Health Technology Assessment 2007; Vol. 11: No. 20

A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease

R Collins, G Cranny, J Burch, R Aguiar-Ibáñez, D Craig, K Wright, E Berry, M Gough, J Kleijnen and M Westwood

May 2007

Health Technology Assessment
NHS R&D HTA Programme
www.hta.ac.uk

How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease

R Collins,[1*] G Cranny,[1] J Burch,[1] R Aguiar-Ibáñez,[1] D Craig,[1] K Wright,[1] E Berry,[2] M Gough,[3] J Kleijnen[1] and M Westwood[1]

[1] Centre for Reviews and Dissemination, University of York, UK
[2] Academic Unit of Medical Physics, University of Leeds, UK
[3] Leeds Teaching Hospitals NHS Trust, UK

* Corresponding author

Declared competing interests of authors: none

Published May 2007

This report should be referenced as follows:

Collins R, Cranny G, Burch J, Aguiar-Ibáñez R, Craig D, Wright K, *et al*. A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease. *Health Technol Assess* 2007;**11**(20).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE and *Science Citation Index Expanded (SciSearch®)* and *Current Contents®*/Clinical Medicine.

NIHR Health Technology Assessment Programme

The Health Technology Assessment (HTA) programme, now part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the costs, effectiveness and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA Programme is needs-led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, the public and consumer groups and professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Secondly, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Thirdly, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer-reviewed by a number of independent expert referees before publication in the widely read monograph series *Health Technology Assessment*.

Criteria for inclusion in the HTA monograph series

Reports are published in the HTA monograph series if (1) they have resulted from work for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 03/07/04. The contractual start date was in May 2004. The draft report began editorial review in December 2005 and was accepted for publication in October 2006. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.

Abstract

A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease

R Collins,[1*] G Cranny,[1] J Burch,[1] R Aguiar-Ibáñez,[1] D Craig,[1] K Wright,[1] E Berry,[2] M Gough,[3] J Kleijnen[1] and M Westwood[1]

[1] Centre for Reviews and Dissemination, University of York, UK
[2] Academic Unit of Medical Physics, University of Leeds, UK
[3] Leeds Teaching Hospitals NHS Trust, UK
* Corresponding author

Objectives: To determine the diagnostic accuracy and cost-effectiveness of duplex ultrasound (DUS), magnetic resonance angiography (MRA), and computed tomography angiography (CTA), as alternatives to contrast angiography (CA), for the assessment of lower limb peripheral arterial disease (PAD).
Data sources: Ten electronic databases were searched in April 2004, with an update in May 2005. Six key journals and bibliographies of included studies were also searched and experts in the field were consulted.
Review methods: Data extraction and quality assessment were performed in duplicate. Data were analysed according to test type and diagnostic threshold. For the economic analysis, a decision tree was developed and a probabilistic sensitivity analysis performed to incorporate statistical uncertainty into the cost-effectiveness analysis.
Results: A total of 113 studies met the inclusion criteria (including six economic evaluations).
For the detection of stenosis greater than 50% in the whole leg, contrast-enhanced (CE) MRA (14 studies) had the highest diagnostic accuracy, with sensitivity ranging from 92 to 99.5% and specificity from 64 to 99%. Two-dimensional (2D) time-of-flight (TOF) MRA (11 studies) was less accurate, with sensitivity ranging from 79 to 94% and specificity from 74 to 92%. 2D phase-contrast (PC) MRA (one study) had a sensitivity of 98% and specificity of 74%. CTA (seven studies) also appeared slightly inferior to CE MRA, with a sensitivity ranging from 89 to 99% and specificity from 83 to 97%, but better than DUS (28 studies), which had a sensitivity ranging from 80 to 98% and specificity from 89 to 99%. There was some indication that CE MRA and DUS were more accurate for detecting stenoses/occlusions above the knee than below the knee or in the pedal artery. The four studies of patient attitudes strongly suggested that patients preferred CE MRA to CA. CA was considered the most uncomfortable test, followed by CE MRA, with CTA being the least uncomfortable. Half of the patients (from a sample who did not suffer from claustrophobia and had no metallic implants) expressed no preference between undergoing TOF MRA or DUS; most of those who did express a preference favoured TOF MRA. In the 55 studies identified for adverse events, MRA was associated with the highest reported proportion. However, the most severe adverse events were more common in patients undergoing CA; although these were rare for both tests. The economic evaluation showed DUS dominated the other alternatives when the whole leg was assessed, by presenting higher effectiveness at a lower cost per quality-adjusted life-year (QALY; i.e. £13,646 per QALY). When the assessment was limited to a section of the leg, either above the knee or below the knee, 2D TOF MRA was the most cost-effective preoperative diagnostic strategy. The incremental cost per QALY for below-the-knee comparisons was equal to £37,024 when 2D TOF MRA was compared with DUS. For above-the-knee comparisons, 2D TOF MRA presented the lowest cost and slightly lower effectiveness compared with CE MRA, with a cost per QALY equal to £13,442.
Conclusions: The results of the review suggest that CE MRA has a better overall diagnostic accuracy than CTA or DUS, and that CE MRA is generally preferred by patients over CA. Where available, CE MRA may be a viable alternative to CA. The only controlled trial suggested that the results of DUS were comparable to

those of CA, in terms of surgical planning and outcome. This finding conflicts with the results of diagnostic accuracy studies, which reported poor estimates of accuracy for DUS in comparison with CA. There was insufficient evidence to evaluate the usefulness of CTA for the assessment of PAD, particularly newer techniques. The results of the economic modelling suggest that for PAD patients for whom the whole leg is evaluated by a preoperative diagnostic test, DUS dominates the other alternatives by presenting higher effectiveness at a lower cost per QALY. However, when the analysis of stenosis is limited to a section of the leg, either above the knee or below the knee, 2D TOF MRA appears to be the most cost-effective preoperative diagnostic strategy. Further research is needed into a number of areas including the relative clinical effectiveness of the available imaging tests, in terms of surgical planning and postoperative outcome.

Contents

Measures of diagnostic test performance and list of abbreviations vii

Executive summary xi

1 Background 1
What is peripheral arterial disease? 1
Epidemiology of PAD in England and Wales 1
Management 1
Diagnostic tests 2

2 Research questions 5
Aim of the project 5
Objectives 5

3 Review methods 7
Search strategy 7
Inclusion criteria 7
Data extraction 7
Quality assessment 8
Data synthesis 9

4 Details of studies included in the review 11
Assessment of stenosis/occlusion 11
Impact of assessment method on patient management/outcome 11
Studies of patient attitudes 11
Adverse events 11
Economic evaluations 11

5 Details of studies excluded from the review 13

6 Results of the review 17
Results of the literature searches 17
Assessment of stenosis/occlusion 17
Impact of assessment method on patient management and outcome 39
Studies of patient attitudes 41
Adverse events 44
Economic evaluations 44

7 Economic modelling 49
The choice of modelling questions 49
Methods 49
Results from the probabilistic cost-effectiveness analysis 68

8 Discussion 79
Methodology 79
Results of the review 81
Results of the review of economic evaluations 86
Results of the economic modelling 86

9 Conclusions 87
Implications for clinical practitioners and decision-makers 87
Implications for research 87

Acknowledgements 89

References 91

Appendix 1 Advisory panel members 121

Appendix 2 Protocol changes 123

Appendix 3 Detailed search strategies 125

Appendix 4 QUADAS and details of criteria for scoring studies 133

Appendix 5 Quality checklist for the included economic evaluations 135

Appendix 6 Included studies evaluating tests to diagnose stenosis/occlusion 137

Appendix 7 Data extraction of included economic evaluations 151

Appendix 8 Parameter distributions used in the probabilistic sensitivity analysis for baseline analysis (1-year time-horizon model) 173

Appendix 9 Cumulative probabilities for the distributions of costs, effectiveness and cost-effectiveness 177

Appendix 10 Cost-effectiveness analysis for 1-year time-horizon model: endarterectomy considered as a PTA procedure 181

Appendix 11 Cost-effectiveness analysis for adjustment of Dirichlet distribution-10 (1-year time-horizon model) 183

Health Technology Assessment reports published to date 185

Health Technology Assessment Programme 199

Measures of diagnostic test performance and list of abbreviations

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader. In some cases, usage differs in the literature, but the term has a constant meaning throughout this review.

Measures of diagnostic test performance

This section summarises the measures of diagnostic test performance used in the review, and how these are calculated.

Stenosis above positive threshold/occlusion

		Present	Absent
Test result	+	*a*	*b*
	–	*c*	*d*

True positive (TP) Correct positive test result: *a* – number of diseased persons with a positive test result

True negative (TN) Correct negative test result: *d* – number of non-diseased persons with a negative test result

False positive (FP) Incorrect positive test result: *b* – number of non-diseased persons with a positive test result

False negative (FN) Incorrect negative test result: *c* – number of diseased persons with a negative test result

Sensitivity $a/(a + c)$ – Proportion of people with the target disorder who have a positive test result

Specificity $d/(b + d)$ – Proportion of people without the target disorder who have a negative test result.

Likelihood ratio (LR) – positive (LR +) – negative (LR –) Describes how many times a person with disease is more likely to receive a particular test result than a person without disease. A likelihood ratio of a positive test result is usually a number greater than 1; a likelihood ratio of a negative test result usually lies between 0 and 1.

$$LR+ = [a/(a + c)]/[b/(b + d)]$$
$$= \text{Sensitivity}/(1 - \text{Specificity})$$
$$LR- = [c/(a + c)]/[d/(b + d)]$$
$$= (1 - \text{Sensitivity})/\text{Specificity}$$

Diagnostic odds ratio (DOR) Used as an overall (single indicator) measure of the diagnostic accuracy of a diagnostic test. It is calculated as the odds of a positive test result among diseased persons, divided by the odds of a positive test result among non-diseased persons. When a test provides no diagnostic evidence then the DOR is 1.0.

$$\text{DOR} = [a/c]/[b/d]$$
$$= [\text{Sensitivity}/(1 - \text{Specificity})]/[(1 - \text{Sensitivity})/\text{Specificity}]$$
$$= LR+ /LR- = ad/bc$$

Predictive value Positive predictive value: the probability of disease among all persons with a positive test result

Positive predictive value (PPV) $= a/(a + b)$

Negative predictive value: the probability of non-disease among all persons with a negative test result

Negative predictive value (NPV) $= d/(c + d)$

Predictive values depend on disease prevalence; the more common a disease is, the more likely it is that a positive test result is right and a negative result is wrong.

continued

Measures of diagnostic test performance *continued*

Receiver operating curve (ROC curve) An ROC curve represents the relationship between the 'true-positive rate' (Sensitivity) and 'false-positive rate' (1 – Specificity). It displays the trade-offs between sensitivity and specificity as a result of varying the threshold for positivity in the case of a continuous test result.

Summary ROC curve (sROC curve) The sROC curve models test accuracy, defined by the log of the diagnostic odds ratio (D = logit(Sensitivity) – logit(1 – Specificity)), as a function of test threshold (S = logit(Sensitivity) + logit(1 – Specificity)). S relates to the positivity threshold: it is 0 in studies where sensitivity equals specificity, it is positive in studies where sensitivity is higher than specificity, and negative in studies where specificity is higher than sensitivity. For a set of primary studies, the following linear regression model is fitted:

$$D = \alpha + \beta S$$

where D (the log odds ratio) and S (the positivity threshold) are calculated for each study from the sensitivity and specificity; α is the estimated intercept (the expected log odds ratio when $S = 0$); and β is the estimated coefficient of S (which indicates whether the log diagnostic odds ratio varies across different thresholds). The estimates of α and β are used to plot the ROC curve by calculating the sensitivity for each value of (1 – Specificity) across the range of observed values. This is calculated using the following equation:

$$\text{Sensitivity} = [1+e^{-\alpha/(1-\beta)}V^{(1+\beta)/(1-\beta)}]^{-1}$$

where V = Specificity/(1 – Specificity).

List of abbreviations

2D	two-dimensional
3D	three-dimensional
AUC	area under the curve
CA	contrast angiography/ arteriography
CDPwATP	correctly diagnosed patient with accurate treatment plan
CDS	colour duplex sonography
CE MRA	contrast-enhanced magnetic resonance angiography
CEAC	cost-effectiveness acceptability curve
CER	cost-effectiveness ratio
CI	confidence interval
CRD	Centre for Reviews and Dissemination
CTA	computed tomography angiography
DOR	diagnostic odds ratio
DSA	digital subtraction angiography/arteriography
DUS	duplex ultrasound scanning
FN	false negative
FP	false positive
ICER	incremental cost-effectiveness ratio
ICUR	incremental cost–utility ratio
LR+	positive likelihood ratio

continued

List of abbreviations *continued*

LR–	negative likelihood ratio
MM	medical management
MR	magnetic resonance
MRA	magnetic resonance angiography
NA	not applicable
NHS EED	NHS Economic Evaluation Database
NPV	negative predictive value
NR	not reported
PAD	peripheral arterial disease
PC MRA	phase-contrast magnetic resonance angiography
PPP	purchasing power parity
PSA	probabilistic sensitivity analysis
PSVR	peak systolic velocity ratio
PTA	percutaneous transluminal angioplasty
PVD	peripheral vascular disease
QALY	quality-adjusted life-year
RCT	randomised controlled trial
ROC	receiver operating characteristic
SD	standard deviation
SE	standard error
sROC	summary receiver operating characteristic
STARD	Standards for Reporting of Diagnostic Accuracy
TN	true negative
TOF	time-of-flight
TOF MRA	time-of-flight magnetic resonance angiography
TP	true positive

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

Lower limb peripheral arterial disease (PAD) is characterised by atheromatous narrowing or occlusion of one or more of the arteries of the leg. Symptoms include intermittent claudication (pain on walking), ischaemic rest pain, ulceration and gangrene. This review concerns the assessment of symptomatic PAD. Intervention decisions utilise information regarding the degree, length and location of stenoses or occlusions. This review summarises the evidence on the role of duplex ultrasound (DUS), magnetic resonance angiography (MRA), and computed tomography angiography (CTA), as alternatives to contrast angiography (CA), for the assessment of PAD.

Objectives

The objectives of this review were:

- to determine the diagnostic accuracy of DUS, MRA and CTA, alone or in combination, for the assessment of lower limb PAD
- to evaluate the impact of these assessment methods on patient management/outcome
- to evaluate the evidence regarding patient attitudes to these technologies
- to summarise available adverse event data associated with these technologies
- to analyse the cost-effectiveness of these technologies using a review of existing cost-effectiveness literature, and decision analysis.

Methods

Data sources

Studies were identified through extensive searches of electronic databases (carried out in April 2004, with update searches in May 2005), handsearching of journals, scanning reference lists of included papers and consultation with experts in the field.

Study selection

Two reviewers independently screened titles and abstracts for relevance. Full papers of potentially relevant studies were assessed for inclusion by one reviewer and checked by a second. Published and unpublished studies in any language were eligible for inclusion.

Inclusion criteria

Separate inclusion criteria, relating to study design, participant characteristics and outcome measures, were derived for each objective.

Data extraction

Data extraction and quality assessment were performed using standardised forms. The quality of the included studies was evaluated using published checklists and criteria. All data extraction was checked by a second reviewer.

Data synthesis

Assessment of stenosis/occlusion

Results were analysed according to test type (MRA, DUS, CTA) and diagnostic threshold (e.g. 50% stenosis, occlusion). Data for different MRA techniques [e.g. time-of-flight (TOF), phase-contrast (PC), contrast-enhanced (CE)] were grouped separately. Data were further grouped according to the area of the leg assessed (whole leg, above knee, below knee, foot). Sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratios were calculated for each data set. Individual study results were presented graphically in receiver operating characteristic (ROC) space. Heterogeneity was investigated using the Q statistic and through visual examination of study results. Pooled estimates of diagnostic test performance were calculated where statistically and clinically meaningful; otherwise, median likelihood ratios and ranges were presented. Insufficient data were available to facilitate the use of subgroup or regression analyses to investigate potential sources of between study heterogeneity (e.g. aspects of methodological quality, presence of co-morbidities or risk factors, image postprocessing techniques, personnel involved in test interpretation).

Impact of assessment method on patient management/outcome

A narrative synthesis was presented.

Studies of patient attitudes

A narrative synthesis was presented.

Adverse events
Results were tabulated and, where more than one study reported a particular adverse event, the range of the proportion of patients experiencing that adverse event was presented.

Economic evaluations
Economic evaluations were described and critically appraised in a narrative summary.

Economic modelling
The objective of the economic analysis was to assess the relative cost-effectiveness of MRA, DUS and CTA compared with CA, from the UK NHS perspective, in order to identify the type and level of stenosis and subsequently formulate a treatment plan for patients with PAD. A decision tree was developed and a probabilistic sensitivity analysis performed to incorporate statistical uncertainty into the cost-effectiveness analysis.

Results

The searches identified 650 potentially relevant studies, of which 113 met the inclusion criteria (including six economic evaluations).

Assessment of stenosis/occlusion (58 studies)
For the detection of stenosis greater than 50% in the whole leg, CE MRA (14 studies) had the highest diagnostic accuracy, with sensitivity ranging from 92 to 99.5% and specificity from 64 to 99%. Two-dimensional (2D) TOF MRA (11 studies) was less accurate, with sensitivity ranging from 79 to 94% and specificity from 74 to 92%. 2D PC MRA (one study) had a sensitivity of 98% and specificity of 74%. CTA (seven studies) also appeared slightly inferior to CE MRA, with a sensitivity ranging from 89 to 99% and specificity from 83 to 97%, but better than DUS (28 studies), which had a sensitivity ranging from 80 to 98% and specificity from 89 to 99%. There was some indication that CE MRA and DUS were more accurate for detecting stenoses/occlusions above the knee than below the knee or in the pedal artery.

Impact of assessment method on patient management/outcome (one study)
This historically controlled trial reported no statistically significant differences in immediate or intermediate-term patient outcomes, following treatment plans based on DUS alone or based on conventional CA alone. However, in a subgroup of 22% of patients having DUS supplementary CA was needed to form a treatment plan.

Studies of patient attitudes (four studies)
These studies strongly suggested that patients preferred CE MRA to CA. CA was considered the most uncomfortable test, followed by CE MRA, with CTA being the least uncomfortable. Half of the patients (from a sample who did not suffer from claustrophobia and had no metallic implants) expressed no preference between undergoing TOF MRA or DUS, while the majority of those who did express a preference favoured TOF MRA.

Adverse events (55 studies)
MRA was associated with the highest proportion of adverse events reported in the studies. However, the most severe adverse events were more common in patients undergoing CA than MRA; although these only occurred in a very small proportion of patients undergoing either test. The most commonly reported adverse events were acute digestive system symptoms associated with CE MRA, unspecified contrast agent-related adverse events associated with CE MRA, minor pain/discomfort during or immediately after DUS, 2D TOF MRA or CE MRA, anxiety associated with 2D TOF MRA, and acute central and peripheral nervous system adverse events associated with CE MRA.

Economic evaluations/modelling
When the whole leg was assessed by a preoperative diagnostic test, DUS dominated the other alternatives by presenting higher effectiveness at a lower cost per quality-adjusted life-year (QALY; i.e. £13,646 per QALY). When the assessment was limited to a section of the leg, either above the knee or below the knee, 2D TOF MRA was the most cost-effective preoperative diagnostic strategy. The incremental cost per QALY for below-the-knee comparisons was equal to £37,024 when 2D TOF MRA was compared with DUS. For above-the-knee comparisons, 2D TOF MRA presented the lowest cost and slightly lower effectiveness compared with the most effective diagnostic strategy (i.e. CE MRA), with a cost per QALY equal to £13,442.

Conclusions

The results of the review suggest that CE MRA has a better overall diagnostic accuracy than CTA or DUS, and that CE MRA is generally preferred by patients over CA. Where available, CE MRA may be a viable alternative to CA.

The only controlled trial of the effectiveness of imaging procedures suggested that the results of DUS were comparable to those of CA, in terms of

surgical planning and outcome. This finding conflicts with the results of diagnostic accuracy studies, which reported poor estimates of accuracy for DUS in comparison with CA.

There was insufficient evidence to evaluate the usefulness of CTA for the assessment of PAD, particularly newer techniques.

The results of the economic modelling suggest that for PAD patients for whom the whole leg is evaluated by a preoperative diagnostic test DUS dominates the other alternatives by presenting higher effectiveness at a lower cost per QALY. However, when the analysis of stenosis is limited to a section of the leg, either above the knee or below the knee, 2D TOF MRA appears to be the most cost-effective preoperative diagnostic strategy.

Recommendations for future research

The following specific questions requiring further research were identified:

- What is the relative clinical effectiveness of the available imaging tests, in terms of surgical planning and postoperative outcome?
- What adverse events occur as a consequence of testing, and what is the relative incidence for the available tests?
- Which tests do patients prefer?
- What is the true diagnostic accuracy of DUS for the detection of 50% or greater stenoses and occlusions and how is this affected by timing of the test and operator skill?
- What are the effects of operator skill/training/experience on measures of test accuracy for all the imaging modalities of interest?
- What is the diagnostic accuracy and clinical effectiveness of tests to image arteries in different areas of the leg, particularly the foot?
- What is the diagnostic accuracy and clinical effectiveness of tests in particular patient subgroups, for example diabetes mellitus?
- Are the prognosis and quality of life of PAD patients different according to whether they have an accurate or an inaccurate treatment plan?

Chapter 1
Background

What is peripheral arterial disease?

Lower limb peripheral arterial disease (PAD) is characterised by atheromatous narrowing or occlusion of one or more of the arteries of the leg. Narrowing (stenosis) of the arteries reduces blood flow through the affected artery and hence to distal tissues and may lead to the development of symptoms. Complete occlusion usually results from superimposed thrombosis within a narrowed artery.

The most common symptom of lower limb PAD is calf pain when walking or, if more proximal arteries such as the common/external iliac arteries or the aorta are narrowed, then pain may develop in the thighs or buttocks. This results in the patient needing to pause during walking, in order to relieve pain. The condition is known as intermittent claudication. Less specific symptoms of lower limb PAD include poor hair and toenail growth and cool feet. When lower limb blood flow is more severely compromised rest pain may develop. Any further deterioration in limb perfusion may result in ulceration or gangrene, both of which may be precipitated by minor trauma.[1] The severity of lower limb PAD can be described using the classification developed by Leriche and Fontaine in the 1920s: stage I, asymptomatic; stage II, intermittent claudication; stage III, ischaemic rest pain; stage IV, focal tissue necrosis with or without ischaemic rest pain.

Risk factors for PAD include advanced age, smoking, hypertension, hyperlipidaemia, diabetes, obesity, physical inactivity and family history.[2] The most important of these risk factors is smoking. The relative risk for a person smoking more than 15 cigarettes a day of developing PAD, compared with a non-smoker, is approximately 9.[2] PAD is also common in diabetes, which is present in around 20% of PAD patients.

Epidemiology of PAD in England and Wales

The prevalence of PAD increases with age. It is estimated that around one in five people over the age of 65 has evidence of PAD on clinical examination, although only around one in four of these will have symptoms.[3] Patients with PAD have an increased risk of other cardiovascular conditions. Patients with symptomatic PAD have a 30% risk of death within 5 years of diagnosis and almost 50% after 10 years.[4] These risks are highest in patients with more severe disease requiring surgery. Approximately half of the deaths at 5 years will be from cardiac causes, with the remainder being due to cerebrovascular events, other vascular causes or non-vascular disease.[3] Further, 5–10% of these patients will suffer a non-fatal cardiovascular event. Patients with asymptomatic disease also have an increased risk of mortality.[4]

It has been estimated that, of every 100 patients presenting to their GP with intermittent claudication, over the next 5 years symptoms will improve in 50, remain stable in 25 and deteriorate in 25. Of the 25 legs that worsen five will need intervention and two to five will need a major amputation.

Management

Management strategies for patients with symptomatic lower limb PAD can be conveniently divided into two categories: those for patients with intermittent claudication (Fontaine stage II) and those for patients with limb-threatening ischaemia (Fontaine stages III and IV).[5] Because of the relatively benign course associated with intermittent claudication, and the risks incurred during and after reconstructive surgery, most patients are managed conservatively, with intervention being reserved for patients in whom there is a significant impact upon quality of life. Although angioplasty (with or without a stent) is a less invasive procedure, similar considerations apply to the use of these techniques.

The choice between angioplasty (with or without a stent) and surgical revascularisation is governed by the extent and severity of the vascular disease. Some patients require primary amputation when the pattern of disease is such that revascularisation is not technically possible. Thus, patients with limb-threatening ischaemia require a detailed

assessment of their vascular disease to allow a suitable treatment plan to be developed.

The most important factors in intervention planning are the distribution of disease and the length and severity of stenoses or occlusions. Thus, while high-grade stenoses (≥50% narrowing) and occlusions of an artery are more likely to exert a significant haemodynamic effect, lesser stenoses can usually be ignored. The length and location of the diseased segment are also important predictors of the success of angioplasty, which is usually reserved for stenoses or occlusions less than 10 cm in length. For any intervention to be successful, diagnostic imaging must also confirm that the vessels proximal to the artery to be treated are relatively disease free, so that there is good inflow of blood as far as the diseased segment. For this reason, when intervention is planned the most proximal lesions are treated first, as these tend to restrict flow to the greatest extent.[6] In addition to confirming that the inflow from proximal vessels is satisfactory, imaging must be capable of demonstrating the patency of the distal arteries below the site of maximum disease. If there is no adequate outflow to the ischaemic limb then proximal intervention will be of limited benefit. Given the importance of a clear demonstration of the proximal inflow, the site of maximum disease and the outflow or run-off, it is important to evaluate the performance of diagnostic imaging techniques within the various arterial segments.

Diagnostic tests

A diagnosis of intermittent claudication can usually be made using the Edinburgh claudication questionnaire, which has a reported specificity of 91% and sensitivity of 99%.[7] Examination of patients with PAD usually reveals weak or absent pulses and a crude numerical measure of disease severity is readily obtained with the ankle/brachial pressure index (ABPI). Further investigations are normally only carried out in patients for whom invasive intervention is considered.[3] A number of imaging techniques may be used to evaluate the lower limb vasculature before intervention. These can be broadly grouped as follows.

Contrast angiography

Contrast angiography (CA) entails the intravascular injection of contrast agent during planar X-ray imaging. Images can be enhanced by background subtraction of a precontrast frame, leaving an image of only the opacified arterial tree. Digital subtraction arteriography (DSA) requires a lower dose of contrast agent (typically 30% versus 76% for screen-film arteriography) owing to superior contrast resolution, which is more comfortable for the patients, so reducing artefacts,[8] and also permits further views if necessary without using an excessive total contrast load. Contrast agent may be injected intra-arterially or intravenously. However, the intravenous technique has serious limitations in terms of image quality, resulting from dilution of the contrast medium, and is not considered in this review. Intra-arterial CA is regarded as the reference standard for the imaging of PAD, and will be treated as the preferred reference standard for those elements of this project that consider diagnostic accuracy. The drawbacks of contrast angiography are those associated with arterial puncture and ionising radiation, the potential nephrotoxicity of iodinated contrast agents, particularly in patients with pre-existing renal impairment, and allergic reactions to the contrast agent. While developments in contrast agents may overcome some of these issues, DSA will continue to carry a small risk.

Magnetic resonance angiography

Magnetic resonance angiography (MRA) is a less invasive alternative to CA. Both time-of-flight (TOF) and phase-contrast (PC) MRA are non-contrast techniques with intravascular blood detected by virtue of its movement compared with static surrounding tissues. Contrast-enhanced (CE) MRA relies on the T1 shortening effect of intravenously administered contrast media circulating in the blood.[9]

TOF techniques use a gradient echo pulse sequence in which protons entering the slice (such as those in flowing blood) are unsaturated compared with static protons and so return a higher signal which forms the basis of the contrast. Compared with the two-dimensional (2D) method, three-dimensional (3D) TOF provides a higher signal-to-noise ratio and shorter imaging times; however, it is more susceptible to saturation effects.[10] Phase-contrast methods rely on phase shifts imparted to protons moving through a gradient magnetic field, whereas stationary protons show no phase change. Technical problems with the use of TOF and PC MRA in peripheral arterial disease include motion artefacts, long acquisition times, low spatial resolution, unreliable visualisation of lesions with high flow and turbulence (excessive signal loss at regions of high grade stenosis), and non-visualisation of patent vessels with reversed blood

flow. All magnetic resonance (MR) studies have the problem of the exclusion of patients with pacemakers and some other metallic implants or who suffer from severe claustrophobia.

Some of the problems described above have been addressed by contrast-enhanced techniques, the most commonly used MRA method for assessment of PAD.[11] CE MRA is flow independent, therefore most of the artefacts due to flow turbulence and slow flow that are problematic in TOF and PC MRA are eliminated, reducing acquisition times and increasing the quality of images.[12] Flow independence also allows in-plane imaging of vessels, reducing the number of image slices needed to cover an extended vascular territory and thereby allowing faster high-resolution imaging. In combination with a moving table this allows the whole of the lower limb vascular tree to be covered in three steps after a single contrast injection.

CE MRA may also visualise patent distal segments not seen with TOF techniques or CA. The potential for adverse events relating to the use of contrast agents is a consideration; however, since contrast media used in MRA are delivered intravenously, the potential complications associated with arterial puncture are avoided.

Computed tomography angiography

Helical computed tomography angiography (CTA) has been widely used for the evaluation of abdominal aortic aneurysms, but has only recently begun to be used in PAD, as newer multidetector row machines have enabled fine collimation to be combined with rapid (arterial phase) contrast-enhanced scanning of the extended ranges needed to cover the lower limb vascular tree.

Although CTA avoids the potential complications associated with arterial puncture, in common with CA it still requires exposure to ionising radiation and the injection of relatively large volumes of contrast material.

Duplex ultrasound

Duplex sonography (strictly meaning the combination of pulsed Doppler sonography with real time B mode ultrasound imaging, but in current practice usually also including colour Doppler scanning) allows the interrogation of Doppler flow patterns in a precisely defined area within the vessel lumen, facilitating the localisation of arterial stenoses. Stenosis is graded by the ratio between the peak systolic velocity of the target/stenosed vessel and adjacent or contralateral non-stenosed vessels: the peak systolic velocity ratio (PSVR). Unlike MRA, CTA and CA, duplex ultrasound (DUS) does not directly provide the familiar 'roadmap' overview of the circulation which facilitates treatment planning. However, a diagram drawn by the ultrasound operator can fulfil a similar role, particularly in distinguishing patients who are candidates for angioplasty from those requiring surgical reconstruction. A further technical drawback of DUS which may limit its utility is the technical difficulty in assessing aortoiliac disease owing to the potential interference by bowel gas and the depth of the vessels. However, the benefits of DUS are that it avoids the possible complications associated with more invasive procedures, it does not involve ionising radiation or the hazards and contraindications associated with strong magnetic fields, and it is relatively cheap and mobile.

Chapter 2

Research questions

Aim of the project

The aim of the review was to determine the best method, or combination of methods, for the diagnosis and assessment of lower limb PAD.

Objectives

The review had several objectives:

- to determine the diagnostic accuracy of DUS, MRA and CTA, alone or in combination, for the assessment of lower limb PAD
- to evaluate the impact of these technologies on patient management/outcome
- to evaluate the evidence on the attitudes of patients to these assessment methods
- to summarise the available data on the adverse events associated with these technologies
- to analyse the cost-effectiveness of the available methods of assessment for PAD using a critical review of the existing cost-effectiveness literature, and decision analysis.

Chapter 3
Review methods

An advisory panel was established. In addition to providing subject-specific input during the review, members of the panel were invited to offer comment on the protocol and draft report. Details of advisory panel members can be found in Appendix 1. The systematic review was undertaken in accordance with the Centre for Reviews and Dissemination (CRD) guidelines for undertaking systematic reviews[13] and published guidelines on the meta-analysis of diagnostic tests.[14,15] Details of protocol changes are presented in Appendix 2.

Search strategy

A database of published and unpublished literature was assembled from systematic searches of electronic sources, handsearching and consultation with experts in the field.

Studies were identified by searching major medical databases such as MEDLINE, EMBASE, BIOSIS Previews, Science Citation Index, LILACS and Pascal from 1996 to April 2004. Update searches were undertaken in May 2005 (see Appendix 3 for detailed search strategies).

In addition, information on studies in progress, unpublished research and research reported in the grey literature was sought from a range of relevant databases, including Inside Conferences, System for Information on Grey Literature in Europe (SIGLE), Dissertation Abstracts Online and the National Technical Information Service (NTIS) database. Six key journals were handsearched: *Radiology* (1965 to January 2005), *Journal of Vascular Intervention and Radiology* (1990 to January 2005), *European Journal of Vascular and Endovascular Surgery* (1999 to February 2005), *American Journal of Roentgenology* (2000 to March 2005), *Journal of Vascular Surgery* (2000 to December 2004 and articles in press) and *Cardiovascular and Interventional Radiology* (2000 to December 2004 and articles in press).

Attempts to identify further studies were made by contacting clinical experts and examining the reference lists of all included articles.

There was no restriction by country of origin or language of publication. The results of the searches were imported into Endnote6 bibliographic management software and deduplicated.

In addition to the literature searches to identify studies of effectiveness, searches were undertaken to inform the economic modelling. These searches were undertaken in MEDLINE, EMBASE and the Cochrane Database of Systematic Reviews. Detailed search strategies are reported in Appendix 3.

Inclusion criteria

Effectiveness studies

Two reviewers screened titles and abstracts for relevance independently, and any disagreements were resolved by consensus. Full papers of potentially relevant studies were obtained and assessed for inclusion by one reviewer and checked by a second. Disagreements were resolved by consensus or referral to a third reviewer when necessary. There were separate inclusion criteria for each section of the review, as shown in *Table 1*.

Economic evaluations

Studies were included in the review if they met the criteria of being full economic evaluations, namely that they included an explicit analysis of both costs and effects for an intervention and at least one comparator[16] and were considered to be useful in answering the research questions relating to cost-effectiveness.

Data extraction

Data extraction was performed by one reviewer and checked by a second. Disagreements were resolved by consensus or referral to a third reviewer when necessary. Non-English-language papers were extracted by one reviewer, accompanied by a speaker of that language. Data extraction from non-English-language studies were not checked by a second reviewer.

Assessment of stenosis/occlusion

Data extraction forms were developed using Microsoft Access. These were piloted on a small sample of studies. The following information was

TABLE 1 *Inclusion criteria for each of the four sections of the review*

	Diagnostic accuracy of DUS/MRA/CTA	Impact on patient management/outcome	Patient acceptability	Adverse events
Study design	Diagnostic cohort or case–control	RCT/CCT	Studies of any design. Case reports were excluded	
Population	Studies that include 20 or more adults (≥18 years) with symptoms suggestive of lower limb PAD			Studies of adults with symptoms suggestive of lower limb PAD
Index tests/ interventions	DUS, MRA or CTA, alone or in combination			
Reference standard	Conventional angiography (CA) or findings at surgery/ follow-up. Studies that reported the use of intravenous CA were excluded		NA	
Outcome measures	Sufficient information to construct 2 × 2 tables of test performance	Any treatment decision or long-term outcome measure (e.g. graft/vessel patency following intervention, morbidity, mortality)	Any reported criteria relating to patient acceptability	Adverse events relating to the index test or to currently used contrast agents

NA, not applicable.

extracted: study details [identifier, aim, study design, country, setting (teaching hospital/non-teaching hospital)], participant details (number of participants, age, gender, whether from a patient subgroup and Fontaine classification, where provided), test details [test(s) evaluated, reference standard, definition of a positive test result, area of the leg assessed, how the results were reported in the studies (leg, artery, arterial segment), time elapsed between index test and reference standard, details of dropouts and exclusions] and results (data to construct a 2 × 2 table).

Impact of assessment method on patient management/outcome

Data were extracted into Microsoft Word. Data were extracted on the test being evaluated, study methodology, management decisions/outcomes reported and results.

Studies of patient attitudes

Data were extracted into Microsoft Word. Data were extracted on the test being evaluated, study methodology and results.

Adverse events

Data were extracted into Microsoft Access. The following information was extracted: study details [identifier, aim, study design, country, setting (teaching hospital/non-teaching hospital)], participant details (number of participants, age, gender, whether from a patient subgroup and Fontaine classification, where provided), test details [test(s) evaluated, reference standard] and type and frequency of adverse events.

Quality assessment

Quality assessment was carried out by one reviewer and checked by a second. Disagreements were resolved by consensus or referral to a third reviewer when necessary. Data specific to the type of study were extracted.

Diagnostic accuracy studies

Quality assessment forms were developed using Microsoft Access. Included diagnostic accuracy studies were assessed for methodological quality using the QUADAS tool.[17] The 14 items of the QUADAS tool check the appropriateness of the patient spectrum composition, whether selection criteria for patients have been described, the appropriateness of the reference standard, whether disease progression bias has been avoided (time lapsed between index test and reference standard was sufficiently short to make a change in disease status unlikely), whether partial and/or

differential verification bias have been avoided (all participants received verification using the same reference standard of diagnosis) and whether incorporation bias has been avoided (the index test did not form part of the reference standard). The checklist also addresses the question of whether the reference standard and index tests have been reported in sufficient detail to permit replication, and whether test review bias, diagnostic review bias and clinical review bias have been avoided (the results of tests have been interpreted independently of each other and with appropriate clinical information available). Finally, the studies were checked with regard to the reporting of uninterpretable results and whether all withdrawals had been accounted for. Item 3 of the QUADAS tool (appropriateness of reference standard) was omitted from this review as the use of a specified, adequate reference standard formed part of the inclusion criteria. Those elements of the QUADAS tool that require specification for individual projects were defined a priori by discussion among the authors. The QUADAS tool, together with details on how studies were scored, is reported in Appendix 4.

Controlled trials and other study designs

The quality of each study was assessed using the appropriate checklist from the CRD guidelines for undertaking systematic reviews.[13]

Economic evaluations

The quality assessment of each included study was undertaken using two methods. First, the quality of economic evaluations was assessed using a modified version of the 35-point checklist developed for authors of economic evaluation submissions to the *British Medical Journal*, to which an additional item was added (item 36) in order to report whether or not the authors had addressed the issue of the generalisability of the results. Each item in the checklist was given one of four responses: (a) yes, (b) no, (c) not clear and (d) not applicable. The checklists were completed independently by two health economists, with discrepancies being discussed and a final agreement reached (see Appendix 5).

Secondly, for each study a critical review (textual) summary was completed following the approach adopted by the NHS Economic Evaluation Database (NHS EED). This includes an appraisal of the validity of the choice of comparator(s), the validity of the analysis of effectiveness results, the validity of the benefit measure used in the economic analysis, the validity of the cost results, and a variety of other important issues, including whether or not the authors compared their results with those of other (similar) studies, whether generalisability was addressed by the authors, and the principal limitations and strengths of the study, and finally the implications of the study in terms of clinical practice and future research.

Data synthesis

Assessment of stenosis/occlusion

Results were analysed according to the imaging tests assessed (DUS, MRA or CTA). Within these groups, tests were further grouped by specific technique where appropriate (e.g. 2D, 3D TOF and CE MRA techniques were analysed separately). Analyses were conducted using Meta-DiSc.[18]

For each individual data set the sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratio (DOR) were calculated from the 2×2 tables. These are presented in tables, grouped by anatomy assessed (whole leg, above or below knee, and foot) and the threshold used in the definition of stenosis/occlusion ($\geq$50%, $\geq$70% or 100%). To account for cells with a value of zero in the 2×2 tables when calculating likelihood ratios and DOR, 0.5 was added to all cells of every 2×2 table, as recommended by Moses and colleagues.[19]

Pooling was only considered where 2×2 data were reported in the same way (e.g. arterial segment, artery or limb) and for the same anatomy and threshold used in the definition of stenosis/occlusion. As some studies presented results for more than one anatomy or threshold, this method avoids the issue of multiple data sets being obtained from the same patients. Within data sets that were considered for pooling, heterogeneity was assessed using statistical tests and also graphically with forest plots of individual study results. Heterogeneity between sensitivities and specificities was assessed using a χ^2 test, and Cochran's Q test was used for likelihood ratios and diagnostic odds ratios. Statistically significant heterogeneity was assumed if $p < 0.1$. When there was evidence of significant statistical or clinical heterogeneity the range was presented for sensitivity and specificity, and the median value (and range) for likelihood ratios. Individual study results were presented plotted in receiver operating characteristic (ROC) space (without a summary curve).

When there was no evidence of statistical heterogeneity, pooled estimates of sensitivity, specificity and likelihood ratios were calculated using a random effects model and presented with their corresponding 95% confidence intervals (CI). In addition, summary ROC (sROC) curves were fitted, estimated by calculating the sensitivity at each value of (1 – Specificity) using the following equation:

$$\text{Sensitivity} = [(1+e^{-\alpha/(1-\beta)}) \times (V^{(1+\beta)/(1-\beta)})]^{-1}$$

where V = Specificity/(1 – Specificity).

α and β were calculated using the following regression equation:

$$D = \alpha + \beta S$$

with D and S being calculated from the sensitivities and specificities of each study:

$$D = [\text{logit (Sensitivity)} - \text{logit (1 - Specificity)}] = \ln (\text{DOR})$$
$$S = [\text{logit (Sensitivity)} + \text{logit (1 - Specificity)}]$$

logit (Sensitivity) = ln[Sensitivity/(1 – Sensitivity)]
logit (1 – Specificity) = ln[(1 – Specificity)/Specificity]

This was estimated by fitting a regression model containing S to the outcome D, which was weighted by the sample size of each study. Beta (β) provides an estimate of the effect upon the DOR of the choice of threshold for a positive test result. If β is 0 (when the line is symmetrical with respect to the line True-positive rate = 1 – False-positive rate), or not statistically significantly different from 0, then the DOR is not affected by the threshold used.

Impact of assessment method on patient management/outcome

A narrative synthesis was presented.

Studies of patient attitudes

A narrative synthesis was presented.

Adverse events

Results were tabulated and when more than one study reported a particular adverse event, the range of the proportions of patients experiencing that adverse event was presented.

Economic evaluations

The identified economic evaluations were described and evaluated in a narrative summary.

Chapter 4

Details of studies included in the review

Assessment of stenosis/occlusion

Fifty-eight diagnostic accuracy studies provided data on tests to diagnose stenosis/occlusion (*Table 2*). A more detailed description of the included diagnostic accuracy studies is presented in Appendix 6. Twenty-six studies evaluated DUS, seven evaluated CTA and 23 evaluated MRA; of which nine evaluated 2D TOF MRA, one evaluated 2D PC MRA and 13 evaluated CE MRA. In addition, one study evaluated both DUS and 2D TOF MRA, and one study evaluated DUS, 2D TOF MRA and CE MRA. Conventional angiography was the reference standard in all studies.

Impact of assessment method on patient management/outcome

One controlled trial provided data on the impact of the assessment method on patient management and/or patient outcomes. The study evaluated DUS in comparison with CA.[77]

Studies of patient attitudes

Four studies reported results relating to patient attitudes. Two studies evaluated MRA and CA,[78,79] one evaluated DUS and MRA,[80] and one evaluated CTA, MRA and CA.[81]

Adverse events

Nine of the diagnostic accuracy studies that met the inclusion criteria for the review provided data on adverse events.[29,30,32,40,41,54,57,60,61] In addition, 46 studies that did not meet the inclusion criteria for the review of diagnostic accuracy reported results relating to adverse events.[78,80,82–125]

Economic evaluations

Six economic evaluations met the inclusion criteria for the review.[126–131] However, one was published in German and the results could not be translated in time to be included.[127] Detailed data extraction,

TABLE 2 *Studies evaluating tests to diagnose stenosis/occlusion*

Study	Index test
Aly, 1998[20]	DUS
Ashleigh, 1993[21]	DUS
Baum, 1995[22]	2D TOF MRA
Baxter, 1993[23]	DUS
Bergamini, 1995[24]	DUS
Bostrom, 2001[25]	DUS
Catalano, 2004[26]	CTA
Cortell, 1996[27]	2D TOF MRA
Cronberg, 2003[28]	CE MRA
Currie, 1995[29]	(1) 2D TOF MRA (2) DUS
Davies, 1992[30]	DUS
Eiberg, 2001[31]	DUS
Eklof, 1998[32]	2D TOF MRA
El-Kayali, 2004[33]	DUS
Fletcher, 1990[34]	DUS
Grassbaugh, 2003[35]	DUS
Hany, 1997[36]	CE MRA
Hatsukami, 1992[37]	DUS
Heuschmid, 2003[38]	CTA
Hirai, 1998[39]	DUS
Hoch, 1996[40]	2D TOF MRA
Hoch, 1999[41]	2D TOF MRA
Hofmann, 2004[42]	DUS
Karacagil, 1996[43]	DUS
Koelemay, 1997[44]	DUS
Koelemay, 1998[45]	DUS
Kreitner, 2000[46]	CE MRA
Lai, 1995[47]	DUS
Lai, 1996[48]	DUS
Laissy, 1998[49]	CE MRA
Legemate, 1991[50]	DUS
Lenhart, 2000[51]	CE MRA
Linke, 1994[52]	DUS
Lundin, 2000[53]	(1) DUS (2) 2D TOF MRA (3) CE MRA
Martin, 2003[54]	CTA
McDermott, 1995[55]	2D TOF MRA
Meaney, 1999[9]	CE MRA
Mergelsberg, 1986[56]	DUS
Portugaller, 2004[57]	CTA
Puls, 2002[58]	CTA
Rieker, 1996[59]	CTA
Rieker, 1997[60]	CTA
Schafer, 2003[61]	CE MRA
Sensier, 1996[62]	DUS
Shaalan, 2003[63]	DUS
Snidow, 1995[64]	2D TOF MRA
Snidow, 1996[65]	CE MRA

continued

TABLE 2 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Index test
Steffens, 1997[66]	2D PC MRA
Steffens, 2003[67]	CE MRA
Sueyoshi, 1999[68]	CE MRA
Timonina, 1999[69]	2D TOF MRA
Vavrik, 2004[70]	CE MRA
Whyman, 1992[71]	DUS
Wilson, 1997[72]	DUS
Winterer, 1999[73]	CE MRA
Yucel, 1993[74]	2D TOF MRA
Zeuchner, 1994[75]	DUS
Zhang, 2005[76]	CE MRA

in the form of NHS EED abstracts, is provided for the five English language studies in Appendix 7. Details about the results of the quality assessment of the economic evaluations using a modified version of the 35-point checklist are reported in Appendix 5.

Chapter 5

Details of studies excluded from the review

In total, 534 of the 647 articles ordered and screened did not meet the inclusion criteria for the review. Eight were duplicate records. The reasons for exclusion of the remaining 526 (*Table 3*) articles are listed below.

1 Study included fewer than 20 participants
2 The results for adult patients could not be extracted separately from those of children
3 Study of patients with aneurysms only
4 Assessment of the complications of CA only
5 Discussion paper; no data
6 Duplicate publication
7 Study included patients with aortic aneurysms, and results for PAD patients could not be extracted separately
8 Study of intravascular ultrasound
9 Letter/editorial
10 Study did not report sufficient data to allow construction of a 2×2 contingency table
11 Study did not include a reference standard
12 Reference standard was not conventional angiography
13 Not a study of MRA, DUS or CTA
14 Not a study of patients with PAD
15 The study included asymptomatic patients and results for symptomatic patients could not be extracted separately, or the symptomatic status of the participants was not reported
16 All patients were hospitalised for reconstruction failure or thrombosis of artery reconstruction
17 Some patients received intravenous rather than intra-arterial catheter angiography
18 The study was a randomised controlled trial (RCT) with no patient outcomes reported.

TABLE 3 *Studies excluded from the review and reasons for exclusion*

AbuRahma, 1980[132] **12**
AbuRahma, 1993[133] **4**
Adriaensen, 2002[134] **6**
Adriaensen, 2004[135] **18**
Agadzhanova, 1986[136] **10**
Alexander, 1987[137] **15**
Alexander, 2002[138] **10**
Allard, 1994[139] **15**
Allard, 1996[140] **5**
Allard, 1999[141] **5**
Alson, 1997[142] **5**
Aly, 1998[143] **6**
Aly, 1998[144] **6**
Aly, 1999[145] **6**
Amano, 1998[146] **1**
Amendt, 1992[147] **8**
Andres, 2003[148] **14**
Andrew, 1989[149] **14**
Archie, 1982[150] **12**
Aronow, 2005[151] **5**
Ascher, 1999[152] **1**
Ascher, 2002[153] **0**
Ascher, 2003[154] **10**
Auerbach, 2004[155] **5**
Avenarius, 2002[156] **10**
Bagi, 1990[157] **10**
Baker, 1978[158] **14**
Baker, 1986[159] **10**
Balas, 1989[160] **5**
Balas, 1990[161] **14**
Balas, 1990[162] **5**
Balbarini, 1995[163] **8**
Balzer, 2000[164] **5**
Balzer, 2000[165] **10**
Balzer, 2000[166] **10**
Barnes, 1977[167] **4**
Barnes, 1979[168] **5**
Barrett, 1992[169] **14**
Barretto, 2003[170] **13**
Bashir, 2003[171] **5**
Battino, 1996[172] **10**
Baum, 1992[173] **10**
Baum, 1992[174] **6**
Baum, 1994[175] **10**
Baum, 1998[176] **5**
Baumgartner, 1993[177] **1**
Baumgartner, 2005[178] **5**
Baun, 2004[179] **5**
Becker, 2003[180] **5**
Belch, 2003[181] **5**
Bendib, 1997[182] **1**
Bendib, 1997[183] **10**
Bendick, 2003[184] **12**
Benhamou, 1997[185] **5**
Beregi, 1997[186] **1**
Bertschinger, 1999[187] **15**
Bertschinger, 2001[188] **15**
Bettmann, 1997[189] **14**
Binkert, 2004[190] **10**
Bizzini Pezzetta, 1999[191] **5**
Bluemke, 1995[192] **5**
Boos, 1995[193] **10**
Borrello, 1993[194] **5**
Bostrom, 2002[195] **10**
Bostrom-Ardin, 2002[196] **10**
Bostrom-Ardin, 2002[197] **10**
Bourlet, 2000[198] **1**
Brillet, 2001[199] **1**
Brillet, 2003[200] **10**
Brismar, 1991[201] **14**
Brummett, 1988[202] **14**
Bruninx, 2002[203] **14**
Bulynin, 1989[204] **11**
Busch, 1999[205] **15**
Busch, 2001[206] **15**
Cairols, 2003[207] **10**
Calligaro, 1996[208] **15**
Cambria, 1993[209] **1**
Cambria, 1997[210] **10**
Campbell, 1986[211] **15**
Cappelli, 1999[212] **11**
Caputo, 1992[213] **14**
Caputo, 1992[214] **5**
Carpenter, 1992[215] **10**
Carpenter, 1994[216] **10**
Carpenter, 1994[217] **7**
Carpenter, 2000[218] **5**
Carriero, 1998[219] **15**
Carriero, 2002[220] **15**
Caster, 1992[221] **7**
Catalano, 2001[222] **10**
Catalano, 2003[223] **5**
Cherro, 2004[224] **1**
Cochran, 2001[225] **14**
Coenegrachts, 2003[226] **3**
Coffi, 2002[227] **12**
Coffi, 2004[228] **1**
Collier, 1990[229] **10**
Comel, 2004[230] **5**
Correas, 1999[231] **5**
Cossman, 1989[232] **15**
Cotroneo, 1997[233] **5**
Cramer, 1990[234] **1**
Cruz, 1986[235] **4**
Currie, 1995[236] **12**
Currie, 1995[237] **11**
Davis, 1997[238] **1**
De Backer, 2000[239] **5**
De Benito-Fernandez, 2004[240] **7**
De Cobelli, 1999[241] **10**
Dehaut, 2000,[242] **14**
Demolis, 1990,[243] **15**
De Morais Filho, 2004[244] **10**
Depairon, 1998[245] **5**
DeSouza, 1991[246] **15**

continued

TABLE 3 *Studies excluded from the review and reasons for exclusion (cont'd)*

De Vries, 1996[247] **5**
Di Cesare, 2001[248] **10**
Diaz, 2000[249] **4**
Dorenbeck, 2002[250] **1**
Dorweiler, 2002[251] **10**
Douek, 1995[252] **14**
Drugova, 1981[253] **15**
Duncan, 1990[254] **11**
Dunne, 1984[255] **1**
Dyet, 2000[256] **5**
Earls, 1998[257] **1**
Earls, 1998[258] **1**
Ebner, 1992[259] **10**
Edwards, 1991[260] **7**
Edwards, 2005[261] **10**
Eiberg, 2001[262] **5**
Eiberg, 2002[263] **5**
Eiberg, 2002[264] **10**
Eiberg, 2003[265] **1**
Ekelund, 1996[266] **5**
Eklof, 1997[267] **6**
Eklof, 1998[268] **6**
Elsharawy, 2002[269] **10**
Elsman, 1995[270] **10**
Elsman, 1996[271] **10**
Elson, 1994[272] **5**
Engeler, 1991[273] **1**
Engelmann, 1997[274] **1**
Ernst, 1998[275] **10**
Fauvel, 1996[276] **15**
Fellner, 1999[277] **9**
Fischer-Colbrie, 1997[278] **10**
Forster, 1999[279] **1**
Froelich, 1997[280] **14**
Fronek, 1976[281] **15**
Fushimi, 1998[282] **13**
Fussl, 2001[283] **5**
Gaylis, 2002[284] **9**
Georgiou, 1993[285] **5**
Gerritsen, 1993[286] **8**
Giannini, 2004[287] **1**
Goldberg, 1997[288] **10**
Goldstein, 1990[289] **14**
Gooding, 1980[290] **1**
Gooding, 1991[291] **15**
Gosling, 1971[292] **11**
Goyen, 2000[293] **5**
Goyen, 2000[294] **11**
Goyen, 2002[295] **1**
Goyen, 2002[296] **5**
Goyen, 2004[297] **5**
Gregor, 2002[298] **10**
Hany, 1998[299] **7**
Hartnell, 2000[300] **9**
Haslam, 1999[301] **10**
Hendrickx, 1997[302] **15**
Hentsch, 2003[303] **10**
Hentsch, 2004[304] **5**
Herborn, 2004[305] **1**
Herborn, 2004[306] **10**
Herrington, 1994[307] **13**
Hertz, 1993[308] **1**
Hessel, 1981[309] **4**
Hiatt, 1992[310] **5**
Hingorani, 2004[311] **10**
Hingorani, 2004[312] **10**
Hirai, 2002[313] **10**
Ho, 1996[314] **10**
Ho, 1997[315] **10**
Ho, 1998[316] **10**
Ho, 1998[317] **10**
Ho, 2003[318] **5**
Ho, 2004[319] **15**
Hobson, 1981[320] **10**
Hofmann, 2002[321] **10**
Holder, 1978[322] **4**
Huber, 1999[323] **15**
Huber, 2000[324] **6**
Huber, 2003[325] **10**
Hudon, 1979[326] **15**
Huljev, 1994[327] **15**
Humphries, 1980[328] **10**
Huppert, 1994[329] **8**
Hussain, 1996[330] **15**
Hynynen, 1996[331] **14**
Illescas, 1986[332] **1**
Inoue, 1994[333] **5**
Ito, 1996[334] **1**
Jacobovicz, 2004[335] **7**
Jacobs, 1998[336] **14**
Jager, 1985[337] **15**
Jager, 1989[338] **5**
Janka, 2001[339] **1**
Janka, 2005[340] **10**
Jezic, 1982[341] **5**
Johnson, 1984[342] **15**
Kaiser, 1995[343] **15**
Kalden, 2000[344] **1**
Kanal, 1990[345] **14**
Karacagil, 1994[346] **10**
Karacagil, 1995[347] **15**
Karagacil, 1996[348] **6**
Karacagil, 1998[349] **10**
Karasch, 1991[350] **10**
Karasch, 1992[351] **6**
Katayama, 1990[352] **14**
Katsamouris, 2001[353] **10**
Katz, 2001[354] **5**
Kaufman, 1982[355] **10**
Kelekis, 1999[356] **10**
Khilnani, 2002[357] **10**
Kita, 1999[358] **1**
Klein, 2003[359] **10**
Koelemay, 1996[360] **5**
Koelemay, 2001[361] **11**
Koelemay, 2001[362] **5**
Koelemay, 2001[363] **10**
Koennecke, 1989[364] **15**
Kohler, 1987[365] **14**
Kohler, 1990[366] **6**
Kojima, 1995[367] **1**
Konkus, 2002[368] **11**
Korogi, 1996[369] **5**
Korst, 1999[370] **1**
Korst, 1999[371] **15**
Krajina, 2001[372] **5**
Kramer, 1998[373] **1**
Kreissig, 2000[374] **10**
Kreitner, 1998[375] **6**
Krombach, 2000[376] **10**
Krug, 1995[377] **10**
Krug, 1995[378] **10**
Laissy, 1995[379] **1**
Laissy, 1995[380] **1**
Lalli, 1980[381] **14**
Lang, 1981[382] **14**
Langholz, 1993[383] **10**
Langholz, 1998[384] **5**
Langsfeld, 1988[385] **7**
Larch, 1997[386] **15**
Lasser, 1997[387] **14**
Lawler, 2003[388] **5**
Lawrence, 1995[389] **1**
Lee, 1998[390] **10**
Legemate, 1989[391] **6**
Legemate, 1991[392] **7**
Leiner, 2004[393] **5**
Leiner, 2005[394] **10**
Leng, 1993[395] **15**
Leng, 2000[396] **5**
Lenhart, 1999[397] **1**
Lenhart, 2001[398] **6**
Lenhart, 2002[399] **11**
Leon, 2002[400] **10**
Levy, 1998[401] **10**
Lewis, 1986[402] **14**
Lewis, 1997[403] **9**
Leyendecker, 1997[404] **10**
Leyendecker, 1998[405] **10**
Ligush, 1998[406] **10**
Limpert, 1987[407] **15**
Link, 1999[408] **15**
Loewe, 2000[409] **10**
Loewe, 2002[410] **15**
Loewe, 2003[411] **15**
Loewe, 2003[412] **5**
Lofberg, 2001[413] **10**
Lossef, 1992[414] **1**
Lujan, 2002[415] **10**
Mackaay, 1995[416] **11**
Maeda, 1996[417] **1**
Makita, 1997[418] **10**
Marcus, 2000[419] **10**
Markovic, 1996[420] **10**
Marshall, 1988[421] **5**
Marti, 2004[422] **10**
Mast, 2001[423] **14**
Masui, 1995[424] **1**
Matsubara, 1984[425] **11**
Matsumura, 2001[426] **15**
Mazzariol, 2000[427] **10**
McCarthy, 1999[428] **10**
McCauley, 1994[429] **10**
McClennan, 1987[430] **14**
Meaney, 1998[431] **10**
Meaney, 2003[432] **5**
Meissner, 2004[433] **1**
Melke, 1983[434] **10**
Mesurolle, 1999[435] **10**
Meuli, 1986[436] **1**
Mills, 1982[437] **4**
Mitsuzaki, 2000[438] **1**
Mohler, 2003[439] **10**
Moneta, 1987[440] **15**
Moneta, 1992[441] **7**
Moneta, 1993[442] **10**
Morasch, 2003[443] **10**
Muller-Buhl, 2003[444] **13**
Mulligan, 1993[445] **1**
Murphy, 2000[446] **5**
Nagashima, 1979[447] **12**
Naidich, 1992[448] **4**
Nau, 2002[449] **5**
Nchimi, 2002[450] **15**
Nelemans, 2000[451] **5**
Nelemans, 2000[452] **5**
Nemcek, 1996[453] **5**
Nicolaides, 1976[454] **10**
Nikolenko, 1987[455] **11**
Nyamekye, 1996[456] **10**
Nzeh, 1998[457] **10**
Oberholzer, 1999[458] **1**
Ofer, 2003[459] **1**
Ohi, 1987[460] **1**
Oliva, 1999[461] **4**
Oser, 1995[462] **13**
Ota, 2004[463] **2**
Owen, 1992[464] **10**
Owen, 1992[465] **10**
Owen, 1993[466] **10**
Pandharipande, 2000[467] **1**
Pandharipande, 2002[468] **1**
Pasterkamp, 1996[469] **12**
Pellerin, 2001[470] **15**
Pellerito, 1993[471] **5**
Pemberton, 1996[472] **10**
Pemberton, 1996[473] **10**
Pemberton, 1997[474] **5**
Perrier, 1998[475] **10**
Phillips, 1980[476] **5**
Phillips, 1993[477] **5**
Pinto, 1996[478] **15**
Pividal, 2001[479] **5**
Pocek, 1999[480] **1**
Polak, 1991[481] **14**
Polak, 1993[482] **5**
Poletti, 2004[483] **1**
Poon, 1993[484] **9**
Poon, 1997[485] **1**
Portig, 2004[486] **5**

continued

TABLE 3 *Studies excluded from the review and reasons for exclusion (cont'd)*

Portugaller, 1998[487] **15**
Portugaller, 2003[488] **15**
Postiglione, 1992[489] **13**
Powe, 1988[490] **4**
Proia, 2001[491] **10**
Prokop, 1997[492] **5**
Quinn, 1993[493] **10**
Quinn, 1997[494] **10**
Quinn, 1998[495] **10**
Radak, 1998[496] **11**
Radak, 1999[497] **12**
Rajagopalan, 2002[498] **5**
Raman, 2002[499] **1**
Ramaswami, 1999[500] **17**
Ranke, 1992[501] **10**
Raptopoulos, 1996[502] **1**
Raptopoulos, 1995[503] **1**
Rathenborg, 2003[504] 16
Reid, 2001[505] **1**
Reimer, 1997[506] **15**
Reimer, 1998[507] **15**
Reimer, 1998[508] **5**
Rezzo, 1982[509] **11**
Ricco, 1983[510] **10**
Richter, 1994[511] **15**
Rieker, 1995[512] **6**
Rieker, 1997[513] **15**
Rizzo, 1990[514] **14**
Rofsky, 1997[515] **1**
Rofsky, 1999[516] **11**
Rofsky, 2000[517] **5**
Rose, 2000[518] **5**
Rose, 2000[519] **5**
Rose, 2001[520] **5**
Rosenfield, 1989[521] **1**
Rosfors, 1993[522] **15**
Rubin, 1999[523] **1**
Rubin, 1999[524] **1**
Rubin, 2000[525] **3**
Rubin, 2001[526] **7**
Ruehm, 2000[527] **15**
Ruehm, 2001[528] **15**
Ruehm, 1999[529] **5**
Ruthlein, 1988[530] **5**
Sacks, 1990[531] **11**
Sacks, 1992[532] **15**
Sacks, 1994[533] **11**
Saito, 1989[534] **14**
Saito, 2004[535] **7**
Savader, 2001[536] **13**
Sawchuk, 1990[537] **11**
Sawchuk, 1997[538] **15**
Schiebler, 1992[539] **10**
Scheibler, 1993[540] **5**
Schindler, 2001[541] **13**
Schmeller, 1993[542] **14**
Schmiedl, 1996[543] **5**
Schneider, 1999[544] **10**
Schoenberg, 2001[545] **1**
Seifert, 1988[546] **14**
Seifert, 1989[547] **15**
Sensier, 1996[548] **6**
Sensier, 1996[549] **9**
Sensier, 1998[550] **15**
Shannon, 1997[551] **1**
Sharafuddin, 2000[552] **10**
Sharafuddin, 2002[553] **1**
Shearman, 1986[7] **10**
Shehadi, 1980[554] **14**
Shehadi, 1982[555] **14**
Sheikh, 1991[556] **1**
Shetty, 1995[557] **1**
Shetty, 1998[558] **1**
Sigstedt, 1978[559] **4**
Sivananthan, 1993[560] **1**
Snidow, 1995[561] **10**
Snidow, 1996[562] **10**
Solomon, 1995[563] **14**
Sorensen, 2003[564] **6**
Sostman, 1996[565] **5**
Soule, 2003[566] **10**
Spinosa, 2000[567] **4**
Spinosa, 2000[568] **5**
Spring, 1997[569] **14**
Spring, 1997[570] **14**
Steffens, 1996[571] **6**
Steffens, 1997[572] **15**
Steffens, 1998[573] **10**
Steffens, 1999[574] **10**
Stoffers, 1997[575] **5**
Strandness, 1978[576] **5**
Sueyoshi, 2000[577] **1**
Sugihara, 2002[578] **10**
Swan, 2002[579] **10**
Szendro, 2001[580] **10**
Tabuchi, 2000[581] **1**
Tala, 1968[582] **1**
Ternovoy, 1999[583] **1**
Tesauro, 1991[584] **13**
Thiele, 1983[585] **5**
Tielbeek, 1996[586] **8**
Tielbeek, 1997[587] **1**
Tomihira, 2002[588] **1**
Torreggiani, 2002[589] **14**
Trusen, 2003[590] **5**
Ubbink, 2001[591] **11**
Uberoi, 2002[592] **15**
Unger, 1995[593] **1**
Van Asten, 1991[594] **12**
Van der Heijden, 1993[595] **15**
Van der Lugt, 1996[596] **10**
Van Lankeren, 1998[597] **8**
Van Rij, 1989[598] **14**
Vashisht, 1992[599] **1**
Velazquez, 1998[600] **5**
Venkataraman, 2003[601] **15**
Vergara, 1996[602] **14**
Verrel, 2002[603] **15**
Visser, 1999[604] **6**
Visser, 2000[605] **5**
Vodnansky, 2001[606] **6**
Vodnansky, 2002[607] **14**
Von Kalle, 2004[608] **11**
Vosshenrich, 1993[609] **15**
Vosshenrich, 1996[610] **7**
Vosshenrich, 1998[611] **10**
Wain, 1999[612] **10**
Walter, 2000[613] **14**
Walton, 1984[614] **15**
Wang, 2001[615] **11**
Wasser, 1999[616] **5**
Watanabe, 1998[617] **1**
Watts, 2001[618] **11**
Weishaupt, 1999[619] **6**
Wendt, 1990[620] **14**
Wesbey, 1985[621] **15**
Westenberg, 2000[622] **1**
Wetzner, 1984[623] **14**
Whelan, 1992[624] **15**
Whiteley, 1996[625] **9**
Whiteley, 1999[626] **13**
Whiting, 2003[17] **14**
Widrich, 1982[627] **4**
Widrich, 1983[628] **4**
Wikstrom, 2000[629] **15**
Wikstrom, 2001[630] **6**
Wilhelm, 2000[631] **10**
Willmann, 2002[632] **6**
Willmann, 2003[633] **15**
Winchester, 1998[634] **15**
Winterer, 2002[635] **10**
Winter-Warnars, 1996[636] **10**
Wixon, 2000[637] **10**
Wolf, 2003[638] **13**
Wolff, 2002[639] **6**
Wright, 1983[640] **3**
Yamaguchi, 1991[641] **6**
Yamashita, 1997[642] **10**
Yamashita, 1998[643] **10**
Yeon Hyeon, 2001[644] **14**
Yilmaz, 2002[645] **14**
Yoshikawa, 1992[646] **14**
Yucel, 1992[647] **5**
Yucel, 1992[648] **1**
Yucel, 1992[649] **1**
Yucel, 1994[650] **9**
Yucel, 1994[651] **5**
Zagoria, 1988[652] **1**
Zakharova, 1990[653] **12**
Zhao, 2003[654] **14**
Zubarev, 1990[655] **10**

Chapter 6

Results of the review

Results of the literature searches

The literature searches identified 8590 references. These were screened for relevance and 650 were considered to be potentially relevant. Copies of three of these articles could not be obtained during the review.[656–658] A total of 647 articles was assessed for inclusion in the review. *Figure 1* shows the flow of studies through the review process and the number of studies excluded according to each of the inclusion criteria. Chapter 5 summarises the studies excluded from the review.

