51.9%)	RR 0.28 (0.14 to 0.58)	373 fewer per 1000 (from 218 fewer to 446 fewer)	⊕⊕OO LOW	CRITICAL
								51.9%		374 fewer per 1000 (from 218 fewer to 446 fewer)		
Serious adverse events up to 2 weeks after procedure - femoropopliteal (follow-up 2 weeks)												
1	randomised trials	very serious[1,3,4]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/48 (6.3%)	2/54 (3.7%)	RR 1.69 (0.29 to 9.68)	26 more per 1000 (from 26 fewer to 321 more)	⊕OOO VERY LOW	CRITICAL
								3.7%		26 more per 1000 (from 26 fewer to 321 more)		
Serious adverse events at 6 months - femoropopliteal (follow-up 6 months)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons with the drug in a contrast medium	Relative (95% CI)	Absolute		
1	randomised trials	very serious[1,3,4]	no serious inconsistency	no serious indirectness	very serious[2]	none	25/48 (52.1%)	30/54 (55.6%)	RR 0.94 (0.65 to 1.35)	33 fewer per 1000 (from 194 fewer to 194 more)	⊕OOO VERY LOW	CRITICAL
								55.6%		33 fewer per 1000 (from 195 fewer to 195 more)		

[1] *Unclear allocation concealment*
[2] *95% CI crosses both MIDs*
[3] *Outcome assessors not blinded*
[4] *Outcome not clearly defined*
[5] *The event rate and sample size do not meet the optimal information size*

5.10.3. Intermittent claudication or critical limb ischemia due to femoropopliteal and/or infrapopliteal lesions

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons	Relative (95% CI)	Absolute		
Mortality at 6 months - femoropopliteal (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[7]	none	0/25 (0%)	0/25 (0%)	-	0 fewer per 1000 (from 70 fewer to 70 more)[2]	⊕⊕OO LOW	IMPORTANT
								0%		-		
Amputation per limb at 6 months - femoropopliteal (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/33 (3%)	3/38 (7.9%)	RR 0.38 (0.04 to 3.52)	49 fewer per 1000 (from 76 fewer to 199 more)	⊕OOO VERY LOW	CRITICAL
								7.9%		49 fewer per 1000 (from 76 fewer to 199 more)		
Target lesion revascularization per limb at 6 months - femoropopliteal (follow-up 6 months)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons	Relative (95% CI)	Absolute		
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/33 (6.1%)	9/38 (23.7%)	RR 0.26 (0.06 to 1.1)	175 fewer per 1000 (from 223 fewer to 24 more)	⊕OOO VERY LOW	CRITICAL
								23.7%		175 fewer per 1000 (from 223 fewer to 24 more)		
Total major adverse events per limb at 6 months - femoropopliteal (follow-up 6 months)												
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	serious[6]	none	4/33 (12.1%)	14/38 (36.8%)	RR 0.33 (0.12 to 0.9)	247 fewer per 1000 (from 37 fewer to 324 fewer)	⊕OOO VERY LOW	CRITICAL
								36.8%		247 fewer per 1000 (from 37 fewer to 324 fewer)		

[1] *Allocation conccealment unclear*
[2] *Calculated by NCGC*
[3] *95% CI crosses both MIDs*
[4] *Outcome assessors not blinded*
[5] *Outcome not clearly defined*
[6] *95% CI crosses one MID*
[7] *The event rate and sample size do not meet the optimal information size*

5.10.4. Critical limb ischemia due to infrapopliteal lesions, adults with diabetes

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons	Relative (95% CI)	Absolute		
Mortality at 12 months (no. of patients) - infrapopliteal (follow-up 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/65 (7.7%)	3/67 (4.5%)	RR 1.72 (0.43 to 6.9)	32 more per 1000 (from 26 fewer to 264 more)	⊕OOO VERY LOW	IMPORTANT
								4.5%		32 more per 1000 (from 26 fewer to 266 more)		
Major amputation at 12 months (no. of limbs) - infrapopliteal (follow-up 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/71 (0%)	1/72 (1.4%)	OR 0.14 (0 to 6.92)	10 fewer per 1000 (from 50 fewer to 20 more)[3]	⊕OOO VERY LOW	CRITICAL
								1.4%		12 fewer per 1000 (from 14 fewer to 75 more)		
Minor amputation at 12 months (no. of limbs) - infrapopliteal (follow-up 12 months)												
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/71 (23.9%)	19/72 (26.4%)	RR 0.91 (0.52 to 1.6)	24 fewer per 1000 (from 127 fewer to 158 more)	⊕OOO VERY LOW	CRITICAL
								26.4%		24 fewer per 1000 (from 127 fewer to 158 more)		
Major adverse events at 12 months (no. of patients) - infrapopliteal (follow-up 12 months)												
1	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	serious[7]	none	20/65 (30.8%)	34/67 (50.7%)	OR 0.44 (0.22 to 0.88)	196 fewer per 1000 (from 32 fewer to 323 fewer)	⊕⊕OO LOW	CRITICAL
								50.8%		196 fewer per 1000 (from 32 fewer to 323 fewer)		
Complete index ulcer healing at 12 months (no. of limbs) - infrapopliteal (follow-up 12 months)												
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	very serious[2]	none	56/65 (86.2%)	43/64 (67.2%)	RR 1.28 (1.05 to 1.56)	188 more per 1000 (from 34 more to 376 more)	⊕OOO VERY LOW	CRITICAL
								67.2%		188 more per 1000 (from		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug coated	Uncoated balloons	Relative (95% CI)	Absolute		
										34 more to 376 more)		
Time to complete ulcer healing up to 12 months (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	very serious[1,4,5]	no serious inconsistency	no serious indirectness	serious [6]	none	65	64	-	MD 0.8 lower (1.34 to 0.26 lower)	⊕OOO VERY LOW	CRITICAL

[1] *Allocation conccealment unclear*
[2] *95% CI crosses both MIDs*
[3] *Absolute risk calculated by NCGC*
[4] *Outcome assessors not blinded*
[5] *Outcome not clearly defined*
[6] *95% CI crosses one MID*
[7] *The event rate and sample size do not meet the optimal information size*

5.11. Autologous vein versus prostethic graft for critical limb ischemia

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Autologous vein	Prosthetic graft	Relative (95% CI)	Absolute		
Amputation at 5 years												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/25 (0%)	8/24 (33.3%)	RR 0.04 (0 to 0.7)	320 fewer per 1000 (from 100 fewer to 333 fewer)	⊕⊕OO LOW	CRITICAL
Peri-operative minor adverse event												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/25 (20%)	4/24 (16.7%)	RR 1.20 (0.37 to 3.94)	33 more per 1000 (from 105 fewer to 490 more)	⊕OOO VERY LOW	CRITICAL
Re-intervention rate at 5 years												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Autologous vein	Prosthetic graft	Relative (95% CI)	Absolute		
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/25 (0%)	2/24 (8.3%)	RR 0.18 (0.01 to 3.87)	68 fewer per 1000 (from 82 fewer to 239 more)	⊕OOO VERY LOW	CRITICAL
Quality of life												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		
Wound healing												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		
Pain												
0	No evidence available					none	-	-	-	-		CRITICAL
								0%		-		

[1] *No details on allocation concealment, blinding or ITT analysis.*
[2] *Very large CI, but no MID included. However, small sample size;*
[3] *No information on allocation concealment, blinding or ITT analysis.*
[4] *Very large CI (including appreciable harm and benefit).*

6. FOREST PLOTS

6.1. Assessment of PAD

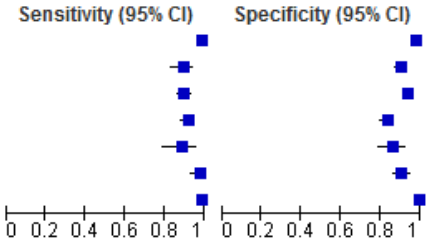
6.1.1. DUS versus CTA versus CE MRA versus 2D TOF MRA versus 3D CE MRA: all compared with the reference standard, DSA

(throughout,'vhi' means very high risk of bias; 'diabetes' means that all patients in the study had diabetes, and 'calc' means the 2x2 table was calculated from the sensitivity, specificity, positive and negative predictive values and the number of patients)

Figure 1 – Forest plot of coupled sensitivities and specificities for imaging tests; whole leg, 50-100% stenosis, all studies

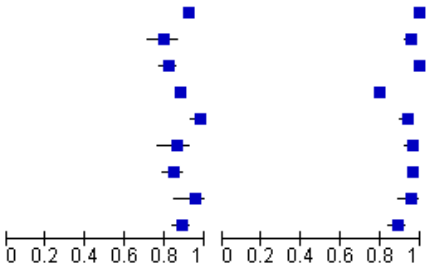
CTA whole leg, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Catalano 2004	251	23	3	860	0.99 [0.97, 1.00]	0.97 [0.96, 0.98]
Heuschmid 2003 vhi	133	40	16	379	0.89 [0.83, 0.94]	0.90 [0.87, 0.93]
Iezzi 2013 vhi	327	61	38	886	0.90 [0.86, 0.93]	0.94 [0.92, 0.95]
Martin 2003 vhi	240	80	21	399	0.92 [0.88, 0.95]	0.83 [0.80, 0.87]
Portugaller 2004	56	17	7	106	0.89 [0.78, 0.95]	0.86 [0.79, 0.92]
Puls 1996	111	20	3	193	0.97 [0.93, 0.99]	0.91 [0.86, 0.94]
Rieker 1996	479	8	6	858	0.99 [0.97, 1.00]	0.99 [0.98, 1.00]



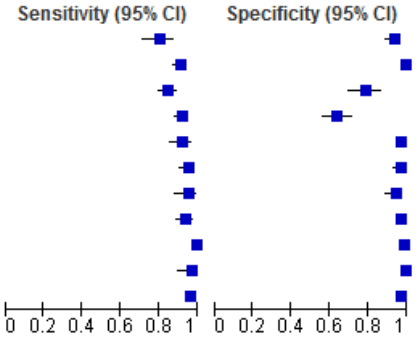
DUS, Whole leg, ≥ 50% stenosis (Bueno calc)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aly 1998	404	27	34	2643	0.92 [0.89, 0.95]	0.99 [0.99, 0.99]
Bergamini 1995	94	13	24	273	0.80 [0.71, 0.87]	0.95 [0.92, 0.98]
Bueno 2010 calc	290	11	66	1207	0.81 [0.77, 0.85]	0.99 [0.98, 1.00]
Eiberg 2010	1358	203	185	789	0.88 [0.86, 0.90]	0.80 [0.77, 0.82]
El-Kayali 2004	123	15	3	216	0.98 [0.93, 1.00]	0.94 [0.90, 0.96]
Hatsukami 2002	73	6	12	152	0.86 [0.77, 0.92]	0.96 [0.92, 0.99]
Legemate 1991	179	30	33	676	0.84 [0.79, 0.89]	0.96 [0.94, 0.97]
Linke 1994	41	4	2	87	0.95 [0.84, 0.99]	0.96 [0.89, 0.99]
Sensier 1996	214	26	28	201	0.88 [0.84, 0.92]	0.89 [0.84, 0.92]



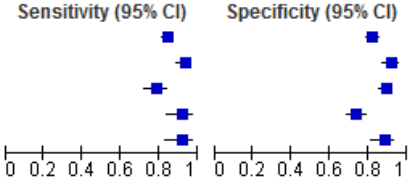
CE MRA, whole leg, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Andreisek 2007 diabetes	84	13	21	182	0.80 [0.71, 0.87]	0.93 [0.89, 0.96]
Bueno 2010 calc	320	11	32	1288	0.91 [0.87, 0.94]	0.99 [0.98, 1.00]
Burbelko 2013 vhi	255	22	47	82	0.84 [0.80, 0.88]	0.79 [0.70, 0.86]
Cronberg 2003	227	62	20	109	0.92 [0.88, 0.95]	0.64 [0.56, 0.71]
Laissy 1998	104	14	9	393	0.92 [0.85, 0.96]	0.97 [0.94, 0.98]
Lapeyre 2005 diabetes	160	4	8	138	0.95 [0.91, 0.98]	0.97 [0.93, 0.99]
Lenhart 2000	79	8	4	129	0.95 [0.88, 0.99]	0.94 [0.89, 0.97]
Schafer 2003	138	13	9	416	0.94 [0.89, 0.97]	0.97 [0.95, 0.98]
Steffens 2003	185	8	1	706	0.99 [0.97, 1.00]	0.99 [0.98, 1.00]
Sueyoshi, 1999	67	3	2	351	0.97 [0.90, 1.00]	0.99 [0.98, 1.00]
Winterer 1999	362	43	14	1361	0.96 [0.94, 0.98]	0.97 [0.96, 0.98]



2D TOF MRA, Whole leg, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Baum 1995	527	101	100	460	0.84 [0.81, 0.87]	0.82 [0.79, 0.85]
Hoch 1996	172	13	12	155	0.93 [0.89, 0.97]	0.92 [0.87, 0.96]
Hoch 1999 vhi	161	37	44	302	0.79 [0.72, 0.84]	0.89 [0.85, 0.92]
Snidow, 1995	80	76	7	215	0.92 [0.84, 0.97]	0.74 [0.68, 0.79]
Yucel, 1993	65	16	6	119	0.92 [0.83, 0.97]	0.88 [0.81, 0.93]



3D CE MRA, whole leg, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Wang 2012	256	5	2	542	0.99 [0.97, 1.00]	0.99 [0.98, 1.00]

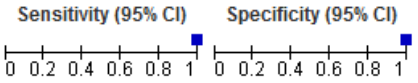


Figure 2 – ROC curve for imaging tests; whole leg, 50-100% stenosis (hierarchical bivariate meta-analysis for all tests; sensitivity analysis for all except CTA, which includes 3 studies at very high risk of bias, and 2D TOF MRA, which includes one at very high risk of bias)

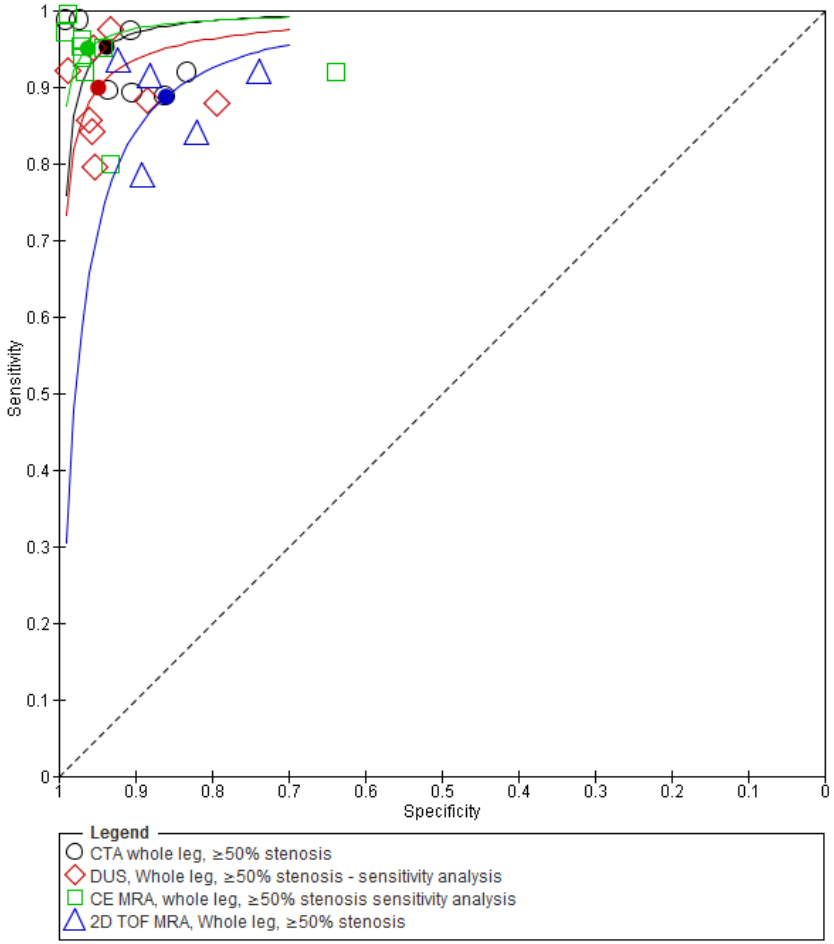
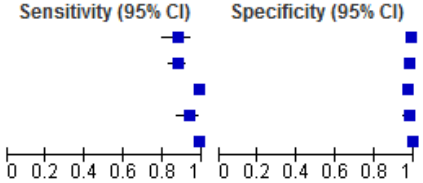


Figure 3 – Forest plot of coupled sensitivities and specificities for imaging tests; whole leg, 70-100% stenosis, all studies

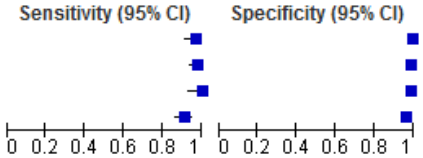
CTA whole leg, ≥ 70% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Heuschmid 2003 vhi	88	7	12	461	0.88 [0.80, 0.94]	0.99 [0.97, 0.99]
Martin 2003 vhi	236	20	34	1022	0.87 [0.83, 0.91]	0.98 [0.97, 0.99]
Napoli 2011	3072	138	41	4141	0.99 [0.98, 0.99]	0.97 [0.96, 0.97]
Rieker 1996	91	6	6	224	0.94 [0.87, 0.98]	0.97 [0.94, 0.99]
Schernthaner 2008	353	5	5	988	0.99 [0.97, 1.00]	0.99 [0.99, 1.00]



CE MRA, Whole leg, ≥ 70% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Schafer 2003	110	3	4	459	0.96 [0.91, 0.99]	0.99 [0.98, 1.00]
Steffens 2003	147	11	4	738	0.97 [0.93, 0.99]	0.99 [0.97, 0.99]
Sueyoshi, 1999	53	4	0	366	1.00 [0.93, 1.00]	0.99 [0.97, 1.00]
Vavrik 2004	170	26	17	661	0.91 [0.86, 0.95]	0.96 [0.95, 0.98]



2D TOF MRA whole leg, ≥ 70% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Yucel, 1993	53	5	6	142	0.90 [0.79, 0.96]	0.97 [0.92, 0.99]

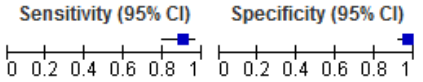


Figure 4 – ROC curve for CTA and CE MRA, whole leg, 70-100% stenosis (sensitivity analysis) – Moses Littenberg analysis

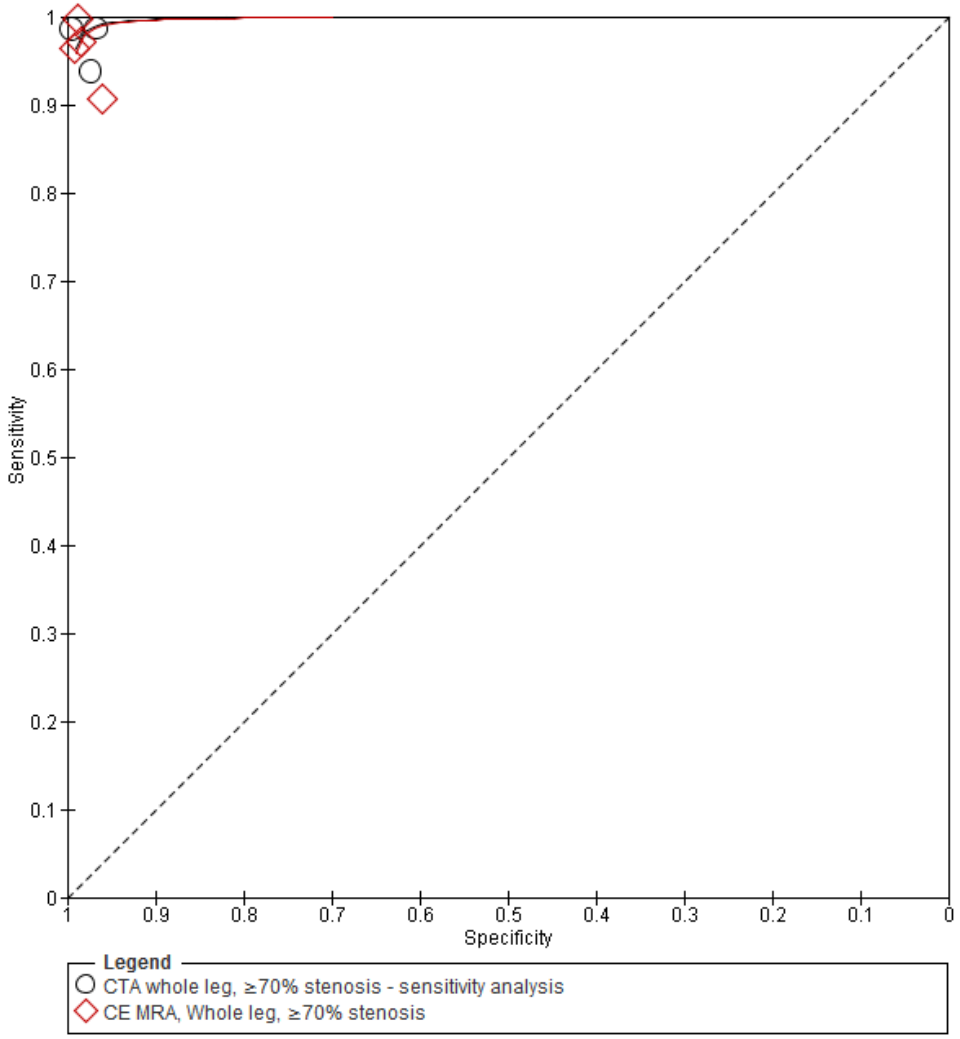
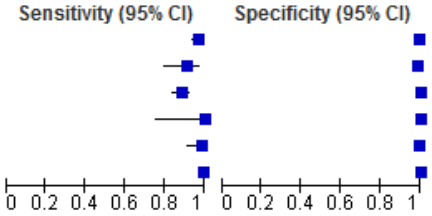


Figure 5 – Forest plot of coupled sensitivities and specificities for imaging tests; whole leg, occlusion, all studies

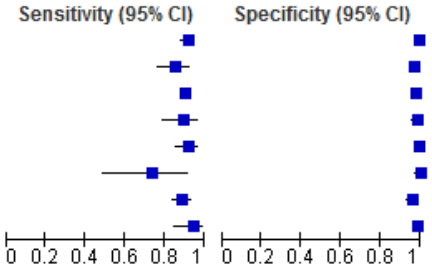
CTA, whole leg, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Catalano 2004	170	5	5	957	0.97 [0.93, 0.99]	0.99 [0.99, 1.00]
Heuschmid 2003 vhi	49	6	5	508	0.91 [0.80, 0.97]	0.99 [0.97, 1.00]
Martin 2003 vhi	202	2	26	1082	0.89 [0.84, 0.92]	1.00 [0.99, 1.00]
Puls 1996	13	0	0	173	1.00 [0.75, 1.00]	1.00 [0.98, 1.00]
Rieker 1996	61	1	1	264	0.98 [0.91, 1.00]	1.00 [0.98, 1.00]
Schernthaner 2008	245	0	2	1104	0.99 [0.97, 1.00]	1.00 [1.00, 1.00]



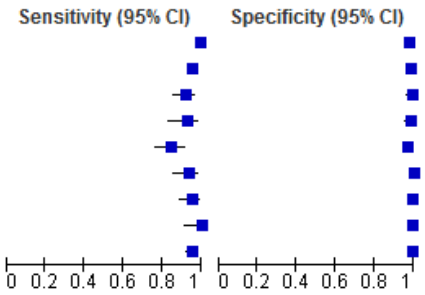
DUS, Whole leg, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aly 1998	272	18	25	2793	0.92 [0.88, 0.94]	0.99 [0.99, 1.00]
Bergamini 1995	76	10	13	305	0.85 [0.76, 0.92]	0.97 [0.94, 0.98]
Bueno 2010 calc	796	15	88	674	0.90 [0.88, 0.92]	0.98 [0.96, 0.99]
Hatsukami 2002	51	3	6	173	0.89 [0.78, 0.96]	0.98 [0.95, 1.00]
Legemate 1991	103	6	9	800	0.92 [0.85, 0.96]	0.99 [0.98, 1.00]
Linke 1994	14	0	5	115	0.74 [0.49, 0.91]	1.00 [0.97, 1.00]
Sensier 1996	166	11	21	271	0.89 [0.83, 0.93]	0.96 [0.93, 0.98]
Zeuchner 1994	50	3	3	266	0.94 [0.84, 0.99]	0.99 [0.97, 1.00]



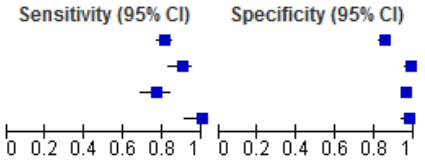
CE MRA, whole leg, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Balzer 2005	331	38	3	1691	0.99 [0.97, 1.00]	0.98 [0.97, 0.98]
Bueno 2010 calc	857	14	41	739	0.95 [0.94, 0.97]	0.98 [0.97, 0.99]
Lapeyre 2005 diabetes	102	2	9	197	0.92 [0.85, 0.96]	0.99 [0.96, 1.00]
Lenhart 2000	54	2	4	160	0.93 [0.83, 0.98]	0.99 [0.96, 1.00]
Meaney 1999	83	16	15	516	0.85 [0.76, 0.91]	0.97 [0.95, 0.98]
Schafer 2003	72	1	5	498	0.94 [0.85, 0.98]	1.00 [0.99, 1.00]
Steffens 2003	85	7	4	804	0.96 [0.89, 0.99]	0.99 [0.98, 1.00]
Sueyoshi, 1999	39	1	0	383	1.00 [0.91, 1.00]	1.00 [0.99, 1.00]
Winterer 1999	255	11	13	1502	0.95 [0.92, 0.97]	0.99 [0.99, 1.00]



2D TOF MRA, Whole leg, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Baum 1995	322	118	76	672	0.81 [0.77, 0.85]	0.85 [0.82, 0.87]
Hoch 1996	101	4	11	236	0.90 [0.83, 0.95]	0.98 [0.96, 1.00]
Hoch 1999 vhi	103	17	31	393	0.77 [0.69, 0.84]	0.96 [0.93, 0.98]
Yucel, 1993	40	4	0	162	1.00 [0.91, 1.00]	0.98 [0.94, 0.99]



3D CE MRA, whole leg, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Wang 2012	115	4	2	684	0.98 [0.94, 1.00]	0.99 [0.99, 1.00]

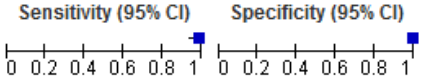


Figure 6 – ROC curve for CTA, DUS and CE MRA, 2D TOF MRA, whole leg, occlusion (sensitivity analysis) – bivariate analysis for all tests except 2D TOF MRA for which the Moses Littenberg analysis was included; CTA had 2 studies at very high risk of bias

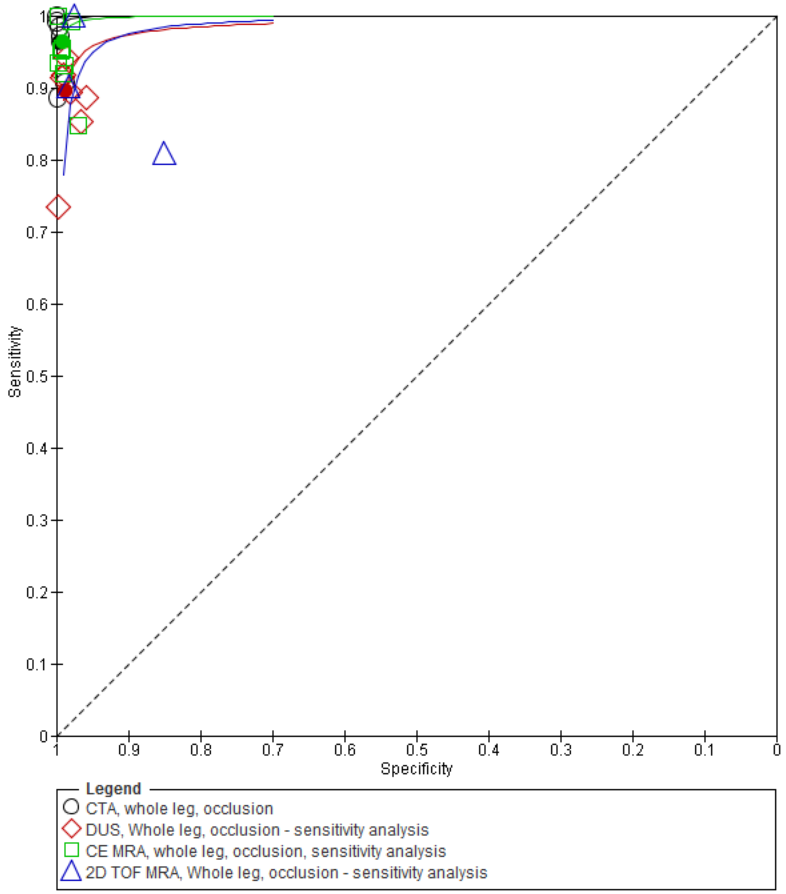
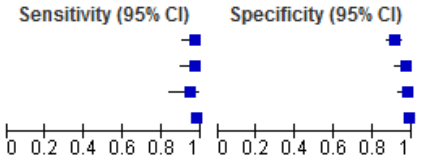


Figure 7 – Forest plot of coupled sensitivities and specificities for imaging tests; above knee, 50-100% stenosis, all studies

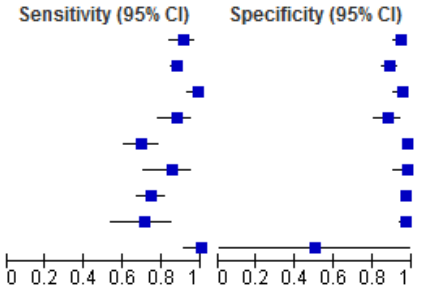
CTA, Above knee, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Portugaller 2004	86	23	3	238	0.97 [0.90, 0.99]	0.91 [0.87, 0.94]
Rieker 1997 (cine axial)	63	4	2	114	0.97 [0.89, 1.00]	0.97 [0.92, 0.99]
Rieker 1997 (MIP)	49	2	3	101	0.94 [0.84, 0.99]	0.98 [0.93, 1.00]
Schernthaner 2008	279	6	6	521	0.98 [0.95, 0.99]	0.99 [0.98, 1.00]



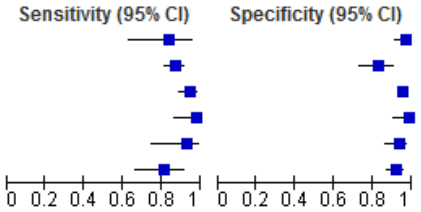
DUS, above knee, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bergamini 1995	83	12	8	194	0.91 [0.83, 0.96]	0.94 [0.90, 0.97]
Eiberg 2010	471	35	64	274	0.88 [0.85, 0.91]	0.89 [0.85, 0.92]
El-Kayali 2004	74	9	1	171	0.99 [0.93, 1.00]	0.95 [0.91, 0.98]
Fletcher 1990	59	12	8	89	0.88 [0.78, 0.95]	0.88 [0.80, 0.94]
Gjonnaess 2006	85	15	37	733	0.70 [0.61, 0.78]	0.98 [0.97, 0.99]
Hatsukami 2002	34	2	6	73	0.85 [0.70, 0.94]	0.97 [0.91, 1.00]
Lai 1996	124	12	42	354	0.75 [0.67, 0.81]	0.97 [0.94, 0.98]
Lundin 2000	27	7	11	207	0.71 [0.54, 0.85]	0.97 [0.93, 0.99]
Whyman 1992	41	1	0	1	1.00 [0.91, 1.00]	0.50 [0.01, 0.99]



CE MRA, above knee, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Andreisek 2007 diabetes	20	3	4	96	0.83 [0.63, 0.95]	0.97 [0.91, 0.99]
Burbelko 2013 vhi	147	14	22	68	0.87 [0.81, 0.92]	0.83 [0.73, 0.90]
Gjonnaess 2006	115	37	7	711	0.94 [0.89, 0.98]	0.95 [0.93, 0.96]
Lapeyre 2005 diabetes	36	1	1	54	0.97 [0.86, 1.00]	0.98 [0.90, 1.00]
Lenhart 2000	24	6	2	83	0.92 [0.75, 0.99]	0.93 [0.86, 0.97]
Lundin 2000	35	18	8	204	0.81 [0.67, 0.92]	0.92 [0.87, 0.95]



2D TOF MRA, above knee,≥ 50%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lundin 2000	35	20	8	197	0.81 [0.67, 0.92]	0.91 [0.86, 0.94]

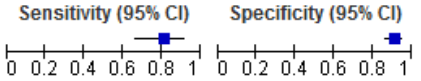


Figure 8 – ROC curve for DUS and CE MRA, above knee, 50-100% stenosis (sensitivity analysis) – bivariate analysis for all tests except CTA, for which the Moses Littenberg analysis was included

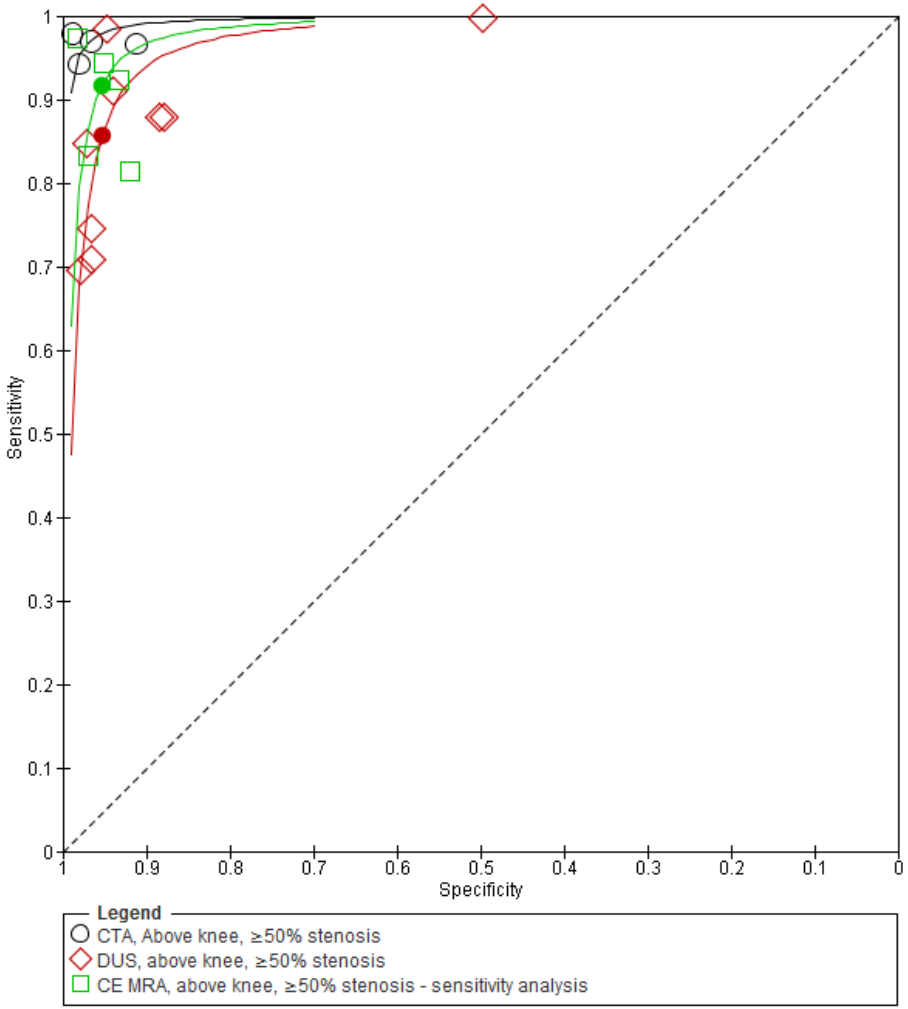


Figure 9 – Forest plot of coupled sensitivities and specificities for imaging tests; above knee, 70-100% stenosis, all studies