A total of 113 studies met the review inclusion criteria. Fifty-eight studies provided data on the diagnostic accuracy of tests to diagnose stenosis/occlusion, nine of which also provided data on adverse events. One controlled trial provided data on the impact of the assessment method on patient management and/or patient outcomes. Four studies that did not meet the inclusion criteria for the review of diagnostic accuracy reported results relating to patient attitudes, two of which also provided data on adverse events. An additional 44 studies that did not meet the inclusion criteria for the review of diagnostic accuracy reported results relating to adverse events. Six economic evaluations met the inclusion criteria for the review.

Seven non-English-language papers were included in the review: five German,[51,56,58,61,90] one French[120] and one Russian.[69] One German-language paper met the inclusion criteria for the review, but could not be translated in time to be included.[127]

Where studies were only published as an abstract and insufficient details were reported to screen studies for inclusion or extract the relevant data, authors were contacted to provide further information. In total, 37 authors were contacted. Four authors replied, providing further information about their study. All four studies were found to fail the inclusion criteria.

Assessment of stenosis/occlusion

A total of 25 studies provided diagnostic accuracy results for MRA: one evaluated 2D PC MRA, ten evaluated 2D TOF MRA (one of these studies investigated both 2D TOF MRA and DUS), 13 evaluated CE MRA, and one evaluated both 2D TOF and CE MRA (in addition to DUS). Seven studies provided diagnostic accuracy results for CTA and 28 studies provided diagnostic accuracy results for DUS.

Most of the studies reported results by arterial segment. The number of arterial segments assessed per patient and their anatomical distribution varied between studies and were incompletely reported. The majority of studies provided accuracy data for more than one anatomical area (e.g. above knee, below knee) and/or more than one stenosis threshold. Pooling of studies was considered only where 2×2 accuracy data were reported in the same way (e.g. arterial segment, artery or limb), for the same anatomy (above knee, below knee or whole leg) and using the same stenosis threshold. Thus, the number and, to some extent, distribution of arterial segments could vary between studies within a grouping considered for pooling. Each study contributed a maximum of one data set to each pooled group.

Differences between studies regarding quality items, test specific details (e.g. the type of coil used and field strength for MRA; PSVR, type of probe, and use of colour for DUS; and the instrument used for CTA), the use of digital subtraction (DSA) as part of the reference standard, sample size, Fontaine classification, date of publication (as a surrogate for technological advances), the inclusion/exclusion of the foot in the scans of the whole leg or below knee, and restriction of the population to a subgroup (e.g. people with diabetes mellitus) were considered as potential explanatory factors for the variability seen between study findings. These issues are discussed in detail below; data were insufficient to allow valid statistical exploration of hypothesised sources of heterogeneity. There was insufficient information regarding the proportion of patients included in the studies with diabetes mellitus, or who were smokers (or had smoked), to consider subgroup analyses for these patient groups.

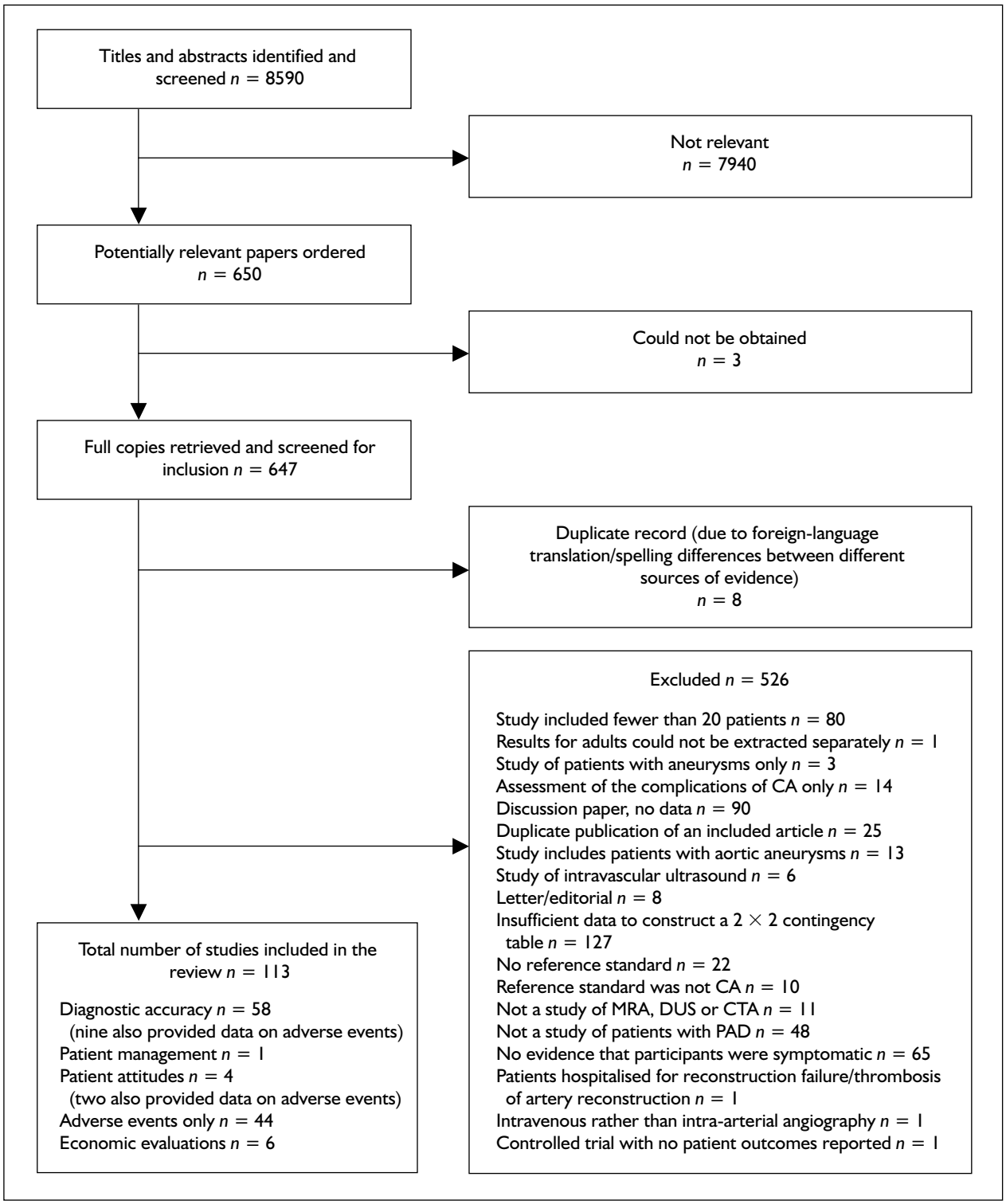


FIGURE 1 *Flowchart of studies through review process*

MRA

One study evaluated 2D PC MRA,[66] 11 evaluated 2D TOF MRA,[22,27,29,32,40,41,53,55,64,69,74] and 14 evaluated CE MRA.[9,28,36,46,49,51,53,61,65,67,68,70,73,76] There were no studies providing results for the assessment of 3D TOF MRA. The full results of the quality assessment using the QUADAS tool for the 25 studies evaluating MRA are presented in *Table 4*. Eighteen studies (72%) did not include an appropriate patient spectrum or failed to provide sufficient details of the patient population for this to be judged, and 12 (48%) did not provide adequate details of the patient selection criteria. The tests themselves were generally well

TABLE 4 *QUADAS evaluation for studies assessing MRA*

Study	Appropriate patient spectrum	Selection criteria described	< 1 month between tests	All received reference standard	Same reference standard	Reference standard independent	Test details well reported	Reference standard details well reported	Test results blind to reference standard	Reference standard blind to test results	Clinical data available	Uninterpretable results reported	Withdrawals explained
2D PC													
Steffens, 1997[66]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
2D TOF													
Baum, 1995[22]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Cortell, 1996[27]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Currie, 1995[29]	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Eklof, 1998[32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Hoch, 1999[41]	No	Yes	Yes	No	Yes	Yes	Yes	No	Unclear	Unclear	No	Unclear	Yes
Hoch, 1996[40]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Unclear
Lundin, 2000[53] (also assessed CE MRA)	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
McDermott, 1995[55]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear
Snidow, 1995[64]	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Timonina, 1999[69]	No	No	Yes	No	No	Yes	Yes	No	Unclear	Unclear	Unclear	Yes	No
Yucel, 1993[74]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
CE													
Cronberg, 2003[28]	Unclear	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Hany, 1997[36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Kreitner, 2000[46]	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Laissy, 1998[49]	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear
Lenhart, 2000[51]	Unclear	No	Yes	No	Yes	Yes	Yes	No	Unclear	Yes	Unclear	Yes	Yes
Meaney, 1999[9]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear	Unclear	Yes	Yes
Schafer, 2003[61]	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Snidow, 1996[65]	No	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Steffens, 2003[67]	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes
Sueyoshi, 1999[68]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Winterer, 1999[73]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes	Unclear	Yes	Yes
Zhang, 2005[76]	No	No	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Vavrik, 2004[70]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes

conducted. Twenty studies (80%) reported having less than a 1-month interval between the index test and reference standard; 1 month was the maximum time interval judged appropriate to minimise the potential impact of disease progression on test results. All patients received the reference standard in 21 studies (84%) and in 24 studies (96%) patients received the same reference standard test. The decision to use the reference test was independent of the MRA results in all the studies. The MRA results were interpreted without knowledge of the reference test results (and vice versa) in 21 studies (84%). Whether or not clinical data were available at the time the results were interpreted was poorly reported, with only one study reporting that clinical data were available.

Further details of the diagnostic accuracy results for the individual MRA techniques are presented below by technique.

2D PC MRA

One study[66] assessed the accuracy of 2D PC MRA for grading lesions, already identified using intra-arterial DSA, at the diagnostic thresholds of 50% stenosis and occlusion. The study assessed grading of stenoses in the whole leg. The sensitivity was 98% and the specificity was 74%. The positive likelihood ratio (LR+) was 3.6 and the negative likelihood ratio (LR–) was 0.03 (*Table 5*).

2D TOF MRA

The 11 studies evaluating 2D TOF MRA[22,27,29,32,40,41,53,55,64,69,74] provided a total of 22 data sets. The results are reported by the anatomy assessed and the full set of diagnostic accuracy results is presented in *Table 5*.

Whole leg

Results for the detection of a stenosis of at least 50% or occlusion were reported by five studies.[22,40,41,64,74] The sensitivity of 2D TOF MRA ranged from 79% (specificity 89%) to 94% (specificity 92%). The specificity ranged from 74% (sensitivity 92%) to 92% (sensitivity 94%). There was evidence of significant statistical heterogeneity between the study results ($p < 0.001$) for all the diagnostic accuracy measures, hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 2*). The median LR+ was 7.1, with a range from 3.5 (LR– of 0.12) to 11.7 (LR– of 0.07). The median LR– was 0.12, with a range from 0.07 (LR+ of 11.7) to 0.24 (LR+ of 7.1).

The study in this group that reported the highest sensitivity (94%), specificity (92%) and LR+ (11.7) and the lowest LR– (0.07)[40] was one of only two that reported Fontaine classification; 62% of the patients had stage IV PAD. More severe pathology in the diseased patients included in a study implies that they are more different from the

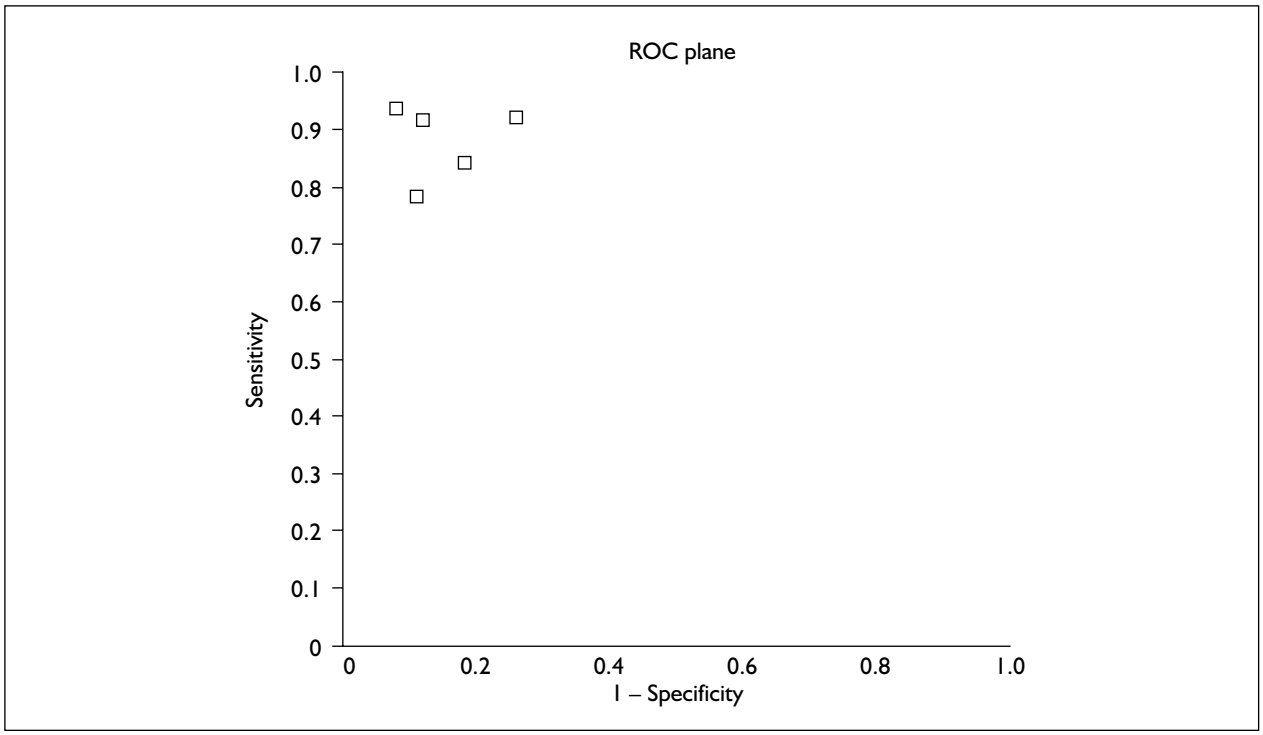


FIGURE 2 *ROC plot for 2D TOF MRA: whole leg, ⩾50% stenosis*

TABLE 5 *Results of studies assessing 2D PC, or 2D TOF MRA, reported by area of leg assessed*

Study	Stenosis threshold	Results reported by	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR
2D PC MRA: whole leg											
Steffens 1997[66]	50–100%	Area of stenosis/ occlusion	229	5	5	14	97.9 (95.1, 99.1)	73.7 (51.2, 88.2)	3.6 (1.7,7.2)	0.03 (0.01, 0.08)	110.0
2D TOF MRA: whole leg, ⩾50% stenosis											
Baum, 1995[22]	50–100%	Segment	527	101	100	460	84.1 (81.0, 86.7)	82.0 (78.6, 85.0)	4.7 (3.9, 5.6)	0.20 (0.16, 0.23)	23.8
Hoch, 1999[41]	50–100%	Segment	161	37	44	302	78.5 (72.4, 83.6)	89.1 (85.3, 92.0)	7.1 (5.2, 9.7)	0.24 (0.19, 0.32)	29.3
Hoch, 1996[40]	50–100%	Segment	172	13	12	155	93.5 (88.9, 96.2)	92.3 (87.2, 95.4)	11.7 (7.0, 19.5)	0.07 (0.04, 0.13)	159.0
Snidow, 1995[64]	50–100%	Segment	80	76	7	215	92.0 (84.3, 96.0)	73.9 (68.5, 78.6)	3.5 (2.9, 4.3)	0.12 (0.06, 0.23)	30.2
Yucel, 1993[74]	50–100%	Segment	65	16	6	119	91.5 (82.8, 96.1)	88.1 (81.6, 92.6)	7.5 (4.7, 11.9)	0.10 (0.05, 0.21)	73.0
2D TOF MRA: whole leg, ⩾70% stenosis											
Yucel, 1993[74]	70–100%	Segment	53	5	6	142	89.8 (79.5, 95.3)	96.6 (92.3, 98.5)	24.0 (10.5, 54.7)	0.11 (0.05, 0.23)	213.3
2D TOF MRA: whole leg, occlusion											
Baum, 1995[22]	100%	Segment	322	118	76	672	80.9 (76.8, 84.5)	85.1 (82.4, 87.4)	5.4 (4.5, 6.4)	0.23 (0.18, 0.28)	23.9
Hoch, 1999[41]	100%	Segment	103	17	31	393	76.9 (69.0 ,83.2)	95.9 (93.5, 97.4)	18.0 (11.3, 28.7)	0.24 (0.18, 0.33)	73.9
Hoch, 1996[40]	100%	Segment	101	4	11	236	90.2 (83.3, 94.4)	98.3 (95.8, 99.4)	48.1 (19.2, 120.4)	0.10 (0.06, 0.18)	463.9
Yucel, 1993[74]	100%	Segment	40	4	0	162	100 (91.2, 100)	97.6 (94.0, 99.1)	36.7 (14.7, 91.3)	0.01 (0.00, 0.20)	2925.0
2D TOF MRA: above knee											
Lundin, 2000[53]	50–100%	Segment	35	20	8	197	81.4 (67.4, 90.3)	90.8 (86.2, 94.0)	8.6 (5.5, 13.3)	0.21 (0.12, 0.39)	40.2
	100%	Segment	13	7	2	238	86.7 (62.1, 96.3)	97.1 (94.2, 98.6)	27.7 (13.3, 57.7)	0.16 (0.05, 0.50)	171.7
Currie, 1995[29]	50–99%	Segment	25	7	10	38	71.4 (54.9, 83.7)	84.4 (71.2, 92.3)	4.3 (2.2, 8.6)	0.35 (0.21, 0.59)	12.5
Timonina, 1999[69]	100%	Artery	36	0	1	163	97.3 (86.2, 99.5)	100 (97.7, 100)	315.1 (19.8, 5020)	0.04 (0.01, 0.19)	7957.0
2D TOF MRA: below knee											
Cortell, 1996[27]	50–100%	Segment	172	10	3	208	98.3 (95.1, 99.4)	95.4 (91.8, 97.5)	20.4 (11.3, 36.9)	0.02 (0.01, 0.06)	978.7
	75–100%	Segment	155	10	3	225	98.1 (94.6, 99.4)	95.7 (92.3, 97.7)	22.0 (12.2, 39.7)	0.02 (0.01, 0.06)	954.2
	100%	Segment	125	7	3	258	97.7 (93.3, 99.2)	97.4 (94.6, 98.7)	34.5 (17.0, 69.9)	0.03 (0.01, 0.08)	1235.9
McDermott, 1995[55]	100%	Segment	95	1	21	99	81.9 (73.9, 87.8)	99.0 (94.6, 99.8)	55.0 (11.2, 269.7)	0.19 (0.13, 0.27)	294.6
	Diseased or occluded	Segment	124	7	15	70	89.2 (83.0, 93.4)	90.9 (82.4,95.5)	9.2 (4.7,18.3)	0.12 (0.08, 0.20)	75.5
Eklof, 1998[32]	50–100%	Artery	59	2	14	31	80.8 (70.3,88.2)	93.9 (80.4, 98.3)	10.9 (3.3, 36.3)	0.21 (0.13, 0.34)	51.7
	100%	Artery	40	10	7	49	85.1 (72.3,92.6)	83.1 (71.5, 90.5)	4.8 (2.7, 8.5)	0.19 (0.10, 0.37)	25.5
2D TOF MRA: foot											
Eklof, 1998[32]	100%	Artery	19	8	3	3	86.4 (66.7,95.3)	27.3 (9.7, 56.6)	1.2 (0.8, 1.8)	0.52 (0.14, 1.93)	2.3

0.5 was added to all values for the calculation of LR+, LR– and DOR.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

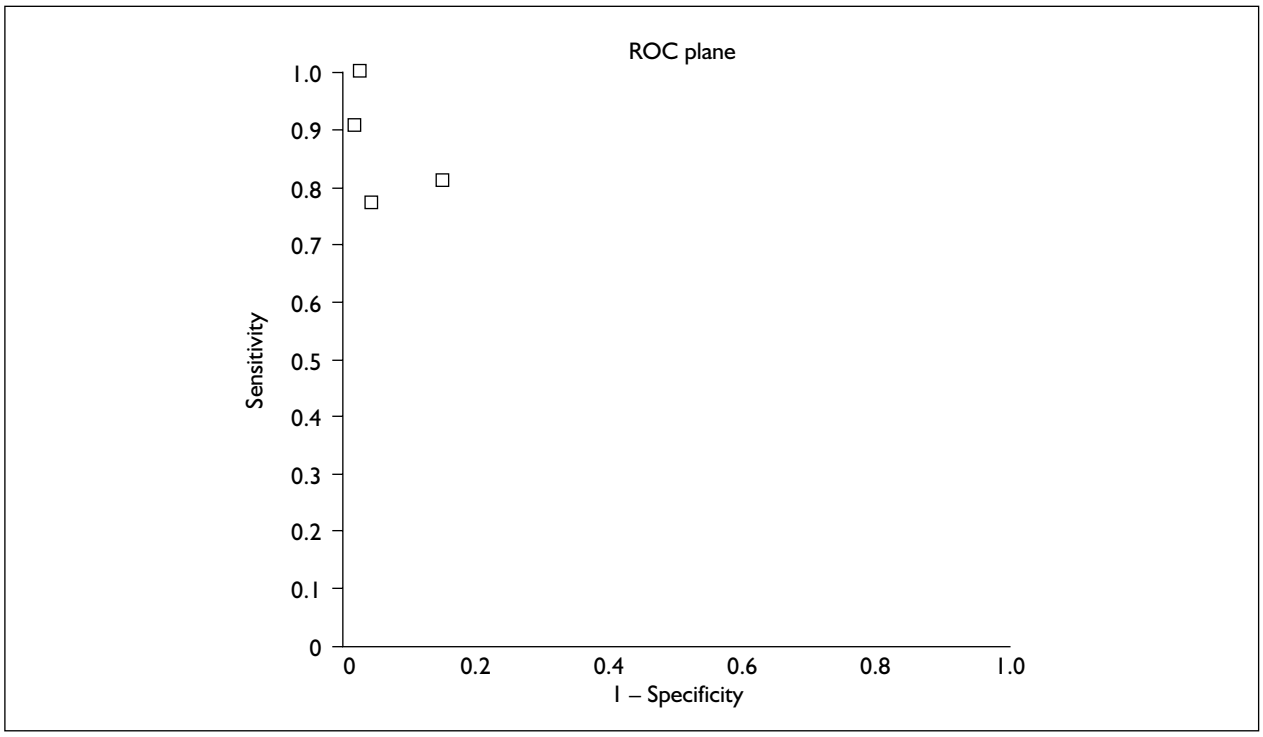


FIGURE 3 *ROC plot for 2D TOF MRA: whole leg, occlusion*

'normal' than would be a less severely diseased population, and hence more easily distinguished. This can give rise to an apparent increase in the performance of diagnostic tests. However, the other study reporting Fontaine classification had only 16% stage IV patients, and this reported similar diagnostic performance: sensitivity of 92%, specificity of 88%, LR+ of 7.5 and LR– of 0.10.[74]

One study[74] provided results for the detection of a stenosis of 70% or greater; the sensitivity was 90% and the specificity was 97% (*Table 5*).

Results for the detection of an occlusion were reported by four studies.[22,40,41,74] The sensitivity ranged from 77% (specificity 96%) to 100% (specificity 98%). The specificity ranged from 85% (sensitivity 81%) to 98% (for two studies with sensitivities of 90% and 100%). Again, there was evidence of significant statistical heterogeneity between the study results ($p = 0.004$ for LR–, $p < 0.001$ for all other measures). The sensitivities and specificities have been plotted in ROC space (*Figure 3*). The median LR+ was 27.4, with a range from 5.4 (LR– of 0.23) to 48.1 (LR– of 0.1). The median LR– was 0.17, with a range from 0.01 (LR+ of 36.7) to 0.24 (LR+ of 18).

Above the knee

Three studies provided results for assessment above the knee, but these did not use similar thresholds and did not report the results in the same way (e.g. arterial segment, artery or limb).[29,53,69] Further details are presented in *Table 5*.

Below the knee

Three studies provided results for assessment below the knee or of the foot;[27,32,55] further details are presented in *Table 5*. Only one study[32] reported separate results for arteries in the foot; for detecting an occlusion the sensitivity was 86% and the specificity was 27%.

CE MRA

Fourteen studies evaluated CE MRA and provided a total of 34 data sets.[9,28,36,46,49,51,53,61,65,67,68,70,73,76] The results are reported by the anatomy assessed and the full set of diagnostic accuracy results is presented in *Table 6*.

Whole leg

Results for the detection of a stenosis of 50% or greater were reported by seven studies.[28,49,51,61,67,68,73] The sensitivity of CE MRA ranged from 92% (for two studies with specificities of 64% and 97%) to 99.5% (specificity 99%). The specificity ranged from 64% (sensitivity 92%) to 99% (for two studies with sensitivities of 97% and 99.5%). There was evidence of significant statistical heterogeneity between the study results ($p = 0.002$ for sensitivity, $p < 0.001$ for all other

TABLE 6 *Results of studies assessing CE MRA, reported by area of leg assessed*

Study	Stenosis threshold	Results reported by	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR
Whole leg, ⩾50% stenosis											
Cronberg, 2003[28]	50–100%	Segment	227	62	20	109	91.9 (87.8, 94.7)	63.7 (56.3, 70.6)	2.5 (2.1, 3.1)	0.13 (0.08, 0.20)	19.4
Laissy, 1998[49]	50–100%	Segment	104	14	9	393	92.0 (85.6, 95.8)	96.6 (94.3, 97.9)	25.8 (15.5, 42.9)	0.09 (0.05, 0.16)	298.5
Lenhart, 2000[51]	50–100%	Segment	79	8	4	129	95.2 (88.3, 98.1)	94.2 (88.9, 97.0)	15.4 (8.0, 29.5)	0.06 (0.02, 0.14)	269.2
Schafer, 2003[61]	51–100%	Segment	138	13	9	416	93.9 (88.8, 96.7)	97.0 (94.9, 98.2)	29.8 (17.6, 50.5)	0.07 (0.04, 0.12)	449.8
Steffens, 2003[67]	51–100%	Segment	185	8	1	706	99.5 (97.0, 99.9)	98.9 (97.8, 99.4)	83.4 (42.8, 162.8)	0.01 (0.00, 0.04)	10278.9
Sueyoshi, 1999[68]	50–100%	Segment	67	3	2	351	97.1 (90.0, 99.2)	99.2 (97.5, 99.7)	97.8 (34.5, 277.7)	0.04 (0.01, 0.12)	2711.6
Winterer, 1999[73]	51–100%	Segment	362	43	14	1361	96.3 (93.8, 97.8)	96.9 (95.9, 97.7)	31.1 (23.2, 41.6)	0.04 (0.02, 0.07)	782.5
Whole leg, ⩾70% stenosis											
Schafer, 2003[61]	76–100%	Segment	110	3	4	459	96.5 (91.3, 98.6)	99.4 (98.1, 99.8)	127.1 (44.7, 361.2)	0.04 (0.02, 0.10)	3223.8
Steffens, 2003[67]	76–100%	Segment	147	11	4	738	97.4 (93.4, 99.0)	98.5 (97.4, 99.2)	63.3 (35.6, 112.4)	0.03 (0.01, 0.07)	2104.9
Sueyoshi, 1999[68]	75–100%	Segment	53	4	0	366	100 (93.2, 100)	98.9 (97.3, 99.6)	81.7 (32.6, 204.7)	0.01 (0.00, 0.15)	8714.6
Vavrik, 2004[70]	70–100%	Segment	170	26	17	661	90.9 (85.9, 94.2)	96.2 (94.5, 97.4)	23.5 (16.2, 34.3)	0.10 (0.06, 0.15)	243.2
Whole leg, occlusion											
Lenhart, 2000[51]	100%	Segment	54	2	4	160	93.1 (83.6, 97.3)	98.8 (95.6, 99.7)	60.2 (17.6, 206.5)	0.08 (0.03, 0.19)	777.5
Meaney, 1999[9]	100%	Segment	83	16	15	516	84.7 (76.3, 90.5)	97.0 (95.2, 98.1)	27.2 (16.8, 44.1)	0.16 (0.10, 0.26)	168.6
Schafer, 2003[61]	100%	Segment	72	1	5	498	93.5 (85.7, 97.2)	99.8 (98.9, 100)	309.8 (62.6, 1533)	0.07 (0.03, 0.16)	4380.8
Steffens, 2003[67]	100%	Segment	85	7	4	804	95.5 (89.0, 98.2)	99.1 (98.2, 99.6)	102.9 (50.4, 210.0)	0.05 (0.02, 0.12)	2038.1
Sueyoshi, 1999[68]	100%	Segment	39	1	0	383	100 (91.0, 100)	99.7 (98.5, 100)	253.5 (51.3, 1252)	0.01 (0.00, 0.20)	20197.7
Winterer, 1999[73]	100%	Segment	255	11	13	1502	95.1 (91.9, 97.1)	99.3 (98.7, 99.6)	125.0 (70.3, 222.5)	0.05 (0.03, 0.09)	2472.7
Above knee, ⩾50% stenosis											
Lenhart, 2000[51]	50–100%	Segment	24	6	2	83	92.3 (75.9, 97.9)	93.3 (86.1, 96.9)	12.6 (5.9, 26.6)	0.10 (0.03, 0.33)	125.9
Lundin, 2000[53]	50–100%	Segment	35	18	8	204	81.4 (67.4, 90.3)	91.9 (87.5, 94.8)	9.7 (6.1, 15.4)	0.21 (0.12, 0.39)	46.2
Hany, 1997[36]	50–100%	Artery	62	7	2	163	96.9 (89.3, 99.1)	95.9 (91.7, 98.0)	21.9 (10.9, 44.2)	0.04 (0.01, 0.14)	545.0
Snidow, 1996[65]	50–100%	Artery	26	6	0	96	100 (87.1, 100)	94.1 (87.8, 97.3)	15.6 (7.4, 32.8)	0.02 (0.00, 0.31)	786.8
Above knee, ⩾70% stenosis											
Vavrik, 2004[70]	70–100%	Segment	86	13	9	468	90.5 (83.0, 94.9)	97.3 (95.4, 98.4)	32.2 (18.9, 54.7)	0.10 (0.06, 0.19)	316.0
Above knee, occlusion											
Lenhart, 2000[51]	100%	Segment	14	0	2	99	87.5 (64.0, 96.5)	100 (96.3, 100)	170.6 (10.7, 2728)	0.15 (0.05, 0.46)	1154.2
Lundin, 2000[53]	100%	Segment	13	0	2	250	86.7 (62.1, 96.3)	100 (98.5, 100)	423.6 (26.4, 6808)	0.16 (0.05, 0.49)	2705.4
Hany, 1997[36]	100%	Artery	19	1	0	214	100 (83.2, 100)	99.5 (97.4, 99.9)	140.4 (28.5, 692.8)	0.03 (0.00, 0.39)	5577.0
Snidow, 1996[65]	100%	Artery	18	0	0	110	100 (82.4, 100)	100 (96.6, 100)	216.2 (13.6, 3438)	0.03 (0.00, 0.41)	8177.0

continued

TABLE 6 *Results of studies assessing CE MRA, reported by area of leg assessed (cont'd)*

Study	Stenosis threshold	Results reported by	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR
Below knee, ⩾50% stenosis											
Kreitner, 2000[46]	50–100%	Segment	27	3	11	33	71.1 (55.2, 83.0)	91.7 (78.2, 97.1)	7.5 (2.7, 20.6)	0.33 (0.20, 0.54)	22.9
Lenhart, 2000[51]	50–100%	Segment	55	2	2	46	96.5 (88.1, 99.0)	95.8 (86.0, 98.8)	18.8 (5.6, 62.8)	0.05 (0.01, 0.15)	412.9
Zhang, 2005[76]	51–100%	Segment	252	31	52	207	82.9 (78.3, 86.7)	87.0 (82.1, 90.7)	6.3 (4.5, 8.7)	0.20 (0.15, 0.25)	31.7
Below knee, ⩾70% stenosis											
Vavrik, 2004[70]	70–100%	Segment	84	13	8	193	91.3 (83.8, 95.5)	93.7 (89.5, 96.3)	13.9 (8.3, 23.4)	0.10 (0.05, 0.19)	142.5
Below knee, occlusion											
Lenhart, 2000[51]	100%	Segment	40	2	2	61	95.2 (84.2, 98.7)	96.8 (89.1, 99.1)	24.1 (7.1, 81.5)	0.06 (0.02, 0.20)	398.5
Zhang, 2005[76]	100%	Segment	200	22	32	288	86.2 (81.2, 90.1)	92.9 (89.5, 95.3)	11.9 (8.0, 17.8)	0.15 (0.11, 0.21)	79.1
Foot											
Zhang, 2005[76]	51–100%	Segment	59	20	16	48	78.7 (68.1, 86.4)	70.6 (58.9, 80.1)	2.6 (1.8, 3.9)	0.31 (0.20, 0.49)	8.5
	100%	Segment	50	11	13	69	79.4 (67.8, 87.5)	86.3 (77.0, 92.1)	5.6 (3.2, 9.6)	0.25 (0.15, 0.40)	22.6

0.5 was added to all values for the calculation of LR+, LR– and DOR.

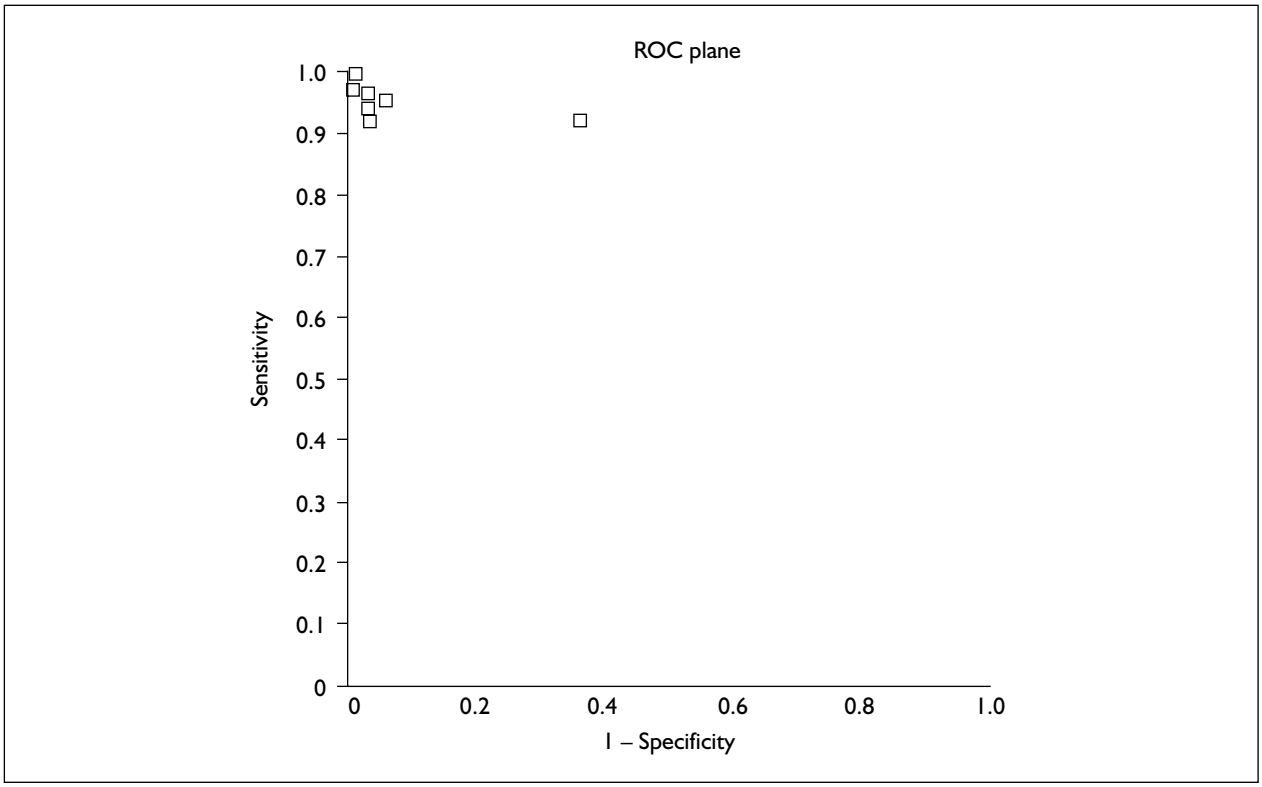


FIGURE 4 *ROC plot for CE MRA: whole leg, ⩾50% stenosis*

measures), hence no pooling was undertaken. One study had a low specificity in comparison with the others;[28] however, there was still statistically significant heterogeneity when the analysis was repeated without this study. The sensitivities and specificities have been plotted in ROC space (*Figure 4*). The median LR+ was 29.8, with a range from 2.5 (LR– of 0.13) to 97.8 (LR– of 0.04). The median LR– was 0.06, with a range from 0.01 (LR+ of 83.4) to 0.13 (LR+ of 2.5).

The study that had a low specificity in comparison with the others[28] was the only study to include the foot in the scan. The diagnostic accuracy of MRA is thought to be lower in the foot than in other areas of the leg and this may have been a factor in this difference.

Results for the detection of a stenosis of 70% or greater were reported by four studies.[61,67,68,70] The sensitivity of CE MRA ranged from 91% (specificity 96%) to 100% (specificity 99%). The specificity ranged from 96% (sensitivity 91%) to 99% (for three studies with sensitivities of 97%, 97% and 100%). There was evidence of significant statistical heterogeneity between the study results ($p = 0.004$ for sensitivity, $p = 0.012$ for LR–, $p < 0.001$ for all other measures), hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 5*). The median LR+ was 72.5, with a range from 23.5 (LR– of 0.1) to 127.1 (LR– of 0.04). The median LR– was 0.04, with a range from 0.01 (LR+ of 81.7) to 0.1 (LR+ of 23.5).

Results for the detection of an occlusion were reported by six studies.[9,51,61,67,68,73] The sensitivity of CE MRA ranged from 85% (specificity 97%) to 100% (specificity 99.7%). The specificity ranged from 97% (sensitivity 85%) to 99.8% (sensitivity 94%). There was evidence of significant statistical heterogeneity between the study results ($p = 0.006$ for sensitivity, $p = 0.005$ for LR–, $p < 0.001$ for all other measures), hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 6*). The median LR+ was 114, with a range from 27.2 (LR– of 0.16) to 309.8 (LR– of 0.07). The median LR– was 0.06, with a range from 0.01 (LR+ of 253.5) to 0.16 (LR+ of 27.2).

Above the knee

Five studies provided results for assessment above the knee, but not all reported results on an arterial segment basis.[36,51,53,65,70] Further details are presented in *Table 6*.

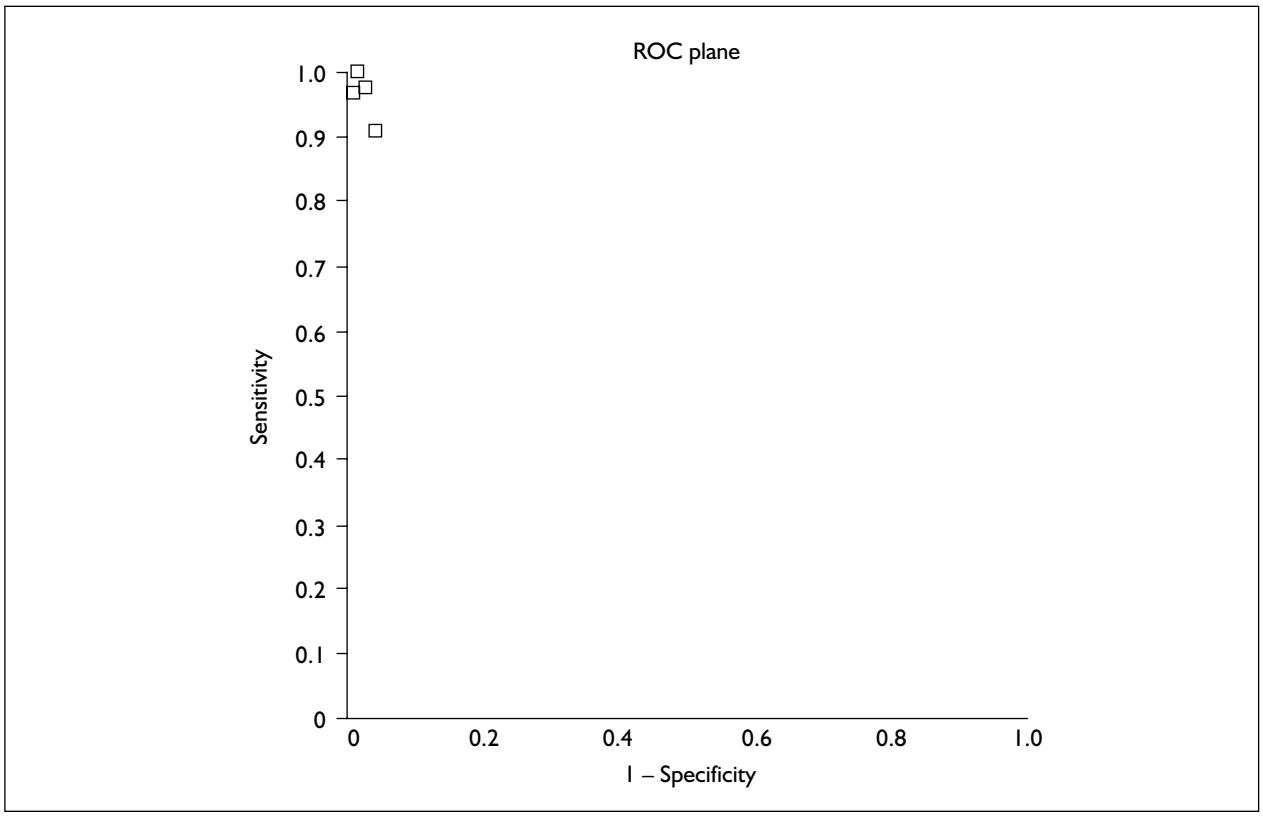


FIGURE 5 *ROC plot for CE MRA: whole leg, ⩾70% stenosis*

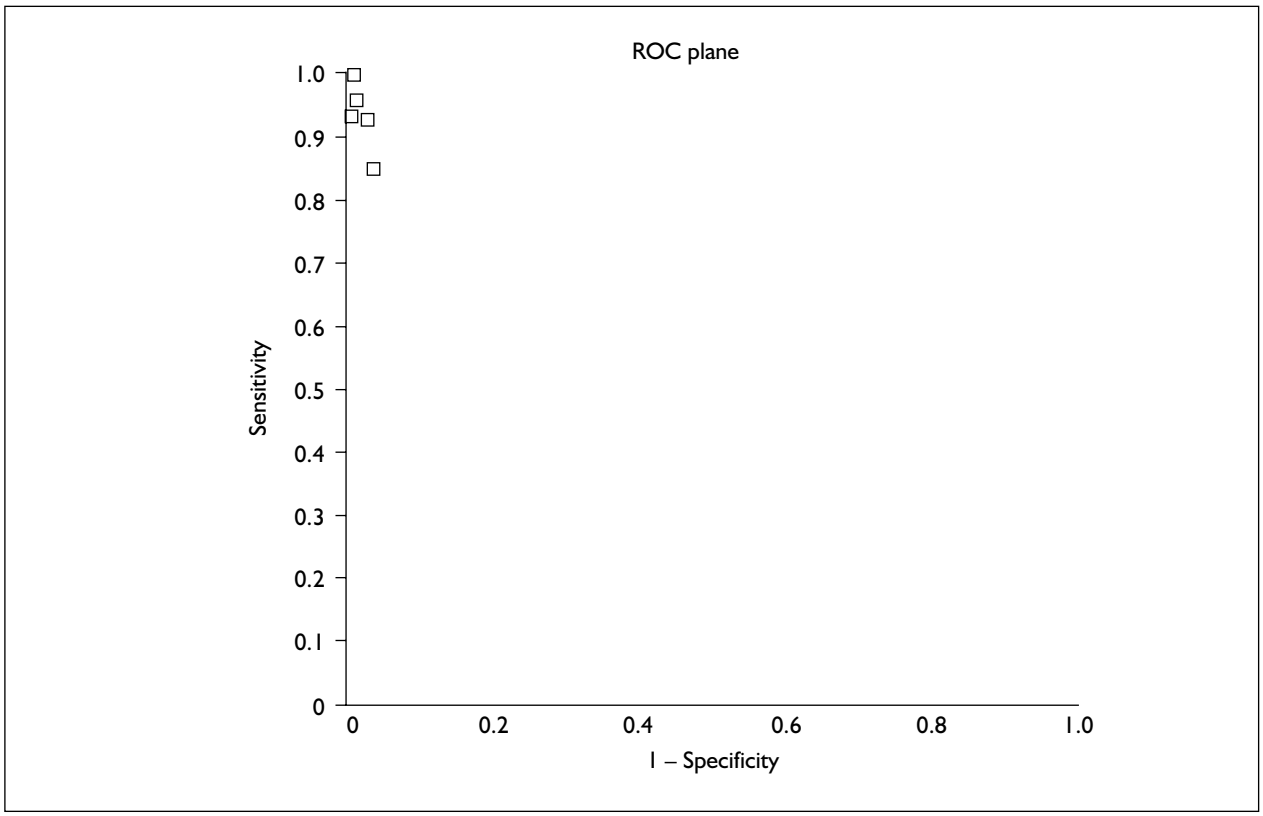


FIGURE 6 *ROC plot for CE MRA: whole leg, occlusion*

Below the knee
Four studies provided results for assessment below the knee or of the foot.[46,51,70,76] Further details are presented in *Table 6*.

Three studies provided results for assessment of stenosis of 50% or greater below the knee using CE MRA. One study in this group was restricted to patients with diabetes mellitus.[46] This study had the lowest sensitivity (71%).

One study[76] assessed the ability of CE MRA to detect stenoses in the foot. For the detection of a stenosis greater than 50%, the sensitivity was 79% and the specificity was 71%; and for the detection of an occlusion, the sensitivity was 79% and the specificity was 86%.

CTA

The full results of the quality assessment using the QUADAS tool, for the seven studies evaluating CTA, are presented in *Table 7*.
Five studies (71%) did not include an appropriate patient spectrum, or failed to provide sufficient details of the patient population for this to be judged, and two (29%) did not provide adequate details of the patient selection criteria. The tests themselves were generally well conducted. Five studies (71%) reported having less than a 1-month interval between the index test and reference standard and all patients received the reference standard in all seven studies. All studies reported that the decision to use the reference test was independent of the CTA results.
The CTA results were interpreted without knowledge of the reference test results (and vice versa) in five studies (71%). Whether or not clinical data were available at the time the results were interpreted was again poorly reported, with no studies reporting that clinical data were available.

The seven studies evaluating CTA provided a total of 22 data sets.[26,38,54,57–60] The full set of diagnostic accuracy results is presented in *Table 8*. All the studies presented the results on an arterial segment basis.

Whole leg
Results for the detection of a stenosis of 50% or greater were reported by six studies.[26,38,54,57–59]
The sensitivity of CTA ranged from 89% (for two studies with specificities of 86% and 91%) to 99% (specificity 97%). The specificity ranged from 83% (sensitivity 92%) to 97% (sensitivity 99%). There was evidence of significant statistical heterogeneity between the study results ($p < 0.001$), hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 7*). The median LR+ was 12, with a range from 5.5 (LR– of 0.1) to 37.1 (LR– of 0.01). The median LR– was 0.11, with a range from 0.01 (LR+ of 37.1) to 0.14 (LR+ of 6.3).

The study in this group that reported the highest sensitivity (99%), specificity (97%) and LR+ (37.1) and the lowest LR– (0.01)[26] was one of two studies that scored 12 out of 13 on the quality assessment, and reported recruiting an appropriate patient spectrum. The other high-quality study reported the next highest sensitivity (97%).[59]

Results for the detection of a stenosis of 70% or greater were reported by three studies.[38,54,59]
There was no evidence of statistical heterogeneity between the study results ($p > 0.1$ for all accuracy measures). The pooled sensitivity was 89% (95% CI 86 to 92%), the pooled specificity was 98% (95% CI 97 to 99%), the pooled LR+ was 44 (95% CI 31.5 to 61.3) and the pooled LR– was 0.12 (95% CI 0.09 to 0.16). The sensitivities and specificities have been plotted with the sROC curve (*Figure 8*). The area under the curve (AUC) was 0.987 and the Q^* index (the point at which sensitivity and specificity are equal) was 0.951.

Results for the detection of an occlusion were reported by five studies.[26,38,54,58,59] There was no evidence of statistical heterogeneity between the study results for specificity, LR+ and LR– ($p > 0.09$), although there was for sensitivity ($p = 0.001$). The sensitivity ranged from 89% (specificity 99.8%) to 100% (specificity 100%). The pooled specificity was 99.5% (95% CI 99.2 to 99.7%), the pooled LR+ was 160.2 (95% CI 76.7 to 334.3), and the pooled LR– was 0.06 (95% CI 0.03 to 0.13). The sensitivities and specificities have been plotted in ROC space (*Figure 9*). There were no obvious differences between the studies to explain the heterogeneity seen.

Above the knee
Two studies reported results for above the knee.[57,60] The study by Rieker[60] gave results for maximum intensity projections and cine axial images separately. Further details are provided in *Table 8*.

Below the knee
Only one study provided data evaluating the accuracy of CTA below the knee.[57] This found a sensitivity of 90% and a specificity of 74% for detecting a stenosis of 50% or greater (*Table 8*).

TABLE 7 *QUADAS evaluation for studies assessing CTA*

Study	Appropriate patient spectrum	Selection criteria described	< 1 month between tests	All received reference standard	Same reference standard	Reference standard independent	Test details well reported	Reference standard details well reported	Test results blind to reference standard	Reference standard blind to test results	Clinical data available	Uninterpretable results reported	Withdrawals explained
Heuschmid, 2003[38]	Unclear	No	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes
Martin, 2003[54]	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Puls, 2002[58]	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Rieker, 1996[59]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Rieker, 1997[60]	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	Yes	Yes
Catalano, 2004[26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Portugaller, 2004[57]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes

TABLE 8 *Results of studies assessing CTA, reported by area of leg assessed*

Study	Stenosis threshold	Results reported by	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR
Whole leg, ⩾50% stenosis											
Heuschmid, 2003[38]	51–100%	Segment	133	40	16	379	89.3 (83.3, 93.3)	90.5 (87.3, 92.9)	9.2 (6.9, 12.4)	0.12 (0.08, 0.19)	75.8
Martin, 2003[54]	50–100%	Segment	327	61	38	886	89.6 (86.0, 92.3)	93.6 (91.8, 95.0)	13.8 (10.8, 17.6)	0.11 (0.08, 0.15)	122.6
Puls, 2002[58]	51–100%	Segment	56	17	7	106	88.9 (78.8, 94.5)	86.2 (79.0, 91.2)	6.3 (4.0, 9.7)	0.14 (0.07, 0.27)	45.8
Rieker, 1996[59]	50–100%	Segment	111	20	3	193	97.4 (92.5, 99.1)	90.6 (85.9, 93.8)	10.1 (6.7, 15.3)	0.03 (0.01, 0.09)	300.7
Catalano, 2004[26]	51–100%	Segment	251	23	3	860	98.8 (96.6, 99.6)	97.4 (96.1, 98.3)	37.1 (24.9, 55.3)	0.01 (0.00, 0.04)	2631.2
Portugaller, 2004[57]	50–100%	Segment	240	80	21	399	92.0 (88.0, 94.7)	83.3 (79.7, 86.4)	5.5 (4.5, 6.7)	0.10 (0.07, 0.15)	55.5
Whole leg, ⩾70% stenosis											
Heuschmid, 2003[38]	76–100%	Segment	88	7	12	461	88.0 (80.2, 93.0)	98.5 (96.9, 99.3)	54.8 (26.8, 111.9)	0.13 (0.07, 0.21)	435.7
Martin, 2003[54]	75–100%	Segment	236	20	34	1022	87.4 (82.9, 90.8)	98.1 (97.1, 98.8)	44.4 (28.9, 68.3)	0.13 (0.10, 0.18)	341.9
Rieker, 1996[59]	75–100%	Segment	91	6	6	224	93.8 (87.2, 97.1)	97.4 (94.4, 98.8)	33.2 (15.5, 70.9)	0.07 (0.03, 0.14)	486.2
Whole leg, occlusion											
Heuschmid, 2003[38]	100%	Segment	49	6	5	508	90.7 (80.1, 96.0)	98.8 (97.5, 99.5)	71.3 (33.1, 153.8)	0.10 (0.05, 0.22)	704.1
Martin, 2003[54]	100%	Segment	202	2	26	1082	88.6 (83.8, 92.1)	99.8 (99.3, 99.9)	383.8 (111.2, 1325)	0.12 (0.08, 0.17)	3308.8
Puls, 2002[58]	100%	Segment	13	0	0	173	100 (77.2, 100)	100 (97.8, 100)	335.6 (21.0, 5354)	0.04 (0.00, 0.54)	9369.0
Rieker, 1996[59]	100%	Segment	61	1	1	264	98.4 (91.4, 99.7)	99.6 (97.9, 99.9)	173.1 (35.1, 854.2)	0.02 (0.00, 0.12)	7229.7
Catalano, 2004[26]	100%	Segment	170	5	5	957	97.1 (93.5, 98.8)	99.5 (98.8, 99.8)	169.6 (73.7, 390.5)	0.03 (0.01, 0.07)	5396.8
Above knee, ⩾50% stenosis											
Rieker, 1997[60]	50–100%	Segment (1)	49	2	3	101	94.2 (84.4, 98.0)	98.1 (93.2, 99.5)	38.9 (11.4, 132.5)	0.07 (0.02, 0.19)	574.2
Rieker, 1997[60]	50–100%	Segment (2)	63	4	2	114	96.9 (89.5, 99.2)	96.6 (91.6, 98.7)	25.4 (10.3, 63.1)	0.04 (0.01, 0.13)	646.3
Portugaller, 2004[57]	50–100%	Segment	86	23	3	238	96.6 (90.6, 98.8)	91.2 (87.1, 94.1)	10.7 (7.3, 15.8)	0.04 (0.02, 0.12)	250.8
Above knee, ⩾70% stenosis											
Rieker, 1997[60]	75–100%	Segment (1)	28	0	0	127	100 (87.9, 100)	100 (97.1, 100)	251.6 (15.8, 4002)	0.02 (0.00, 0.27)	14535.0
Rieker, 1997[60]	75–100%	Segment (2)	30	0	0	153	100 (88.6, 100)	100 (97.6, 100)	303.0 (19.0, 4825)	0.02 (0.00, 0.25)	18727.0
Above knee, occlusion											
Rieker, 1997[60]	100%	Segment (1)	39	0	2	114	95.1 (83.9, 98.7)	100 (96.7, 100)	216.3 (13.6, 3441)	0.06 (0.02, 0.20)	3618.2
Rieker, 1997[60]	100%	Segment (2)	48	1	2	132	96.0 (86.5, 98.9)	99.2 (95.9, 99.9)	85.0 (17.3, 417.7)	0.05 (0.01, 0.17)	1713.7
Below knee, ⩾50% stenosis											
Portugaller, 2004[57]	50–100%	Segment	154	57	18	161	89.5 (84.1, 93.3)	73.9 (67.6, 79.2)	3.4 (2.7, 4.3)	0.15 (0.09, 0.22)	23.5

0.5 was added to all values for the calculation of LR+, LR– and DOR.
The study by Rieker[60] reported separate results for different CTA images: (1) maximum intensity projections and (2) cine axial images.

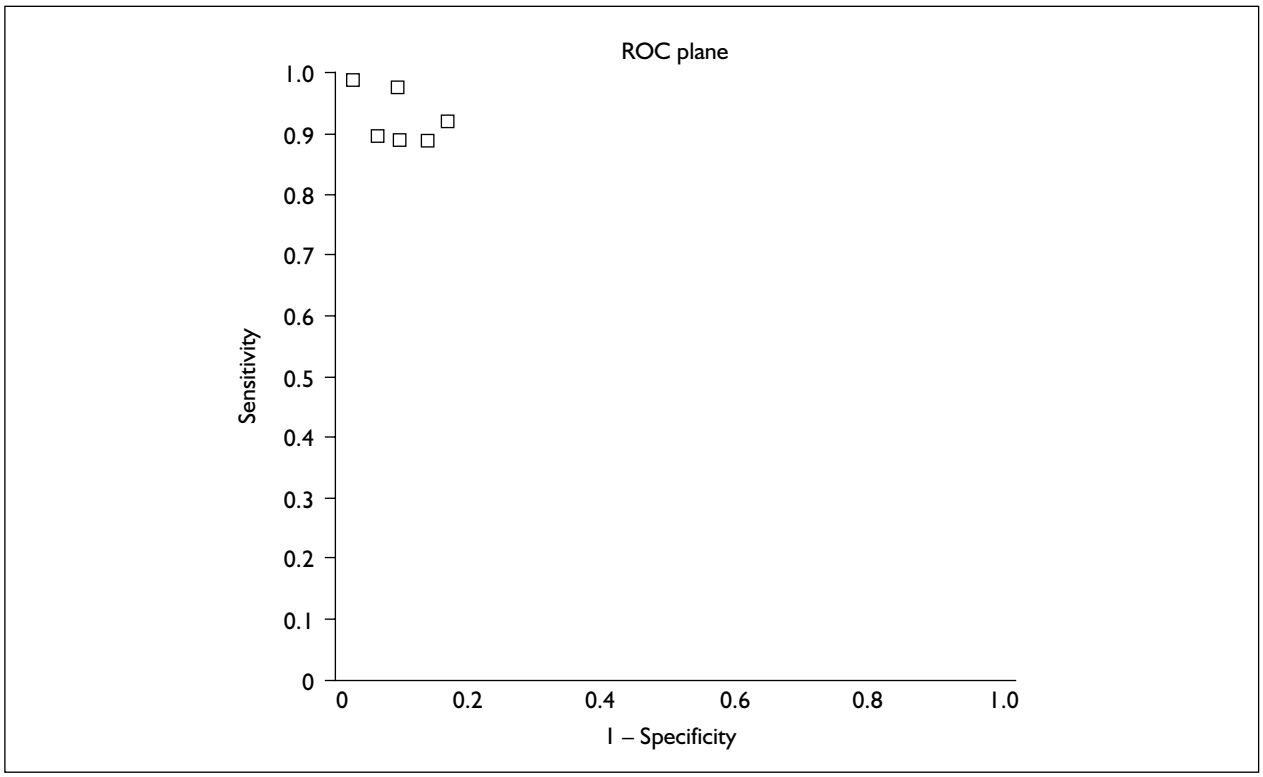


FIGURE 7 *ROC plot for CTA: whole leg, ⩾50% stenosis*

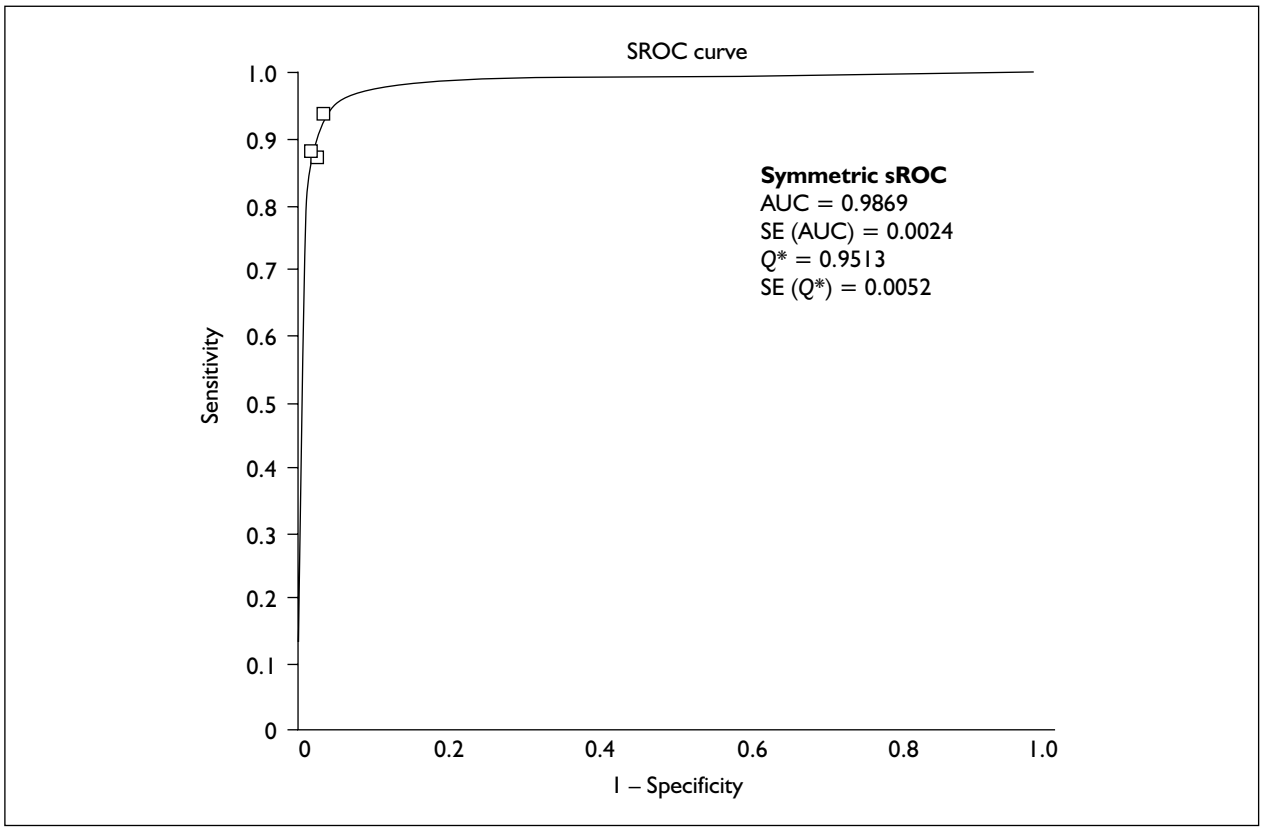


FIGURE 8 *ROC plot for CTA: whole leg, ⩾70% stenosis*

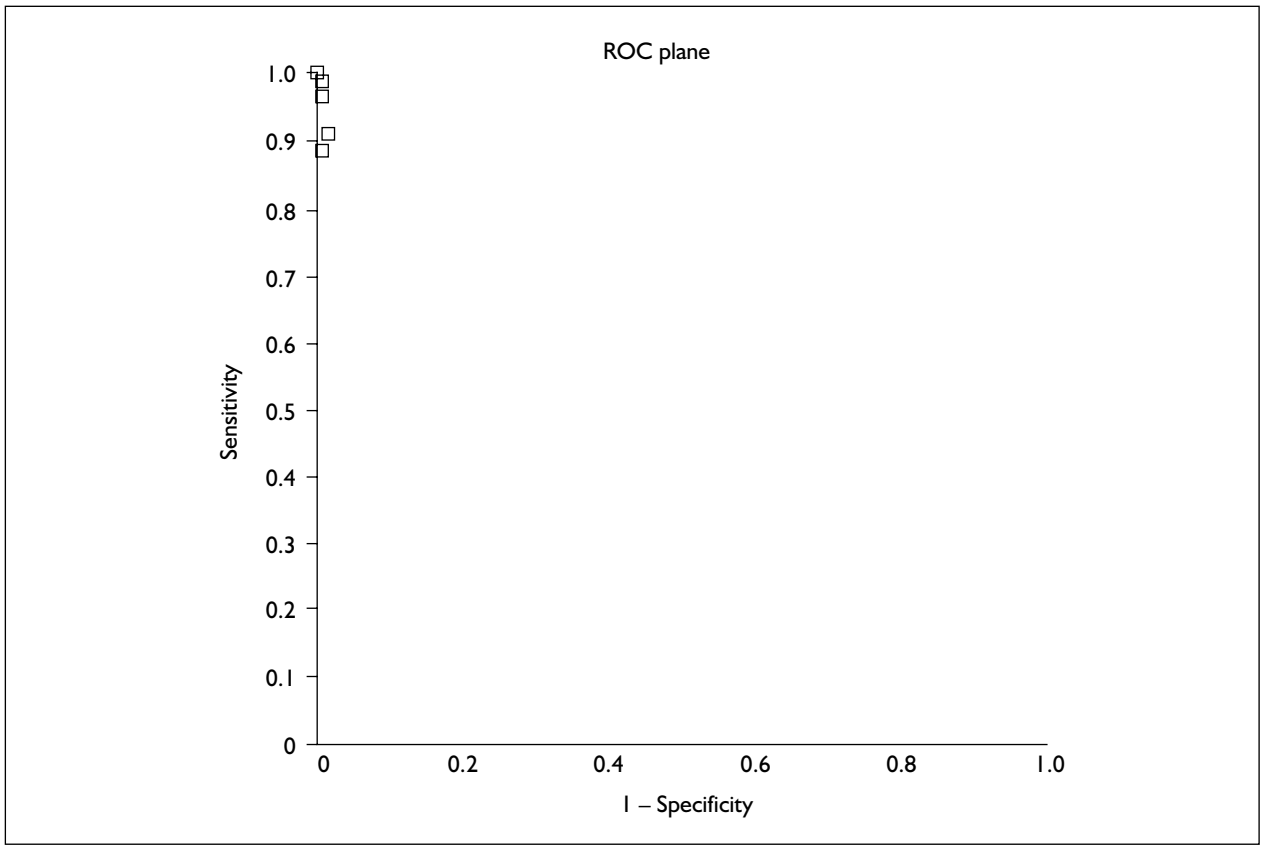


FIGURE 9 *ROC plot for CTA: whole leg, occlusion*

DUS

The full results of the quality assessment using the QUADAS tool for the 28 studies evaluating DUS are presented in *Table 9*. Twenty studies (71%) did not include an appropriate patient spectrum or failed to provide sufficient details of the patient population for this to be judged. Sixteen studies (57%) did not provide sufficient details of the patient selection criteria. Only 18 studies (64%) reported having less than a 1-month interval between the index test and reference standard. In all 28 studies, all patients received the same reference standard test and the decision to use the reference test was independent of the DUS results in 27 (96%) of these. The DUS results were interpreted without knowledge of the reference test results in 20 studies (71%) and the reference test results were interpreted without knowledge of the DUS results in 23 studies (82%). Whether or not clinical data were available at the time the results were interpreted was again poorly reported, with only one study reporting that clinical data were available.

The 28 studies evaluating DUS provided a total of 56 data sets.[20,21,23–25,29–31,33–35,37,39,42–45,47,48,50,52,53,56,62,63,71,72,75] The full set of diagnostic accuracy results is presented in *Table 10*. Seven studies presented results by limb[21,23,30,31,47,56,63] and one presented results by artery;[35] the rest were presented on an arterial segment basis.

Whole leg

Results for the detection of a stenosis of 50% or greater, with results reported by arterial segment, were reported by seven studies.[20,24,33,37,50,52,62] The sensitivity of DUS ranged from 80% (specificity 96%) to 98% (specificity 94%). The specificity ranged from 89% (sensitivity 88%) to 99% (sensitivity 92%). There was evidence of significant statistical heterogeneity between the study results ($p < 0.001$ for all measures), hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 10*). The median LR+ was 19.3, with a range from 7.6 (LR– of 0.13) to 89.5 (LR– of 0.08). The median LR– was 0.13, with a range from 0.03 (LR+ of 14.6) to 0.22 (LR+ of 16.9). A study with a particularly low sensitivity (79.7%) was the only study in this group with an unacceptable delay between conducting the index test and reference standard.[24]

Results for the detection of an occlusion, on an arterial segment basis, were reported by seven

TABLE 9 *QUADAS evaluation for studies assessing DUS*

Study	Appropriate patient spectrum	Selection criteria described	< 1 month between tests	All received reference standard	Same reference standard	Reference standard independent	Test details well reported	Reference standard details well reported	Test results blind to reference standard	Reference standard blind to test results	Clinical data available	Uninterpretable results reported	Withdrawals explained
Aly, 1998[20]	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes
Ashleigh, 1993[21]	Unclear	No	No	Yes	Yes	Yes	Yes	No	Unclear	Unclear	Unclear	Yes	Yes
Bergamini, 1995[24]	Unclear	No	No	Yes	Yes	Yes	Yes	No	Unclear	Yes	Unclear	Yes	Yes
Bostrom, 2001[25]	No	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Currie, 1995[29]	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Davies, 1992[30]	Unclear	No	Yes	Unclear	Yes	Yes	No	No	Unclear	Unclear	Unclear	Unclear	No
Eiberg, 2001[31]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Unclear	Yes	Yes
Fletcher, 1990[34]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Hatsukami, 1992[37]	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Hirai, 1998[39]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Unclear	Unclear
Hofmann, 2004[42]	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	No	No
Karacagil, 1996[43]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	No	No
Koelemay, 1998[45]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Koelemay, 1997[44]	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Lai, 1995[47]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	No	No
Lai, 1996[48]	Unclear	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Unclear	No
Linke, 1994[52]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Lundin, 2000[53]	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mergelsberg, 1986[56]	Unclear	No	Yes	Yes	Yes	Unclear	Yes	No	Unclear	Unclear	Unclear	Yes	Yes
Sensier, 1996[62]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Shaalan, 2003[63]	No	Yes	Unclear	Yes	Yes	Yes	No	No	Yes	Unclear	Unclear	Yes	Yes
Wilson, 1997[72]	Yes	Yes	Unclear	Yes	Yes	Yes	No	No	Yes	Yes	Unclear	Yes	Yes
Zeuchner, 1994[75]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Grassbaugh, 2003[35]	No	No	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
El-Kayali, 2004[33]	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Whyman, 1992[71]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes	Unclear	Yes	Yes
Baxter, 1993[23]	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	Unclear	Yes
Legemate, 1991[50]	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes

TABLE 10 *Results of studies assessing DUS, reported by area of leg assessed*

Study	Stenosis threshold	Results reported by	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR
Whole leg, ≥50% stenosis											
Aly, 1998[20]	50–100%	Segment	404	27	34	2643	92.2 (89.3, 94.4)	99.0 (98.5, 99.3)	89.5 (61.6, 129.9)	0.08 (0.06, 0.11)	1127.1
Bergamini, 1995[24]	50–100%	Segment	94	13	24	273	79.7 (71.5, 85.9)	95.5 (92.4, 97.3)	16.9 (9.9, 28.6)	0.22 (0.15, 0.31)	78.1
Hatsukami, 1992[37]	50–100%	Segment	73	6	12	152	85.9 (76.9, 91.7)	96.2 (92.0, 98.2)	20.9 (9.8, 44.6)	0.15 (0.09, 0.25)	138.0
Linke, 1994[52]	50–100%	Segment	41	4	2	87	95.3 (84.5, 98.7)	95.6 (89.2, 98.3)	19.3 (7.8, 47.6)	0.06 (0.02, 0.20)	322.8
Sensier, 1996[62]	50–100%	Segment	214	26	28	201	88.4 (83.8, 91.9)	88.5 (83.7, 92.1)	7.6 (5.3, 10.9)	0.13 (0.09, 0.19)	57.2
El-Kayali, 2004[33]	50–100%	Segment	123	15	3	216	97.6 (93.2, 99.2)	93.5 (89.6, 96.0)	14.6 (9.0, 23.6)	0.03 (0.01, 0.08)	492.9
Legemate, 1991[50]	50–100%	Segment	179	30	33	676	84.4 (78.9, 88.7)	95.8 (94.0, 97.0)	19.5 (13.7, 27.8)	0.16 (0.12, 0.22)	118.8
Ashleigh, 1993[21]	50–100%	Limb	69	2	0	5	100 (94.7, 100)	71.4 (35.9, 91.8)	3.2 (1.1, 8.9)	0.01 (0.00, 0.17)	305.8
Baxter, 1993[23]	50–100%	Limb	32	1	3	4	91.4 (77.6, 97.0)	80.0 (37.6, 96.4)	3.6 (0.9, 14.5)	0.13 (0.04, 0.39)	27.9
Whole leg, occlusion											
Aly, 1998[20]	100%	Segment	272	18	25	2793	91.6 (87.9, 94.2)	99.4 (99.0, 99.6)	139.0 (88.1, 219.2)	0.09 (0.06, 0.12)	1613.6
Bergamini, 1995[24]	100%	Segment	76	10	13	305	85.4 (76.6, 91.3)	96.8 (94.3, 98.3)	25.6 (14.0, 46.7)	0.16 (0.09, 0.25)	164.9
Hatsukami, 1992[37]	100%	Segment	51	3	6	173	89.5 (78.9, 95.1)	98.3 (95.1, 99.4)	44.9 (15.9, 127.2)	0.11 (0.06, 0.24)	392.8
Linke, 1994[52]	100%	Segment	14	0	5	115	73.7 (51.2, 88.2)	100 (96.8, 100)	168.2 (10.4, 2709)	0.28 (0.14, 0.56)	609.0
Sensier, 1996[62]	100%	Segment	166	11	21	271	88.8 (83.4, 92.5)	96.1 (93.2, 97.8)	21.8 (12.3, 38.5)	0.12 (0.08, 0.18)	182.8
Zeuchner, 1994[75]	100%	Segment	50	3	3	266	94.3 (84.6, 98.1)	98.9 (96.8, 99.6)	72.1 (25.4, 204.8)	0.07 (0.02, 0.18)	1098.6
Legemate, 1991[50]	100%	Segment	103	6	9	800	92.0 (85.4, 95.7)	99.3 (98.4, 99.7)	113.7 (52.8, 245.0)	0.08 (0.05, 0.16)	1341.7
Ashleigh, 1993[21]	100%	Limb	36	7	6	27	85.7 (72.2, 93.3)	79.4 (63.2, 89.7)	4.0 (2.1, 7.6)	0.19 (0.09, 0.40)	20.6
Whole leg, other stenosis thresholds											
Zeuchner, 1994[75]	50–99%	Segment	12	1	4	305	75.0 (50.5, 89.8)	99.7 (98.2, 99.9)	150.5 (29.7, 761.7)	0.27 (0.12, 0.59)	565.7
Ashleigh, 1993[21]	Suitability for angioplasty	Limb	25	7	4	42	86.2 (69.4, 94.5)	85.7 (73.3, 92.9)	5.7 (2.9, 11.1)	0.18 (0.07, 0.42)	32.1
Lai, 1995[47]	Selection for angioplasty	Limb	14	9	9	54	60.9 (40.8, 77.8)	85.7 (75.0, 92.3)	4.1 (2.1, 8.0)	0.46 (0.28, 0.77)	8.8
Above knee, ≥50% stenosis											
Bergamini, 1995[24]	50–100%	Segment	83	12	8	194	91.2 (83.6, 95.5)	94.2 (90.1, 96.6)	15.0 (8.7, 25.8)	0.10 (0.05, 0.19)	152.9
Fletcher, 1990[34]	50–100%	Segment	59	12	8	89	88.1 (78.2, 93.8)	88.1 (80.4, 93.1)	7.1 (4.2, 12.1)	0.14 (0.08, 0.27)	50.1
Hatsukami, 1992[37]	50–100%	Segment	34	2	6	73	85.0 (70.9, 92.9)	97.3 (90.8, 99.3)	25.6 (7.5, 87.2)	0.16 (0.08, 0.33)	156.0
Lai, 1996[48]	50–100%	Segment	124	12	42	354	74.7 (67.6, 80.7)	96.7 (94.4, 98.1)	21.9 (12.6, 38.0)	0.26 (0.20, 0.34)	83.1
Lundin, 2000[53]	50–100%	Segment	27	7	11	207	71.1 (55.2, 83.0)	96.7 (93.4, 98.4)	20.2 (9.7, 42.0)	0.31 (0.19, 0.50)	66.2
El-Kayali, 2004[33]	50–100%	Segment	74	9	1	171	98.7 (92.8, 99.8)	95.0 (90.8, 97.3)	18.7 (10.0, 34.7)	0.02 (0.00, 0.10)	896.6
Whyman, 1992[71]	51–100%	Segment	41	1	0	1	100 (91.4, 100)	50.0 (9.5, 90.5)	2.0 (0.6, 6.1)	0.02 (0.00, 0.47)	83.0
Eiberg, 2001[31]	50–100%	Limb	50	8	1	35	98.0 (89.7, 99.7)	81.4 (67.4, 90.3)	5.0 (2.7, 9.2)	0.04 (0.01, 0.17)	140.6
Shaalan, 2003[63]	50–100%	Limb	97	12	5	100	95.1 (89.0, 97.9)	89.3 (82.2, 93.8)	8.6 (5.1, 14.5)	0.06 (0.03, 0.14)	142.5

continued

TABLE 10 *Results of studies assessing DUS, reported by area of leg assessed (cont'd)*

Study	Stenosis threshold	Results reported by	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR
Above knee, ⩾70% stenosis											
Fletcher, 1990[34]	75–100%	Segment	14	2	0	40	100 (78.5, 100)	95.2 (84.2, 98.7)	16.6 (5.0, 55.6)	0.04 (0.00, 0.54)	469.8
Lai, 1996[48]	76–100%	Segment	83	8	44	397	65.4 (56.7, 73.1)	98.0 (96.2, 99.0)	31.2 (15.8, 61.3)	0.36 (0.28, 0.45)	87.7
Above knee, occlusion											
Currie, 1995[29]	100%	Segment	25	4	5	146	83.3 (66.4, 92.7)	97.3 (93.3, 99.0)	27.6 (10.9, 69.6)	0.18 (0.09, 0.39)	150.9
Fletcher, 1990[34]	100%	Segment	45	7	5	111	90.0 (78.6, 95.7)	94.1 (88.3, 97.1)	14.2 (7.0, 28.5)	0.12 (0.05, 0.25)	123.0
Hatsukami, 1992[37]	100%	Segment	29	0	1	85	96.7 (83.3, 99.4)	100 (95.7, 100)	163.7 (10.3, 2599)	0.05 (0.01, 0.23)	3363.0
Hirai, 1998[39]	100%	Segment	64	0	1	454	98.5 (91.8, 99.7)	100 (99.2, 100)	889.3 (55.7, 14201)	0.02 (0.00, 0.11)	39087.0
Lai, 1996[48]	100%	Segment	50	0	12	470	80.6 (69.1, 88.6)	100 (99.2, 100)	755.1 (47.2, 12088)	0.20 (0.12, 0.33)	3801.6
Lundin, 2000[53]	100%	Segment	13	1	1	237	92.9 (68.5, 98.7)	99.6 (97.7, 99.9)	143.4 (28.8, 713.3)	0.10 (0.02, 0.46)	1425.0
Whyman, 1992[71]	100%	Segment	26	1	0	16	100 (87.1, 100)	94.1 (73.0, 99.0)	11.8 (2.5, 54.6)	0.02 (0.00, 0.32)	583.0
Davies, 1992[30]	100%	Limb	27	1	1	36	96.4 (82.3, 99.4)	97.3 (86.2, 99.5)	24.0 (5.0, 115.6)	0.05 (0.01, 0.26)	446.1
Mergelsberg, 1986[56]	100%	Limb	25	6	1	17	96.2 (81.1, 99.3)	73.9 (53.5, 87.5)	3.5 (1.8, 6.8)	0.08 (0.02, 0.37)	45.8
Above knee, other stenosis thresholds											
Bostrom, 2001[25]	Suitable for endovascular intervention	Segment	93	11	6	53	93.9 (87.4, 97.2)	82.8 (71.8, 90.1)	5.3 (3.1, 9.0)	0.08 (0.04, 0.17)	66.9
Hirai, 1998[39]	50–99%	Segment	43	3	9	399	82.7 (70.3, 90.6)	99.3 (97.8, 99.7)	94.5 (33.0, 270.2)	0.18 (0.10, 0.32)	522.7
Davies, 1992[30]	50–99%	Limb	16	1	1	47	94.1 (73.0, 99.0)	97.9 (89.1, 99.6)	29.9 (6.2, 145.6)	0.09 (0.02, 0.40)	348.3
Below knee, ⩾50% stenosis											
Bergamini, 1995[24]	50–100%	Segment	11	1	16	79	40.7 (24.5, 59.3)	98.8 (93.3, 99.8)	22.2 (4.3, 115.1)	0.60 (0.44, 0.82)	36.9
Hatsukami, 1992[37]	50–100%	Segment	27	1	6	44	81.8 (65.6, 91.4)	97.8 (88.4, 99.6)	24.8 (5.1, 120.7)	0.20 (0.10, 0.40)	125.5
Karacagil, 1996[43]	51–100%	Segment	211	47	36	186	85.4 (80.5, 89.3)	79.8 (74.2, 84.5)	4.2 (3.2, 5.4)	0.18 (0.14, 0.25)	22.8
El-Kayali, 2004[33]	50–100%	Segment	49	6	2	45	96.1 (86.8, 98.9)	88.2 (76.6, 94.5)	7.6 (3.7, 15.7)	0.05 (0.02, 0.18)	138.6
Below knee, occlusion											
Hatsukami, 1992[37]	100%	Segment	25	0	5	48	83.3 (66.4, 92.7)	100 (92.6, 100)	80.6 (5.1, 1277)	0.18 (0.08, 0.38)	449.7
Karacagil, 1996[43]	100%	Segment	199	44	34	203	85.4 (80.3, 89.4)	82.2 (76.9, 86.5)	4.8 (3.6, 6.2)	0.18 (0.13, 0.25)	26.4
Koelemay, 1998[45]	100%	Segment	457	77	324	655	58.5 (55.0, 61.9)	89.5 (87.0, 91.5)	5.5 (4.4, 6.9)	0.46 (0.43, 0.51)	11.9
Koelemay, 1997[44]	100%	Segment	84	21	33	121	71.8 (63.0, 79.2)	85.2 (78.4, 90.1)	4.8 (3.2, 7.1)	0.33 (0.25, 0.45)	14.3
Wilson, 1997[72]	100%	Segment	80	1	5	36	94.1 (87.0, 97.5)	97.3 (86.2, 99.5)	23.7 (4.9, 113.9)	0.07 (0.03, 0.15)	356.2
Grassbaugh, 2003[35]	100%	Artery	36	6	12	56	75.0 (61.2, 85.1)	90.3 (80.5, 95.5)	7.2 (3.4, 15.2)	0.28 (0.18, 0.46)	25.4

continued

TABLE 10 *Results of studies assessing DUS, reported by area of leg assessed (cont'd)*

Study	Stenosis threshold	Results reported by	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR
Below knee, other stenosis thresholds											
Koelemay, 1998[45]	Severe stenosis	Segment	813	99	257	344	76.0 (73.3, 78.4)	77.7 (73.5, 81.3)	3.4 (2.8, 4.0)	0.31 (0.28, 0.35)	10.9
Koelemay, 1997[44]	Severe and occluded	Segment	136	23	52	48	72.3 (65.5, 78.2)	67.6 (56.1, 77.3)	2.2 (1.6, 3.1)	0.41 (0.31, 0.55)	5.4
Foot											
Hofmann, 2004[42]	Target vessels suitable for surgery	Segment	54	11	30	45	64.3 (53.6, 73.7)	80.4 (68.2, 88.7)	3.2 (1.9, 5.5)	0.45 (0.33, 0.61)	7.1

0.5 was added to all values for the calculation of LR+, LR– and DOR.

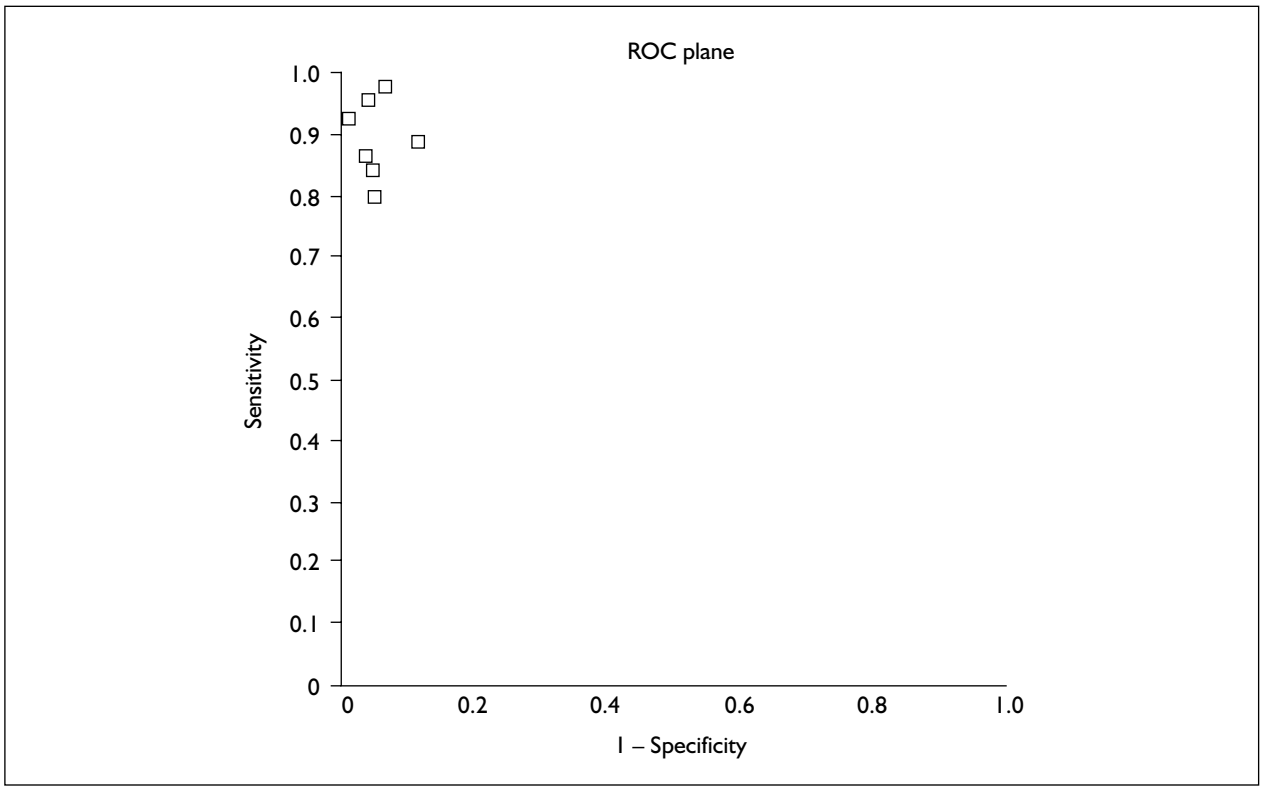


FIGURE 10 *ROC plot for DUS: whole leg, ⩾50% stenosis*

studies.[20,24,37,50,52,62,75] There was evidence of significant statistical heterogeneity between the study results ($p < 0.001$) for all accuracy measures apart from sensitivity ($p = 0.18$), therefore only results for sensitivity were pooled. The pooled sensitivity was 90% (95% CI 88 to 92%). The specificity ranged from 96% (sensitivity 89%) to 100% (sensitivity 74%). The sensitivities and specificities have been plotted in ROC space (*Figure 11*). The median LR+ was 72.1, with a range from 21.8 (LR– of 0.12) to 168.2 (LR– of 0.28). The median LR– was 0.11, with a range from 0.07 (LR+ of 72.1) to 0.28 (LR+ of 168.2).

Although there was no evidence of statistically significant between-study heterogeneity in sensitivity values, one study reported a notably low sensitivity (74%).[52] Of the three studies that reported Fontaine classification, this was the only study restricted to people with Fontaine stage II PAD. A possible explanation for the observed lower sensitivity may therefore be the theoretically greater difficulty in distinguishing patients at the milder end of the disease spectrum from the 'normal' population. The statistically significant heterogeneity for LR– disappeared when this study was removed from the analysis ($p = 0.35$).

Above the knee

Results for the detection of a stenosis of 50% or greater, on an arterial segment basis, were reported by seven studies.[24,33,34,37,48,53,71] The sensitivity of DUS ranged from 71% (specificity 97%) to 100% (specificity 50%). The specificity ranged from 50% (sensitivity 100%) to 97% (for three studies with sensitivities of 71%, 75% and 85%). There was evidence of significant statistical heterogeneity between the study results ($p < 0.001$ for all measures), hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 12*). The median LR+ was 18.7, with a range from 2.0 (LR– of 0.02) to 25.6 (LR– of 0.16). The median LR– was 0.14, with a range from 0.02 (two studies: LR+ of 2.0 and 18.7) to 0.31 (LR+ of 20.2).

One study had an outlying value for specificity of 50%.[71] None of the variables considered appeared to offer an explanation for this result, and when this study was removed from the analysis heterogeneity between the studies was still statistically significant ($p < 0.05$). The study that reported the lowest sensitivity (71%),[53] was the only study to use a PSVR of 2.5 as the cut-off for 50% stenosis (one study did not report PSVR and all the others used 2.0).

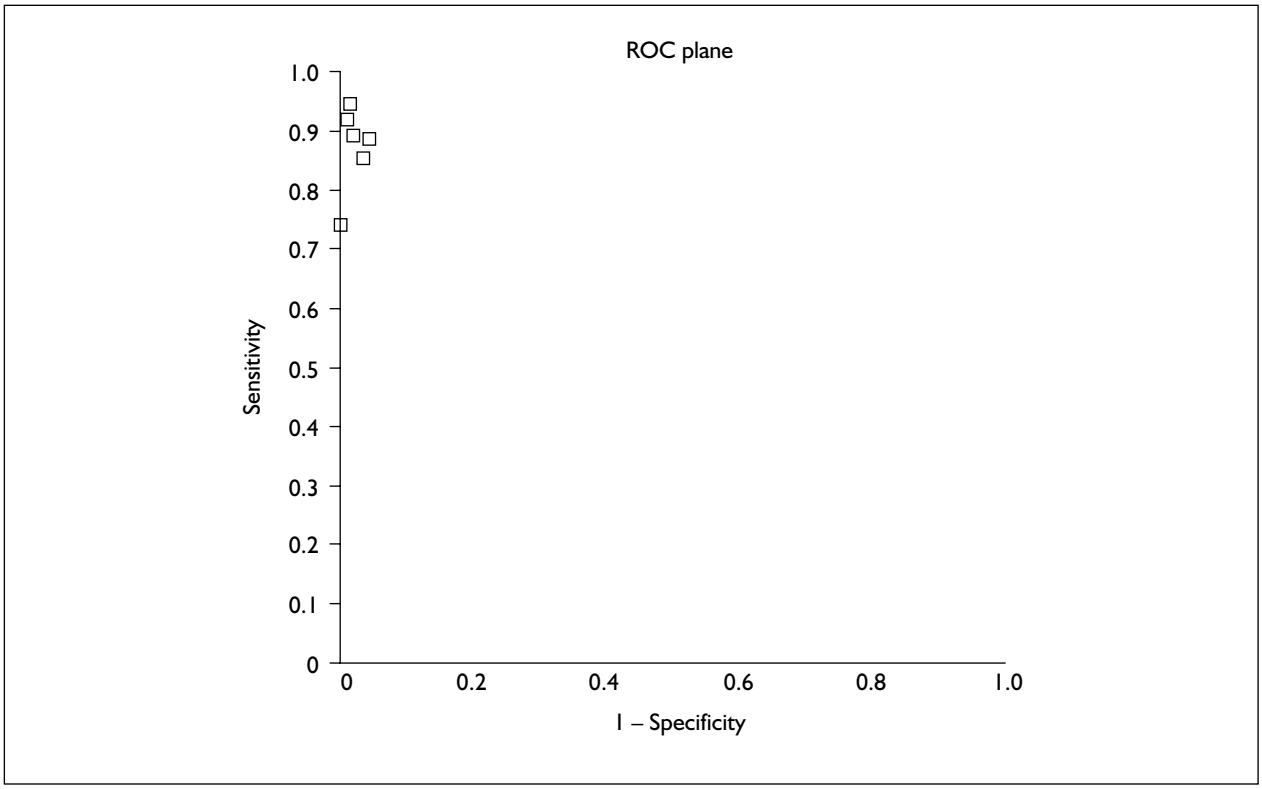


FIGURE 11 *ROC plot for DUS: whole leg, occlusion*

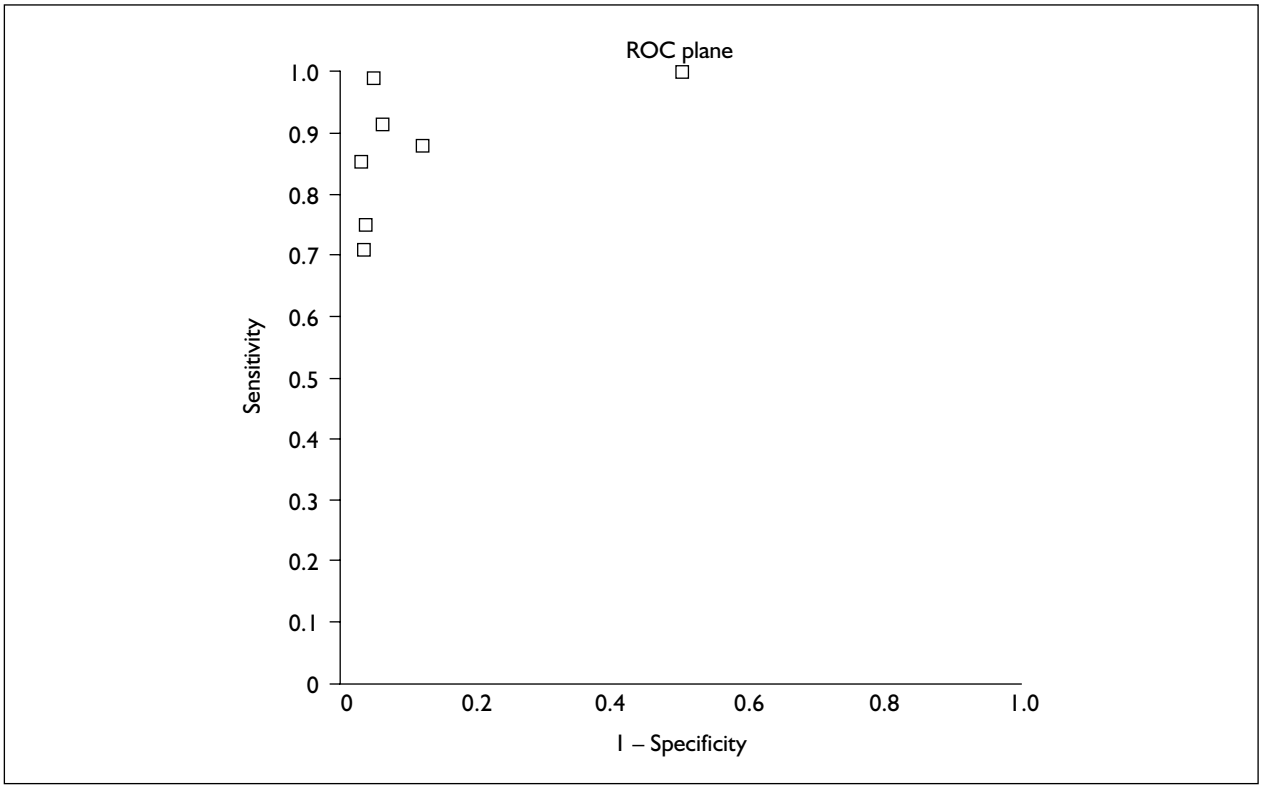


FIGURE 12 *ROC plot for DUS: above knee, ⩾50% stenosis*

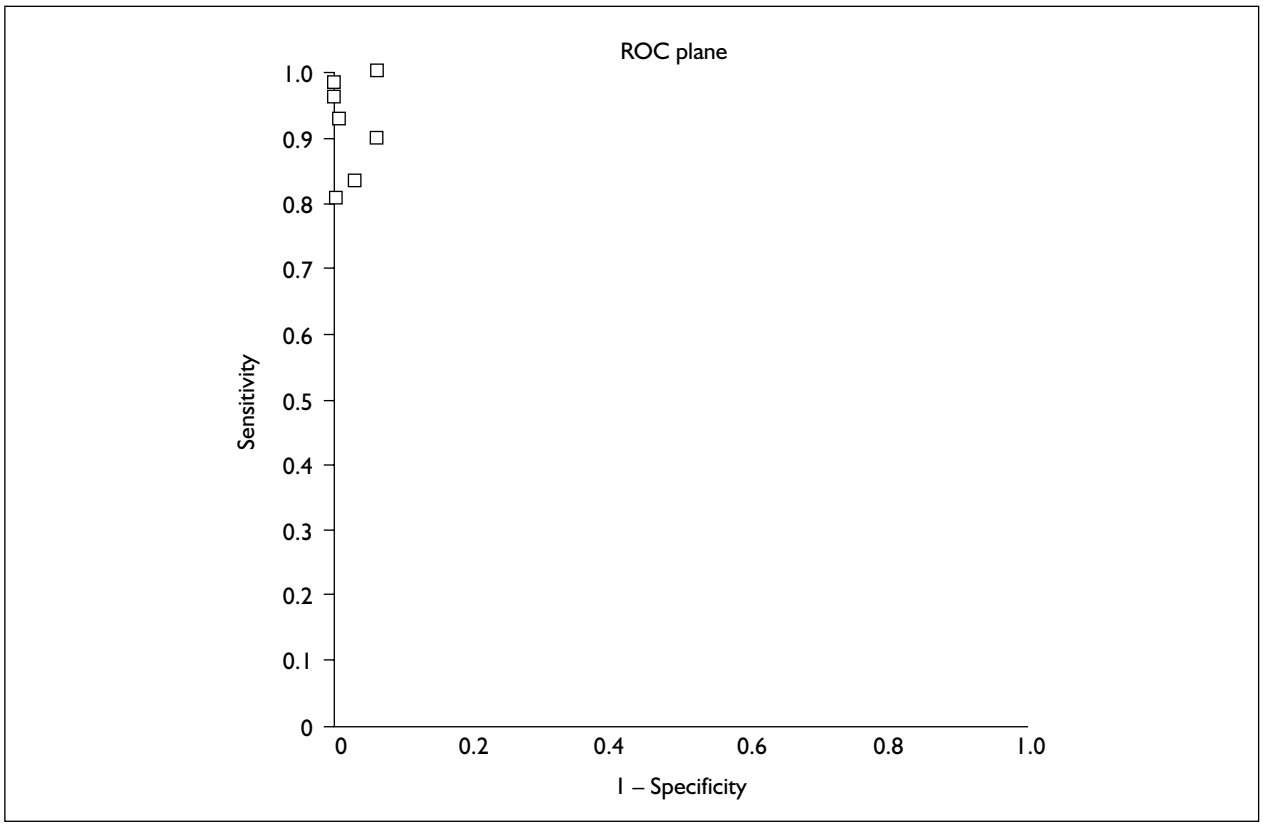


FIGURE 13 *ROC plot for DUS: above knee, occlusion*

Two studies provided results for the accuracy of DUS in detecting a stenosis of 75% or greater.[34,48] The two studies had very different sensitivities, one reporting a sensitivity of 100%[34] and the other of 65.4%,[48] with corresponding specificities of 95% and 98%, respectively (*Table 10*). The study with the higher sensitivity had an acceptable time between the index test and reference standard, whereas the other study did not.

Results for the detection of an occlusion, on an arterial segment basis, were reported by seven studies.[29,34,37,39,48,53,71] The sensitivity of DUS ranged from 81% (specificity 100%) to 100% (specificity 94%). The specificity ranged from 94% (for two studies with sensitivities of 90% and 100%) to 100% (for three studies with sensitivities of 81%, 97% and 99%). There was evidence of significant statistical heterogeneity between the study results ($p = 0.002$ for sensitivity, $p = 0.03$ for LR–, $p < 0.001$ for specificity and LR+), hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 13*). The median LR+ was 143.4, with a range from 11.8 (LR– of 0.02) to 889.3 (LR– of 0.02). The median LR– was 0.1, with a range from 0.02 (two studies: LR+ of 11.8 and 889.3) to 0.2 (LR+ of 755.1).

One study reported the highest sensitivity (100%), and the lowest specificity (94%), LR+ (11.8) and LR– (0.02).[71] Another study reported the lowest sensitivity (81%), the highest specificity (100%) and LR– (0.2), and second highest LR+ (755.1).[48] When comparing these two studies, as the extremes of the data set, one had an acceptable time between the index test and reference standard,[71] whereas the other did not.

Below the knee

Results for the detection of a stenosis of 50% or greater, on an arterial segment basis, were reported by four studies.[24,33,37,43] The sensitivity of DUS ranged from 41% (specificity 99%) to 96% (specificity 88%). The specificity ranged from 80% (sensitivity 85%) to 99% (sensitivity 41%). There was evidence of significant statistical heterogeneity between the study results ($p = 0.01$ for LR+, $p < 0.001$ for all others), hence no pooling was undertaken. One study had an outlying value for sensitivity of 41%.[24] None of the variables considered appeared to offer an explanation for this result, and when this study was removed from the analysis heterogeneity between the studies was still statistically significant. The sensitivities and specificities have been plotted in ROC space (*Figure 14*). The median LR+ was 14.9, with a

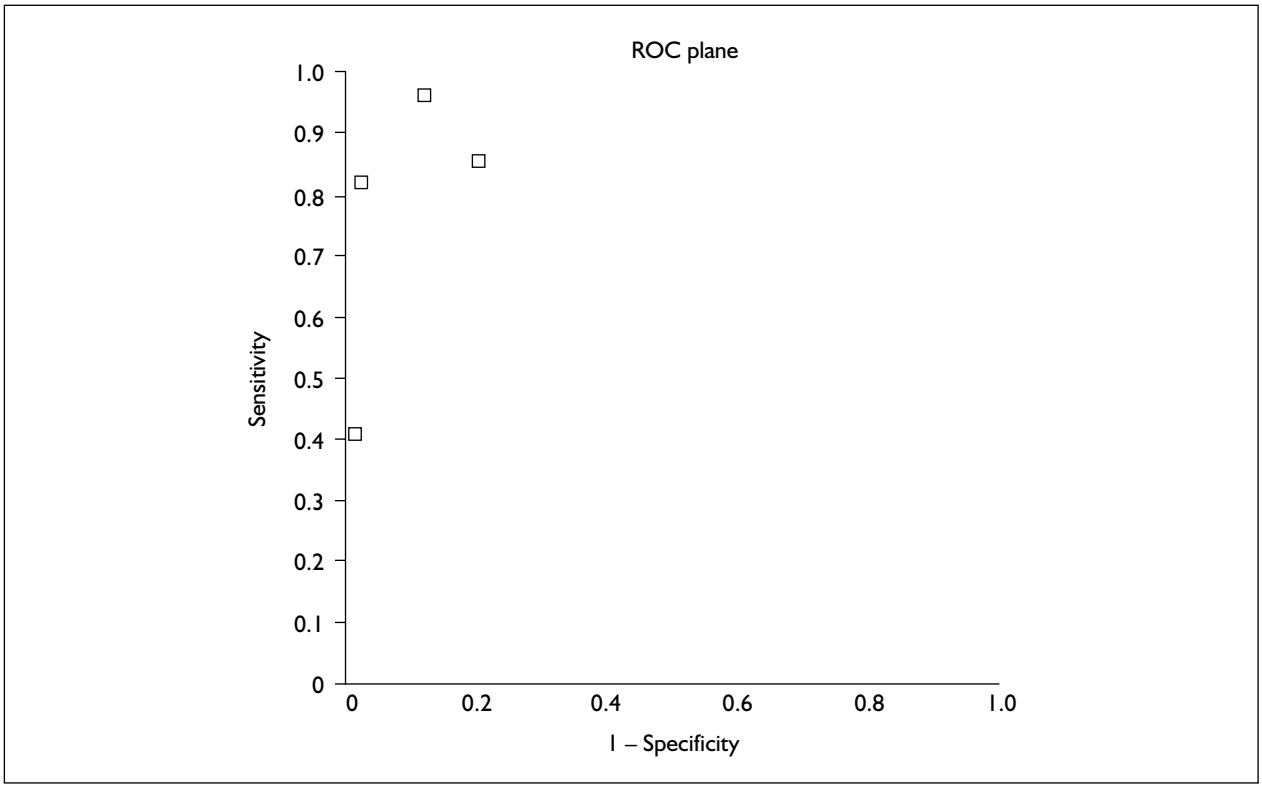


FIGURE 14 *ROC plot for DUS: below knee, ⩾50% stenosis*

range from 4.2 (LR– of 0.18) to 24.8 (LR– of 0.2). The median LR– was 0.19, with a range from 0.05 (LR+ of 7.6) to 0.6 (LR+ of 22.2).

Results for the detection of an occlusion, on an arterial segment basis, were reported by five studies.[37,44–46,72] The sensitivity of DUS ranged from 59% (specificity 90%) to 94% (specificity 97%). The specificity ranged from 82% (sensitivity 85%) to 100% (sensitivity 83%). There was evidence of significant statistical heterogeneity between the study results ($p = 0.06$ for LR+, $p < 0.001$ for all others), hence no pooling was undertaken. The sensitivities and specificities have been plotted in ROC space (*Figure 15*). The median LR+ was 5.5, with a range from 4.8 (two studies: LR– of 0.18 and 0.33) to 80.6 (LR– of 0.18). The median LR– was 0.18 with a range from 0.07 (LR+ of 23.7) to 0.46 (LR+ of 5.5).

One study reported a particularly low sensitivity (59%) compared with the other studies in this group.[45] This study was the highest quality study, responding positively to 12 of the 13 quality criteria. It was also one of only two studies to include the foot in the scan, with the other study reporting the next lowest sensitivity (72%).[44]

Only one study assessed the ability of DUS to detect stenoses in the foot separately.[42] For the detection of target vessels suitable for surgery the sensitivity was 64% and the specificity was 80%.

Impact of assessment method on patient management and outcome

One controlled trial was identified that met the inclusion criteria for the review in relation to the impact of the assessment method on patient management and outcomes.[77] The study was a prospective assessment of DUS involving 114 consecutive patients with lower leg ischaemia who underwent DUS alone (unless CA was indicated) between April 1997 and September 1998. The DUS results served as the basis for the treatment plan, which was decided jointly by the vascular surgeons and interventional radiologist, and comprised conservative treatment, percutaneous transluminal angioplasty or surgical revascularisation. These patients were compared with a historical control group, herein referred to as the CA group, of 113 consecutive patients with lower leg ischaemia who had participated in an earlier study between February 1995 and March 1997, with the same inclusion criteria. All patients

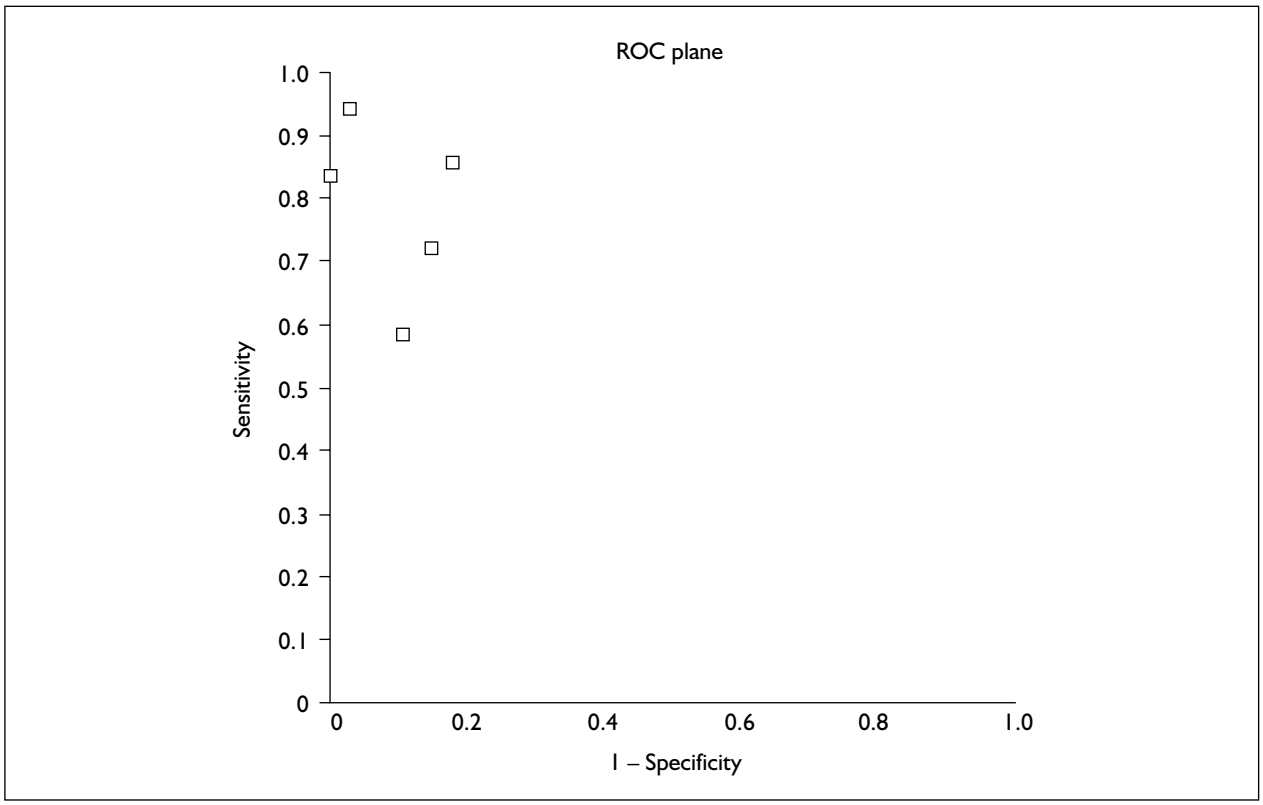


FIGURE 15 *ROC plot for DUS: below knee, occlusion*

in the CA group had undergone intra-arterial DSA, which had served as the basis for the treatment plan, formulated by the same vascular surgeons and interventional radiologist. Complications occurring within 30 days, 12-month and 24-month patency rates, survival rates and limb salvage rates were recorded and compared between the two groups. There were no significant differences between the DUS group and the CA group in terms of patient characteristics (such as co-morbidities and prior interventions), indications for specific treatment or the type of treatment that the patients underwent.

Using DUS, 125 limbs were assessed in the 114 included patients and 119 limbs were assessed using CA in the 113 patients in the historical control group. For 97 of the 125 limbs (78%) the management plan was based on DUS without the need for CA. However, additional CA was necessary before a femorocrural bypass graft when DUS detected multiple patent or partially patent crural arteries (18 patients), although DUS suggested an identical treatment to CA in 14 of these patients. In four patients DUS could not visualise all popliteal or crural arteries, making CA necessary. The management plan was conservative treatment for 33 limbs in the DUS group and 21 in the CA group, percutaneous transluminal angioplasty for 25 limbs in the DUS group and 31 in the CA group, femoropopliteal bypass graft for 29 limbs in each group, femorocrural bypass graft for 29 limbs in the DUS group and 37 limbs in the CA group, and other surgical procedures for eight limbs in the DUS group and one limb in the CA group. One patient in the DUS group died of acute myocardial infarction before their operation. Follow-up was available for 113 patients in the DUS group (99%) and 111 patients in the CA group (98%).

Five patients (4%) in the DUS group and eight patients (7%) in the CA group died within 30 days; 2-year survival was 83% in the DUS group and 74% in the CA group. After a femoropopliteal bypass graft, the 2-year primary patency rate was 75% in the DUS group and 58% in the CA group, the 2-year secondary patency rate was 93% in the DUS group and 80% in the CA group, and the limb salvage rate was 93% in the DUS group and 92% in the CA group. After a femorocrural bypass graft the 1-year primary patency rate was 35% in the DUS group and 54% in the CA group, the 1-year secondary patency rate was 73% in the DUS group and 85% in the CA group, and the limb salvage rate was 74% in the DUS group and 82%

in the CA group. There were no statistically significant differences between the DUS group and the CA group in terms of immediate and intermediate-term outcomes.

The authors concluded that in a vascular unit with wide expertise in DUS of the lower leg arteries, management of patients with severe lower leg ischaemia can be based on DUS in most patients without negative effects on clinical outcome within 30 days and at 2-years' follow-up.

The lack of randomisation and inability to blind either the patients or clinicians to the investigation being performed increases the potential for bias. As this trial used a historical control group it is possible that other factors occurring within the time-frame of the trial might have affected the results. The use of the same inclusion criteria for both groups helps to reduce differences between the groups; the authors present details of the characteristics of the two groups and found no statistically significant differences between them. There were also no significant differences between the type of treatment that the patients underwent. However, the authors do not comment on other factors that could have had a major influence upon outcomes, particularly graft patency, such as the nature of the graft material, whether smoking patients continued to smoke and the use of antiplatelet drugs. Follow-up was high in both groups. This trial appears to have been well conducted and the results are likely to be reliable. However, no data were collected relating to patient acceptability or adverse events of the investigations, other than mortality within 30 days.

Studies of patient attitudes

Four studies reported results relating to patient attitudes.[78–81] The results of the studies strongly suggest that CE MRA is preferred by patients over CA;[78,79,81] statistically significantly more patients preferred CE MRA if having to undergo testing again in the future ($p = 0.01$)[78] and CE MRA scored statistically significantly better on a rating scale, compared with CA ($p = 0.0001$ and $p = 0.0002$).[78,79] In terms of level of discomfort, CA was found to be the most uncomfortable, followed by CE MRA, with CTA being the least uncomfortable; again, this result was statistically significant ($p = 0.016$).[81] The majority of patients (from a sample who did not suffer from claustrophobia and had no metallic implants) had no preference between undergoing TOF MRA or DUS, while the majority of those who did express a preference preferred TOF MRA.[80] Within the same population there was no significant difference between TOF MRA and DUS on a scale that rated how bothersome the tests were.[80] Each of the studies assessing patient attitudes is described below.

One study surveyed 98 of 117 patients who had undergone both TOF MRA and DUS in the pretreatment work-up of PAD, as part of a clinical study.[80] The reasons the other 19 patients who underwent TOF MRA and DUS did not participate were communication problems between the institutions conducting the study ($n = 12$), participant refusal ($n = 5$), hearing problem making telephone interview impossible ($n = 1$) and patient missed DUS appointment ($n = 1$). Fifty-one per cent of patients had undergone DUS before TOF MRA and 49% had undergone TOF MRA before DUS. The time between the two tests was on average 4.2 days.

Patients were sent a questionnaire that asked which imaging test they would prefer if they were to require testing in the future, with a rating scale with scores ranging from 0 (not bothersome at all) to 10 (extremely bothersome) and specific questions on whether patients experienced discomfort due to the imaging test (the results of this part of the survey are presented in the section 'Adverse events', p. 44). Patients were interviewed by telephone after receiving the questionnaire. On average, the interviews took place approximately 10 days after the test, at which time 34% of patients knew the result for both tests, 22% knew only the DUS result, 4% knew only the TOF MRA result and 40% did not know either test result.

Fifty per cent of respondents had no preference for either TOF MRA or DUS, 41% expressed a preference for TOF MRA and 9% expressed a preference for DUS. The average rating scale scores were not significantly different between the two procedures [1.6 for TOF MRA (SD 2.1) and 1.7 (SD 2.2) for DUS; $p = 0.53$]. There was a slight, but statistically significant correlation between the rating scale scores of TOF MRA and DUS (Spearman's correlation coefficient 0.52, $p < 0.01$) and a statistically significant inverse association between the rating scale score for TOF MRA and the age of the patient (Spearman's correlation coefficient –0.21, $p = 0.04$). Knowledge of the test result, gender, time between test and interview and the order of performance of the MRA and DUS did not influence the rating scale

scores. Patients who reported adverse events due to the imaging test gave higher rating scale scores (i.e. more bothersome), as might be expected. The authors concluded that their results suggest that the majority of patients have no preference between TOF MRA and DUS in the diagnostic work-up of PAD. Among those patients who do have a preference, TOF MRA was preferred over DUS.

Although the authors state that the section of the questionnaire regarding adverse events was piloted before this study, they do not mention whether the other sections of the questionnaire were also piloted. There was a high response rate to the questionnaire and reasons for non-participation were presented. The proportion of participants undergoing TOF MRA first was approximately the same as the proportion undergoing DUS first. Both the time between the two tests and the time between the tests and interviews was short, thus reducing the potential for recall bias. The authors assessed whether there was any correlation between the rating scale scores and certain study and patient characteristics. This survey appears to have been well conducted and the results are likely to be reliable. However, as the authors point out, this survey may not be representative of all patients undergoing pretreatment work-up of PAD, as 18% (25 patients) of the initial patient population did not participate in the clinical study, from which this sample was drawn, 4% of whom (one patient) did not participate because of an implanted cardiac pacemaker, 8% (two patients) because the scanner was not available and 8% (two patients) because they were claustrophobic.

Another study surveyed 30 patients who had undergone both CE MRA and CA for the assessment of PAD as part of a diagnostic accuracy study.[78] Patients were interviewed in person ($n = 2$) or via the telephone ($n = 28$). Seventeen patients underwent CA first and 13 underwent CE MRA first. Patients were interviewed a mean of 30 weeks after the last test they had undergone.

Patients were asked the strength of their agreement (on a scale of 1 to 5) with a statement that they would consent to have the test done again, which test they would prefer if they were to require testing in the future and their experience of the test on a scale from 0 (neutral experience) to –10 (extremely unpleasant experience). Patients were also assessed using a willingness-to-pay approach, where they were asked what percentage of their income they would pay to avoid undergoing the test in future (without compromising their healthcare), and a time trade-off approach, where they were asked whether they would undergo the test if they could be guaranteed an extra 2 years of healthy life in addition to the (5 or 10) years they already have. Patients were also surveyed in relation to adverse events (the results of this part of the survey are presented in the 'Adverse events' section, p. 44). Twenty-nine patients were willing to respond to the willingness-to-pay questions, 28 responded to the time trade-off questions and all 30 patients responded to the other questions.

More patients agreed that they would consent to have CE MRA done again than CA, and the difference was statistically significant ($p = 0.01$). One patient expressed no preference as to which test they would prefer if they required testing in the future, 28 patients stated a preference for CE MRA and one patient stated a preference for CA. The mean score relating to their experience of the tests was –1.1 for CE MRA and –3.8 for CA, and the difference was statistically significant ($p = 0.0002$). Using the willingness-to-pay approach, patients were willing to pay a mean of 2.12% of their annual income to avoid CE MRA and a mean of 7.41% of their annual income to avoid CA, and the difference was statistically significant ($p = 0.01$). However, 16 of the 29 patients who responded to this question were unwilling to pay an amount above zero to avoid either CE MRA or CA. The median required survival gain to undergo CE MRA was 10.5 days (range 0–547) and for CA was 52.5 days (range 0–1095) (given a 10-year life expectancy); the difference was not statistically significant. The authors concluded that their findings indicate a strong preference for CE MRA over CA.

The authors state that their utilities questionnaires were piloted before use. The proportion of participants undergoing CE MRA first was approximately the same as the proportion undergoing CA first. The authors did not state the time interval between patients undergoing CE MRA and CA. The potential for recall bias is very high in this study, owing to the delay between the last test and the interview. However, the authors state that they read a short paragraph summarising each procedure to the patient to help them to remember the details of the procedure, and that patients showed no difficulties in remembering the particulars of their procedures. Given the consistently, and statistically significantly, better score for CE MRA over CA, the authors' conclusion is likely to be reliable.

A further study surveyed 38 patients who had undergone both CE MRA and CA for the assessment of PAD as part of a diagnostic accuracy study.[79] The original sample size was 40, but two patients refused to participate at the time of interview as they were not comfortable with the questionnaire format. Patients were interviewed via telephone. Twenty-eight patients underwent CA first and 12 underwent CE MRA first. The time between the two tests was a mean of 28 days. Patients were interviewed a mean of 8 weeks after the last test they had undergone. Half of the patients were asked about their preferences for CE MRA before CA and half were asked about their preferences for CA before CE MRA.

Patients were asked to keep in mind a typical week with their symptoms before the performance of MRA or CA. They were then given the option of (1) having the test they had received (e.g. CA), with the associated pain, discomfort and other adverse effects, with the physician having immediate access to the results and immediate treatment, or (2) having a hypothetical 'ideal' test, which takes very little time to perform and where there is no associated pain or other adverse effects, but where the results require a certain amount of time to analyse. The patient is initially given the hypothetical waiting time of 4 weeks for the ideal test results and subsequent treatment and a bisection method was used to work towards the patient's point of indifference to which test they received. Patients were also asked to rate their experience of the test from 0 (neutral experience) to –10 (extremely unpleasant experience).

Patients were willing to wait a mean of 42.1 days after the ideal test for results and treatment, rather than having to undergo CA, and a mean of 16.1 days to avoid having to undergo CE MRA; the difference was 26.0 days and was statistically significant ($p = 0.0001$). The mean score relating to their experience of the tests was –3.73 for CA and –1.05 for CE MRA, and the difference was statistically significant ($p = 0.0001$). The authors concluded that their findings indicate a clear preference for CE MRA, in agreement with known literature.

The main aim of this study was to validate the 'wait trade-off' method. More patients underwent CA before CE MRA, which increases the potential for order/sequential bias. The time interval between the two tests was relatively short, as was the average time between the last test and the interview, reducing the potential for recall bias. Although this study has some limitations, the potential biases are unlikely to have had a major impact on the overall conclusions.

Another diagnostic accuracy study that compared CE MRA and CTA with CA in 46 consecutive patients also measured patient acceptance for each modality, although this was not a stated objective of the study.[81] All patients underwent CA, CE MRA and CTA within 1 week, CA was always performed first and half of the patients underwent CE MRA before CTA, while half underwent CTA before CE MRA. After all three examinations had been performed, patients were asked to give a subjective score of discomfort using a 10-cm visual analogue scale, the left end of the scale representing 'no discomfort, excellently tolerated' and the right end of the scale representing 'very uncomfortable, hardly tolerable'. The distance between the left end of the scale and the patient's mark was measured and the patient acceptance for each modality was expressed in millimetres. After completing the visual analogue scale, patients were asked which of the following factors provided the most discomfort during all three procedures: confinement, keeping still, noise, puncture of a vessel, application of a pressure bandage, nothing, or other.

CA was the most uncomfortable procedure, with a mean discomfort score of 41.0 mm (SD 33.0), followed by CE MRA, with a mean discomfort score of 27.9 mm (SD 25.7). CTA was the least uncomfortable, with a mean discomfort score of 15.5 mm (SD 19.8). The difference was statistically significant between CA and CTA ($p < 0.001$), between CE MRA and CTA ($p = 0.016$), and between CA and CE MRA ($p = 0.037$). The most disturbing factors were noise and having to keep still for CE MRA, and puncture of a vessel and application of a pressure bandage for CA. The authors conclude that CTA was better accepted by patients.

The authors do not state whether their questionnaire was piloted before use. The proportion of participants undergoing CE MRA before CTA was the same as the proportion undergoing CTA before CE MRA. However, all patients underwent CA first, which increases the potential for order/sequential bias. The time between the three tests was short; however, the authors do not state the length of time between patients undergoing the tests and completing the visual analogue scale or questionnaire, and therefore the potential for recall bias cannot be assessed. Although this study has some limitations, the potential biases mentioned above are unlikely to have had a major impact on the overall conclusions.

Adverse events

Only nine of the diagnostic accuracy studies that met the inclusion criteria for the review provided data on adverse events. In addition, 46 studies that did not meet the inclusion criteria for the review of diagnostic accuracy reported results relating to adverse events. Therefore, a total of 55 studies contributed adverse event data. The lack of adverse event data reported by diagnostic accuracy studies cannot be interpreted as no adverse events having occurred. The criteria used to determine whether adverse events were procedure related (e.g. temporal relation to procedure) and the methods by which adverse event data were sought and recorded varied by study and were not always reported. This section should therefore only be regarded as a guide to the spectrum of adverse events reported, and not an accurate assessment of their actual or relative frequency. *Table 11* shows the number of studies reporting each adverse event, with the total number of patients in the studies, and the proportion of patients suffering the adverse event, for 53 of the 55 studies. The other two studies reported adverse event data, but did not report the number of patients affected; these data are presented at the end of this section.

As shown in *Table 11*, MRA was associated with the highest proportion of adverse events reported in the studies. However, the two major adverse events (death and severe vascular adverse events) were reported in a higher proportion of patients who underwent CA than MRA, although the proportion of patients undergoing CA that suffered these adverse events was still very low [2% death (one patient) compared with 0.5% (one patient) for CE MRA and up to 5% severe vascular adverse events compared with 0.5% for CE MRA]. However, it should be noted that only two studies reported that a patient had died; therefore, a figure of 2% is an unrealistic overestimate of the death rate in the total population undergoing CA.

Contrast agents were responsible for some of the reported adverse events, although generally the proportion of patients suffering significant contrast agent-related adverse events was low. However, studies reported up to 25% of patients suffering from unspecified contrast agent-related adverse events associated with CE MRA, although the study that reported the highest proportion of contrast agent-related adverse events was designed to evaluate the dose response and safety of the contrast agent.[101]

The most commonly reported adverse events were minor pain/discomfort during or immediately after DUS (22% of patients), minor pain/discomfort during or immediately after 2D TOF MRA (17% of patients), minor pain/discomfort during or immediately after CE MRA (up to 10% of patients), acute digestive system symptoms associated with CE MRA (up to 10% of patients), anxiety associated with 2D TOF MRA (up to 10% of patients), and acute central and peripheral nervous system adverse events associated with CE MRA (up to 10% of patients).

The two studies that reported adverse event data, but did not report the number of patients affected, reported acute change in renal function after administration of contrast agent, anxiety, minor pain/discomfort during or immediately postprocedure and unspecified adverse events, all related to CA.

Economic evaluations

Of the five included English-language studies, none was conducted in the UK; one was conducted in the USA,[131] one in Sweden,[126] two in The Netherlands,[128,130] and one failed to state where it had been carried out.[129] Given the setting of the studies, the cost data are likely to have only limited generalisability to the UK framework. Four out of the five studies were modelling studies and derived their effectiveness data from reviews of published literature, while the fifth derived its effectiveness data from a single clinical trial.[126] The perspective adopted in the modelling studies was that of society; the single study was undertaken from the perspective of the hospital. None of the published models compared the four imaging techniques and treatment strategies at the same time (i.e. MRA, DUS, CTA and CA). However, where appropriate, effectiveness data, cost/resource information and health outcome data were used to inform the decision-analytical modelling undertaken for this review. The structured abstracts for each of the studies are shown in Appendix 7.

Geitung and colleagues[126] assessed the use of DUS as a preoperative tool for examination of the aorta, pelvic and lower limb vessels compared with CA (which was considered to be the gold standard). The aim of the study was to establish whether it would be cost-effective to replace the current practice of preoperative CA with preoperative DUS. The economic analysis evaluated diagnostic results on consecutive

TABLE 11 *Adverse events reported*

Adverse event	Test	No. of studies	% of patients affected
Acute cardiac signs and symptoms	CE MRA	2 (n = 879)	0.00–0.42
Acute central and peripheral nervous system adverse events (weakness/paralysis/dizziness)	CE MRA	3 (n = 591)	1.48–10.00
Acute change in biochemical measures of renal function after gadolinium infusion	CE MRA	1 (n = 136)	1.48
Acute digestive system adverse events (nausea/diarrhoea/taste perversion)	CE MRA	3 (n = 591)	0.74–10.00
Acute renal failure after gadolinium infusion (patients had baseline chronic renal insufficiency)	CA	1 (n = 42)	9.52
Acute renal failure after gadolinium infusion (patients had baseline chronic renal insufficiency)	CE MRA	1 (n = 218)	1.38
Anxiety	2D TOF MRA	1 (n = 40)	10.00
Anxiety	CA	1 (n = 23)	4.35
Anxiety	CE MRA	1 (n = 98)	8.16
Anxiety	DUS	1 (n = 98)	1.02
Death (from haemorrhage due to dissection of an external iliac artery following CA)	CA	1 (n = 52)	1.92
Death (deemed as possibly related to the study drug by the principal investigator. Immediate cause of death was atherosclerotic cardiovascular disease)	CE MRA	1 (n = 238)	0.42
Minor pain/discomfort during or immediately after procedure	2D TOF MRA	1 (n = 12)	16.67
Minor pain/discomfort during or immediately after procedure	CA	1 (n = 35)	8.57
Minor pain/discomfort during or immediately after procedure	CE MRA	5 (n = 719)	0.23–10.20
Minor pain/discomfort during or immediately after procedure	DUS	1 (n = 98)	22.45
Minor vascular adverse events	CA	2 (n = 133)	2.17–7.32
Minor vascular adverse events	CE MRA	2 (n = 571)	0.74–2.30
Severe unspecified adverse events	CE MRA	1 (n = 274)	1.09
Severe unspecified contrast agent-related adverse events	CE MRA	3 (n = 740)	0.00–0.78
Severe vascular adverse events	CA	2 (n = 111)	1.09–5.26
Severe vascular adverse events	CE MRA	1 (n = 435)	0.46
Skin adverse events (irritation/rash)	CE MRA	2 (n = 673)	0.23–0.42
Skin adverse events (irritation/rash)	CTA	1 (n = 49)	2.04
Unspecified adverse events	2D TOF MRA	3 (n = 62)	0.00[a]
Unspecified adverse events	3D TOF MRA	1 (n = 49)	0.00[a]
Unspecified adverse events	CA	11 (n = 355)	0.00[a]
Unspecified adverse events	CE MRA	9 (n = 618)	0.00–6.67
Unspecified adverse events	CTA	5 (n = 179)	0.00[a]
Unspecified adverse events	DUS	4 (n = 181)	0.00[a]
Unspecified adverse events	PC-MRA	1 (n = 19)	0.00[a]
Unspecified contrast agent-related adverse events	CA	4 (n = 125)	0.00[a]
Unspecified contrast agent-related adverse events	CE MRA	10 (n > 1334)	0.00–24.79
Unspecified contrast agent-related adverse events	DUS	1 (n = 14)	0.00[a]

[a] Study stated that no adverse events/contrast agent-related adverse events occurred.

patients examined with both DUS and CA, then compared the outcomes obtained.