CTA, Above knee, ≥ 70% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Iezzi 2013 vhi	33	5	1	25	0.97 [0.85, 1.00]	0.83 [0.65, 0.94]
Rieker 1997 (cine axial)	30	0	0	153	1.00 [0.88, 1.00]	1.00 [0.98, 1.00]
Rieker 1997 (MIP)	28	0	0	127	1.00 [0.88, 1.00]	1.00 [0.97, 1.00]
Schafer 2003	192	4	2	614	0.99 [0.96, 1.00]	0.99 [0.98, 1.00]

DUS, above knee, ≥ 70% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fletcher 1990	14	2	0	40	1.00 [0.77, 1.00]	0.95 [0.84, 0.99]
Lai 1996	83	8	44	397	0.65 [0.56, 0.74]	0.98 [0.96, 0.99]

CE MRA, above knee, ≥ 70% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Vavrik 2004	86	13	9	468	0.91 [0.83, 0.96]	0.97 [0.95, 0.99]

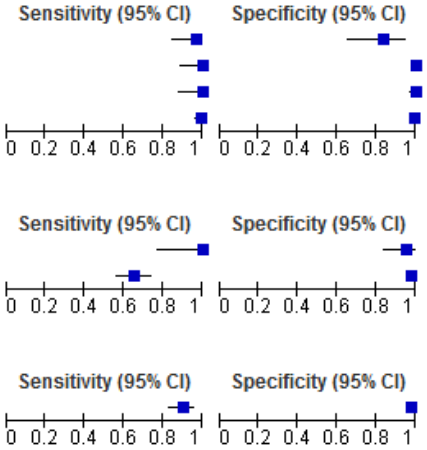


Figure 10 – Forest plot of coupled sensitivities and specificities for imaging tests; above knee, occlusion, all studies

CTA, Above knee, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rieker 1997 (cine axial)	48	1	2	132	0.96 [0.86, 1.00]	0.99 [0.96, 1.00]
Rieker 1997 (MIP)	39	0	2	114	0.95 [0.83, 0.99]	1.00 [0.97, 1.00]
Schernthaner 2008	107	0	2	703	0.98 [0.94, 1.00]	1.00 [0.99, 1.00]

DUS, above knee, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Currie 1995	25	4	5	146	0.83 [0.65, 0.94]	0.97 [0.93, 0.99]
Davies 1992 vhi	27	1	1	36	0.96 [0.82, 1.00]	0.97 [0.86, 1.00]
Fletcher 1990	45	7	5	111	0.90 [0.78, 0.97]	0.94 [0.88, 0.98]
Hatsukami 2002	29	0	1	85	0.97 [0.83, 1.00]	1.00 [0.96, 1.00]
Hirai 1998	64	0	1	454	0.98 [0.92, 1.00]	1.00 [0.99, 1.00]
Lai 1996	50	0	12	470	0.81 [0.69, 0.90]	1.00 [0.99, 1.00]
Lundin 2000	13	1	1	237	0.93 [0.66, 1.00]	1.00 [0.98, 1.00]
Mergelsberg 1986 vhi	25	6	1	17	0.96 [0.80, 1.00]	0.74 [0.52, 0.90]
Whyman 1992	26	1	0	16	1.00 [0.87, 1.00]	0.94 [0.71, 1.00]

CE MRA, above knee, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Hany 1997	19	1	0	214	1.00 [0.82, 1.00]	1.00 [0.97, 1.00]
Lapeyre 2005 diabetes	13	0	0	79	1.00 [0.75, 1.00]	1.00 [0.95, 1.00]
Lenhart 2000	14	0	2	99	0.88 [0.62, 0.98]	1.00 [0.96, 1.00]
Lundin 2000	13	0	2	250	0.87 [0.60, 0.98]	1.00 [0.99, 1.00]
Snidow 1996	18	0	0	110	1.00 [0.81, 1.00]	1.00 [0.97, 1.00]

2D TOF MRA, above knee,occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lundin 2000	13	7	2	238	0.87 [0.60, 0.98]	0.97 [0.94, 0.99]

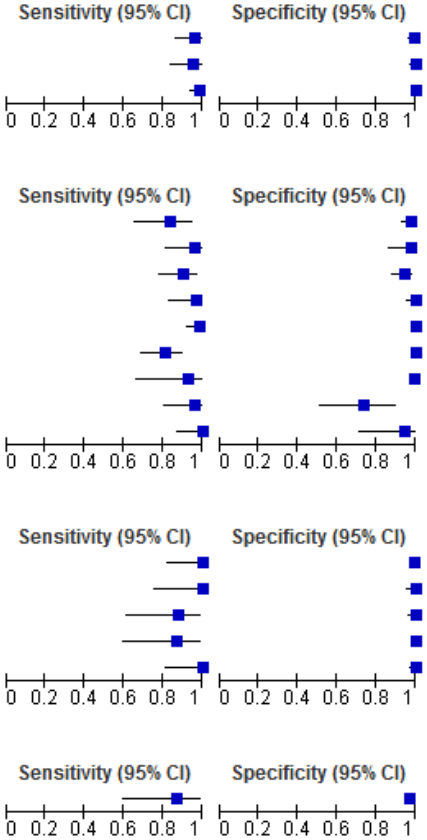


Figure 11 – ROC curve for DUS and CE MRA, above knee, occlusion (sensitivity analysis) - bivariate analysis for all tests, 0s replaced by 1s

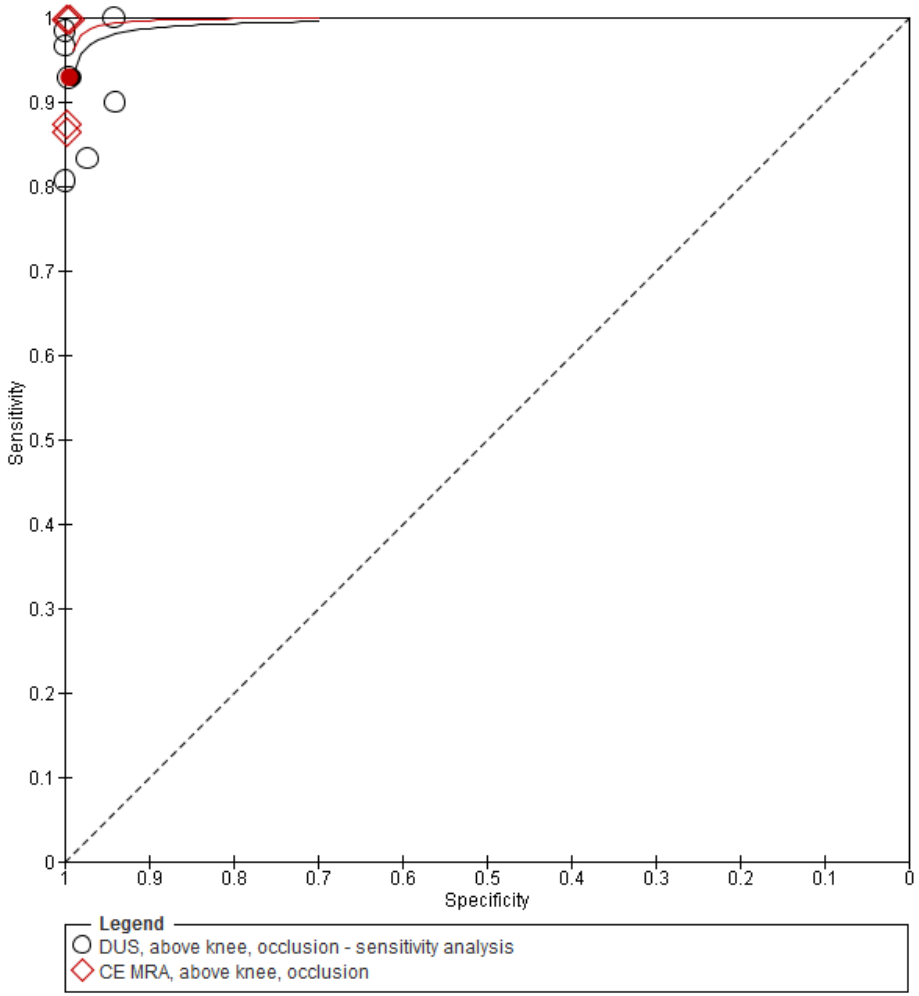


Figure 12 – Forest plot of coupled sensitivities and specificities for imaging tests; below knee, 50-100% stenosis, all studies

CTA, Below knee, ≥ 50% stenosis

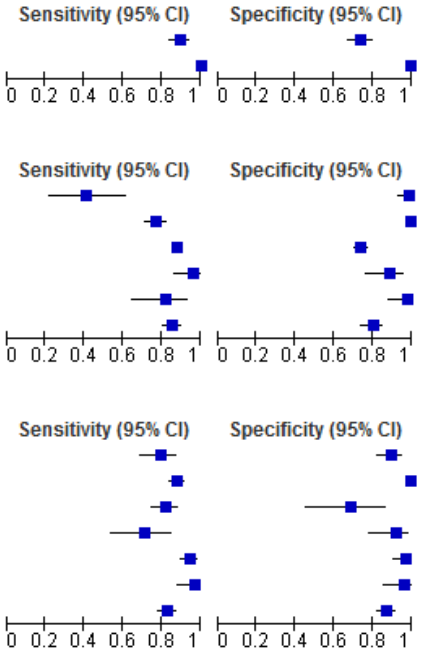
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Portugaller 2004	154	57	18	161	0.90 [0.84, 0.94]	0.74 [0.67, 0.80]
Schernthaner 2008	200	2	0	337	1.00 [0.98, 1.00]	0.99 [0.98, 1.00]

DUS, below knee, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bergamini 1995	11	1	16	79	0.41 [0.22, 0.61]	0.99 [0.93, 1.00]
Bueno 2010 calc	191	6	57	613	0.77 [0.71, 0.82]	0.99 [0.98, 1.00]
Eiberg 2010	879	180	120	511	0.88 [0.86, 0.90]	0.74 [0.71, 0.77]
El-Kayali 2004	49	6	2	45	0.96 [0.87, 1.00]	0.88 [0.76, 0.96]
Hatsukami 2002	27	1	6	44	0.82 [0.65, 0.93]	0.98 [0.88, 1.00]
Karacagil 1996	211	47	36	186	0.85 [0.80, 0.90]	0.80 [0.74, 0.85]

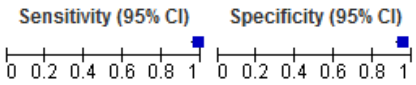
CE MRA, below knee, ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Andreisek 2007 diabetes	64	10	17	86	0.79 [0.69, 0.87]	0.90 [0.82, 0.95]
Bueno 2010 calc	234	3	32	646	0.88 [0.83, 0.92]	1.00 [0.99, 1.00]
Burbelko 2013 vhi	109	7	24	15	0.82 [0.74, 0.88]	0.68 [0.45, 0.86]
Kreitner 2000 diabetes	27	3	11	33	0.71 [0.54, 0.85]	0.92 [0.78, 0.98]
Lapeyre 2005 diabetes	124	3	7	84	0.95 [0.89, 0.98]	0.97 [0.90, 0.99]
Lenhart 2000	55	2	2	46	0.96 [0.88, 1.00]	0.96 [0.86, 0.99]
Zhang 2005	252	31	52	207	0.83 [0.78, 0.87]	0.87 [0.82, 0.91]



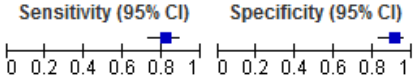
2D TOF MRA, below knee,≥ 50%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cortell 1996	172	10	3	208	0.98 [0.95, 1.00]	0.95 [0.92, 0.98]



CE MRA Time resolved sequence, below knee (calf only) ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Andreisek 2007 diabetes	77	9	17	88	0.82 [0.73, 0.89]	0.91 [0.83, 0.96]



CE MRA Time resolved sequence, below knee (calf and foot) ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Andreisek 2007 diabetes	100	15	34	141	0.75 [0.66, 0.82]	0.90 [0.85, 0.95]

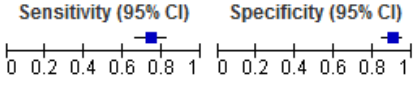


Figure 13 – ROC curve for DUS and CE MRA, below knee, 50-100% stenosis (sensitivity analysis); bivariate analysis for DUS and CE-MRA

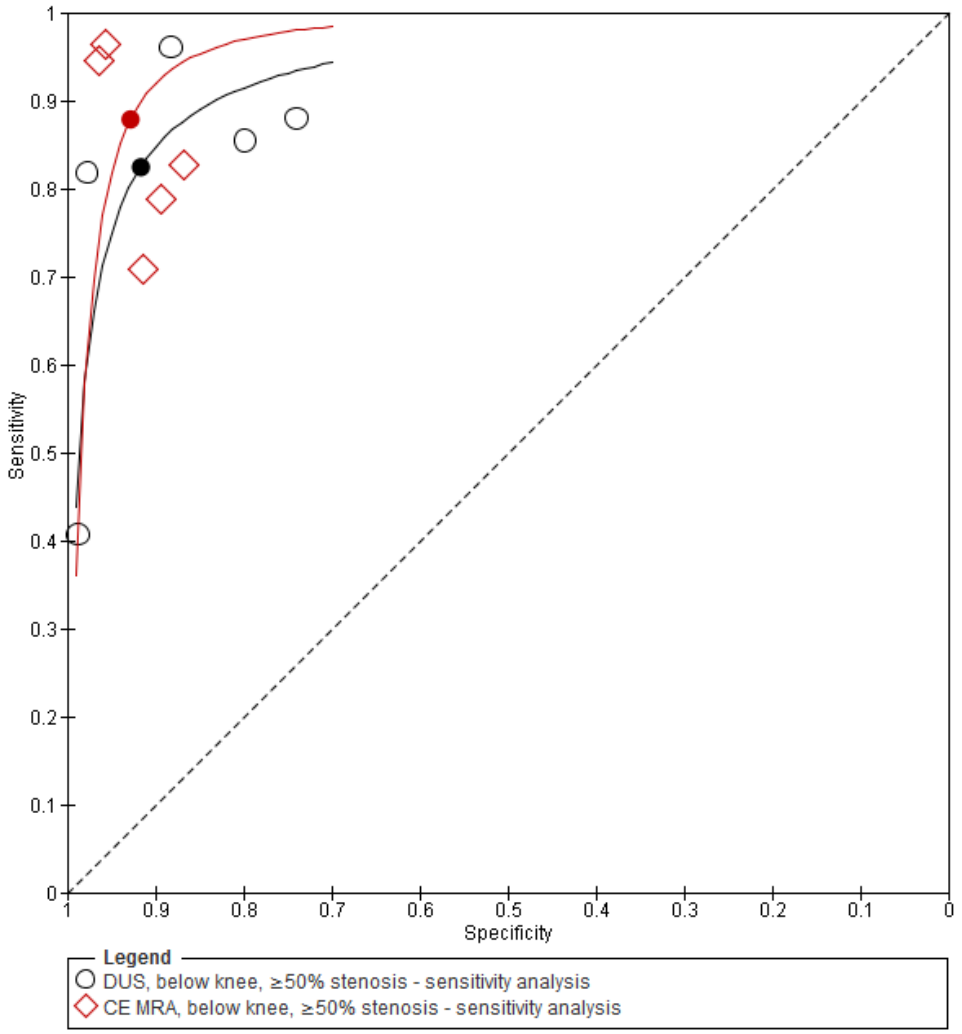


Figure 14 – Forest plot of coupled sensitivities and specificities for imaging tests; below knee, 70-100% stenosis, all studies

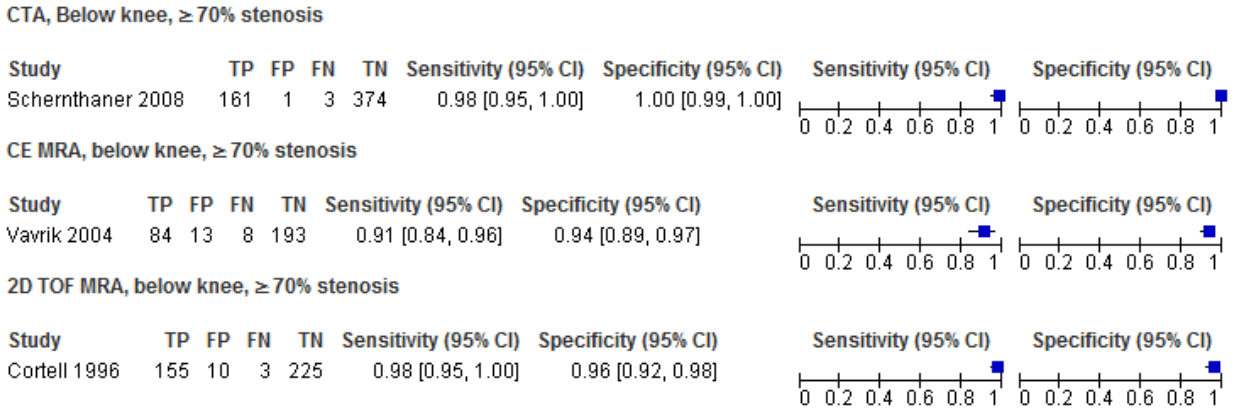


Figure 15 – Forest plot of coupled sensitivities and specificities for imaging tests; below knee, occlusion, all studies

CTA, Below knee, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Schernthaner 2008	138	0	0	401	1.00 [0.97, 1.00]	1.00 [0.99, 1.00]

DUS, below knee, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bueno 2010 calc	461	11	63	331	0.88 [0.85, 0.91]	0.97 [0.94, 0.98]
Grassbaugh 2003	36	6	12	56	0.75 [0.60, 0.86]	0.90 [0.80, 0.96]
Hatsukami 2002	25	0	5	48	0.83 [0.65, 0.94]	1.00 [0.93, 1.00]
Karacagil 1996	199	44	34	203	0.85 [0.80, 0.90]	0.82 [0.77, 0.87]
Koelemay 1997	84	21	33	121	0.72 [0.63, 0.80]	0.85 [0.78, 0.91]
Koelemay 1998	457	77	324	655	0.59 [0.55, 0.62]	0.89 [0.87, 0.92]
Wilson 1997	80	1	5	36	0.94 [0.87, 0.98]	0.97 [0.86, 1.00]

CE MRA, below knee, occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bueno 2010 calc	516	11	28	359	0.95 [0.93, 0.97]	0.97 [0.95, 0.99]
Lapeyre 2005 diabetes	89	2	9	118	0.91 [0.83, 0.96]	0.98 [0.94, 1.00]
Lenhart 2000	40	2	2	61	0.95 [0.84, 0.99]	0.97 [0.89, 1.00]
Zhang 2005	200	22	32	288	0.86 [0.81, 0.90]	0.93 [0.89, 0.95]

2D TOF MRA, below knee, occluded

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cortell 1996	125	7	3	258	0.98 [0.93, 1.00]	0.97 [0.95, 0.99]
McDermott 1995 diabetes	95	1	21	99	0.82 [0.74, 0.88]	0.99 [0.95, 1.00]

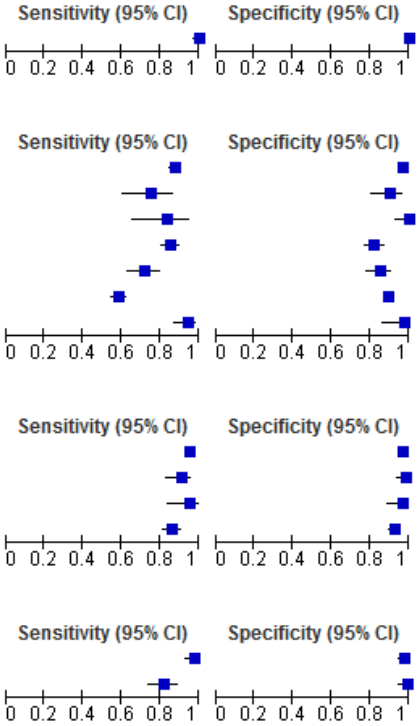


Figure 16 – ROC curve for DUS and CE MRA, below knee, occlusion (sensitivity analysis), bivariate analysis for DUS test only, CE MRA had a Moses Littenberg analysis

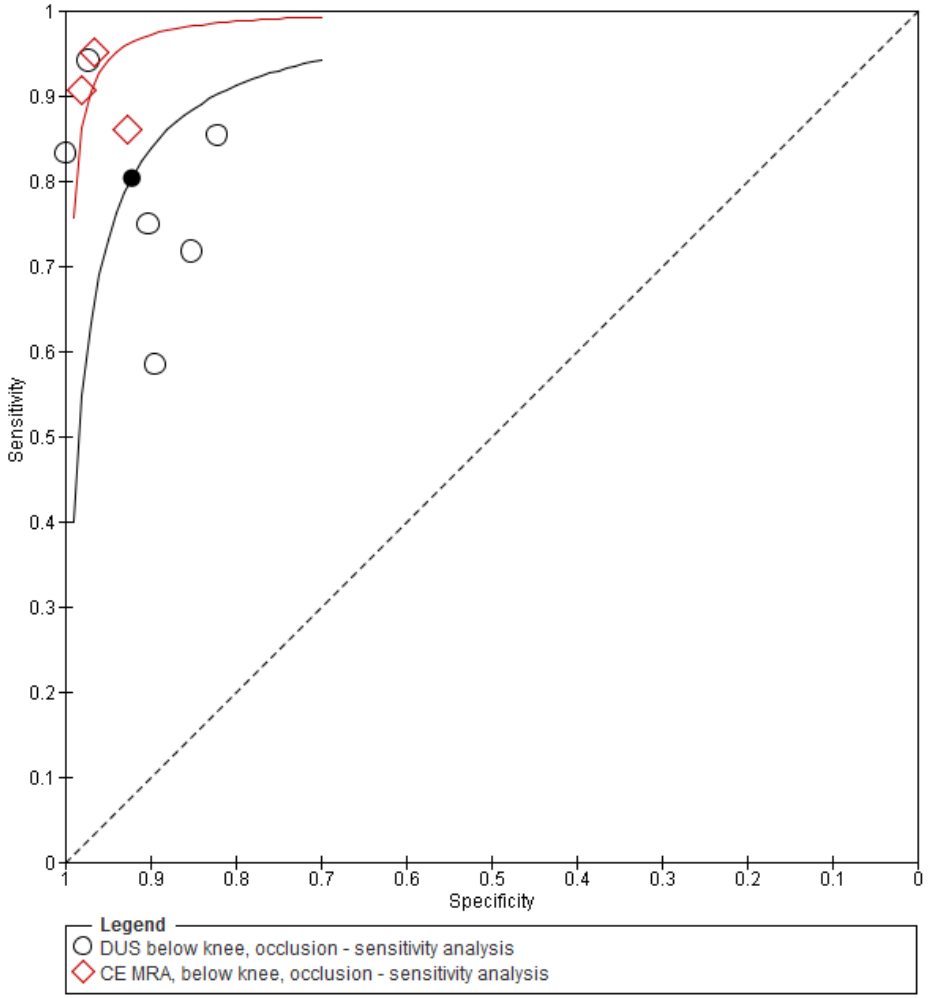
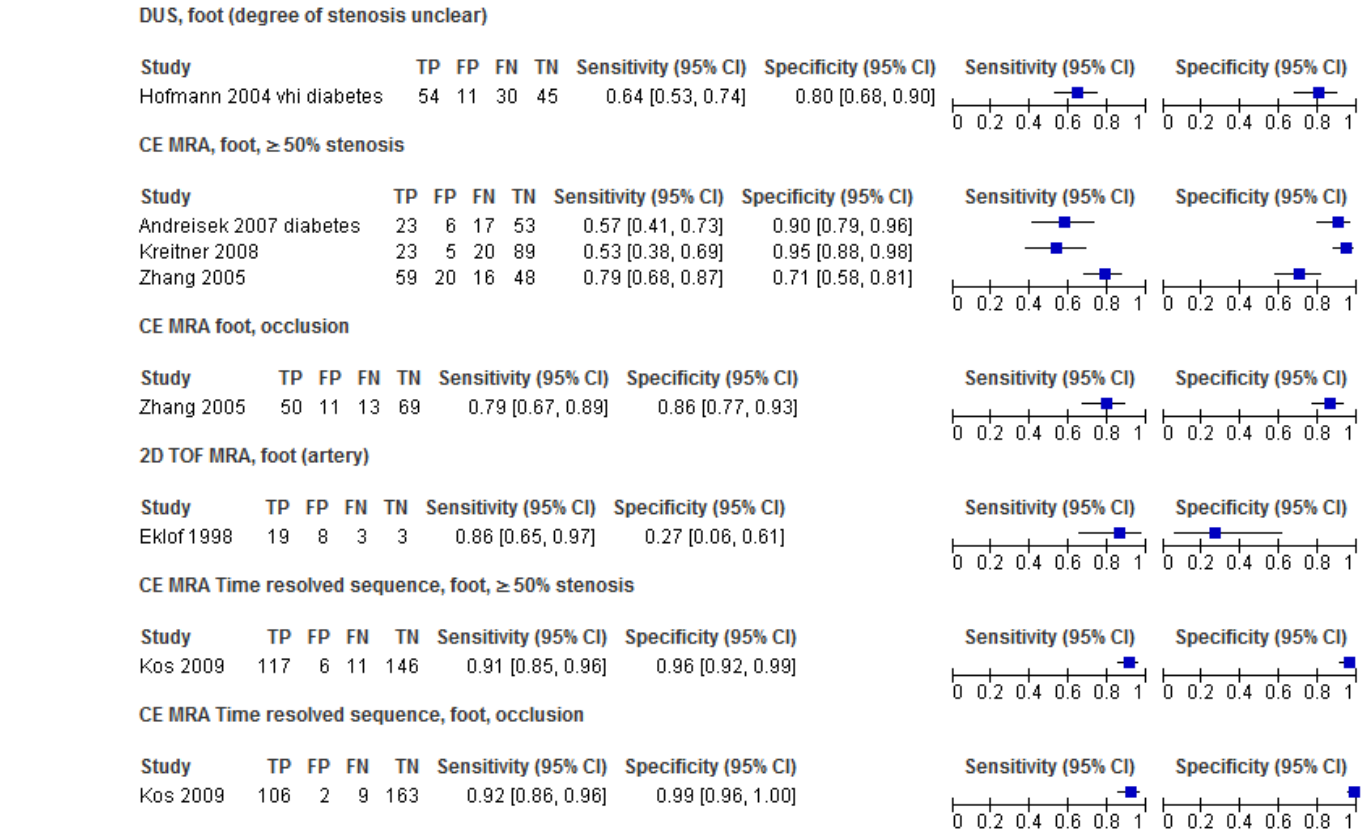
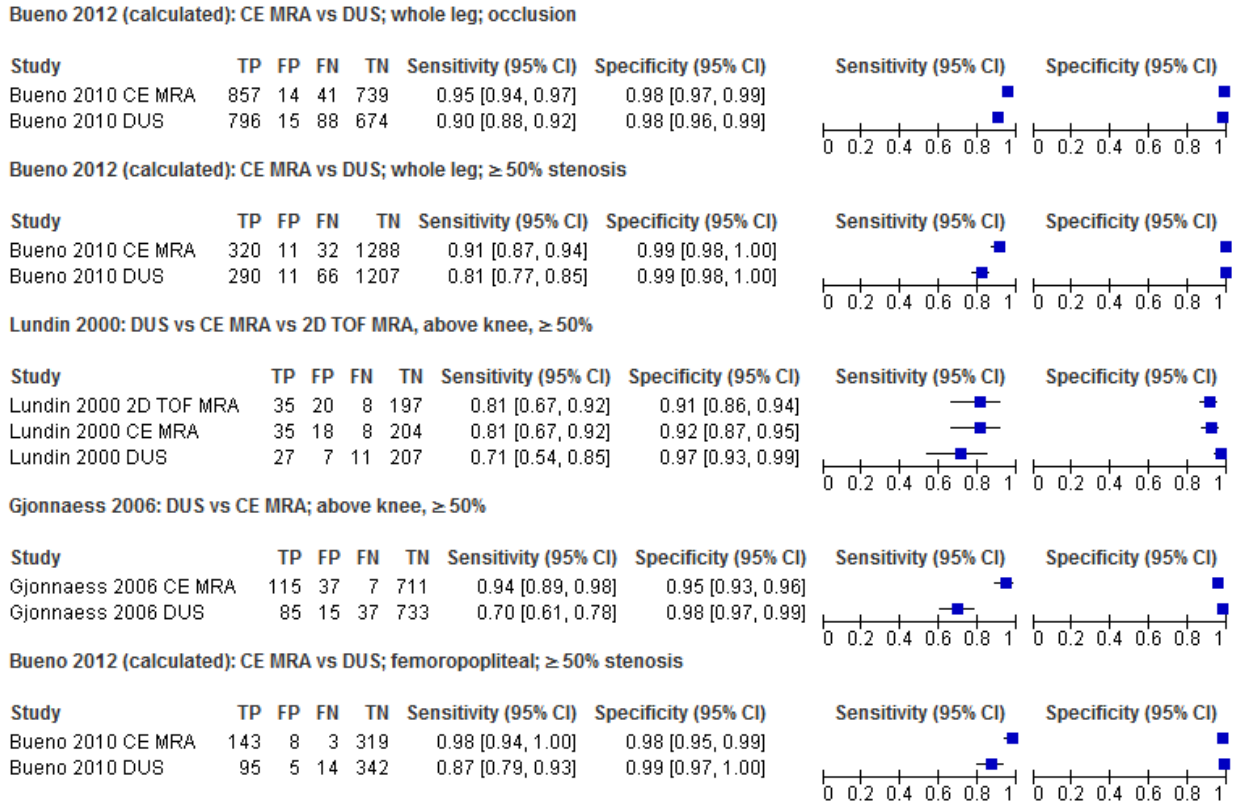


Figure 17 – Forest plot of coupled sensitivities and specificities for imaging tests; foot, all studies



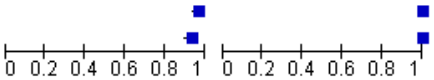
6.1.2. *DUS versus CTA versus CE MRA versus 2D TOF MRA: all compared with the reference standard, DSA – studies with more than one index test*

Figure 18 – Forest plot of coupled sensitivities and specificities for imaging tests; foot, studies with more than one index test



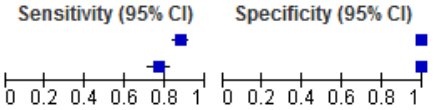
Bueno 2012 (calculated): CE MRA vs DUS; femoropopliteal; occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bueno 2010 CE MRA	197	0	6	270	0.97 [0.94, 0.99]	1.00 [0.99, 1.00]
Bueno 2010 DUS	188	0	13	256	0.94 [0.89, 0.97]	1.00 [0.99, 1.00]



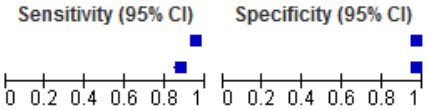
Bueno 2012 (calculated): CE MRA vs DUS; below knee; ≥ 50% stenosis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bueno 2010 CE MRA	234	3	32	646	0.88 [0.83, 0.92]	1.00 [0.99, 1.00]
Bueno 2010 DUS	191	6	57	613	0.77 [0.71, 0.82]	0.99 [0.98, 1.00]



Bueno 2012 (calculated): CE MRA vs DUS; below knee; occlusion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bueno 2010 CE MRA	516	11	28	359	0.95 [0.93, 0.97]	0.97 [0.95, 0.99]
Bueno 2010 DUS	461	11	63	331	0.88 [0.85, 0.91]	0.97 [0.94, 0.98]



6.1.3. Diagnostic meta-analysis using bivariate hierarchical modelling

Figure 19 – ROC curve showing diagnostic meta-analysis: DUS, whole leg, 50-100% stenosis – sensitivity analysis

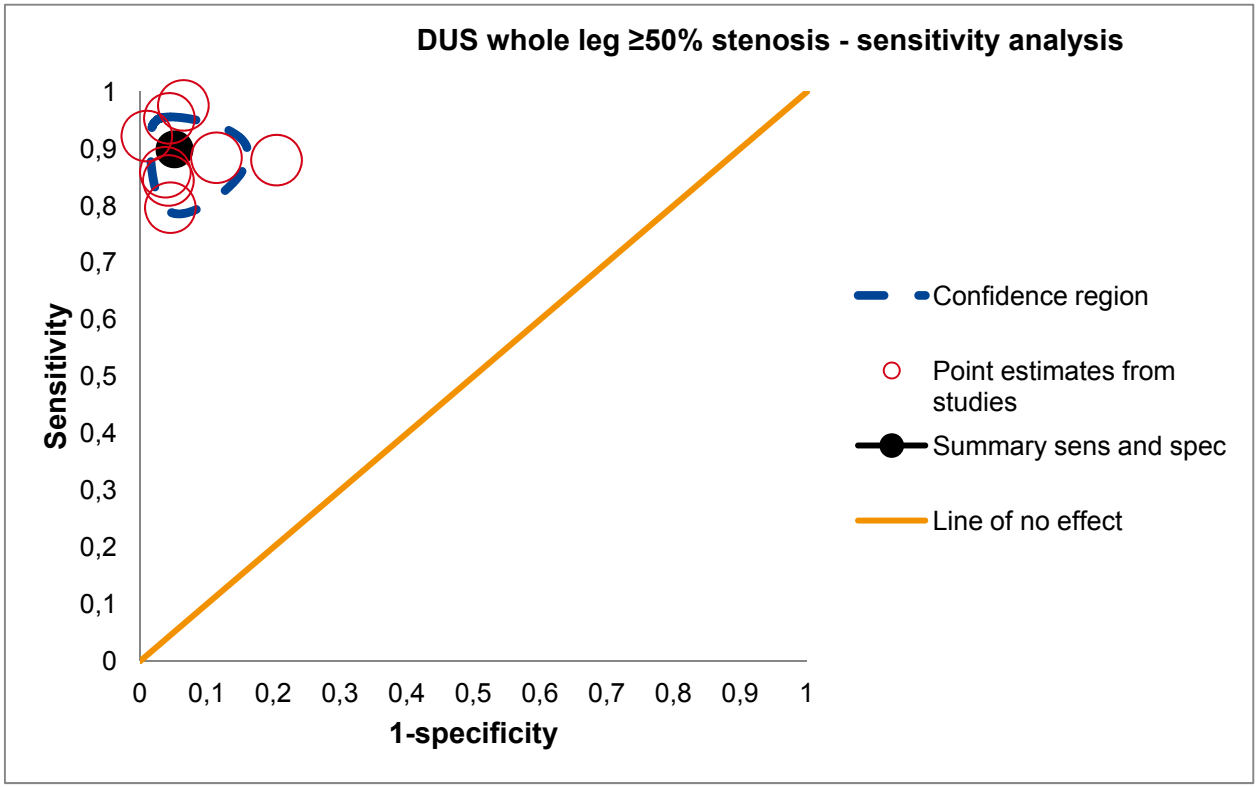


Figure 20 – ROC curve showing diagnostic meta-analysis: CE-MRA, whole leg, 50-100% stenosis – sensitivity analysis