The study was conducted in Sweden from the perspective of the hospital. The direct costs were obtained from the study hospital and included a mixture of both costs and prices. The effectiveness data were derived from a cohort of 53 consecutively referred patients who underwent both diagnostic procedures. The results obtained showed a number of diagnostic discrepancies between the two techniques, which could potentially lead to reoperations, delayed operations and overtreatment. No summary measure of benefit was derived so, in effect, a cost–consequence approach was adopted. The observational nature of the study design is subject to a number of limitations.

The cost analyses found that the cost savings obtained from using DUS (due to avoidance of hospitalisation and lower costs for the test) would be outweighed by the cost of reoperations, delayed operations and overtreatment. The authors

concluded that DUS of the aorta and arteries of the pelvis and lower limb is not a cost-effective option for preoperative examination.

Yin and colleagues[131] developed a decision tree to evaluate the use of MRA in the preoperative evaluation of patients with limb-threatening PAD, but the degree of stenosis was not reported. The main objective of the economic analysis was to evaluate MRA compared with CA. However, a secondary aim was to determine a diagnostic accuracy threshold that MRA was required to reach before it would become a cost-effective alternative to CA.

The study population comprised a hypothetical cohort of patients undergoing angiography. The model inputs (effectiveness data, utility data and costs) were derived from published literature and, when necessary, were augmented by expert/author opinion. Full details of the review were not reported; consequently, it is not possible to establish whether the best available evidence was used to populate the decision tree. Full details of the structure of the decision tree were reported. The measure of benefit used was the number of quality-adjusted life-years (QALYs). These were not directly measured, but were based on assumed quality-of-life values which, in turn, were based upon the Quality of Well-Being Scale. Benefits were discounted at an annual rate of 5%.

The study was conducted from a societal perspective, and included both the direct costs to the hospital, which were derived from Medicare sources, and indirect costs, in the form of productivity losses, which were derived from US national average daily earnings. All costs were subjected to discounting at an annual rate of 5%.

An incremental cost–utility ratio was calculated to combine costs and QALYs; the base case showed that the incremental cost per QALY saved with MRA over CA was US$25,895. Univariate sensitivity analysis showed that the results were sensitive to variations in some of the sensitivity parameters used in the model.

In addition, the authors assessed MRA in combination with CA compared with CA alone. The results obtained showed that the combined approach produced an incremental cost per QALY saved of $29,305 relative to CA alone.

The threshold analysis showed that, when the sensitivity and specificity of CA were 95%, MRA would have to have at least 90% sensitivity and 85% specificity for it to be a cost-effective option at a threshold of $30,000 per QALY.

The authors highlighted several limitations to their analysis and concluded that their results indicate that MRA could prove to be a cost-effective alternative to CA as a preoperative diagnostic tool in patients with limb-threatening PAD. In addition, they stressed that further research is required to address many of the data limitations found and to corroborate the findings of their study. It is also worth noting that, given the publication date of this paper, techniques used and treatment pathways are likely to have changed significantly.

Visser and colleagues[129] aimed to evaluate alternative pretreatment imaging work-up procedures followed by treatment. The imaging techniques included MRA, DUS and DSA. A Markov model was developed to compare the alternative strategies over a lifetime horizon. The main objective of the evaluation was to assess the cost-effectiveness of MRA, DSA and DUS for the pretreatment imaging work-up of patients with lifestyle-limiting intermittent claudication. The comparator chosen was exercise therapy without imaging work-up. The analysis was conducted for two different treatment scenarios, namely minimally invasive (i.e. where treatment was limited to angioplasty or an exercise programme for those patients not suitable for angioplasty) and invasive (where bypass was performed if patients were not suitable for angioplasty).

The study population comprised a hypothetical cohort of 60-year-old men with a 1-year history of severe unilateral claudication, an initial ankle brachial index of 0.70 and no history of coronary artery disease. The model parameters were derived from published literature and augmented by authors' assumptions. It is not clear whether a systematic review of the literature was conducted to identify the best available evidence with which to populate the model, although the authors did identify and use several meta-analyses of RCTs. The measure of benefit used in the economic analysis was QALYs; these were also obtained from the literature review. QALYs were discounted at an annual rate of 3%.

The direct costs included in the analysis were those of both the health service and the patient. The costs, including technical and professional fees, for the three alternative imaging techniques were derived from Medicare reimbursement rates. All other costs were derived from the literature.

Although the authors stated that the analysis was conducted from a societal perspective, indirect costs were not discussed. Costs were discounted at an annual rate of 3%.

Cost-effectiveness was determined by excluding dominated and extended dominated strategies (i.e. strategies that were less effective and more costly), then calculating the incremental cost–utility ratio (ICUR). For the minimally invasive scenario the ICUR for MRA yielded $35,000 per QALY compared with no diagnostic work-up; DSA had an ICUR of $471 per QALY compared with MRA. DUS was dominated by MRA. For the invasive scenario, DSA had an ICUR of $179,000 per QALY compared with no imaging work-up. MRA and DUS were both dominated by DSA. The model was also evaluated for relevant subpopulations, namely 40-year-old men and 70-year-old men, with results showing ICURs lower than for the base-case analysis. In addition, several sensitivity analyses were conducted, which showed that the results obtained were not sensitive to changes in the diagnostic test characteristics. The authors highlight a number of limitations to the study; these are mainly concerned with the model assumptions made to develop fully a tractable model.

The authors concluded that the differences in costs and effectiveness among diagnostic imaging strategies for the baseline patient population were slight. MRA or DUS could replace intra-arterial DSA without substantial loss in effectiveness and with a slight cost reduction. They also state that their results suggest that a clinical study should focus on the decision-making process and workflow in clinical practice.

Visser and colleagues[128] undertook an analysis to determine the societal cost-effectiveness of a variety of management strategies including the imaging work-up and treatment for patients with intermittent claudication. (See abstract in Appendix 7 for full details of the strategies compared.) A previously developed Markov model was enhanced to evaluate appropriately the relevant strategies. The population was modelled over a lifetime from the time the initial diagnostic work-up was performed. The comparator chosen was conservative treatment in which all patients entered a supervised exercise programme.

The study population comprised a hypothetical cohort of previously untreated 60-year-old patients presenting with severe unilateral claudication of at least 1 year's duration, who had at least one significant lesion that was located predominantly suprainguinal or infrainguinal, an ankle brachial index of 0.70 and no history of coronary artery disease. The model parameters were obtained from published sources; it is not apparent whether a systematic review of the literature was performed and as such it is not possible to assess whether the best available evidence was used to populate the decision model. The measure of benefit used in the economic evaluation was QALYs; these were mainly derived using time trade-off values obtained from the literature. All benefits were discounted at an annual rate of 3%.

The direct costs included those incurred by both the hospital and patients; these were obtained directly from the hospital and the literature and, when necessary, augmented by the authors' assumptions. Productivity costs (indirect costs) were excluded from the analysis as most patients with PAD would be retired. Given that the population being modelled comprised 60-year-old patients, this justification for excluding productivity losses may be flawed. Costs were discounted at an annual rate of 3%.

Cost-effectiveness was determined by excluding dominated and extended dominated strategies, then calculating the incremental ICUR. The strategy of MRA plus percutaneous transluminal angioplasty (PTA)/supervised exercise had an ICUR of €20,138 per QALY compared with no test plus exercise strategy. The strategy of DSA plus PTA/bypass surgery/supervised exercise had an ICUR of €130,557 per QALY compared with MRA plus PTA/supervised exercise. All other strategies were inferior by either dominance or extended dominance. The analysis was also undertaken for a subpopulation of 40-year-old and 70-year-old men. Several parameters were varied in sensitivity analyses, which suggests that the results are very sensitive to changes in the costs of MRA.

The authors concluded that for the population modelled, non-invasive imaging modalities could replace intra-arterial DSA without an important loss in effectiveness and at a minimal cost reduction. In addition, management strategies that include bypass surgery were more effective, but their incremental costs were very high.

Visser and colleagues[130] evaluated the cost-effectiveness of a new imaging modality, multidetector row CTA, compared with that of gadolinium-enhanced MRA. The objective of the study was to determine the costs, sensitivity for detection of stenoses and proportion of equivocal

results that would make the new imaging examination cost-effective compared with gadolinium-enhanced MRA. The analysis was conducted for two treatment scenarios: minimally invasive and invasive (as defined above). A Markov model was used to simulate the lifetime cost-effectiveness of the comparative strategies.

The population comprised a hypothetical cohort of 60-year-old men with symptoms of severe unilateral claudication for 1 year, an ankle brachial index of 0.70 and no history of coronary artery disease. The model parameters were obtained from a review of published literature and when necessary augmented by the authors' assumptions. Full details of the review process were not reported, although the authors selected and used a number of published meta-analyses. The measure of benefit used in the analysis was QALYs. Estimated health values were obtained from the literature review and discounted at an annual rate of 3%.

Although the authors state that the analysis was conducted from a societal perspective, no indirect costs (productivity losses) were included. The direct costs included were those of the healthcare system and were derived from the literature. Healthcare resource utilisation data were based on the authors' assumptions. All costs were discounted at an annual rate of 3%.

The analyses showed that for the minimally invasive treatment scenario, with the use of a societal willingness-to-pay threshold of $100,000 per QALY, CTA was equivalent to MRA in terms of cost-effectiveness if the cost of the modality was $420, the sensitivity for detection of significant stenosis was 90%, and 20% of patients required additional work-up owing to equivocal CTA results. For the invasive treatment scenario, with the use of the same willingness-to-pay threshold, CTA was equivalent to MRA in terms of cost-effectiveness if the cost of the modality was $673, the sensitivity for detection of significant stenosis was 95%, and 20% of patients required additional work-up owing to equivocal CTA results. Sensitivity analyses showed that these results did not change substantially when the societal willingness-to-pay threshold was varied.

The authors concluded that multidetector row CTA, as compared with currently used imaging modalities such as MRA, has the potential to be cost-effective in the evaluation of patients with intermittent claudication. They also suggested that the role of new imaging modalities that have fairly good preliminary results could be assessed by performing a pragmatic RCT in which the new modality could be compared with the imaging modality currently in use.

One further study was identified that met the inclusion criteria for the review, but a full translation was not obtained in time for it to be included.[127]

Chapter 7
Economic modelling

The choice of modelling questions

The objective of the economic analysis was the assessment of the relative cost-effectiveness of MRA, DUS and CTA compared with CA (which was considered to be the gold-standard preoperative diagnostic test) for the assessment and treatment planning of PAD patients.

Both a short-term and a long-term model were developed to evaluate the costs and outcomes of the different preoperative diagnostic strategies considered at analysis over different time-horizons.

- The short-term model focused on the period of diagnosis and formulation of the treatment plans. It aimed to estimate the cost per correctly diagnosed patient for whom an accurate treatment plan was formulated; an accurate treatment plan was defined as one that did not require modification during the procedure.
- The long-term model considered not only the diagnosis and formulation of treatment plans, but also follow-up of the patients, including community care (i.e. 1 year time-horizon). In this case, the objective was to estimate the cost per QALY related to each of the diagnostic tests.

The perspective adopted was that of the UK NHS. A wider societal perspective may have been more appropriate, but given that the prevalence of PAD is low among people younger than 65,[659] it is unlikely that productivity losses would have a major impact on the results obtained.

The data that were obtained from the systematic review have enabled comparisons of the accuracy of the tests not only for the whole leg, but also for above-the-knee and below-the-knee comparisons, analysed by arterial segment. *Table 12* highlights the potential comparisons to be performed across the alternative diagnostic imaging techniques in terms of the available diagnostic accuracy data obtained from the systematic review, according to the type of test, how the results were reported (e.g. arterial segment, artery or limb) and the degree of stenosis.

The boundary of 50–100% stenosis was considered for the base-case analysis to diagnose and plan treatment for PAD patients. There are two additional diagnostic thresholds that are considered relevant for the diagnosis and treatment planning of PAD patients: 0–49% or 100% versus 50–99%, and 0–99% versus 100%.[660] However, it was not possible to consider these latter thresholds in the economic analysis, since data were mainly reported for the former threshold (i.e. 0–49% versus 50–100%).

The fact that some relevant data required to populate the decision models were not available for CTA led to the exclusion of this test from the economic evaluation (see below).

In line with the inclusion criteria for the study population that were used in the systematic review, the type of patients considered in the model was those with symptoms suggestive of lower limb PAD, either with intermittent claudication (Fontaine stage II) or with limb-threatening ischaemia (Fontaine stage III or IV), who needed to undergo lower limb vascular imaging to formulate an appropriate treatment plan for their condition.

Methods

Structure of the model and choice of the input parameters

A decision tree was developed, using the software package Data Professional (TreeAge Software), to synthesise experimental data about sensitivity and specificity of the tests with resource use, survival and utility values associated with the alternative preoperative diagnostic tests and consequent treatment plans (*Figures 16–19*). The initial aim of the model was to estimate the costs and consequences of performing preoperative vascular tests (MRA, CTA or DUS), compared with the gold standard (i.e. CA). Since only limited data were available for CTA, it was decided to exclude this diagnostic test from the economic analysis.

The input parameters and strategies were primarily based on the clinical studies and economic evaluations that were identified in the

TABLE 12 *Potential test comparisons to be performed in terms of how the results were reported and the degree of stenosis considered for the diagnosis of PAD*

			MRA	CTA	DUS
Whole leg	50–100%	Segment	Yes	Yes	Yes
		Lesion	Yes	–	–
		Artery	–	–	–
	100%	Segment	Yes	Yes	Yes
		Lesion	–	–	–
		Artery	–	–	–
Above knee	50–100%	Segment	Yes	Yes	Yes
		Lesion	–	–	–
		Artery	Yes	–	–
	100%	Segment	Yes	Yes	Yes
		Lesion	–	–	–
		Artery	Yes	–	–
Below knee	50–100%	Segment	Yes	Yes	Yes
		Lesion	–	–	–
		Artery	Yes	–	–
	100%	Segment	Yes	–	Yes
		Lesion	–	–	–
		Artery	Yes	–	Yes
Foot	50–100%	Segment	–	–	–
		Lesion	–	–	–
		Artery	–	–	–
	100%	Segment	Yes	–	–
		Lesion		–	–
		Artery	Yes	–	–

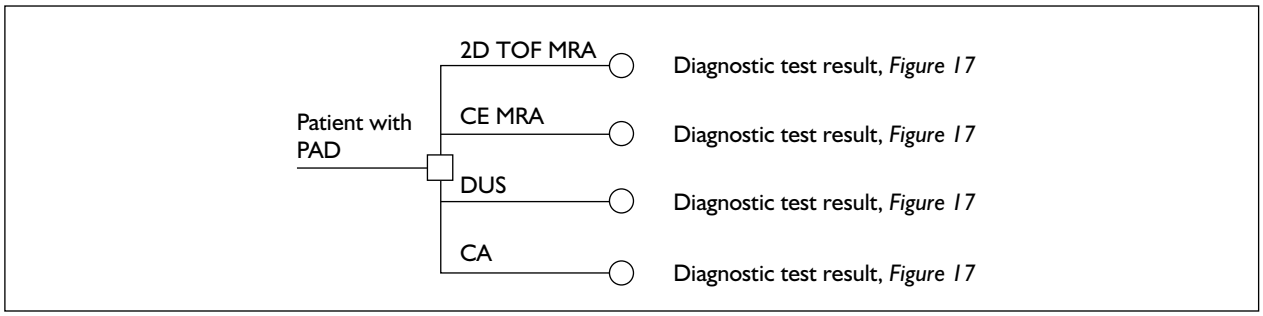


FIGURE 16 *Decision tree 1: preoperative diagnostic tests compared*

systematic review. In addition, other studies identified by screening the references of the included economic evaluations were reviewed to retrieve additional data that were required.

The structure of the decision tree was principally based on a previously developed model,[660] which evaluated the cost-effectiveness of MRA compared with CA in the diagnosis and management of patients with PAD. This model reflected the relevant features related to the preoperative diagnosis and subsequent treatment for PAD patients, although some aspects of the model were simplified (mainly those related to the possible treatments for PAD patients, following the results obtained from the diagnostic test).

Several issues were investigated to progress the structure and accuracy of this previous model. One issue was the concern that some patients may obtain an inconclusive test result and, therefore, may need to undergo an additional diagnostic test. Moreover, there are some contraindications to undergoing MRA (e.g. experiencing claustrophobia or having a pacemaker[128]). These issues are commented on in the following subsections.

Comparators

The model starts by comparing the ability of several preoperative diagnostic tests to accurately determine the severity of lesions and formulate an appropriate interventional treatment plan for

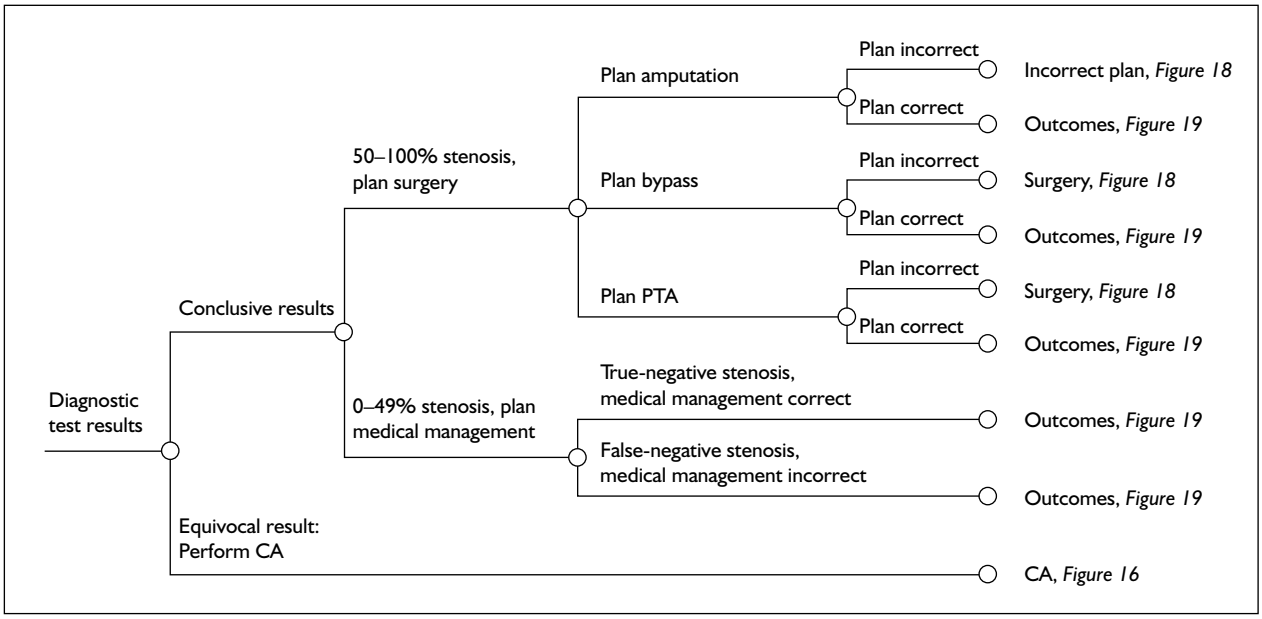


FIGURE 17 *Decision tree II: diagnostic results after initial testing*

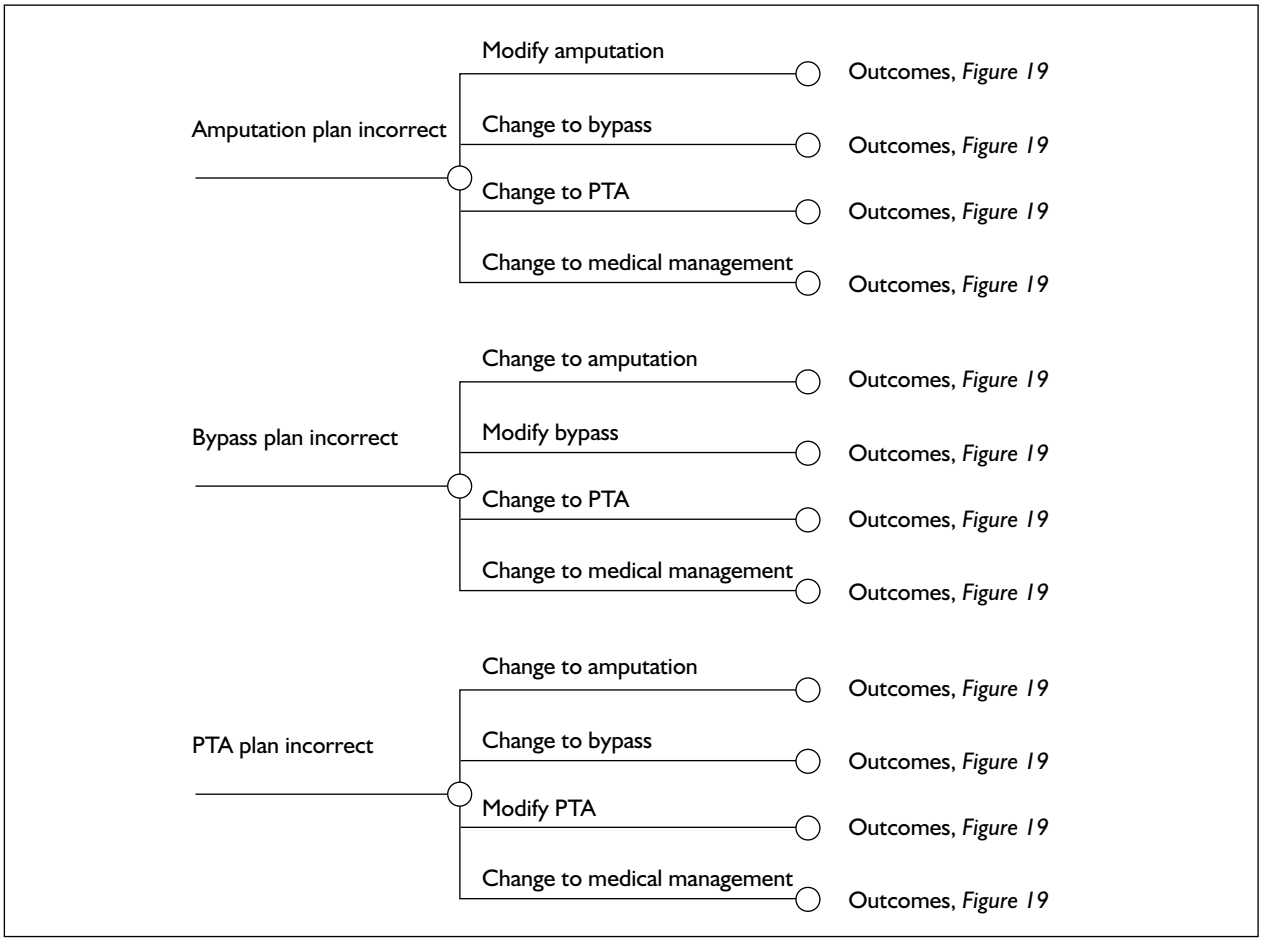


FIGURE 18 *Decision tree III: incorrect treatment plans*

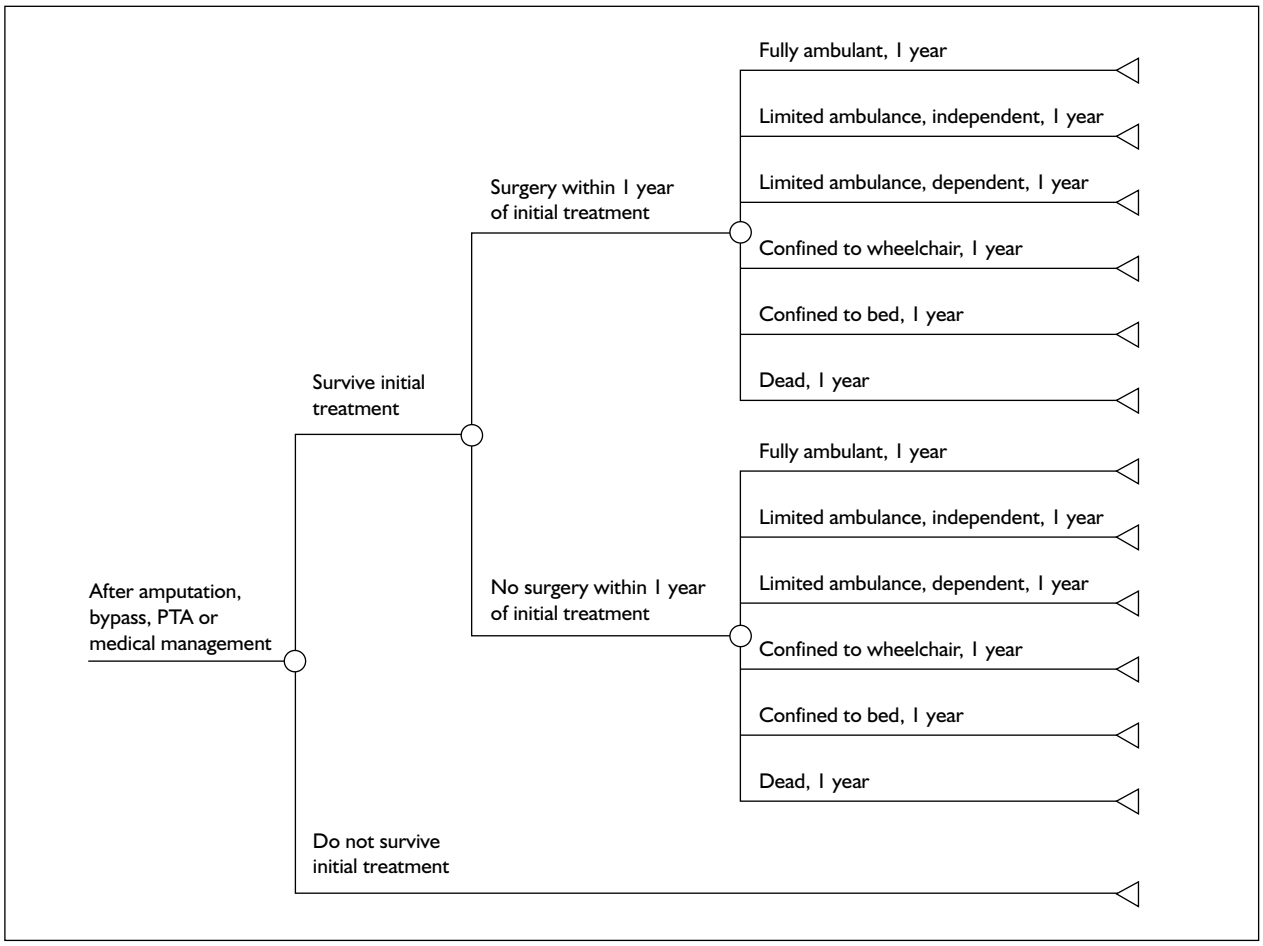


FIGURE 19 *Decision tree IV: outcome at 1 year*

patients with symptomatic PAD. The choice of the diagnostic tests to be included in the analysis was initially based on those tests assessed in the systematic review (i.e. DUS, MRA, or CTA). Nevertheless, as indicated above, owing to the unavailability of relevant data related to the use of CTA (none of the included or excluded studies reported information about how patients would be managed according to the results of a preoperative CTA test), and in consultation with the expert panel, the decision was taken to exclude this diagnostic test from the economic analysis. The model structure considered two MRA techniques, 2D TOF MRA and CE MRA, as separate diagnostic techniques, while CA was included as the reference standard for the imaging of PAD. In total, there were four preoperative diagnostic techniques evaluated in the economic analysis (*Figure 16*):

- 2D TOF MRA
- CE MRA
- DUS
- CA.

Contraindications for the diagnostic tests or inconclusive test results

The economic literature review suggested that preoperative diagnostic tests might not be appropriate for all PAD patients, or may not always provide a definite result.[126,128–130] For the case purpose of the model, it was considered that an equivocal test result could be obtained if there was a contraindication for the patient to undergo the test, if there was a technical failure of the test, or if a treatment plan could not be formulated from the test results.[128]

Overall, for those patients with inconclusive test results, any diagnostic test could be subsequently performed, as a secondary test, to determine the severity of lesion and derive the appropriate treatment plan for the patient (with the exception of those patients with contraindications, for whom only some specific tests could be performed). The initial intention was to consider that any of the diagnostic tests could have been performed as the secondary test. However, data about accuracy of the diagnostic tests being serially performed owing

TABLE 13 *Estimated probabilities of having inconclusive test results with the imaging modalities*

	Base case	Range	Sources
Additional work-up with CA for equivocal 2D-MRA results	0	–	Eklof, 1998[32]
Additional work-up with CA for equivocal CE MRA results	0.09	0.06–0.14	Visser, 2003[128]
Additional work-up with CA for equivocal DUS results	0.23	0.08–0.37	Visser, 2003[128]
Additional work-up with CA for equivocal CA results	0.05	–	Geitung, 1996[126]

to initial inconclusive results were not available in any of the included studies. As a solution to this problem, it was assumed that after an inconclusive test result (or for those patients with contraindications for MRA), CA would be undergone to obtain a final conclusive result that would allow the formulation of the appropriate treatment plans. In this situation, CA was assumed to be 100% sensitive and specific. It was further assumed that after performing CA as a secondary test to obtain definite results, all the data associated with this branch were similar to those in the main branch of CA.

Three of the economic evaluations reviewed reported the probabilities that MRA and DUS would lead to equivocal test results.[128–130] The baseline values for these probabilities were chosen from one of these studies.[128] Based on the information reported by Geitung and colleagues,[126] it was assumed that 5% of patients would require repeated CA because of inconclusive findings (*Table 13*).

Accuracy of the tests

For the base-case analysis, a conclusive test result would indicate that the patient has no stenoses of 50% or higher in the limb under investigation (test negative) or stenoses between 50 and 100% (test positive) in that limb, i.e. the unit of analysis is the limb.

Regarding the accuracy of the diagnostic tests, the baseline data included in the model were the probabilities that the test indicated a degree of stenosis of less than 50% versus 50% or higher (p[T(+)]), and the negative predictive values (NPVs) for stenosis of 0–49% versus 50–100%. These probabilities were obtained from the studies included in the systematic review (*Table 14*). Sample sizes were used to weight the studies in order to obtain pooled estimates of the means and standard errors (SEs) for calculating these probabilities. As CA was considered the reference standard, it was assumed to have 100% sensitivity and specificity. Therefore, the average probability of having a positive test with CA was equal to the prevalence of PAD obtained by pooling the results of the studies included in the systematic review.

The model considers the patient as the focus of analysis. However, in the studies included in the systematic review results were mostly reported by arterial segment, although some studies presented results by artery[32,36,65] or limb[21,23,31,63] as the unit of analysis. Consequently, the units of analysis tested were not independent of each other because one patient could have several segments or arteries evaluated, and either one or both legs. No information was reported in the studies about the accuracy of the test results on a patient basis. As such, it was necessary to assume that the estimates of sensitivity and specificity were equivalent, independent of how the results were reported (e.g. arterial segment, artery or limb). This was an appropriate assumption given that it has been shown that this issue affects only the precision of sensitivity and specificity estimates.[661] It has been further assumed that each patient entering the model has one leg evaluated. While the authors acknowledge that it may be possible with certain techniques to image more that one limb at a time, it was considered impractical to evaluate both legs in one session with 2D TOF MRA, according to expert opinion. Therefore, outcomes have been reported per patient, per leg.

The probability of having a positive test result with CA was estimated as the prevalence of stenosis 50% or greater among the total number of patients in the included studies that evaluated 2D TOF MRA, CE MRA or DUS versus CA.

Treatment plans

Based on the result obtained with the diagnostic test a treatment plan will be formulated for each patient. Following the model structure, patients diagnosed with 50% or more stenosis could be treated with PTA, bypass or amputation, according to the choice of the surgeon, depending on the technical options and the clinical state of the patient, while patients diagnosed with less than 50% stenosis would be treated with medical management. This is a simplification of the reality,

TABLE 14 *Pooled estimates associated with the accuracy of the diagnostic tests (0–49% versus 50–100% stenosis for the whole leg) derived from the systematic review*

	p[T(+)]	SE (*p*[T(+)])	NPV	SE (NPV)	Sources
2D TOF MRA	0.468	0.0097	0.881	0.0087	Baum, 1995,[22] Hoch, 1996,[40] Hoch, 1999,[41] Snidow, 1995,[64] Yucel, 1993[74]
CE MRA	0.271	0.0064	0.983	0.0023	Cronberg, 2003,[28] Laissy, 1998,[49] Lenhart, 2000,[51] Schafer, 2003,[61] Steffens, 2003,[67] Sueyoshi,1999,[68] Winterer, 1999[73]
DUS	0.222	0.0055	0.969	0.0028	Aly, 1998,[20] Ashleigh, 1993,[21] Baxter, 1993,[23] Bergamini, 1995,[24] El-Kayali, 2004,[33] Hatsukami, 1992[37] Legemate, 1991,[50] Linke, 1994,[52] Sensier, 1996[62]
CA	0.279	0.0039	1	–	Aly, 1998,[20] Ashleigh, 1993,[21] Baum, 1995,[22] Baxter, 1993,[23] Bergamini, 1995,[24] Cronberg, 2003,[28] El-Kayali, 2004,[33] Hatsukami, 1992,[37] Hoch, 1996,[40] Hoch, 1999,[41] Laissy, 1998,[49] Legemate, 1991,[50] Lenhart, 2000,[51] Linke, 1994,[52] Schafer, 2003,[61] Sensier, 1996,[62] Snidow, 1995,[64] Steffens, 2003,[67] Sueyoshi, 1999,[68] Winterer, 1999,[73] Yucel, 1993[74]

since other options are available for the treatment of patients with PAD. For example, endovascular stents have been used after PTA to improve health outcomes for specific subgroups of patients with intermittent claudication. However, a systematic review comparing the use of stents after PTA with PTA alone found no significant differences in the outcomes when studies were combined, and concluded that there is no clear evidence that stent following angioplasty should be recommended.[662] This supports the decision of choosing PTA alone for the model. Patients with intermittent claudication could also be recommended to undergo exercise programmes, which may improve maximal walking distance,[663] but a lack of clear evidence led to the exclusion of this alternative from the model.

In this sense, the alternative treatments considered for patients diagnosed with less than 50% stenosis could be not only medical management but also angioplasty, which has shown short-term clinical benefits for patients. In the present model, only medical management was finally considered, since there is doubt about the value of angioplasty in the long-term for this type of patient.[664] When formulating a treatment plan the surgeon would, in practice, consider a number of factors in addition to the degree of stenosis, such as the length and position of stenosis, and the presence of co-morbidities affecting suitability for surgery.

Literature suggests that both MRA and DUS may not correctly identify the degree of stenosis in all patients; in which case, an inaccurate plan may be formulated.[33,40,41,126] In addition, although CA is assumed to be 100% sensitive and specific, the treatment plan chosen will depend to some extent on the interpretation of the test results (i.e. images obtained) by the radiologist and the surgeon (i.e. it is subject to inter-observer variability), which may also lead to the formulation of an inaccurate treatment plan.[40,41]

For those patients for whom an inaccurate surgical intervention is chosen, there is the possibility of identifying the error and changing the type of treatment during the procedure.[33,40,41,126]

The probabilities associated with the treatment plans chosen by surgeons according to the results of each of the imaging tests were obtained from four studies included in the systematic review. Two of these studies provided information about how patients would be managed using the results of the MRA test compared with those of CA,[40,41] while two other studies provided information about treatment plans for patients undergoing DUS.[33,126]

The types of data to be identified from these papers were:

- the treatment plans initially formulated according to each diagnostic test
- the number and type of inaccurate treatment plans formulated using each test
- the treatments that were actually performed according to the intraoperative findings

- the type of change made for each inaccurate treatment plan to manage the patient appropriately.

The aim was to identify:

- the probabilities that a patient would be initially managed with PTA, bypass or amputation according to the results of the preoperative test
- the probability that the initial plan was inaccurate
- the probability that an inaccurate plan would be managed by modifying the intervention or changing the management plan.

However, some of these studies failed to report all the information in a homogeneous way. Moreover, results were reported in different units of analysis (i.e. by arterial segment, leg or patient), or in some instances the unit of analysis was not clearly specified. To interpret and extract data that could be used for the estimation of these probabilities, several assumptions had to be made based on the conjecture of the researchers dealing with the papers.

Related to the interpretation of these studies was the fact that some of them included patients who had undergone endarterectomy. Endarterectomy is a surgical procedure which, like bypass grafting, generally requires either a regional (epidural or spinal) or a general anaesthetic. For some peripheral stenoses or occlusions, usually of the common/external iliac or superficial femoral arteries, a remote endarterectomy may be performed. This is a less invasive procedure, which involves passing an instrument along the artery from an incision in the groin. Nevertheless, endarterectomy carries risks that are similar to both bypass grafting (i.e. perioperative complications such as haemorrhage, vessel occlusion by thrombolysis of embolism, infection and risk from general anaesthesia) and PTA (vessel rupture, thrombolysis or embolism). For this reason, two sets of parameters were obtained to populate the model; for the base-case analysis endarterectomy was grouped with bypass grafting, although a sensitivity analysis was performed to quantify the effect of including people with endarterectomy in the PTA group.

To obtain pooled estimates for the probabilities related to the accuracy of the treatment plans formulated (i.e. the probabilities of having PTA, bypass or amputation after the diagnostic test results, the probabilities of having an inaccurate treatment plan given the type of treatment formulated, and the probabilities of changing from an inaccurate plan to another intervention), the estimates from the studies were weighted by their sample size (*Tables 15–17*).

A relevant issue to highlight at this point is that the distribution of patient characteristics may not have been similar across studies. In two of the studies used for these estimations[33,41] patients were stated to be symptomatic, but no further characteristics about their severity were reported. In another study[40] 18% (8/45) of patients were Fontaine II, 20% (9/45) were Fontaine III and 62% (28/45) were Fontaine IV. This seems to be a disproportionate number with severe disease,

TABLE 15 *Estimated probabilities of having PTA, bypass or amputation as the initially formulated treatment plan according to diagnostic test result*

	CA	MRA	DUS
Amputation			
El-Kayali, 2004[33]	–	–	0.11
Hoch, 1996[40]	0.06	0.06	–
Hoch, 1999[41]	0.04	0.00	–
Pooled estimate	0.05	0.03	0.11
Bypass			
El-Kayali, 2004[33]	–	–	0.49
Hoch, 1996[40]	0.56	0.58	–
Hoch, 1999[41]	0.67	0.78	–
Pooled estimate	0.62	0.68	0.49
PTA			
El-Kayali, 2004[33]	–	–	0.41
Hoch, 1996[40]	0.38	0.36	–
Hoch, 1999[41]	0.29	0.22	–
Pooled estimate	0.33	0.29	0.41

TABLE 16 *Estimated probabilities of having an inaccurate treatment plan*

	CA	MRA	DUS
Inaccurate amputation			
El-Kayali, 2004[33]	–	–	0.00
Hoch, 1996[40]	0.33	0.33	–
Hoch, 1999[41]	1	0.00	–
Pooled estimate	0.66	0.17	0.00
Inaccurate bypass			
El-Kayali, 2004[33]	–	–	0.11
Hoch, 1996[40]	0.07	0.10	–
Hoch, 1999[41]	0.00	0.11	–
Pooled estimate	0.04	0.10	0.11
Inaccurate PTA			
El-Kayali, 2004[33]	–	–	0.07
Hoch, 1996[40]	0.11	0.06	–
Hoch, 1999[41]	0.07	0.00	–
Pooled estimate	0.09	0.03	0.07

which will almost certainly have led to a relatively high number of amputations in this study. The last of these studies[126] did not report relevant characteristics for the patients evaluated (only age and gender). Consequently, the samples in these studies may not have been representative of the general population of symptomatic PAD patients.

Effectiveness of treatments undergone after diagnosis

The model considers that, after a specific treatment plan has been followed, intervention-related mortality may occur. Otherwise, the patient survives and may or may not require further surgery within the first year.

Following bypass, 6% of patients would die within 30 days from causes related to the intervention, while for PTA none of the patients would experience intervention-related mortality.[396] The probability of amputation-related mortality was assumed to be the same as that after bypass.[665]

Once an intervention has been undergone, a patient may require a secondary procedure within 1 year (*Table 18*). Data about the percentage of patients who would undergo secondary procedures within 1 year, and about the type of procedure undergone, were scarce. Some assumptions were therefore formulated:

- Amputation was regarded as an end-point for a given incidence of disease, and therefore the proportion of patients with primary amputation that required further PTA or bypass graft within a year was assumed to be zero.
- Similarly, the proportion of patients who had a PTA after bypass graft was assumed to be zero on the basis that after bypass, PTA would only be performed at a new disease site. The use of PTA to treat stenosis of bypass grafts was not considered as this is outside the scope of the current project.

Health states

Patients could end in one of six health states: (1) fully ambulant; (2) limited ambulance and independent; (3) limited ambulance and dependent; (4) non-ambulant and using a wheelchair; (5) bedridden; or (6) dead (*Table 19*). The probability that a patient ended in each one of these health states depended on whether the initial treatment plan was correct or not, and whether complications such as graft failure, amputation or death occurred.[660]

An adjustment was performed for the probabilities related to the prognosis after amputation for patients with 50–100% stenosis, medical management for patients with 50–100% stenosis, and amputation for patients with less than 50% stenosis, to overcome the problem that they did not sum up to one in the original study.[660]

In addition, these probabilities were adjusted to account for the fact that some patients may undergo further revascularisation within 1 year. In this case the probabilities of ending in a less favourable health state would increase (*Table 20*). For example, the probability of ending in a health state of independency and full mobility for a patient initially treated with bypass and

TABLE 17 *Estimated probabilities of changing plan after inaccurate plan formulation*

	CA	MRA	DUS
Amputation incorrect			
Modify amputation			
El-Kayali, 2004[33]	–	–	0
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	1	0	–
Hoch, 1999[41]	0	0	–
Pooled estimate	0.51	0	0
Change to bypass			
El-Kayali, 2004[33]	–	–	0
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	0	0	–
Hoch, 1999[41]	1	0	–
Pooled estimate	0.49	0	0
Change to PTA			
El-Kayali, 2004[33]	–	–	0
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	0	0	–
Hoch, 1999[41]	0	0	–
Pooled estimate	0	0	0
Change to MM			
El-Kayali, 2004[33]	–	–	0
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	0	0	–
Hoch, 1999[41]	0	0	–
Pooled estimate	0	0	0
Bypass incorrect			
Change to amputation			
El-Kayali, 2004[33]	0	0	–
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	–	–	0
Hoch, 1999[41]	0	0	–
Pooled estimate	0	0	0
Modify bypass			
El-Kayali, 2004[33]	1	0.67	–
Geitung, 1996[126]	–	–	0.82
Hoch, 1996[40]	–	–	1
Hoch, 1999[41]	0	0	–
Pooled estimate	1	0.34	0.91
Change to PTA			
El-Kayali, 2004[33]	0	0.33	–
Geitung, 1996[126]	–	–	0.18
Hoch, 1996[40]	–	–	0
Hoch, 1999[41]	0	1	–
Pooled estimate	0	0.66	0.09
Change to MM			
El-Kayali, 2004[33]	0	0	–
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	–	–	0
Hoch, 1999[41]	0	0	–
Pooled estimate	0	0	0

continued

TABLE 17 *Estimated probabilities of changing plan after inaccurate plan formulation (cont'd)*

	CA	MRA	DUS
PTA incorrect			
Change to amputation			
El-Kayali, 2004[33]	–	–	0
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	0	0	–
Hoch, 1999[41]	0	0	–
Pooled estimate	0	0	0
Change to bypass			
El-Kayali, 2004[33]	–	–	0
Geitung, 1996[126]	–	–	1
Hoch, 1996[40]	0	0	–
Hoch, 1999[41]	1	0	–
Pooled estimate	0.49	0.00	0.49
Modify PTA			
El-Kayali, 2004[33]	–	–	0
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	1	1	–
Hoch, 1999[41]	0	0	–
Pooled estimate	0.51	1.00	0.00
Change to MM			
El-Kayali, 2004[33]	–	–	1
Geitung, 1996[126]	–	–	0
Hoch, 1996[40]	0	0	–
Hoch, 1999[41]	0	0	–
Pooled estimate	0	0	0.51

MM, medical management.

TABLE 18 *Probability of having a revascularisation procedure among patients undergoing surgery within 1 year after initial treatment*

	Amputation	Bypass	PTA	Total probability of surgery within 1 year	Sources
After amputation	1.00	0.00	0.00	0.56	Peters, 1998[666] Assumption
After bypass	0.78	0.22	0.00	0.18	Holm, 1991[667]
After PTA	0.52	0.05	0.43	0.40	Holm, 1991[667]
After MM	0.07	0.19	0.74	0.27	Vascular Surgical Society of Great Britain and Ireland, 2003[668] Expert opinion

subsequently requiring further surgery within 1 year was estimated as follows:

ProbFMb_Byp_surg =
ProbByp_surgAmp*ProbFMb_Amp +
ProbByp_surgByp*ProbFMb_Byp +
ProbByp_surgPTA*ProbFMb_PTA

where ProbFMb_Byp_surg is the probability of ending in a health state of independency and full mobility for a patient treated initially with bypass and requiring further surgery within 1 year, ProbByp_surgAmp is the probability that the revascularisation procedure performed within 1 year was amputation, ProbFMb_Amp is the probability of ending fully ambulant after initial amputation, ProbByp_surgByp is the probability that the revascularisation procedure performed within 1 year was bypass, ProbFMb_Byp is the probability of ending fully ambulant after initial bypass, ProbByp_surgPTA is the probability that the revascularisation procedure performed within 1 year was PTA; and ProbFMb_PTA is the probability of ending fully ambulant after initial PTA.

TABLE 19 *Health states at 1 year after diagnosis and treatment of PAD patients*

Event	Probability	Source
Stenosis 50–100%, amputation		
Full mobility	0.04	Berry, 2002,[660] Davies, 1991,[669] assumption
Limited mobility, independent	0.18	Berry, 2002[660]
Limited mobility, dependent	0.2	Berry, 2002[660]
Wheelchair	0.32	Berry, 2002[660]
Bedridden	0.01	Berry, 2002[660]
Dead	0.25	Berry, 2002[660]
Stenosis 50–100%, bypass		
Full mobility	0.05	Berry, 2002[660]
Limited mobility, independent	0.29	Berry, 2002[660]
Limited mobility, dependent	0.32	Berry, 2002[660]
Wheelchair	0.19	Berry, 2002[660]
Bedridden	0.01	Berry, 2002[660]
Dead	0.14	Berry, 2002[660]
Stenosis 50–100%, PTA		
Full mobility	0.05	Berry, 2002[660]
Limited mobility, independent	0.26	Berry, 2002[660]
Limited mobility, dependent	0.29	Berry, 2002[660]
Wheelchair	0.28	Berry, 2002[660]
Bedridden	0.01	Berry, 2002[660]
Dead	0.11	Berry, 2002[660]
Stenosis 50–100%, MM		
Full mobility	0.04	Berry, 2002,[660] Davies, 1991,[669] assumption
Limited mobility, independent	0.18	Berry, 2002[660]
Limited mobility, dependent	0.2	Berry, 2002[660]
Wheelchair	0.32	Berry, 2002[660]
Bedridden	0.01	Berry, 2002[660]
Dead	0.25	Berry, 2002[660]
Stenosis <50%, amputation		
Full mobility	0.04	Berry, 2002,[660] Davies, 1991,[669] assumption
Limited mobility, independent	0.18	Berry, 2002[660]
Limited mobility, dependent	0.2	Berry, 2002[660]
Wheelchair	0.32	Berry, 2002[660]
Bedridden	0.01	Berry, 2002[660]
Dead	0.25	Berry, 2002[660]
Stenosis <50%, bypass		
Full mobility	0.06	Berry, 2002[660]
Limited mobility, independent	0.33	Berry, 2002[660]
Limited mobility, dependent	0.36	Berry, 2002[660]
Wheelchair	0.14	Berry, 2002[660]
Bedridden	0	Berry, 2002[660]
Dead	0.11	Berry, 2002[660]
Stenosis <50%, PTA		
Full mobility	0.07	Berry, 2002[660]
Limited mobility, independent	0.37	Berry, 2002[660]
Limited mobility, dependent	0.4	Berry, 2002[660]
Wheelchair	0.16	Berry, 2002[660]
Bedridden	0	Berry, 2002[660]
Dead	0	Berry, 2002[660]
Stenosis <50%, MM		
Full mobility	0.07	Berry, 2002[660]
Limited mobility, independent	0.37	Berry, 2002[660]
Limited mobility, dependent	0.4	Berry, 2002[660]
Wheelchair	0.16	Berry, 2002[660]
Bedridden	0	Berry, 2002[660]
Dead	0	Berry, 2002[660]

TABLE 20 *Probabilities of ending in different health states for patients undergoing further revascularisation procedures within 1 year*

Health state	After initial amputation	After initial bypass	After initial PTA	After initial MM (50–100% stenosis)
Full mobility	0.040	0.042	0.045	0.049
Limited mobility, independent	0.180	0.204	0.230	0.260
Limited mobility, dependent	0.200	0.226	0.254	0.289
Wheelchair, dependent	0.320	0.291	0.268	0.266
Bedridden	0.010	0.010	0.010	0.010
Dead	0.250	0.226	0.194	0.126

For those patients who initially underwent primary amputation and subsequently required further surgery within the first year of treatment, it was assumed that the probabilities of ending in the different health states were the same as for initial amputation (although this was considered to be the best case scenario in relation to these parameters).

Life expectancy and quality of life

Life expectancy for those patients dying within the first year was assumed to be 6 months to account for differences in survival times through the year. For those patients experiencing intervention-related mortality, life expectancy was assumed to be zero since these patients are more likely to die during or just after the intervention. Evidence about long-term survival according to each of the possible health states was uncertain,[660] which led to limiting the period of analysis to 1 year for the long-term model.

Health utility values were assigned to each of the possible health states according to those previously published[660] (*Table 21*). QALYs were estimated by multiplying the health utility values by the estimated life expectancy.

Following expert opinion, it was assumed that those patients undergoing a revascularisation procedure within the first year after initial treatment would experience a reduction in their quality of life of 30%, 15% or 5% during the period of recovery (which was estimated to be 2 months), depending on whether the revascularisation procedure undergone was PTA, bypass or amputation, respectively. To estimate the utilities associated with the possible end health states after revascularisation within 1 year, these reductions in quality of life were weighted by the probabilities that the type of procedure undergone would be PTA, bypass or amputation. For example, the utility associated with the health state of a patient initially managed with medical

TABLE 21 *Utility values of health states following treatment of PAD*

Health state	Utility value
Full mobility	
Amputation	0.83
Critical limb ischaemia	0.83
Claudication	0.83
Limited mobility, independent:	
Amputation	0.56
Critical limb ischaemia	0.73
Claudication	0.78
Limited mobility, dependent:	
Amputation	0.56
Critical limb ischaemia	0.69
Claudication	0.69
Wheelchair, dependent	0.46
Bedridden	0.33
Dead	0.00

Source: Berry *et al*. (2002).[660]

treatment, requiring a revascularisation procedure during the first year of treatment and ending with full mobility, was estimated as follows:

$$UMM\_surg = [10/12 + 2/12 * (1 - 0.30 * Prob\_MM\_surgAmp - 0.15 * Prob\_MM\_surgByp - 0.05 * Prob\_MM\_surgPTA)] * U\_FMb$$

where UMM_surg is the utility obtained by a patient receiving initially medical treatment and requiring a revascularisation procedure within 1 year after initial treatment, Prob_MM_surgAmp, Prob_MM_surgByp and Prob_MM_surgPTA are the probabilities that a patient under initial medical management (MM) and requiring a revascularisation procedure within 1 year would undergo amputation, bypass or PTA, respectively, and U_FMb is the utility associated with the health state of being independent and with full mobility for those patients not requiring further interventions within 1 year (*Table 22*).

TABLE 22 *Utilities for patients undergoing further revascularisation procedures within one year*

Health state	After amputation	After bypass	After PTA	After MM (50–100% stenosis)	After MM (0–49% stenosis)
Full mobility	0.789	0.793	0.800	0.818	0.818
Limited mobility, independent	0.532	0.698	0.704	0.719	0.744
Limited mobility, dependent	0.532	0.659	0.665	0.680	0.680
Wheelchair, dependent	0.437	0.440	0.443	0.453	0.453
Bedridden	0.314	0.318	0.318	0.325	0.325
Dead	0.266	0.330	0.333	0.340	0.340

Costing

The perspective adopted for the economic evaluation was that of the service provider (UK NHS). According to this perspective, the costs included in the economic analysis were the direct medical costs incurred in performing the preoperative diagnostic tests (and secondary CA for those inconclusive tests or those patients with contraindications), costs of treatments (i.e. PTA, bypass, amputation, medical management, and costs derived from intervention-related mortality) and follow-up costs.

The costs of major complications associated with CA[128] were also included in the economic evaluation. Other diagnostic procedure-related costs incurred due to adverse events were excluded as the adverse events obtained from the systematic review were not considered representative of the actual adverse events experienced by patients while undergoing the preoperative diagnostic tests (since not all the studies reported information about adverse events). Moreover, most of the adverse events reported in the studies did not imply an incurrence of costs, and when they did, the costs were considered to be negligible.

The costs of the vascular interventions included theatre time and the time spent in the intensive care unit, the high-dependency unit and other inpatient wards. The cost of the amputation was averaged according to the percentage of patients undergoing amputations at the below- and above-knee level (i.e. 40% of the amputations performed would be at the below-knee level, according to UK data).[670]

In addition, there were costs related to the adjustment of the treatment plans that were inaccurately formulated after the diagnostic result. The probability that an initially formulated amputation would be changed to medical treatment is remote (a zero probability was observed in the primary studies providing these types of data).[33,40,41,126] However, the possibility exists that a patient with limb-threatening ischaemia requiring amputation may decide not to undergo the procedure and to receive only medical treatment. Therefore, the costs of changing from amputation to medical management were assumed to be zero. In the unlikely case that a treatment plan was changed from bypass to medical treatment, the associated costs were assumed to be those of a normal bypass. The costs incurred while changing other types of inaccurately formulated treatment plans are reported in *Table 23*.

A retrospective study evaluating data from the Trent Regional Database (UK) reported data about the rates of secondary procedures undergone by patients with PAD within the same admission considering a follow-up period of 2 years (1995–1997).[670] As the authors stated, these rates were likely to be underestimated. However, they were used in the present analysis to estimate more accurately the costs associated with the surgical procedures undergone. The fact that some patients may require further surgery within the same admission was also considered in the cost estimation (*Table 24*).

The costs of outpatient visits related to the vascular procedure undergone have been included[670] (*Table 25*) and were estimated according to the type of vascular procedure. In the case of either amputation or bypass, the patient incurred a total of three outpatient visits, whereas in the case of PTA only two outpatient visits were required.

The costs associated with any additional surgery required at 1 year were estimated according to the proportion of patients that would experience recurrent ischaemia at 1 year and, consequently, would require further intervention (*Table 18*). The costs incurred in performing the preoperative diagnostic tests, the costs due to inconclusive test results and those of CA complications (when this test was performed) were also included in the cost estimation of surgery within 1 year after initial treatment.

TABLE 23 *Resource use and costs associated with diagnostic procedures and follow-up*

	Resource use		Unit costs (£ 2004)			Estimated costs (£ 2004)		
	Average	**Range (95% CI)**	**Source**	**Average**	**Range**	**Source**	**Average**	**Range**
Preoperative diagnostic tests								
CA								
CA, including capital equipment	1	No range	Berry, 2002[660]	492.30	432.79–704.37	Berry, 2002[660]	536.80	215.56–914.04
Complications of CA	–	–	Visser, 2003[129]	–	–	Visser, 2003[129]	5740.35	3183.47–8300.33
MRA								
MRA, including capital equipment	1	No range	Berry, 2002[660]	462.00	450.10–502.04	Berry, 2002[660]	462.00	450.10–502.04
DUS								
DUS	1	No range		92.49	72.90–134.34	DH, 2004[671]	92.49	72.90–134.34
Amputation								
Above-knee primary								
Theatre time (minutes)	125	100–150	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	1081.98	907.51–1132.02
Intensive care unit (hours)	6	5–7.2	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	312.42	283.21–341.36
High-dependency unit (hours)	4	3.3–5	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	23	20.75–25.47 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	4852.66	4554.04–5151.29
							6328.02	5825.36–6705.99
Above-knee plan changed to bypass								
Theatre time (minutes)	312	No range	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	2700.61	2265.14–2825.51
Intensive care unit (hours)	4	3.58–5.36	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	208.28	188.80–227.58
High-dependency unit (hours)	4	2.94–4.4	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	14	13.51–25.5	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	2953.79	2772.02–3135.57
							5943.65	5306.57–6269.98
Above-knee revision, readmission								
Theatre time (minutes)	114	83–144	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	986.76	827.65–1032.40
Intensive care unit (hours)	6	5–7.2	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	312.42	283.21–341.36
High-dependency unit (hours)	4	3.3–5	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	23	20.75–25.47 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	4852.66	4554.04–5151.29
							6232.81	5745.50–6606.38
Below knee primary								
Theatre time (minutes)	156	125–187	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	1350.31	1132.57–1412.76
Intensive care unit (hours)	6	5–7.2	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	312.42	283.21–341.36
High dependency unit (hours)	4	3.3–5	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	23	20.75–25.47 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	4852.66	4554.04–5151.29
							6596.35	6050.42–6986.73

continued

TABLE 23 *Resource use and costs associated with diagnostic procedures and follow-up (cont'd)*

	Resource use		Unit costs (£ 2004)			Estimated costs (£ 2004)		
	Average	**Range (95% CI)**	**Source**	**Average**	**Range**	**Source**	**Average**	**Range**
Below-knee plan changed to bypass								
Theatre time (minutes)	312	No range	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	2700.61	2265.14–2825.51
Intensive care unit (hours)	4	3.58–5.36	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	208.28	188.80–227.58
High-dependency unit (hours)	4	2.94–4.4	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	14	13.51–25.5	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	2953.79	2772.02–3135.57
							5943.65	5306.57–6269.98
Below-knee revision, readmission								
Theatre time (minutes)	114	83–144	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	986.76	827.65–1032.40
Intensive care unit (hours)	6	5–7.2	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	312.42	283.21–341.36
High-dependency unit (hours)	4	3.3–5	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	23	20.75–25.47 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	4852.66	4554.04–5151.29
							6232.81	5745.50–6606.38
Bypass								
Bypass primary								
Theatre time (minutes)	199	190–318	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	1722.51	1444.75–1802.17
Intensive care unit (hours)	4	3.58–5.36	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	208.28	188.80–227.58
High-dependency unit (hours)	4	2.94–4.4	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	14	13.51–25.5	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	2953.79	2772.02–3135.57
							4965.55	4486.18–5246.64
Bypass plan changed to amputation								
Theatre time (minutes)	199	190–318	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	1722.51	1444.75–1802.17
Intensive care unit (hours)	4	3.58–5.36	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	208.28	188.80–227.58
High-dependency unit (hours)	4	2.94–4.4	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	14	13.51–25.5	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	2953.79	2772.02–3135.57
							4965.55	4486.18–5246.64
Bypass plan changed to PTA								
Theatre time (minutes)	199	190–318	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	1722.51	1444.75–1802.17
Intensive care unit (hours)	0	No range	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	0.00	0.00–0.00
High-dependency unit (hours)	0	No range	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	0.00	0.00–0.00
Other inpatient ward (days)	3	2.29–3.18 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	632.96	594.00–671.91
							2355.46	2038.76–2474.08

continued

TABLE 23 *Resource use and costs associated with diagnostic procedures and follow-up (cont'd)*

	Resource use		Unit costs (£ 2004)			Estimated costs (£ 2004)		
	Average	**Range (95% CI)**	**Source**	**Average**	**Range**	**Source**	**Average**	**Range**
Bypass revision, readmission								
Theatre time (minutes)	199	190–318	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	1722.51	1444.75–1802.17
Intensive care unit (hours)	4	3.58–5.36	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	208.28	188.80–227.58
High-dependency unit (hours)	4	2.94–4.4	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	14	13.51–25.5	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	2953.79	2772.02–3135.57
							4965.55	4486.18–5246.64
PTA								
PTA primary								
Theatre time (minutes)	63	50–75	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	545.32	457.38–570.54
Intensive care unit (hours)	0	No range	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	0.00	0.00–0.00
High-dependency unit (hours)	0	No range	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	0.00	0.00–0.00
Other inpatient ward (days)	3	2.29–3.18 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	632.96	594.00–671.91
							1178.27	1051.39–1242.44
PTA plan changed to bypass								
Theatre time (minutes)	261	No range	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	2259.16	1894.87–2363.65
Intensive care unit (hours)	4	3.58–5.36	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	208.28	188.80–227.58
High-dependency unit (hours)	4	2.94–4.4	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	14	13.51–25.5	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	2953.79	2772.02–3135.57
							5502.21	4936.31–5808.12
PTA plan changed to amputation								
Theatre time (minutes)	219	No range	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	1895.62	1589.95–1983.29
Intensive care unit (hours)	6	5–7.2	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	312.42	283.21–341.36
High-dependency unit (hours)	4	3.3–5	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	80.97	80.61–81.33
Other inpatient ward (days)	23	20.75–25.47 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	4852.66	4554.04–5151.29
							7141.67	6507.80–7557.27
PTA plan changed to MM	–	–	Visser, 2003[129]	–	–	Visser, 2003[129]	245.36	122.68–368.04
PTA revision, readmission								
Theatre time (minutes)	63	50–75	Berry, 2002[660]	8.66	7.26–9.06	Berry, 2002[660]	545.32	457.38–570.54
Intensive care unit (hours)	0	No range	Berry, 2002[660]	52.07	47.20–56.89	Berry, 2002[660]	0.00	0.00–0.00
High-dependency unit (hours)	0	No range	Berry, 2002[660]	20.24	20.15–20.33	Berry, 2002[660]	0.00	0.00–0.00
Other inpatient ward (days)	3	2.29–3.18 (95% CI)	Berry, 2002[660]	210.99	198.00–223.97	Berry, 2002[660]	632.96	594.00–671.91
							1178.27	1051.39–1242.44
Mortality from vascular interventions	–	–	Visser, 2003[129]	–	–	Visser, 2003[129]	9906.04	3067.01–17051.00

continued

TABLE 23 *Resource use and costs associated with diagnostic procedures and follow-up (cont'd)*

	Resource use		Unit costs (£ 2004)			Estimated costs (£ 2004)		
	Average	**Range (95% CI)**	**Source**	**Average**	**Range**	**Source**	**Average**	**Range**
Long-term costs								
Full mobility	1	No range	Berry, 2002[660]	0.00	–	Berry, 2002[660]	0.00	–
Limited mobility, independent	1	No range	Berry, 2002[660]	771.45	0.00–1541.82	Berry, 2002[660]	771.45	0.00–1541.82
Limited mobility, dependent	1	No range	Berry, 2002[660]	7290.35	1541.82–13038.89	Berry, 2002[660]	7290.35	1541.82–13038.89
Wheelchair	1	No range	Berry, 2002[660]	13169.81	11387.79–14950.74	Berry, 2002[660]	13169.81	11387.9–14950.74
Bedridden	1	No range	Berry, 2002[660]	22150.20	14950.74–29348.59	Berry, 2002[660]	22150.20	14950.74–29348.59
Medical management (i.e. aspirin; mg per day; unit cost per day; estimated cost per year)	75	No range	BNF, 2005[672]	0.04	0.01–0.06	BNF, 2005[672]	14.66	3.47–20.21

BNF, British National Formulary; DH, Department of Health.

TABLE 24 *Probabilities of patients undergoing a secondary procedure within the same admission*

Primary procedure	Amputation	Bypass	PTA
Amputation	0.04	0.13	0.13
Bypass	0.00	0.29	0.00
PTA	0.00	0.00	0.05

Source: Michaels *et al*. (2000).[670]

TABLE 25 *Number of outpatient visits per admission according to the vascular procedure undergone*

Vascular procedure	Outpatient visits
Amputation	3
Bypass	3
PTA	2

Source: Michaels *et al*. (2000).[670]

Independently of whether or not patients undergo an invasive treatment intervention, medical management, consisting of antiplatelet therapy (generally aspirin),[171] is recommended for all patients with PAD. Therefore, the cost of medical management with aspirin (300 mg per day) for all patients was also included in the economic analysis. Moreover, it has been stated that patients should follow risk-factor modification therapies, such as smoking cessation, and controlling hyperlipidaemia, diabetes and hypertension.[151,673] However, these costs were not considered in the economic analysis since these risk-factor modification therapies appeared to be underused.[151,670]

The short-term model included only the costs of performing the diagnostic procedures plus any additional costs incurred while formulating and performing an incorrect plan (*Table 26*). This was estimated as the costs of performing the initially incorrect treatment plan and changing it subsequently during the intervention minus the costs that would have been incurred in case the appropriate treatment plan had been performed initially. In the cases in which an initially incorrect PTA, bypass or amputation were modified, there were no data available that allowed an estimation of these differential costs; therefore, they were assumed to be zero (since the costs associated with these modifications are likely to be very similar to performing the appropriate plan initially). There was a lack of information about the costs of changing from bypass to medical management, and therefore it was assumed to be equal to the cost of changing from PTA to medical management. This may have led to an underestimation of these costs, since bypass is a more invasive and more expensive procedure than PTA. However, it is expected that the difference would not have a significant impact on the final cost-effectiveness results. In addition, the costs of changing from incorrect amputation to PTA were assumed to be equal to those of changing from incorrect amputation to bypass. In this case, these costs may have been overestimated for the same reason as previously explained, although, as before, this overestimation is not expected to affect relevantly the results of the economic analysis.

The costs per incorrect treatment plan were estimated as the cost average of having incorrect amputation, bypass or PTA weighted by the corresponding probabilities of these events happening.

For example, the costs incurred when an incorrect amputation was formulated after MRA and had to be changed or modified was estimated as follows:

```
cIncAmp_MRA = pIncAmp_Amp_MRA *
cIncAmp_Amp + pIncAmp_Byp_MRA *
cIncAmp_Byp + pIncAmp_PTA_MRA *
cIncAmp_PTA + pIncAmp_MM_MRA *
cIncAmp_MM
```

where cIncAmp_MRA was the additional costs incurred when an incorrect amputation plan was formulated and had to be changed or modified after MRA results, pIncAmp_Amp_MRA, pIncAmp_Byp_MRA, pIncAmp_PTA_MRA and pIncAmp_MM_MRA were the probabilities of having an initially inaccurate amputation plan followed by an appropriate modification to alternative amputation, bypass, PTA or medical management, respectively, after an MRA test result; and cIncAmp_Amp, cIncAmp_Byp, cIncAmp_PTA and cIncAmp_MM were the additional costs incurred when an incorrect amputation plan had to be modified to another amputation, bypass, PTA or medical management.

All costs were adjusted for inflation, using the Pay and Prices Indices for Hospital and Community Health Services (HCHS), in order to reflect 2004 costs in UK sterling pounds (£). Owing to the limited time-horizon of the analysis, 1 year, discounting was not relevant, and as such, has not been conducted.

Costs were obtained from a variety of sources and, where necessary, these have been converted to UK

TABLE 26 *Incremental costs incurred while formulating and performing an incorrect treatment plan*

	Estimated costs (£ 2004)		
	Average	**Range**	**Source**
Amputation			
Modify amputation	0	–	Assumption
Amputation changed to bypass	978.11	820.39–1023.34	Berry, 2002,[660] Michaels, 2000[670]
Amputation changed to PTA	978.11	820.39–1023.34	Assumption (same as for bypass)
Amputation changed to MM	0	–	Assumption
Bypass			
Bypass plan changed to amputation	706.31	592.42–738.98	Assumption (based on Berry, 2002[660] for PTA)
Modify bypass	0	–	
Bypass plan changed to PTA	1177.19	987.37-1231.63	Berry, 2002[660]
Bypass plan changed to MM	0	–	Assumption (i.e. same as for bypass)
PTA			
PTA plan changed to amputation	706.31	592.42–738.98	Berry, 2002[660]
PTA plan changed to bypass	536.66	450.12–561.48	Berry, 2002[660]
Modify PTA	0	–	Assumption
PTA plan changed to MM	245.36	122.68–368.04	Visser, 2003[129]

costs using purchasing power parity (PPP) indices.[674] For example, the costs related to CA complications, the mortality costs associated with the vascular interventions and the extra costs due to planned but not performed PTA were obtained in an aggregate manner and from other settings[129] and were converted into UK cost data using the PPP indices.

Cost-effectiveness analysis

Incremental analysis of costs and consequences

To compare the costs and consequences of the alternative diagnostic imaging techniques, cost-effectiveness ratios (CERs) were estimated as the cost per unit of health benefit gained in the economic analysis. In the short-term model, the CER was estimated as the cost per correctly diagnosed patient for whom an accurate treatment plan was formulated (CDPwATP). In the long-term model, the CER was calculated as the cost per QALY gained.

Those strategies with lower effectiveness and higher costs (i.e. dominated strategies) were eliminated from the analysis, and incremental cost-effectiveness ratios (ICERs) were estimated for the remaining strategies as the incremental cost per correctly diagnosed patient for whom an accurate treatment plan was formulated in the case of the short-term model, and as the incremental cost per QALY gained in the case of the long-term model, when two alternative diagnostic imaging techniques were compared.

Dealing with uncertainty

A probabilistic sensitivity analysis (PSA) was performed to incorporate statistical uncertainty into the cost-effectiveness analysis. This allowed assessment of the effect of varying simultaneously different variables on the study results (on both costs and consequences). Appropriate parameter distributions were chosen, according to the nature of the variables, for those input parameters for which suitable data were available. Beta distributions were generally used for the probability parameters where only two categories of events were possible (i.e. test result showing 50–100% degree of stenosis versus 0–49%; management plan incorrect versus correct, etc.). For those input parameters presenting more than two categories of events, a Dirichlet distribution was used in order to account for the polychotomous nature of the variable. A Dirichlet distribution was applied for the following types of events:

- After a 50–100% degree of stenosis was detected with the test, there were three possible events: amputation, bypass or PTA.
- An incorrectly formulated treatment plan could end in amputation, bypass, PTA or medical management.

Some of these events had a zero probability according to the data retrieved from the studies reporting information about the formulation of the treatment plans after the diagnostic test results (see *Tables 16* and *17*). For example, the observed probability of changing from an initially

formulated incorrect bypass to amputation was zero for all the tests considered at analysis. However, the fact that some of the events were not observed in these trials does not mean that they cannot occur in clinical practice. A Bayesian approach was adopted in order to overcome the problem of zero counts encountered for some of the probabilities within the multivariate distributions. Following the method proposed by Briggs,[675] an uninformative prior distribution was specified by assuming it as uniform (i.e. all the possible events had the same probability of happening). This prior distribution was combined with the observed counts to obtain the posterior Dirichlet distribution for these model parameters. However, the number of observed counts in the retrieved studies was very low and consequently there was concern that a prior uniform distribution combined with the observed counts could considerably bias the likelihood of events happening, weighting the probabilities in favour of those events less likely to happen. To ensure that the observed data dominated the prior distribution, the observed counts were multiplied by 1000, therefore making the probabilities of those events non-observed in the clinical trials very low, but still possible. Further analyses were performed to assess the impact of using this adjustment: in sensitivity analyses the observed counts were multiplied by 100 and by 10.

The probabilistic distributions assigned to the event 'formulation of an incorrect amputation after DUS', and all subsequent events associated with changes of initial incorrectly formulated amputation after DUS, were assumed to be the same as those observed after MRA, to overcome the problem of observing zero counts. This was based on the fact that DUS presented a distribution of observed counts more similar to that presented by MRA than that of CA.

Given the type of data available for the cost parameters (i.e. means and ranges), it was necessary to assume that the lower and upper values of the ranges were those corresponding to the interquartile ranges.[676] After assuming a normal distribution for these parameters, the standard errors of the costs were estimated. To ensure that the cost results simulated could not become negative, a gamma distribution was fitted using the method of moments approach.

No information about the covariance structure that correlates parameters was available. Therefore, it had to be assumed that the parameters varied independently.

The distributions assigned to the parameters used in the baseline PSA for the 1-year time horizon model have been reported in Appendix 8.

Cost-effectiveness acceptability curves (CEACs) were used to summarise uncertainty. CEACs assess what the chance is for each alternative diagnostic test to be cost-effective according to the willingness to pay per unit of health benefit obtained (in the long-term model, per QALY, and in the short-term model, per CDPwATP). Reporting of incremental results by means of CEACs overcomes the problem of interpreting confidence intervals for ICERs when these are negative.[677]

The accuracy of the tests for above-the-knee and below-the-knee comparisons, separately, considering a threshold of 50–100% stenosis, was assessed in the sensitivity analysis. Only one included study evaluated the results for the above-the-knee diagnosis with 2D TOF MRA, two included studies assessed CE MRA, and seven studies assessed DUS. For the below-the-knee comparisons, only one study assessed the results with 2D TOF MRA, three studies assessed CE MRA and four assessed DUS. To perform the simulation, it had to be assumed that the distribution of the parameters after the results of the diagnostic tests would be the same independently of whether the whole leg or only a section of the leg was assessed. For those parameters obtained from a unique study, a probabilistic distribution was not assigned and, therefore, they were left as deterministic.

Results from the probabilistic cost-effectiveness analysis

Short-term model

The results for the baseline short-term model (*Table 27*) show that 2D TOF MRA was the least effective and least costly strategy, achieving a correct diagnosis followed by an accurate formulated treatment plan in 88.9% of the cases, at a cost of £492 per CDPwATP. CE MRA and DUS were more effective and more costly than 2D TOF MRA, both obtaining 96.2% of CDPwATP at a cost of £697 and £657 per CDPwATP, respectively. CE MRA was found to be dominated by DUS since it obtained the same effectiveness but at a higher average cost per diagnosed patient. The most effective strategy, but also the most expensive, was CA, with 97.8% of CDPwATP, at a cost of £2558 per CDPwATP.

TABLE 27 *Baseline cost-effectiveness results for the short-term model*

		Mean	SD	Minimum	Median	Maximum
2D TOF MRA	Cost (£ 2004)	492	16	444	492	544
	CDPwATP	0.889	0.014	0.839	0.89	0.922
	CER	554	24	492	552	647
CE MRA	Cost (£ 2004)	697	56	564	689	923
	CDPwATP	0.962	0.007	0.933	0.962	0.979
	CER	725	59	589	717	968
DUS	Cost (£ 2004)	657	138	371	639	1,250
	CDPwATP	0.962	0.008	0.926	0.963	0.979
	CER	682	144	387	665	1,300
CA	Cost (£ 2004)	2,558	628	1,271	2,494	5,196
	CDPwATP	0.978	0.008	0.944	0.979	0.996
	CER	2,617	644	1,308	2,544	5,271

TABLE 28 *Baseline incremental cost-effectiveness results (short-term model)*

Strategy	Cost	Incremental cost	Effectiveness	Incremental effectiveness	C/E	Incremental C/E (ICER)
2D TOF MRA	492.0264	–	0.889271	–	553.2918	–
DUS	656.5048	164.4785	0.962042	0.072771	682.4077	2,260.223
CE MRA	696.8975	40.39268	0.961704	–0.00034	724.6486	Dominated
CA	2,557.801	1901.296	0.977604	0.015563	2616.396	122,171.4

The results of the incremental analysis are shown in *Table 28*. The results show that the incremental cost incurred by DUS to obtain an additional CDPwATP was £2260, compared with 2D TOF MRA. Whereas every additional CDPwATP obtained with CA compared with DUS incurred an additional cost of £122,171, which would appear to be an excessive cost if compared with the implicit ICER threshold used by the National Institute for Health and Clinical Excellence (NICE) to approve pharmaceutical products.[678]

The cost-effectiveness plane for the above results is presented in *Figure 20*.

The uncertainty captured in the PSA can be seen visually in the scatterplot (*Figure 21*). It is clear that in terms of costs, CA (top right cloud) has a wide dispersion of points, compared with 2D TOF MRA (bottom left cloud), which presents a high dispersion in terms of effectiveness, but shows more tightly clustered results in terms of costs. The similarities presented by DUS and CE MRA (bottom right clouds) in terms of costs and effectiveness can be observed from the plot, although DUS tends to be have a more highly concentrated scattering of points in a slightly lower cost band, and therefore it would appear to dominate CE MRA.

A CEAC represents the probability that a health technology falls in the right section of the cost-effectiveness plane,[677] which means that, when compared with another health technology, it achieves higher effectiveness (at higher, the same or at lower cost). The interpretation of the CEACs has been performed according to that presented by Fenwick and colleagues,[679] which described the CEACs as a graphic transformation of the cost-effectiveness plane, representing the joint densities of the incremental costs and effects.

According to this interpretation, DUS in some cases results in cost-savings as the curve does not cut the *y*-axis at zero. However, health gains are not obtained through all of its density since the curve does not asymptote to 1. A similar situation is found for the CEAC of CE MRA, although the health gains obtained are lower than with DUS. The fact that the CEAC for DUS is the curve that most closely approaches 1 when the willingness-to-pay threshold increases indicates that DUS is the alternative that most frequently shows health benefits through its density (even if it does not always achieve health benefits) (*Figure 22*).

The CEAC for 2D TOF MRA also shows some cost-savings, although not always health gains (again, since the curve does not asymptote to 1).

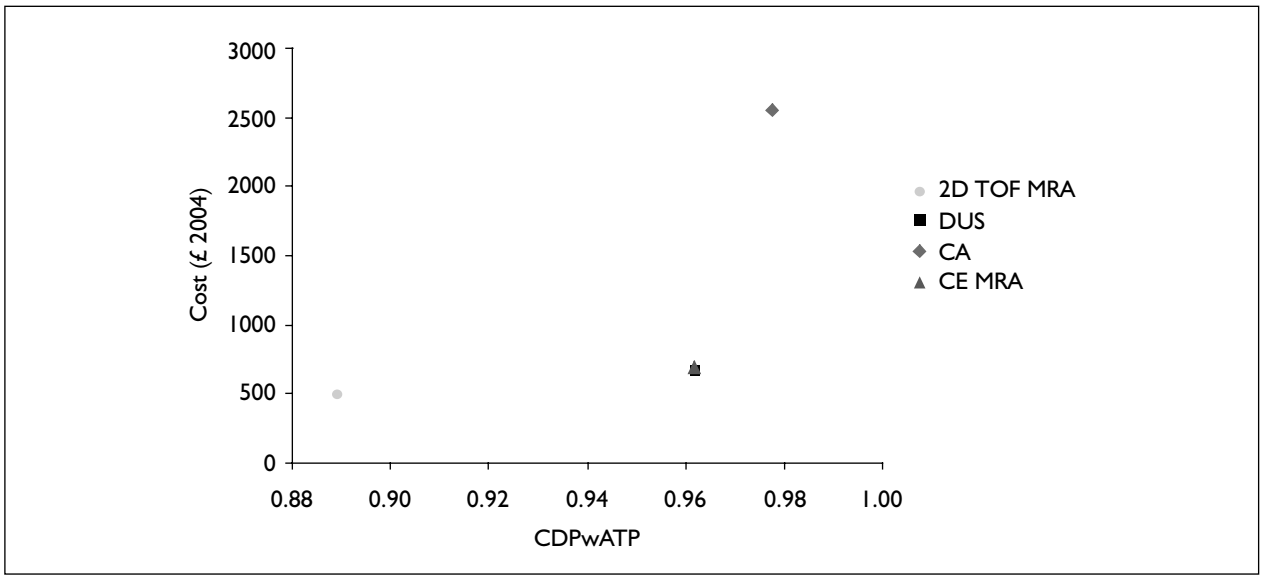


FIGURE 20 *Cost-effectiveness plane for baseline analysis (short-term model)*

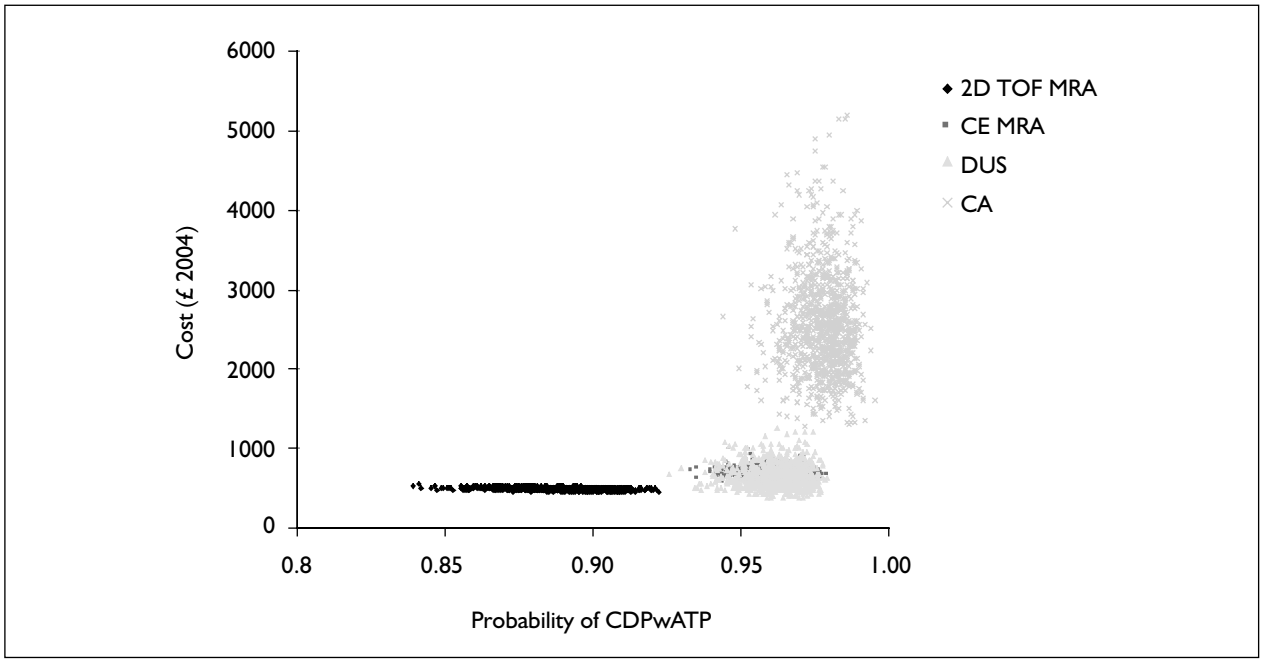


FIGURE 21 *Scatter plot for PSA (baseline short-term model)*

CA is the more costly alternative and, in addition, it shows lower effectiveness. This is displayed by the fact that its CEAC does not cut the *y*-axis at 0 and asymptotes to a value higher than 0 but much lower than 1 (indicating the existence of health benefits, but not throughout its density).

Long-term model

The results of the baseline analysis for the 1-year time-horizon model are reported in *Table 29*. It can be observed from the results that DUS and CA are the diagnostic procedures associated with the highest health benefit, obtaining 0.64 QALYs for the 1-year period considered. CE MRA achieves an insignificantly lower number of QALYs for the first year (0.639), while 2D TOF MRA is the diagnostic procedure with the lowest health benefits (0.61 QALYs). In terms of costs, DUS was the diagnostic procedure with the lowest costs. Since DUS presented the highest effectiveness at the lowest cost, it was the dominant strategy for the baseline analysis. Consequently, an incremental cost-effectiveness analysis was not performed for the baseline analysis of the 1-year

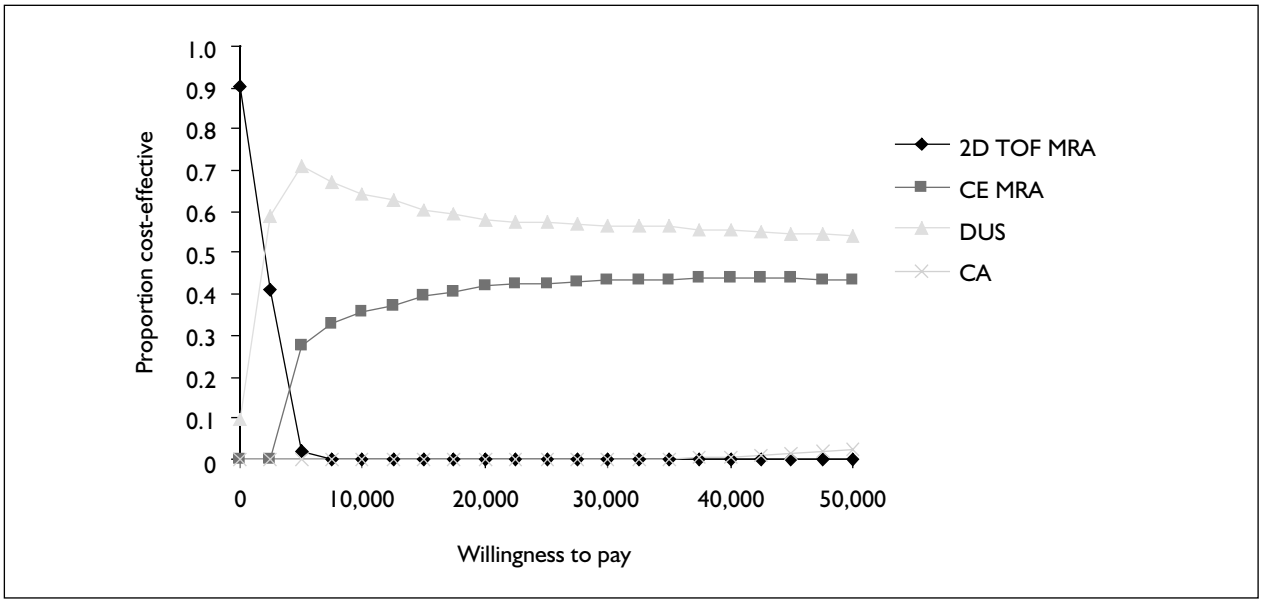


FIGURE 22 *CEACs of the alternative diagnostic preoperative tests for baseline short-term model. CEAC of 2D TOF MRA, CE MRA and DUS versus CA. The lines give the probability that the relevant strategy is cost-effective for a given willingness to pay per CDPwATP.*

TABLE 29 *Baseline cost-effectiveness results for 1-year time-horizon model*

		Mean	SD	Minimum	Median	Maximum
2D TOF MRA	Cost (£ 2004)	10,688	1,096	8,159.66	10,590.96	15,657.72
	QALYs	0.61	0.002	0.603	0.609	0.613
	CER	17,549	1,802	13,339	17,427	25,722
CE MRA	Cost (£ 2004)	9,092	1,119	6,599	9,005	14,088
	QALYs	0.639	0.001	0.635	0.639	0.642
	CER	14,222	1,752	10,302	14,093	22,051
DUS	Cost (£ 2004)	8,734	1,138	6,275	8,639	13,820
	QALYs	0.64	0.002	0.632	0.64	0.644
	CER	13,646	1,782	9,764	13,490	21,617
CA	Cost (£ 2004)	11,509	1,409	8,232	11,385	17,732
	QALYs	0.64	0.001	0.635	0.64	0.642
	CER	17,990	2,205	12,854	17,784	27,678

time-horizon model as all the other strategies considered were dominated. The baseline results are presented in *Table 29*. The findings show that the cost incurred with DUS to obtain one QALY was £13,646.

Figure 23 presents the cost-effectiveness plane for the above results. In addition, the cumulative probabilities for the distributions of costs, health benefits (i.e. QALYs) and cost-effectiveness ratios (with their corresponding 10/50/90 percentiles) are reported in Appendix 9.

The scatterplot represented in *Figure 24* shows the dispersion regarding cost-effectiveness estimators for the different samples drawn from the PSA. CA (top right cloud) presents the widest dispersion in costs, being the health benefits at 1 year around 0.64 QALYs. The health benefits for DUS (bottom right cloud) are similar to those of CA (top right cloud), although the costs are at a lower level. 2D TOF MRA (top left cloud) is associated with the lowest effectiveness for all sampling. The position of the sampling clouds shows that DUS (bottom right cloud) appears to dominate the other strategies.

The CEACs for the baseline long-term model show that the densities of DUS and CE MRA involve cost-savings at some points (since the curves do not cut the *y*-axis at 0) and also health benefits (although not for their entire densities

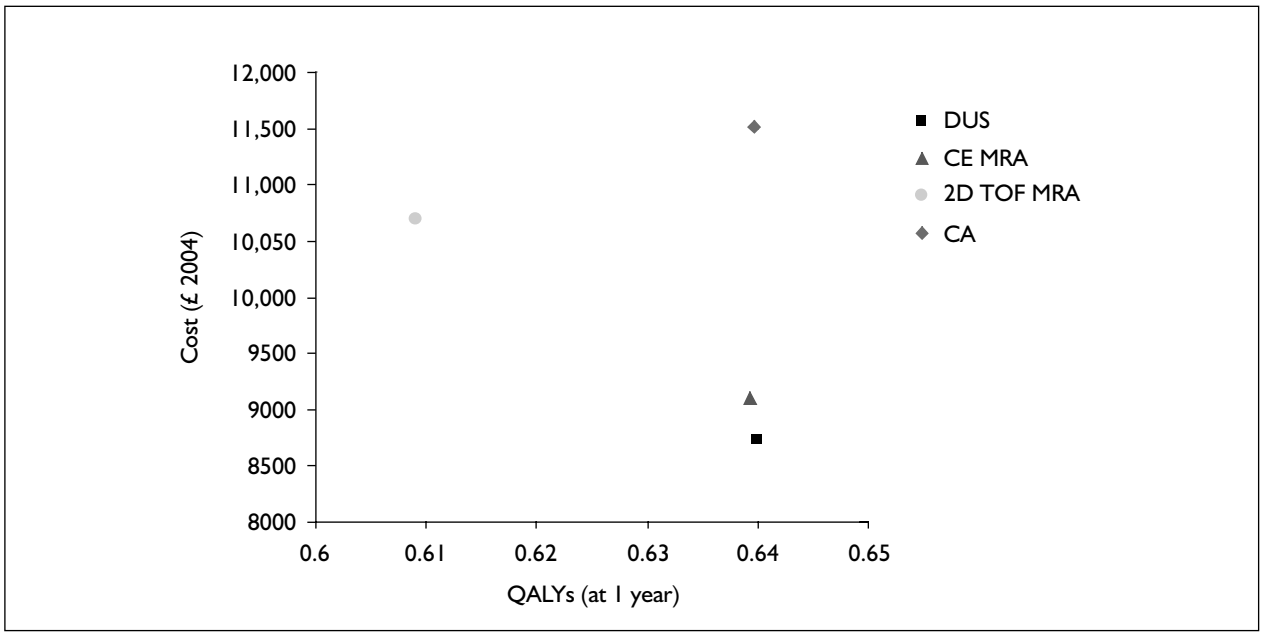


FIGURE 23 *Cost-effectiveness plane for baseline analysis (1-year time-horizon model)*

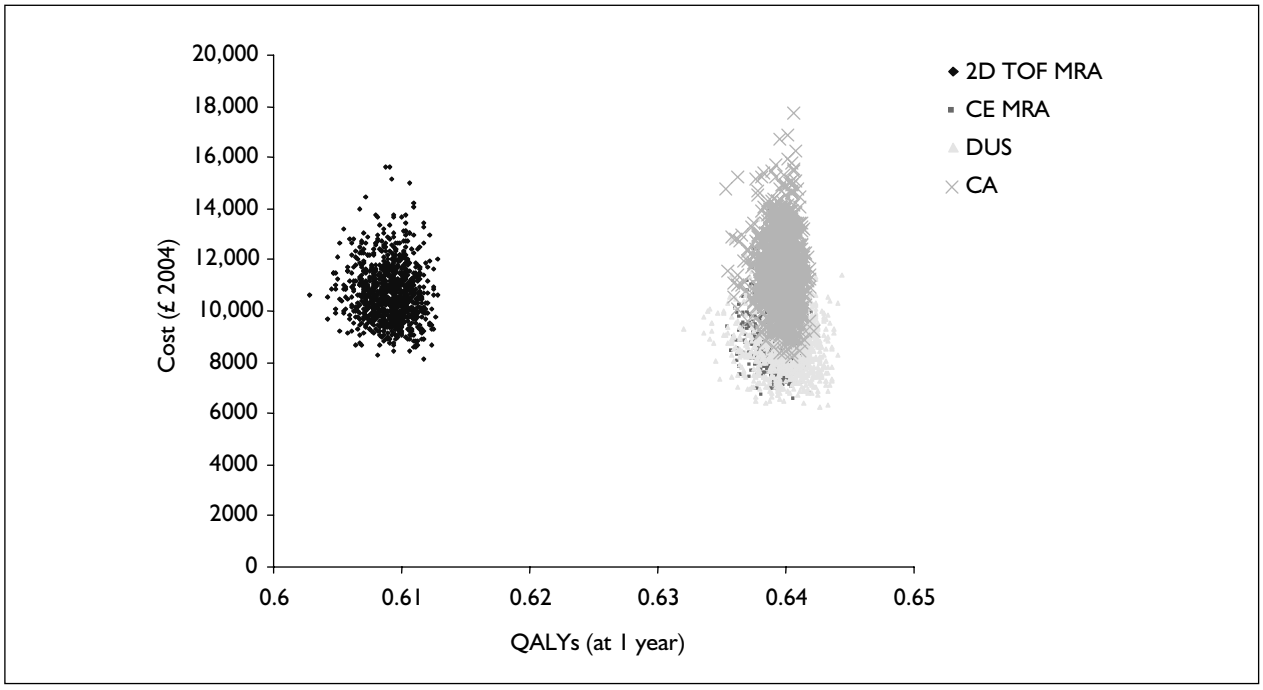


FIGURE 24 *Scatterplot for PSA (baseline 1-year time-horizon model)*

since the curves asymptote to a value lower than 1). Both 2D TOF MRA and CA CEACs show that cost-savings are not obtained at any point of their density curves, since they cut the *y*-axis at 0. Moreover, they have the lowest effectiveness since none of their densities appears to involve health gains compared with the other preoperative diagnostic imaging tests. This is reflected by the fact that the curves for both 2D TOF MRA and CA lie on the *x*-axis. Therefore, 2D TOF MRA and CA are clearly dominated, as shown in *Figure 25*.

Change of assumption: endarterectomy considered as a PTA procedure

When endarterectomy was included as a PTA procedure, the impact on the cost-effectiveness

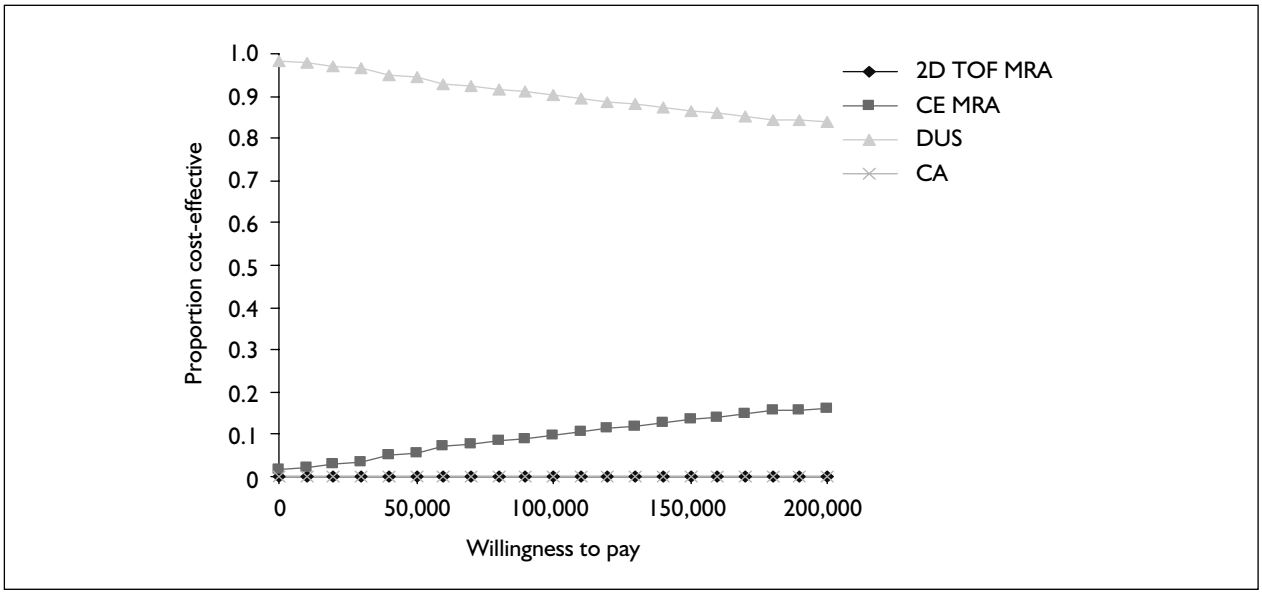


FIGURE 25 *CEACs of the alternative diagnostic preoperative tests for baseline 1-year time-horizon model*

results was negligible. As this change of assumption had minimal impact on the results obtained all results of this analysis are presented in Appendix 10.

Impact of adjustments in Dirichlet distributions

The adjustments performed to the Dirichlet distributions to ensure that the observed data dominated the prior distribution appeared to have a negligible impact on the cost-effectiveness results obtained. The results obtained corresponding to the adjustment of the observed data by multiplying it by 10 are reported in Appendix 11. (For the baseline analysis data were adjusted by multiplying the observed data by 1000.) It can be observed from the simulation results that, overall, there was a very slight increase in the average costs for 2D TOF MRA, CE MRA and DUS, with the same or slightly lower effectiveness results. DUS continued as the dominant strategy, presenting the highest health benefits and the lowest costs.

This is an expected result as the probabilities assigned to those non-observed events by means of the adjustments in the Dirichlet distributions were very low. The adjustments, therefore, allowed us to assign probabilistic distributions to some relevant effectiveness parameters without affecting the cost-effectiveness results.

Above-the-knee comparison

When the accuracy of the tests was considered to assess their cost-effectiveness for stenoses above the knee, the results were considerably different from those obtained in the baseline analysis. As can be observed from *Table 30*, there was a reduction in the average cost per patient undergoing either 2D TOF MRA or CE MRA, in addition to a slight increase in the effectiveness in terms of the number of QALYs obtained during the first year after initial treatment. This led to a reduction in the cost-effectiveness ratios associated with 2D TOF MRA and CE MRA (which became £8628 and £8761 per QALY gained, respectively). In contrast, the average costs related to DUS increased, while there was a slight reduction in the number of QALYs gained after performing this diagnostic test. DUS became more expensive and less effective compared with 2D TOF MRA and CE MRA, and therefore it became a dominated strategy. In this analysis, as previously, CA maintained its condition as a dominated strategy, as it was found to be more expensive and of slightly lower effectiveness than either 2D TOF MRA or CE MRA.

MRA became the preferred strategy when the accuracy of the tests was assessed for stenoses above the knee. As shown in *Table 31*, 2D TOF MRA obtained a slightly lower level of effectiveness compared with CE MRA, although the incremental costs incurred with CE MRA, compared with 2D TOF MRA, in order to gain an additional QALY were very high (i.e. £122,687 per additional QALY gained). Therefore, when above-the-knee comparisons were considered as the unit of diagnosis for PAD patients, the preoperative

TABLE 30 *Cost-effectiveness results for above-the-knee comparisons (1-year time-horizon model)*

		Mean	SD	Minimum	Median	Maximum
2D TOF MRA	Cost (£ 2004)	8,628	1,130	6,175	8,489	14,581
	QALYs	0.642	0.001	0.639	0.642	0.643
	CER	13,442	1,761	9,632	13,224	22,701
CE MRA	Cost (£ 2004)	8,761	1,139	6,238	8,637	14,624
	QALYs	0.643	0.002	0.637	0.643	0.649
	CER	13,627	1,777	9,674	13,432	22,666
DUS	Cost (£ 2004)	9,104	1,143	6,485	8,969	15,056
	QALYs	0.631	0.003	0.622	0.631	0.637
	CER	14,424	1,816	10,264	14,188	23,712
CA	Cost (£ 2004)	11,454	1,414	8,188	11,330	18,350
	QALYs	0.64	0.001	0.633	0.64	0.644
	CER	17,889	2,211	12,849	17,702	28,772

TABLE 31 *Incremental cost-effectiveness results for above-the-knee comparisons (1-year time-horizon model)*

Strategy	Cost	Incremental cost	Effectiveness	Incremental effectiveness	C/E	Incremental C/E (ICER)
2D TOF MRA	8,628.311	–	0.641904	–	13,441.76	–
CE MRA	8,761.333	133.0225	0.642988	0.001084	13,625.97	122,686.7
DUS	9,103.687	342.3536	0.631169	–0.01182	14,423.52	Dominated
CA	11,454.18	2692.847	0.640283	–0.0027	17,889.24	Dominated

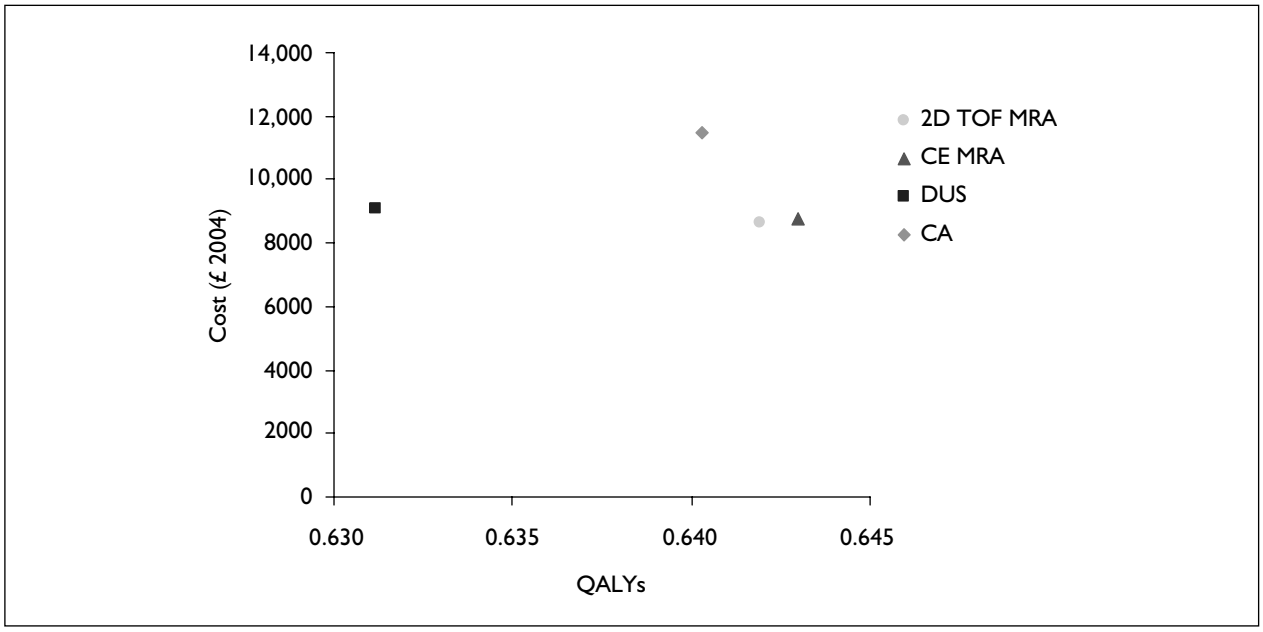


FIGURE 26 *Cost-effectiveness plane for above-the-knee comparisons (1-year time-horizon model)*

diagnostic strategy that appeared to be more cost-effective was 2D TOF MRA (with a cost per QALY equal to £8628).

The cost-effectiveness plane for the above results is presented in *Figure 26*.

The scatterplot represented in *Figure 27* shows that when above-the-knee comparisons are considered as the basis of analysis, the differences in the overall sampling of the alternative strategies appeared less clearly defined for 2D TOF MRA, CE MRA and CA, since all points are dispersed in

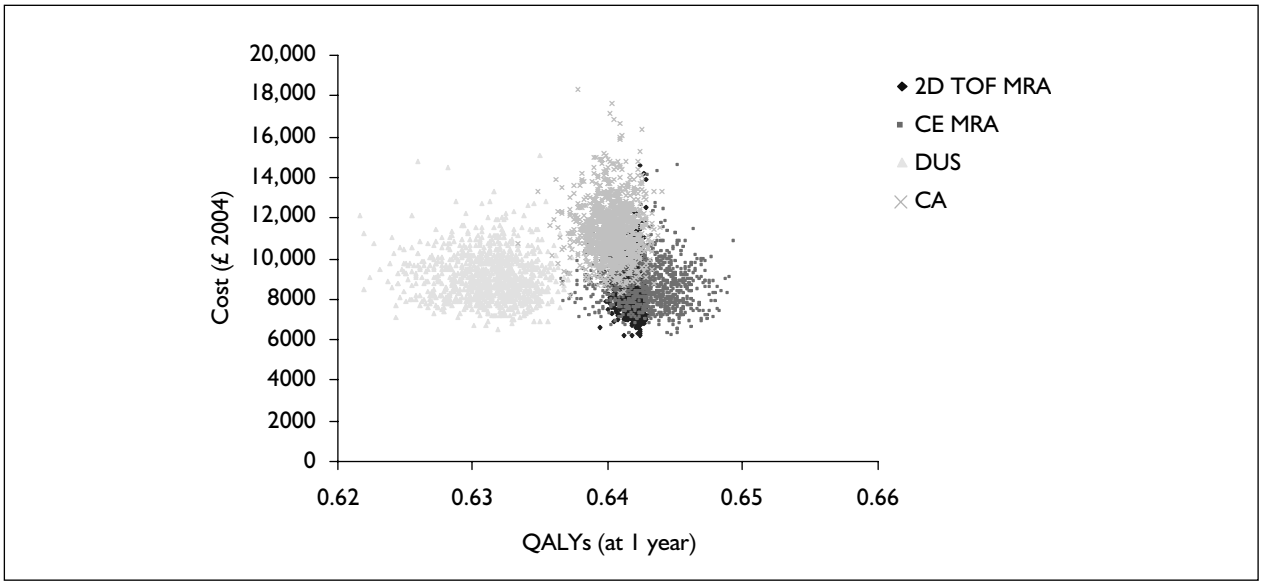


FIGURE 27 *Scatterplot for PSA for above-the-knee comparisons (1-year time-horizon model)*

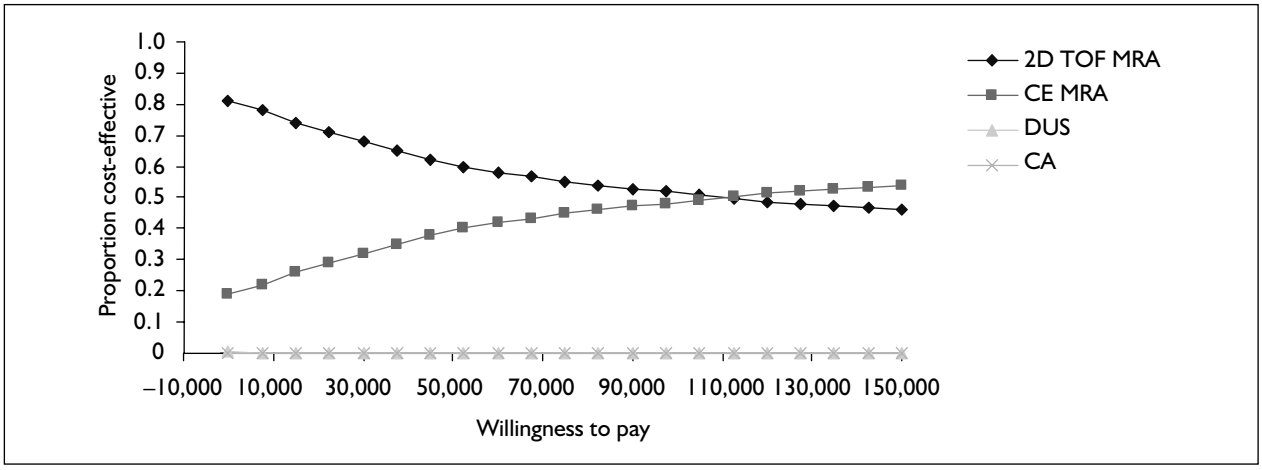


FIGURE 28 *CEACs of the alternative diagnostic preoperative tests for above-the-knee comparisons (1-year time-horizon model)*

a concentrated, more specific area of the scatterplot for these diagnostic strategies. DUS is shown to be the diagnostic strategy with a more differentiated sampling compared with the others. The CEAC for the above-the-knee comparison is shown in *Figure 28*.

Below-the-knee comparisons

According to the data retrieved for below-the-knee comparisons, the results of the economic analysis show an increase in the average costs for CE MRA, DUS and CA. The overall health benefits obtained were lower in comparison with the health benefits observed in the analysis assessing comparisons for the whole leg (baseline analysis).

As in the baseline analysis, DUS presented the lowest costs among the diagnostic imaging strategies considered (£10,260 per patient), although these were higher than those obtained from the baseline analysis (i.e. £8734) (*Table 32*). CE MRA was dominated by DUS and 2D TOF MRA since it achieved lower health benefits at a higher cost per patient (i.e. 0.606 QALYs at 1 year at a cost of £10,798 per patient), and therefore it was excluded from the incremental cost-effectiveness analysis (*Table 33*).

The incremental cost incurred with 2D TOF MRA to obtain an additional QALY, compared with DUS, was equal to £37,024. However, since the difference in health benefits between CA and 2D TOF MRA was very low, each additional QALY obtained with CA, compared with 2D TOF MRA, implied an additional cost of £4,928,686. According to these results,

TABLE 32 *Cost-effectiveness results for below-the-knee comparisons (1-year time-horizon model)*

		Mean	SD	Minimum	Median	Maximum
2D TOF MRA	Cost (£ 2004)	10,570	1,139	7,720	10,427	15,084
	QALYs	0.616	0.001	0.61	0.616	0.618
	CER	17,154	1,850	12,537	16,917	24,551
CE MRA	Cost (£ 2004)	10,798	1,136	7,689	10,659	15,286
	QALYs	0.606	0.002	0.596	0.606	0.614
	CER	17,833	1,888	12,672	17,612	25,406
DUS	Cost (£ 2004)	10,260	1,148	7,267	10,119	14,762
	QALYs	0.608	0.004	0.593	0.608	0.618
	CER	16,882	1,903	11,943	16,678	24,164
CA	Cost (£ 2004)	12,913	1,400	9,073	12,824	17,647
	QALYs	0.617	0.002	0.606	0.617	0.622
	CER	20,942	2,277	14,657	20,796	28,770

TABLE 33 *Incremental cost-effectiveness results for below-the-knee comparisons (1-year time-horizon model)*

Strategy	Cost	Incremental cost	Effectiveness	Incremental effectiveness	C/E	Incremental C/E (ICER)
DUS	10,259.65	–	0.607802	–	16,879.92	–
2D TOF MRA	10,569.59	309.9456	0.616173	0.008371	17,153.6	37,024.29
CE MRA	10,798.4	228.8103	0.605562	–0.01061	17,832.05	Dominated
CA	12,913.43	2343.836	0.616649	0.000476	20,941.3	4,928,686

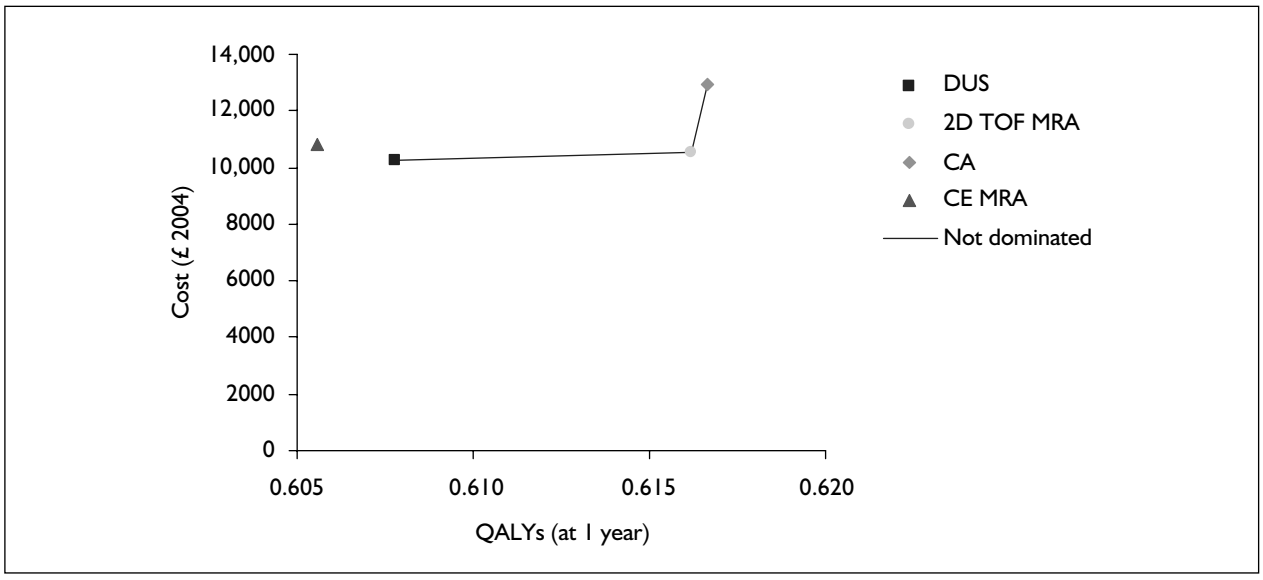


FIGURE 29 *Cost-effectiveness plane for below-the-knee comparisons (1-year time-horizon model)*

2D TOF MRA appears to be a cost-effective preoperative diagnostic strategy when below-the-knee comparisons are considered as the basis for the analysis.

The cost-effectiveness plane for the above results is presented in *Figure 29*.

In a similar manner to the findings obtained when comparisons above the knee were considered, the scatterplot presented in *Figure 30* shows that for below-the-knee comparisons the differences in the overall sampling of the alternative strategies appear to be less clearly defined. Again, dispersion is concentrated around a specific area

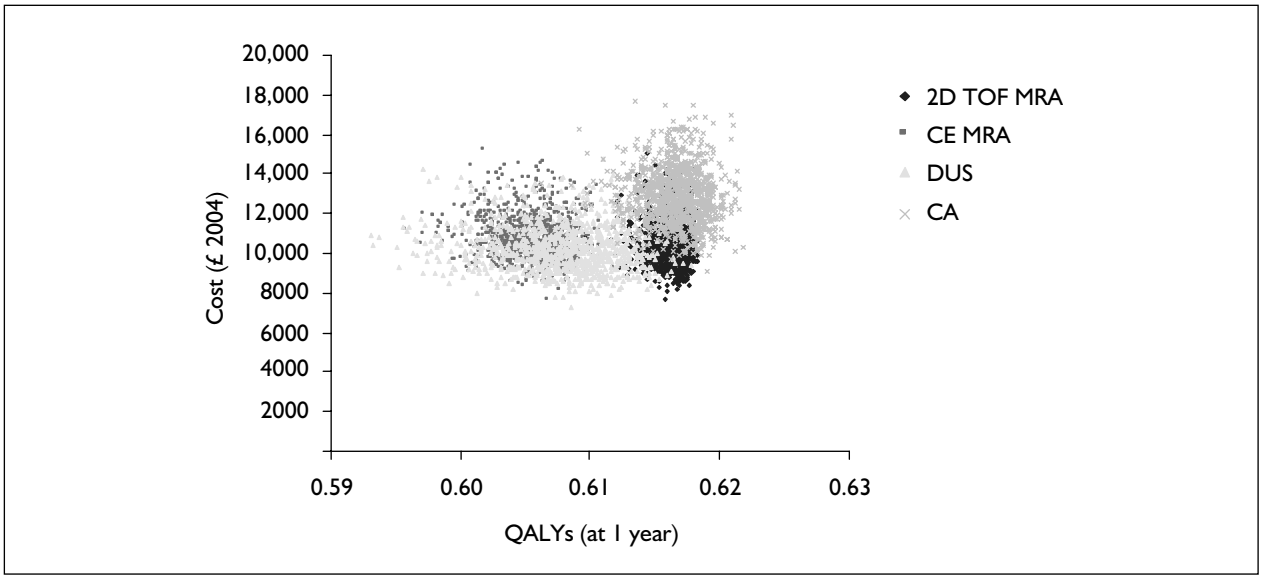


FIGURE 30 *Scatterplot for PSA for below-the-knee comparisons (1-year time-horizon model)*

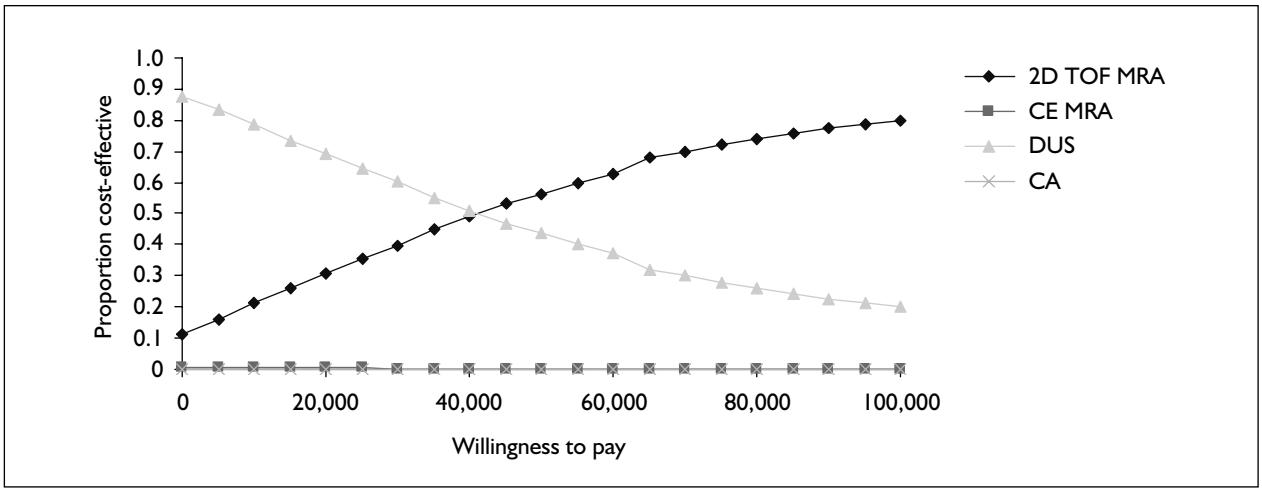


FIGURE 31 *CEACs of the alternative diagnostic preoperative tests for below-the-knee comparisons (1-year time-horizon model)*

of the scatterplot, although differences in effectiveness and costs are still easily observed. DUS is the diagnostic strategy presenting highest dispersion, but given the wider standard deviations related to its average costs and health benefits (see *Table 32*) this was an expected result.

The graph represented in *Figure 31* shows the CEACs obtained from the analysis of the alternative diagnostic preoperative tests at 1 year, considering below-the-knee comparisons. It can be observed that when the values for the willingness to pay are low, DUS is the strategy with greatest probability of being cost-effective, which may be due to the fact that it is the imaging strategy with the lowest costs for below-the-knee comparisons. However, since 2D TOF MRA shows a slightly higher effectiveness at a lower cost, compared with DUS, the probability of 2D TOF MRA being the cost-effective imaging strategy increases at higher values for the willingness to pay.

Chapter 8
Discussion

This chapter is divided into two main sections, the first covering methodological issues associated with the literature review and economic modelling and the second covering the findings of the review and modelling.

Methodology

Review methodology

Extensive literature searches were conducted in an attempt to locate all relevant studies. These included electronic searches of a variety of resources, scanning the references of included studies, contacting experts in the field and handsearching. The search strategy was developed to maximise sensitivity, at the expense of reducing specificity. Therefore, large numbers of citations were identified and screened, many of which did not meet the inclusion criteria for the review. However, owing to deficiencies in specific indexing terms for diagnostic accuracy studies, it was felt that a more sensitive search strategy was necessary.[680]

The possibility of publication bias remains a potential problem for all systematic reviews. The extent to which publication bias is an issue for diagnostic studies remains unclear. For intervention studies there is a clear cut-off defining a 'positive result'; that is, whether there is a significant difference in outcome between the treatment and control groups, and whether this difference favours the intervention. This is not the case for studies of diagnostic accuracy, which are essentially a measure of agreement between the results of the index test and a reference standard. It is possible, and indeed likely, that studies reporting higher estimates of test performance will more often be published, but the extent to which this occurs is unclear. Similarly, it is possible that tests will not perform as well in the clinical setting as may be indicated by reports from research studies. There is evidence that publication bias is a particular problem for studies with a small sample size, although these data are not specific to the diagnostic literature.[681,682] This review was restricted to studies that included at least 20 patients, meaning that this type of publication bias is less likely to be a problem.

Clear inclusion criteria were set out in the protocol for this review. It is therefore explicit exactly which studies were eligible for inclusion. A list of studies has been provided that appeared initially relevant, but which did not meet all of the inclusion criteria for the review.

All studies contributing results to the section of the review relating to diagnostic accuracy were assessed for methodological quality using QUADAS. Individual components of methodological quality, specific to diagnostic accuracy studies, could therefore be assessed using criteria developed by an evidence-based method.[683] However, where studies are poorly reported the information that may be derived from quality assessment becomes limited. It cannot be known whether an unreported QUADAS item reflects a true methodological flaw or poor reporting of a study that may be methodologically sound. It should also be noted that the QUADAS tool does not contain any criteria to assess the impact of inter-observer variability. Since the interpretation of imaging studies is inherently subjective, the impact of characteristics of the observers (e.g. training, experience) upon measures of accuracy is likely to be of particular interest. The Standards for Reporting of Diagnostic Accuracy (STARD) initiative has recommended reporting of observer characteristics, but very little evidence was found of reporting of such information by the studies included in this review. While poor reporting remains a widespread problem, it is almost impossible to assess the impact of components of methodological quality on the results of systematic reviews of diagnostic tests. The STARD initiative has provided clear guidance for the reporting of diagnostic accuracy studies[684,685] and its uptake should improve all aspects of the evaluation of diagnostic accuracy. The full results of the quality assessment using the QUADAS tool were tabulated and a narrative summary was presented.

The methodological quality of studies with other study designs was assessed using the appropriate checklist from the CRD guidelines for undertaking systematic reviews,[13] and a narrative summary of study quality was presented.

The processes of study selection, data extraction and quality assessment were carried out by one reviewer and checked by a second, with disagreements resolved by consensus or referred to a third reviewer when necessary. This reduces the potential for reviewer error or bias.

Sensitivity, specificity and likelihood ratios were used to summarise estimates of test performance. Ranges in sensitivity and specificity were reported and results of individual studies plotted in ROC space. ROC plots provide an easy to interpret visual summary of all the studies included in a review. They enable the reader quickly to assess the variability between studies, the accuracy of the test and whether there appears to be a threshold effect, without the potentially misleading effect of pooling using an sROC where there is significant unexplained statistical heterogeneity between study results. SROC curves were only presented where there was no evidence of significant heterogeneity. Likelihood ratios were also presented, as it has been suggested that these are the measure that physicians find easiest to interpret.[686] Pooled likelihood ratios were not calculated, for the majority of data groupings, owing to the presence of statistically significant heterogeneity; instead, the median values and ranges were presented. A general problem with pooled likelihood ratios as summary measures is that positive and negative likelihood ratios are pooled individually. These measures are likely to be correlated within an individual study and ignoring this correlation may be problematic. This is an area of current research in the methodology of diagnostic meta-analysis.

Further analyses using regression methods to investigate reasons for the observed heterogeneity were not performed. As results for more than one stenosis threshold and arterial segment were reported by some studies, these studies provided multiple sets of diagnostic accuracy results for the same patients. The standard sROC regression analysis is used to investigate the effects of differing cut-off thresholds, study quality and other study-level factors on the DOR. To perform an sROC analysis would require the pooling of only one data set from each study, reducing the number of studies available for analysis and potentially introducing bias by the choice of data sets to include. Therefore, the reviewers chose not to perform multiple regression modelling to investigate QUADAS components as they were restricted by the small numbers of similar data sets considered for pooling; it is recommended that at least ten outcomes are needed for each factor in the model.[687] Further research into statistical methods accounting for multiple sets of accuracy results within a study is ongoing, but these methods are complex and have not yet been fully evaluated in practice.[688,689]

A further consideration in this review was the way the results were reported, as studies reported results by arterial segment, artery, limb or area of stenosis/occlusion. The majority of studies reported results using arterial segment as the unit of analysis and, for consistency, only segmental results were considered for pooling. The 'clustering' of analysis units is a common feature of diagnostic accuracy studies, for example arteries within a patient, or segments within an artery. This means that there is likely to be correlation between results within each patient and this should be accounted for in any statistical analyses. However, estimates of sensitivity, specificity and likelihood ratios are not affected by this issue; it is the calculation of their variance that needs to take into account the clustering.[661] This means that the estimates of diagnostic accuracy in this review are likely to be accurate, but their 95% confidence intervals may be too narrow because they have ignored the multiple segments within each patient. This is less of a concern for systematic reviews such as this one, where all data sets are reported individually and pooling and statistical comparisons are limited. However, it should be considered where primary diagnostic accuracy studies or meta-analyses make statistical comparisons between diagnostic accuracy parameters for two or more diagnostic methods.

Modelling methodology

The economic model developed aimed to assess the relative cost-effectiveness of MRA, DUS and CTA when compared with CA (which was considered to be the gold-standard preoperative diagnostic test) for the assessment and treatment planning of PAD patients. It was developed keeping in mind the intrinsic properties of good decision-analytical models identified by the Consensus Conference on Guidelines on Economic Modelling in Health Technology Assessment.[690]

A detailed reporting of the sources, the methods used to perform the economic evaluation and the assumptions formulated has been presented to ensure the transparency of the analysis and enhance the interpretability and the applicability of the study results, and to allow ready reproducibility of the analysis.

Modelling guidelines suggest that all relevant comparators should be included in the model, independently of whether or not they represent currently accepted clinical practice.[691] However, in this case a lack of data led to the exclusion of one relevant comparator, CTA. The authors acknowledge that this may have an effect on the results obtained. However, the inclusion of CTA was not viable given that no data were available to populate the model for this diagnostic test. The only alternative available was to use expert opinion to obtain efficacy estimates; this was deemed unrealistic by the clinical experts.

The structure of the decision model was based on a previously published model,[660] which was enhanced to allow clinical practice to be better represented. As with any decision model the structure is a simplification of reality, the main purpose of which is to synthesise different types of data to inform resource allocation. A problem inherent to modelling studies in general is that it is often necessary to oversimplify the structure. PAD is a very complex disease and this model structure, like any other, has limitations compared with clinical reality.

Guidelines on economic modelling in health technology assessment suggest that the time-horizon considered for the model should be long enough to incorporate all the relevant cost and benefit differences between the alternatives compared.[691,692] Data were not available about the prognosis of patients on a long-term basis according to whether they underwent a treatment that had initially been accurately or inaccurately formulated, and how this may affect their quality of life. Therefore, the time-horizon of the study was limited to 1 year.

For this analysis, treatments postdiagnosis have been considered as chance nodes, determined by the clinician's choice of appropriate treatment. This was done to reflect clinical practice, since the treatment path to be followed will actually depend on the choice of the surgeon according to his interpretation of the test results and other clinical characteristics of the patient. However, the structure of the model could be modified to consider that treatments after diagnosis become decision nodes, which would allow the best pathway to be identified not only for diagnosis, but also for the planning of treatments.

The present model could be further enhanced by incorporating serial tests, using a variety of assumptions about the relationship between tests (both assumptions of independency of tests and dependency of tests could be investigated). As with many diagnostic procedures the complexity of testing variations that occur in clinical practice are poorly reported in the literature, which in turn makes modelling the scenario impossible without the use of wild assumptions.

For the short-term model a specific measure of health benefit was identified according to what the clinicians considered a relevant outcome for the diagnostic tests in a short-term period (i.e. the percentage of patients who would be correctly diagnosed according to the test results and for whom an appropriate treatment plan was formulated according to the judgement of the vascular surgeon). The measure of health benefits used in the long-term model was the number of QALYs, which is a generic measure that allows the comparison of the results of these interventions with those of different types of intervention.

Probabilistic sensitivity analysis was undertaken to address the existing uncertainty surrounding the input variables used to populate the model, which were obtained by merging data from a variety of sources (medical literature, expert opinion and assumptions). Scatter plots on the cost-effectiveness plane and cost-effectiveness acceptability curves were reported, which are the most appropriate way of presenting the results according to the NICE guide to the methods of technology appraisal.[692]

Results of the review

The electronic literature searches were conducted in May 2004 and updated in May 2005. The update searches identified an additional two studies that provided data on tests to diagnose stenosis/occlusion that were eligible for inclusion in the review. In addition, three studies that did not meet the inclusion criteria for the review of diagnostic accuracy, but which reported results relating to adverse events, were identified by the update searches. This indicates the rapidly evolving nature of vascular imaging research. As the update search represents the approximate number of studies being indexed in electronic medical databases per year that would have been eligible for inclusion in this review, it can be used to assess how rapidly this area of research is growing and to evaluate how soon the data in this review will be out of date.

The data obtained from studies meeting the inclusion criteria for the review were insufficient to

facilitate the development of any evidence-based algorithm.

The studies identified and included in the review focused on assessing the level of stenosis or occlusion to assist in the formulation of a treatment plan. Although no studies were identified that investigated diagnostic techniques merely to confirm the diagnosis of PAD, there is no reason to believe that the diagnostic accuracy of the tests would be different when used to confirm the diagnosis of PAD in symptomatic patients, with a similar spectrum of disease, presenting to primary care.

The quality of the included diagnostic accuracy studies was generally good with respect to the test descriptions, blinding and independence of the reference standard. However, other aspects were poorly reported. Most studies either did not include an appropriate patient spectrum or failed to report sufficient details of the included patients for this to be assessed. Around half of the MRA and DUS studies did not describe the method used to select patients for the study, although this was better reported by the CTA studies, with 71% reporting patient selection criteria. This may be due to the impact of STARD on the more recently reported studies. The most poorly reported quality item, across all the tests, was the availability of clinical data when the test results were interpreted, with 86% of the studies being classed as unclear as they did not discuss the availability of other data. In around 30% of studies it was not clear whether the test results were interpreted without knowledge of the reference standard results, which is a major source of potential bias. In general, both tests were performed in a short period (within 1 month of each other) for around 80% of the CTA and DUS studies, reducing the potential for disease progression bias. The test and reference standard were performed within an acceptable time-frame in only 64% of the DUS studies. This may reflect a difference in the application of DUS in clinical practice, with this test more likely to be used as an early 'screening' procedure, and tests that are viewed as able to produce the classic 'road map' used to assess patients for intervention. However, the potential for disease progression bias indicated by the observed delay in many studies makes objective assessment of the diagnostic performance of DUS difficult.