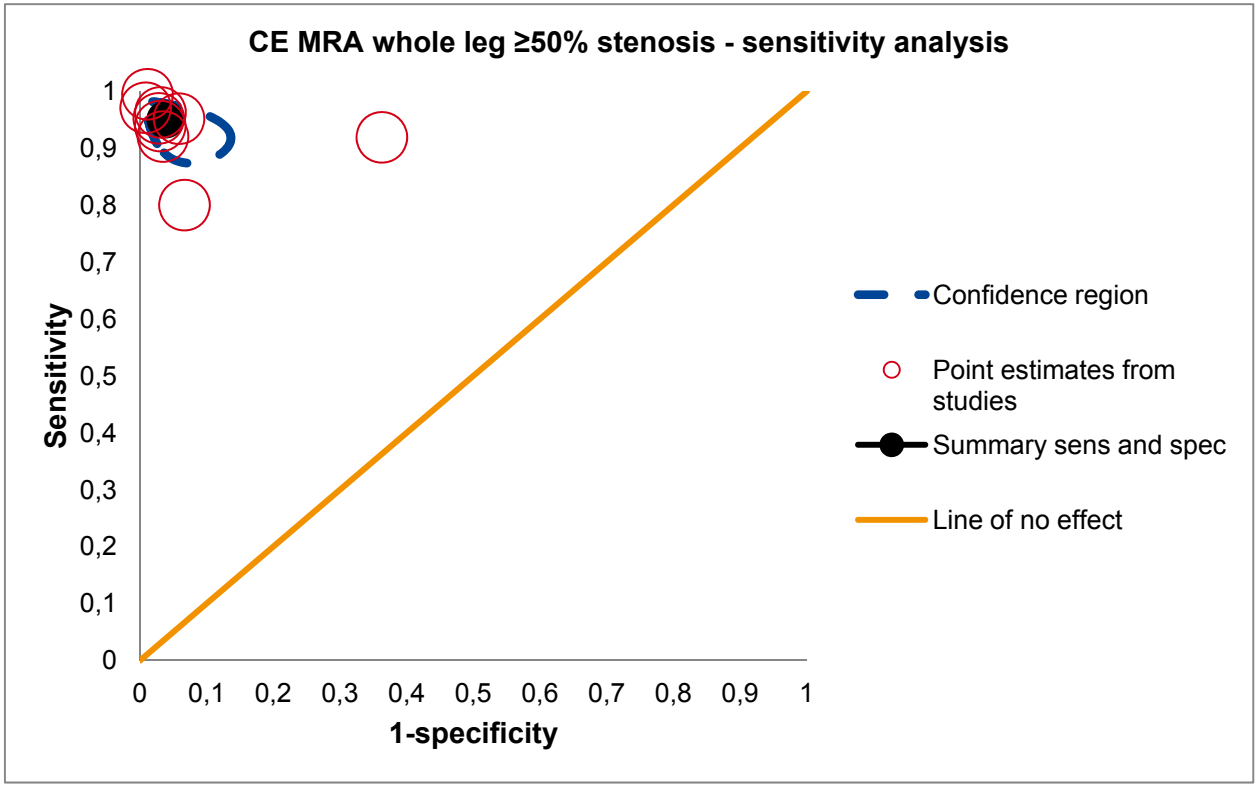


Figure 21 – ROC curve showing diagnostic meta-analysis: 2D TOF-MRA, whole leg, 50-100% stenosis – full dataset

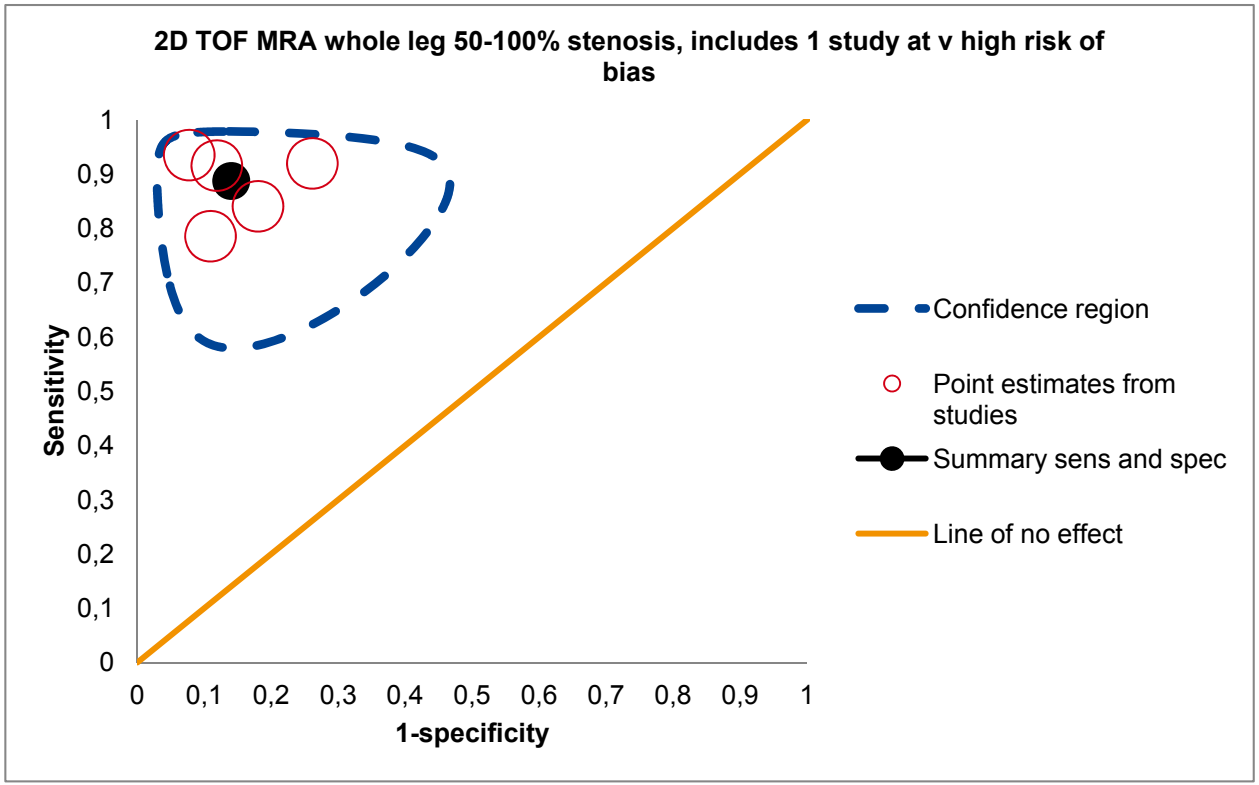


Figure 22 – ROC curve showing diagnostic meta-analysis: CTA, whole leg, 50-100% stenosis; full dataset

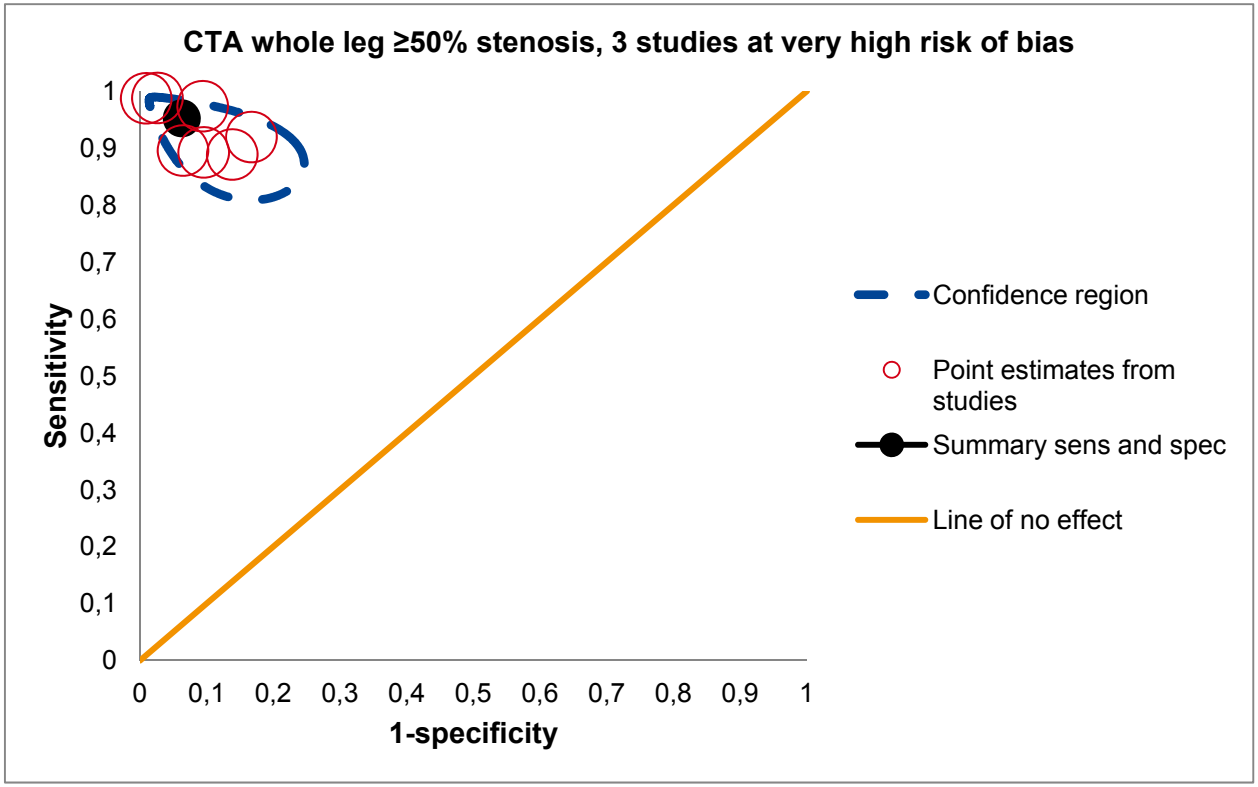


Figure 23 – ROC curve showing diagnostic meta-analysis: DUS, whole leg, occlusion – sensitivity analysis

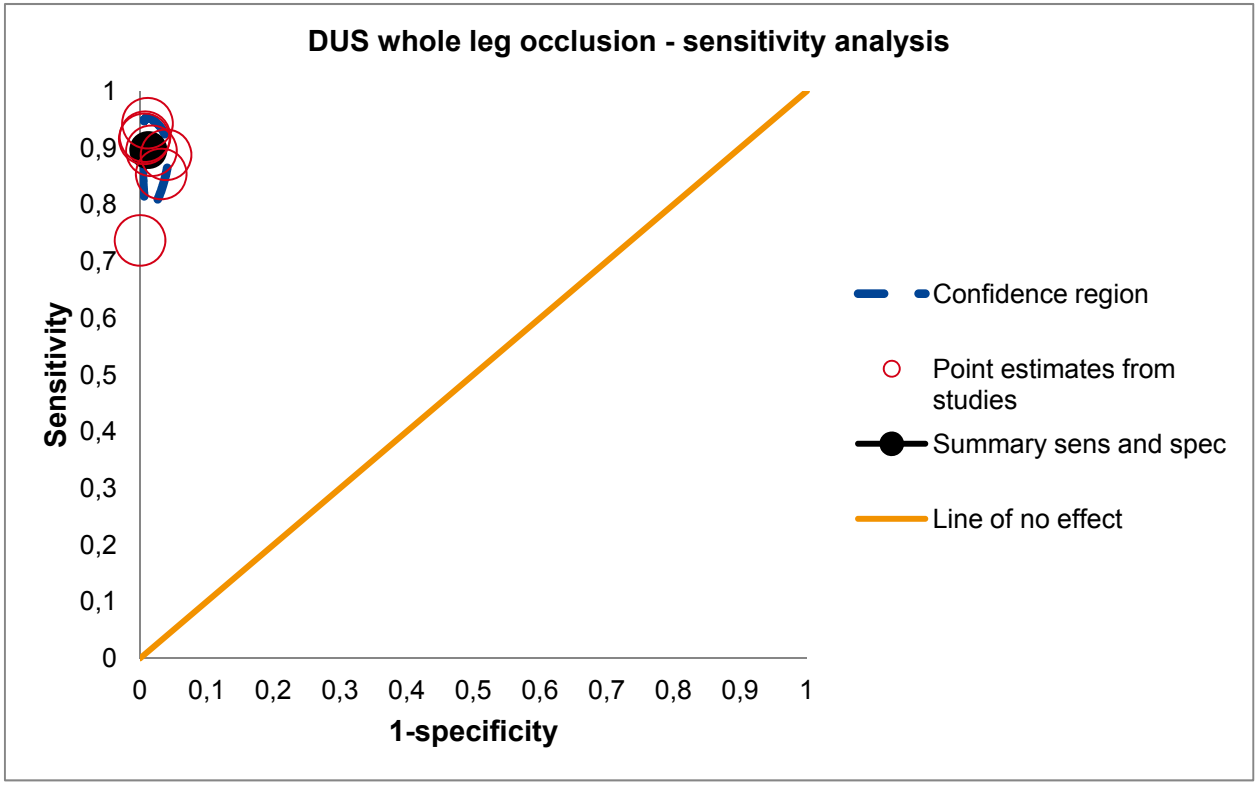


Figure 24 – ROC curve showing diagnostic meta-analysis: CTA, whole leg, occlusion – full dataset

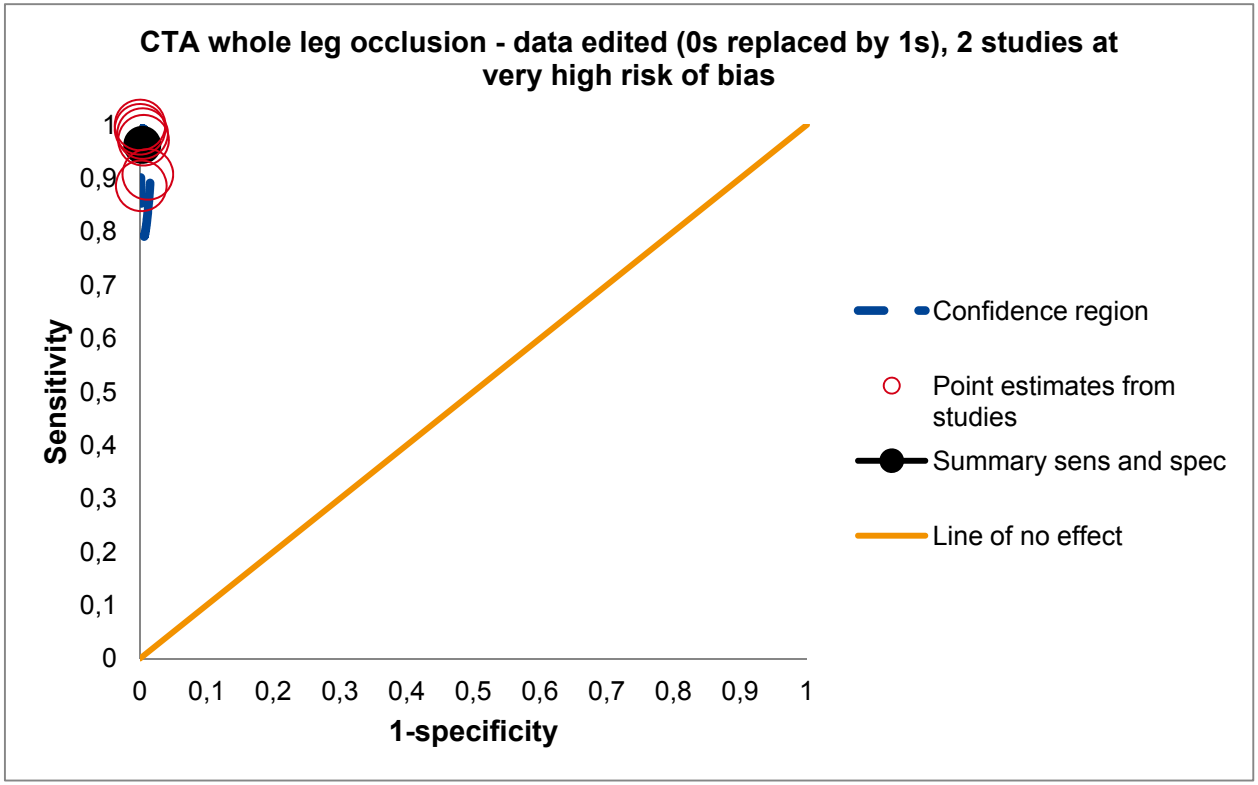


Figure 25 – ROC curve showing diagnostic meta-analysis: CE MRA, whole leg, occlusion – sensitivity analysis

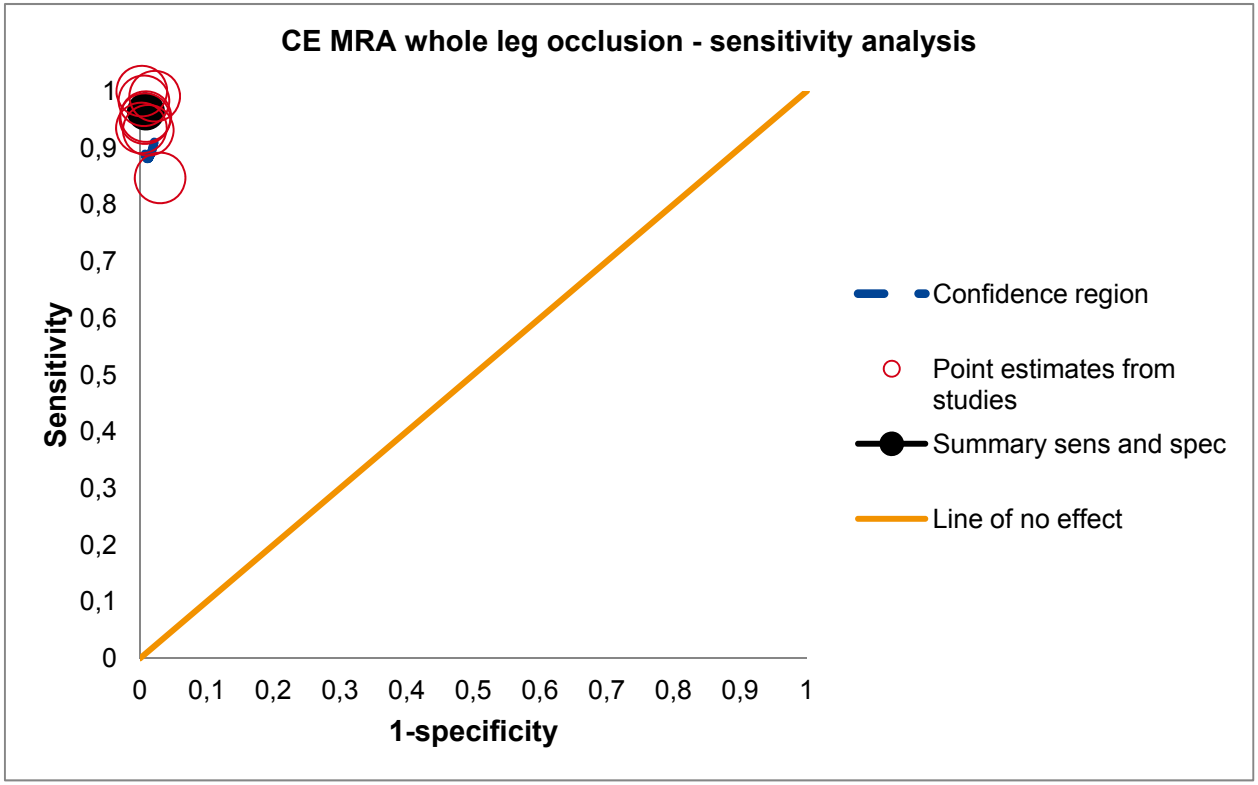


Figure 26 – ROC curve showing diagnostic meta-analysis: DUS, above knee, 50-100% stenosis

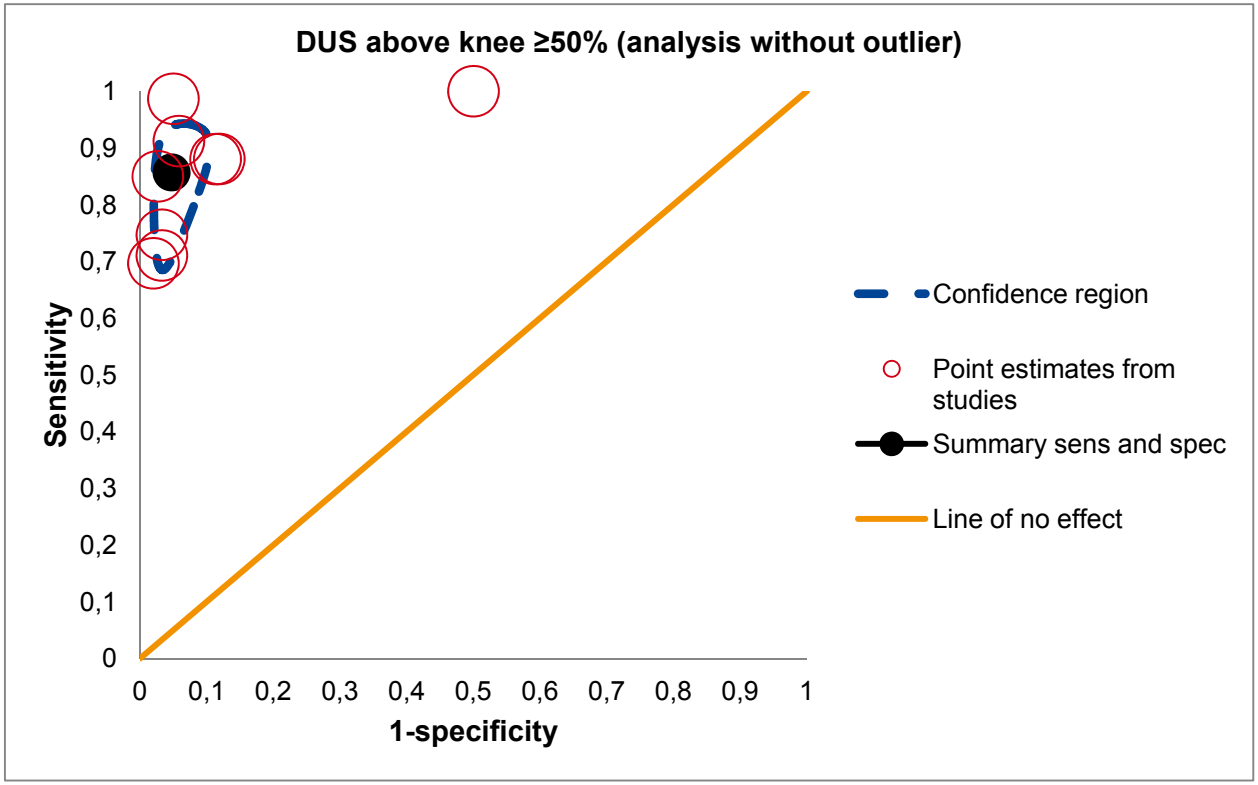


Figure 27 – ROC curve showing diagnostic meta-analysis: CE MRA, above knee, 50-100% stenosis; sensitivity analysis

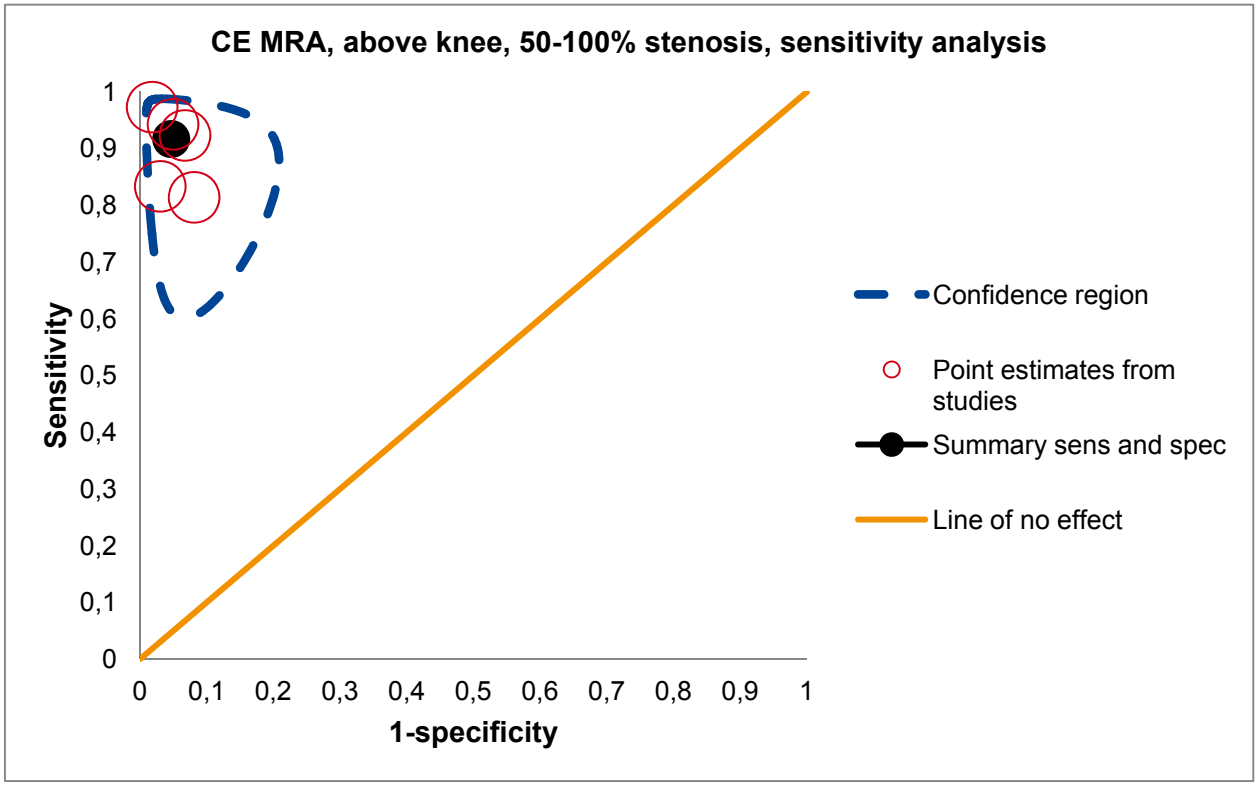


Figure 28 – ROC curve showing diagnostic meta-analysis: DUS, above knee, 50-100% stenosis; sensitivity analysis

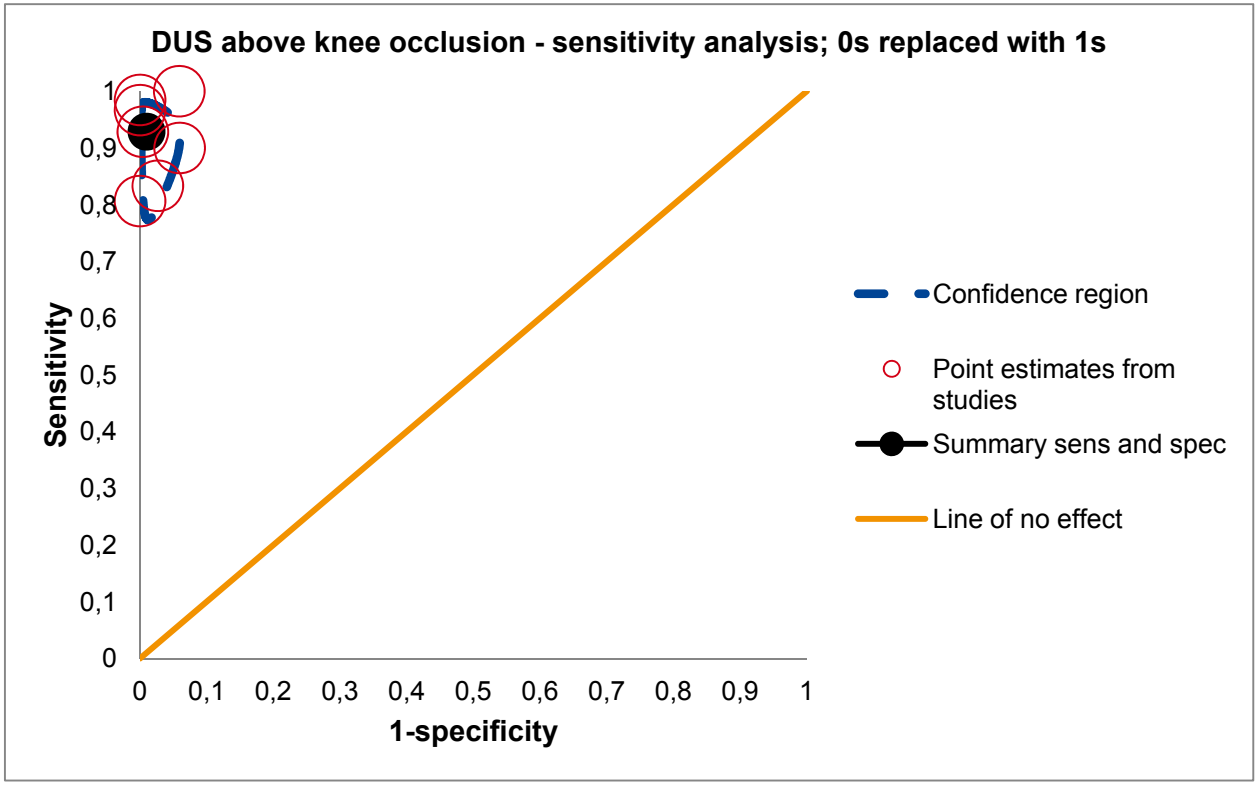


Figure 29 – ROC curve showing diagnostic meta-analysis: CE MRA, above knee, occlusion

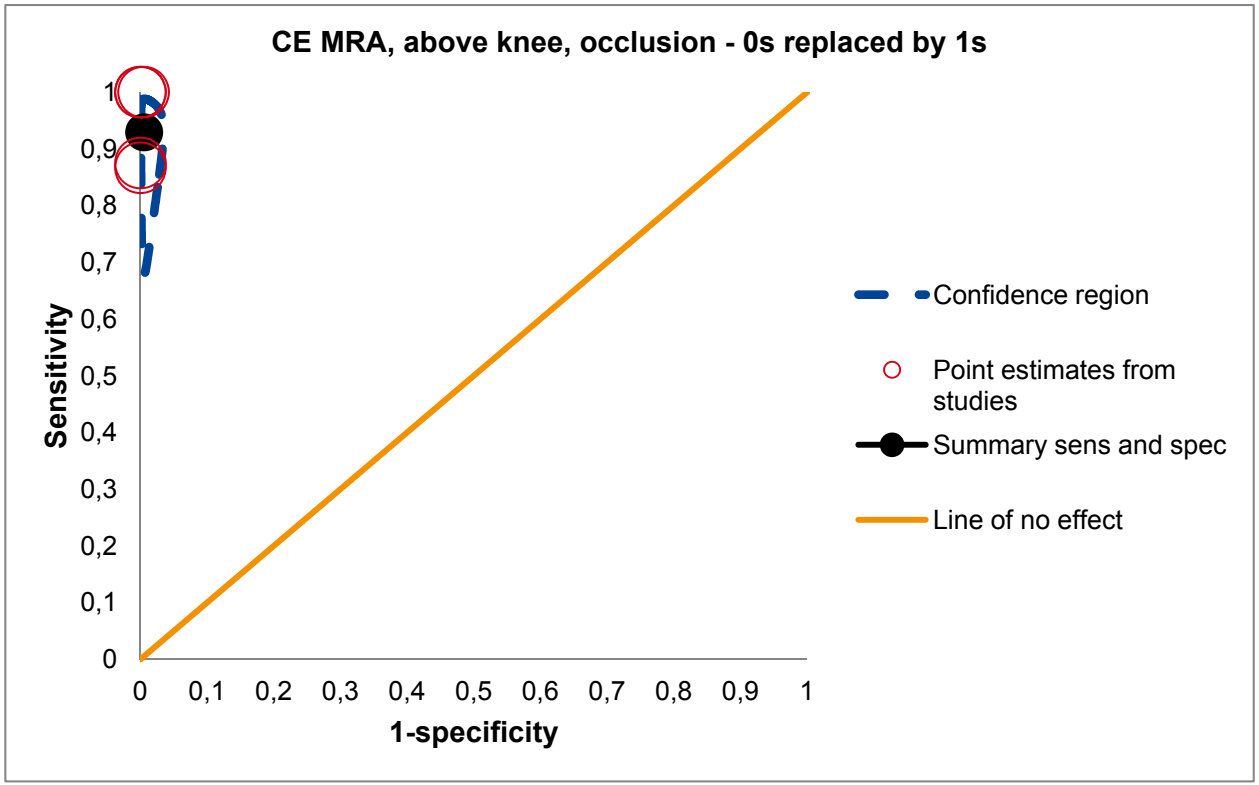


Figure 30 – ROC curve showing diagnostic meta-analysis: DUS, below knee, 50-100% stenosis – sensitivity analysis

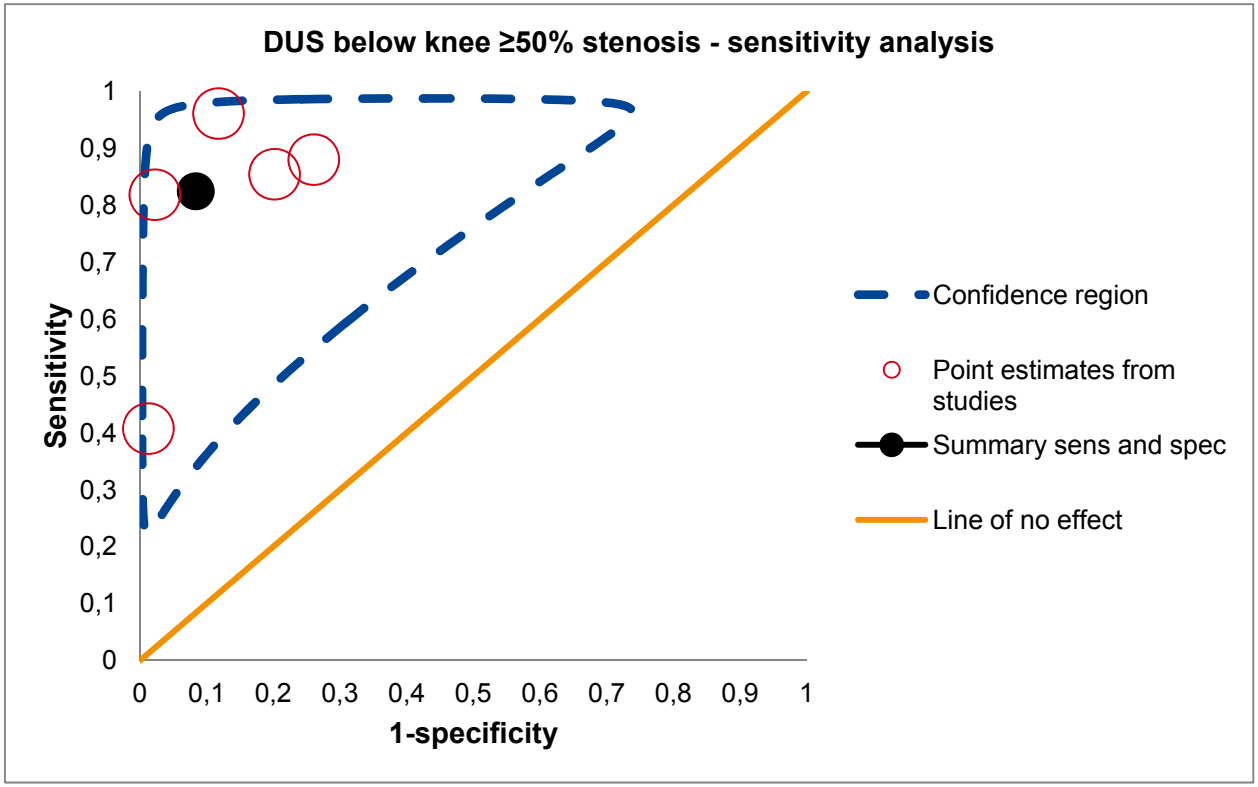


Figure 31 – ROC curve showing diagnostic meta-analysis: CE-MRA, below knee, 50-100% stenosis – sensitivity analysis

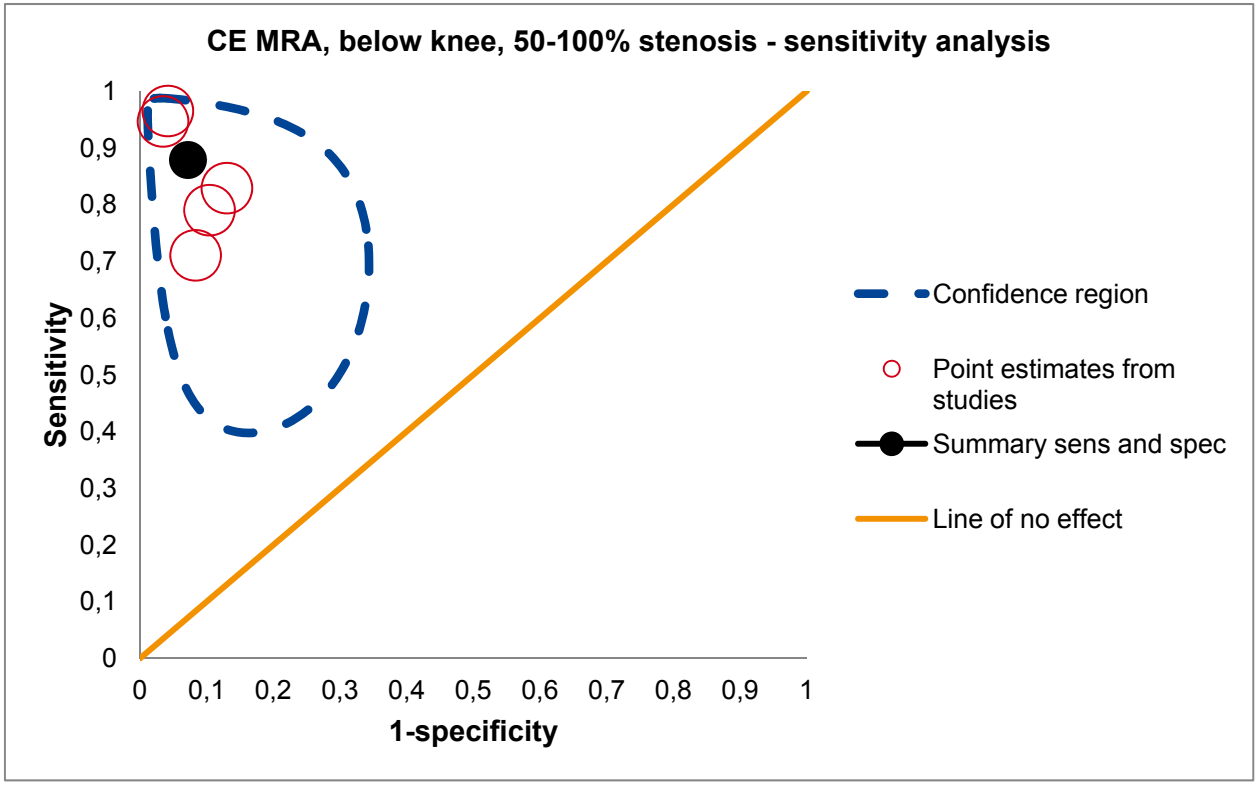
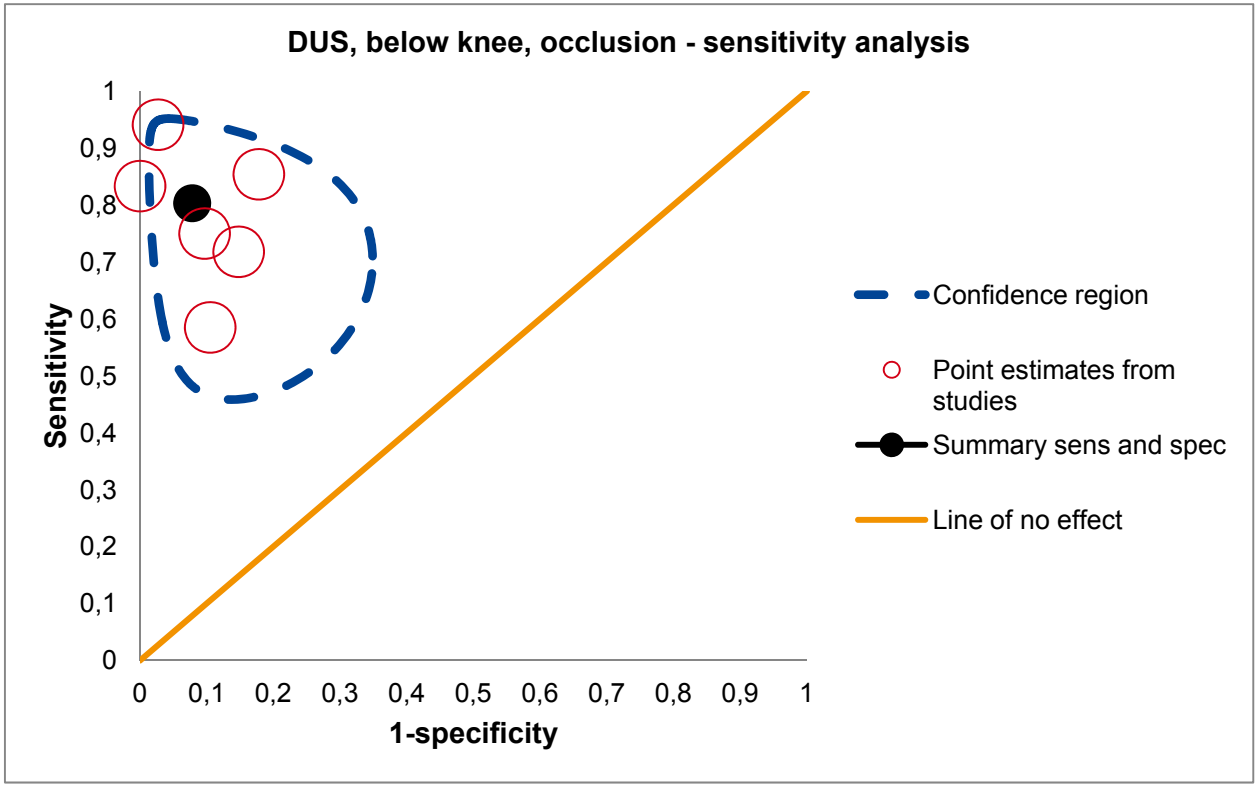
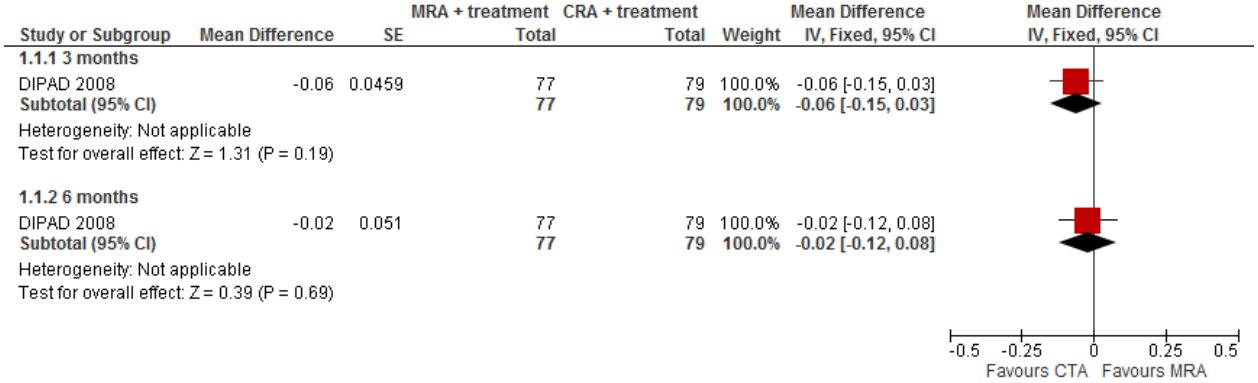


Figure 32 – ROC curve showing diagnostic meta-analysis: DUS, below knee, 50-100% occlusion – sensitivity analysis



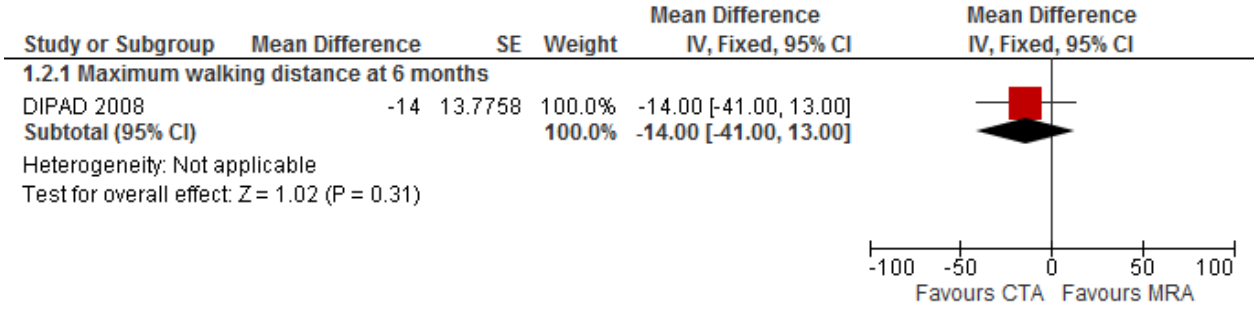
6.1.4. Test and treat forest plots: MRA plus treatment versus CTA plus treatment

Figure 33 – Forest plot of CE MRA plus treatment versus CTA plus treatment: outcome: Change in Eq 5d adjusted* analysis at 3 months and 6 months



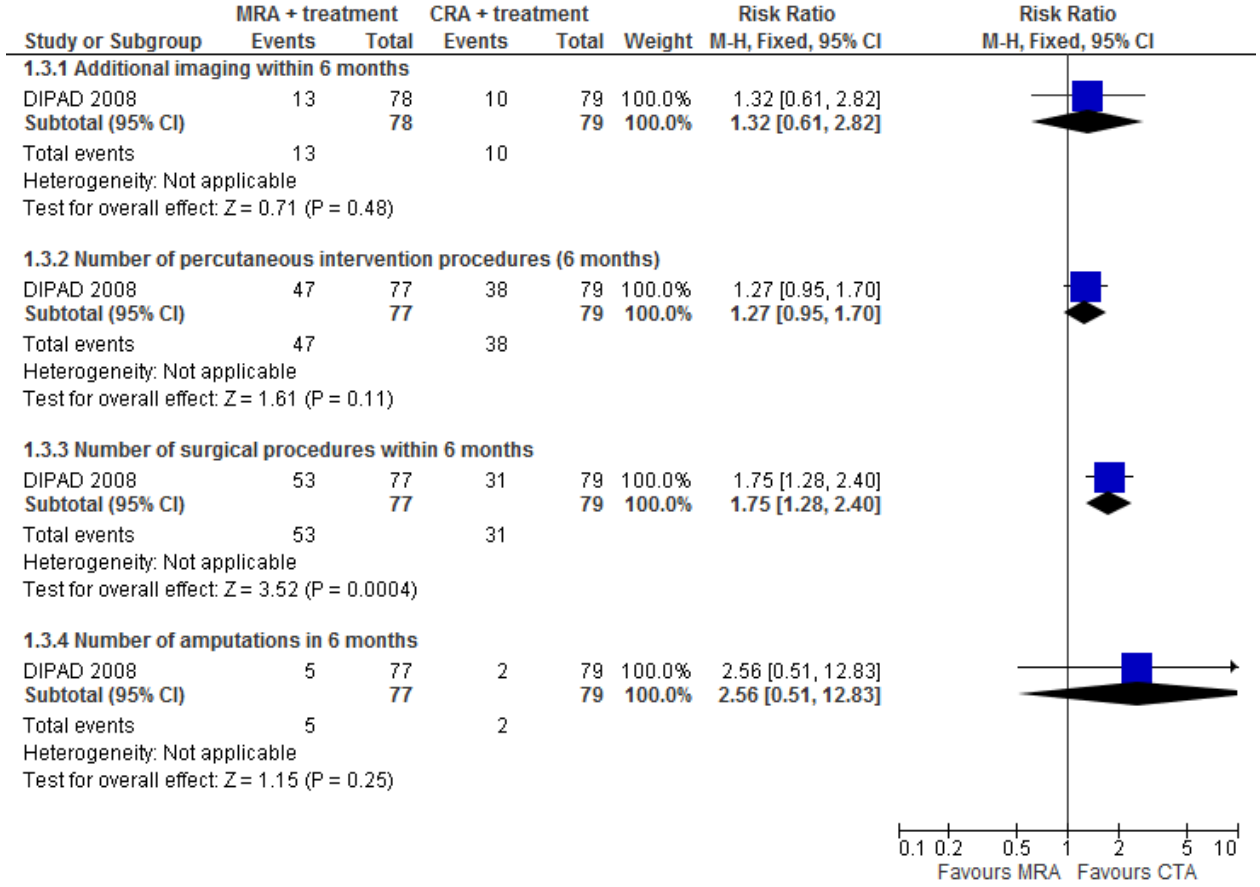
adjusted for baseline Eq 5d score, severity (IC or CLI), diabetes, renal disease, cerebrovascular disease, cardiac disease at baseline and rank order.

Figure 34 – Forest plot of CE MRA plus treatment versus CTA plus treatment: outcome: change in maximum walking distance adjusted* analysis at 6 months



adjusted for baseline walking distance, severity (IC or CLI), diabetes, renal disease, cerebrovascular disease, cardiac disease at baseline and rank order.

Figure 35 – Forest plot of CE MRA plus treatment versus CTA plus treatment: outcomes: additional imaging, number of percutaneous intervention procedures, number of surgical procedures and number of amputations within 6 months (frequencies, not number of people)



6.1.5. Test and treat forest plots: MRA plus treatment versus DUS plus treatment

Figure 36 – Forest plot of CE MRA plus treatment versus DUS plus treatment: outcome: Change in Eq 5d, unadjusted analysis at 3 months and 6 months

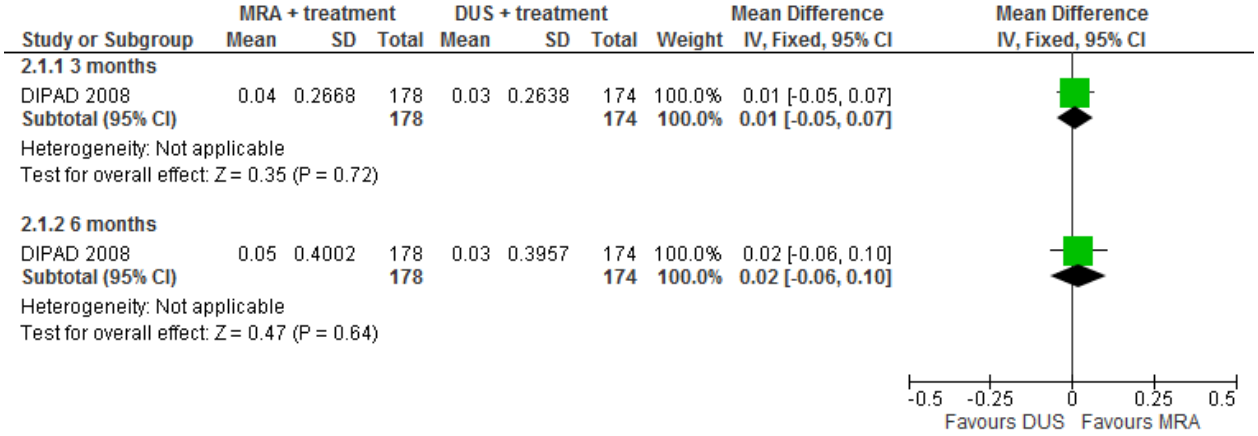


Figure 37 – Forest plot of CE MRA plus treatment versus DUS plus treatment: outcome: Change in walking distance unadjusted analysis at 6 months

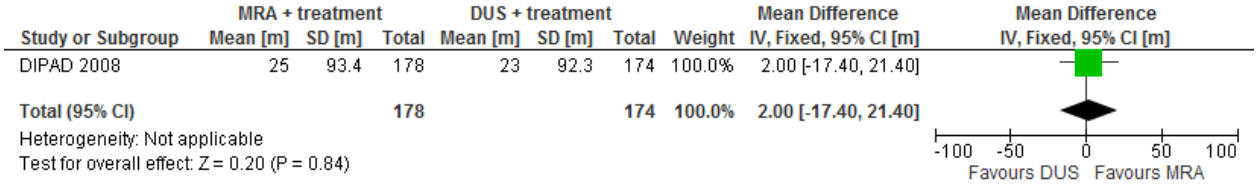
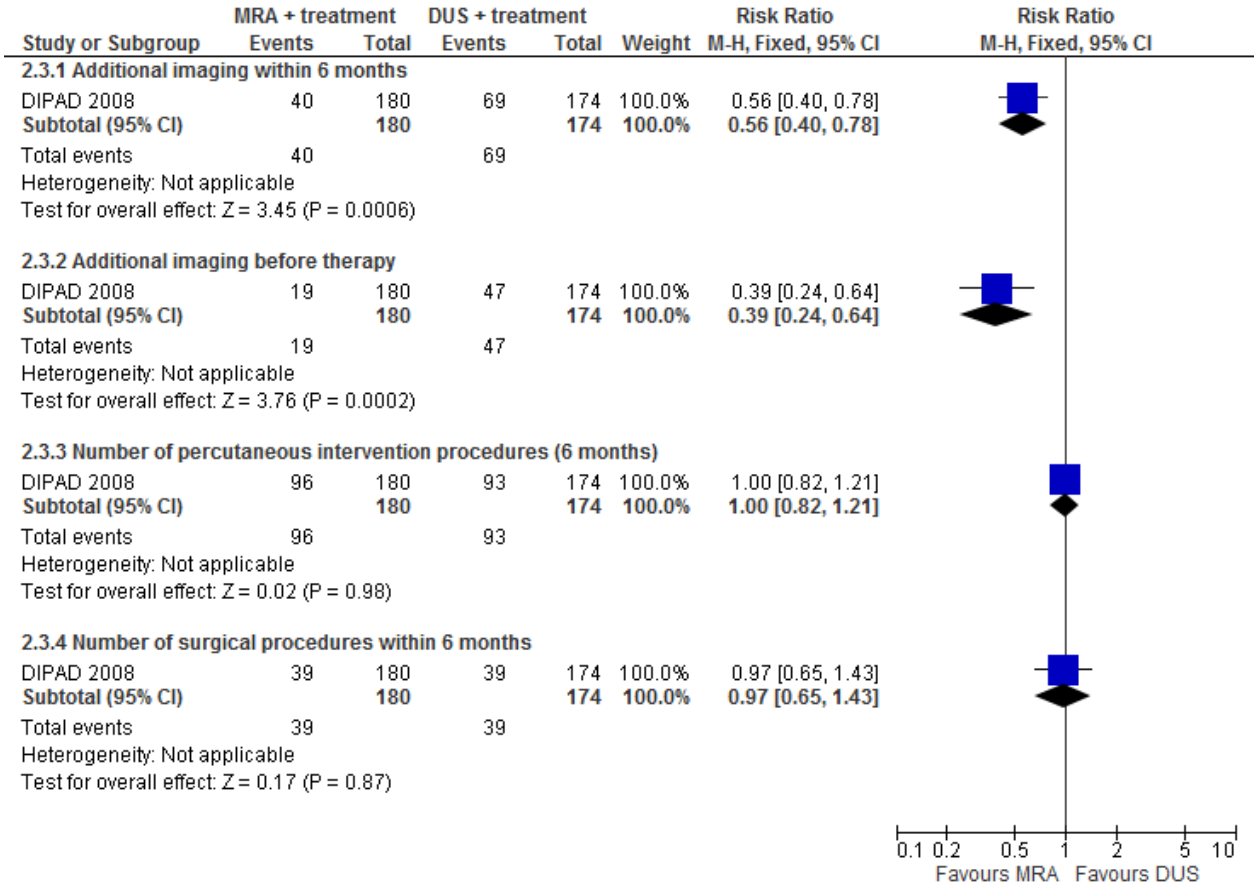


Figure 38 – Forest plot of CE MRA plus treatment versus DUS plus treatment: outcomes: additional imaging, number of percutaneous intervention procedures, number of surgical procedures within 6 months (frequencies, not number of people)



6.2. Selective versus primary stenting

6.2.1. Intermittent claudication - aortoiliac lesions

Figure 39 – Forest plot of selective versus primary stenting with angioplasty: IC, aortic lesions, outcome: Mortality at 3 months

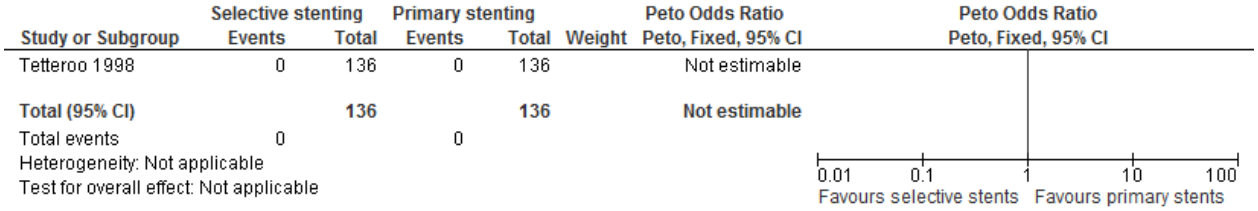


Figure 40 Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Mortality at 1 year

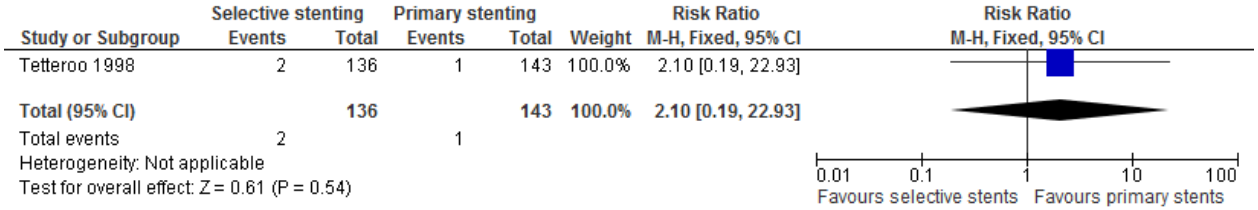


Figure 41 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Mortality at 2 years

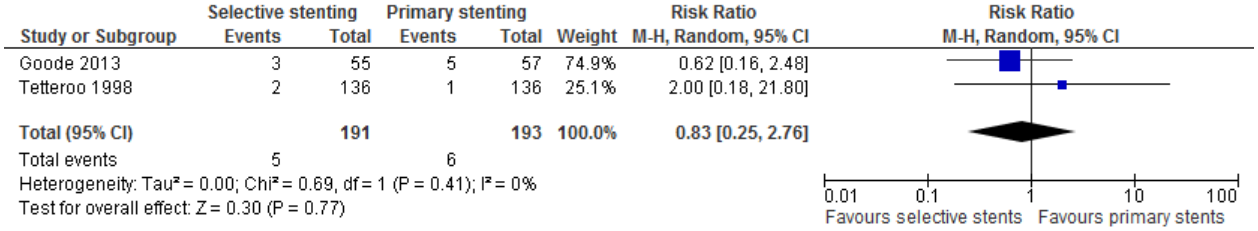


Figure 42 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Mortality at 5 years

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Klein, 2004	22	136	21	143	100.0%	1.10 [0.64, 1.91]
Total (95% CI)		**136**		**143**	**100.0%**	**1.10 [0.64, 1.91]**
Total events	22		21			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.73)

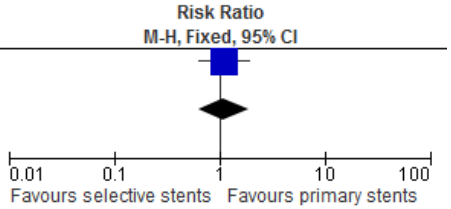


Figure 43 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Amputation at 5 years

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Klein, 2004	8	136	3	143	100.0%	2.80 [0.76, 10.35]
Total (95% CI)		**136**		**143**	**100.0%**	**2.80 [0.76, 10.35]**
Total events	8		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.55 (P = 0.12)

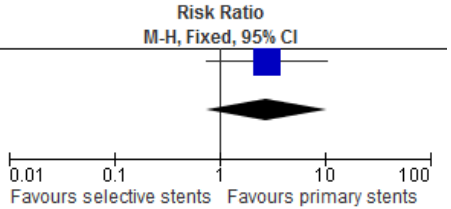


Figure 44 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Re-intervention at 3 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tetteroo 1998	2	136	2	143	100.0%	1.05 [0.15, 7.36]
Total (95% CI)		**136**		**143**	**100.0%**	**1.05 [0.15, 7.36]**
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.05 (P = 0.96)

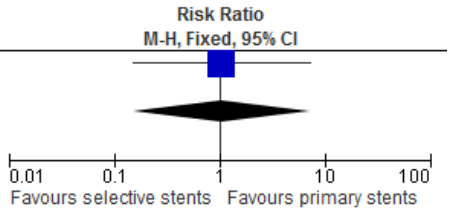


Figure 45 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Re-intervention at 1 year

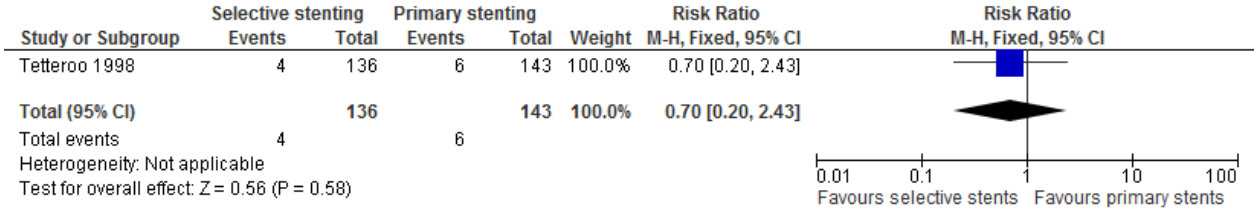


Figure 46 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Re-intervention at 2 years

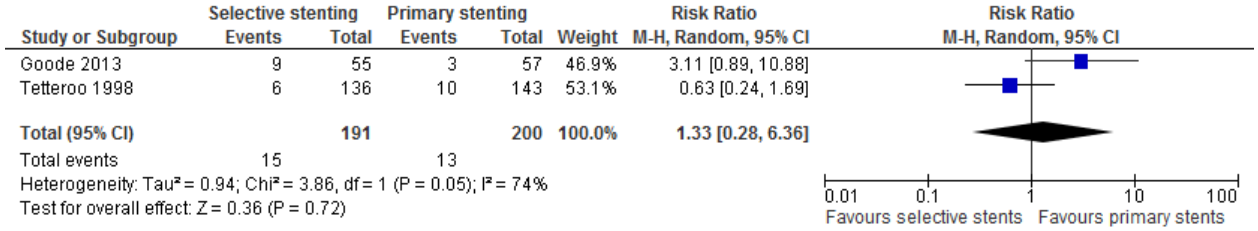


Figure 47 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, reported by arterial segment, outcome: Re-intervention Hazard ratio up to 8 years data

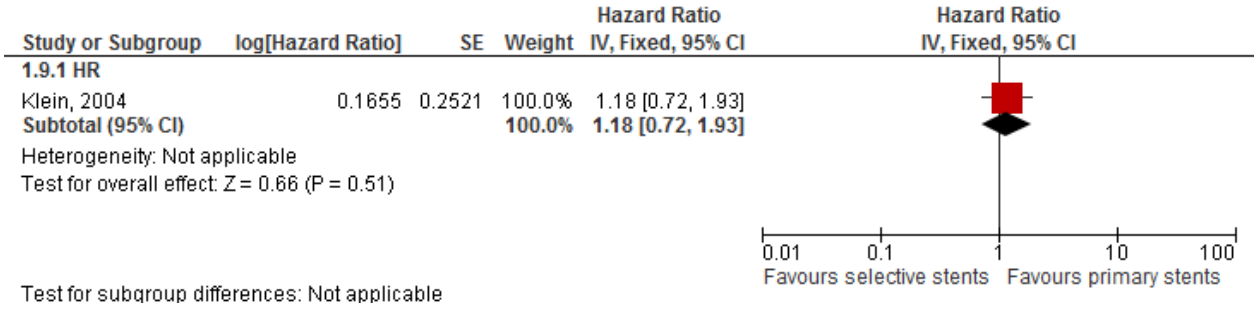


Figure 48 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, reported by arterial segment, outcome: Re-intervention at 5 years

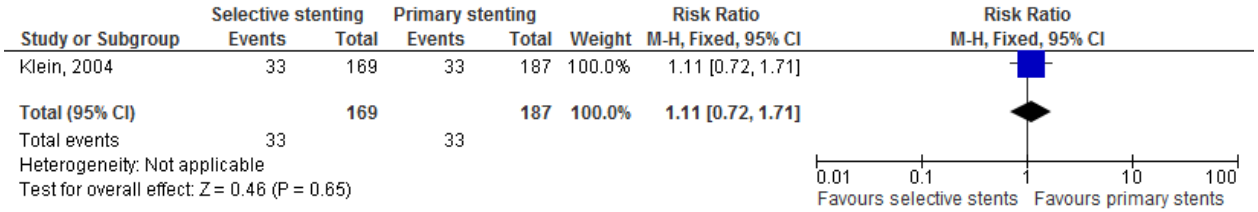


Figure 49 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, reported by arterial segment, outcome: Re-intervention at 8 years

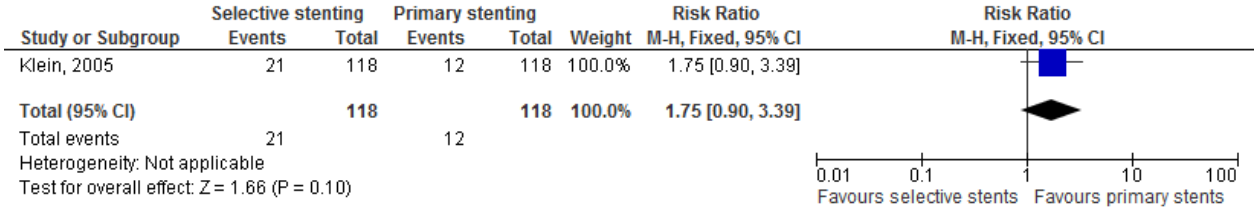


Figure 50 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Complications/adverse events at 30 days

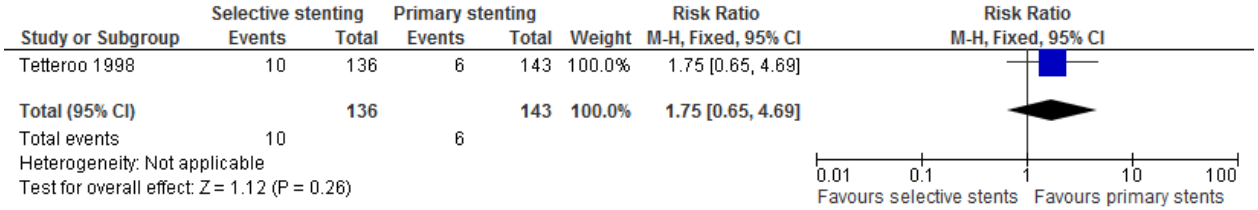


Figure 51 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Major complications at 2 years

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Goode 2013	11	55	3	57	100.0%	3.80 [1.12, 12.89]
Total (95% CI)		**55**		**57**	**100.0%**	**3.80 [1.12, 12.89]**
Total events	11		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.14 (P = 0.03)

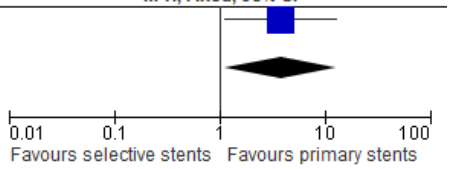


Figure 52 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Walking distance at 3 months

Study or Subgroup	Selective stenting Mean	SD	Total	Primary stenting Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bosch 1999	255	64	136	263	57	143	100.0%	-8.00 [-22.25, 6.25]
Total (95% CI)			**136**			**143**	**100.0%**	**-8.00 [-22.25, 6.25]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)

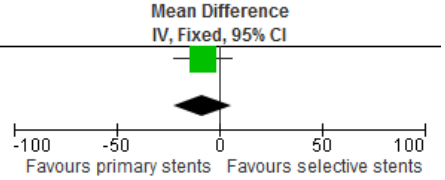


Figure 53 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Walking distance at 1 year

Study or Subgroup	Selective stenting Mean	SD	Total	Primary stenting Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bosch 1999	263	65	136	261	58	143	100.0%	2.00 [-12.48, 16.48]
Total (95% CI)			**136**			**143**	**100.0%**	**2.00 [-12.48, 16.48]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.27 (P = 0.79)

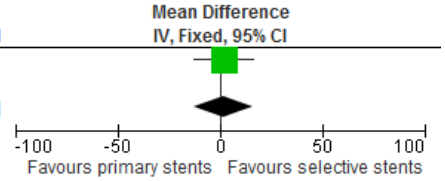
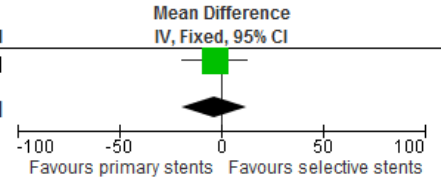


Figure 54 – Forest plot of selective versus primary stenting with angioplasty: IC, aortailliac lesions, outcome: Walking distance at 2 years

Study or Subgroup	Selective stenting Mean	SD	Total	Primary stenting Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bosch 1999	255	68	136	258	68	143	100.0%	-3.00 [-18.96, 12.96]
Total (95% CI)			**136**			**143**	**100.0%**	**-3.00 [-18.96, 12.96]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.37 (P = 0.71)



6.2.2. Intermittent claudication - femoropopliteal lesions

Figure 55 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Mortality at 30 days

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Laird, 2010	0	72	0	134		Not estimable
Total (95% CI)		**72**		**134**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

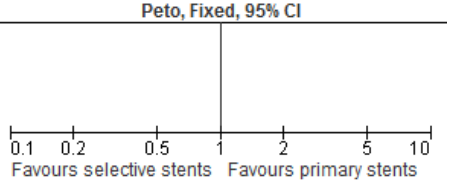


Figure 56 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, randomized by limb, outcome: Mortality at 30 days

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Cejna 2001	2	77	0	77	100.0%	7.49 [0.46, 120.79]
Total (95% CI)		**77**		**77**	**100.0%**	**7.49 [0.46, 120.79]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.42 (P = 0.16)

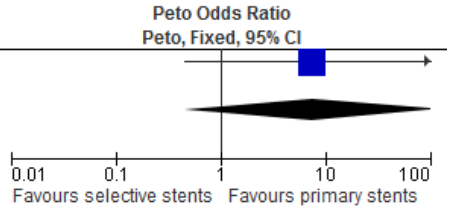


Figure 57 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Mortality at 6 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Schillinger 2006	0	53	0	51		Not estimable
Total (95% CI)		**53**		**51**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

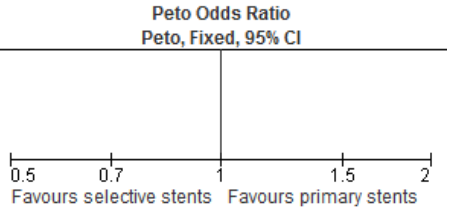


Figure 58 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Mortality at 1 year

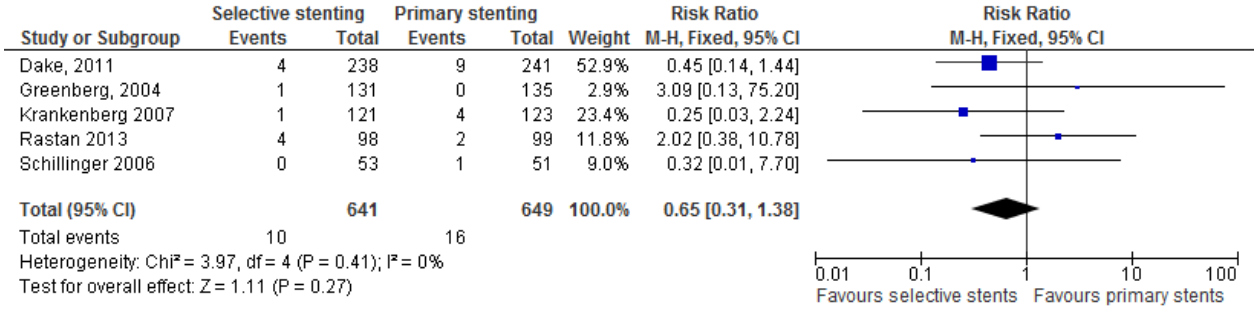


Figure 59 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, randomized by limb, outcome: Mortality at 1 year