When considering the diagnostic accuracy for detecting stenosis/occlusion, CE MRA had the best overall performance, with nearly all the studies reporting sensitivities and specificities of over 90%. MRA was associated with the highest proportion of adverse events reported in the studies. However, the most severe adverse events (death and severe vascular adverse events) were more common in patients undergoing CA than MRA, although they only occurred in a very small proportion of patients undergoing either test. The increased likelihood of suffering a mild adverse event does not appear to affect patients' preferences for MRA over CA, as the results of three patient attitude surveys strongly suggest that MRA is preferred by patients over CA. The contrast agent was responsible for some of the reported adverse events, although generally the proportion of patients suffering contrast agent-related adverse events was very low. The most commonly reported adverse events associated with CE MRA were acute digestive system symptoms, minor pain/discomfort, and acute central and peripheral nervous system adverse events. The most commonly reported adverse events associated with 2D TOF MRA were minor pain/discomfort and anxiety.

Overall, the performance of CE MRA appeared superior to that of 2D TOF MRA, which also showed more variation in diagnostic accuracy. This is consistent with the findings of previous systematic reviews.[362,660] However, one study assessing 2D TOF MRA in arteries below the knee reported results comparable to CE MRA,[27] with a sensitivity of 98% and specificity of 95% for the detection of stenoses of 50% or higher. It should also be noted that a simple comparison of accuracy for the detection of degree of stenosis, cannot fully assess the ability of a procedure to produce the 'vascular road map'. Factors such as length and grouping of stenoses are not considered. The relative ability of procedures to provide a complete and clinically useful picture is therefore difficult, if not impossible, to assess using diagnostic accuracy studies alone. It also seems unlikely that further evidence relating to 3D TOF MRA will become available given the overriding enthusiasm for CE MRA among radiologists.

For CTA, there was less heterogeneity between the results for the detection of stenoses of 70% or greater, or an occlusion, with CTA having a higher specificity (above 97%) than sensitivity (above 87%) for the whole leg. This indicates that CTA may be useful for 'ruling in' the presence of higher grade stenosis, but its overall performance in detecting stenoses of 50% or above was slightly inferior to CE MRA. However, the application of CTA to the assessment of PAD remains a relatively

recent development and its contribution to effective surgical planning remains to be explored. No studies investigating the diagnostic accuracy of the new 64-slice CTA were identified, as this is a very new development in CTA technology. A survey of patient attitudes towards CA, MRA and CTA found that in terms of level of discomfort CA was found to be the most uncomfortable, followed by MRA, with CTA being the least uncomfortable. Only one study reported mild adverse events associated with CTA (skin adverse events), which occurred in a very small proportion of the study population.

The performance of DUS was inferior to both CE MRA and CTA. Again, the specificity of DUS tended to be higher than the sensitivity (specificity above 89% and sensitivity above 74% for the whole leg). There was more heterogeneity among the study sensitivities for DUS and the lower overall sensitivity means that DUS may miss some significant stenoses. This may be of particular concern if DUS were to be used to screen patients before surgical planning. However, although the sensitivity of DUS may be inadequate for the detection of individual lesions, it is unlikely to classify wrongly a whole limb as 'normal' and thus inappropriately screen out a patient from further investigation. Sensitivities were generally adequate for DUS studies reporting data by limb. DUS may be useful for broader diagnostic classification (e.g. is this patient suitable for PTA or bypass graft?), although data are not currently available to assess this adequately. It should also be noted that the long delay between the index test and reference standard, apparent in some studies, is likely to reduce estimates of sensitivity. The only trial of the effectiveness of imaging procedures, in terms of surgical planning and patient outcome, found DUS and CA to be comparable, a result which is seemingly at odds with poor estimates of diagnostic accuracy. A survey of patient attitudes found that the majority of patients (from a sample who did not suffer from claustrophobia and had no metallic implants) had no preference between undergoing MRA or DUS, while the majority of those who did express a preference preferred MRA. There was no significant difference between MRA and DUS on a scale rating how bothersome the tests were. This conclusion may be open to question, however, since patients experiencing claustrophobia (an important reason for patient dissatisfaction with MRA) were excluded from the relevant study. Only two studies reported adverse events associated with DUS: anxiety occurred in a very small proportion of the study population in one study, and minor pain/discomfort during or immediately after the procedure was reported in 22% of patients in one study.

There were some differences in diagnostic performance of individual imaging techniques with respect to the area of leg being assessed. CE MRA was more accurate for detecting stenoses above the knee than below the knee. Only one CE MRA study[76] provided separate results for the foot and these were less accurate (sensitivity of 79%, specificity of 71% for detecting stenosis of 50% or above). There was insufficient evidence to judge CTA (only one study provided results below the knee), although its accuracy above the knee was high (sensitivity above 96% and specificity above 91%). The results were similar for DUS, with the overall accuracy tending to be higher for the assessment of stenoses above the knee. The one DUS study that provided separate results for the foot[42] reported a low sensitivity of 64% and a specificity of 80% for detecting vessels suitable for surgery. The assessment of potential outflow vessels in the foot appears to be a problematic area and one that warrants further research, particularly with respect to newer technologies such as CTA.

Only nine of the diagnostic accuracy studies that met the inclusion criteria for the review provided data on adverse events. The lack of adverse event data reported by the majority of included diagnostic accuracy studies cannot be interpreted as no adverse events having occurred. Therefore, the results of this review in relation to adverse events are unlikely to be a complete picture of all adverse events occurring in the included diagnostic accuracy studies. In addition to this potential source of bias, the reporting of adverse events was subjective; therefore, an adverse event categorised as 'severe' in one study may not have been classed as 'severe' in another.

Heterogeneity

There are various potential sources of heterogeneity between the studies. These include the spectrum of patients included, the interval between the reference standard and index test, other quality criteria, test-specific details, technological advancement (using the date of publication as a surrogate) and the extent of the scan (inclusion/exclusion of the foot). Operator bias may also be a source of heterogeneity; however, insufficient data were reported in the included studies for the impact of this bias to be assessed.

Quality criteria

Spectrum bias may help to explain some of the heterogeneity seen between studies. A study may

underestimate or overestimate the accuracy of a test by investigating a selected population. Factors that may affect the measures of accuracy include the severity of disease in the population studied, demographics and co-morbidity.[17] Population-based differences may be a factor in the heterogeneity seen in CE MRA studies, with two studies that reported recruiting an appropriate patient spectrum reporting the lowest sensitivity and specificity in their groups.[9,70] One of these studies also reported that clinical data were not available when interpreting scans,[70] which may also be a factor in lower accuracy. The major factor in spectrum-related heterogeneity is likely to be the proportion of patients at each stage of the disease process included in the studies. It may be expected that studies recruiting a high proportion of patients with less severe disease (Fontaine stage II) may underestimate overall accuracy, as identifying less severe stenosis, with fewer symptoms, may be more difficult. Conversely, studies recruiting a high proportion of patients with more severe disease (Fontaine stage IV) may overestimate overall accuracy. This hypothesis is supported by the 2D TOF MRA study that had the highest proportion of patients with Fontaine stage IV in its grouping, and reported the highest sensitivity and specificity.[40] In addition, a DUS study restricted to Fontaine stage II reported the lowest sensitivity and highest specificity in its group.[52] However, contrary to this, a CE MRA study with the highest proportion of patients with Fontaine stage IV in its group reported the lowest sensitivity and specificity.[28]

The delay between the index test and reference standard is likely to affect significantly measures of diagnostic performance where disease progression is relatively rapid. Where the reference standard is conducted a clinically significant time after the index test, estimates of the sensitivity of the index test are likely to be reduced. This is borne out by the data presented in this review, where timing of tests seemed to have an effect on the diagnostic measures for all three technologies evaluated.[28,34,48,54,59,71] In the studies reporting a delay of over 1 month between tests 33 patients received the index test first and eight patients received the reference standard first in one study,[54] and it was unclear which test was first in the other.[24] It is therefore possible that the patient's condition deteriorated during this time, making it easier to diagnose, and therefore underestimating the accuracy of the index test. Similarly, the reference standard may be detecting clinically significant disease that simply was not present at the time of the index test.

Whether withdrawals and dropouts were reported, and the reasons explained, appeared to have some relation to the diagnostic measures. This may reflect the type of patients that withdrew, with withdrawals being unequal across the patient spectrum and potentially resulting in an underestimate or overestimation of diagnostic accuracy. The 2D TOF MRA study that did not explain withdrawals from the study had the highest proportion of patients with Fontaine stage IV, and reported the highest sensitivity and specificity.[40] The failure to explain withdrawals and dropouts may imply selective reporting, or that the patients who dropped out may have been from the less severe stages of disease; both scenarios could have led to an overestimation of the accuracy of the index test. In this study, however, it appears that certain segments were not imaged in all patients, which may imply that the scans for these segments were uninterpretable, or were not imaged for unspecified reasons. Omitting these results from the analysis may have overestimated the diagnostic accuracy of the index test.

Most studies that reported whether interpreters were blinded to the results of the index test when interpreting results of the reference standard (and vice versa) stated that the interpreters were blinded. However, for a large proportion of studies, it was unclear whether interpreters were blinded or not. Therefore, the impact of blinding the interpreters on the reported diagnostic accuracy could not be investigated. The vast majority of studies also did not report whether other clinical data were available to interpreters.

Test-specific details

One criterion that requires defining when undertaking DUS is the PSVR used to diagnose a specified level of stenosis. The majority of the studies either did not report the PSVR, or used a PSVR of 2.0 as representing 50% stenosis. In one analysis of 50% or more stenosis, above the knee, one study used 2.5 for 50% stenosis, with the others using 2.0 or not reporting the PSVR. The study that used 2.5 reported the lowest sensitivity and highest specificity.[53] By choosing a higher PSVR for the diagnosis of 50% or greater stenosis, the difference in flow rate between stenosed and non-stenosed sections of artery will need to be greater to produce a positive result, requiring a greater severity of stenosis. Therefore, stenosis of lesser severity may be missed, reducing the sensitivity. However, the number of false-positive results would also be reduced, so increasing specificity. There was no evidence that the type of

probe used during the DUS had any effect on the accuracy of the test.

The only other test-specific detail identified that may have had an impact on the diagnostic accuracy measures was related to the reference standard, and was seen in the group of CE MRA studies diagnosing 50% stenosis or more in below-the-knee scans. The study reporting the highest sensitivity and specificity stated that the location of the catheter during the reference standard angiography was aortic,[51] whereas the other studies identified the puncture site, but not the position of the catheter.[46,76] However, it is more likely that the exclusion of the foot from the images explains the superior diagnostic accuracy reported in this study (see below).[51] There was no clear pattern between technological advancement (using the date of publication as a surrogate) and diagnostic measures.

Inclusion of the foot

In general, the inclusion of the foot in the scan seems to decrease the diagnostic accuracy of CE MRA and DUS. The arteries in the foot are deemed to be more difficult to visualise using CA owing to dilution of contrast material, slow flow and difficulties in timing of imaging relative to the arterial injection.[593] These factors may, therefore, also be an issue during CE MRA. The small size of the arteries and greater movement of the foot during imaging also contribute to the problems of imaging the arteries of the foot.[76] The only CE MRA study to include the foot in the evaluation of 50% or greater stenoses in the whole leg reported the lowest sensitivity and specificity,[28] and a CE MRA study evaluating below the knee that did not include the foot reported the highest sensitivity and specificity in that group.[51] Only four DUS studies included the foot in the scan. Three of these were grouped together evaluating occlusions below the knee. Two reported the two lowest sensitivities,[44,45] and the other the lowest specificity.[43] The effect of including the foot when undertaking a CTA scan was less clear, and was based on just two studies giving contrasting results.[26,54] Both of these studies were included in two analyses. In studies evaluating 50% stenosis or more in the whole leg, one reported the highest sensitivity and specificity,[26] whereas the other[54] reported one of the lowest sensitivities, with a similar value to that of the study reporting the lowest sensitivity that did not include the foot.[58] In the group evaluating occlusions in the whole leg, one study again reported the lowest sensitivity,[54] whereas the other reported the second highest sensitivity.[26] Both studies reported a specificity over 99% in this category. It is possible that the difference in results between these studies is related to quality, as the study reporting the lower diagnostic accuracy did not include an appropriate patient spectrum, had an unacceptable delay between the index test and reference standard, and did not report the Fontaine classification (or its equivalent) of the participants.[54] The performance of all imaging technologies in the foot is an area that requires further evaluation.

Gaps in the evidence

The review was limited by the lack of high-quality, well-reported studies. The searches located only a single controlled trial. This used a historical control group and could be subject to selection and interpretation bias. The majority of the available studies were diagnostic cohorts, with most having small sample sizes. Data regarding the influence of imaging technologies upon the surgical planning and postoperative outcome for patients with PAD are urgently needed. These cannot be provided by diagnostic accuracy studies. The most reliable and appropriate methodology is the RCT. A well-designed RCT could provide information on the influence of tests on treatment decisions and patient outcomes in patients with PAD. Health economic data could be collected simultaneously. Advantages of an RCT include: the measurement of directly relevant clinical and economic outcomes (as opposed to the ability to detect a specific diagnostic feature), no requirement for a reference standard (the diagnostic accuracy study design is dependent on the assumption that the result of a reference standard test is always correct, whereas the RCT design allows direct comparison of new tests with the reference standard without this potentially flawed assumption), and a comparative measure can incorporate all information provided by a test (including that which is not readily defined).

Several potential barriers to carrying out an RCT require consideration. There may be ethical objections; despite the lack of good-quality accuracy data, withholding a particular test may be deemed unethical. This may be a more persuasive argument for some tests, where diagnostic accuracy data are stronger. The same could be said for institutions where certain technologies are used as part of the routine assessment of PAD. The feasibility of carrying out an RCT may also be questioned, primarily regarding the refinements in the technology over time and the logistic problems associated with the availability of the technologies and concerning the potentially large sample size required for such an RCT. Where resources are too

scarce, an RCT might be impractical, and a judgement as to when a technology is sufficiently refined to warrant investigation in an RCT is required.

Results of the review of economic evaluations

There exists some discrepancy in the literature regarding the most cost-effective imaging technique for PAD patients, according to the results observed in the economic evaluations included in the systematic review. One of the studies[126] found that DUS was not cost-effective as a preoperative imaging technique because of its low sensitivity. Two studies[128,129] compared MRA, DUS and CA followed by treatment among PAD patients with intermittent claudication, and concluded that differences in costs and effectiveness were slight and either MRA or DUS could replace CA without a substantial reduction in effectiveness and with a minor cost reduction. Yin and colleagues[131] compared MRA with CA as a preoperative diagnostic test for patients with limb-threatening peripheral vascular disease and concluded that MRA was cost-effective, either alone or in combination with selective use of CA. CTA was compared with MRA in a further study[130] for the evaluation of patients with intermittent claudication, the conclusion being that CTA has the potential to be cost-effective. (See Appendix 7 for more details of these studies.) What seems clear from these results is that non-invasive imaging techniques appear to have a place in the preoperative diagnosis of PAD patients.

Results of the economic modelling

When the short-term model was considered, the most cost-effective imaging modality appeared to be DUS, which presented a cost of £2617 per CDPwATP and an incremental cost per additional CDPwATP obtained, compared with 2D TOF MRA, equal to £2260. One year after initial treatment, DUS remained the dominant strategy, incurring a cost per QALY of £13,646. The assumption about whether endarterectomy was included as a bypass or as a PTA procedure did not have an impact on the cost-effectiveness results. The adjustments performed to overcome the problem of zero counts for some of the events considered in the decision model also had no impact.

However, when test performance was related to a specific area of the leg (i.e. either above- or below-the-knee comparisons), the preoperative diagnostic strategy that appeared to be more cost-effective was 2D TOF MRA, with a cost per QALY equal to £8628 for above-the-knee comparisons, and an incremental cost per additional QALY equal to £37,024, when 2D TOF MRA was compared with DUS.

It seems relevant to highlight that these cost-effectiveness results do not depend exclusively on the accuracy of the tests, but also on the accuracy of the clinician's decision about the best treatment to formulate for each patient according to type and severity of stenosis and other relevant factors.

In conclusion, these results suggest that for PAD patients for whom the whole leg is evaluated by a preoperative diagnostic test, in order to identify the type and level of stenosis and subsequently formulate a treatment plan, DUS dominates the other alternatives by presenting higher effectiveness at a lower cost per QALY. However, when analysis of stenosis is limited to a section of the leg, either above the knee or below the knee, 2D TOF MRA appears to be the most cost-effective preoperative diagnostic strategy.

Chapter 9
Conclusions

Implications for clinical practitioners and decision-makers

The results of the review suggest that CE MRA has the best overall diagnostic accuracy of the three index tests evaluated. Where available, CE MRA may be a viable alternative to CA.

CE MRA was generally preferred by patients over CA. Where reported, there was a greater number of adverse events associated with CE MRA than with CA. However, these were mild and do not appear to affect patient preferences. The most severe adverse events were more common in patients undergoing CA. It should be noted that reporting of adverse event data and patient attitudes was poor.

The only controlled trial of the effectiveness of imaging procedures suggested that the results of DUS were comparable to those of CA, in terms of surgical planning and outcome. This finding conflicts with the results of diagnostic accuracy studies, which reported poor estimates of accuracy for DUS in comparison with CA.

The overall diagnostic performance of CTA in detecting stenoses of 50% or more was inferior to CE MRA. However, the results for the performance of CTA to image arteries of the foot appear promising. As the assessment of PAD is a relatively new application for this technology, there was insufficient evidence to evaluate the usefulness of CTA in this area.

The results of the economic modelling suggest that once the accuracy and effectiveness of the tests (in terms of surgical planning and outcome) are combined with their associated costs, DUS dominates the other alternatives, presenting higher effectiveness at a lower cost per QALY. This outcome is in line with the results shown by the only trial included in the systematic review assessing the effectiveness of imaging procedures.

However, when analysis of stenosis was limited to a section of the leg, either above the knee or below the knee, the findings show 2D TOF MRA to be the most cost-effective preoperative diagnostic strategy. This result was in accordance with the overall findings of the systematic review.

Implications for research

Quality assessment highlighted limitations in the methodological and reporting quality of many studies included in this review. Future evaluations of diagnostic tests should follow the STARD guidelines for reporting of diagnostic accuracy studies.[684,685] The following specific questions require further research.

What is the relative clinical effectiveness of the available imaging tests, in terms of surgical planning and postoperative outcome?

Diagnostic accuracy studies will not provide information on effectiveness or cost-effectiveness. The diagnostic accuracy study is designed to compare the results obtained from new tests with those of the reference standard of diagnosis (which are assumed always to be correct); it is therefore inherently not capable of comparing tests in terms of their ultimate impact upon patient outcomes. The diagnostic accuracy studies included in this review compare imaging tests with the reference standard purely in terms of their ability to detect a predefined level of stenosis at a given point in the vasculature. They do not provide an overall picture of the relative contributions of the images obtained to therapeutic decision-making, or of any consequent impact upon patient outcomes. To address these issues, a large, multicentre RCT is required. Ideally, those imaging modalities that are of primary interest for surgical planning (CT and CE MRA) would be evaluated in more than one centre included in the RCT, in an attempt to avoid performance bias. Such a trial would provide direct and robust information on the influence of a test on treatment planning and patient outcome.

Health economic data could be collected simultaneously, allowing an examination of cost-effectiveness. The availability of data on the management of patients after testing currently restricts the scope of economic modelling.

Recognising that the establishment of large-scale RCTs is particularly problematic in rapidly evolving fields such as vascular imaging, a compromise approach may be to establish a multicentre tracker study. Such a study should enable the collection of data comparing the numbers of misdiagnoses, and the relative health status and health-related quality of life resulting from alternative imaging strategies.

What adverse events occur as a consequence of testing, and what is the relative incidence for the available tests?

Future studies should consider methods appropriate for the collection of adverse event data.

Which testing options do patients prefer?

Further research, which is well designed, conducted and reported, is required in this area. Future studies should consider collection of data on patient attitudes.

What is the true diagnostic accuracy of DUS in comparison with CA, for the detection of stenoses of 50% or greater and occlusions?

Existing diagnostic accuracy studies on DUS have a number of methodological weaknesses, which are highlighted in this report. Further well-designed diagnostic accuracy studies may provide additional useful information. Particular consideration should be given to the time between the index test and reference standard, and assessment of the influence of operator skill/experience on accuracy.

What are the effects of operator skill/training/experience on measures of test accuracy for all the imaging modalities of interest?

Future studies should report details of observers and allow collection of data on inter-observer variability.

What is the diagnostic accuracy and clinical effectiveness of tests to image arteries in different areas of the lower limbs, particularly the foot?

Future studies should allow collection of data on effectiveness and diagnostic performance of tests, which is specific to their application in the foot.

What is the diagnostic accuracy and clinical effectiveness of tests in clinically important patient subgroups, such as diabetes mellitus?

Future studies should allow collection of data on effectiveness and diagnostic performance of tests, which is specific to clinically important patient subgroups.

In addition, the available literature showed a lack of data about how patients are managed after the results of diagnostic tests are obtained; these were required to populate the economic model. It is not clear from the literature whether the prognosis and quality of life of patients who had an inaccurately formulated treatment plan and underwent a change of procedure would be significantly different from those of patients who were correctly diagnosed and managed from the outset. Further research on these topics is required, which could take the form of an observational study of patients with PAD presenting different levels of severity, over the long term.

If the allocation of treatment pathway were to be modelled, further research in this area would also be required to allow these decisions to be captured and accurately represented. Such a model would reflect different treatment plans to be performed according to the specific clinical characteristics of patients obtained by means of the preoperative diagnostic testing. Therefore, the model should consider:

- choice of treatments available (for patients with the same characteristics, which is the most cost-effective treatment to choose for the patient?)
- the treatment chosen by the clinicians according to the test results.

Both options could be taken into account to develop alternative treatment scenarios for patients according to the patient characteristics reflected by the test results. A model of this nature was outside the scope of this project owing to time constraints and the lack of available data that would have made such a model a viable option. However, it is recommended that a patient simulation model, considering the above issues, be performed to assess the long-term cost-effectiveness of preoperative imaging diagnostic tests for PAD patients.

Acknowledgements

We would like to thank the following individuals and groups for their valuable contributions to this project: Professor Mark Sculpher from the Centre for Health Economics, University of York, and Professor Jonathan Michaels from the Academic Vascular Unit, University of Sheffield, for their assistance with the economic modelling section of the review. We also thank the members of the advisory panel for commenting on the protocol and draft report and for provision of advice during the review process.

Contribution of authors

Ros Collins (Research Fellow) was the lead reviewer responsible for study selection, data extraction, validity assessment, data analysis and writing the report. Gillian Cranny (Research Fellow) was involved in data extraction, validity assessment, data analysis and writing the report. Jane Burch (Research Fellow) was involved in study selection, data extraction, validity assessment, data analysis and writing the report. Raquel Aguiar-Ibáñez (Health Economist) was involved in the cost-effectiveness section, study selection, data extraction, development of the economic model and report writing. Dawn Craig (Health Economist) was involved in the cost-effectiveness section, study selection, data extraction, development of the economic model and report writing. Kath Wright (Information Officer) devised the search strategy, carried out the literature searches and wrote the search methodology sections of the report. Elizabeth Berry (Senior Lecturer) provided advice and commented on drafts of the report. Michael Gough (Consultant Vascular Surgeon) provided advice and commented on drafts of the report. Jos Kleijnen (Director of Centre for Reviews and Dissemination, University of York) provided advice and commented on drafts of the report. Marie Westwood (Senior Research Fellow) provided input at all stages, commented on drafts of the report and took overall responsibility for the review.

References

1. Beard J. Chronic lower limb ischaemia. *BMJ* 2000; **320**:854–7.
2. Drug treatment of peripheral arterial disease. *Bandolier* 1996:29–34. URL: http://www.jr2.ox.ac.uk/bandolier/band29/b29-4.html. Accessed October 2005.
3. Burns P, Gough S, Bradbury A. Management of peripheral arterial disease in primary care. *BMJ* 2003;**326**:585–8.
4. Tierney S, Fennessy F, Hayes D. Secondary prevention of peripheral vascular disease. *BMJ* 2000;**320**:1262–5.
5. *Management of peripheral arterial disease (PAD)*. TransAtlantic Inter-Society Consensus (TASC). URL: http://www.tasc-pad.org/html/homepage.htm. Accessed October 2005.
6. Brewster DC, Perler BA, Robison JG, Darling AC. Aortofemoral graft for multilevel occlusive disease: predictors of success and need for distal bypass. *Arch Surg* 1982;**117**:1593–600.
7. Shearman CP, Gwynn BR, Curran FT, Gannon MX, Simms MH. Non-invasive femoropopliteal assessment: is that angiogram really necessary? *BMJ* 1986;**293**:1086–9.
8. Gates MD, Hartnell GG. Optimized diagnostic angiography in high-risk patients with severe peripheral vascular disease. *Radiographics* 2000; **20**:121–33.
9. Meaney JF, Ridgway JP, Chakraverty S, Robertson I, Kessel D, Radjenovic A, *et al*. Stepping-table gadolinium-enhanced digital subtraction MR angiography of the aorta and lower extremity arteries: preliminary experience. *Radiology* 1999; **211**:59–67.
10. Hesselink JR. *MR angiography: techniques and applications*. University of California, San Diego, CA. URL: http://spinwarp.ucsd.edu/NeuroWeb/Text/br-120.htm. Accessed October 2005.
11. Westwood ME, Kelly S, Berry E, Bamford JM, Gough MJ, Airey CM, *et al*. How to undertake a clinically relevant systematic review in a rapidly evolving field: magnetic resonance angiography. *Int J Technol Assess Health Care* 2002;**18**:24–32.
12. Tripathi R, Batra A, Taneja M, Kaushik SB, Kumaran S. Three-dimensional contrast-enhanced magnetic resonance angiography: our preliminary experience. *Indian Journal of Radiology and Imaging* 2002;**12**:179–88.
13. NHS Centre for Reviews and Dissemination. *Undertaking systematic reviews of research on effectiveness. CRD's guidance for those carrying out or commissioning reviews*. 2nd ed. CRD Report No. 4. York: NHS Centre for Reviews and Dissemination, University of York; 2001.
14. Irwig L, Macaskill P, Glasziou P, Fahey M. Meta-analytic methods for diagnostic test accuracy. *J Clin Epidemiol* 1995;**48**:119–30.
15. Irwig L, Tostesen ANA, Gatsonis C, Lau J, Colditz G, Chalmers TC, *et al*. Guidelines for meta-analyses evaluating diagnostic tests. *Ann Intern Med* 1994;**120**:667–76.
16. NHS Centre for Reviews and Dissemination. *Improving access to cost-effectiveness information for health care decision making: the NHS Economic Evaluation Database*. CRD Report No. 6. York: NHS Centre for Reviews and Dissemination, University of York; 2001.
17. Whiting P, Rutjes A, Reitsma J, Bossuyt P, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol* 2003;**3**. URL: http://www.biomedcentral.com/1471-2288/3/25. Accessed October 2005.
18. Zamora J, Muriel A, Abraira V. *Meta-DiSc for Windows: a software package for the meta-analysis of diagnostic tests*. In XI Cochrane Colloquium. Barcelona; 2003. URL: http://www.hrc.es/investigacion/metadisc.html. Accessed October 2005.
19. Moses L, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. *Stat Med* 1993;**12**:1293–316.
20. Aly SAAF. *Duplex ultrasound in the assessment of peripheral arterial disease*. PhD thesis, London University; 1998.
21. Ashleigh RJ, Farrell A. The use of colour flow Doppler ultrasound in the selection of patients for femoropopliteal angioplasty. *Journal of Interventional Radiology* 1993;**8**:133–8.
22. Baum RA, Rutter CM, Sunshine JH, Blebea JS, Blebea J, Carpenter JP, *et al*. Multicenter trial to evaluate vascular magnetic resonance angiography of the lower extremity. American College of Radiology Rapid Technology Assessment Group. *JAMA* 1995;**274**:875–80.

23. Baxter G, Polak J. Lower limb colour flow imaging: a comparison with ankle: brachial measurements and angiography. *Clin Radiol* 1993; **47**:91–5.

24. Bergamini TM, Tatum CM Jr, Marshall C, Hall-Disselkamp B, Richardson JD. Effect of multilevel sequential stenosis on lower extremity arterial duplex scanning. *Am J Surg* 1995; **169**:564–6.

25. Bostrom A, Karacagil S, Lofberg AM, Ljungman C, Nyman R, Logason K, *et al*. Selection of patients with lower limb arterial occlusive disease for endovascular treatment of the iliac arteries with duplex scanning. *Vasc Surg* 2001;**35**:437–42.

26. Catalano C, Fraioli F, Laghi A, Napoli A, Bezzi M, Pediconi F, *et al*. Infrarenal aortic and lower-extremity arterial disease: diagnostic performance of multi-detector row CT angiography. *Radiology* 2004;**231**:555–63.

27. Cortell ED, Kaufman JA, Geller SC, Cambria RP, Rivitz SM, Waltman AC. MR angiography of tibial runoff vessels: imaging with the head coil compared with conventional arteriography. *AJR Am J Roentgenol* 1996;**167**:147–51.

28. Cronberg CN, Sjoberg S, Albrechtsson U, Leander P, Lindh M, Norgren L, *et al*. Peripheral arterial disease. Contrast-enhanced 3D MR angiography of the lower leg and foot compared with conventional angiography. *Acta Radiol* 2003; **44**:59–66.

29. Currie IC, Jones AJ, Wakeley CJ, Tennant WG, Wilson YG, Baird RN, *et al*. Non-invasive aortoiliac assessment. *Eur J Vasc Endovasc Surg* 1995;**9**:24–8.

30. Davies AH, Magee TR, Parry R, Hayward J, Murphy P, Cole SEA, *et al*. Duplex ultrasonography and pulse-generated run-off in selecting claudicants for femoropopliteal angioplasty. *Br J Surg* 1992;**79**:894–6.

31. Eiberg JP, Jensen F, Gronvall Rasmussen JB, Schroeder TV. Screening for aortoiliac lesions by visual interpretation of the common femoral Doppler waveform. *Eur J Vasc Endovasc Surg* 2001; **22**:331–6.

32. Eklof H, Smedby O, Ljungman C, Karacagil S, Bergqvist D, Ahlstrom H. 2D inflow MR angiography in severe chronic leg ischemia. *Acta Radiol* 1998;**39**:663–8.

33. El-Kayali A, Al-Bakry A, Iqbal K, Al-Salman M, Rabee H, Al-Smayer S, *et al*. Accuracy of duplex scan in the management of chronic leg ischaemia. *Emirates Medical Journal* 2004;**22**:53–6.

34. Fletcher JP, Kershaw LZ, Chan A, Lim J. Noninvasive imaging of the superficial femoral artery using ultrasound Duplex scanning. *J Cardiovasc Surg (Torino)* 1990;**31**:364–7.

35. Grassbaugh JA, Nelson PR, Rzucidlo EM, Schermerhorn ML, Fillinger MF, Powell RJ, *et al*. Blinded comparison of preoperative duplex ultrasound scanning and contrast arteriography for planning revascularization at the level of the tibia. *J Vasc Surg* 2003;**37**:1186–90.

36. Hany TF, Debatin JF, Leung DA, Pfammatter T. Evaluation of the aortoiliac and renal arteries: comparison of breath-hold, contrast-enhanced, three-dimensional MR angiography with conventional catheter angiography. *Radiology* 1997;**204**:357–62.

37. Hatsukami TS, Primozich JF, Zierler RE, Harley JD, Strandness DE Jr, Moneta GL, *et al*. Color Doppler imaging of infrainguinal arterial occlusive disease. *J Vasc Surg* 1992;**16**:527–33.

38. Heuschmid M, Krieger A, Beierlein W, Luz O, Kuettner A, Kopp AF, *et al*. Assessment of peripheral arterial occlusive disease: comparison of multislice-CT angiography (MS-CTA) and intraarterial digital subtraction angiography (IA-DSA). *Eur J Med Res* 2003;**8**:389–96.

39. Hirai T, Ohishi H, Kichikawa K, Yoshimura H, Uchida H. Ultrasonographic screening for arterial occlusive disease in the pelvis and lower extremities. *Radiat Med* 1998;**16**:411–16.

40. Hoch JR, Tullis MJ, Kennell TW, McDermott J, Acher CW, Turnipseed WD. Use of magnetic resonance angiography for the preoperative evaluation of patients with infrainguinal arterial occlusive disease. *J Vasc Surg* 1996;**23**:792–800.

41. Hoch JR, Kennell TW, Hollister MS, Sproat IA, Swan JS, Acher CW, *et al*. Comparison of treatment plans for lower extremity arterial occlusive disease made with electrocardiography-triggered two-dimensional time-of-flight magnetic resonance angiography and digital subtraction angiography. *Am J Surg* 1999;**178**:166–72.

42. Hofmann WJ, Walter J, Ugurluoglu A, Czerny M, Forstner R, Magometschnigg H. Preoperative high-frequency duplex scanning of potential pedal target vessels. *J Vasc Surg* 2004;**39**:169–75.

43. Karacagil S, Lofberg AM, Granbo A, Lorelius LE, Bergqvist D. Value of duplex scanning in evaluation of crural and foot arteries in limbs with severe lower limb ischaemia: a prospective comparison with angiography. *Eur J Vasc Endovasc Surg* 1996;**12**:300–3.

44. Koelemay MJ, Legemate DA, van Gurp J, Ponson AE, Reekers JA, Jacobs MJ. Colour duplex scanning and pulse-generated run-off for assessment of popliteal and cruropedal arteries before peripheral bypass surgery. *Br J Surg* 1997; **84**:1115–19.

45. Koelemay MJ, Legemate DA, de Vos H, van Gurp JA, Reekers JA, Jacobs MJ. Can

cruropedal colour duplex scanning and pulse generated run-off replace angiography in candidates for distal bypass surgery? *Eur J Vasc Endovasc Surg* 1998;**16**:13–18.

46. Kreitner KF, Kalden P, Neufang A, Duber C, Krummenauer F, Kustner E, *et al*. Diabetes and peripheral arterial occlusive disease: prospective comparison of contrast-enhanced three-dimensional MR angiography with conventional digital subtraction angiography. *AJR Am J Roentgenol* 2000;**174**:171–9.

47. Lai DT, Huber D, Glasson R, Grayndler V, Evans J, Hogg J, *et al*. Colour-coded duplex ultrasonography in selection of patients for transluminal angioplasty. *Australas Radiol* 1995; **39**:243–5.

48. Lai DT, Huber D, Glasson R, Grayndler V, Evans J, Hogg J, *et al*. Colour duplex ultrasonography versus angiography in the diagnosis of lower-extremity arterial disease. *Cardiovasc Surg* 1996; **4**:384–8.

49. Laissy JP, Debray MP, Menegazzo D, Rangheard AS, Benamer H, Charlier P, *et al*. Prospective evaluation of peripheral arterial occlusive disease by 2D MR subtraction angiography. *J Magn Reson Imaging* 1998;**8**:1060–5.

50. Legemate D, Teeuwen C, Hoeneveld H. Spectral analysis in duplex scanning of aortoiliac and femoro-popliteal arterial disease. *Ultrasound Med Biol* 1991;**17**:769–76.

51. Lenhart M, Herold T, Volk M, Seitz J, Manke C, Zorger N, *et al*. [Table-feed gadolinium-enhance MR angiography of the lower extremity arteries. Imaging with a dedicated peripheral vascular coil system. Preliminary experience]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2000;**172**:992–9.

52. Linke RJ, Davies RP, Giles AJ, Walsh JA, Thompson BW. Colour duplex ultrasound: a screening modality for femoropopliteal disease in patients with intermittent claudication. *Australas Radiol* 1994;**38**:320–3.

53. Lundin P, Svensson A, Henriksen E, Jonason T, Forssell C, Backbro B, *et al*. Imaging of aortoiliac arterial disease. Duplex ultrasound and MR angiography versus digital subtraction angiography. *Acta Radiol* 2000;**41**:125–32.

54. Martin ML, Tay KH, Flak B, Fry PD, Doyle DL, Taylor DC, *et al*. Multidetector CT angiography of the aortoiliac system and lower extremities: a prospective comparison with digital subtraction angiography. *AJR Am J Roentgenol* 2003; **180**:1085–91.

55. McDermott VG, Meakem TJ, Carpenter JP, Baum RA, Stolpen AH, Holland GA, *et al*. Magnetic resonance angiography of the distal lower extremity. *Clin Radiol* 1995;**50**:741–6.

56. Mergelsberg M, Brecht T, Christ F. [Diagnosis of arterial occlusive disease by ultrasonography]. *Dtsch Med Wochenschr* 1986;**111**:1055–8.

57. Portugaller HR, Schoellnast H, Hausegger KA, Tiesenhausen K, Amann W, Berghold A. Multislice spiral CT angiography in peripheral arterial occlusive disease: a valuable tool in detecting significant arterial lumen narrowing. *Eur Radiol* 2004;**14**:1681–7.

58. Puls R, Knollmann F, Werk M, Gebauer B, Gaffke G, Steinkamp H, *et al*. [Multi-slice spiral CT: 3D CT angiography for evaluating therapeutically relevant stenosis in peripheral arterial occlusive disease]. *Rontgenpraxis* 2002; **54**:141–7.

59. Rieker O, Duber C, Schmiedt W, von Zitzewitz H, Schweden F, Thelen M. Prospective comparison of CT angiography of the legs with intraarterial digital subtraction angiography. *AJR Am J Roentgenol* 1996;**166**:269–76.

60. Rieker O, Dueber C, Neufang A, Pitton M, Schweden F, Thelen M. CT angiography versus intraarterial digital subtraction angiography for assessment of aortoiliac occlusive disease. *AJR Am J Roentgenol* 1997;**169**:1133–8.

61. Schafer FK, Schafer PJ, Jahnke T, Walluscheck K, Priebe M, Hentsch A, *et al*. [First clinical results in a study of contrast enhanced magnetic resonance angiography with the 1.0 molar gadobutrol in peripheral arterial occlusive disease-comparison to intraarterial DSA]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2003;**175**:556–64.

62. Sensier Y, Hartshorne T, Thrush A, Handford H, Nydahl S, London NJ. The effect of adjacent segment disease on the accuracy of colour duplex scanning for the diagnosis of lower limb arterial disease. *Eur J Vasc Endovasc Surg* 1996;**12**:238–42.

63. Shaalan WE, French-Sherry E, Castilla M, Lozanski L, Bassiouny HS. Reliability of common femoral artery hemodynamics in assessing the severity of aortoiliac inflow disease. *J Vasc Surg* 2003;**37**:960–9.

64. Snidow JJ, Harris VJ, Trerotola SO, Cikrit DF, Lalka SG, Buckwalter KA, *et al*. Interpretations and treatment decisions based on MR angiography versus conventional arteriography in symptomatic lower extremity ischemia. *J Vasc Interv Radiol* 1995;**6**:595–603.

65. Snidow JJ, Johnson MS, Harris VJ, Margosian PM, Aisen AM, Lalka SG, *et al*. Three-dimensional gadolinium-enhanced MR angiography for aortoiliac inflow assessment plus renal artery screening in a single breath hold. *Radiology* 1996; **198**:725–32.

66. Steffens JC, Link J, Muller-Hulsbeck S, Freund M, Brinkmann G, Heller M. Cardiac-gated two-

dimensional phase-contrast MR angiography of lower extremity occlusive disease. *AJR Am J Roentgenol* 1997;**169**:749–54.

67. Steffens JC, Schafer FK, Oberscheid B, Link J, Jahnke T, Heller M, *et al*. Bolus-chasing contrast-enhanced 3D MRA of the lower extremity. Comparison with intraarterial DSA. *Acta Radiol* 2003;**44**:185–92.

68. Sueyoshi E, Sakamoto I, Matsuoka Y, Ogawa Y, Hayashi H, Hashmi R, *et al*. Aortoiliac and lower extremity arteries: comparison of three-dimensional dynamic contrast-enhanced subtraction MR angiography and conventional angiography. *Radiology* 1999;**210**:683–8.

69. Timonina EA, Sinitsin VE, Shiryaev AA, Levitsky IV, Akchurin RS, Ternovoy SK. The use of magnetic resonance angiography for assessment of stenotic and occlusive lesions of arteries of lower extremities in patients with intermittent claudication. *Kardiologiya* 1999; **39**:14–19.

70. Vavrik J, Rohrmoser GM, Madani B, Ersek M, Tscholakoff D, Bucek RA. Comparison of MR angiography versus digital subtraction angiography as a basis for planning treatment of lower limb occlusive disease. *J Endovasc Ther* 2004; **11**:294–301.

71. Whyman M, Gillespie I, Ruckley C, Allan P, Fowkes F. Screening patients with claudication from femoropopliteal disease before angioplasty using Doppler colour flow imaging. *Br J Surg* 1992;**79**:907–9.

72. Wilson YG, George JK, Wilkins DC, Ashley S. Duplex assessment of run-off before femorocrural reconstruction. *Br J Surg* 1997;**84**:1360–3.

73. Winterer JT, Laubenberger J, Scheffler K, Neumann K, Bayraktarli YR, Allmann KH, *et al*. Contrast-enhanced subtraction MR angiography in occlusive disease of the pelvic and lower limb arteries: results of a prospective intraindividual comparative study with digital subtraction angiography in 76 patients. *J Comput Assist Tomogr* 1999;**23**:583–9.

74. Yucel EK, Kaufman JA, Geller SC, Waltman AC. Atherosclerotic occlusive disease of the lower extremity: prospective evaluation with two-dimensional time-of-flight MR angiography. *Radiology* 1993;**187**:637–41.

75. Zeuchner J, Geitung JT, Lukes P, Gothlin JH. Angiography and color-flow duplex ultrasonography in the evaluation of peripheral ischemic occlusive arterial-disease. *Acta Radiol* 1994;**35**:270–4.

76. Zhang HL, Khilnani NM, Prince MR, Winchester PA, Golia P, Veit P, *et al*. Diagnostic accuracy of time-resolved 2D projection MR for symptomatic intrapopliteal arterial occlusive disease. *AJR Am J Roentgenol* 2005;**184**:938–47.

77. Koelemay MJ, Legemate DA, de Vos H, van Gurp AJ, Balm R, Reekers JA, *et al*. Duplex scanning allows selective use of arteriography in the management of patients with severe lower leg arterial disease. *J Vasc Surg* 2001;**34**:661–7.

78. Swan JS, Fryback DG, Lawrence WF, Katz DA, Heisey DM, Hagenauer ME, *et al*. MR and conventional angiography: work in progress toward assessing utility in radiology. *Acad Radiol* 1997;**4**:475–82.

79. Swan JS, Fryback DG, Lawrence WF, Sainfort F, Hagenauer ME, Heisey DM. A time-tradeoff method for cost-effectiveness models applied to radiology. *Med Decis Making* 2000;**20**:79–88.

80. Visser K, Bosch JL, Leiner T, van Engelshoven JM, Passchier J, Hunink MG. Patients' preferences for MR angiography and duplex US in the work-up of peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2003;**26**:537–43.

81. Willmann JK, Wildermuth S, Pfammatter T, Roos JE, Seifert B, Hilfiker PR, *et al*. Aortoiliac and renal arteries: prospective intraindividual comparison of contrast-enhanced three-dimensional MR angiography and multi-detector row CT angiography. *Radiology* 2003;**226**:798–811.

82. Adamis MK, Li W, Wielopolski PA, Kim D, Sax EJ, Kent KC, *et al*. Dynamic contrast-enhanced subtraction MR angiography of the lower extremities: initial evaluation with a multisection two-dimensional time-of-flight sequence. *Radiology* 1995;**196**:689–95.

83. Balzer JO, Loewe C, Davis K, Goyen M, Leiner T, Meaney JF, *et al*. Safety of contrast-enhanced MR angiography employing gadobutrol 1.0 M as contrast material. *Eur Radiol* 2003;**13**:2067–74.

84. Baum RA, Grist TM, Stillman AE, D'Agostino R, Bis KG, Malden ES. MR angiography using AngioMARK (MS-325), an intravascular blood pool contrast agent, in patients with peripheral vascular disease. *Radiology* 1999;**213P**:481.

85. Bezooijen R, Van Den Bosch HCM, Tielbeek AV, Thelissen GRP, Visser K, Hunink MGM, *et al*. Peripheral arterial disease: sensitivity-encoded multiposition MR angiography compared with intraarterial angiography and conventional multiposition MR angiography. *Radiology* 2004; **231**:263–71.

86. Fellner FA, Janka R, Fellner C, Wutke R, Lang W, Requardt M, *et al*. MR angiography of peripheral arteriosclerotic occlusive disease. In *High-tech Medicine, World Congress*, 2000, Hanover, Germany. Bologna: Monduzzi; 2000. pp. 323–6.

87. Glickerman DJ, Obregon RG, Schmiedl UP, Harrison SD, Macaulay SE, Simon HE, *et al*.

Cardiac-gated MR angiography of the entire lower extremity: a prospective comparison with conventional angiography. *AJR Am J Roentgenol* 1996;**167**:445–51.

88. Goyen M, Herborn CU, Vogt FM, Kroger K, Verhagen R, Yang F, *et al*. Using a 1 M Gd-chelate (gadobutrol) for total-body three-dimensional MR angiography: preliminary experience. *J Magn Reson Imaging* 2003;**17**:565–71.

89. Ho KY, de Haan MW, Oei TK, Koster D, Kessels AG, Janevski BK, *et al*. MR angiography of the iliac and upper femoral arteries using four different inflow techniques. *AJR Am J Roentgenol* 1997;**169**:45–53.

90. Hosten N, Puls R, Sahimbas O, Balzer J, Urbank A, Felix R. [Color Doppler ultrasonography in peripheral artery occlusive disease: continuous application of a signal enhancer]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1998;**169**:495–8.

91. Huber TS, Back MR, Ballinger RJ, Culp WC, Flynn TC, Kubilis PS, *et al*. Utility of magnetic resonance arteriography for distal lower extremity revascularization. *J Vasc Surg* 1997;**26**: 415–23.

92. Ishikawa M, Morimoto N, Sasajima T, Kubo Y. Three-dimensional computed tomographic angiography in lower extremity revascularization. *Surg Today* 1999;**29**:243–7.

93. Jakobsen JA, Berg KJ, Laerum F, Kendall B. The influence of iodinated contrast media on renal function, with special reference to iopentol. In Laerum F, editor. *Iopentol: clinical trials with a new non ionic contrast medium: Proceedings of the Nycomed Scientific Symposium*, 1989, Paris, France. Excerpta Medica; 1989. pp. 63–72.

94. Jones L, Pressdee DJ, Lamont PM, Baird RN, Murphy KP. A phase contrast (PC) rephase/dephase sequence of magnetic resonance angiography (MRA): a new technique for imaging distal run-off in the pre-operative evaluation of peripheral vascular disease. *Clin Radiol* 1998; **53**:333–7.

95. Krause UJ, Pabst T, Kenn W, Wittenberg G, Hahn D. Time-resolved contrast-enhanced magnetic resonance angiography of the lower extremity. *Angiology* 2004;**55**:119–25.

96. Kroencke TJ, Krause UJ, Klaus H, Taupitz M, Hamm BK. Contrast-enhanced magnetic resonance angiography with gadodiamide compared to digital subtraction angiography in the evaluation of peripheral arterial occlusive disease: a phase III multi-centre pilot study. *Radiology* 2001;**221**:454.

97. Loewe C, Cejna M, Lammer J, Thurnher SA. Contrast-enhanced magnetic resonance angiography in the evaluation of peripheral bypass grafts. *Eur Radiol* 2000;**10**:725–32.

98. London NJM, Nydahl S, Hartshorne T, Bolia A, Bell PRF, Fishwick G. Color-coded Doppler ultrasonography to diagnose and guide angioplasty of lower-limb arterial lesions. *Br J Surg* 1995;**82**:557.

99. Mohler ER. Results of four multicenter, phase III, magnetic resonance angiography (MRA) trials with MS-325, a blood pool contrast agent, for the detection of vascular disease in the aortoiliac, renal, and pedal regions. *J Am Coll Cardiol* 2004; **43**:352A.

100. Mulligan SA, Matsuda T, Lanzer P, Gross GM, Routh WD, Keller FS, *et al*. Peripheral arterial occlusive disease: prospective comparison of MR angiography and color duplex US with conventional angiography. *Radiology* 1991; **178**:695–700.

101. Perreault P, Edelman MA, Baum RA, Yucel EK, Weisskoff RM, Shamsi K, *et al*. MR angiography with gadofosveset trisodium for peripheral vascular disease: phase II trial. *Radiology* 2003; **229**:811–20.

102. Pesaresi A, Costarelli L, Valeri G, Lorenzoni A, Alborino S, Alo F. Gd-BOPTA enhanced MR angiography of peripheral arteries: comparison with DSA. *Radiology* 2000;**217**:132–3.

103. Roberts DA, Leung D, Solomon J, Sehgal M, Farner M, Baum R, *et al*. A prospective comparison of highly-optimized bolus-chase MRA with infrapopliteal 2D TOF MRA in patients with peripheral vascular disease. *Proceedings of the International Society for Magnetic Resonance in Medicine* 2000;**8**:1811.

104. Romano M, Amato B, Markabaoui K, Tamburrini O, Salvatore M. [Multidetector row computed tomographic angiography of the abdominal aorta and lower limbs arteries: a new diagnostic tool in patients with peripheral arterial occlusive disease]. *Minerva Cardioangiol* 2004; **52**:9–17.

105. Sarkar R, Ro KM, Obrand DI, Ahn SS. Lower extremity vascular reconstruction and endovascular surgery without preoperative angiography. *Am J Surg* 1998;**176**:203–7.

106. Swan JS, Kennell TW, Acher CW, Heisey DM, Grist TM, Korosec FR, *et al*. Magnetic resonance angiography of aorto-iliac disease. *Am J Surg* 2000; **180**:6–12.

107. Tins B, Oxtoby J, Patel S. Comparison of CT angiography with conventional arterial angiography in aortoiliac occlusive disease. *Br J Radiol* 2001;**74**:219–25.

108. Ubbink DT, Legemate DA, Llull JB. Color-flow duplex scanning of the leg arteries by use of a new echo-enhancing agent. *J Vasc Surg* 2002; **35**:392–6.

109. van der Zaag ES, Legemate DA, Nguyen T, Balm R, Jacobs MJ. Aortoiliac reconstructive surgery based upon the results of duplex scanning. *Eur J Vasc Endovasc Surg* 1998;**16**:383–9.

110. Vogt KC, Rasmussen JG, Skovgaard LT, Just S, Schroeder TV. Quantification of iliac artery stenoses: a methodological comparative study between intravascular ultrasound, arteriography and duplex scanning. *Ultrasound Med Biol* 1998; **24**:963–70.

111. Weishaupt D, Ruhm SG, Binkert CA, Schmidt M, Patak MA, Steybe F, *et al*. Equilibrium-phase MR angiography of the aortoiliac and renal arteries using a blood pool contrast agent. *AJR Am J Roentgenol* 2000;**175**:189–95.

112. Wikstrom J. On contrast-enhanced magnetic resonance angiography of the aortoiliac arteries. *Acta Radiol* 2001;**42** (Suppl):1–30.

113. Wikstrom J, Wasser MN, Pattynama PMT, Bonomo L, Hamm B, Del Maschio A, *et al*. Gadobenate dimeglumine-enhanced magnetic resonance angiography of the pelvic arteries. *Invest Radiol* 2003;**38**:504–15.

114. Wolff SD. Results of diagnostic trials of magnetic resonance angiography with MS-325, a blood pool contrast agent, for the detection of peripheral vascular disease in the aortoiliac region. *Am J Cardiol* 2002;**90**:TCT335.

115. Wolosker N, Nakano L, D'Hippolito G, Rosoky RA, Borri ML, Wolosker AM. Gadolinium magnetic angioresonance in the study of aortoiliac disease. *Angiology* 2003;**54**:163–8.

116. Wyttenbach R, Gianella S, Alerci M, Braghetti A, Cozzi L, Gallino A. Prospective blinded evaluation of Gd-DOTA- versus Gd-BOPTA-enhanced peripheral MR angiography, as compared with digital subtraction angiography. *Radiology* 2003; **227**:261–9.

117. Ito K, Kumazaki T. [Sequential gadolinium-enhanced magnetic resonance angiography of the aortoiliac and the femoropopliteal arteries with repetitive administration of low-dose contrast agent]. *J Nippon Med Sch* 2000;**67**:421–8.

118. Leiner T, Tordoir JHM, Kessels AGH, Nelemans PJ, Schurink GW, Kitslaar PJEHM, *et al*. Comparison of treatment plans for peripheral arterial disease made with multi-station contrast medium-enhanced magnetic resonance angiography and duplex ultrasound scanning. *J Vasc Surg* 2003; **37**:1255–62.

119. London NJM, Nydahl S, Hartshorne T, Fishwick G. Use of colour duplex imaging to diagnose and guide angioplasty of lower limb arterial lesions. *Br J Surg* 1999;**86**:911–15.

120. Walter F, Leyder B, Fays J, Bronner JF, Lehalle B, Blum A, *et al*. Intêrét de l'artério-scanner dans le bilan des artériopathies des membres inférieurs: étude préliminaire. *J Radiol* 2001;**82**:473–9.

121. Winterer JT, Strecker R, Lohrmann C, Schaefer O, Ghanem N, Bley T, *et al*. [Background suppression using magnetization preparation for contrast-enhanced 3D MR angiography of the pelvic and lower leg arteries]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2003;**175**:28–31.

122. Sam AD, Morasch MD, Collins J, Song G, Chen R, Pereles FS. Safety of gadolinium contrast enhanced angiography in patients with chronic renal insufficiency. *J Vasc Surg* 2003;**38**:313–18.

123. Krause U, Kroencke T, Spielhaupter E, Taupitz M, Kenn W, Hamm B, *et al*. Contrast-enhanced magnetic resonance angiography of the lower extremities: standard-dose vs. high-dose gadodiamide injection. *J Magn Reson Imaging* 2005;**21**:449–54.

124. Leiner T, Kessels AG, Schurink GW, Kitslaar PJ, de Haan MW, Tordoir JH, *et al*. Comparison of contrast-enhanced magnetic resonance angiography and digital subtraction angiography in patients with chronic critical ischemia and tissue loss. *Invest Radiol* 2004;**39**:435–44.

125. Romano M, Mainenti PP, Imbriaco M, Amato B, Markabaoui K, Tamburrini O, *et al*. Multidetector row CT angiography of the abdominal aorta and lower extremities in patients with peripheral arterial occlusive disease: diagnostic accuracy and interobserver agreement. *Eur J Radiol* 2004; **50**:303–8.

126. Geitung JT, Wikstrom T, Zeuchner J, Gothlin JH. Cost-effectiveness of colour duplex sonography compared with angiography of the pelvis and lower limb. *Eur Radiol* 1996;**6**:481–4.

127. Meindl T, Berger K, Knollmann F, Zurbrugg H, Maurer J. [Cost–utility analysis of contrast-enhanced MR angiography with automated table-translation for diagnosis and therapy planning in patients with peripheral vascular disease]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2003; **175**:981–90.

128. Visser K, de Vries SO, Kitslaar PJEHM, van Engelshoven JMA, Hunink MGM. Cost-effectiveness of diagnostic imaging work-up and treatment for patients with intermittent claudication in the Netherlands. *Eur J Vasc Endovasc Surg* 2003;**25**:213–23.

129. Visser K, Kuntz KM, Donaldson MC, Gazelle GS, Hunink MGM. Pretreatment imaging workup for patients with intermittent claudication: a cost-effectiveness analysis. *J Vasc Interv Radiol* 2003; **14**:53–62.

130. Visser K, Kock MCJM, Kuntz KM, Donaldson MC, Gazelle GS, Hunink MGM. Cost-effectiveness targets for multi-detector row CT angiography in

the work-up of patients with intermittent claudication. *Radiology* 2003;**227**:647–56.

131. Yin D, Baum RA, Carpenter JP, Langlotz CP, Pentecost MJ. Cost-effectiveness of MR angiography in cases of limb-threatening peripheral vascular disease. *Radiology* 1995; **194**:757–64.

132. AbuRahma AF, Boland J, Diethrich EB. Correlation of the resting and exercise Doppler ankle/arm index to angiographic findings. *Angiology* 1980;**31**:331–6.

133. AbuRahma A, Robinson P, Boland J. Complications of arteriography in a recent series of 707 cases: factors affecting outcome. *Ann Vasc Surg* 1993;**7**:122–9.

134. Adriaensen ME, Kock MC, Stijnen T, Van Sambeek MR, Pattynama PM, Hunink MG. Diagnostic and therapeutic impact of CT angiography compared with digital subtraction angiography for peripheral arterial disease. *Radiology* 2002;**225**:157.

135. Adriaensen ME, Kock MC, Stijnen T, van Sambeek MR, van Urk H, Pattynama PM, *et al*. Peripheral arterial disease: therapeutic confidence of CT versus digital subtraction angiography and effects on additional imaging recommendations. *Radiology* 2004;**233**:385–91.

136. Agadzhanova LP. Doppler ultrasonography in the diagnosis of diseases of the lower limb vessels. *Vestn Akad Med Nauk SSSR* 1986;**2**:83–9.

137. Alexander K, Hundeshagen H, Heintz P, Emter M, Wagner HH, Korfel A. [Preliminary clinical experience with noninvasive magnetic resonance angiography]. *Vasa* 1987;**20**:176.

138. Alexander JQ, Leos SM, Katz SG. Is duplex ultrasonography an effective single modality for the preoperative evaluation of peripheral vascular disease? *Am Surg* 2002;**68**:1107–10.

139. Allard L, Cloutier G, Durand L, Roederer G, Langlois Y. Limitations of ultrasonic duplex scanning for diagnosing lower limb arterial stenoses in the presence of adjacent segment disease. *J Vasc Surg* 1994;**19**:650–7.

140. Allard L, Cloutier G, Durand LG. Évaluation par écho-Doppler duplex des stenoses artérielles des membres inférieurs en presence de lesions étagees. *Arteres Veines* 1996;**15**:51–60.

141. Allard L, Cloutier G, Guo Z, Durand L-G. Review of the assessment of single level and multilevel arterial occlusive disease in lower limbs by duplex ultrasound. *Ultrasound Med Biol* 1999;**25**:495–502.

142. Alson MD, Lang EV, Kaufman JA. Pedal arterial imaging. *J Vasc Interv Radiol* 1997;**8**:9–18.

143. Aly S, Jenkins MP, Zaidi FH, Coleridge Smith PD, Bishop CC. Duplex scanning and effect of multisegmental arterial disease on its accuracy in lower limb arteries. *Eur J Vasc Endovasc Surg* 1998; **16**:345–9.

144. Aly S, Sommerville K, Adiseshiah M, Raphael M, Coleridge Smith PD, Bishop CC. Comparison of duplex imaging and arteriography in the evaluation of lower limb arteries. *Br J Surg* 1998; **85**:1099–102.

145. Aly S, Shoab S, Bishop C. Inter-observer variation. An alternative method of assessing the role of ultrasonic imaging in clinical decision-making in lower limb arterial disease. *Int Angiol* 1999; **18**:220–4.

146. Amano Y, Gemma K, Kawamata H, Kumazaki T. Fat-suppressed gadolinium-enhanced three-dimensional magnetic resonance angiography adequately depicts the status of iliac arteries following atherectomy and stent placement. *Cardiovasc Intervent Radiol* 1998;**21**:345–7.

147. Amendt K, Schoemig A, Wilhelm C, Hsu E, Weiss T, Diehm C, *et al*. [Intravascular ultrasound (IVUS) in patients with peripheral arterial occlusive disease (PAOD)]. *Vasa* 1992;**21**:27–38.

148. Andres A, Revilla Y, Ramos A, Gonzalez E, Vereda MS, Praga M, *et al*. Helical computed tomography angiography is the most efficient test to assess vascular calcifications in the iliac arterial sector in renal transplant candidates. *Transplant Proc* 2003;**35**:1682–3.

149. Andrew E, Sveen K, Lambrecths M, Lillevold PE, Laerum F, Kendall B. Total iopentol profile. Overall results from clinical trials. In Laerum F, editor. *Iopentol: clinical trials with a new non ionic contrast medium: Proceedings of the Nycomed Scientific Symposium*; 1989. Paris, France. Excerpta Medica; 1989. pp. 189–97.

150. Archie JPJ, Feldtman RW. Determination of the hemodynamic significance of iliac artery stenosis by noninvasive doppler ultrasonography. *Surgery* 1982;**91**:419–24.

151. Aronow WS. Management of peripheral arterial disease. *Cardiol Rev* 2005;**13**:61–8.

152. Ascher E, Mazzariol F, Hingorani A, Salles-Cunha S, Gade P. The use of duplex ultrasound arterial mapping as an alternative to conventional arteriography for primary and secondary infrapopliteal bypasses. *Am J Surg* 1999; **178**:162–5.

153. Ascher E, Hingorani A, Markevich N, Costa T, Kallakuri S, Khanimoy Y. Lower extremity revascularisation without preoperative contrast arteriography: experience with duplex ultrasound arterial mapping in 485 cases. *Ann Vasc Surg* 2002; **16**:108–14.

154. Ascher E, Hingorani A, Markevich N, Schutzer R, Kallakuri S. Acute lower limb ischemia: the value

of duplex ultrasound arterial mapping (DUAM) as the sole preoperative imaging technique. *Ann Vasc Surg* 2003;**17**:284–9.

155. Auerbach EG, Martin ET. Magnetic resonance imaging of the peripheral vasculature. *Am Heart J* 2004;**148**:755–63.

156. Avenarius JK, Breek JC, Lampmann LE, van Berge Henegouwen DP, Hamming JF. The additional value of angiography after colour-coded duplex on decision making in patients with critical limb ischaemia. A prospective study. *Eur J Vasc Endovasc Surg* 2002;**23**:393–7.

157. Bagi P, Sillesen H, Bitsch K, Hansen H. Doppler waveform analysis in evaluation of occlusive arterial disease in the lower limb: comparison with distal blood pressure measurement and arteriography. *Eur J Vasc Surg* 1990;**4**:305–11.

158. Baker ML, Dairymple GV. Biological effects of diagnostic ultrasound: a review. *Radiology* 1978; **126**:479–83.

159. Baker A, Prytherch D, Evans D, Bell P. Doppler ultrasound assessment of the femoro-popliteal segment: comparison of different methods using ROC curve analysis. *Ultrasound Med Biol* 1986; **12**:473–82.

160. Balas P, Strano A, Novo S. Panarterial ultrasonography: a non invasive evaluation of the peripheral arterial system. *Adv Vasc Pathol* 1989; **1**:9–12.

161. Balas P, Pangratis N. [Panarterial ultrasonography: noninvasive evaluation of the peripheral arterial system]. *Grud Serdechnososudistaia Khir* 1990; **11**:43–4.

162. Balas P, Pangratis N. Panarterial ultrasonography. A noninvasive evaluation of the peripheral arterial system. *Int Angiol* 1990;**9**:4–7.

163. Balbarini A, Petronio AS, Buttitta F, Baglini R, Limbruno U, Biadi O, *et al*. Intravascular ultrasound: clinical applications. *Cardiovasc Imag* 1995;**7**:123–31.

164. Balzer JO, Davis K, Vahldiek G, Vogl TJ. Contrast enhanced MRA (CE-MRA) for treatment planning and follow-up in peripheral arterial occlusive disease. Part I. *Imaging Decisions* 2000; **4**:2–14.

165. Balzer JO, Herzog C, Thalhammer C, Pira A, Engelmann KS, Vogl TJ. Multidetector CT angiography in the evaluation of peripheral arterial occlusive disease. *Radiology* 2000;**217**:593.

166. Balzer JO, Mack MG, Thalhammer C, Pira A, Hammerstingl RM, Vogl TJ. The role of contrast enhanced MR angiography in treatment planning and follow-up of peripheral arterial occlusive disease: comparison to CT angiography and DSA findings. *Radiology* 2000;**217**:238.

167. Barnes RW, Slaymaker EE, Hahn FJY. Thromboembolic complications of angiography for peripheral arterial disease: prospective assessment by doppler ultrasound. *Radiology* 1977; **122**:459–61.

168. Barnes RW. Noninvasive diagnostic techniques in peripheral vascular disease. *Am Heart J* 1979; **97**:241–58.

169. Barrett BJ, Parfrey PS, McDonald JR, Hefferton DM, Reddy ER, McManamon PJ. Nonionic low-osmolality versus ionic high-osmolality contrast material for intravenous use in patients perceived to be at high risk: randomized trial. *Radiology* 1992;**183**:105–10.

170. Barretto S, Ballman KV, Rooke TW, Kullo IJ. Early-onset peripheral arterial occlusive disease: clinical features and determinants of disease severity and location. *Vasc Med* 2003;**8**:95–100.

171. Bashir R, Cooper CJ. Evaluation and medical treatment of peripheral arterial disease. *Curr Opin Cardiol* 2003;**18**:436–43.

172. Battino A. [Doppler echography and the diagnosis of popliteal arterial occlusion]. *J Mal Vasc* 1996; **21**:213–14.

173. Baum RA, Owen R, Carpenter JP, Holland GA, Kressel HY, Cope C. MR angiography of the peripheral vascular system: comparison with conventional angiography. *Radiology* 1992;**185**:133.

174. Baum RA, Owen R, Carpenter JP, Perloff LJ. Peripheral vascular diagnosis with magnetic-resonance angiography. *Circulation* 1992;**86**:I-243.

175. Baum R, Holland G, Carpenter J, Pentecost M, Cope C. MR angiography as the primary imaging approach to the patient with symptomatic peripheral ischemia. *J Vasc Interv Radiol* 1994; **194**:14.