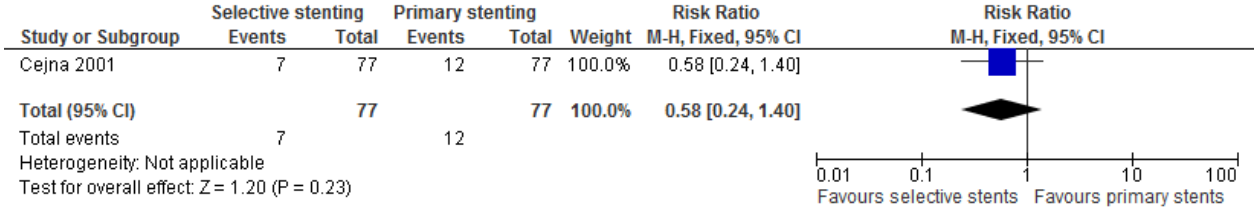


Figure 60 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, randomized by limb, outcome: Amputation at 30 days

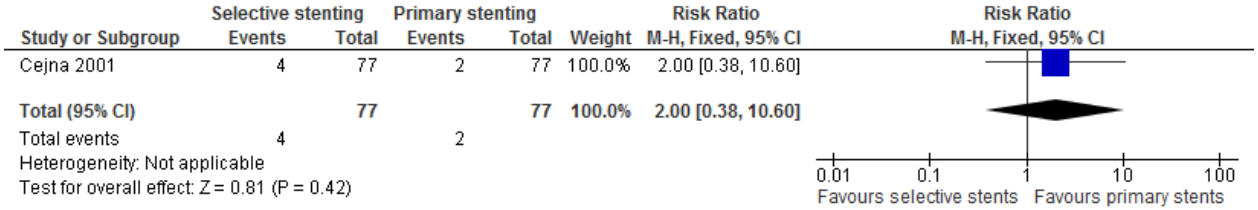


Figure 61 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Amputation at 6 months

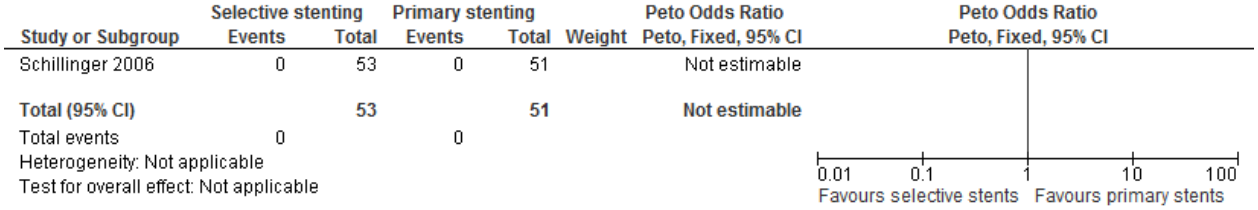


Figure 62 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Amputation at 1 year

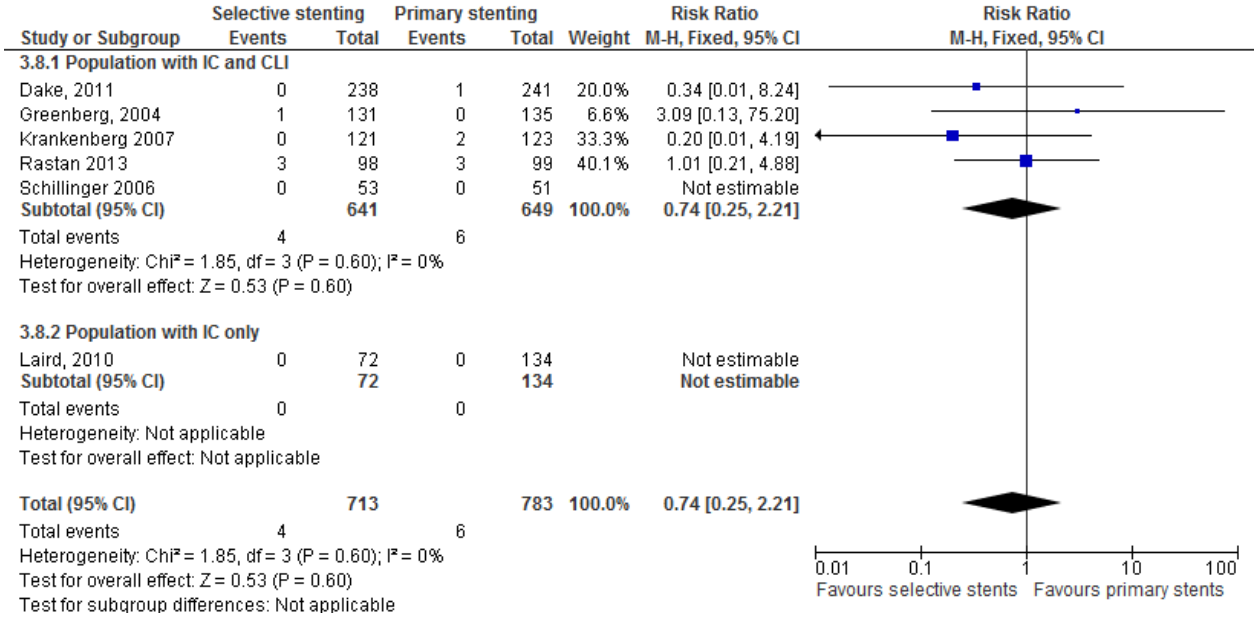


Figure 63 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Amputation at 2 years



Figure 64 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: TLR/TVR Hazard ratio

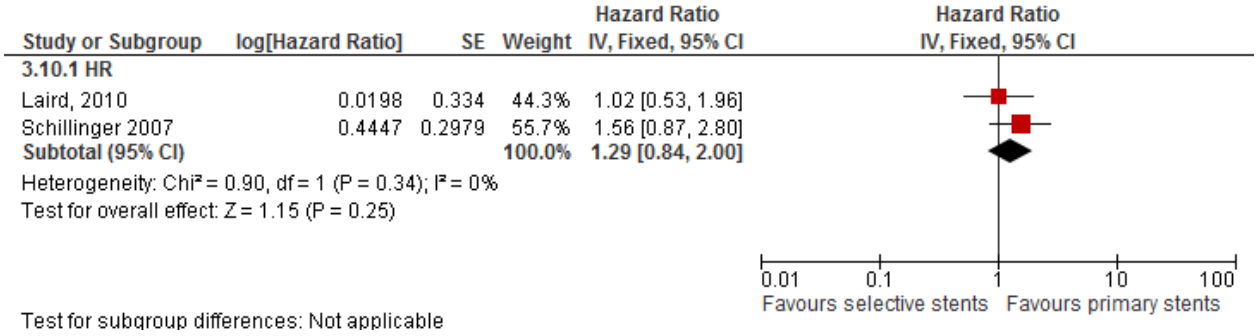


Figure 65 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: TLR at 6 months

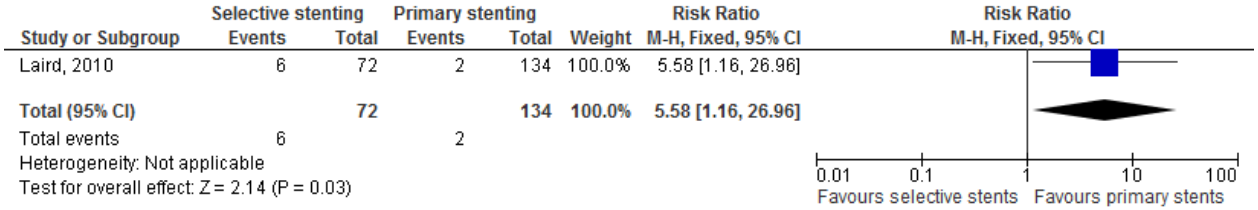


Figure 66 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: TLR at 1 year

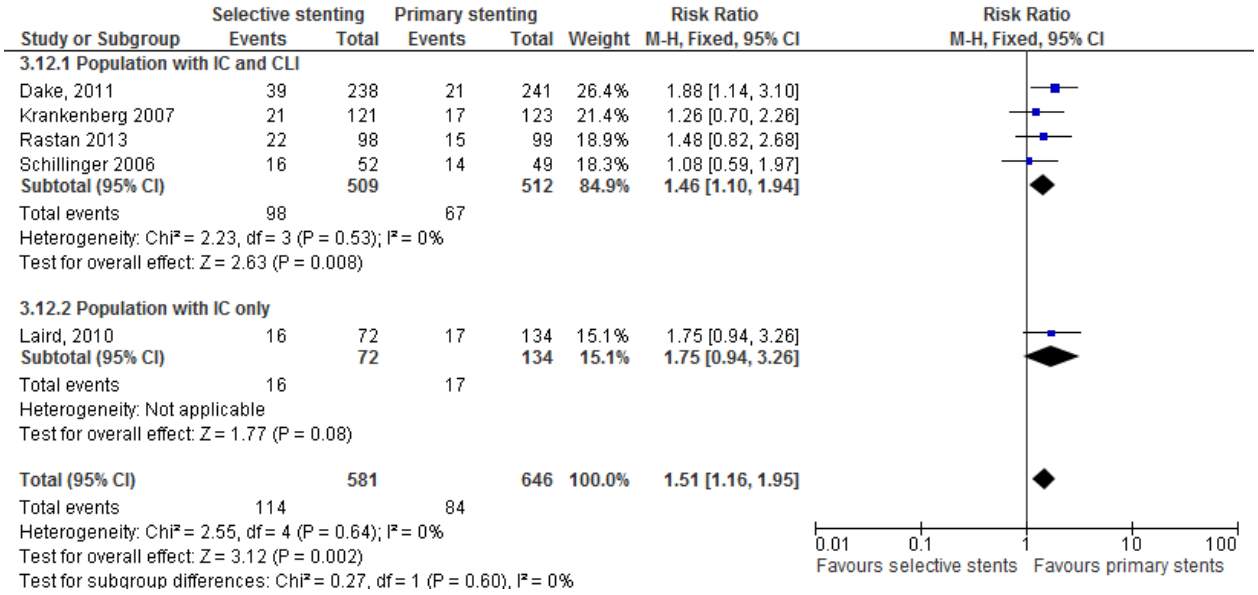


Figure 67 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, randomized by limb, outcome: TLR at 1 year

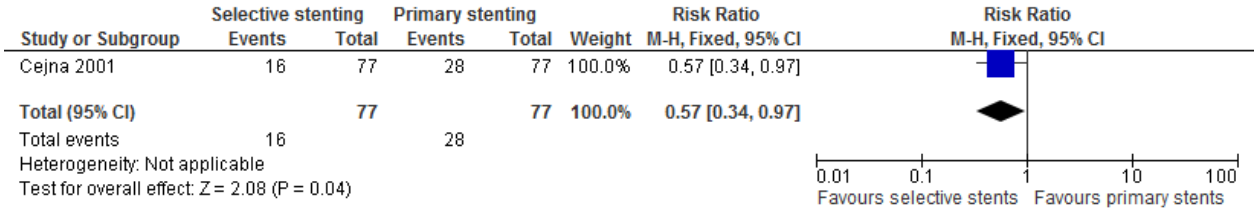


Figure 68 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: TLR at 2 years

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schillinger 2007	28	52	17	46	100.0%	1.46 [0.93, 2.29]
Total (95% CI)		**52**		**46**	**100.0%**	**1.46 [0.93, 2.29]**
Total events	28		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.63 (P = 0.10)

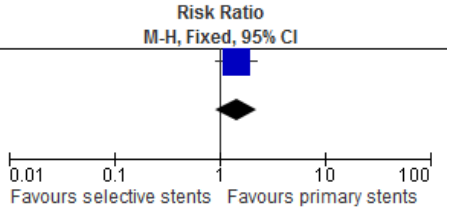


Figure 69 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: TLR at 3 years

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Laird, 2010	22	72	30	134	100.0%	1.36 [0.85, 2.18]
Total (95% CI)		**72**		**134**	**100.0%**	**1.36 [0.85, 2.18]**
Total events	22		30			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.30 (P = 0.19)

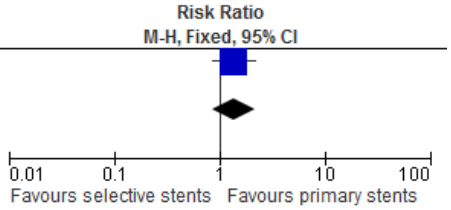


Figure 70 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Perioperative complications

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dick 2009	1	36	0	32	5.0%	2.68 [0.11, 63.45]
Krankenberg 2007	5	121	8	123	75.4%	0.64 [0.21, 1.89]
Rastan 2013	3	127	2	119	19.6%	1.41 [0.24, 8.27]
Schillinger 2006	0	53	0	51		Not estimable
Total (95% CI)		**337**		**325**	**100.0%**	**0.89 [0.37, 2.11]**
Total events	9		10			

Heterogeneity: Chi² = 1.09, df = 2 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.27 (P = 0.79)

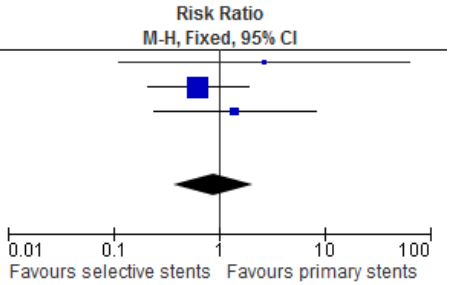


Figure 71 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, randomized by limb, outcome: Major complications at 30 days

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cejna 2001	6	77	7	77	100.0%	0.86 [0.30, 2.43]
Total (95% CI)		**77**		**77**	**100.0%**	**0.86 [0.30, 2.43]**
Total events	6		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.29 (P = 0.77)

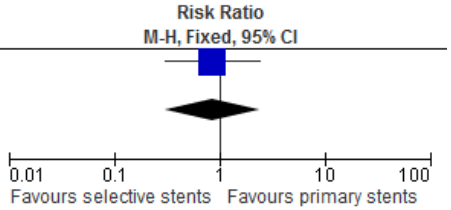


Figure 72 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Major complications at 6 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Laird, 2010	5	72	9	134	100.0%	1.03 [0.36, 2.97]
Total (95% CI)		**72**		**134**	**100.0%**	**1.03 [0.36, 2.97]**
Total events	5		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.06 (P = 0.95)

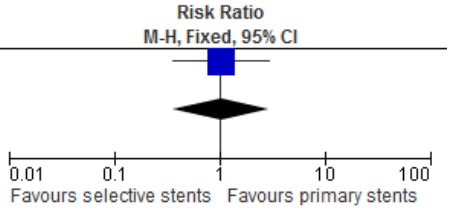


Figure 73 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Major complications at 9 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Greenberg, 2004	21	131	22	135	100.0%	0.98 [0.57, 1.70]
Total (95% CI)		**131**		**135**	**100.0%**	**0.98 [0.57, 1.70]**
Total events	21		22			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.06 (P = 0.95)

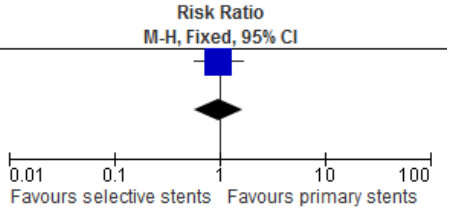


Figure 74 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Major complications at 1 year

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Laird, 2010	8	72	19	134	100.0%	0.78 [0.36, 1.70]
Total (95% CI)		**72**		**134**	**100.0%**	**0.78 [0.36, 1.70]**
Total events	8		19			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.54)

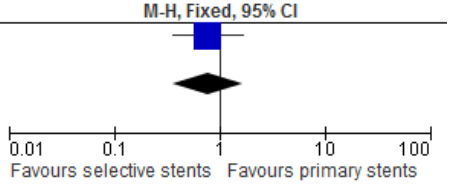


Figure 75 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: QoL (change in SF8 at 1 year)

Study or Subgroup	Selective stenting Mean	SD	Total	Primary stenting Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Laird, 2010	5.9	11.2	72	5.7	11.2	134	100.0%	0.20 [-3.01, 3.41]
Total (95% CI)			**72**			**134**	**100.0%**	**0.20 [-3.01, 3.41]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.90)

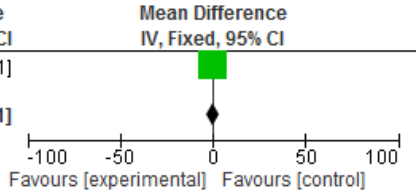


Figure 76 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: QoL (change in SF8 at 3 years)

Study or Subgroup	Selective stenting Mean	SD	Total	Primary stenting Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Laird, 2010	6.9	12.2	72	5.4	11.3	134	100.0%	1.50 [-1.91, 4.91]
Total (95% CI)			**72**			**134**	**100.0%**	**1.50 [-1.91, 4.91]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)

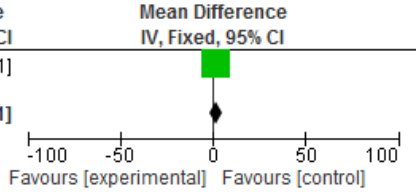


Figure 77 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Walking distance at 6 months

Study or Subgroup	Selective stenting Mean	SD	Total	Primary stenting Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Dick 2009	600	265.62	39	800	265.62	34	100.0%	-200.00 [-322.15, -77.85]
Total (95% CI)			**39**			**34**	**100.0%**	**-200.00 [-322.15, -77.85]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.21 (P = 0.001)

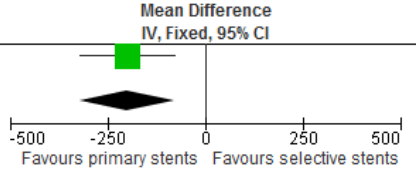


Figure 78 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Walking distance at 1 year

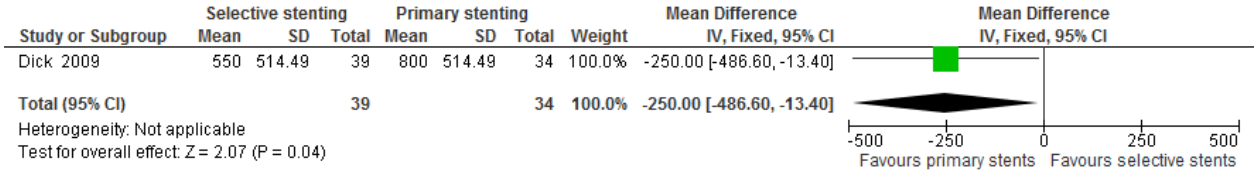
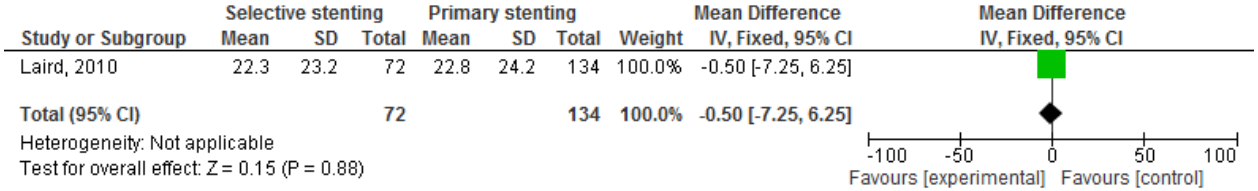


Figure 79 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Walking score at 1 year



6.2.3. Intermittent claudication - infrapopliteal lesions (person randomized)

Figure 80 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Mortality at 1 year

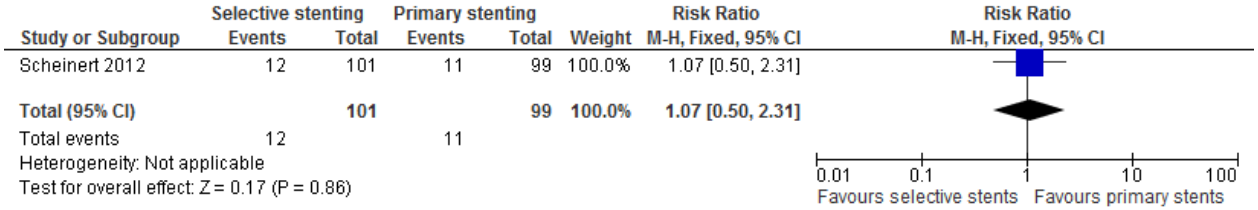


Figure 81 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: Amputation at 1 year

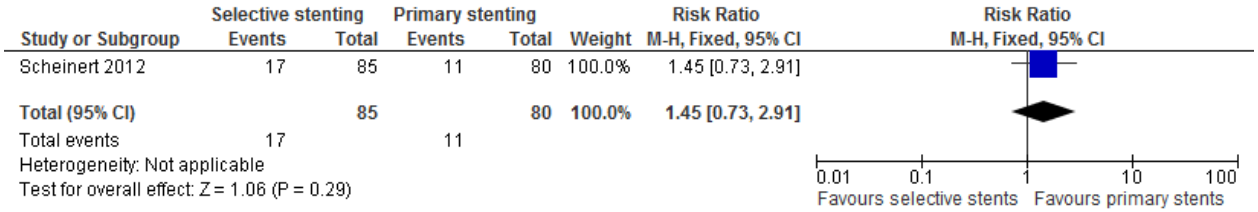
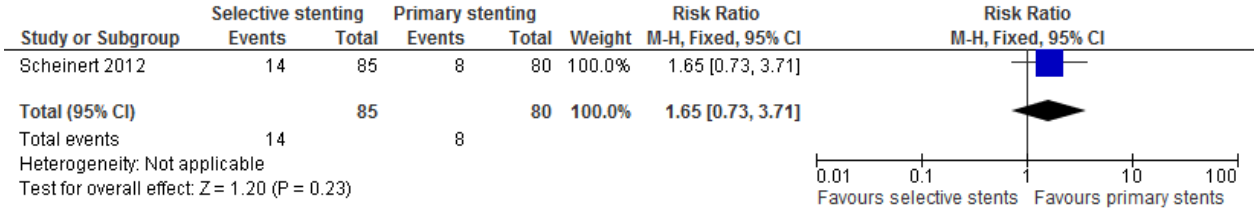


Figure 82 – Forest plot of selective versus primary stenting with angioplasty: IC, femoropopliteal lesions, outcome: TLR at 1 year



6.2.4. Critical limb ischemia - infrapopliteal lesions (person randomized)

Figure 83 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: Mortality at 3 months

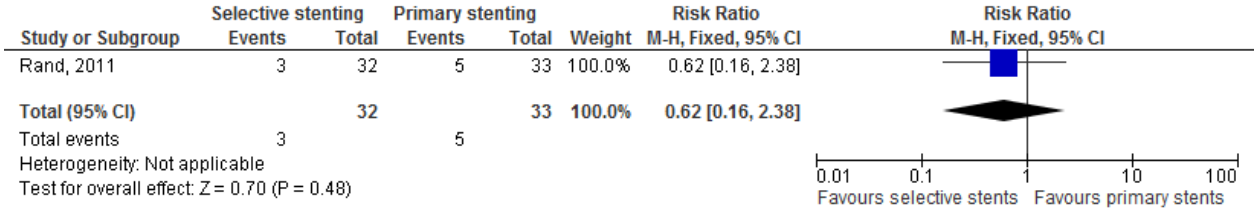


Figure 84 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: Mortality at 9 months

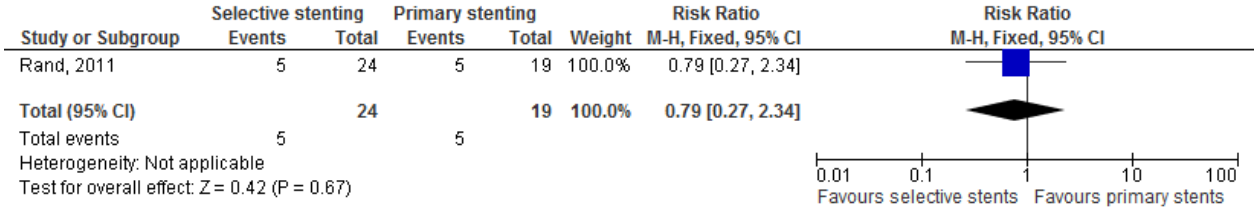


Figure 85 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: Amputation at 3 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rand, 2011	4	32	6	33	100.0%	0.69 [0.21, 2.21]
Total (95% CI)		**32**		**33**	**100.0%**	**0.69 [0.21, 2.21]**
Total events	4		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

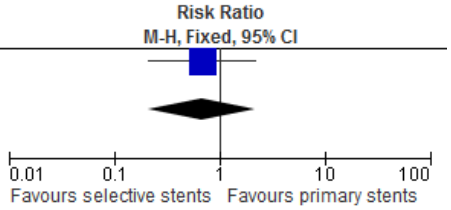


Figure 86 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: Amputation at 6 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rand 2006	1	27	2	24	100.0%	0.44 [0.04, 4.60]
Total (95% CI)		**27**		**24**	**100.0%**	**0.44 [0.04, 4.60]**
Total events	1		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)

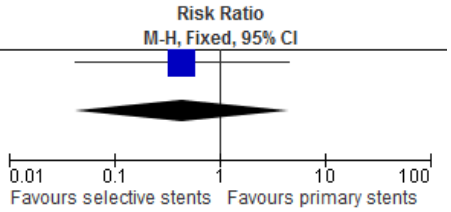


Figure 87 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: Amputation at 9 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rand, 2011	7	24	10	19	100.0%	0.55 [0.26, 1.18]
Total (95% CI)		**24**		**19**	**100.0%**	**0.55 [0.26, 1.18]**
Total events	7		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.53 (P = 0.13)

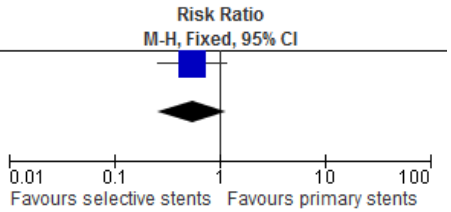


Figure 88 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: TLR at 3 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Rand, 2011	0	32	1	33	100.0%	0.14 [0.00, 7.03]
Total (95% CI)		**32**		**33**	**100.0%**	**0.14 [0.00, 7.03]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.32)

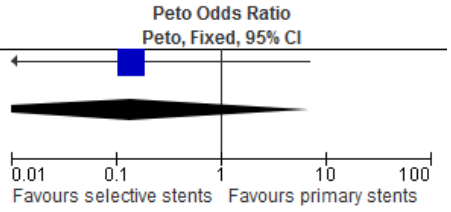


Figure 89 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: TLR at 6 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Rand 2006	0	27	1	24	100.0%	0.12 [0.00, 6.06]
Total (95% CI)		**27**		**24**	**100.0%**	**0.12 [0.00, 6.06]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)

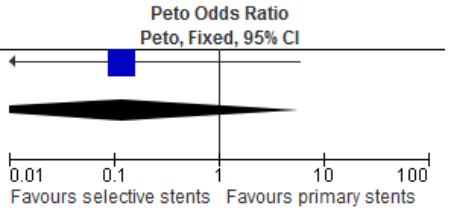


Figure 90 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: TLR at 9 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rand, 2011	6	24	7	19	100.0%	0.68 [0.27, 1.68]
Total (95% CI)		**24**		**19**	**100.0%**	**0.68 [0.27, 1.68]**
Total events	6		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.84 (P = 0.40)

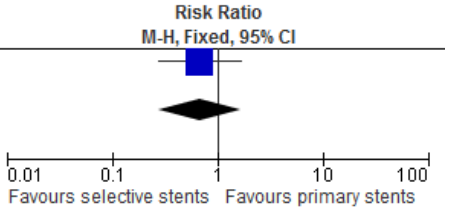
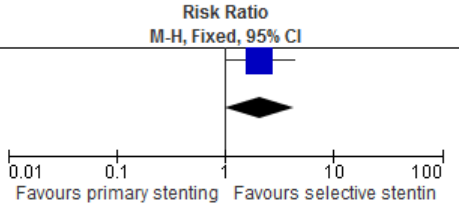


Figure 91 – Forest plot of selective versus primary stenting with angioplasty: CLI, femoropopliteal lesions, outcome: Complete ulcer healing at 12 months

Study or Subgroup	Selective stenting Events	Total	Primary stenting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brodmann, 2011	16	20	5	13	100.0%	2.08 [1.01, 4.28]
Total (95% CI)		**20**		**13**	**100.0%**	**2.08 [1.01, 4.28]**
Total events	16		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)



6.3. Bare metal versus drug eluting stents

6.3.1. Intermittent claudication, femoro-popliteal lesions

Figure 92 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Mortality at 6 months.

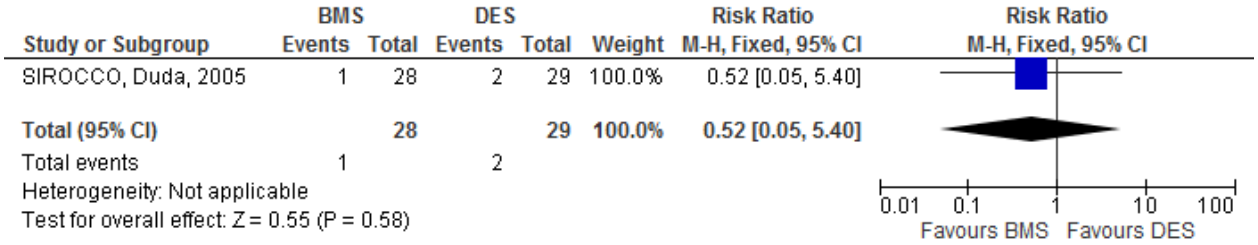


Figure 93 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Mortality at 12 months.

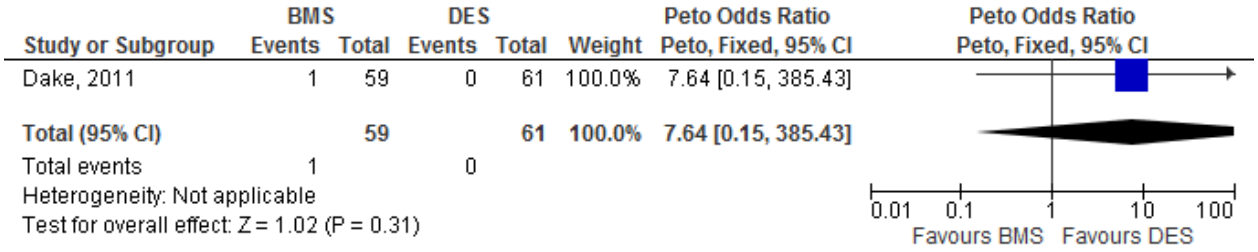


Figure 94 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Mortality at 24 months.

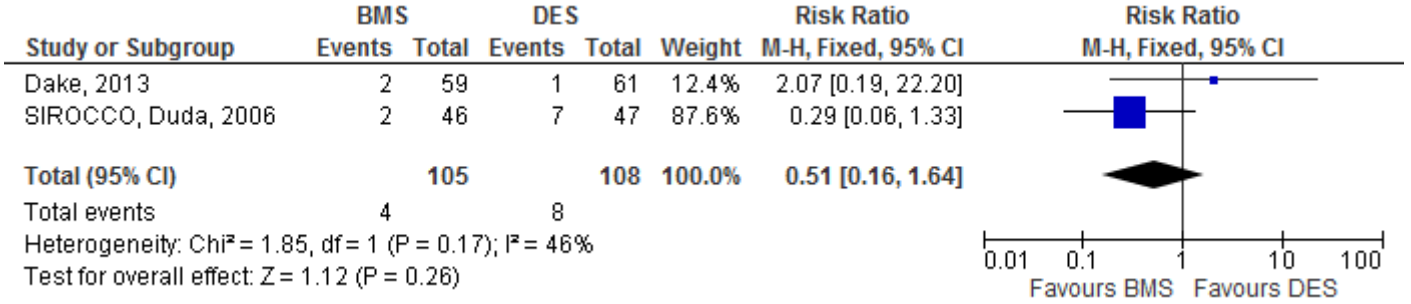


Figure 95 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Mortality at 36 months.

Study or Subgroup	BMS Events	BMS Total	DMS Events	DMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Geraghty, 2013	9	72	3	76	100.0%	3.17 [0.89, 11.23]
Total (95% CI)		**72**		**76**	**100.0%**	**3.17 [0.89, 11.23]**
Total events	9		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.78 (P = 0.07)

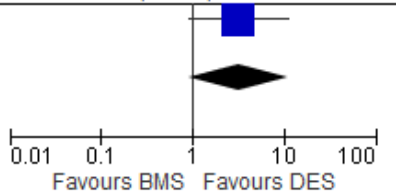


Figure 96 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Procedure/device related deaths at 12 months

Study or Subgroup	BMS Events	BMS Total	DES Events	DES Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Dake, 2011	0	59	0	61		Not estimable
Total (95% CI)		**59**		**61**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

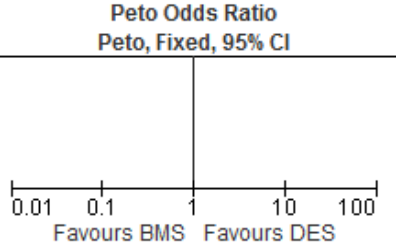


Figure 97 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Amputation at 24 months.

Study or Subgroup	BMS Events	BMS Total	DES Events	DES Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
SIROCCO, Duda, 2006	0	46	0	47		Not estimable
Total (95% CI)		**46**		**47**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

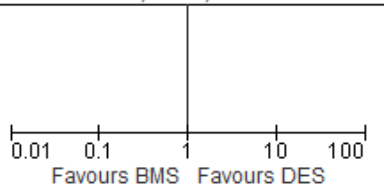


Figure 98 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 TLR at 6 months.

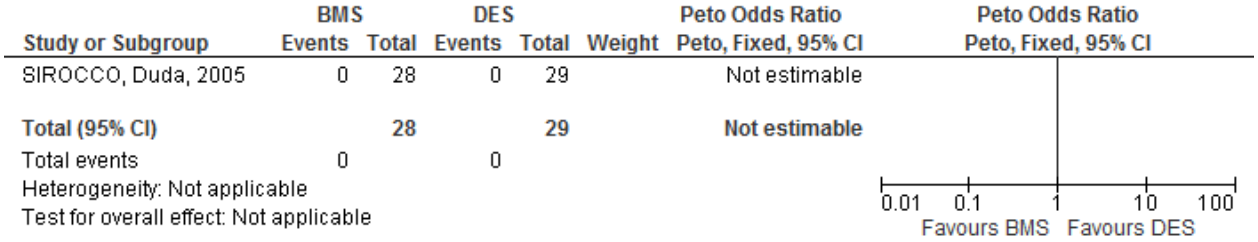


Figure 99 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 TLR at 24 months (HR)

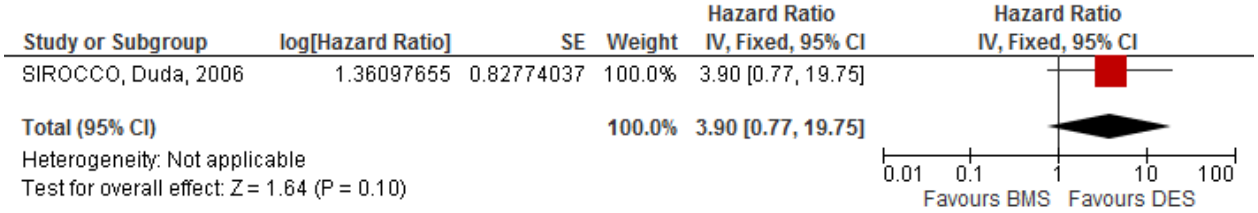


Figure 100 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 TLR in patients at 36 months

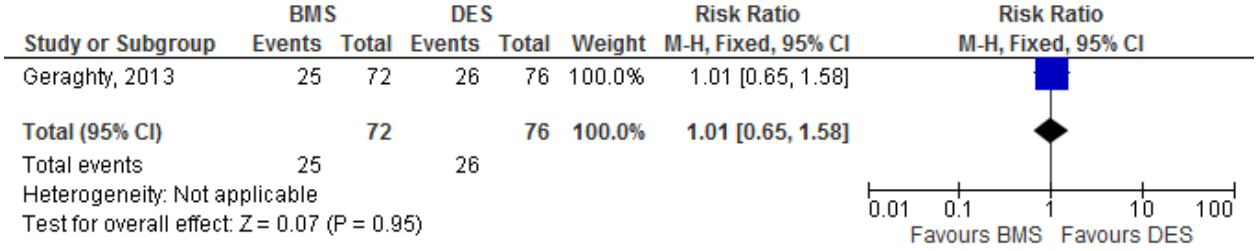


Figure 101 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 TLR by lesions at 36 months

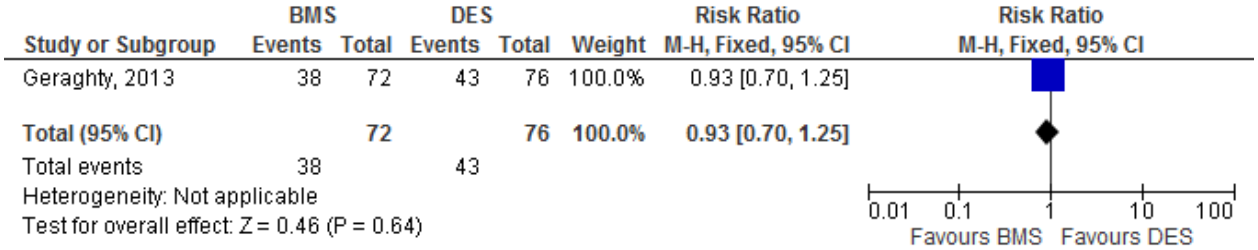


Figure 102 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 TVR at 6 months

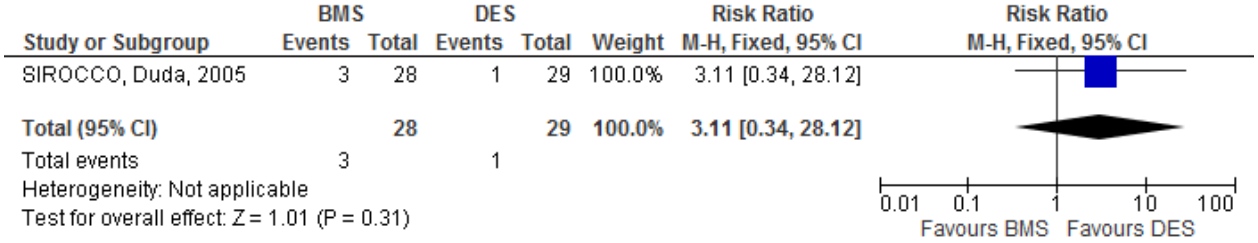


Figure 103 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 TVR at 24 months (HR)

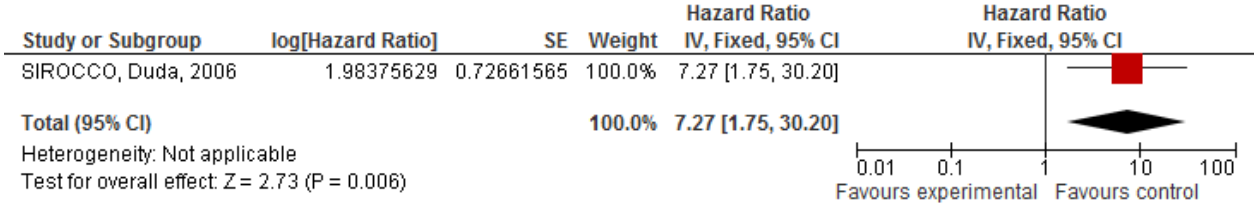


Figure 104 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Revascularisation procedure on contralateral leg before discharge at 6 months.

Study or Subgroup	BMS Events	BMS Total	DES Events	DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SIROCCO, Duda, 2005	2	28	2	29	100.0%	1.04 [0.16, 6.86]
Total (95% CI)		**28**		**29**	**100.0%**	**1.04 [0.16, 6.86]**
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.97)

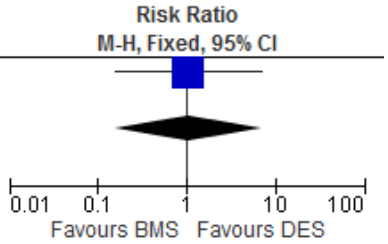


Figure 105 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Revascularisation procedure on contralateral leg after discharge at 6 months.

Study or Subgroup	BMS Events	BMS Total	DES Events	DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SIROCCO, Duda, 2005	2	28	3	29	100.0%	0.69 [0.12, 3.83]
Total (95% CI)		**28**		**29**	**100.0%**	**0.69 [0.12, 3.83]**
Total events	2		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.42 (P = 0.67)

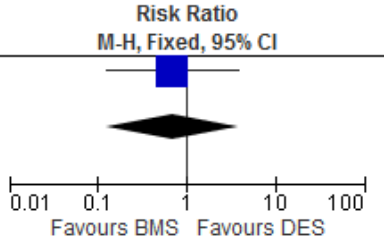


Figure 106 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Peri-procedural complications.

Study or Subgroup	Favours BMS Events	Favours BMS Total	DES Events	DES Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Geraghty, 2013	1	72	0	76	100.0%	7.81 [0.15, 394.22]
Total (95% CI)		**72**		**76**	**100.0%**	**7.81 [0.15, 394.22]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.03 (P = 0.30)

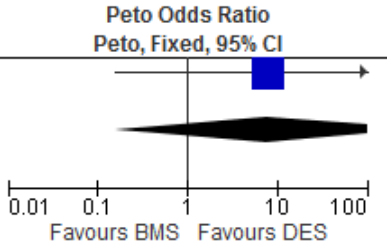


Figure 107 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Major adverse events at 6 months.

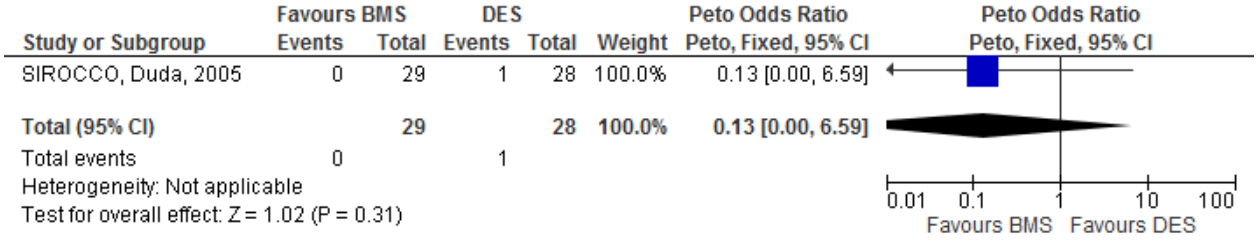


Figure 108 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Quality of life (SF-36) at 1 month

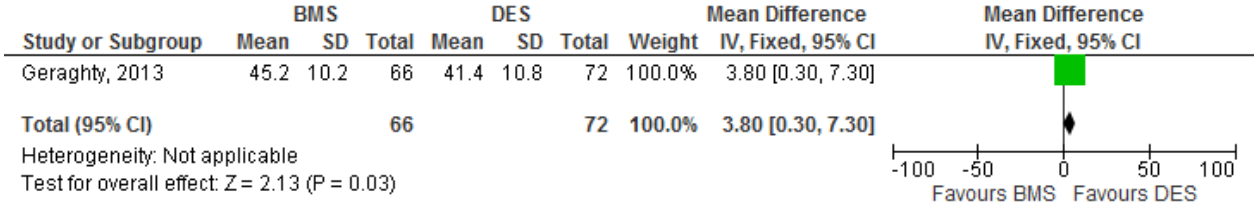


Figure 109 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Quality of life (SF-36) at 6 months.

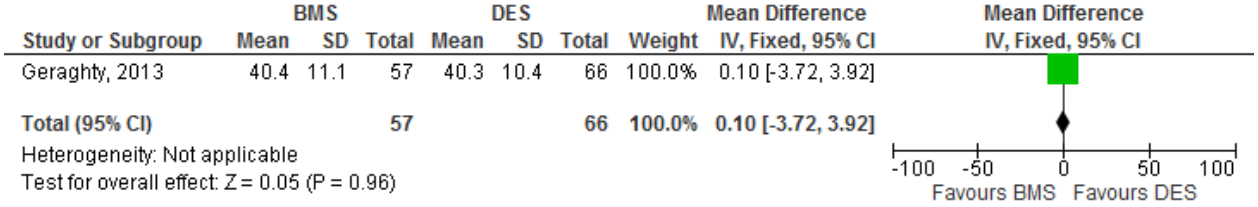


Figure 110 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Quality of life (SF-36) at 12 months.

	BMS			DES				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Geraghty, 2013	40.5	11.7	52	39.8	10.7	62	100.0%	0.70 [-3.45, 4.85]	
Total (95% CI)			**52**			**62**	**100.0%**	**0.70 [-3.45, 4.85]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)

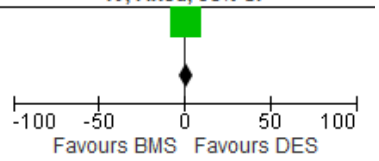


Figure 111 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Quality of life (SF-36) at 24 months.

	BMS			DES				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Geraghty, 2013	39.8	11.5	43	40.6	10.9	48	100.0%	-0.80 [-5.42, 3.82]	
Total (95% CI)			**43**			**48**	**100.0%**	**-0.80 [-5.42, 3.82]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.73)

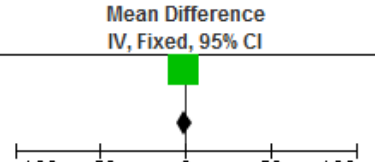
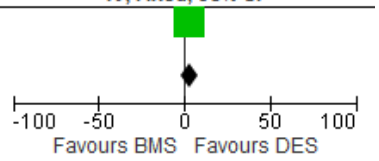


Figure 112 – Forest plot of bare-metal stent versus drug-eluting stent: IC, femoro-popliteal lesions, outcome: 1.1 Quality of life (SF-36) at 36 months.

	BMS			DES				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Geraghty, 2013	41.9	11.7	39	38.7	10.5	45	100.0%	3.20 [-1.58, 7.98]	
Total (95% CI)			**39**			**45**	**100.0%**	**3.20 [-1.58, 7.98]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.31 (P = 0.19)



6.3.2. *Intermittent claudication, infra-geniculate lesions*

Figure 113 – Forest plot of bare-metal stent versus drug-eluting stent: IC, infra-geniculate lesions, outcome: 1.1 Mortality at 12 months.

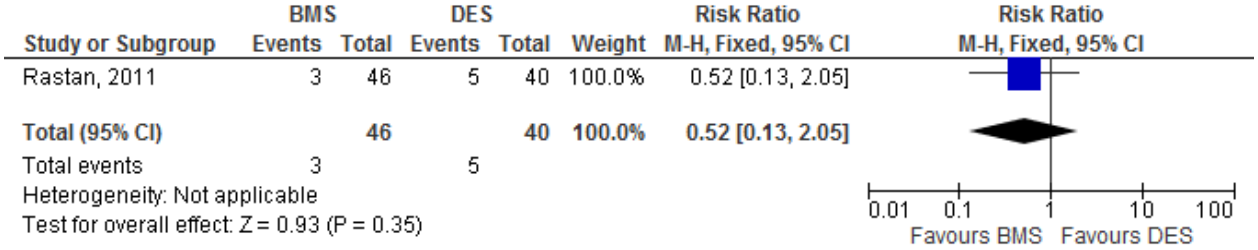


Figure 114 – Forest plot of bare-metal stent versus drug-eluting stent: IC, infra-geniculate lesions, outcome: 1.1 Mortality at 1200 days.

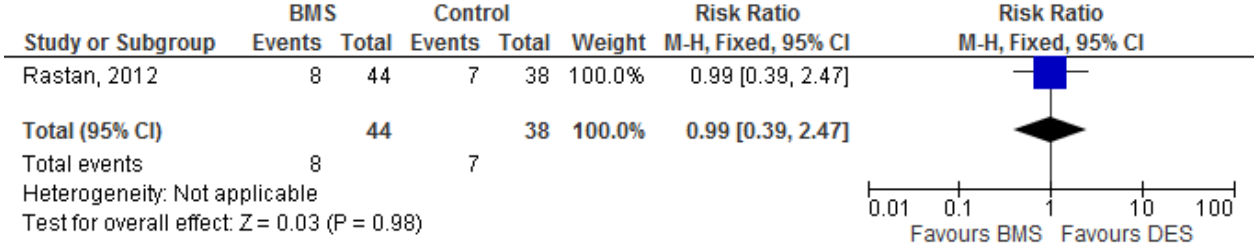


Figure 115 – Forest plot of bare-metal stent versus drug-eluting stent: IC, infra-geniculate lesions, outcome: 1.1 Amputation at 1 year.

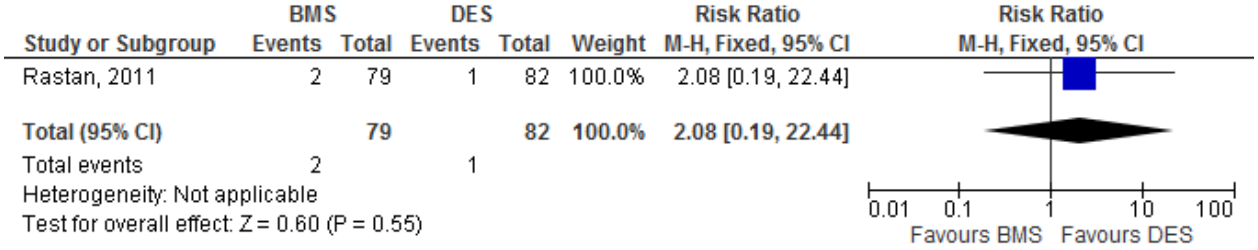


Figure 116 – Forest plot of bare-metal stent versus drug-eluting stent: IC, infra-geniculate lesions, outcome: 1.1 Amputation at 1200 days.

Study or Subgroup	BMS Events	BMS Total	Control Events	Control Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Rastan, 2012	2	44	0	38	100.0%	6.60 [0.40, 108.15]
Total (95% CI)		**44**		**38**	**100.0%**	**6.60 [0.40, 108.15]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.32 (P = 0.19)

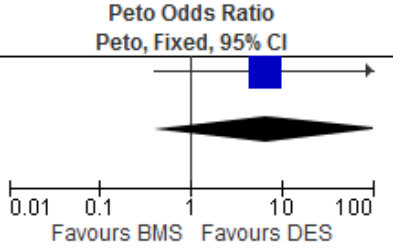


Figure 117 –Forest plot of bare-metal stent versus drug-eluting stent: IC, infra-geniculate lesions, outcome: 1.1 Re-intervention at 1 year.

Study or Subgroup	BMS Events	BMS Total	DES Events	DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rastan, 2011	7	79	8	82	100.0%	0.91 [0.35, 2.39]
Total (95% CI)		**79**		**82**	**100.0%**	**0.91 [0.35, 2.39]**
Total events	7		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.85)

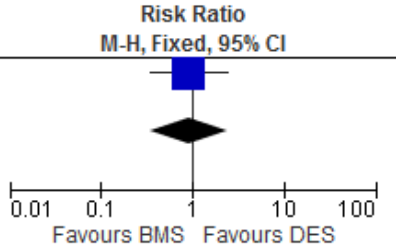


Figure 118 – Forest plot of bare-metal stent versus drug-eluting stent: IC, infra-geniculate lesions, outcome: 1.1 TLR at 12 months in patients.

Study or Subgroup	BMS Events	BMS Total	DES Events	DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rastan, 2011	8	46	2	40	100.0%	3.48 [0.78, 15.44]
Total (95% CI)		**46**		**40**	**100.0%**	**3.48 [0.78, 15.44]**
Total events	8		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)

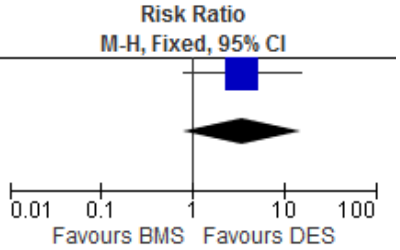
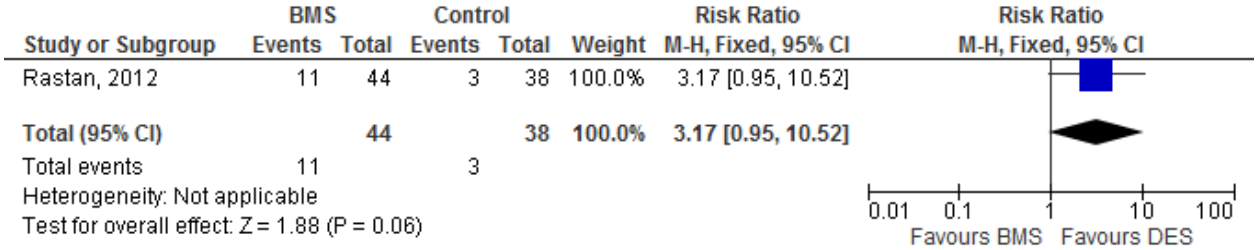


Figure 119 – Forest plot of bare-metal stent versus drug-eluting stent: IC, infra-geniculate lesions, outcome: 1.1 TVR at 1200 days.



6.3.3. Criticial Limb Ischemia, infra-geniculate lesions

Figure 120 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 Mortality (hazard ratio).

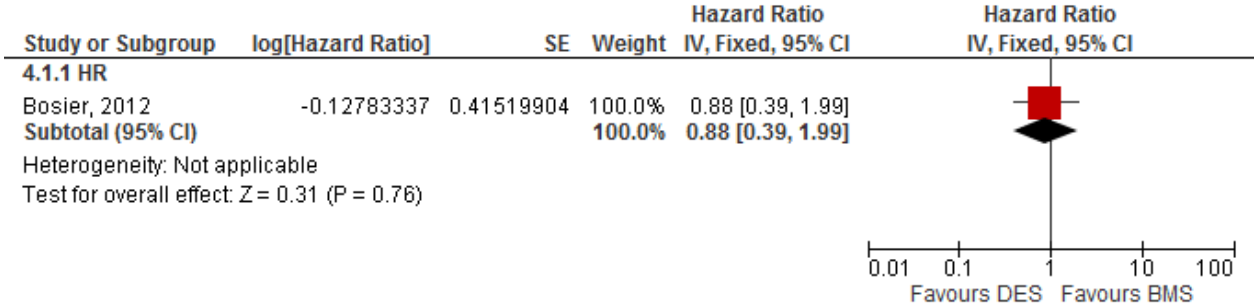


Figure 121 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 Mortality at 12 months.

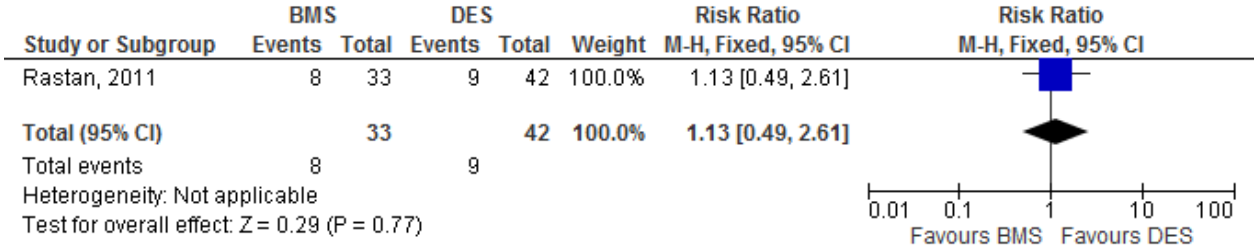


Figure 122 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 Mortality at 1200 days.

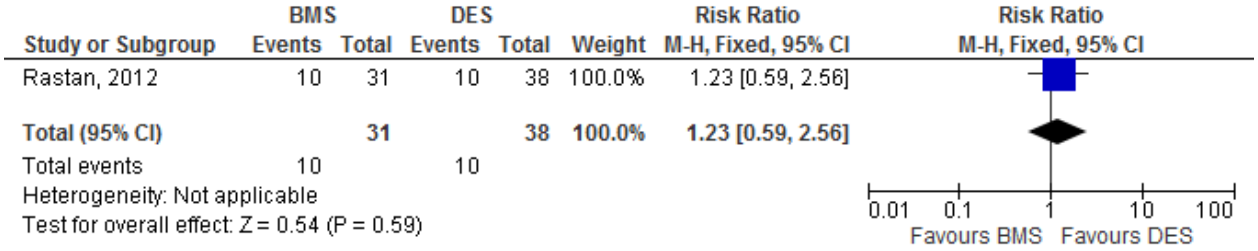


Figure 123 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 Amputation at 12 months.

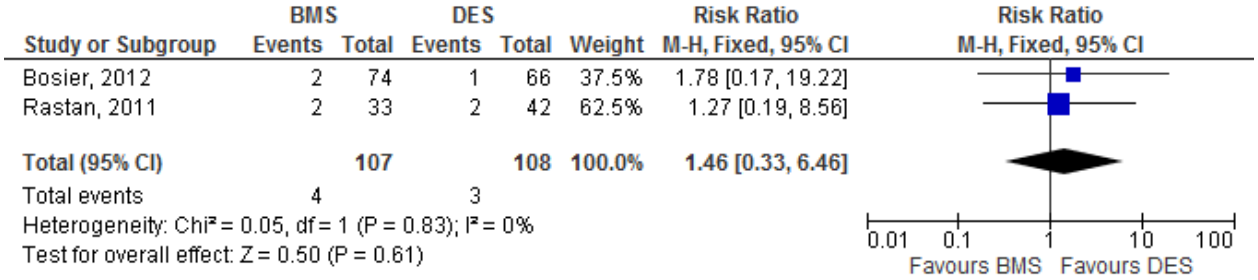


Figure 124 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 Amputation at 1200 days.

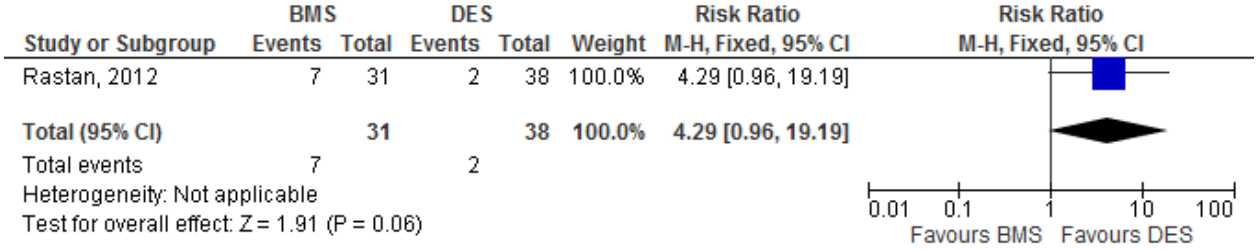


Figure 125 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 TLR (hazard ratio)

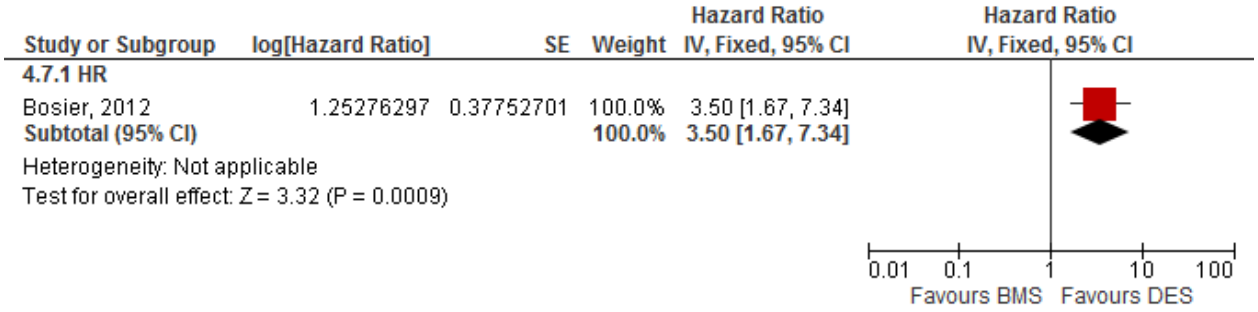


Figure 126 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 TLR by patient at 12 months.

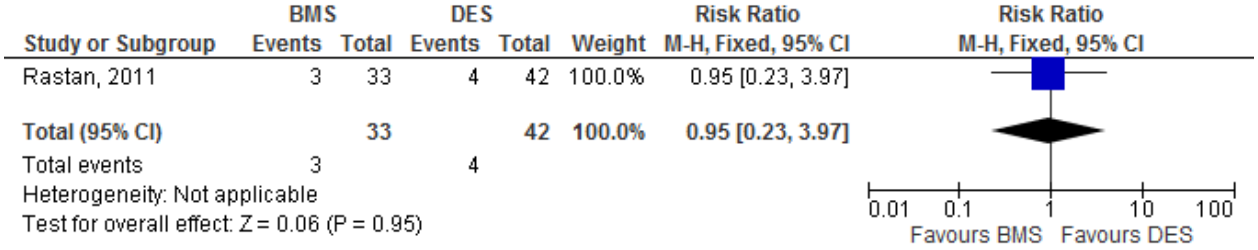


Figure 127 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, infra-geniculate lesions, outcome: 1.1 TVR at 1200 days.

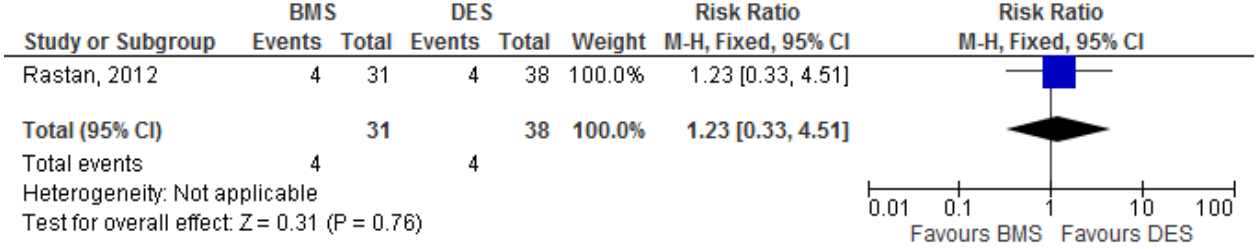
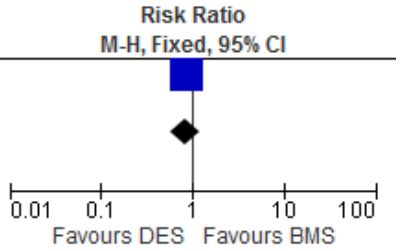


Figure 128 – Forest plot of bare-metal stent versus drug-eluting stent: CLI, femoro-popliteal lesions, outcome: 1.1 Wound healing at 12 months

Study or Subgroup	BMS Events	BMS Total	DES Events	DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rastan, 2011	14	21	19	24	100.0%	0.84 [0.58, 1.21]
Total (95% CI)		**21**		**24**	**100.0%**	**0.84 [0.58, 1.21]**
Total events	14		19			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.92 (P = 0.36)



6.4. Autologous vein versus prosthetic bypass

Figure 129 – Forest plot of autologous vein versus prosthetic bypass: IC, femoro-popliteal lesions, outcome: 1.1 Mortality at 30 days

Study or Subgroup	Autologous vein Events	Autologous vein Total	Prosthetic bypass Events	Prosthetic bypass Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Ballotta, 2003	0	51	0	51		Not estimable
Klinkert et al, 2002	0	75	0	76		Not estimable
Solakovic, 2008	0	60	0	61		Not estimable
Total (95% CI)		**186**		**188**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

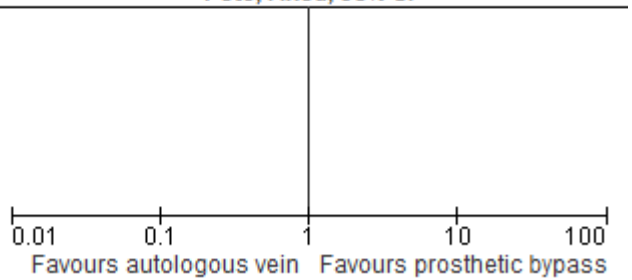


Figure 130 – Forest plot of autologous vein versus prosthetic bypass: IC, femoro-popliteal lesions, outcome: 1.1 Mortality at 2 years

Study or Subgroup	Autologous vein Events	Total	Prosthetic bypass Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tofigh, 2007	6	47	6	49	100.0%	1.04 [0.36, 3.00]
Total (95% CI)		**47**		**49**	**100.0%**	**1.04 [0.36, 3.00]**
Total events	6		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.08 (P = 0.94)

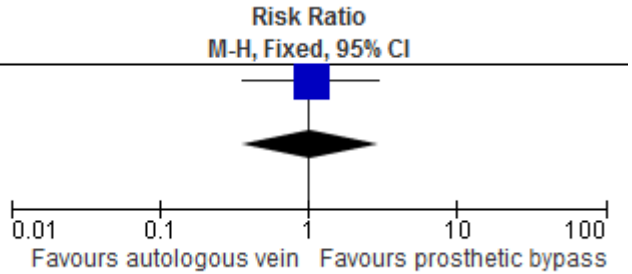


Figure 131 – Forest plot of autologous vein versus prosthetic bypass: IC, femoro-popliteal lesions, outcome: 1.1 Amputation at 30 days

Study or Subgroup	Autologous vein Events	Total	Prosthetic bypass Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Ballotta, 2003	0	51	0	51		Not estimable
Total (95% CI)		**51**		**51**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

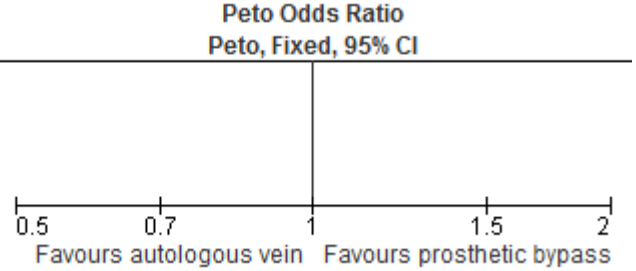


Figure 132 – Forest plot of autologous vein versus prosthetic bypass: IC, femoro-popliteal lesions, outcome: 1.1 Amputation at 5 years

Study or Subgroup	Autologous vein Events	Total	Prosthetic bypass Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ballotta, 2003	0	51	0	51		Not estimable
Klinkert et al, 2002	2	75	2	76	50.0%	1.01 [0.15, 7.01]
Solakovic, 2008	2	60	2	61	50.0%	1.02 [0.15, 6.99]
Total (95% CI)		**186**		**188**	**100.0%**	**1.01 [0.26, 3.97]**
Total events	4		4			

Heterogeneity: Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.02 (P = 0.98)

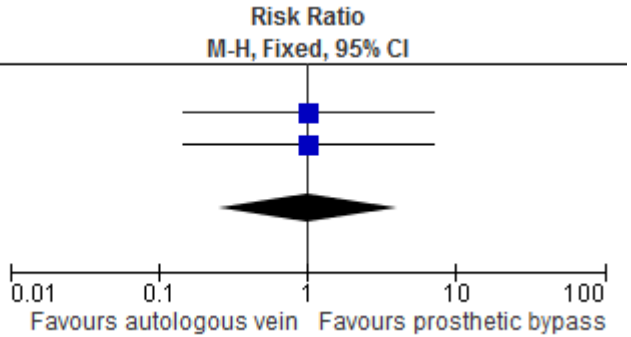


Figure 133 – Forest plot of autologous vein versus prosthetic bypass: IC, femoro-popliteal lesions, outcome: 1.1 Re-intervention at 2 years

Study or Subgroup	Autologous vein Events	Total	Prosthetic bypass Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burger et al, 2000	1	75	4	76	100.0%	0.25 [0.03, 2.21]
Total (95% CI)		**75**		**76**	**100.0%**	**0.25 [0.03, 2.21]**
Total events	1		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.21)

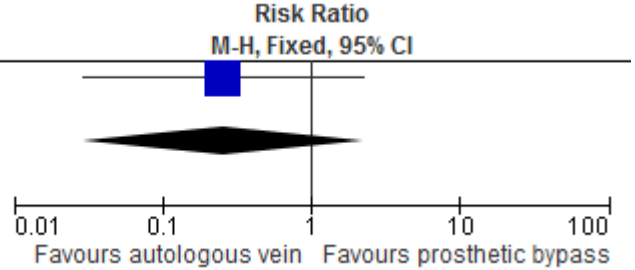


Figure 134 – Forest plot of autologous vein versus prosthetic bypass: IC, femoro-popliteal lesions, outcome: 1.1 Re-intervention at 5 years

	Autologous vein		Prosthetic bypass			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Ballotta, 2003	1	51	5	51	15.2%	0.20 [0.02, 1.65]
Klinkert et al, 2002	5	75	16	76	48.5%	0.32 [0.12, 0.82]
Solakovic, 2008	4	60	12	61	36.3%	0.34 [0.12, 0.99]
Total (95% CI)		**186**		**188**	**100.0%**	**0.31 [0.16, 0.60]**
Total events	10		33			

Heterogeneity: Chi² = 0.19, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 3.43 (P = 0.0006)

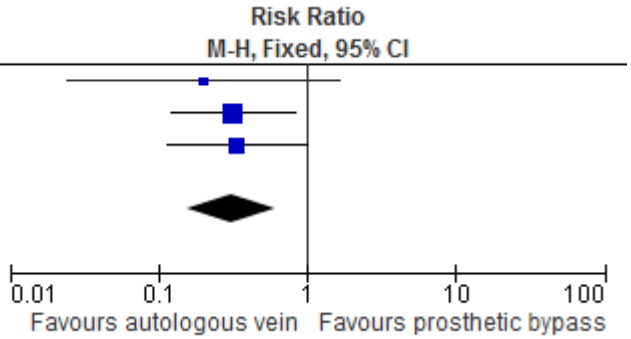
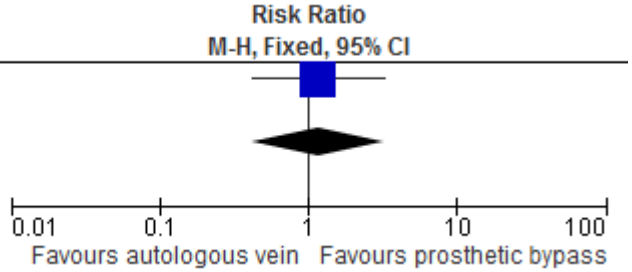


Figure 135 – Forest plot of autologous vein versus prosthetic bypass: IC, femoro-popliteal lesions, outcome: 1.1 Peri-operative complications at 30 days

	Autologous vein		Prosthetic bypass			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Ballotta, 2003	7	51	6	51	100.0%	1.17 [0.42, 3.23]
Total (95% CI)		**51**		**51**	**100.0%**	**1.17 [0.42, 3.23]**
Total events	7		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.30 (P = 0.77)



6.5. Drug-coated balloon angioplasty

6.5.1. Drug coated balloons vs uncoated balloons – IC and CLI, femoro-popliteal lesions

Figure 136 – Forest plot of drug coated balloons versus uncoated balloons: IC and CLI, femoro-popliteal lesions, outcome: 1.1 Mortality at 6 months