176. Baum RA. Peripheral vascular diagnosis using magnetic resonance angiography. *Semin Interv Radiol* 1998;**15**:135–48.

177. Baumgartner I, Maier SE, Koch M, Schneider E, Vonschulthess GK, Bollinger A. [Magnetic-resonance arteriography, duplex sonography and conventional arteriography for evaluating peripheral arterial occlusive disease]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1993;**159**:167–73.

178. Baumgartner I, Schainfeld R, Graziani L. Management of peripheral vascular disease. *Annu Rev Med* 2005;**56**:249–72.

179. Baun J. Practical arterial evaluation of the lower extremity. *Journal of Diagnostic Medical Sonography* 2004;**20**:5–14.

180. Becker CR, Wintersperger B, Jakobs TF. Multi-detector-row CT angiography of peripheral arteries. *Semin Ultrasound CT MR* 2003;**24**:268–79.

181. Belch JJF, Topol EJ, Agnelli G, Bertrand M, Califf RM, Clement DL, *et al*. Critical issues in peripheral arterial disease detection and management: a call to action. *Arch Intern Med* 2003;**163**:884–92.

182. Bendib K, Berthezene Y, Croisille P, Villard J, Douek PC. Assessment of complicated arterial bypass grafts: value of contrast-enhanced subtraction magnetic resonance angiography. *J Vasc Surg* 1997;**26**:1036–42.

183. Bendib K, Vaudoux M, Croisille P, Berthezene Y, Douek P. 3D gadolinium-enhanced subtraction MR imaging angiography of the lower limb arteries compared to X-ray angiography for evaluation of vascular occlusive disease. *Radiology* 1997;**205**:463.

184. Bendick PJ, Bove PG, Long GW, Zelenock GB, Brown OW, Shanley CJ. Efficacy of ultrasound scan contrast agents in the noninvasive follow-up of aortic stent grafts. *J Vasc Surg* 2003;**37**:381–5.

185. Benhamou AC, Dadon M, Emmerich J, Fontaine P, Got I, Guillausseau PJ, *et al*. Lower limb arteriopathy in the diabetic patient. *Diabetes Metab* 1997;**23**:541–8.

186. Beregi J-P, Djabbari M, Desmoucelle F, Willoteaux S, Wattinne L, Louvegny S. Popliteal vascular disease: evaluation with spiral CT angiography. *Radiology* 1997;**203**:477–83.

187. Bertschinger K, Ruehm SG, Cassina P, Hany TF, Debatin JF. Peripheral arterial bypass grafts: three-dimensional MR angiography vs DSA. *Radiology* 1999;**213P**:480.

188. Bertschinger K, Cassina PC, Debatin JF, Ruehm SG. Surveillance of peripheral arterial bypass grafts with three-dimensional MR angiography: comparison with digital subtraction angiography. *AJR Am J Roentgenol* 2001;**176**:215–20.

189. Bettmann MA, Heeren T, Greenfield A, Goudey C. Adverse events with radiographic contrast agents: results of the SCVIR Contrast Agent Registry. *Radiology* 1997;**203**:611–20.

190. Binkert CA, Baker PD, Petersen BD, Szumowski J, Kaufman JA. Peripheral vascular disease: blinded study of dedicated calf MR angiography versus standard bolus-chase MR angiography and film hard-copy angiography. *Radiology* 2004;**232**:860–6.

191. Bizzini Pezzetta G, Depairon M, von Segesser L, Hayoz D. [Vascular surveillance after peripheral artery interventions]. *Schweiz Med Wochenschr* 1999; **129**:413–19.

192. Bluemke D, Chambers T. Spiral CT angiography: an alternative to conventional angiography. *Radiology* 1995;**195**:317–39.

193. Boos M, Schlegel E, Cramer BM. [Magnitude contrast angiography in peripheral occlusive vascular-disease of the lower-limbs]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1995;**163**:45–52.

194. Borrello JA. MR angiography versus conventional X-ray angiography in the lower extremities: everyone wins. *Radiology* 1993; **187**:615–17.

195. Bostrom A, Ljungman C, Hellberg A, Logason K, Barlin T, Ostholm G, *et al*. Duplex scanning as the sole preoperative imaging method for infrainguinal arterial surgery. *Eur J Vasc Endovasc Surg* 2002;**23**:140–5.

196. Bostrom-Ardin A, Karacagil S, Hellberg A, Ljungman C, Logason K, Ostholm G. Surgical reconstruction without preoperative angiography in patients with aortoiliac occlusive disease. *Ann Vasc Surg* 2002;**16**:273–8.

197. Bostrom-Ardin A, Lofberg AM, Hellberg A, Andren B, Ljungman C, Logason K, *et al*. Selection of patients with infrainguinal arterial occlusive disease for percutaneous transluminal angioplasty with duplex scanning. *Acta Radiol* 2002;**43**:391–5.

198. Bourlet P, De Fraissinnette B, Garcier JM, Lipiecka E, Privat C, Ravel A, *et al*. [Comparative assessment of helical CT-angiography, 2D TOF MR-angiography and 3D gadolinium enhanced MRA in aorto-iliac occlusive disease]. *J Radiol* 2000;**81**:1619–25.

199. Brillet PY, Tassart M, Bazot M, Le Blanche AF, Allaire E, Boudghene F. [Investigation of peripheral vascular bed in critical lower limb ischemia: comparative study between arteriography and magnetic resonance angiography]. *J Mal Vasc* 2001;**26**:31–8.

200. Brillet PY, Vayssairat M, Tassart M, Deux JF, Bazot M, Allaire E, *et al*. Gadolinium-enhanced MR angiography as first-line preoperative imaging in high-risk patients with lower limb ischemia. *J Vasc Interv Radiol* 2003;**14**:1139–45.

201. Brismar J, Jacobsson BF, Jorulf H. Miscellaneous adverse effects of low-versus high-osmolality contrast media: a study revised. *Radiology* 1991; **179**:19–22.

202. Brummett RE, Talbot JM, Charuhas P. Potential hearing loss resulting from MR imaging. *Radiology* 1988;**169**:539–40.

203. Bruninx G, Salame H, Wery D, Delcour C. [Doppler study of gluteal arteries. A useful tool for excluding gluteal arterial pathology and an important adjunct to lower limb Doppler studies]. *J Mal Vasc* 2002;**27**:12–17.

204. Bulynin VI, Martem'Yanov SV, Esipenko VV, Kazanskii VN. Potential benefits of Doppler ultrasonography in the diagnosis of occlusive aorto-iliac diseases. *Kardiologiya* 1989;**29**:96–8.

205. Busch H, Hoffmann H, Metzner C, Oettinger W. MR angiographie der unteren extremitaten mit automatischer Tischverschiebung (MobiTrak) im Vergleich zur i.a. DSA [MR angiography of the lower extremities with an automatic table translation (Mobitrak) compared to i.a. DSA]. *Fortschr Rontgensr* 1999;**170**:275–83.

206. Busch HP, Hoffmann HG, Rock J, Schneider C. [MR angiography of pelvic and leg vessels with automatic table movement technique ('Mobi-Trak') – clinical experience with 450 studies]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2001;**173**:405–9.

207. Cairols MA, Marti X, Vila R, Ballon-Carazas H. [Value and limitations of Doppler mapping in the management of ischemic patients]. *Angiologia* 2003;**55**:S112–24.

208. Calligaro KD, Musser DJ, Chen AY, Dougherty MJ, McAffee-Bennett S, Doerr KJ, *et al*. Duplex ultrasonography to diagnose failing arterial prosthetic grafts. *Surgery* 1996;**120**:455–9.

209. Cambria RP, Yucel EK, Brewster DC, L'Italien G, Gertler JP, LaMuraglia GM, *et al*. The potential for lower extremity revascularization without contrast arteriography: experience with magnetic resonance angiography. *J Vasc Surg* 1993;**17**:1050–6.

210. Cambria RP, Kaufman JA, L'Italien GJ, Gertler JP, LaMuraglia GM, Brewster DC, *et al*. Magnetic resonance angiography in the management of lower extremity arterial occlusive disease: a prospective study. *J Vasc Surg* 1997;**25**:380–9.

211. Campbell W, Fletcher E, Hands L. Assessment of the distal lower limb arteries: a comparison of arteriography and Doppler ultrasound. *Ann R Coll Surg Engl* 1986;**68**:37–9.

212. Cappelli R, Bicchi M, Arrigucci S, Boschi S, Guerrini M, Forconi S. [Critical leg ischemia in elderly patients: evaluation of two different Iloprost treatments on the efficacy, tolerance, change in the quality of life and in self-sufficiency]. *Minerva Cardioangiol* 1999;**47**:81–8.

213. Caputo GR, Masui T, Gooding GAW, Chang JM, Higgins CB. Popliteal and tibioperoneal arteries: feasibility of two-dimensional time-of-flight MR angiography and phase velocity mapping. *Radiology* 1992;**182**:387–92.

214. Caputo GR, Higgins CB. Magnetic resonance angiography and measurement of blood flow in the peripheral vessels. *Invest Radiol* 1992; **27**:S97–102.

215. Carpenter JP, Owen RS, Baum RA, Cope C, Barker CF, Berkowitz HD, *et al*. Magnetic-resonance angiography of peripheral runoff vessels. *J Vasc Surg* 1992;**16**:807–15.

216. Carpenter JP, Baum RA, Holland GA, Barker CF, Wilkerson D, O'Donnell TF, *et al*. Peripheral vascular-surgery with magnetic-resonance angiography as the sole preoperative imaging modality. *J Vasc Surg* 1994;**20**:861–71.

217. Carpenter JP, Owen RS, Holland GA, Baum RA, Barker CF, Perloff LJ, *et al*. Magnetic resonance angiography of the aorta, iliac, and femoral arteries. *Surgery* 1994;**116**:17–23.

218. Carpenter JP. Noninvasive assessment of peripheral vascular occlusive disease. *Adv Skin Wound Care* 2000;**13**:84–5.

219. Carriero A, Gatta S, Baratto M, Marano R, Aulisa R, Bonomo L. [Angiography compared to high resolution magnetic resonance and digital angiography in atherosclerosis of the iliac-femoral arteries]. *Radiol Med (Torino)* 1998; **95**:165–9.

220. Carriero A, Maggialetti A, Pinto D, Salcuni M, Mansour M, Petronelli S, *et al*. Contrast-enhanced magnetic resonance angiography MoBI-trak in the study of peripheral vascular disease. *Cardiovasc Intervent Radiol* 2002;**25**:42–7.

221. Caster J, Cummings C, Moneta G, Taylor L, Porter J. Accuracy of tibial artery duplex mapping. *J Vasc Technol* 1992;**16**:63–8.

222. Catalano C, Fraioli F, Bezzi M, Laghi A, Napoli A, Pediconi F. Multi-slice spiral CT angiography in the evaluation of patients with peripheral arterial disease. *Radiology* 2001;**221**:454.

223. Catalano C, Napoli A, Fraioli F, Venditti F, Votta V, Passariello R. Multidetector-row CT angiography of the infrarenal aortic and lower extremities arterial disease. *Eur Radiol* 2003;**13**:M88–93.

224. Cherro A, Alegroni P, Grinfeld D, Ferrari P, Solerno R, Gagliardi J, *et al*. Angiografía por resonancia magnética con gadolinio versus angiografía convencional en diagnóstico de vasculopatía de miembros inferiores [Gadolinium enhanced magnetic resonance angiography versus conventional angiography for lower extremity arterial disease diagnostic]. *Rev Argent Cardiol* 2004;**72**:356–60.

225. Cochran ST, Bomyea K, Sayre JW. Trends in adverse events after IV administration of contrast media. *AJR Am J Roentgenol* 2001;**176**:1385–8.

226. Coenegrachts K, Rigauts H, De Letter J. Prediction of aortoiliac stent graft length: comparison of a semiautomated computed tomography angiography method and calibrated aortography. *J Comput Assist Tomogr* 2003;**27**:284–8.

227. Coffi SB, Ubbink DT, Zwiers I, van Gurp JAM, Legemate DA. Improved assessment of the hemodynamic significance of borderline iliac stenoses with use of hyperemic duplex scanning. *J Vasc Surg* 2002;**36**:575–80.

228. Coffi SB, Ubbink DT, Zwiers I, van Gurp JAM, Hanson D, Legemate DA. Contrast-enhanced

duplex scanning of criral arteries by means of continuous infusion of Levovist. *J Vasc Surg* 2004; **39**:517–22.

229. Collier P, Wilcox G, Brooks D. Improved patient selection for angioplasty utilizing color Doppler imaging. *Am J Surg* 1990;**160**:171–4.

230. Comel S, Douek P, Moulin P, Vaudoux M, Marelund B. Contrast-enhanced MR angiography of the foot: anatomy and clinical application in patients with diabetes. *AJR Am J Roentgenol* 2004; **182**:1435–42.

231. Correas JM, Boespflug O, Hamida K, El Rody F, Melki P, Helenon O, *et al*. Doppler ultrasonography of peripheral vascular disease: the potential for ultrasound contrast agents. Multiple perspectives in MR contrast. *J Comput Assist Tomogr* 1999;**23**:S119–27.

232. Cossman DV, Ellison JE, Wagner WH, Carroll RM, Treiman RL, Foran RF, *et al*. Comparison of contrast arteriography to arterial mapping with color-flow duplex imaging in the lower extremities. *J Vasc Surg* 1989;**10**:522–9.

233. Cotroneo AR, Manfredi R, Settecasi C, Prudenzano R, Di Stasi C. Angiography and MR-angiography in the diagnosis of peripheral arterial occlusive disease in diabetic patients. *Rays* 1997; **22**:579–90.

234. Cramer BM, Schlegel E, Boos M, Laub G. MR angiography of vessels in the pelvic region and the lower extremities for occlusive arterial disease. *Electromedica* 1990;**58**:89–98.

235. Cruz C, Hricak H, Samhouri F, Smith RF, Eyler WR, Levin NW. Contrast media for angiography: effect on renal function. *Radiology* 1986;**158**:109–12.

236. Currie I, Wilson Y, Baird R, Lamont P. Postocclusive hyperaemic duplex scan: a new method of aortoiliac assessment. *Br J Surg* 1995; **82**:1226–9.

237. Currie IC, Wilson YG, Baird RN, Lamont PM. Treatment of intermittent claudication: the impact on quality of life. *Eur J Vasc Endovasc Surg* 1995; **10**:356–61.

238. Davis CP, Schopke WD, Seifert B, Schneider E, Pfammatter T, Debatin JF. MR angiography of patients with peripheral arterial disease before and after transluminal angioplasty. *AJR Am J Roentgenol* 1997;**168**:1027–34.

239. De Backer TL, Duprezb DA, Clement DL. [Peripheral vascular disease in diabetes mellitus. Non-invasive diagnosis]. *Tijdschr Geneeskd* 2000; **56**:807–12.

240. De Benito-Fernandez L, Bueno-Bertomeu A, Utrilla-Fernandez F, Fernandez-Heredero A, Ros-Vidal R, Acin-Garcia F. [The use of Doppler ultrasound to evaluate the aortoiliac region. A comparison with arteriography]. *Angiologia* 2004;**56**:17–28.

241. De Cobelli FA, Vanzulli A, Scifo P, Brasca L, Venturini M, Del Maschio A. Evaluation of aortoiliac and lower extremities arteries with automatically moving-bed infusion-tracking 3D dynamic gadolinium-enhanced MR angiography (MRA). *Radiology* 1999;**213P**:480.

242. Dehaut S, Ditschuneit HH, Kratzer W. Perfusion measurements with power-Doppler ultrasound in fine subcutaneous arterioles. *Int J Obes* 2000; **24**:S45.

243. Demolis P, Asmar R, Levy B, Manent PJ, Safar M. Étude non invasive de l'hémodynamique des artères péripheriques par Doppler pulse couple a l'échographie bidimensionnelle: étude préliminaire. *Arch Mal Coeur Vaiss* 1990;**83**:1335–41.

244. de Morais Filho D, Miranda F, Peres MJD, Barros N, Buriham E, Salles-Cunha SX. Segmental waveform analysis in the diagnosis of peripheral arterial occlusive diseases. *Ann Vasc Surg* 2004; **18**:714–24.

245. Depairon M. [Non-invasive methods for evaluation and follow-up of arteriopathy of the lower extremities]. *Rev Med Suisse Romande* 1998; **118**:833–7.

246. DeSouza N, King D, Pilgrim P, Bates P, Reidy J, Gosling R. Quickscan: Doppler ultrasound emulation of angiography – its value prior to arteriography in peripheral vascular disease. *Br J Radiol* 1991;**64**:479–84.

247. de Vries SO, Hunink MG, Polak JF. Summary receiver operating characteristic curves as a technique for meta-analysis of the diagnostic performance of duplex ultrasonography in peripheral arterial disease. *Acad Radiol* 1996; **3**:361–9.

248. Di Cesare E, Giordano AV, Santarelli B, Cariello G, Marsili L, Barile A, *et al*. [MR-angiography with contrast bolus vs digital angiography in peripheral arterial occlusive disease of the legs]. *Radiol Med (Torino)* 2001;**102**:55–61.

249. Diaz LP, Pabon IP, Garcia JA, Lopez MAdlC. Assessment of CO_2 arteriography in arterial occlusive disease of the lower extremities. *J Vasc Interv Radiol* 2000;**11**:163–9.

250. Dorenbeck U, Seitz J, Volk M, Strotzer M, Lenhart M, Feuerbach S, *et al*. Evaluation of arterial bypass grafts of the pelvic and lower extremities with gadolinium-enhanced magnetic resonance angiography: comparison with digital subtraction angiography. *Invest Radiol* 2002; **37**:60–4.

251. Dorweiler B, Neufang A, Kreitner K-F, Schmiedt W, Oelert H. Magnetic resonance angiography

unmasks reliable target vessels for pedal bypass grafting in patients with diabetes mellitus. *J Vasc Surg* 2002;**35**:766–72.

252. Douek PC, Revel D, Chazel S, Falise B, Villard J, Amiel M. Fast MR angiography of the aortoiliac arteries and arteries of the lower extremity: value of bolus-enhanced, whole-volume subtraction technique. *AJR Am J Roentgenol* 1995;**165**:431–7.

253. Drugova B, Puchmayer V, Zapletalova J, Krivanek J. [Comparison of arteriography of the lower extremities with noninvasive angiological methods]. *Ceska Radiologie* 1981;**35**:15–23.

254. Duncan G, Wilson JA, Maclennan WJ. Prevalence and diagnosis of peripheral vascular disease in elderly people living at home. *Journal of Clinical Experimental Gerontology* 1990;**12**:229–40.

255. Dunne AP, Grant EG, Richardson JD, Walsh DB. Duplex ultrasound of the femoral artery and other selected vessels a retrospective study. *Radiology* 1984;**153**:297.

256. Dyet JF, Nicholson AA, Ettles DFE. Vascular imaging and intervention in peripheral arteries in the diabetic patient. *Diabetes Metab Res Rev* 2000; **16**:S16–22.

257. Earls JP, Patel NH, Smith PA, Desena S, Meissner MH. Gadolinium-enhanced three-dimensional MR angiography of the aorta and peripheral arteries: evaluation of a multistation examination using two gadopentetate dimeglumine infusions. *AJR Am J Roentgenol* 1998;**171**:599–604.

258. Earls JP, Desena S, Bluemke DA. Gadolinium-enhanced three-dimensional MR angiography of the entire aorta and iliac arteries with dynamic manual table translation. *Radiology* 1998;**209**:844–9.

259. Ebner C, Gschwendtner M, Dobetsberger E, Zeidler G, Bohmig HJ, Nesser HJ. [Combined duplex/color Doppler sonography in the evaluation of the intervention result in peripheral arteries]. *Vasa* 1992;**21**:26.

260. Edwards J, Coldell D, Goldman M, Strandness D. The role of duplex scanning in the selection of patients for transluminal angioplasty. *J Vasc Surg* 1991;**13**:69–74.

261. Edwards AJ, Wells IP, Roobottom CA. Multidetector row CT angiography of the lower limb arteries: a prospective comparison of volume-rendered techniques and intra-arterial digital subtraction angiography. *Clin Radiol* 2005;**60**:85–95.

262. Eiberg JP, Lundorf E, Thomsen C, Schroeder TV. Peripheral vascular surgery and magnetic resonance arteriography – a review. *Eur J Vasc Endovasc Surg* 2001;**22**:396–402.

263. Eiberg JP, Lundorf E, Thomsen C, Schroeder TV. [Magnetic resonance arteriography in peripheral vascular surgery]. *Ugeskr Laeger* 2002;**164**:2490–4.

264. Eiberg JP, Madycki G, Hansen MA, Christiansen S, Gronvall Rasmussen JB, Schroeder TV. Ultrasound imaging of infrainguinal arterial disease has a high interobserver agreement. *Eur J Vasc Endovasc Surg* 2002;**24**:293–9.

265. Eiberg JP, Hansen MA, Jensen F, Gronvall Rasmussen JB, Schroeder TV. Ultrasound contrast-agent improves imaging of lower limb occlusive disease. *Eur J Vasc Endovasc Surg* 2003;**25**:23–8.

266. Ekelund L, Sjoeqvist L, Thuomas KA, Asberg B. MR angiography of abdominal and peripheral arteries: techniques and clinical applications. *Acta Radiol* 1996;**37**:3–13.

267. Eklof H, Smedby O, Ljungman C, Loefberg AM. MRA evaluation of lower leg arteries in patients with critical ischemia. *Cardiovasc Intervent Radiol* 1997;**20**:S75.

268. Eklof H, Smedby OE, Ljungman C, Karacagil S, Bergqvist D, Ahlstroem H. 2D inflow MR angiography in severe chronic leg ischemia. *Acta Radiol* 1998;**39**:663–8.

269. Elsharawy M, Elzayat E. A fast track arterial duplex ultrasound performed by vascular surgeons. Is the time now? *Int Angiol* 2002;**21**:374–8.

270. Elsman BH, Legemate DA, van der Heijden FH, de Vos HJ, Mali WP, Eikelboom BC. Impact of ultrasonographic duplex scanning on therapeutic decision making in lower-limb arterial disease. *Br J Surg* 1995;**82**:630–3.

271. Elsman BH, Legemate DA, van der Heyden FW, de Vos H, Mali WP, Eikelboom BC. The use of color-coded duplex scanning in the selection of patients with lower extremity arterial disease for percutaneous transluminal angioplasty: a prospective study. *Cardiovasc Intervent Radiol* 1996; **19**:313–16.

272. Elson JD, Raymond RA. Lower extremity ischemia: interventions to preserve quality of life. *Postgrad Med* 1994;**95**:96–108.

273. Engeler CE, Yedlicka JW, Letourneau JG, Castaneda-Zuniga WR, Hunter DW, Amplatz K. Intravascular sonography in the detection of arteriosclerosis and evaluation of vascular interventional procedures. *AJR Am J Roentgenol* 1991;**156**:1087–90.

274. Engelmann MG, Wintersberg B, Von Smekal A, Hofling B, Reiser M. Contrast enhanced 3 dimensional magnetic resonance angiography (MRA) of coronary bypass grafts: preliminary results of an angiographically controlled study. *Circulation* 1997;**96**:133.

275. Ernst RD, Kawashima A, Middlebrook MR, Tamm EP, Kramer LA, Sandler CM. Run-off MR angiography following a single injection of gadodiamide: evaluation of aortoiliac and peripheral arteries. *Radiology* 1998;**209P**:456–7.

276. Fauvel G, Chaillou P, Lescalie F, Patra P, Planchon B. [Evaluation of a computer graphic representation of echo-Doppler (Echotrace) in the assessment of atherosclerosis of the legs]. *J Mal Vasc* 1996;**21**:136–40.

277. Fellner F, Janka R, Fellner C, Lang W, Bautz W. Post occlusion visualization of peripheral arteries with 'floating table' MR angiography. *Magn Reson Imaging* 1999;**17**:1235.

278. Fischer-Colbrie W, Jogestrand T, Wiklund B, Calissendorff B. Duplex ultrasonographic vs angiographic measurements in short-term follow-up after percutaneous transluminal angioplasty. *J Vasc Invest* 1997;**3**:149–55.

279. Forster BB, Johnstone RD, Shannon HM, Machan LS, Whittall KP, Trepanier PJ, *et al*. Quantification of hemodynamic improvement after superficial femoral artery angioplasty by cine phase contrast MR angiography. *AJR Am J Roentgenol* 1999;**173**:1564–6.

280. Froelich JJ, Hoppe M, Nahrstedt C, Barth KH, Wagner HJ, Klose KJ. The precise determination of vascular lumen and stent diameters: correlation among calibrated angiography, intravascular ultrasound, and pressure-fixed specimens. *Cardiovasc Intervent Radiol* 1997;**20**:452–6.

281. Fronek A, Coel M, Bernstein EF. Quantitative ultrasonographic studies of lower extremity flow velocities in health and disease. *Circulation* 1976; **53**:957–60.

282. Fushimi H, Kubo M, Inoue T, Yamada Y, Matsuyama Y, Kameyama M. Peripheral vascular reactions to smoking – profound vasoconstriction by atherosclerosis. *Diabetes Res Clin Pract* 1998; **42**:29–34.

283. Fussl R, Stork T. [Symptoms, diagnosis and conservative treatment of peripheral arterial disease]. *Med Welt* 2001;**52**:74–9.

284. Gaylis H, Geiss LS, Gregg E, Engelgau MM, Ram RP, Eberhardt MS, *et al*. Diagnosis and treatment of peripheral arterial disease. *JAMA* 2002;**287**:313–16.

285. Georgiou D, Bleiweis MS, Brundage BH. Ultrafast computed tomography in the diagnosis of diseases of great vessels: peripheral vascular imaging. *Am J Card Imaging* 1993;**7**:120–7.

286. Gerritsen GP, Gussenhoven EJ, The SH, Pieterman H, van der Lugt A, Li W, *et al*. Intravascular ultrasonography before and after intervention: *in vivo* comparison with angiography. *J Vasc Surg* 1993;**18**:31–40.

287. Giannini M, Almeida Rollo H, Bonetti Yoshida W, Lastoria S, Moura R, de Abreu Maffei FH. Value of ultrasonographic contrast in duplex scanning of leg arteries. Comparison with conventional duplex scanning and arteriography. *Int Angiol* 2004; **23**:263–9.

288. Goldberg RM, Gianturco LE, Feldman L, Yucel EK. Prospective two institution trial of MR angiography versus x-ray angiography for peripheral vascular treatment planning. *Radiology* 1997;**205**:463.

289. Goldstein HA, Kashanian FK, Blumetti RF, Holyoak WL, Hugo FP, Blumenfield DM. Safety assessment of gadopentetate dimeglumine in US clinical trials. *Radiology* 1990;**174**:17–23.

290. Gooding GAW. Ultrasonography of the iliac arteries. *Radiology* 1980;**135**:161–3.

291. Gooding GAW, Perez S, Rapp JH, Krupski WC. Lower-extremity vascular grafts placed for peripheral vascular disease: prospective evaluation with duplex doppler sonography. *Radiology* 1991; **180**:379–86.

292. Gosling R, Dunbar G, King D. The quantitative analysis of occlusive peripheral arterial disease by a nonintrusive ultrasonic technique. *Angiology* 1971;**22**:52–5.

293. Goyen M, Ruehm SG, Debatin JF. MR-angiography: the role of contrast agents. *Eur J Radiol* 2000;**34**:247–56.

294. Goyen M, Heuser LJG. Improved peripheral MRA using multi-velocity-encoding phase contrast-enhanced MRA techniques. *Acta Radiol* 2000; **41**:139–41.

295. Goyen M, Quick HH, Debatin JF, Ladd ME, Barkhausen J, Herborn CU, *et al*. Whole-body three-dimensional MR angiography with a rolling table platform: initial clinical experience. *Radiology* 2002;**224**:270–7.

296. Goyen M, Ruehm SG, Debatin JF, Hagspiel KD, Matsumoto AH. MR angiography for assessment of peripheral vascular disease. *Radiol Clin North Am* 2002;**40**:835–46.

297. Goyen M, Debatin JF. Gadopentetate dimeglumine-enhanced three-dimensional MR-angiography: dosing, safety, and efficacy. *J Magn Reson Imaging* 2004;**19**:261–73.

298. Gregor M, Tombach B, Hentsch A, Reimer P. Peripheral run-off CE-MRA with a 1.0 molar gadolinium chelate (Gadovist) with intraarterial DSA comparison. *Acad Radiol* 2002;**9**:S398–400.

299. Hany TF, Schmidt M, Davis CP, Gohde SC, Debatin JF. Diagnostic impact of four postprocessing techniques in evaluating contrast-enhanced three-dimensional MR angiography. *AJR Am J Roentgenol* 1998;**170**:907–12.

300. Hartnell G. MR angiography compared with digital subtraction angiography. *AJR Am J Roentgenol* 2000;**175**:1188–9.

301. Haslam PJ, Thornton F, Lee MJ. A comparison of bolus chased 3D gadolinium enhanced MRA with conventional angiography in patients with

peripheral vascular disease: is MRA sufficient to plan therapy? *Cardiovasc Intervent Radiol* 1999; **22**:S88.

302. Hendrickx P, Roth U, Grunert JH. [Value of Doppler color ultrasonography in diagnosis of arterial occlusive disease of the lower extremity. A direct comparison with percutaneous angiography]. *Ultraschall Med* 1997;**18**:116–23.

303. Hentsch A, Aschauer MA, Balzer JO, Brossman J, Busch HP, Davis K, *et al*. Gadobutrol-enhanced moving-table magnetic resonance angiography in patients with peripheral vascular disease: a prospective, multi-center blinded comparison with digital subtraction angiography. *Eur Radiol* 2003; **13**:2103–14.

304. Hentsch A. Importance of CE-MRA in various body regions: comparison with i.a. DSA. *Eur Radiol* 2004;**14**:M8–11.

305. Herborn CU. Peripheral contrast-enhanced 3D MRA with 1.0 M gadobutrol. *Eur Radiol* 2004; **14**:M23–5.

306. Herborn CU, Goyen M, Quick HH, Bosk S, Massing S, Kroeger K, *et al*. Whole-body 3D MR angiography of patients with peripheral arterial occlusive disease. *AJR Am J Roentgenol* 2004; **182**:1427–34.

307. Herrington DM, Kim LS, Miller ME, Mitchell SE, Walford GD, Dobs AS. Visual and quantitative computerized assessment of disease severity on peripheral angiograms. *J Vasc Interv Radiol* 1994; **5**:595–602.

308. Hertz SM, Baum RA, Owen RS, Holland GA, Logan DR, Carpenter JP. Comparison of magnetic resonance angiography and contrast arteriography in peripheral arterial stenosis. *Am J Surg* 1993; **166**:112–16.

309. Hessel SJ, Adams DF, Abrams HL. Complications of angiography. *Radiology* 1981;**138**:273–81.

310. Hiatt WR, Jones DN. The role of hemodynamics and duplex ultrasound in the diagnosis of peripheral arterial disease. *Curr Opin Cardiol* 1992; **7**:805–10.

311. Hingorani A, Ascher E, Markevich N, Kallakuri S, Hou A, Schutzer R, *et al*. Magnetic resonance angiography versus duplex arteriography in patients undergoing lower extremity revascularization: which is the best replacement for contrast arteriography? *J Vasc Surg* 2004; **39**:717–22.

312. Hingorani A, Ascher E, Markevich N, Kallakuri S, Schutzer R, Yorkovich W, *et al*. A comparison of magnetic resonance angiography, contrast arteriography, and duplex arteriography for patients undergoing lower extremity revascularization. *Ann Vasc Surg* 2004;**18**:294–301.

313. Hirai N, Imakita S, Higashi M, Tanaka R, Naito H. Utility of multidetector-row CT angiography for the diagnosis of arterial occlusive disease of lower extremities. *Radiology* 2002;**225**:160–1.

314. Ho KY, DeHaan MW, Oei TK, Kitslaar P, VanEngelshoven JM. Cardiac-triggered time-of-flight MR angiography and nonsubtracted and subtracted gadolinium-enhanced MR angiography of the iliac arteries compared with conventional X-ray angiography. *Radiology* 1996;**201**:376.

315. Ho KY, Leiner T, DeHaan MW, Kessels AG, Kitslaar P, VanEngelshoven JM. Moving bed infusion tracking: a new MR angiographic technique for imaging the peripheral arteries. *Radiology* 1997;**205**:301.

316. Ho K, De Haan MW, Kessels AGH, Kitslaar P, Van Engelshoven JMA. Peripheral vascular tree stenoses: detection with subtracted and nonsubtracted MR angiography. *Radiology* 1998; **206**:673–81.

317. Ho KYJAM, Leiner T, De Haan Michiel W, Kessels Alfons GH, Kitslaar Peter JEHM, Van Engelshoven Joseph MA. Peripheral vascular tree stenoses: evaluation with moving-bed infusion-tracking MR angiography. *Radiology* 1998;**206**:683–92.

318. Ho VB, Corse WR, Bluemke DA. MR angiography of the abdominal aorta and peripheral vessels. *Radiol Clin North Am* 2003;**41**:115–44.

319. Ho CF, Wu MH, Wu HM, Chang CY, Chen MC, Chou TY. Comparison of auto-moving table contrast-enhanced 3-D MRA and iodinated contrast-enhanced DSA for evaluating the lower-extremity arteries. *J Chin Med Assoc* 2004;**67**:511–20.

320. Hobson IR, Berry SM, Katocs AS Jr, Marsters CE, O'Donnell JA, Jamil Z, *et al*. Real-time B-mode ultrasonography of the femoral arteries: comparison to contrast arteriography. *Am Surg* 1981;**47**:262–7.

321. Hofmann WJ, Forstner R, Kofler B, Binder K, Ugurluoglu A, Magometschnigg H. Pedal artery imaging: a comparison of selective digital subtraction angiography, contrast enhanced magnetic resonance angiography and duplex ultrasound. *Eur J Vasc Endovasc Surg* 2002; **24**:287–92.

322. Holder JC, Dairymple GV. Choosing a contrast material for aortofemoral runoff angiography. *Radiology* 1978;**128**:787–8.

323. Huber AM, Heuck AF, Helmberger TK, Billing A, Heiss M, Reiser MF. Contrast-enhanced MR angiography of the iliac and peripheral arteries: a dynamic measurement on three levels. *Radiology* 1999;**213P**:480.

324. Huber A, Heuck A, Baur A, Helmberger T, Waggershauser T, Billing A, *et al*. Dynamic contrast-enhanced MR angiography from the

distal aorta to the ankle joint with a step-by-step technique. *AJR Am J Roentgenol* 2000;**175**:1291–8.

325. Huber A, Scheidler J, Wintersperger B, Baur A, Schmidt M, Requardt M, *et al*. Moving-table MR angiography of the peripheral runoff vessels: comparison of body coil and dedicated phased array coil systems. *AJR Am J Roentgenol* 2003; **180**:1365–73.

326. Hudon G, Fagret D, Bourassa MG, Lesperance J. [Diagnostic use of directional Doppler ultrasound in the assessment of cerebral and peripheral vascular disease]. *Union Med Can* 1979; **108**:1215–22.

327. Huljev D, Rasic Z. [The role of color doppler sonography in the diagnosis of atherosclerotic changes in arteries of the lower extremities]. *Lijec Vjesn* 1994;**116**:198–204.

328. Humphries KN, Hames TK, Smith SWJ, Cannon VA. Quantitative assessment of the common femoral to popliteal arterial segment using continuous wave Doppler ultrasound. *Ultrasound Med Biol* 1980;**6**:99–105.

329. Huppert PE, Duda SH, Braunschweig R, Voelker W, Fenchel G, Claussen CD. [Transvenoese Sonographie peripherer arterieller Gefaesse. Erste klinische Ergebnisse]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1994;**160**:222–7.

330. Hussain ST, Smith RE, Wood RFM, Bland M. Observer variability in volumetric blood flow measurements in leg arteries using duplex ultrasound. *Ultrasound Med Biol* 1996;**22**:287–91.

331. Hynynen K, Chung AH, Colucci V, Jolesz FA. Potential adverse effects of high-intensity focused ultrasound exposure on blood vessels *in vivo*. *Ultrasound Med Biol* 1996;**22**:193–201.

332. Illescas FF, Baker ME, McCann R, Cohan RH, Silverman PM, Dunnick NR. CT evaluation of retroperitoneal hemorrhage associated with femoral arteriography. *AJR Am J Roentgenol* 1986; **146**:1289–92.

333. Inoue Y, Iwai T, Endo M. Color Doppler ultrasonography in peripheral arteries. *Respiration and Circulation* 1994;**42**:1055–60.

334. Ito K, Kato J, Okada S, Tajima N, Hosaka J, Kumazaki T. 3D contrast MR angiography of lower extremity: additional imaging with subtraction. *Nippon Acta Radiol* 1996;**56**:66–7.

335. Jacobovicz C, Timi JRR, França LHG, Júnior S, Jorge H, Nakahara J. Avaliação do eco-Doppler na predição da necessidade de arteriografia do território aorto-ilíaco em pacientes submetidos a revascularização arterial infra-inguinal [Evaluation of the accuracy of Doppler ultrasonography to rule out the need for aortoiliac arteriography before infrainguinal arterial reconstruction]. *Journal Vascular Brasileiro* 2004;**3**:5–12.

336. Jacobs JE, Birnbaum BA, Langlotz CP. Contrast media reactions and extravasation: relationship to intravenous injection rates. *Radiology* 1998; **209**:411–16.

337. Jager K, Phillips D, Martin R. Noninvasive mapping of lower limb arterial lesions. *Ultrasound Med Biol* 1985;**11**:515–21.

338. Jager K, Eichlisberger R, Widmer LK. [Value of ultrasound in the diagnosis of peripheral vascular disease]. *Ther Umsch* 1989;**46**:204–12.

339. Janka R, Fellner FA, Fellner C, Requardt M, Lang W, Wutke R, *et al*. [Fully automated floating table MR angiography of pelvic and leg arteries: initial clinical results]. *Rontgenpraxis* 2001;**54**:62–70.

340. Janka R, Fellner C, Wenkel E, Lang W, Bautz W, Fellner FA. Contrast-enhanced MR angiography of peripheral arteries including pedal vessels at 1.0 T: feasibility study with dedicated peripheral angiography coil. *Radiology* 2005;**235**:319–26.

341. Jezic DV, Stonesifer GL. Computed-tomography for non-invasive imaging of the iliac arteries. *South Med J* 1982;**75**:1385–8.

342. Johnson K, Kassam M, Koers J, Cobbold R, MacHattie D. Comparative study of four methods for quantifying Doppler ultrasound waveforms from the femoral artery. *Ultrasound Med Biol* 1984; **10**:1–12.

343. Kaiser U, Do DD, Triller J, Mahler F. [Follow-up of patients with stents of the iliac arteries by color duplex ultrasound]. *Schweiz Med Wochenschr* 1995; **125**:11–19.

344. Kalden P, Kreitner KF, Oberholzer K, Pitton M, Krummenauer F, Requardt M, *et al*. [Contrast media-enhanced 3D MR angiography of peripheral arteries using an automatic tracking technique at 1.0 Tesla]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2000;**172**:978–84.

345. Kanal E, Shellock FG, Talagala L. Safety considerations in MR imaging. *Radiology* 1990; **176**:593–606.

346. Karacagil S, Lofberg AM, Almgren B, Granbo A, Jonsson ML, Lorelius LE, *et al*. [Duplex ultrasound scanning for diagnosis of aortoiliac and femoropopliteal arterial disease]. *Vasa* 1994; **23**:325–9.

347. Karacagil S, Granbo A, Jonsson ML, Bergqvist D. [Arterial surgery of the extremities without angiography. A simpler preoperative survey with color Doppler]. *Lakartidningen* 1995;**92**:3692–3.

348. Karagacil S, Lofberg A, Granbo A, Lorelius L, Bergqvist D. Value of duplex scanning in evaluation of crural and foot arteries in limbs with severe lower limb ischaemia: a prospective comparison with angiograph. *Eur J Vasc Endovasc Surg* 1996;**12**:300–3.

349. Karacagil S, Bergqvist D. Lower extremity arterial reconstructions based on duplex scanning without preoperative angiography. *J Vasc Invest* 1998; **4**:99–102.

350. Karasch T, Rieser R, Neuerburg-Heusler D. [The determination of occlusion length and localization in leg arteries: color duplex sonography versus angiography]. *Vasa* 1991;**20**:295–6.

351. Karasch T, Rieser R, Grun B, Strauss AL, Neuerburg-Heusler D, Roth FJ, *et al*. [Determination of the length of the occlusion in extremity arteries: color duplex ultrasound versus angiography]. *Ultraschall Med* 1992;**14**:247–54.

352. Katayama H, Yamaguchi K, Kozuka T, Takashima T, Seez P, Matsuura K. Adverse reactions to ionic and nonionic contrast media. A report from the Japanese Committee on the Safety of Contrast Media. *Radiology* 1990;**175**:621–8.

353. Katsamouris AN, Giannoukas AD, Tsetis D, Kostas T, Petinarakis I, Gourtsoyiannis N. Can ultrasound replace arteriography in the management of chronic arterial occlusive disease of the lower limb? *Eur J Vasc Endovasc Surg* 2001; **21**:155–9.

354. Katz DS, Hon M. CT angiography of the lower extremities and aortoiliac system with a multi-detector row helical CT scanner: promise of new opportunities fulfilled. *Radiology* 2001; **221**:7–10.

355. Kaufman SL, Barth KH, Kadir S, Williams GM, Smith GW, Stonesifer GLJ, *et al*. Hemodynamic measurements in the evaluation and follow-up of transluminal angioplasty of the iliac and femoral arteries. *Radiology* 1982;**142**:329–36.

356. Kelekis NL, Semelka RC, Worawattanakul S, Molina PL, Mauro MA. Magnetic resonance imaging of the abdominal aorta and iliac vessels using combined 3-D gadolinium-enhanced MRA and gadolinium-enhanced fat-suppressed spoiled gradient echo sequences. *Magn Reson Imaging* 1999;**17**:641–51.

357. Khilnani NM, Winchester PA, Prince MR, Vidan E, Trost DW, Bush HL Jr, *et al*. Peripheral vascular disease: combined 3D bolus chase and dynamic 2D MR angiography compared with x-ray angiography for treatment planning. *Radiology* 2002;**224**:63–74.

358. Kita M, Mitani Y, Tanihata H, Sato M, Takizawa O, Laub G. Three-phase gadolinium infusion in moving-table three-dimensional MR angiography. *Nippon Acta Radiol* 1999;**59**:888–90.

359. Klein WM, Schlejen PM, Eikelboom BC, van der Graaf Y, Mali WP. MR angiography of the lower extremities with a moving-bed infusion-tracking technique. *Cardiovasc Intervent Radiol* 2003;**26**:1–8.

360. Koelemay MJ, den Hartog D, Prins MH, Kromhout JG, Legemate DA, Jacobs MJ. Diagnosis of arterial disease of the lower extremities with duplex ultrasonography. *Br J Surg* 1996;**83**:404–9.

361. Koelemay MJ, Legemate DA, van Gurp JA, de Vos H, Balm R, Jacobs MJ. Interobserver variation of colour duplex scanning of the popliteal, tibial and pedal arteries. *Eur J Vasc Endovasc Surg* 2001;**21**:160–4.

362. Koelemay MJ, Lijmer JG, Stoker J, Legemate DA, Bossuyt PM. Magnetic resonance angiography for the evaluation of lower extremity arterial disease: a meta-analysis. *JAMA* 2001;**285**:1338–45.

363. Koelemay MJW, Legemate DA, Reekers JA, Koedam NA, Balm R, Jacobs M. Interobserver variation in interpretation of arteriography and management of severe lower leg arterial disease. *Eur J Vasc Endovasc Surg* 2001;**21**:417–22.

364. Koennecke H, Fobbe G, Hamed M, Wolf K. [Diagnosis of arterial vascular diseases of the lower extremities with color-coded duplex sonography]. *Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr* 1989;**151**:42–6.

365. Kohler TR. Duplex scanning for diagnosis of aortoiliac and femoropopliteal disease. *Circulation* 1987;**76**:1074–80.

366. Kohler TR, Andros G, Porter JM, Clowes A, Goldstone J, Johansen K, *et al*. Can duplex scanning replace arteriography for lower extremity arterial disease? *Ann Vasc Surg* 1990;**4**:280–7.

367. Kojima KY, Szumowski J, Sheley RC, Quinn SF. Lower extremities: MR angiography with a unilateral telescopic phased-array coil. *Radiology* 1995;**196**:871–5.

368. Konkus CJ, Czum JM, Jacobacci JT. Contrast-enhanced MR angiography of the aorta and lower extremities with routine inclusion of the feet. *AJR Am J Roentgenol* 2002;**179**:115–17.

369. Korogi Y, Hirai T, Takahashi M. Intravascular ultrasound imaging of peripheral arteries as an adjunct to balloon angioplasty and atherectomy. *Cardiovasc Intervent Radiol* 1996;**19**:1–9.

370. Korst MBJM, Van der Vliet JA, Heijstraten FJ, Boll APM. Comparative study among contrast-enhanced MRA, colour Doppler sonography and intra-arterial DSA in the diagnosis of stenosis of the aorta and the iliac arteries. *Cardiovasc Intervent Radiol* 1999;**22**:S88.

371. Korst MB, Van der Vliet JA, Heijstraten FM, Klemm PL, Van Langen H, Barentsz JO. Comparative study of normal dose contrast-enhanced MR angiography, color duplex ultrasound and intra-arterial DSA in the diagnosis of stenosis of aorta and iliac arteries. *Radiology* 1999;**213P**:354–5.

372. Krajina A. [Arteriography in the diagnosis of arterial ischaemia of lower extremities]. *Cesk Radiol* 2001;**55**:135–7.

373. Kramer SC, Gorich J, Aschoff AJ, Orend KH, Mickley V, Sokiranski R, *et al*. Diagnostic value of spiral-CT angiography in comparison with digital subtraction angiography before and after peripheral vascular intervention. *Angiology* 1998; **49**:599–606.

374. Kreissig R, Knollmann FD, Steinkamp HJ, Boettcher HD, Ehrenstein T, Felix R. Evaluation of multi-slice helical CT angiography for the assessment of peripheral artery disease. *Radiology* 2000;**217**:593–4.

375. Kreitner KF, Kalden P, Neufang A, Dueber C, Laub GA, Krummenauer F. Diabetes and peripheral arterial occlusive disease: prospective comparison of a contrast-enhanced subtraction 3D-MR-angiography with conventional DSA. *Radiology* 1998;**209P**:456.

376. Krombach GA, Adam G, Nolte-Ernsting C, Haage P, Tacke J, Schurmann K, *et al*. Single bolus contrast-enhanced 3-D MRA of the aortoiliac and lower limb arteries: comparison with DSA. *Cardiovasc Intervent Radiol* 2000;**23**:S114–15.

377. Krug B, Kugel H, Harnischmacher U, Heindel W, Altenburg A, Fischbach R, *et al*. [Peripheral occlusive arterial diseases: comparison of diagnostic value of MRA and DSA]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1995;**162**:112–19.

378. Krug B, Kugel H, Harnischmacher U, Heindel W, Fischbach R, Altenburg A, *et al*. Diagnostic performance of digital subtraction angiography (DSA) and magnetic resonance angiography (MRA): preliminary results in vascular occlusive disease of the abdominal and lower-extremity arteries. *Eur J Radiol* 1995;**19**:77–85.

379. Laissy JP, Falise B, Mousseaux E. Investigation of the lower limb vessels by magnetic resonance angiography (MRA): cardiovascular applications in MRI. *Ann Radiol (Paris)* 1995;**38**:79–90.

380. Laissy JP, Limot O, Henry-Feugeas MC, Karrillon G, Hackworth CA, Julliard JM, *et al*. Iliac artery patency before and immediately after percutaneous transluminal angioplasty: assessment with time-of-flight MR angiography. *Radiology* 1995;**197**:455–9.

381. Lalli AF. Contrast media reactions: data analysis and hypothesis. *Radiology* 1980;**134**:1–12.

382. Lang EK, Foreman J, Schiegel JU, Leslie C, List A, McCormick P. The incidence of contrast medium induced acute tubular necrosis following arteriography. *Radiology* 1981;**138**:203–6.

383. Langholz J, Stolke O, Behrendt C, Blank B, Fessler B, Heidrich H. [Color-coded duplex ultrasound of lower leg arteries – image reliability with reference to Fontaine stages]. *Ultraschall Med* 1993;**14**:279–84.

384. Langholz J. Investigation of peripheral arterial disease: the expanding role of echo-enhanced color flow Doppler and duplex sonography. *Eur J Ultrasound* 1998;**7**:S53–61.

385. Langsfeld M, Nepute J, Hershey F, Thorpe L, Auer A, Binnington H. The use of deep duplex scanning to predict hemodynamically significant aortoiliac stenoses. *J Vasc Surg* 1988;**7**:395–9.

386. Larch E, Minar E, Ahmadi R, Schnurer G, Schneider B, Stumpflen A, *et al*. Value of color duplex sonography for evaluation of tibioperoneal arteries in patients with femoropopliteal obstruction: a prospective comparison with anterograde intraarterial digital subtraction angiography. *J Vasc Surg* 1997;**25**:629–36.

387. Lasser EC, Lyon SG, Berry CC. Reports on contrast media reactions: analysis of data from reports to the US Food and Drug Administration. *Radiology* 1997;**203**:605–10.

388. Lawler LP, Fishman EK. Multidetector row computed tomography of the aorta and peripheral arteries. *Cardiol Clin* 2003;**21**:607–29.

389. Lawrence JA, Kim D, Kent KC, Stehling MK, Rosen MP, Raptopoulos V. Lower extremity spiral CT angiography versus catheter angiography. *Radiology* 1995;**194**:903–8.

390. Lee HM, Wang Y, Sostman HD, Schwartz LH, Khilnani NM, Trost DW, *et al*. Distal lower extremity arteries: evaluation with two-dimensional MR digital subtraction angiography. *Radiology* 1998;**207**:505–12.

391. Legemate D, Teeuwen C, Hoeneveld H, Ackerstaff R, Eikelboom B. The potential of duplex scanning to replace aorto-iliac and femoropopliteal angiography. *Eur J Vasc Surg* 1989;**3**:49–54.

392. Legemate D, Teeuwen G, Hoeneveld H. Value of duplex scanning compared with angiography and pressure measurements in the assessment of aortoiliac lesions. *Br J Surg* 1991; **78**:1003–8.

393. Leiner T. Contrast-enhanced MRA in the workup of peripheral arterial occlusive disease. *Imaging Decisions* 2004;**8**:20–8.

394. Leiner T, Kessels AGH, Nelemans PJ, Vasbinder GBC, de Haan MW, Kitslaar P, *et al*. Peripheral arterial disease: comparison of color duplex US and contrast-enhanced MR angiography for diagnosis. *Radiology* 2005;**235**:699–708.

395. Leng GC, Whyman MR, Donnan PT, Ruckley CV, Gillespie I, Fowkes FGR, *et al*. Accuracy and reproducibility of duplex ultrasonography in grading femoropopliteal stenoses. *J Vasc Surg* 1993;**17**:510–7.

396. Leng G, Davis M, Baker D. *Bypass surgery for chronic lower limb ischaemia. Cochrane Database of Systematic Reviews 2000* (Issue 3). Wiley Interscience; 2000. Accessed October 2005.

397. Lenhart M, Djavidani B, Volk M, Strotzer M, Manke C, Requardt M, *et al*. [Contrast medium-enhanced MR angiography of the pelvic and leg vessels with an automated table-feed technique]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1999; **171**:442–9.

398. Lenhart M, Herold T, Manke C, Link J, Feuerbach S, Voelk M. Table-feed gadolinium-enhanced MR angiography of the lower extremity arteries: imaging with a dedicated peripheral vascular coil system. Preliminary experience. *Radiology* 2001;**221**:122.

399. Lenhart M, Finkenzeller T, Paetzel C, Strotzer M, Mann S, Djavidani B, *et al*. [Contrast-enhanced MR angiography in the routine work-up of the lower extremity arteries]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2002;**174**:1289–95.

400. Leon M, Mohler E. Results of a dose-ranging diagnostic trial of magnetic resonance angiography with MS-325, a blood pool contrast agent, for the detection of vascular occlusive disease in the aortoiliac region. *J Am Coll Cardiol* 2002;**39**:368A.

401. Levy MM, Baum RA, Carpenter JP. Endovascular surgery based solely on noninvasive preprocedural imaging. *J Vasc Surg* 1998;**28**:995–1003.

402. Lewis P, Psaila JV, Davies WT, McCarty K, Woodcock JP. Measurement of volume flow in the human common femoral artery using a duplex ultrasound system. *Ultrasound Med Biol* 1986; **12**:777–84.

403. Lewis DR, Baird RN, Irvine CD, Lamont PM. Colour flow duplex imaging of occlusive arterial disease of the lower limb. *Br J Surg* 1997;**84**:1625.

404. Leyendecker JR, Johnson SP, Diffin DC, Elsass K, Bifano SL. Time-of-flight MR arteriography of below-knee arteries with maximum-intensity-projection reconstruction: is interpretation of the axial source images helpful? *AJR Am J Roentgenol* 1997;**169**:1145–9.

405. Leyendecker JR, Elsass KD, Johnson SP, Diffin DC, Cull DL, Light JT, *et al*. The role of infrapopliteal MR angiography in patients undergoing optimal contrast angiography for chronic limb-threatening ischemia. *J Vasc Interv Radiol* 1998;**9**:545–51.

406. Ligush J Jr, Reavis SW, Preisser JS, Hansen KJ. Duplex ultrasound scanning defines operative strategies for patients with limb-threatening ischemia. *J Vasc Surg* 1998;**28**:482–90.

407. Limpert JD, Vogelzang RL, Yao JST. Computed tomography of aortoiliac atherosclerosis. *J Vasc Surg* 1987;**5**:814–19.

408. Link J, Steffens JC, Brossmann J, Graessner J, Hackethal S, Heller M. Iliofemoral arterial occlusive disease: contrast-enhanced MR angiography for preinterventional evaluation and follow-up after stent placement. *Radiology* 1999; **212**:371–7.

409. Loewe CL, Cejna M, Grgurin M, Wolf F, Schoder M, Lammer J, *et al*. Contrast-enhanced magnetic resonance angiography using moving bed imaging on a 1.0 Tesla system in the diagnosis of peripheral arterial occlusive disease. *Cardiovasc Intervent Radiol* 2000;**23**:S99.

410. Loewe C, Schoder M, Rand T, Hoffmann U, Sailer J, Kos T, *et al*. Peripheral vascular occlusive disease: evaluation with contrast-enhanced moving-bed MR angiography versus digital subtraction angiography in 106 patients. *AJR Am J Roentgenol* 2002;**179**:1013–21.

411. Loewe C, Cejna M, Schoder M, Loewe-Grgurin M, Wolf F, Lammer J, *et al*. Contrast material-enhanced, moving-table MR angiography versus digital subtraction angiography for surveillance of peripheral arterial bypass grafts. *J Vasc Interv Radiol* 2003;**14**:1129–37.

412. Loewe C. Peripheral MR angiography. *Semin Ultrasound CT MR* 2003;**24**:280–315.

413. Lofberg AM, Karacagil S, Hellberg A, Bostrom A, Ljungman C, Ostholm G. The role of duplex scanning in the selection of patients with critical lower-limb ischemia for infrainguinal percutaneous transluminal angioplasty. *Cardiovasc Intervent Radiol* 2001;**24**:229–32.

414. Lossef SV, Rajan SS, Patt RH, Carvlin M, Calcagno D, Gomes MN, *et al*. Gadolinium-enhanced magnitude contrast MR angiography of popliteal and tibial arteries. *Radiology* 1992; **184**:349–55.

415. Lujan S, Criado E, Puras E, Izquierdo LM. Duplex scanning or arteriography for preoperative planning of lower limb revascularisation. *Eur J Vasc Endovasc Surg* 2002;**24**:31–6.

416. Mackaay AJ, Beks PJ, Dur AH, Bischoff M, Scholma J, Heine RJ, *et al*. The distribution of peripheral vascular disease in a Dutch Caucasian population: comparison of type II diabetic and non-diabetic subjects. *Eur J Vasc Endovasc Surg* 1995;**9**:170–5.

417. Maeda H. A prospective comparison of magnetic resonance angiography and conventional angiography in peripheral arterial occlusive disease. *Nichidai Igaku Zasshi* 1996;**55**:252–6.

418. Makita S, Ohira A, Murakami H, Itoh S, Hiramori K. Noninvasive detection of iliac artery disease and prediction of its severity from Doppler spectral analysis in common femoral artery. *Angiology* 1997;**48**:615–21.

419. Marcus CD, Ladam-Marcus V, Bigot J. Clement C, Bonnet-Gausserand FM, Menanteau BP. CT angiography of iliac artery stenoses: evaluation with volume rendering technique. *Radiology* 2000; **217**:593.

420. Markovic N, Zdravkoci M, Brajovkic M, Dedic N. Importance of Doppler ultrasonography in diagnosis of macroangiopathia diabetica. *Int Angiol* 1996;**15**:38.

421. Marshall M. [Doppler ultrasonographic diagnostics in peripheral arterial-disease]. *Herz* 1988;**13**:358–71.

422. Marti X, Cairols-Castellote MA, Vila R, Rancanõ-Ferreiro J, Romera A. [The role of duplex arterial mapping in decision making in critical ischaemia in lower limbs]. *Angiologia* 2004;**56**:433–43.

423. Mast BA. Comparison of magnetic resonance angiography and digital subtraction angiography for visualization of lower extremity arteries. *Ann Plast Surg* 2001;**46**:261–4.

424. Masui T, Caputo GR, Bowersox JC, Higgins CB. Assessment of popliteal arterial occlusive disease with 2D time-of-flight MRA. *J Comput Assist Tomogr* 1995;**19**:449–54.

425. Matsubara J, Ohta T, Shionoya S, Horibe T. [Non-invasive ultrasonic imaging of the peripheral arterial diseases]. *Japanese Journal of Medical Ultrasonics* 1984;**11**:16–23.

426. Matsumura K, Sato K, Hashida K, Utsumi N, Ishizawa T. [Contrast-enhanced subtraction MR angiography of the systemic aorta and lower extremity arteries for vascular intervention: use of stepping-table method on a 0.5 T system]. *Japanese Journal of Interventional Cardiology* 2001;**16**:130–6.

427. Mazzariol F, Ascher E, Hingorani A, Gunduz Y, Yorkovich W, Salles-Cunha S. Lower extremity revascularisation without preoperative contrast angiography in 185 cases: lessons learned with duplex ultrasound arterial mapping. *Eur J Vasc Endovasc Surg* 2000;**19**:509–15.

428. McCarthy MJ, Nydahl S, Hartshorne T, Naylor AR, Bell PRF, London NJM. Colour-coded duplex imaging and dependent Doppler ultrasonography in the assessment of cruropedal vessels. *Br J Surg* 1999;**86**:33–7.

429. McCauley TR, Monib A, Dickey KW, Clemett J, Meier GH, Egglin TK, *et al*. Peripheral vascular occlusive disease: accuracy and reliability of time-of-flight MR angiography. *Radiology* 1994; **192**:351–7.

430. McClennan BL. Low-osmolality contrast media: premises and promises. *Radiology* 1987;**162**:1–8.

431. Meaney JFM, Robertson I, Chakravarti S, Selvakumar S, Scott J, Vowden P, *et al*. Fast contrast-enhanced magnetic resonance angiography of the aorta and lower extremity vessels using a novel approach. *Br J Surg* 1998; **85**:17.

432. Meaney JF. Magnetic resonance angiography of the peripheral arteries: current status. *Eur Radiol* 2003;**13**:836–52.

433. Meissner OA, Verrel F, Tato F, Siebert U, Ramirez H, Ruppert V, *et al*. Magnetic resonance angiography in the follow-up of distal lower-extremity bypass surgery: comparison with duplex ultrasound and digital subtraction angiography. *J Vasc Interv Radiol* 2004;**15**:1269–77.

434. Melke JP, Luizy F, Laurian C, Fainas G, Riche MC, Chauffour J, *et al*. Apport de l'ultrasonographie Doppler et de l'échotomographie à la stratégie de l'angioplastie transluminale. *Angeiologie* 1983; **36**:67–76.

435. Mesurolle BD, Qanadli SD, El Hajjam M, Mignon F, Chagnon S, Lacombe P. Dual-slice helical CT angiography of occlusive arterial disease of the lower extremities: work in progress. *Radiology* 1999;**213P**:353–4.

436. Meuli RA, Wedeen VJ, Geller SC, Edelman RR, Frank LR, Brady TJ, *et al*. MR gated subtraction angiography: evaluation of lower extremities. *Radiology* 1986;**159**:411–18.

437. Mills SR, Wertman DE, Heatson DK, Moore AV, Bates M, Allen S, *et al*. Study of safety and tolerance of iopamidol in peripheral arteriography. *Radiology* 1982;**145**:57–8.

438. Mitsuzaki K, Yamashita Y, Sakaguchi T, Ogata I, Takahashi M, Hiai Y. Abdomen, pelvis and extremities: diagnostic accuracy of dynamic contrast-enhanced turbo MR angiography compared with conventional angiography-initial experience. *Radiology* 2000;**216**:909–15.

439. Mohler ER. Results of MS-325-13: a phase III magnetic resonance angiography (MRA) trial with MS-325, a blood pool contrast agent, for the detection of aortoiliac occlusive disease (AIOD). *Circulation* 2003;**108**:453–4.

440. Moneta G, Strandness D. Peripheral arterial duplex scanning. *J Clin Ultrasound* 1987;**15**:645–51.

441. Moneta G, Yeager R, Antonovic R. Accuracy of lower extremity arterial duplex mapping. *J Vasc Surg* 1992;**15**:275–84.

442. Moneta GL, Yeager RA, Lee RW, Porter JM. Noninvasive localization of arterial occlusive disease: a comparison of segmental Doppler pressures and arterial duplex mapping. *J Vasc Surg* 1993;**17**:578–82.

443. Morasch MD, Collins J, Pereles FS, Carr JC, Eskandari MK, Pearce WH, *et al*. Lower extremity stepping-table magnetic resonance angiography

with multilevel contrast timing and segmented contrast infusion. *J Vasc Surg* 2003;**37**:62–71.

444. Muller-Buhl U, Engeser P, Klimm HD, Wiesemann A. Quality of life and objective disease criteria in patients with intermittent claudication in general practice. *Fam Pract* 2003;**20**:36–40.

445. Mulligan SA, Doyle M, Matsuda T, Koslin DB, Kenney PJ, Barton RE, *et al*. Aortoiliac disease: two-dimensional inflow MR angiography with lipid suppression. *J Magn Reson Imaging* 1993;**3**:829–34.

446. Murphy BE. Magnetic resonance angiography: the optimal tool for screening peripheral vascular disease and planning percutaneous interventions. *J Endovasc Ther* 2000;**7**:I-26.

447. Nagashima T. [Study of chronic arterial occlusive disease of the lower extremities by ultrasonic blood rheograph]. *Journal of the Nagoya Medical Association* 1979;**102**:45–66.

448. Naidich JB, Crystal KS, Stein HL. Not so rapid progression of peripheral vascular disease after diagnostic angiography. *Radiology* 1992;**182**:15–17.

449. Nau JY. Artériographie et échographie-Doppler dans l'artériopathie oblitérante des membres inférieurs. *Med Hyg (Geneve)* 2002;**60**:2037.

450. Nchimi A, Brisbois D, Donkers E, Biquet JF, Saive C, Jadot A, *et al*. [MR aortofemorography versus DSA: prospective evaluation]. *J Belge Radiol* 2002;**85**:246–51.

451. Nelemans PJ, Leiner T, De Vet HC, Van Engelshoven JM. Meta-analysis of the diagnostic performance of magnetic resonance angiography in patients with peripheral arterial disease. *Radiology* 2000;**217**:238.

452. Nelemans PJ, Leiner T, de Vet Henrica CW, van Engelshoven Joseph MA. Peripheral arterial disease: meta-analysis of the diagnostic performance of MR angiography. *Radiology* 2000; **217**:105–14.

453. Nemcek A. Contrast material reactions. *J Vasc Interv Radiol* 1996;**7**:541.

454. Nicolaides A, Gordon-Smith I, Dayandas J, Eastcott H. The value of Doppler blood velocity tracings in the detection of aortoiliac disease in patients with intermittent claudication. *Surgery* 1976;**80**:774–8.

455. Nikolenko NY, Golovina VM, Soldatkina LV, Kalmykova ND, Burtsev VI. Impulse doppler arteriography in the diagnosis of atherosclerosis of the carotid and femoral arteries in outpatient clinical practice. *Ter Arkh* 1987;**59**:37–9.

456. Nyamekye I, Sommerville K, Raphael M, Adiseshiah M, Bishop C. Non-invasive assessment of arterial stenoses in angioplasty surveillance: a comparison with angiography. *Eur J Vasc Endovasc Surg* 1996;**12**:471–81.

457. Nzeh DA, Allan PL, McBride K, Gillespie I, Ruckley CV. Comparison of colour Doppler ultrasound and digital subtraction angiography in the diagnosis of lower limb arterial disease. *Afr J Med Med Sci* 1998;**27**:177–80.

458. Oberholzer K, Kreitner KF, Kalden P, Requardt M, Pitton M, Mildenberger P, *et al*. [MR angiography of peripheral vessels with automatic tracking table technique at 1.0 in comparison with intra-arterial digital subtraction angiography]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1999; **171**:240–3.

459. Ofer A, Nitecki SS, Linn S, Epelman M, Fischer D, Karram T, *et al*. Multidetector CT angiography of peripheral vascular disease: a prospective comparison with intraarterial digital subtraction angiography. *AJR Am J Roentgenol* 2003;**180**:719–24.