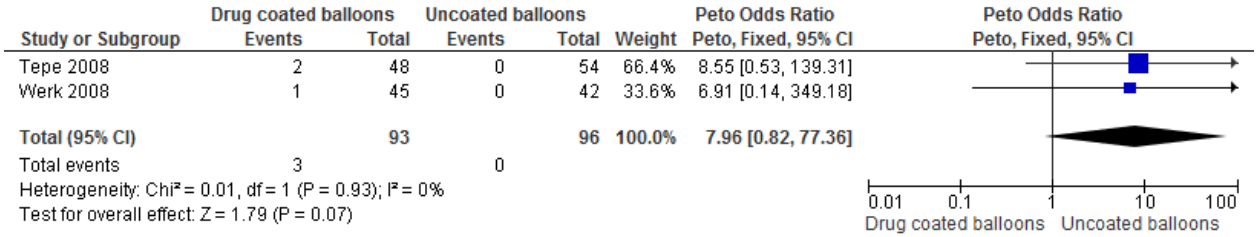


Figure 137 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Mortality at 18 to 24 months

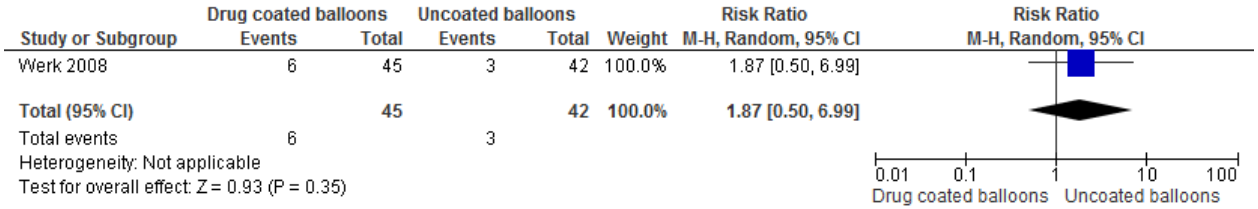


Figure 138 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Amputation at 6 months

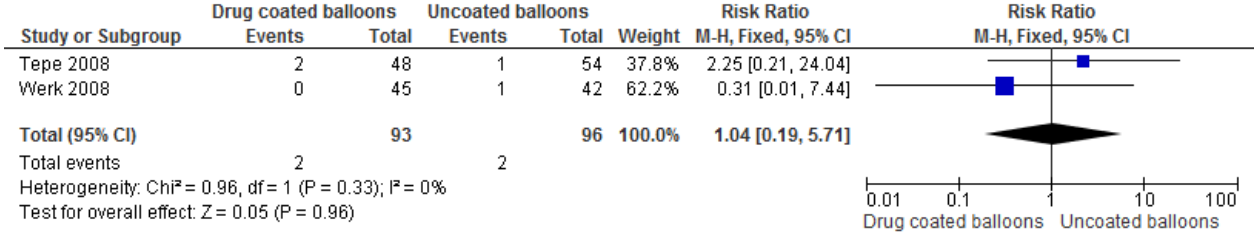


Figure 139 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Amputation at 18 to 24 months

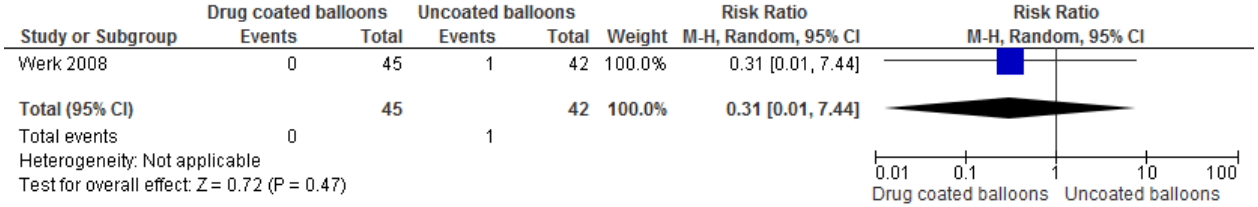


Figure 140 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Target lesion revascularization at 6 months

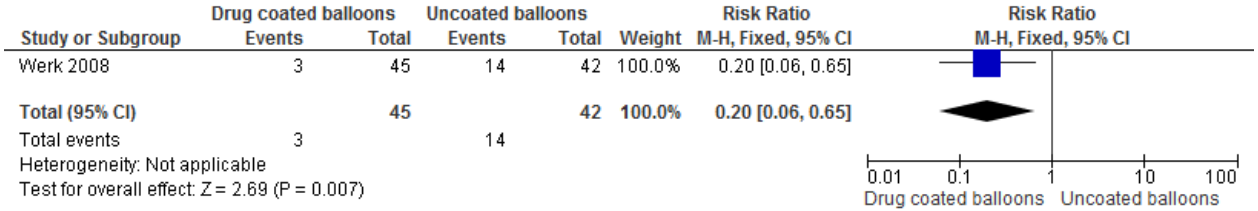


Figure 141 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Target lesion revascularization at 12 months

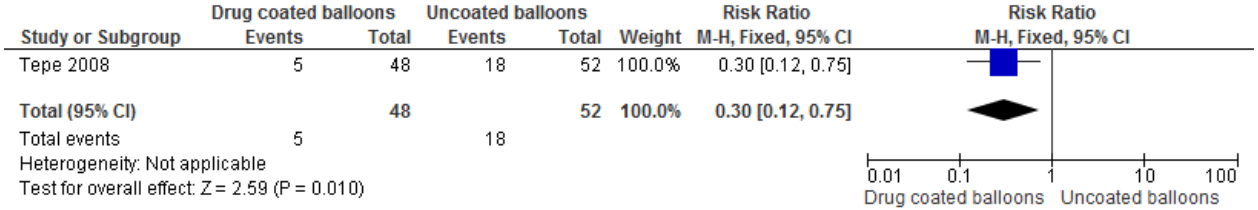


Figure 142 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Target lesion revascularization at 18 to 24 months

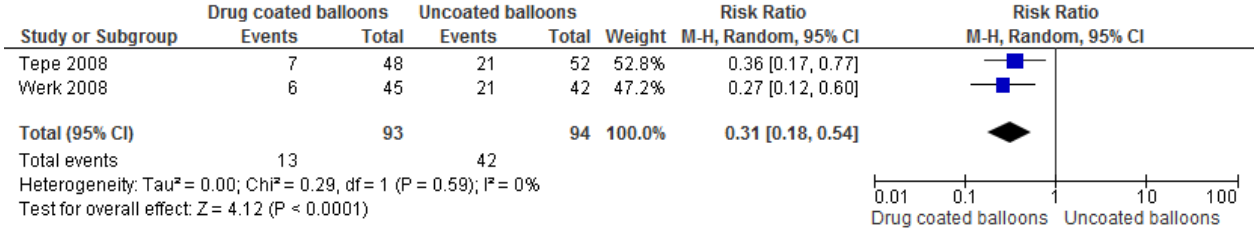


Figure 143 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Serious adverse events up to 2 weeks

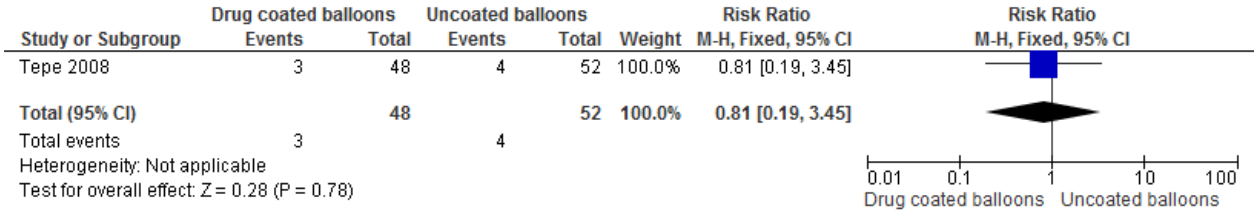
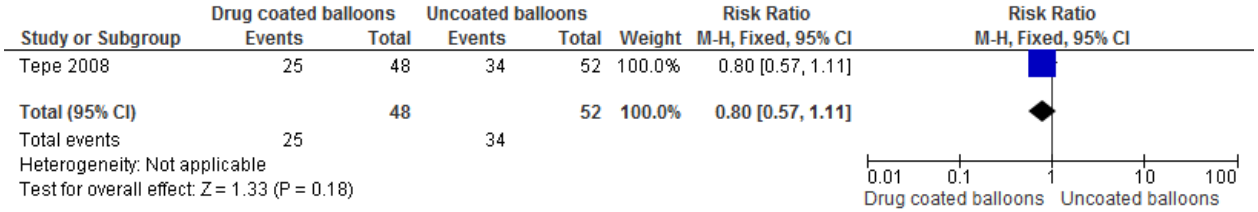


Figure 144 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Serious adverse events at 6 months



6.5.2. Drug coated balloons vs uncoated balloons with drug contrast medium – IC and CLI, femoro-popliteal lesions

Figure 145 – Forest plot of drug coated balloons versus uncoated balloons: IC and CLI, femoro-popliteal lesions, outcome: 1.1 Mortality at 6 months

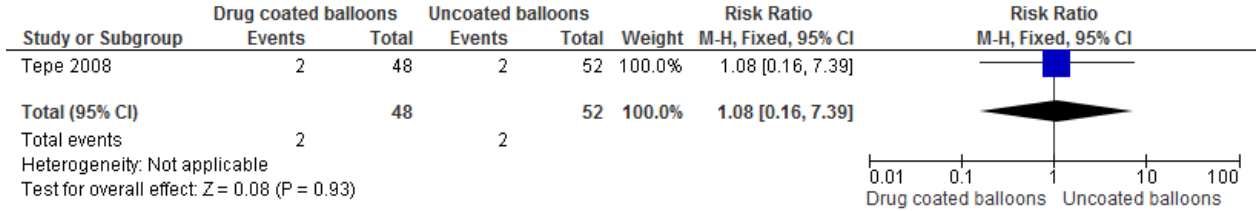


Figure 146 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Amputation at 6 months

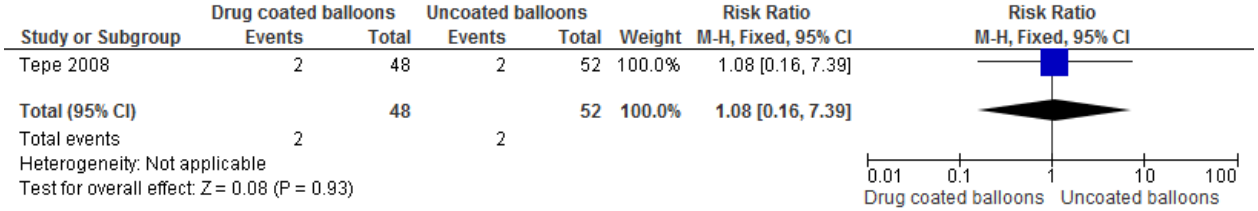


Figure 147 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Target lesion revascularization at 12 months

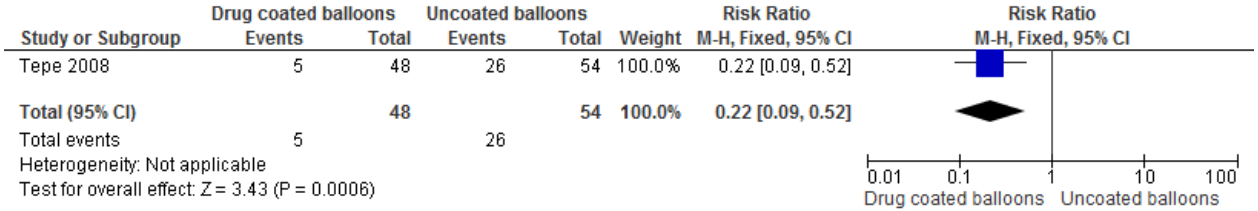


Figure 148 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Target lesion revascularization at 18 to 24 months

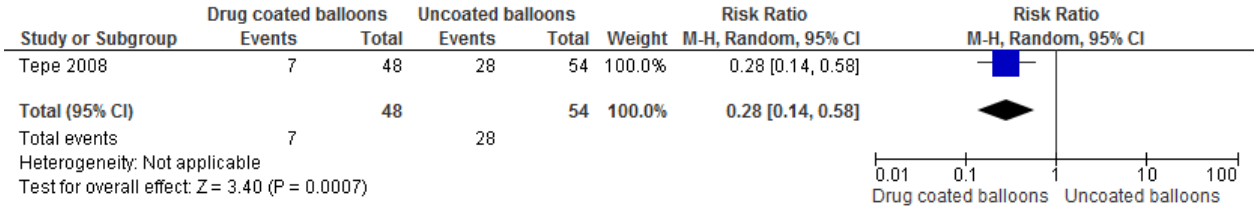


Figure 149 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Serious adverse events up to 2 weeks

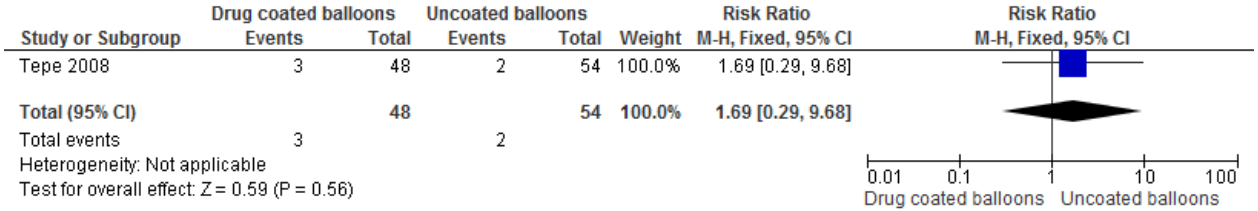
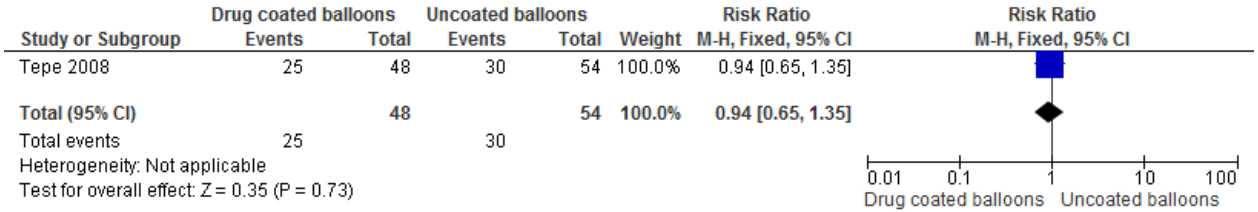


Figure 150 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal lesions, outcome: 1.1 Serious adverse events at 6 months



6.5.3. Drug coated balloons vs uncoated balloons– IC and CLI, femoro-popliteal and infra-popliteal lesions

Figure 151 – Forest plot of drug coated balloons versus uncoated balloons: IC and CLI, femoro-popliteal and infra-popliteal lesions, outcome: 1.1 Mortality at 6 months

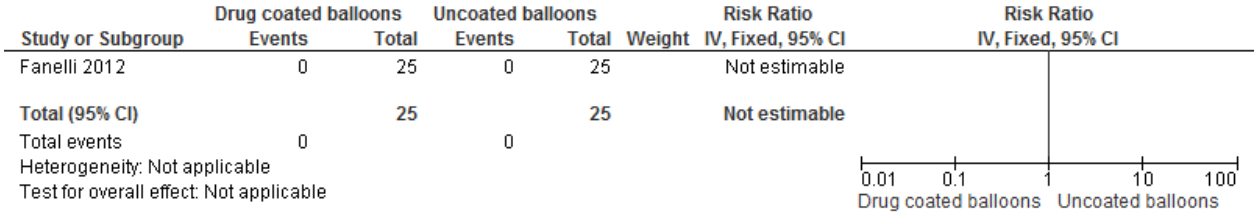


Figure 152 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal and infra-popliteal lesions, outcome: 1.1 Amputation at 6 months

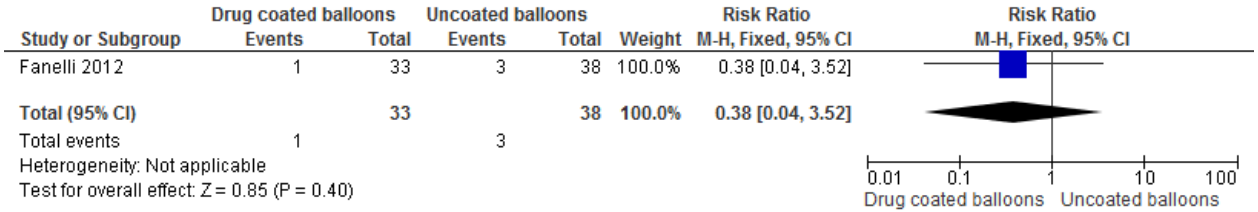


Figure 153 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal and infra-popliteal lesions, outcome: 1.1 Target lesion revascularization at 6 months

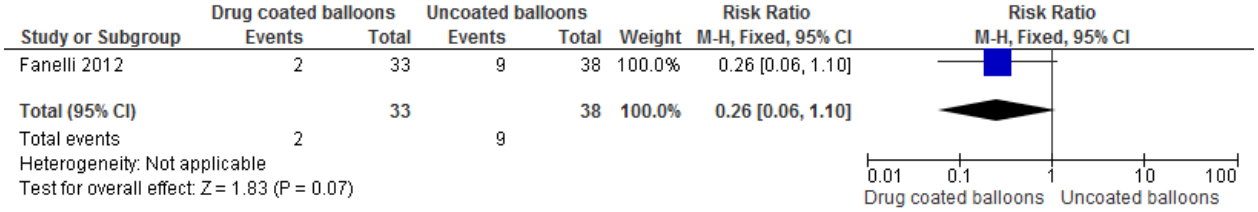
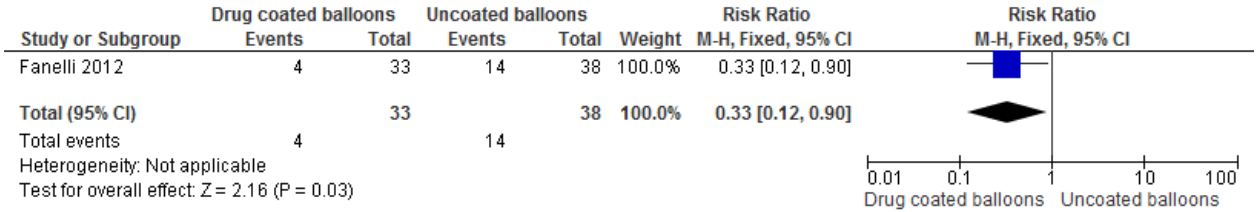


Figure 154 – Forest plot of drug coated balloons versus uncoated balloons: IC, femoro-popliteal and infra-popliteal lesions, outcome: 1.1 Total major adverse events at 6 months



6.5.4. Drug coated balloons vs uncoated balloons – diabetic patients with CLI, infra-popliteal lesions

Figure 155 – Forest plot of drug coated balloons versus uncoated balloons: diabetic patients with CLI, infra-popliteal lesions, outcome: 1.1 Mortality at 12 months (by no. of people)

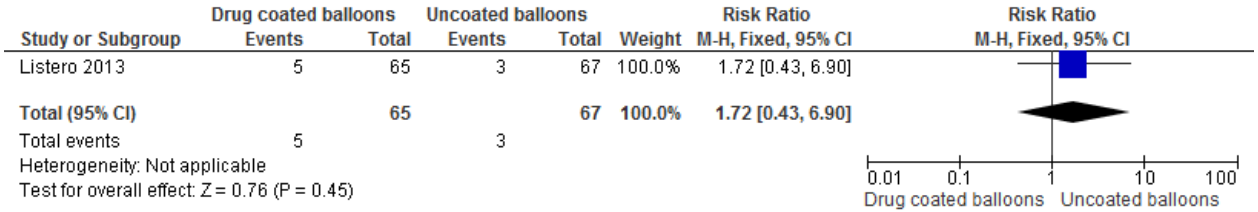


Figure 156 – Forest plot of drug coated balloons versus uncoated balloons: diabetic patients with CLI, infra-popliteal lesions, outcome: 1.1 Major amputation at 12 months (by no. of limbs)

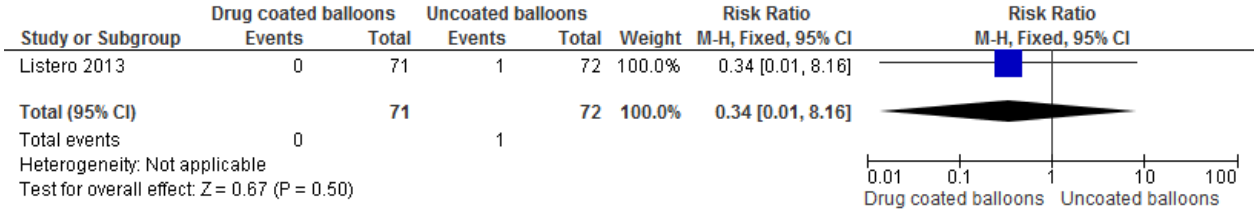


Figure 157 – Forest plot of drug coated balloons versus uncoated balloons: diabetic patients with CLI, infra-popliteal lesions, outcome: 1.1 Minor amputation at 12 months (by no. of limbs)

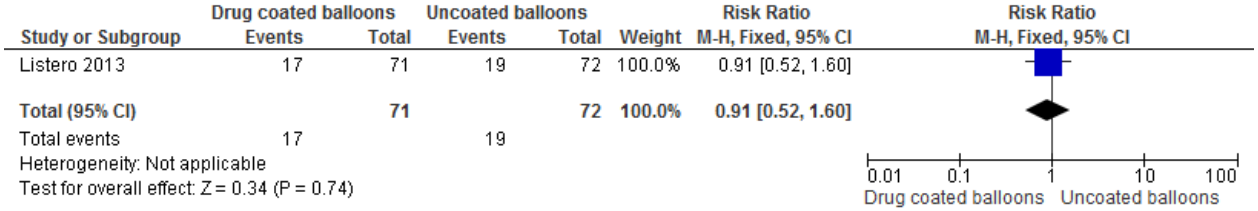


Figure 158 – Forest plot of drug coated balloons versus uncoated balloons: diabetic patients with CLI, infra-popliteal lesions, outcome: 1.1 Major adverse events at 12 months

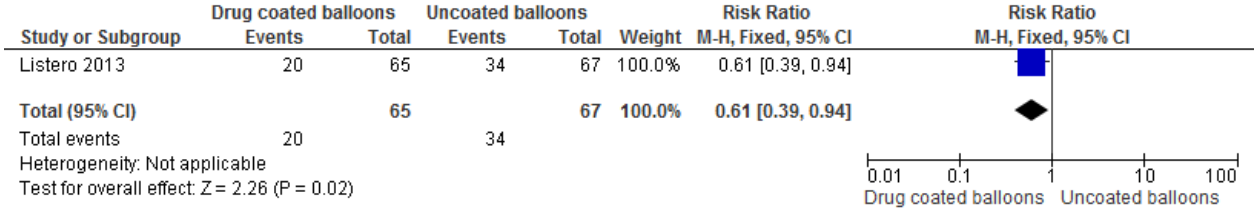


Figure 159 – Forest plot of drug coated balloons versus uncoated balloons: diabetic patients with CLI, infra-popliteal lesions, outcome: 1.1 Complete index ulcer healing at 12 months

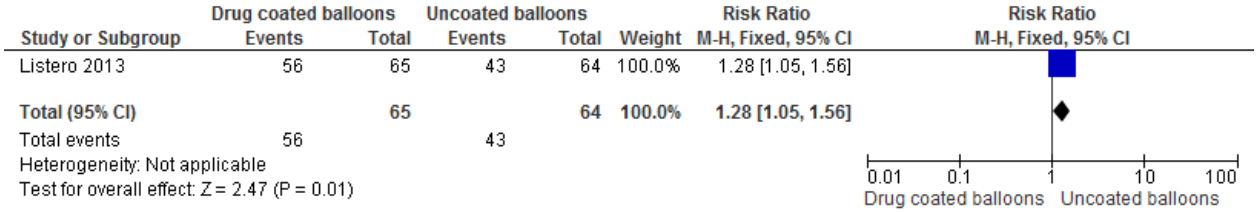
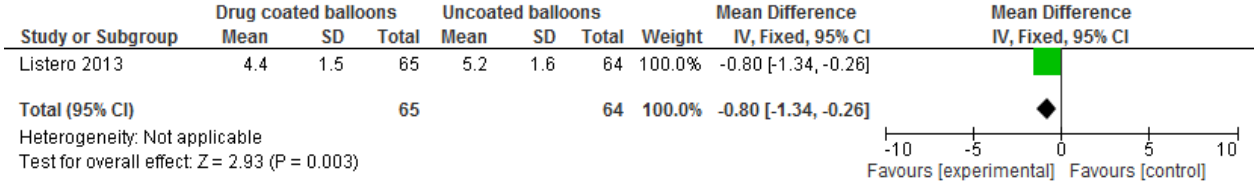


Figure 160 – Forest plot of drug coated balloons versus uncoated balloons: diabetic patients with CLI, infra-popliteal lesions, outcome: 1.1 Time to complete index ulcer healing at 12 months



7. METHODS FOR META-ANALYSIS

7.1. Diagnostic meta-analysis

Diagnostic meta-analysis was conducted where 5 or more similar studies were identified that compared the index test to the reference standard. The test accuracy for the studies was pooled using the bivariate method modelled in WinBUGS® by; the advantage of this approach is that it produces summary estimates of sensitivity and specificity that account for the correlation between the two. Other advantages of this method have been described elsewhere[119,161,162].

Analysis

The bivariate method utilises a logistic regression on the true positives, true negatives, false positives and false negatives reported in the sudies and is parameterised as follows[119,161,162]:

The model above was fitted in WinBUGS®. Using the output from WinBUGS®, we constructed and plotted confidence regions and, where appropriate ROC curves, using methods outlined by Novelli et al[107] in Microsoft Excel®.

As it was a Bayesian analysis, the evidence distribution is weighted by a distribution of prior beliefs. Vague non-informative priors were used for all parameters. For each analysis, a series of 50,000 burn-in simulations were run to allow convergence and then a further 100,000 simulations were run to produce the outputs. Convergence was assessed by investigating density plots, auto correlation plots and history plots for parameters of interest. Where appropriate, additional simulations were run.

In cases where cell counts were 0, 1 was added to each category (true positives, false positives, true negatives, false negatives) to ensure the model was able to run, whilst not significantly distorting the results.

WinBUGS® code

Model

```
{

for (i in 1:NS)

        {

        TotP[i]<-TP[i] + FN[i]
        TotN[i]<-FP[i] + TN[i]
        TP[i] ~ dbin(p[i , 1] , TotP[i])
        TN[i] ~ dbin(p[i , 2]  , TotN[i])

                for (j in 1:2)

                {
                logit(p[i , j]) <- MeanS[i , j]
                }
MeanS[i , 1:2] ~ dmnorm(md[] , sigma[,])
        }
        sigma[1:2,1:2]~dwish(R[,] , 2)
        Sigma.sq[1:2,1:2] <- inverse(sigma[,])

                for (i in 1:2)
                        {
                        parms[i] <- exp(md[i])/(1+exp(md[i]))
                        }

        sens <- parms[1]
        spec<- parms[2]


                for (i in 1:2)
                        {
                        md[i] ~ dnorm(0 , 0.001)
                        }
```

```
                    sensitivity.bar <- exp(md[1])/(1+ exp(md[1]))
            specificity.bar <- exp(md[2])/(1+exp(md[2]))


    }


}
```

Data

```
list(NS= Number of studies goes here)

list(R = structure(
        .Data = c(1, 0,
              0, 1), .
        Dim = c(2, 2))
```

Cell Counts for each strategy are entered below, in place of the ni values

TP=True positives
FP=False positives
FN=False negatives
TN=True negatives

```
TP[]    FP[]    FN[]    TN[]
n1      n2      n3      n4
END
```

Initial conditions

```
list(md=c(0,0))
```

8. CONSULTATION OF STAKEHOLDERS

Each recommendation was scored on a 5-point scale indicating the stakeholder's agreement with the recommendation: a score of '1' indicates 'completely disagree', '2' indicates 'somewhat disagree', '3' indicates 'unsure', '4' indicates 'somewhat agree', and '5' indicates 'completely agree'. The scores were anonymized and summarized into a median score, range and % of 'agree'-scores (score '4' and '5'), and served as a basis for the discussion during the stakeholders meeting.

The results are presented below, together with the final decisions (to be read at zoom level 190%).

Item	Recommendation(s)	Strength	Level of evidence	Min	Max	Med	%4-5	Comments	Decision
Imaging for revascularization in peripheral arterial disease	Offer duplex ultrasound as first-line imaging to all people with peripheral arterial disease for whom revascularisation is being considered	Weak	Low - Very low	2	4	3	25%	03: Very low level of evidence that duplex ultrasound acutally guides the work up in patients in whom revascularieation is considered.	**Consider** duplex ultrasound as first-line imaging **in** people with **intermittent claudication** for whom revascularisation is being considered
	Offer contrast-enhanced magnetic resonance angiography to people with peripheral arterial disease who need further imaging (after duplex ultrasound) before considering revascularisation	Strong	Moderate - Low	4	5	4,5	100%		Recommendation accepted
	Offer computed tomography angiography to people with peripheral arterial disease who need further imaging (after duplex ultrasound) if contrast-enhanced magnetic resonance angiography is contraindicated or not tolerated	Strong	Moderate - Low	3	5	4,5	75%		Recommendation accepted
Management of intermittent claudication	Consider a trial of best medical treatment including supervised exercise in patients presenting with intermittent claudication	Weak	Very low	2	5	4	50%		Recommendation accepted
	If after a trial of best medical treatment including supervised exercise treatment clinical results are insufficient in patients with intermittent claudication, then consider angioplasty or bypass surgery in addition, taking into account the following factors: • Type and length of lesion; • Availability of vein; • Patient preferences; • Symptoms; • Expertise of medical team	Weak	Very low	2	5	3	50%	03: This is a critical issue: in whom should revascularisation (angioplasty or surgery) be considered? I would add a comment. In general, revascularisation should only be considered in patients with significant disability, (i.e. inability to perform normal work or serious impairment of activities important to the patient.)This criteria should be dominant over "type of lesion, availability of vein, expertise of the medical team	If after a trial of best medical treatment including supervised exercise treatment clinical results are insufficient in patients with **incapacitating** intermittent claudication, then consider angioplasty or bypass surgery in addition, taking into account the following factors: • Type and length of lesion; • Availability of vein; • Patient preferences; • Symptoms; • Expertise of medical team
	Consider primary stenting in patients with intermittent claudication due to aorto-iliac disease undergoing revascularization with angioplasty	Weak	Very low	3	4	3,5	50%	02: If associated with aneurysm, consider covered stent	Recommendation accepted
	Consider primary stenting in patients with intermittent claudication due to femoropopliteal disease undergoing revascularization with angioplasty, taking into account the following factors: • Length of the lesion; • Complexity of the lesion; • Calcification; • Location	Weak	Low	3	5	3,5	50%	02: Factors should be defined, eg. What is indicated in short vs long lesions, calcified or not, stenosis vs. occlusion? 04: a lot of randomized trials show benefit for primary stenting in lesions longer than 5cm, DEB will probably change this approach as their results show better results than POBA	Consider primary stenting **or drug-coated balloon angioplasty** in patients with intermittent claudication due to femoropopliteal disease undergoing revascularization with angioplasty, taking into account the following factors: • Length of the lesion; • Complexity of the lesion; • Calcification; • Location
	In the absence of evidence based on RCTs, use bare metal stents in patients with intermittent claudication due to aorto-iliac disease undergoing revascularization with angioplasty and stenting	Strong	Very low	4	5	4,5	100%		Recommendation accepted
	Consider drug-eluting stents in patients with intermittent claudication due to femoropopliteal disease undergoing revascularization with angioplasty and stenting	Weak	Very low	3	4	3	25%	Argument against DES = few positive data + high cost	Consider **bare metal stents** in patients with intermittent claudication due to femoropopliteal disease undergoing revascularization with angioplasty and stenting
	Consider autologous vein grafting in patients with intermittent claudication due to femoropopliteal disease undergoing bypass surgery	Weak	Low	2	5	3,5	50%		Recommendation accepted
Management of critical limb ischemia	In addition to best medical treatment, offer angioplasty or bypass surgery for treating people with critical limb ischaemia who require revascularisation, taking into account factors including: • Comorbidities; • Pattern of disease; • Availability of a vein; • Patient preference; • Availability of technical expertise	Weak	Very low	3	5	5	75%		Recommendation accepted
	Consider primary stenting in patients with critical limb ischaemia due to aorto-iliac disease undergoing revascularization with angioplasty	Weak	Very low	3	5	4,5	75%		Recommendation accepted
	Consider primary stenting in patients with critical limb ischaemia due to femoropopliteal disease undergoing revascularization with angioplasty, taking into account the following factors: • Length of the lesion; • Complexity of the lesion; • Calcification; • Location	Weak	Very low	3	4	3,5	50%	02: Factors should be defined, eg. What is indicated in short vs long lesions, calcified or not, stenosis vs. occlusion?	Consider primary stenting **or drug-coated balloon angioplasty** in patients with critical limb ischaemia due to femoropopliteal disease undergoing revascularization with angioplasty, taking into account the following factors: • Length of the lesion; • Complexity of the lesion; • Calcification; • Location
	Consider drug-coated balloon angioplasty in patients with critical limb ischaemia due to femoropopliteal disease undergoing revascularization with angioplasty	Weak	Very low	3	4	3	25%	02: Cost-effective study is necessary in Belgium	Merge with previous recommendation
	Consider selective stenting in patients with critical limb ischaemia due to infrageniculate disease undergoing revascularization with angioplasty	Weak	Very low	3	5	3,5	50%	02: Only in failed POBA	Consider **balloon angioplasty with bail-out** stenting in patients with critical limb ischaemia due to infrageniculate disease undergoing revascularization with angioplasty
	In the absence of evidence based on RCTs, use bare metal stents in patients with critical limb ischemia due to aorto-iliac disease undergoing revascularization with angioplasty and stenting	Strong	Very low	3	5	4	75%	02: If associated with aneurysm, consider covered stent	In the absence of evidence based on RCTs, **don't** use **drug-eluting** stents in patients with critical limb ischemia due to aorto-iliac disease undergoing revascularization with angioplasty and stenting
	Consider drug-eluting stents in patients with critical limb ischemia due to femoropopliteal disease undergoing revascularization with angioplasty and stenting	Weak	Very low	3	3	3	0%	02: Positive emerging data but not enough for guidelines! Cost-effective study necessary	Consider **bare metal** stents in patients with critical limb ischemia due to femoropopliteal disease undergoing revascularization with angioplasty and stenting
	Consider drug-eluting stents in patients with critical limb ischemia due to infrageniculate disease undergoing revascularization with angioplasty and stenting	Weak	Very low	2	3	3	0%	02: Positive emerging data but not enough for guidelines! Cost-effective study necessary 03: According to my understanding and our discussion, in patients with infrageniculate disease, drug-eluting stents were not recommended.	Consider drug-eluting stents in patients with critical limb ischemia **and short, focal lesions** due to infrageniculate disease undergoing revascularization with angioplasty and stenting
	Consider autologous vein graft in patients with critical limb ischemia due to femoropopliteal or infrageniculate disease taking into account the following factors: • Availability of a vein; • Quality of the vein; • Location of the lesion (above or below the knee); • Comorbidity; • Urgency of the intervention	Weak	Very low	4	5	5	100%	02: When failed angioplasty	Recommendation accepted
Policy recommendation	The appropriateness of reimbursement of drug-coated balloons should be evaluated by means of a cost-effectiveness analysis using Belgian health care data			2	5	4,5	75%	04: in Germany they already did that	Recommendation accepted
	The appropriateness of reimbursement of supervised exercise treatment for patients with PAD and intermittent claudication should be evaluated by means of a cost-effectiveness analysis using Belgian health care data								Add this recommendation
Research recommendation	Future clinical studies should determine the subpopulations that have the highest benefit with drug-coated balloons			2	5	5	75%		Recommendation accepted
	Future clinical studies should confirm the few available positive data about the effectiveness of drug-eluting stents in patients with intermittent claudication or critical limb ischemia due to femoropopliteal disease, before the appropriateness of reimbursement can be evaluated								Add this recommendation

9. NOMENCLATURE CODES

9.1. Overview

AMB	HOS	Description NL	Description FR	Cost (01-01-2014)
Bypass surgery				
235093	235104	Revascularisatie van een slagader van de ledematen door endarteriëctomie, endoaneurysmorrhafie, pontage of resectie met enten of anastomose	Revascularisation d'une artère des membres par andartérectomie, endoanévrismorraphie, pontage ou résection, avec greffe ou anastomose	€ 508,01
235115	235126	Revascularisatie van een slagader van de ledematen door pontage of resectie, met enten van de vena saphena interna, inclusief het nemen van de ent	Revascularisation d'une artère des membres par pontage ou résection avec greffe de la saphène interne, y compris la prise du greffon	€ 762,01
235211	235222	Revascularisatie van een tibiale slagader met prothese of met autologe vaatent, inclusief het nemen van de ent, te bewijzen met postoperatieve angiografie	Revascularisation d'une artère tibiale avec prothèse ou avec greffe vasculaire, y compris le prélèvement du greffon, à démontrer par angiographie postopératoire	€ 952,51
237031	237042	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies illiaques bilatérales	€ 952,51
237053	237064	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën, geassocieerd met een andere vasculaire reconstructie, met uitzondering van de iliacale (bij voorbeeld : mesenteriale, renale of femorale revascularisatie)	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies illiaques bilatérales, associées à une autre reconstruction vasculaire, à l'exception des illiaques (par exemple : revascularisation mésentérique, rénale ou fémorale)	€ 1.079,52
237075	237086	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën, geassocieerd met verscheidene vasculaire reconstructies, met uitzondering van de iliacale	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies iliaques bilatérales, associées à une reconstruction vasculaire multiple, iliaque exceptée	€ 1.270,02

AMB	HOS	Description NL	Description FR	Cost (01-01-2014)
237171	237182	Unilaterale aortofemorale, aorto-iliacale of iliacofemorale overbrugging	Pontage aortofémoral, aorto-iliacal ou iliacofémoral unilatéral	€ 889,01
715676	715680	Vaatent gebruikt voor femoro-popliteale bypass (boven de knie)	Greffe vasculaire utilisée pour un bypass fémoro-poplité (au-dessus du genou)	€ 800,81
715713	715724	Vaatent gebruikt voor femoro-distale bypass	Greffe vasculaire utilisée pour un bypass fémoro-distal	€ 1.226,24
715750	715761	Vaatent gebruikt voor aorta-iliacale bypass	Greffe vasculaire utilisée pour un bypass aorto-iliaque	€ 600,61
715772	715783	Vaatent gebruikt voor aorta-femorale bypass	Greffe vasculaire utilisée pour un bypass aorto-fémoral	€ 600,61
715794	715805	Vaatent gebruikt voor ilio-femorale bypass	Greffe vasculaire utilisée pour un bypass ilio-fémoral	€ 600,61
715956	715960	Rechte vaatent gebruikt voor vasculaire bypass, die niet gedefinieerd is in de verstrekkingen 715676-715680, 715691-715702, 715713-715724, 715735-715746, 715750-715761, 715772-715783, 715794-715805, 715816-715820, 715831-715842, 715853-715864, 715875-715886, 715890-715901, 715912-715923 en 715934-715945	Greffe vasculaire droite utilisée pour un bypass vasculaire, qui n'est pas défini dans les prestations 715676-715680, 715691-715702, 715713-715724, 715735-715746, 715750-715761, 715772-715783, 715794-715805, 715816-715820, 715831-715842, 715853-715864, 715875-715886, 715890-715901, 715912-715923 et 715934-715945	€ 600,61
Angioplasty				
589050	589061	Percutane endovasculaire dilatatie met of zonder plaatsing van stents(s) onder controle door medische beeldvorming van een artiriële vernauwing en/of occlusie inclusief de manipulaties en controles tijdens de behandeling en al het gebruikte materieel, exclusief de dilatatiecatheter(s), de farmaca en en de contrastmiddelen . Voor de andere slagaders dan de coronaire	Dilatation endovasculaire percutanée avec ou sans placement de stent(s) sous contrôle d'imagerie médicale d'une sténose et/ou occlusion d'une artère, y compris les manipulations et contrôles pendant le traitement et tout le matériel utilisé, à l'exclusion du ou des cathéter(s) de dilatation et des produits pharmaceutique et de contraste . Pour les artères autres que les artères coronaires	€ 610,69
589072	589083	Bijkomend honorarium bij de verstrekking nr 589050 - 589061 voor de dilatatie van een of meerdere bijkomende vernauwing(en) van een andere arteriële as, voor de andere slagaders dan de coronaire, maximum per operatiezitting	Honoraires supplémentaires lors de la prestation n° 589050 - 589061 pour la dilatation d'une ou plusieurs sténose(s) complémentaire(s) d'un autre axe artériel, pour les artères autres que les coronaires, maximum par séance opératoire	€ 305,35

AMB	HOS	Description NL	Description FR	Cost (01-01-2014)
589094	589105	Percutane endovasculaire dilatatie onder controle door medische beeldvorming van een arteriële vernauwing en/of occlusie, inclusief de manipulaties en controles, tijdens de behandeling en al het gebruikte materieel, exclusief de dilatatiecatheter(s), de farmaca en de contrastmiddelen. Voor de andere slagaders dan de coronaire tijdens een heelkundige bewerking, maximum per operatiezitting	Dilatation endovasculaire percutanée sous contrôle d'imagerie médicale d'une sténose et/ou occlusion d'une artère, y compris les manipulations et contrôles pendant le traitement et tout le matériel utilisé, à l'exclusion du ou des cathéter(s) de dilatation et des produits pharmaceutiques et de contraste Pour les artères autres que les coronaires au cours d'une intervention chirurgicale, maximum par séance opératoire	€ 343,51
683616	683620	Geheel van dilatatiemateriaal en stent(s) gebruikt bij revascularisatie van de onderste ledematen, aorto-iliacaal, femoraal, (infra)popliteaal niveau	Ensemble du matériel de dilatation et du (des) stent(s) utilisés lors de la revascularisation des membres inférieurs, niveau aorto-iliaque, fémoral, (infra) poplité	€ 1.401,42
683653	683664	Geheel van dilatatiemateriaal en stent(s) gebruikt bij revascularisatie van een arterie aan de contralaterale zijde of van een andere anatomische as, met uitzondering van de carotisbloedvaten	Ensemble du matériel de dilatation et du (des) stent(s) utilisés lors de la revascularisation d'une artère controlatérale ou d'un autre axe anatomique, à l'exception des vaisseaux carotidiens	€ 1.021,04
683734	683745	Geheel van dilatatiemateriaal gebruikt bij revascularisatie van de onderste ledematen, aorto-iliacaal, femoraal, (infra)popliteaal niveau	Ensemble du matériel de dilatation utilisé lors de la revascularisation des membres inférieurs, niveau aorto-iliaque, fémoral, (infra) poplité	€ 464,92
683771	683782	Geheel van dilatatiemateriaal gebruikt bij revascularisatie van een arterie aan de contralaterale zijde of van een andere anatomische as, met uitzondering van de carotisbloedvaten	Ensemble du matériel de dilatation utilisé lors de la revascularisation d'une artère controlatérale ou d'un autre axe anatomique, à l'exception des vaisseaux carotidiens	€ 258,29

9.2. Evolution of use of nomenclature codes

Code	2008	2009	2010	2011
235093-235104	€ 2.218.014,66	€ 2.331.543,39	€ 2.396.932,93	€ 2.365.939,29
235115-235126	€ 1.099.952,08	€ 1.073.181,44	€ 921.644,25	€ 891.557,12
235211-235222	€ 1.096.748,44	€ 1.135.029,51	€ 1.153.943,27	€ 1.094.837,23
237031-237042	€ 428.882,33	€ 440.822,24	€ 346.998,43	€ 372.498,29
237053-237064	€ 368.984,08	€ 306.259,73	€ 281.662,06	€ 251.117,88
237075-237086	€ 1.896.246,52	€ 2.075.529,39	€ 1.042.217,56	€ 1.097.483,26
237171-237182	€ 810.515,20	€ 770.121,31	€ 783.588,19	€ 838.967,64
715676-715680				€ 280.103,38
715713-715724				€ 330.137,99
715750-715761				€ 37.762,43
715772-715783				€ 16.731,90
715794-715805				€ 106.069,78
715956-715960				€ -
Bypass surgery	**€ 7.919.343,31**	**€ 8.132.487,01**	**€ 6.926.986,69**	**€ 7.683.206,19**
589050-589061	€ 9.233.218,00	€ 9.509.370,27	€ 10.363.405,28	€ 11.088.693,99
589072-589083	€ 1.730.351,39	€ 1.888.956,09	€ 2.257.235,53	€ 2.369.629,12
589094-589105	€ 593.464,46	€ 685.508,60	€ 484.776,48	€ 507.503,75
683616-683620	€ 17.419.951,16	€ 16.558.913,64	€ 14.761.522,06	€ 15.604.149,66
683653-683664	€ 2.607.131,30	€ 2.713.356,41	€ 2.297.311,72	€ 2.453.925,57
683734-683745	€ 2.607.965,78	€ 2.966.015,05	€ 3.313.382,29	€ 3.431.168,67
683771-683782	€ 608.266,54	€ 785.170,03	€ 1.036.197,54	€ 1.106.038,07
Angioplasty	**€ 34.800.348,63**	**€ 35.107.290,09**	**€ 34.513.830,90**	**€ 36.561.108,83**

10. RIZIV/INAMI EXPENDITURE ANALYSIS

10.1. Case selection

All hospital stays of 2012, one day and inpatient, with at least one of the nomenclature numbers in Table 10 are selected.

Table 10 – RIZIV-INAMI nomenclature selection codes

Group	Code	Label NL	Label FR
Surgery	235093	Revascularisatie van een slagader van de ledematen door endarteriëctomie, endoaneurysmorrhafie, pontage of resectie met enten of anastomose	Revascularisation d'une artère des membres par andartérectomie, endoanévrismorraphie, pontage ou résection, avec greffe ou anastomose
Surgery	235104	Revascularisatie van een slagader van de ledematen door endarteriëctomie, endoaneurysmorrhafie, pontage of resectie met enten of anastomose	Revascularisation d'une artère des membres par andartérectomie, endoanévrismorraphie, pontage ou résection, avec greffe ou anastomose
Surgery	235115	Revascularisatie van een slagader van de ledematen door pontage of resectie, met enten van de vena saphena interna, inclusief het nemen van de ent	Revascularisation d'une artère des membres par pontage ou résection avec greffe de la saphène interne, y compris la prise du greffon
Surgery	235126	Revascularisatie van een slagader van de ledematen door pontage of resectie, met enten van de vena saphena interna, inclusief het nemen van de ent	Revascularisation d'une artère des membres par pontage ou résection avec greffe de la saphène interne, y compris la prise du greffon
Surgery	235211	Revascularisatie van een tibiale slagader met prothese of met autologe vaatent, inclusief het nemen van de ent, te bewijzen met postoperatieve angiografie	Revascularisation d'une artère tibiale avec prothèse ou avec greffe vasculaire, y compris le prélèvement du greffon, à démontrer par angiographie postopératoire
Surgery	235222	Revascularisatie van een tibiale slagader met prothese of met autologe vaatent, inclusief het nemen van de ent, te bewijzen met postoperatieve angiografie	Revascularisation d'une artère tibiale avec prothèse ou avec greffe vasculaire, y compris le prélèvement du greffon, à démontrer par angiographie postopératoire
Surgery	237031	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies illiaques bilatérales
Surgery	237042	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies illiaques bilatérales
Surgery	237053	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën, geassocieerd met een andere vasculaire reconstructie, met uitzondering van de iliacale (bij voorbeeld : mesenteriale, renale of femorale revascularisatie)	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies illiaques bilatérales, associées à une autre reconstruction vasculaire, à l'exception des illiaques (par exemple : revascularisation mésentérique, rénale ou fémorale)

Group	Code	Label NL	Label FR
Surgery	237064	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën, geassocieerd met een andere vasculaire reconstructie, met uitzondering van de iliacale (bij voorbeeld : mesenteriale, renale of femorale revascularisatie)	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies illiaques bilatérales, associées à une autre reconstruction vasculaire, à l'exception des illiaques (par exemple : revascularisation mésentérique, rénale ou fémorale)
Surgery	237075	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën, geassocieerd met verscheidene vasculaire reconstructies, met uitzondering van de iliacale	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies iliaques bilatérales, associées à une reconstruction vasculaire multiple, iliaque exceptée
Surgery	237086	Heelkunde op de aortabifurcatie onder de nierslagaders : resectie van de aortabifurcatie, tweezijdige intra-abdominale pontages, tweezijdige iliacale endarteriëctomieën, geassocieerd met verscheidene vasculaire reconstructies, met uitzondering van de iliacale	Chirurgie du carrefour aortique en dessous des artères rénales : résection du carrefour aortique, pontages intra-abdominaux bilatéraux, endartérectomies iliaques bilatérales, associées à une reconstruction vasculaire multiple, iliaque exceptée
Surgery	237171	Unilaterale aortofemorale, aorto-iliacale of iliacofemorale overbrugging	Pontage aortofémoral, aorto-iliacal ou iliacofémoral unilatéral
Surgery	237182	Unilaterale aortofemorale, aorto-iliacale of iliacofemorale overbrugging	Pontage aortofémoral, aorto-iliacal ou iliacofémoral unilatéral
Endovascular	589050	Percutane endovasculaire dilatatie met of zonder plaatsing van stents(s) onder controle door medische beeldvorming van een artiriële vernauwing en/of occlusie inclusief de manipulaties en controles tijdens de behandeling en al het gebruikte materieel, exclusief de dilatatiecatheter(s), de farmaca en en de contrastmiddelen . Voor de andere slagaders dan de coronaire	Dilatation endovasculaire percutanée avec ou sans placement de stent(s) sous contrôle d'imagerie médicale d'une sténose et/ou occlusion d'une artère, y compris les manipulations et contrôles pendant le traitement et tout le matériel utilisé, à l'exclusion du ou des cathéter(s) de dilatation et des produits pharmaceutique et de contraste . Pour les artères autres que les artères coronaires
Endovascular	589061	Percutane endovasculaire dilatatie met of zonder plaatsing van stents(s) onder controle door medische beeldvorming van een artiriële vernauwing en/of occlusie inclusief de manipulaties en controles tijdens de behandeling en al het gebruikte materieel, exclusief de dilatatiecatheter(s), de farmaca en en de contrastmiddelen . Voor de andere slagaders dan de coronaire	Dilatation endovasculaire percutanée avec ou sans placement de stent(s) sous contrôle d'imagerie médicale d'une sténose et/ou occlusion d'une artère, y compris les manipulations et contrôles pendant le traitement et tout le matériel utilisé, à l'exclusion du ou des cathéter(s) de dilatation et des produits pharmaceutique et de contraste . Pour les artères autres que les artères coronaires
Endovascular	589094	Percutane endovasculaire dilatatie onder controle door medische beeldvorming van een arteriële vernauwing en/of occlusie, inclusief de manipulaties en controles, tijdens de behandeling en al het gebruikte materieel, exclusief de dilatatiecatheter(s), de farmaca en de contrastmiddelen. Voor de andere slagaders dan de coronaire tijdens een heelkundige bewerking, maximum per operatiezitting	Dilatation endovasculaire percutanée sous contrôle d'imagerie médicale d'une sténose et/ou occlusion d'une artère, y compris les manipulations et contrôles pendant le traitement et tout le matériel utilisé, à l'exclusion du ou des cathéter(s) de dilatation et des produits pharmaceutiques et de contraste Pour les artères autres que les coronaires au cours d'une intervention chirurgicale, maximum par séance opératoire
Endovascular	589105	Percutane endovasculaire dilatatie onder controle door medische beeldvorming van een arteriële vernauwing en/of occlusie, inclusief de manipulaties en controles, tijdens de behandeling en al het gebruikte materieel, exclusief de dilatatiecatheter(s), de farmaca en de contrastmiddelen. Voor de andere slagaders dan de coronaire tijdens een heelkundige bewerking, maximum per operatiezitting	Dilatation endovasculaire percutanée sous contrôle d'imagerie médicale d'une sténose et/ou occlusion d'une artère, y compris les manipulations et contrôles pendant le traitement et tout le matériel utilisé, à l'exclusion du ou des cathéter(s) de dilatation et des produits pharmaceutiques et de contraste Pour les artères autres que les coronaires au cours d'une intervention chirurgicale, maximum par séance opératoire

Group	Code	Label NL	Label FR
Endovascular	589175	Percutaan inbrengen onder controle door medische beeldvorming van endovasculaire catheters met het oog op de rekanalisatie van een gedocumenteerde vasculaire occlusie, door fibrinolyse, door mechanische rekanalisatie, door aanwending van energie (thermische, laser, radiofrequentie) en door aspiratie inclusief de manipulaties en controles tijdens de behandeling en het gebruikte materiaal, exclusief de angioplastiekcatheters, de farmaca en contrastmiddelen. Voor de andere bloedvaten dan de coronaire	Introduction percutanée sous contrôle d'imagerie médicale de cathéters endovasculaires visant à la recanalisation d'une occlusion vasculaire documentée, par fibrinolyse, par recanalisation mécanique, par utilisation d'énergie (thermique, laser, radiofréquence) et par aspiration, y compris les manipulations et contrôles pendant le traitement ainsi que le matériel utilisé, à l'exclusion des cathéters d'angioplastie, des produits pharmaceutiques et de contraste. Pour les vaisseaux autres que les vaisseaux coronaires
Endovascular	589186	Percutaan inbrengen onder controle door medische beeldvorming van endovasculaire catheters met het oog op de rekanalisatie van een gedocumenteerde vasculaire occlusie, door fibrinolyse, door mechanische rekanalisatie, door aanwending van energie (thermische, laser, radiofrequentie) en door aspiratie inclusief de manipulaties en controles tijdens de behandeling en het gebruikte materiaal, exclusief de angioplastiekcatheters, de farmaca en contrastmiddelen. Voor de andere bloedvaten dan de coronaire	Introduction percutanée sous contrôle d'imagerie médicale de cathéters endovasculaires visant à la recanalisation d'une occlusion vasculaire documentée, par fibrinolyse, par recanalisation mécanique, par utilisation d'énergie (thermique, laser, radiofréquence) et par aspiration, y compris les manipulations et contrôles pendant le traitement ainsi que le matériel utilisé, à l'exclusion des cathéters d'angioplastie, des produits pharmaceutiques et de contraste. Pour les vaisseaux autres que les vaisseaux coronaires
Endovascular	589256	Andere percutane endovasculaire arterioplastie dan de dilatatie met ballonnetje (atherectomie, laser, rotatieve endarteriectomie) onder controle door medische beeldvorming, inclusief de manipulatie en controles tijdens de behandeling alsmede het gebruikte materieel, met uitsluiting van de angioplastiecatheters, de farmaceutische produkten en de contrastmiddelen : Voor andere slagaders dan de kransslagaders	Artérioplastie endovasculaire percutanée autre que la dilatation par ballonnet (athérectomie, laser, endartériectomie rotative) sous contrôle d'imagerie médicale, y compris les manipulations de contrôles pendant le traitement ainsi que le matériel utilisé, à l'exclusion des cathéters d'angioplastie, des produits pharmaceutiques et de contraste : Pour les artères autres que les artères coronaires
Endovascular	589260	Andere percutane endovasculaire arterioplastie dan de dilatatie met ballonnetje (atherectomie, laser, rotatieve endarteriectomie) onder controle door medische beeldvorming, inclusief de manipulatie en controles tijdens de behandeling alsmede het gebruikte materieel, met uitsluiting van de angioplastiecatheters, de farmaceutische produkten en de contrastmiddelen : Voor andere slagaders dan de kransslagaders	Artérioplastie endovasculaire percutanée autre que la dilatation par ballonnet (athérectomie, laser, endartériectomie rotative) sous contrôle d'imagerie médicale, y compris les manipulations de contrôles pendant le traitement ainsi que le matériel utilisé, à l'exclusion des cathéters d'angioplastie, des produits pharmaceutiques et de contraste : Pour les artères autres que les artères coronaires
Endovascular	589271	Percutane endovasculaire dilatatie met ballonnetje, naar aanleiding van het verrichten van de verstrekking nr. 589256 - 589260	Dilatation endovasculaire percutanée par ballonnet, à l'occasion de l'exécution de la prestation n° 589256 - 589260
Endovascular	589282	Percutane endovasculaire dilatatie met ballonnetje, naar aanleiding van het verrichten van de verstrekking nr. 589256 - 589260	Dilatation endovasculaire percutanée par ballonnet, à l'occasion de l'exécution de la prestation n° 589256 - 589260

10.2. Method

All analyses and graphics are produced with SAS 9.3 and R 3.1.

10.3. Expenditure calculation

For each stay, all RIZIV-INAMI expenditures are summed. The per diem lump sum is replaced by a 100% per diem price to account for the dual financing of hospital stays. Each stay is classified as either angioplasty, bypass surgery, or both based on the presence of the nomenclature selection codes (Table 10). The qualification of the care giver(s) is identified for each stay.

10.4. Hospital stay selection

Prior to the expenditure calculation, some stays were removed from the selection. Table 11 depicts the reasons.

Table 11 – Hospital stay selection

Reason	N	N left	%	% left
All stays with at least one selection code	26041	26041	100%	100%
Stays with both bypass surgery and angioplasty	2165	23876	8.3%	91.7%
Stays with multiple physician qualifications for the selected interventions	116	23760	0.5%	91.2%

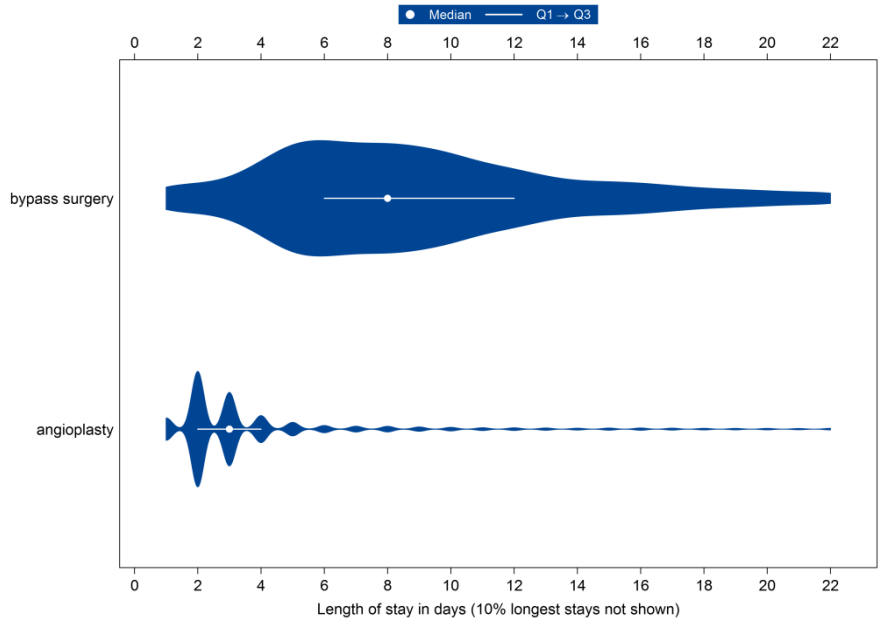
10.5. Results

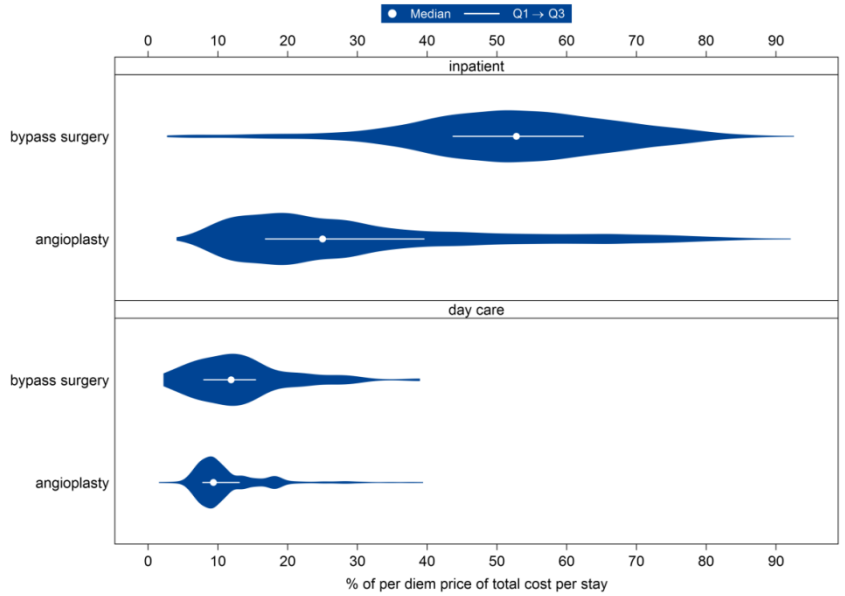
10.5.1. Inpatient and day care

	day care		inpatient		total	
	N	% row	N	% row	N	% all
angioplasty	1224	6,8%	16834	93,2%	18058	76,0%
bypass surgery	90	1,6%	5612	98,4%	5702	24,0%
Total	1314	5,5%	22446	94,5%	23760	100,0%

10.5.2.

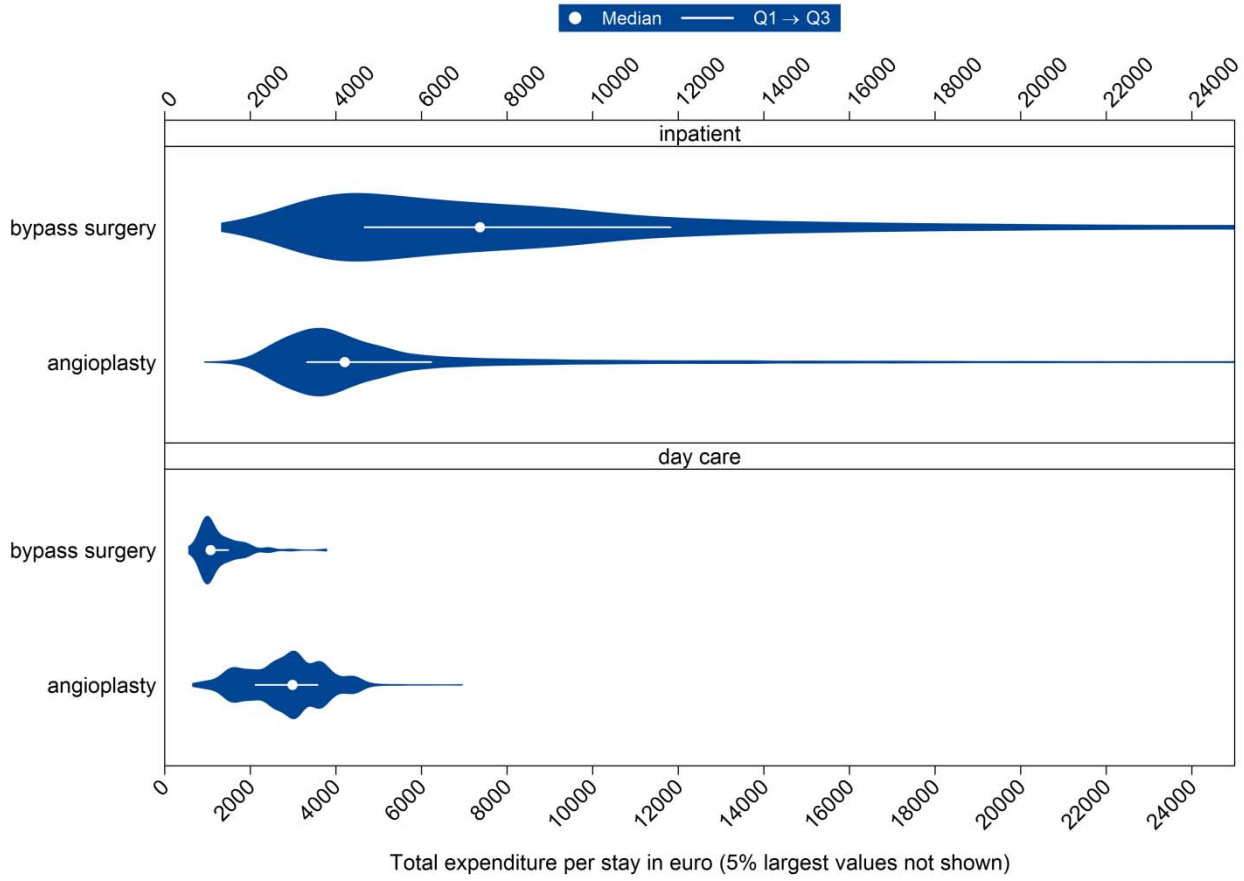
10.5.3. Length of stay and per diem part expenditure





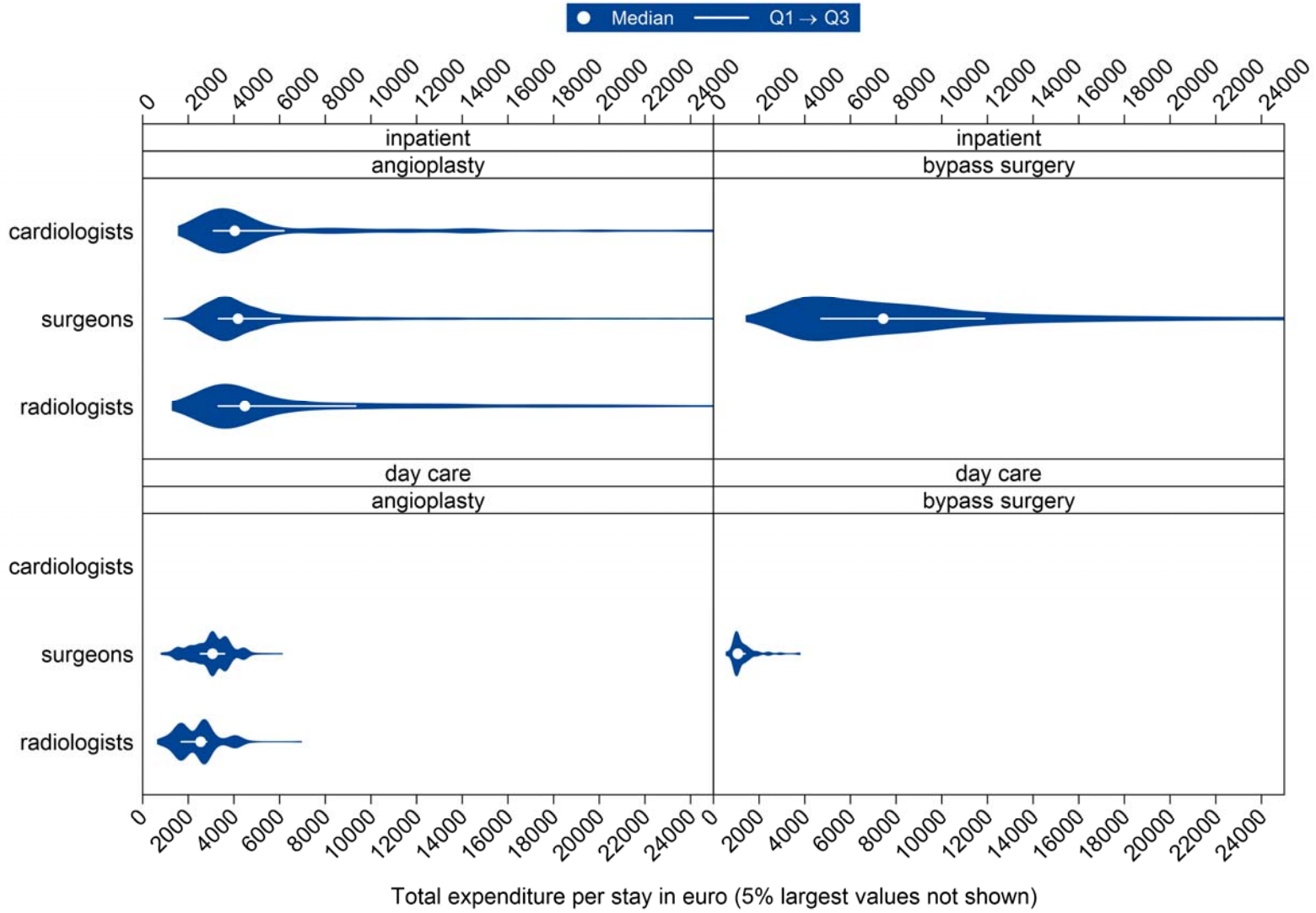
10.5.4. Expenditure by intervention type and hospital stay type

intervention	stay type	n	median	Q1	Q3	min	max	mean	sd
angioplasty	day care	1224	€ 2 985,73	€ 2 119,06	€ 3 571,30	€ 654,66	€ 6 952,05	€ 2 831,80	€ 898,42
	inpatient	16834	€ 4 207,03	€ 3 323,44	€ 6 225,69	€ 934,03	€ 299 147,22	€ 7 302,38	€ 11 055,03
bypass surgery	day care	90	€ 1 071,95	€ 973,18	€ 1 482,36	€ 563,99	€ 3 784,45	€ 1 276,47	€ 517,14
	inpatient	5612	€ 7 366,69	€ 4 669,33	€ 11 820,74	€ 1 330,87	€ 190 796,14	€ 11 196,71	€ 13 376,95



10.5.5. Expenditure by intervention type, hospital stay type, and qualification

intervention	stay type	Qualification	n	median	Q1	Q3	min	max	mean	sd
angioplasty	day care	surgeons	872	€ 3 062,67	€ 2 532,88	€ 3 588,74	€ 814,36	€ 6 117,09	€ 3 013,22	€ 828,32
		radiologists	340	€ 2 542,49	€ 1 691,83	€ 2 803,12	€ 654,66	€ 6 952,05	€ 2 405,14	€ 905,90
		other	<= 50	€ 1 532,47	€ 1 192,53	€ 2 531,28	€ 659,83	€ 2 953,52	€ 1 736,88	€ 760,51
	inpatient	surgeons	14637	€ 4 179,37	€ 3 324,32	€ 6 013,77	€ 934,03	€ 299 147,22	€ 7 000,00	€ 10 374,97
		radiologists	1948	€ 4 478,75	€ 3 313,96	€ 9 332,94	€ 1 303,01	€ 211 196,38	€ 9 499,36	€ 14 248,42
		cardiologists	201	€ 4 037,99	€ 3 104,22	€ 6 185,89	€ 1 572,55	€ 28 698,39	€ 6 186,00	€ 5 392,90
		other	<= 50	€ 5 050,23	€ 4 123,87	€ 10 815,17	€ 2 540,99	€ 230 978,53	€ 15 025,87	€ 37 716,17
bypass surgery	day care	surgeons	59	€ 1 067,36	€ 993,52	€ 1 379,18	€ 563,99	€ 3 784,45	€ 1 278,04	€ 541,53
		other	<= 50	€ 1 109,89	€ 888,00	€ 1 715,14	€ 575,28	€ 2 436,49	€ 1 273,48	€ 475,84
	inpatient	surgeons	5537	€ 7 436,12	€ 4 708,05	€ 11 873,10	€ 1 436,40	€ 190 796,14	€ 11 242,91	€ 13 405,74
		other	75	€ 3 770,54	€ 2 204,97	€ 6 926,58	€ 1 330,87	€ 59 283,64	€ 7 786,09	€ 10 570,30


Median
Q1 → Q3
0
2000
4000
6000
8000
10000
12000
14000
16000
18000
20000
22000
24000
inpatient
angioplasty
inpatient
bypass surgery
cardiologists
surgeons
radiologists
day care
angioplasty
day care
bypass surgery
cardiologists
surgeons
radiologists
Total expenditure per stay in euro (5% largest values not shown)

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