460. Ohi M, Takeda K, Matsumura K, Tashiro T, Terada N, Hirano T, *et al*. [Clinical usefulness of CT and MRI in the diagnosis of popliteal artery occlusive diseases]. *Rinsho Hoshasen* 1987; **32**:1625–8.

461. Oliva VL, Denbow N, Therasse E, Common AA, Harel C, Giroux M-F, *et al*. Digital subtraction angiography of the abdominal aorta and lower extremities: carbon dioxide versus iodinated contrast material. *J Vasc Interv Radiol* 1999; **10**:723–31.

462. Oser RF, Picus D, Hicks ME, Darcy MD, Hovsepian DM. Accuracy of DSA in the evaluation of patency of infrapopliteal vessels. *J Vasc Interv Radiol* 1995;**6**:589–94.

463. Ota H, Takase K, Igarashi K, Chiba Y, Haga K, Saito H, *et al*. MDCT compared with digital subtraction angiography for assessment of lower extremity arterial occlusive disease: importance of reviewing cross-sectional images. *AJR Am J Roentgenol* 2004;**182**:201–9.

464. Owen RS, Baum RA, Carpenter JP, Holland GA, Shlanskygoldberg R, Cope C. Identification and quantification of peripheral vascular stenoses with MR angiography. *Radiology* 1992;**185**:277.

465. Owen RS, Carpenter JP, Baum RA, Perloff LJ, Cope C. Magnetic resonance imaging of angiographically occult runoff vessels in peripheral arterial occlusive disease. *N Engl J Med* 1992;**326**:1577–81.

466. Owen RS, Baum RA, Carpenter JP, Holland GA, Cope C. Symptomatic peripheral vascular disease: selection of imaging parameters and clinical evaluation with MR angiography. *Radiology* 1993; **187**:627–35.

467. Pandharipande PV, Lee VS, Reuss PM, Charles HW, Rosen RJ, Rofsky NM. Stable table two-station bolus chase MR angiography: a simple, effective, and low-cost alternative approach to the evaluation

of peripheral vascular disease. *Radiology* 2000; **217**:239.

468. Pandharipande PV, Lee VS, Reuss PM, Charles HW, Rosen RJ, Krinsky GA, *et al*. Two-station bolus-chase MR angiography with a stationary table: a simple alternative to automated-table techniques. *AJR Am J Roentgenol* 2002;**179**:1583–9.

469. Pasterkamp G, Spijkerboer Anje M, Mali Willem PTM, Borst C. Residual stenosis determined by intravascular ultrasound and duplex ultrasound after balloon angioplasty of the superficial femoral artery. *Ultrasound Med Biol* 1996;**22**:801–6.

470. Pellerin M, Coquille F, Hubert M, Lagrange C, Piquois A, Scherrer A. [Comparison between arteriography and magnetic resonance angiography in patients with leg peripheral arterial disease]. *J Radiol* 2001;**82**:237–43.

471. Pellerito JS. Ultrasound examination of the peripheral arteries. *J Cardiovasc Diagn Proced* 1993;**11**:269–75.

472. Pemberton M, Nydahl S, Hartshorne T, Naylor AR, Bell PR, London NJ. Colour-coded duplex imaging can safely replace diagnostic arteriography in patients with lower-limb arterial disease. *Br J Surg* 1996;**83**:1725–8.

473. Pemberton M, Nydahl S, Hartshorne T, Naylor AR, Bell PR, London NJ. Can lower limb vascular reconstruction be based on colour Duplex imaging alone? *Eur J Vasc Endovasc Surg* 1996; **12**:452–4.

474. Pemberton M, London NJ. Colour flow duplex imaging of occlusive arterial disease of the lower limb. *Br J Surg* 1997;**84**:912–19.

475. Perrier E, Dubayle P, Boyer B, Mousseaux E, Larroque P, Vergos M, *et al*. [Comparison of magnetic resonance angiography with injection of gadolinium and conventional arteriography of the ilio-femoral arteries]. *J Radiol* 1998;**79**:1493–8.

476. Phillips DJ, Powers JE, Eyer MK, Blackshear WMJ, Bodily KC, Strandness DWJ, *et al*. Detection of peripheral vascular disease using the duplex scanner Iii. *Ultrasound Med Biol* 1980;**6**:205–18.

477. Phillips JJ. Vascular imaging with magnetic resonance and computed tomography: peripheral vascular imaging. *Am J Card Imaging* 1993; **7**:128–37.

478. Pinto F, Lencioni R, Napoli V, Petrucci R, Vignali C, Armillotta N, *et al*. Peripheral ischemic occlusive arterial disease: comparison of color Doppler sonography and angiography. *J Ultrasound Med* 1996;**15**:697–704.

479. Pividal R. Échographie-Doppler et artériopathie oblitérante des membres inférieurs. *Annal Cardiol Angeiol (Paris)* 2001;**50**:112–18.

480. Pocek M, Fiaschetti V, Maspes F, Gandini R. Moving-bed infusion-tracking MR angiography of lower limb arteries compared with DSA in the evaluation of vascular occlusive disease. *Cardiovasc Intervent Radiol* 1999;**22**:S156.

481. Polak JF, Karmel MI, Meyerovitz MF. Accuracy of color Doppler flow mapping for evaluation of the severity of femoropopliteal arterial disease: a prospective study. *J Vasc Interv Radiol* 1991; **2**:471–6.

482. Polak J. Arterial sonography: efficacy for the diagnosis of arterial disease of the lower limb extremity. *AJR Am J Roentgenol* 1993;**161**:235–43.

483. Poletti P-A, Rossett A, Didier D, Bachmann P, Verdun FR, Rutschmann O, *et al*. Subtraction CT angiography of the lower limbs: a new technique for the evaluation of acute arterial occlusion. *AJR Am J Roentgenol* 2004;**183**:1445–8.

484. Poon FW, Baxter GM. Colour flow imaging for lower limb arterial disease. *Clin Radiol* 1993;**48**:145.

485. Poon E, Yucel EK, Pagan-Marin H, Kayne H. Iliac artery stenosis measurements: comparison of two-dimensional time-of-flight and three-dimensional dynamic gadolinium-enhanced MR angiography. *AJR Am J Roentgenol* 1997; **169**:1139–44.

486. Portig I, Maisch B. Nichtinvasive diagnostische Methoden der Makro- und Mikroangiopathie der peripheren Gefaesse und Karotiden. *Herz* 2004; **29**:17–25.

487. Portugaller HR, Hausegger KA, Schoellnast H, Pilhatsch A. The value of CT-angiography in the assessment of aortoiliac occlusive disease. *Cardiovasc Intervent Radiol* 1998;**21**:S135.

488. Portugaller HR, Schoellnast H, Tauss J, Tiesenhausen K, Hausegger KA. Semitransparent volume-rendering CT angiography for lesion display in aortoiliac arteriosclerotic disease. *J Vasc Interv Radiol* 2003;**14**:1023–30.

489. Postiglione A, Cicerano U, Gallotta G, Gnasso A, Lamenza F, Rubba P, *et al*. Prevalence of peripheral arterial disease and related risk factors in elderly institutionalized subjects. *Gerontology* 1992;**38**:330–7.

490. Powe NR, Steinberg EP, Erickson JE, Moore RD, Smith CR, White RI, *et al*. Contrast medium-induced adverse reactions: economic outcome. *Radiology* 1988;**169**:163–8.

491. Proia R, Walsh D, Nelson P, Connors J, Powell R, Zwolak R. Early results of infragenicular revascularization based solely on duplex arteriography. *J Vasc Surg* 2001;**33**:1165–70.

492. Prokop M, Debatin JF. MRI contrast media – new developments and trends. CTA vs. MRA. *Eur Radiol* 1997;**7**:299–306.

493. Quinn SF, Demlow TA, Hallin RW, Eidemiller LR, Szumowski J. Femoral MR-angiography versus conventional angiography: preliminary results. *Radiology* 1993;**189**:181–4.

494. Quinn SF, Sheley RC, Szumowski J, Shimakawa A. Evaluation of the iliac arteries: comparison of two-dimensional time of flight magnetic resonance angiography with cardiac compensated fast gradient recalled echo and contrast-enhanced three-dimensional time of flight magnetic resonance angiography. *J Magn Reson Imaging* 1997;**7**:197–203.

495. Quinn SF, Sheley RC, Semonsen KG, Leonardo VJ, Kojima K, Szumowski J. Aortic and lower-extremity arterial disease: evaluation with MR angiography versus conventional angiography. *Radiology* 1998;**206**:693–701.

496. Radak D, Labs KH, Jager KA, Ilijevski N, Bojic M. [Doppler sonography diagnosis of restenosis after percutaneous transluminal angioplasty: sensitivity and specificity of the pedal-brachial index in relation to changes in absolute arterial blood pressure]. *Srp Arh Celok Lek* 1998;**126**:83–91.

497. Radak D, Labs KH, Jager KA, Bojic M, Popovic AD. Doppler-based diagnosis of restenosis after femoropopliteal percutaneous transluminal angioplasty: sensitivity and specificity of the ankle/brachial pressure index versus changes in absolute pressure values. *Angiology* 1999; **50**:111–22.

498. Rajagopalan S, Prince M. Magnetic resonance angiographic techniques for the diagnosis of arterial disease. *Cardiol Clin* 2002;**20**:501–12.

499. Raman R, Raman B, Hundt W, Stucker D, Napel SS, Rubin GD. Improved speed of bone removal in CT angiography (CTA) using automated targeted morphological separation: method and evaluation in CTA of the lower extremity occlusive disease (LEOD). *Radiology* 2002;**225**:647.

500. Ramaswami G, Al-Kutoubi A, Nicolaides AN, Dhanjil S, Griffin M, Belcaro G, *et al*. The role of duplex scanning in the diagnosis of lower limb arterial disease. *Ann Vasc Surg* 1999;**13**:494–500.

501. Ranke C, Creutzig A, Alexander K. Duplex scanning of the peripheral arteries – correlation of the peak velocity ratio with angiographic diameter reduction. *Ultrasound Med Biol* 1992; **18**:433–40.

502. Raptopoulos V, Rosen MP, Kent KC, Kuestner LM, Sheiman RG, Pearlman JD. Sequential helical CT angiography of aortoiliac disease. *AJR Am J Roentgenol* 1996;**166**:1347–54.

503. Raptopoulos VD, Rosen MP, Kent KC, Kuestner L, Sheiman RG. Double-spiral CT angiography of aortoiliac disease. *Radiology* 1995;**197**:213–14.

504. Rathenborg LK, Hill-Madsen B, Felthus JL, Jansen VD, Just SR, Sillesen HH. [Validation of Doppler ultrasonographic scanning for the detection of stenoses in peripheral vascular reconstructions]. *Ugeskr Laeger* 2003;**165**:2096–8.

505. Reid SK, Pagan-Marin HR, Menzoian JO, Woodson J, Yucel EK. Contrast-enhanced moving-table MR angiography: prospective comparison to catheter arteriography for treatment planning in peripheral arterial occlusive disease. *J Vasc Interv Radiol* 2001;**12**:45–53.

506. Reimer P, Wilhelm M, Lentschig M, Wortler K, Boettger U, Heinecke A, *et al*. [Phase-contrast MR angiography of the lower extremity. Comparison of methods and clinical application]. *Radiologe* 1997;**37**:572–8.

507. Reimer P, Wilhelm M, Lentschig M, Wortler K, Marx C, Allkemper T, *et al*. [Combined use of ECK-triggered 2D-phase contrast MR angiography and 2D-time-of-flight MR angiography for planning and follow up before and after vascular intervention of pelvic and leg arteries]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1998;**168**:243–9.

508. Reimer P, Landwehr P. Non-invasive vascular imaging of peripheral vessels. *Eur Radiol* 1998; **8**:858–72.

509. Rezzo R, Bertoglio C, Stabilini L, Tallero G. [Doppler ultrasonography in the diagnosis of arteriopathy in the lower extremities]. *Minerva Cardioangiol* 1982;**30**:269–74.

510. Ricco J-B, Pearce W, Yao J. The use of operative prebypass arteriography and Doppler ultrasound recordings to select patients for extended femoral-distal bypass. *Ann Surg* 1983;**198**:646–53.

511. Richter CS, Biamino G, Niemann VT, Ragg C, Felix R. [CT angiography and arterial DSA in the evaluation of occlusive processes in pelvic arteries. Initial results]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1994;**161**:154–60.

512. Rieker O, Dueber C, Schmiedt W, Schweden FJ, Pitton MB, Thelen M. CT angiography versus intraarterial DSA in patients with peripheral arterial occlusive disease. *Radiology* 1995; **197**:144–5.

513. Rieker O, Mildenberger P, Neufang A, von Zitzewitz H, Schweden F, Thelen M. [CT angiography in arterial occlusive disease: comparison of 3 rendering techniques]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1997; **167**:361–70.

514. Rizzo RJ, Flinn WR, Yao JST, McCarthy WJ, Vogelzang RL, Pearce WH. Computed tomography for evaluation of arterial disease in the popliteal fossa. *J Vasc Surg* 1990;**11**:112–19.

515. Rofsky NM, Johnson G, Adelman MA, Rosen RJ, Krinsky GA, Weinreb JC. Peripheral vascular

disease evaluated with reduced-dose gadolinium-enhanced MR angiography. *Radiology* 1997; **205**:163–9.

516. Rofsky NM, Morana G, Adelman MA, Lee VS, Krinsky GA. Improved gadolinium-enhanced subtraction MR angiography of the femoropopliteal arteries: reintroduction of osseous anatomic landmarks. *AJR Am J Roentgenol* 1999; **173**:1009–11.

517. Rofsky NM, Adelman MA. MR angiography in the evaluation of atherosclerotic peripheral vascular disease. *Radiology* 2000;**214**:325–38.

518. Rose SC. Noninvasive vascular laboratory for evaluation of peripheral arterial occlusive disease. Part I – Hemodynamic principles and tools of the trade. *J Vasc Interv Radiol* 2000; **11**:1107–14.

519. Rose SC. Noninvasive vascular laboratory for evaluation of peripheral arterial occlusive disease. Part II – Clinical applications: chronic, usually atherosclerotic, lower extremity ischemia. *J Vasc Interv Radiol* 2000;**11**:1257–75.

520. Rose SC. Noninvasive vascular laboratory for evaluation of peripheral arterial occlusive disease. Part III – Clinical applications: nonatherosclerotic lower extremity arterial conditions and upper extremity arterial conditions and upper extremity arterial disease. *J Vasc Interv Radiol* 2001;**12**:11–18.

521. Rosenfield K, Kelly S, Fields C. Non-invasive assessment of peripheral vascular disease by colour flow Doppler/two-dimensional ultrasound. *Am J Cardiol* 1989;**64**:247–51.

522. Rosfors S, Eriksson M, Hoglund N, Johansson G. Duplex ultrasound in patients with suspected aorto-iliac occlusive disease. *Eur J Vasc Surg* 1993; **7**:513–17.

523. Rubin GD, Schmidt AJ, Logan LJ, Olcott C, Dake MD. Detection and characterization of lower extremity occlusive disease with multidetector-row CT angiography. *Radiology* 1999;**213P**:353.

524. Rubin GD, Schmidt AJ, Logan LJ, Olcott C, Zarins CK, Napel S, *et al*. Multi-detector row CT angiography of lower extremity occlusive disease: a new application for CT scanning. *Radiology* 1999;**210**:588.

525. Rubin GD, Shiau MC, Leung AN, Kee ST, Logan LJ, Sofilos MC. Aorta and iliac arteries: single versus multiple detector-row helical CT angiography. *Radiology* 2000;**215**:670–6.

526. Rubin GD, Schmidt AJ, Logan LJ, Sofilos MC. Multi-detector row CT angiography of lower extremity arterial inflow and runoff: initial experience. *Radiology* 2001;**221**:146–58.

527. Ruehm SG, Hany TF, Pfammatter T, Schneider E, Ladd M, Debatin JF. Pelvic and lower extremity arterial imaging: diagnostic performance of three-dimensional contrast-enhanced MR angiography. *AJR Am J Roentgenol* 2000;**174**:1127–35.

528. Ruehm SG, Nanz D, Baumann A, Schmid M, Debatin JF. 3D contrast-enhanced MR angiography of the run-off vessels: value of image subtraction. *J Magn Reson Imaging* 2001;**13**:402–11.

529. Ruehm SG, Debatin JF. Kontrastverstaerkte 3D-MR-angiographie in thorax, abdomen und peripherie: Vasculaere Diagnostik und Intervention [Contrast-enhanced 3D MR angiography in the chest, abdomen and lower extremities]. *Radiologe* 1999;**39**:100–9.

530. Ruthlein VM, Dennig K, Rudolph W. [Color Doppler ultrasonography (angiodynography) for assessment of the arterial vascular beds in the lower extremities]. *Herz* 1988;**13**:378–81.

531. Sacks D, Robinson ML, Marinelli DL, Perlmutter GS. Evaluation of the peripheral arteries with duplex ultrasound angioplasty. *Radiology* 1990;**176**:39–44.

532. Sacks D, Robinson ML, Marinelli DL, Perlmutter GS. Peripheral arterial Doppler ultrasonography: diagnostic criteria. *J Ultrasound Med* 1992;**11**:95–103.

533. Sacks D, Robinson ML, Summers TA, Marinelli DL. The value of duplex sonography after peripheral artery angioplasty in predicting subacute restenosis. *AJR Am J Roentgenol* 1994; **162**:179–83.

534. Saito Y, Yodono H, Tarusawa K, Sasaki T, Akimura R, Takahashi KKS, *et al*. MR-angiography with intravenous administration of gadolinium DTPA. *Nippon Acta Radiol* 1989;**49**:688–90.

535. Saito Y, Noda H, Itabashi Y, Miura H, Sasaki T, Tsuji T, *et al*. [Table-moving MRA of the lower extremities in patients with arterial occlusive disease]. *Japanese Journal of Clinical Radiology* 2004; **49**:547–54.

536. Savader SJ, Porter DJ, Ehrman KO, Haikal LC. The legs for life screening for peripheral vascular disease: compliance with physician recommendations in moderate- and high-risk assessed patients. *J Vasc Interv Radiol* 2001;**12**:33–7.

537. Sawchuk AP, Flanigan DP, Tober JC, Eton D, Schwarcz TH, Eldrup-Jorgensen J, *et al*. A rapid accurate noninvasive technique for diagnosing critical and subcritical stenoses in aortoiliac arteries. *J Vasc Surg* 1990;**12**:158–67.

538. Sawchuk AP. Simplified screening of lower extremity arterial bypasses. *Vasc Surg* 1997;**31**:535–41.

539. Schiebler ML, Listerud J, Holland G, Owen R, Baum R, Kressel HY. Magnetic resonance angiography of the pelvis and lower extremities: work in progress. *Invest Radiol* 1992;**27**:S90–6.

540. Scheibler M, Listerud J, Baum R. Magnetic resonance arteriography of the pelvis and lower extremities. *Magn Reson Q* 1993;**9**:152–87.

541. Schindler N, Calligaro KD, Lombardi J, Dougherty MJ, Raviola CA, D'Orazio E. Has arteriography gotten a bad name? Current accuracy and morbidity of diagnostic contrast arteriography for aortoiliac and lower extremity arterial disease. *Ann Vasc Surg* 2001;**15**:417–20.

542. Schmeller W, Welzel J, Plettenberg A. Lokalization und Auspraegungsgrad der Dermatoliposklerose lassen sich mittels 20 MHz-Sonographie gut beurteilen. *Vasa* 1993; **22**:219–26.

543. Schmiedl UP, Yuan C, Nghiem HV, Winter TC, Freeny PC. MR angiography of the peripheral vasculature. *Semin Ultrasound CT MR* 1996;**17**:404–11.

544. Schneider P, Ogawa D, Rush M. Lower extremity revascularizaton without contrast arteriography: a prospective study of operation based upon duplex mapping. *Cardiovasc Surg* 1999;**7**:699–703.

545. Schoenberg SO, Londy FJ, Licato P, Williams DM, Wakefield T, Chenevert TL. Multiphase-multistep gadolinium-enhanced MR angiography of the abdominal aorta and runoff vessels. *Invest Radiol* 2001;**36**:283–91.

546. Seifert H, Jager K, Johl H, Bollinger A. [Duplex scanning in the diagnosis of peripheral artery circulatory disorders]. *Schweiz Med Wochenschr* 1988;**118**:554–7.

547. Seifert H, Jager K. [Clinical use of duplex ultrasound in peripheral arterial occlusive disease]. *Vasa* 1989;**27**:404–6.

548. Sensier Y, Hartshorne T, Thrush A, Nydahl S, Bolia A, London NJ. A prospective comparison of lower limb colour-coded duplex scanning with arteriography. *Eur J Vasc Endovasc Surg* 1996; **11**:170–5.

549. Sensier YJ, London NJ. Colour duplex ultrasound assessment of lower limb arterial disease: the effect of adjacent disease. *Ultrasound Med Biol* 1996; **22**:365–6.

550. Sensier Y, Fishwick G, Owen R, Pemberton M, Bell PR, London NJ. A comparison between colour duplex ultrasonography and arteriography for imaging infrapopliteal arterial lesions. *Eur J Vasc Endovasc Surg* 1998;**15**:44–50.

551. Shannon H, Machan LS, Forster BB, Whittall KP. Quantification of blood flow pre- and post-superficial femoral and popliteal artery angioplasty using CINE phase contrast MR angiography. *Radiology* 1997;**205**:464.

552. Sharafuddin MJ, Wroblicka JT, Sun S, Essig M, Schoenberg SO, Yuh WT. Percutaneous vascular intervention based on gadolinium-enhanced MR angiography. *J Vasc Interv Radiol* 2000; **11**:739–46.

553. Sharafuddin MJ, Stolpen AH, Sun S, Leusner CR, Safvi AA, Hoballah JJ, *et al*. High-resolution multiphase contrast-enhanced three-dimensional MR angiography compared with two-dimensional time-of-flight MR angiography for the identification of pedal vessels. *J Vasc Interv Radiol* 2002;**13**:695–702.

554. Shehadi WH, Toniolo G. Adverse reactions to contrast media: a report from the Committee on Safety of Contrast Media of the International Society of Radiology. *Radiology* 1980;**137**:299–302.

555. Shehadi WH. Contrast media adverse reactions: occurrence, recurrence, and distribution patterns. *Radiology* 1982;**143**:11–17.

556. Sheikh KH, Davidson CJ, Kisslo KB, Harrison JK, Himmelstein SI, Kisslo J, *et al*. Comparison of intravascular ultrasound, external ultrasound and digital angiography for evaluation of peripheral artery dimensions and morphology. *Am J Cardiol* 1991;**67**:817–22.

557. Shetty AN, Shirkhoda A, Bis KG. Contrast-enhanced 3D breath-hold MR-angiography: application in abdominal and iliac vessels. *Radiology* 1995;**197**:516–17.

558. Shetty AN, Shirkhoda A, Bis KG, Ellwood R, Debiao LI. 3D breath-hold contrast-enhanced MRA: a preliminary experience in aorta and iliac vascular disease. *J Comput Assist Tomogr* 1998; **22**:179–85.

559. Sigstedt B, Lunderquist A. Complications of angiographic examinations. *AJR Am J Roentgenol* 1978;**130**:45–60.

560. Sivananthan UM, Ridgway JP, Bann K, Verma SP, Cullingworth J, Ward J, *et al*. Fast magnetic resonance angiography using turbo-FLASH sequences in advanced aortoiliac disease. *Br J Radiol* 1993;**66**:1103–10.

561. Snidow JJ, Aisen AM, Harris VJ, Trerotola SO, Johnson MS, Sawchuk AP, *et al*. Iliac artery MR angiography: comparison of three-dimensional gadolinium-enhanced and two-dimensional time-of-flight techniques. *Radiology* 1995;**196**:371–8.

562. Snidow JJ, Harris VJ, Johnson MS, Cikrit DF, Lalka SG, Sawchuk AP, *et al*. Iliac artery evaluation with two-dimensional time-of-flight MR angiography: update. *J Vasc Interv Radiol* 1996; **7**:213–20.

563. Solomon S, Katz SD, Stevenson-Smith W, Yellin EL, Lejemtel TH. Determination of vascular impedance in the peripheral circulation by transcutaneous pulsed Doppler ultrasound. *Chest* 1995;**108**:515–21.

564. Sorensen AG. Results of MS-325-13: a phase III magnetic resonance angiography trial with MS-325, a blood pool contrast agent, for the detection of aortoiliac occlusive disease. *Am J Cardiol* 2003; **92**:81L.

565. Sostman HD, Beam CA. Evaluation of the quality of clinical research studies of magnetic resonance angiography: 1991–1994. *J Magn Reson Imaging* 1996;**6**:33–8.

566. Soule B, Hingorani A, Ascher E, Kallakuri S, Yorkovich W, Markevich N, *et al*. Comparison of magnetic resonance angiography (MRA) and duplex ultrasound arterial mapping (DUAM) prior to infrainguinal arterial reconstruction. *Eur J Vasc Endovasc Surg* 2003;**25**:139–46.

567. Spinosa DJ, Angle JF, Hagspiel KD, Kern JA, Hartwell GD, Matsumoto AH. Lower extremity arteriography with use of iodinated contrast material or gadodiamide to supplement CO_2 angiography in patients with renal insufficiency. *J Vasc Interv Radiol* 2000;**11**:35–43.

568. Spinosa DJ, Hagspiel KD, Matsumoto AH, Hartwell GD. Gadolinium-based contrast agents in angiography and interventional radiology: uses and techniques. *J Vasc Interv Radiol* 2000;**11**:985–90.

569. Spring DB, Bettmann MA, Barkan HE. Deaths related to iodinated contrast media reported spontaneously to the US Food and Drug Administration, 1978–1994: effect of the availability of low-osmolality contrast media. *Radiology* 1997;**204**:333–7.

570. Spring DB, Bettmann MA, Barkan HE. Nonfatal adverse reactions to iodinated contrast media: spontaneous reporting to the US Food and Drug Administration 1978–1994. *Radiology* 1997; **204**:325–32.

571. Steffens JC, Link J, MuellerHuelsbeck S, Brinkmann G, Heller M. Use of a combination of 2D phase-contrast and triggered 2D time-of-flight MR angiography to identify patients suitable for interventional treatment of peripheral artery occlusive disease. *Radiology* 1996;**201**:377.

572. Steffens JC, Link J, Fronius M, MuellerHuelsbeck S, Brinkmann G, Heller M. Evaluation of peripheral artery occlusive disease by high-resolution contrast-enhanced 3D MR angiography. *Radiology* 1997;**205**:462.

573. Steffens JC, Link J, Graessner J, Brossmann J. Bolus-chasing 3D-contrast-enhanced MR angiography: first results in patients with lower extremity occlusive disease. *Cardiovasc Intervent Radiol* 1998;**21**:S90.

574. Steffens JC, Link J, Schwarzenberg H, Mueller-Huelsbeck S, Brinkmann G, Heller M. Lower extremity occlusive disease: diagnostic imaging with a combination of cardiac-gated 2D phase-contrast and cardiac-gated 2D time-of-flight MRA. *J Comput Assist Tomogr* 1999;**23**:7–12.

575. Stoffers H, Legemate DA, Prins MH. [Non-invasive diagnosis in peripheral artery diseases]. *HART Bulletin* 1997;**28**:190–4.

576. Strandness D. The use of ultrasound in the evaluation of peripheral vascular disease. *Prog Cardiovasc Dis* 1978;**20**:403–22.

577. Sueyoshi E, Sakamoto I, Matsuoka Y, Hayashi H, Hayashi K. Symptomatic peripheral vascular tree stenosis: comparison of subtracted and nonsubtracted 3D contrast-enhanced MR angiography with fat suppression. *Acta Radiol* 2000;**41**:133–8.

578. Sugihara E, Kim T, Kawata S, Kumano S, Murakami T, Nakamura H. Evaluation of arterial stenosis of lower extremities with multidetector-row CT angiography (MDCTA): comparison to conventional digital subtraction angiography (DSA). *Radiology* 2002;**225**:160.

579. Swan JS, Carroll TJ, Kennell TW, Heisey DM, Korosec FR, Frayne R, *et al*. Time-resolved three-dimensional contrast-enhanced MR angiography of the peripheral vessels. *Radiology* 2002;**225**:43–52.

580. Szendro G, Lumelsky D, Klimov A, Faingersh I. Computed tomographic angiography of the peripheral vasculature: role and applications in vascular surgery. *Harefuah* 2001;**140**:306–10.

581. Tabuchi K. Evaluation of MR angiography and blood flow measurement in abdominal and peripheral arterial occlusive disease. *Dokkyo Journal of Medical Sciences* 2000;**27**:299–309.

582. Tala P, Laustela E, Kerminen T, Eerola S, Lieto JV. Ultrasound echography in peripheral vascular occlusion. *Ann Chir Gynaecol Fenn* 1968;**57**:501–5.

583. Ternovoy SK, Sinitsyn VE, Artioukhina E, Dadvani S, Timonina E, Kondrashin S. Use of electron-beam computed tomography (EBCT) for preoperative evaluation of the iliac and femoral arteries: comparison to translumbar angiography. *Radiology* 1999;**213P**:353.

584. Tesauro P, Accarino B, Schilliro F, Maraziti A, Delvecchio E. Diagnostic-imaging of peripheral vascular diseases – a personal experience. *Arch Gerontol Geriatr* 1991;Suppl. 2:367–70.

585. Thiele B, Strandeness D. Accuracy of angiographic quantification of peripheral atherosclerosis. *Prog Cardiovasc Dis* 1983;**26**:223–36.

586. Tielbeek AV, Vroegindeweij D, Buth J, Schol FPG, Mali WPTM. Comparison of intravascular ultrasonography and intraarterial digital subtraction angiography after directional atherectomy of short lesions in femoropopliteal arteries. *J Vasc Surg* 1996;**23**:436–45.

587. Tielbeek AV, Vroegindeweij D, Gussenhoven EJ, Buth J, Landman GHM. Evaluation of directional atherectomy studied by intravascular ultrasound in femoropopliteal artery stenosis. *Cardiovasc Intervent Radiol* 1997;**20**:413–19.

588. Tomihira A, Hino Y, Sugihara M. [Stepping table gadolinium-enhanced three-dimensional MR angiography in arterial occlusive disease of the pelvic and lower extremity arteries]. *Jpn J Clin Radiol* 2002;**47**:525–33.

589. Torreggiani WC, Varghese J, Haslam P, McGrath F, Munk PL, Lee MJ. Prospective comparison of MRA with catheter angiography in the assessment of patients with aortoiliac occlusion before surgery or endovascular therapy. *Clin Radiol* 2002; **57**:625–31.

590. Trusen A, Beissert M, Hahn D. Color Doppler US findings in the diagnosis of arterial occlusive disease of the lower limb. *Acta Radiol* 2003; **44**:411–18.

591. Ubbink DT, Fidler M, Legemate DA. Interobserver variability in aortoiliac and femoropopliteal duplex scanning. *J Vasc Surg* 2001;**33**:540–5.

592. Uberoi R, Sarker B, Coleman J, Mudawi A, Ashour H. Duplex follow-up of aorto-iliac stents. *Eur J Vasc Endovasc Surg* 2002;**23**:331–5.

593. Unger EC, Schilling JD, Awad AN, McIntyre KE, Yoshino MT, Pond GD, *et al*. MR angiography of the foot and ankle. *J Magn Reson Imaging* 1995; **5**:1–5.

594. Van Asten W, Beijneveld W, Pieters B. Assessment of aortoiliac obstructive disease by Doppler spectrum analysis of blood flow velocities in the common femoral artery at rest and during reactive hypreremia. *Surgery* 1991;**109**:633–9.

595. Van der Heijden F, Legemate DA, Van Leeuwen MS, Mali WPM, Eikelboom BC. Value of Duplex scanning in the selection of patients for percutaneous transluminal angioplasty. *Eur J Vasc Surg* 1993;**7**:71–6.

596. Van der Lugt A, Gussenhoven EJ, Pasterkamp G, Bom N, Posthuma DJ, Stijnen T. Interobserver reproducibility of qualitative and quantitative analysis of intravascular ultrasound images before and after peripheral balloon angioplasty. *Ultrasound Med Biol* 1996;**22**:399–404.

597. Van Lankeren W, Gussenhoven EJ, Pieterman H, Van Sambeek MRHM, Van der Lugt A. Comparison of angiography and intravascular ultrasound before and after balloon angioplasty of the femoropopliteal artery. *Cardiovasc Intervent Radiol* 1998;**21**:367–74.

598. Van Rij AM, Packer SGK, Morrison ND, Thomson IA. The role of CT scan in aorto-iliac arterial disease. *J Cardiovasc Surg (Torino)* 1989; **30**:24.

599. Vashisht R, Ellis MR, Skidmore C, Blair SD, Greenhalgh RM, O'Malley MK. Colour-coded duplex ultrasonography in the selection of patients for endovascular surgery. *Br J Surg* 1992; **79**:1030–1.

600. Velazquez OC, Baum RA, Carpenter JP, Baum RA. Magnetic resonance angiography in peripheral vascular surgery: the role of CTA and MRA in interventional radiology. *Semin Interv Radiol* 1998; **15**:149–62.

601. Venkataraman S, Semelka RC, Weeks S, Braga L, Vaidean G. Assessment of aorto-iliac disease with magnetic resonance angiography using arterial phase 3-D gradient-echo and interstitial phase 2-D fat-suppressed spoiled gradient-echo sequences. *J Magn Reson Imaging* 2003;**17**:43–53.

602. Vergara M, Seguel S. Adverse reactions to contrast media in CT: effects of temperature and ionic property. *Radiology* 1996;**199**:363–6.

603. Verrel F, Meissner O, Ruppert V, Ramirez H, Tato F, Steckmeier B. [Value of MR angiography in follow-up after cruro-pedal bypass surgery]. *Kongressbd Dtsch Ges Chir Kongr* 2002;**119**:627–30.

604. Visser K, Hunink MG. Diagnostic imaging of peripheral arterial occlusive disease: a meta-analysis of gadolinium-enhanced magnetic resonance angiography and color-guided duplex ultrasonography. *Radiology* 1999;**213P**:354.

605. Visser K, Hunink MG. Peripheral arterial disease: gadolinium-enhanced MR angiography versus color-guided duplex US: a meta-analysis. *Radiology* 2000;**216**:67–77.

606. Vodnansky P. *Prinos barevne duplexni ultrasonografie u nemocnych s ischemickou chorobou dolnich koncetin [Contribution of colour coded duplex ultrasound in patients with peripheral arterial occlusive disease]*. Dr Thesis, Hradec Kralove 1, Charles University in Prague; 2001.

607. Vodnansky P, Elias P, Lojik M, Krajina A, Fridrich J. [The accuracy of colour-coded duplex ultrasound in patients with peripheral arterial occlusive disease – comparison with angiography]. *Cesk Radiol* 2002;**56**:171–7.

608. von Kalle T, Gerlach A, Hatopp A, Klinger S, Prodehl P, Arlart IP. [Contrast-enhanced MR angiography (CEMRA) in peripheral arterial occlusive disease (PAOD): conventional moving table technique versus hybrid technique]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 2004;**176**:62–9.

609. Vosshenrich R, Fischer U, Grabbe E. [Initial experiences with the MR magnitude contrast angiography of the lower extremities]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1993;**159**:393–7.

610. Vosshenrich R, Fischer U, Funke M, Grabbe E. [2-D-time-of-flight MR angiography of the peripheral blood vessels. Experimental and

clinical studies on value of this method in arterial occlusive diseases]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 1996;**164**:25–30.

611. Vosshenrich R, Kopka L, Castillo E, Bottcher U, Graessner J, Grabbe E. Electrocardiograph-triggered two-dimensional time-of-flight versus optimized contrast-enhanced three-dimensional MR angiography of the peripheral arteries. *Magn Reson Imaging* 1998;**16**:887–92.

612. Wain RA, Berdejo GL, Delvalle WN, Lyon RT, Sanchez LA, Suggs WD, *et al*. Can duplex scan arterial mapping replace contrast arteriography as the test of choice before infrainguinal revascularization? *J Vasc Surg* 1999;**29**:100–9.

613. Walter F, Fays J, Thuillier L, Ludig T, Blum AG, Roland J. Evaluation of multislice CT angiography in the assessment of lower limb arteriopathies. *Radiology* 2000;**217**:594.

614. Walton L, Martin T, Collins M. Prospective assessment of the aorto-iliac segment by visual interpretation of frequency analysed Doppler waveforms – a comparison with arteriography. *Ultrasound Med Biol* 1984;**10**:27–32.

615. Wang Y, Winchester PA, Khilnani NM, Lee HM, Watts R, Trost DW, *et al*. Contrast-enhanced peripheral MR angiography from the abdominal aorta to the pedal arteries: combined dynamic two-dimensional and bolus-chase three-dimensional acquisitions. *Invest Radiol* 2001;**36**:170–7.

616. Wasser MN. Magnetic resonance angiography of peripheral vascular disease. *J Comput Assist Tomogr* 1999;**23**:S129–33.

617. Watanabe Y, Dohke M, Okumura A, Amoh Y, Ishimori T, Oda K, *et al*. Dynamic subtraction MR angiography: first-pass imaging of the main arteries of the lower body. *AJR Am J Roentgenol* 1998;**170**:357–60.

618. Watts R, Wang Y, Prince MR, Winchester PA, Khilnani NM, Kent KC. Anatomically tailored *k*-space sampling for bolus-chase three-dimensional MR digital subtraction angiography. *Radiology* 2001;**218**:899–904.

619. Weishaupt D, Ruehm SG, Binkert CA, Patak MA, Steybe F, Debatin JF. Equilibrium phase MR-angiography of the aorto-iliac and renal arteries using an intravascular contrast agent. *Radiology* 1999;**213P**:270–1.

620. Wendt RE, III, Nitz W, Morrisett JD, Hedrick TD. A technique for flow-enhanced magnetic resonance angiography of the lower extremities. *Magn Reson Imaging* 1990;**8**:723–8.

621. Wesbey GE, Higgins CB, Amparo EG, Hale JD, Kaufman L, Pogany AC. Peripheral vascular disease: correlation of MR imaging and angiography. *Radiology* 1985;**156**:733–9.

622. Westenberg JJM, Van Der Geest RJ, Wasser MNJM, Van Der Linden EL, Van Walsum T, Van Assen HC, *et al*. Vessel diameter measurements in gadolinium contrast-enhanced three-dimensional MRA of peripheral arteries. *Magn Reson Imaging* 2000; **18**:13–22.

623. Wetzner SM, Kiser LC, Bezreh JS. Duplex ultrasound imaging: vascular applications. *Radiology* 1984;**150**:507–14.

624. Whelan JF, Barry MH, Moir JD. Color flow Doppler ultrasonography: comparison with peripheral arteriography for the investigation of peripheral vascular disease. *J Clin Ultrasound* 1992;**20**:369–74.

625. Whiteley M. Diagnosis of arterial disease of the lower extremities with duplex ultrasonography. *Br J Surg* 1996;**83**:867.

626. Whiteley MS, Galland RB. Assessing arterial inflow before infra-inguinal bypass grafting: a survey of the members of the Vascular Surgical Society of Great Britain and Ireland. *Cardiovasc Surg* 1999; **7**:70–3.

627. Widrich WC, Robbins AH, Rommel AJ, Andrews R. Iopamidol: a non-ionic contrast agent for peripheral arteriography. *Radiology* 1982;**145**:53–5.

628. Widrich WC, Beckman CF, Robbins AH, Scholz FJ, Srinivasan MK, Hayes EJ, *et al*. Iopamidol and meglumine diatrizoate: comparison of effects on patient discomfort during aortofemoral arteriography. *Radiology* 1983;**148**:61–4.

629. Wikstrom J, Holmberg A, Johansson L, Lofberg AM, Smedby O, Karacagil S, *et al*. Gadolinium-enhanced magnetic resonance angiography, digital subtraction angiography and duplex of the iliac arteries compared with intra-arterial pressure gradient measurements. *Eur J Vasc Endovasc Surg* 2000;**19**:516–23.

630. Wikstrom JL. *On contrast-enhanced magnetic resonance angiography of the aortoiliac arteries*. PhD Thesis, Uppsala Universitet; 2001.

631. Wilhelm KE, Conrad R, Remig J, Gieseke J, Schild H. Gadolinium-enhanced MR-angiography of the lower extremity arteries with an automated table-feed technique. *Cardiovasc Intervent Radiol* 2000;**23**:S114.

632. Willmann JK, Wildermuth S, Lutz AM, Pfammatter T, Marincek B, Weishaupt D. Aorto-iliac and renal arteries: prospective intraindividual comparison of contrast-enhanced three-dimensional MR angiography and multi-detector row CT angiography. *Radiology* 2002; **225**:400.

633. Willmann JK, Mayer D, Banyai M, Desbiolles LM, Verdun FR, Seifert B, *et al*. Evaluation of peripheral arterial bypass grafts with multi-detector row CT angiography: comparison with

duplex US and digital subtraction angiography. *Radiology* 2003;**229**:465–74.

634. Winchester PA, Lee HM, Khilnani NM, Wang Y, Trost DW, Bush HL Jr, *et al*. Comparison of two-dimensional MR digital subtraction angiography of the lower extremity with x-ray angiography. *J Vasc Interv Radiol* 1998;**9**:891–9.

635. Winterer JT, Schaefer O, Uhrmeister P, Zimmermann-Paul G, Lehnhardt S, Altehoefer C, *et al*. Contrast enhanced MR angiography in the assessment of relevant stenoses in occlusive disease of the pelvic and lower limb arteries: diagnostic value of a two-step examination protocol in comparison to conventional DSA. *Eur J Radiol* 2002;**41**:153–60.

636. Winter-Warnars HA, van der Graaf Y, Mali WP. Interobserver variation in duplex sonographic scanning in the femoropopliteal tract. *J Ultrasound Med* 1996;**15**:421–8.

637. Wixon CL, Mills JL, Westerband A, Hughes JD, Ihnat DM. An economic appraisal of lower extremity bypass graft maintenance. *J Vasc Surg* 2000;**32**:1–12.

638. Wolf U, Wolf M, Choi JH, Levi M, Choudhury D, Hull S, *et al*. Localized irregularities in hemoglobin flow and oxygenation in calf muscle in patients with peripheral vascular disease detected with near-infrared spectrophotometry. *J Vasc Surg* 2003;**37**:1017–26.

639. Wolff S. Results of a multicenter phase III trial of magnetic resonance angiography (MRA) with MS-325 for the detection of peripheral vascular disease in the aortoiliac region. *Circulation* 2002; **106**:691.

640. Wright CH, Thomas ML, Young AE. Computed tomography in the assessment of peripheral arterial disease. *Australas Radiol* 1983; **27**:174–7.

641. Yamaguchi K, Katayama H, Takashima T, Kozuka T, Seez P, Matsuura K. Prediction of severe adverse reactions to ionic and nonionic contrast media in Japan: evaluation of pretesting. A report from the Japanese Committee on the Safety of Contrast Media. *Radiology* 1991;**178**:363–7.

642. Yamashita Y, Mitsuzaki K, Tang Y, Namimoto T, Takahashi M. Gadolinium-enhanced breath-hold three-dimensional time-of-flight MR angiography of the abdominal and pelvic vessels: the value of ultrafast MP-RAGE sequences. *J Magn Reson Imaging* 1997;**7**:623–8.

643. Yamashita Y, Mitsuzaki K, Ogata I, Takahashi M, Hiai Y. Three-dimensional high-resolution dynamic contrast-enhanced MR angiography of the pelvis and lower extremities with use of a phased array coil and subtraction: diagnostic accuracy. *J Magn Reson Imaging* 1998;**8**:1066–72.

644. Yeon Hyeon C, Lae Hyun P, Han BK. Biphasic and discontinuous injection of contrast material for thin-section helical CT angiography of of the whole aorta and iliac arteries. *AJR Am J Roentgenol* 2001;**176**:454–6.

645. Yilmaz S, Altinbas H, Senol U, Sindel T, Mete A, Lüleci E. Common peroneal nerve palsy after retrograde popliteal artery puncture. *Eur J Vasc Endovasc Surg* 2002;**23**:467–9.

646. Yoshikawa H. Late adverse reactions to nonionic contrast media. *Radiology* 1992;**183**:737–40.

647. Yucel EK, Gift DA. Magnetic-resonance angiography of the lower-extremity and renal-arteries. *Semin Ultrasound CT MR* 1992;**13**:291–302.

648. Yucel EK, Dumoulin CL, Waltman AC. MR angiography of lower-extremity arterial disease: preliminary experience. *J Magn Reson Imaging* 1992;**2**:303–9.

649. Yucel E, Kaufman JA, Geller SC, Waltman AC. Time-of-flight MR-angiography in the evaluation of lower-extremity arterial-occlusive disease. *Radiology* 1992;**185**:132–3.

650. Yucel EK. Roles of Doppler sonography and femoral arteriography in diagnosing ischemic changes in the foot. *AJR Am J Roentgenol* 1994; **163**:218–19.

651. Yucel EK. Femoropopliteal angioplasty: can we predict success with duplex sonography? *AJR Am J Roentgenol* 1994;**162**:184–6.

652. Zagoria RZ, D'Souza VJ, Sharling ES. Prosthetic arterial graft occlusion: a complication of tourniquet use during arteriography. *Radiology* 1988;**167**:121–2.

653. Zakharova GN, Balatsky OA, Burov Yu A, Klyachkin ML. [The possibilities of ultrasonic dopplerography and multilevel manometry in appraisal of lesions of the lower limb arteries]. *Grud Serdechnososudistaia Khir* 1990;**9**:47–50.

654. Zhao X, Jiang F, She Y, Zhu X, Bai H, He Y, *et al*. The investigation of clinical application of colorful Doppler ultrasound on vascular disease of lower limb. *Zhongguo Linchuang Kangfu* 2003;**7**:328–9.

655. Zubarev AR, Larin SI, Koshkin VM. [The possibilities of Doppler sonography in evaluating the distal vascular channel in chronic obliterating diseases of the lower limb arteries]. *Grud Serdechnososudistaia Khir* 1990;(12)4–7.

656. Airiian PE, Bakhtiozin RF, Dzhordzhikiia RK. [Color duplex scanning in morphological and functional assessment of lower limb arterial occlusions]. *Angiol Sosud Khir* 2004;**10**:45–50.

657. Cherro A, Sarmiento R. Angiografía por resonancia magnética con gadolinio versus angiografía convencional en diagnóstico de vasculopatía de miembros inferiores [respuesta]

[Gadolinium enhanced magnetic resonance angiography versus conventional angiography for lower extremity arterial disease diagnostic] [answer]. *Rev Argent Cardiol* 2004;**72**:496–7.

658. Zierler R, Strandness D. Duplex scanning for the diagnosis of aortoiliac and lower extremity arterial disease. *J Vasc Technol* 1987;**11**:99–102.

659. Fowkes F. Peripheral vascular disease. In Raftery J, Stevens A, editors. *Health care needs assessment: the epidemiology based needs assessment reviews*. Oxford: Radcliffe Publishing. URL: http://hcna.radcliffe-oxford.com/pvd.htm. Accessed October 2005.

660. Berry E, Kelly S, Westwood ME, Davies LM, Gough MJ, Bamford JM, *et al*. The cost-effectiveness of magnetic resonance angiography for carotid artery stenosis and peripheral vascular disease: a systematic review. *Health Technol Assess* 2002;**6**(7).

661. Zhou X, Obuchowski N, McClish D. *Statistical methods in diagnostic medicine*. New York: John Wiley & Sons; 2002.

662. Bachoo P, Thorpe P. Endovascular stents for intermittent claudication. *Cochrane Database of Systematic Reviews* 2002, Issue 4, Art. No: CD003228. DOI: 10.1002/14651858.CD003228. Chichester: Wiley Interscience; 2002. Accessed October 2005.

663. Girolami B, Bernardi E, Prins MH, ten Cate JW, Hettiarachchi R, Prandoni P, *et al*. Treatment of intermittent claudication with physical training, smoking cessation, pentoxifylline, or nafronyl: a meta-analysis. *Arch Intern Med* 1999;**159**:337–45.

664. Fowkes FGR, Gillespie IN. Angioplasty (versus non-surgical management) for intermittent claudication. *Cochrane Database of Systematic Reviews* 1998, Issue 2, Art. No: CD000017. DOI: 10.1002/14651858.CD000017. Chichester: Wiley Interscience; 2002. Accessed October 2005.

665. Brothers T, Rios G, Robison J, Elliot B. Justification of intervention for limb-threatening ischemia: a surgical decision analysis. *Cardiovasc Surg* 1999;**7**:62–9.

666. Peters TG. Distal foot amputation with limb salvage. *Jacksonville Medicine* 1998. URL: http://www.dcmsonline.org. Accessed October 2005.

667. Holm J, Arfvidsson B, Jivegard L, Lundgren F, Lundholm K, Schersten T, *et al*. Chronic lower limb ischaemia. A prospective randomised controlled study comparing the 1-year results of vascular surgery and percutaneous transluminal angioplasty (PTA). *Eur J Vasc Surg* 1991;**5**:517–22.

668. The Vascular Surgical Society of Great Britain and Ireland. *The provision of vascular services 2004*. London; 2003. URL: http://www.vascular society.org.uk/Docs/Provision%20of%20 Vascular%20Services.pdf. Accessed October 2005.

669. Davies L, Noone M, Drummond M, Cheshire N, Wolfe J. *Technology assessment in the development of guidelines for vascularising the ischaemic leg*. Discussion paper. Report No. 89. York: Centre for Health Economics, University of York; 1991.

670. Michaels J, Brazier J, Palfreyman S, Shackley P, Slack R. Cost and outcome implications of the organisation of vascular services. *Health Technol Assess* 2000;**4**(11).

671. Department of Health. *NHS reference costs 2004: NHS trust reference cost index*. 2004. URL: http://www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4105545&chk=znAfqu. Accessed October 2005.

672. Joint Formulary Committee. *British national formulary*. 50th ed. British Medical Association and Royal Pharmaceutical Society of Great Britain; 2005. URL: http://www.bnf.org/bnf/bnf/current/openat/index.htm. Accessed October 2005.

673. Hiatt WR. Medical treatment of peripheral arterial disease and claudication. *N Engl J Med* 2001; **344**:1608–21.

674. Organisation for Economic Co-operation and Development. *Purchasing Power Parities (PPP), PPP Data*. OECD; 2005. URL: http://www.oecd.org/linklist/0,2678,en_2649_34357_2734617_1_1_1_1,00.html. Accessed October 2005.

675. Briggs A. Probabilistic sensitivity analysis for decision trees with multiple branches: use of the Dirichlet distribution in a Bayesian framework. *Med Decis Making* 2003;**23**:341–50.

676. Briggs A, Sculpher M, Dawson J, Fitzpatrick R, Murray R, Murray D, *et al*. *Modelling the cost-effectiveness of primary hip replacement: how cost-effective is the Spectron compared to the Charnley prosthesis?* CHE Technical Paper Series 28. York: Centre for Health Economics, University of York; 2003.

677. Briggs A. Handling uncertainty in cost-effectiveness models. *Pharmacoeconomics* 2000;**17**:479–500.

678. Birch S, Gafni A. The 'NICE' approach to technology assessment: an economics perspective. *Health Care Manage Sci* 2004;**7**:35–41.

679. Fenwick E, O'Brien BJ, Briggs A. Cost-effectiveness acceptability curves: facts, fallacies and frequently asked questions. *Health Econ* 2004; **13**:405–15.

680. Deville W, Bezemer P, Bouter L. Publications on diagnostic test evaluation in family medicine journals: an optimal search strategy. *J Clin Epidemiol* 2000;**53**:65–9.

681. Begg C, Berlin J. Publication bias and dissemination of clinical research. *J Natl Cancer Inst* 1989;**81**:107–15.

682. Dickersin K, Chan S, Chalmers T, Sacks H, Smith H. Publication bias and clinical trials. *Control Clin Trials* 1987;**8**:343–53.

683. Whiting P, Rutjes AWS, Dinnes J, Reitsma JB, Bossuyt PMM, Kleijnen J. Development and validation of methods for assessing the quality of diagnostic accuracy studies. *Health Technol Assess* 2004;**8**(25).

684. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, *et al*. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. *BMJ* 2003;**326**:41–4.

685. Bossuyt PMM, Reitsma JB, Bruns D, Gatsonis C, Glasziou P, Irwig L, *et al*. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. *Ann Intern Med* 2003; **138**:W1–12.

686. Steurer J, Fischer J, Bachmann L, Koller M, ter Riet G. Communicating test accuracy terms to practising physicians: a controlled study. *BMJ* 2002;**324**:824–6.

687. Altman D. *Practical statistics for medical research*. London: Chapman & Hall; 1991.

688. Rutter CM, Gatsonis C. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Stat Med* 2001;**20**: 2865–84.

689. Macaskill P. Empirical Bayes estimates generated in a hierarchical summary ROC analysis agreed closely with those of a full Bayesian analysis. *J Clin Epidemiol* 2004;**57**:925–32.

690. Signatories to the consensus statement. Decision analytic modelling in the economic evaluation of health technologies: a consensus statement. *Pharmacoeconomics* 2000;**17**:443–4.

691. Sculpher M, Fenwick E, Claxton K. Assessing quality in decision analytic cost-effectiveness models: a suggested framework and example of application. *Pharmacoeconomics* 2000;**17**: 461–77.

692. National Institute for Clinical Excellence. *Guide to the methods of technology appraisal*. London: NICE; 2004. p. 54. URL: http://www.nice.org.uk/pdf/TAP_Methods.pdf. Accessed October 2005.

Appendix 1

Advisory panel members

Professor Ian Watt
Department of Health Sciences
University of York

Professor Mark Sculpher
Centre for Health Economics
University of York

Appendix 2

Protocol changes

Inclusion criteria

Studies with fewer than 20 participants were excluded, other than for adverse events.

Appendix 3

Detailed search strategies

The core search strategy used for this review was as follows:

(iliac adj (arter$ or vein$ or vessel$))
(femoral adj (arter$ or vein$ or vessel)
(popliteal adj (arter$ or vein$ or vessel)
(tibial adj (arter$ or vein$ or vessel)
(peroneal adj (arter$ or vein$ or vessel$))
(genicular adj (arter$ or vein$ or vessel$))
(saphenous adj (vein$ or vessel$))
femoropopliteal
iliofemoral
aortoiliac
infrapopliteal
(tibial runoff adj (arter$ or vein$ or vessel$))
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
(lower limb$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
(lower extremit$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
(leg adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
peripheral vascular
peripheral arter$
14 or 15 or 16 or 17 or 18
exp ultrasonography, doppler, duplex/
exp ultrasonography, doppler, color/
exp magnetic resonance angiography/
exp tomography, x-ray computed/
duplex ultrasound
echography
ct angiography
mr angiography
mra.ab,ti.
(mr adj2 angiograph$)
(mri adj2 angiograph$)
cta.ti,ab.
(duplex adj2 ultrasound)
20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
19 and 33
Animals/
Human/
35 not (35 and 36)
33 not 37

This strategy was designed for searching the MEDLINE electronic database (on Ovid), and was adapted, as appropriate, for all other databases searched, taking into account differences in indexing terms and search syntax for each database. Search strategies were not designed to restrict the retrieved results by study type. Full details of all the databases searched and search strategies used are provided below.

MEDLINE: Ovid

The MEDLINE database was searched from 1996 to April week 4 2004 on 10 May 2004 and the following strategy was used. An update search was undertaken on 11 May 2005 covering the period May 2004 to 2005 April week 4.

(iliac adj (arter$ or vein$ or vessel$))
(femoral adj (arter$ or vein$ or vessel)
(popliteal adj (arter$ or vein$ or vessel)
(tibial adj (arter$ or vein$ or vessel)
(peroneal adj (arter$ or vein$ or vessel$))
(genicular adj (arter$ or vein$ or vessel$))
(saphenous adj (vein$ or vessel$))
femoropopliteal
iliofemoral
aortoiliac
infrapopliteal
(tibial runoff adj (arter$ or vein$ or vessel$))
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
(lower limb$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
(lower extremit$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
(leg adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
peripheral vascular
peripheral arter$
14 or 15 or 16 or 17 or 18
exp ultrasonography, doppler, duplex/
exp ultrasonography, doppler, color/
exp magnetic resonance angiography/
exp tomography, x-ray computed/
duplex ultrasound
echography
ct angiography
mr angiography
mra.ab,ti.

(mr adj2 angiograph$)
(mri adj2 angiograph$)
cta.ti,ab.
(duplex adj2 ultrasound)
20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
19 and 33
Animals/
Human/
35 not (35 and 36)
33 not 37

EMBASE: Ovid

The EMBASE database was searched from 1980 to week 19 2004 on 10 May 2004 and the following strategy was used. An update search was undertaken on 11 May 2005 covering the period 2004 week 20 to 2005 week 19.

(iliac adj (arter$ or vein$ or vessel$))
(femoral adj (arter$ or vein$ or vessel$))
(popliteal adj (arter$ or vein$ or vessel$))
(tibial adj (arter$ or vein$ or vessel$))
(peroneal adj (arter$ or vein$ or vessel$))
(genicular adj (arter$ or vein$ or vessel$))
(saphenous adj (vein$ or vessel$))
femoropopliteal
iliofemoral
aortoiliac
infrapopliteal
(tibial runoff adj (arter$ or vein$ or vessel$))
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
(lower limb$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
(lower extremit$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
(leg adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive))
peripheral vascular
peripheral arter
13 or 14 or 15 or 16 or 17 or 18
duplex ultrasound
echography
ct angiography
mr angiography
mra.ab,ti.
(mr adj2 angiograph$)
(mri adj2 angiograph$)
cta.ti,ab.
(duplex adj2 ultrasound
exp echography/
exp computer assisted tomography/
((duplex or doppler) adj2 ultrasonograph$)
20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
19 and 32
human/
nonhuman/
34 not (34 and 35)
33 not 36

BIOSIS Previews: Dialog

The Biosis Previews database was searched from 1969 to May week 2 2004 on 14 May 2004 and the following strategy was used. An update search was undertaken on 12 May 2005 covering the period May 2004 to May 2005.

S1 iliac(w)(arter? Or vein? Or vessel?)/ti,ab,de
s2 femoral(w)(arter? Or vein? Or vessel?)/ti,ab,de
s3 popliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s4 tibial(w)(arter? Or vein? Or vessel?)/ti,ab,de
s5 peroneal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s6 genicular(w)(arter? Or vein? Or vessel?)/ti,ab,de
s7 saphenous(w)(arter? Or vein? Or vessel?)/ti,ab,de
s8 femoropopliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s9 iliofemoral/ti,ab,de
s10 aortoiliac/ti,ab,de
s11 infrapopliteal/ti,ab,de
s12 (tibial(w)runoff)(2w)(vein? Or arter? Or vessel?)/ti,ab,de
s13 (lower(w)limb?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s14 (lower(w)extremit?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s15 leg(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s16 peripheral(w)vascular/ti,ab,de
s17 peripheral(w)arter?/ti,ab,de
s18 s1:s17
s19 doppler(2w)ultrasonograph?/ti,ab,de
s20 magnetic(w)resonance(w)angiograph?/ti,ab,de
s21 computed(2w)tomography/ti,ab,de
s22 duplex(w)ultrasound/ti,ab,de
s23 echography/ti,ab,de
s24 ct(w)angiograph?/ti,ab,de
s25 mra/ti,ab
s26 mr(w)angiograph?/ti,ab,de
s27 mri(w)angiograph?/ti,ab,de
s28 cta/ti,ab

s29 s19:s28
s30 s18 and s29

Science Citation Index: ISI Web of Knowledge

The Science Citation Index database was searched from 1981 to May 2004 on 10 May 2004 and the following strategy was used. An update search was undertaken on 11 May 2005 covering the period 1981 to 11 May 2005.

TS=((iliac or femoral or popliteal or tibial or peroneal or genicular or saphenous) same (arter* or vein* or vessel*))
TS=(femoropopliteal or iliofemoral or aortoiliac or infrapopliteal)
TS=(tibial same runoff same (arter* or vein* or vessel*))
TS=(((lower limb*) or (lower extremit*) or leg) same (iscaehi* or ischemi* or arter* or vein* or vessel* or vascular or occlusive))
TS=((peripheral vascular) or (peripheral arter*))
#1 OR #2 OR #3 OR #4 OR #5
TS=(ultrasonograph* same doppler)
TS=(magnetic resonance angiograph*)
TS=(computed same tomograph*)
TS=((duplex ultrasound) or echography)
TS=(ct same angiograph*)
TS=((mr or mri) same angiograph*)
#7 or #8 or #9 or #10 or #11 or #12
#6 and #13

NTIS: Dialog

The NTIS database was searched from 1964 to week 2 May 2004 on 14 May 2004 and the following strategy was used. An update search was undertaken on 12 May 2005 covering the period May 2004 to April 2005.

S1 iliac(w)(arter? Or vein? Or vessel?)/ti,ab,de
s2 femoral(w)(arter? Or vein? Or vessel?)/ti,ab,de
s3 popliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s4 tibial(w)(arter? Or vein? Or vessel?)/ti,ab,de
s5 peroneal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s6 genicular(w)(arter? Or vein? Or vessel?)/ti,ab,de
s7 saphenous(w)(arter? Or vein? Or vessel?)/ti,ab,de
s8 femoropopliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s9 iliofemoral/ti,ab,de
s10 aortoiliac/ti,ab,de
s11 infrapopliteal/ti,ab,de
s12 (tibial(w)runoff)(2w)(vein? Or arter? Or vessel?)/ti,ab,de
s13 (lower(w)limb?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s14 (lower(w)extremit?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s15 leg(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s16 peripheral(w)vascular/ti,ab,de
s17 peripheral(w)arter?/ti,ab,de
s18 s1:s17
s19 doppler(2w)ultrasonograph?/ti,ab,de
s20 magnetic(w)resonance(w)angiograph?/ti,ab,de
s21 computed(2w)tomography/ti,ab,de
s22 duplex(w)ultrasound/ti,ab,de
s23 echography/ti,ab,de
s24 ct(w)angiograph?/ti,ab,de
s25 mra/ti,ab
s26 mr(w)angiograph?/ti,ab,de
s27 mri(w)angiograph?/ti,ab,de
s28 cta/ti,ab
s29 s19:s28
s30 s18 and s29

LILACS: via http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/

The LILACS database was searched from 1982 to May 2004 on 14 May 2004 and the following strategy was used. An update search was undertaken on 13 May 2005 covering the period 1982 to 13 May 2005.

((iliac AND arter$) OR (iliac AND vein$) OR (iliac AND vessel$) OR (femoral AND arter$) OR (femoral AND vein$) OR (femoral AND vessel$) OR (popliteal AND arter$) OR (popliteal AND vein$) OR (poplitealL AND vessel$) OR (tibial AND arter$) OR (tibial AND vein$) OR (tibial AND vessel$) OR (peroneal AND arter$) OR (peroneal AND vein$) OR (peroneal AND vessel$) OR (genicular AND arter$) OR (genicular and vein$) OR (genicular AND vessel$) OR (saphenous AND arter$) OR (saphenous AND vein$) OR (saphenous AND vessel$) OR (femoropoliteal AND arter$) OR (femoropopliteal AND vein$) OR (femoropopliteal AND vessel$) OR (iliofemoral) OR (aortoiliac) OR (infrapopliteal) OR (lower AND limb$ AND ischaemi$) OR (lower AND limb$ AND ischemi$)

OR (lower AND limb$ AND arter$) OR (lower AND limb$ AND vein$) OR (lower AND limb$ AND vessel$) OR (lower AND limb$ AND vascular) OR (lower AND limb$ AND occlusive) OR (lower AND extremit$ AND ischaemi$) OR (lower AN! D extremit$ AND ischemi$) OR (lower AND extremit$ AND arter$) OR (lower AND extremit$ AND vein$) OR (lower AND extremit$ AND vessel$) OR (lower AND extremit$ and vascular) OR (lower AND extremit$ and occlusive) OR (leg AND limb$ AND ischaemi$) OR (leg AND limb$ AND ischemi$) OR (leg AND limb$ AND arter$) OR (leg AND limb$ AND vein$) OR (leg AND limb$ AND vessel$) OR (leg AND limb$ and vascular) OR (leg AND limb$ and occlusive) OR (peripheral AND vascular) OR (peripheral AND arter$)) and ((doppler AND ultrasonograph$) OR (magnetic AND resonance AND angiograph$) OR (computed AND tomograph$) OR (duplex AND ultrasound) OR (echocography) OR (ct AND angiograph$) OR (MR AND angiograph$) OR (MRI AND angiograph$))

SIGLE: WebSPIRS

The SIGLE database was searched from 1980 to May 2004 on 19 May 2004 and the following strategy was used.

#1 iliac adj (arter* or vein* or vessel*)
#2 femoral adj (arter* or vein* or vessel*)
#3 popliteal adj (arter* or vein* or vessel*)
#4 tibial adj (arter* or vein* or vessel*)
#5 peroneal adj (arter* or vein* or vessel*)
#6 genicular adj (arter* or vein* or vessel*)
#7 saphenous adj (arter* or vein* or vessel*)
#8 femoropopliteal
#9 iliofemoral
#10 aortoiliac
#11 infrapopliteal
#12 (tibial runoff) adj (arter* or vein* or vessel*)
#13 (lower limb*) adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)
#14 (lower extremit*) adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)
#15 leg adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)
#16 peripheral vascular
#17 peripheral arter*
#18 (aortoiliac) or (iliofemoral) or (femoropopliteal) or (saphenous adj (arter* or vein* or vessel*)) or (genicular adj (arter* or vein* or vessel*)) or (peroneal adj (arter* or vein* or vessel*)) or (tibial adj (arter* or vein* or vessel*)) or (popliteal adj (arter* or vein* or vessel*)) or (femoral adj (arter* or vein* or vessel*)) or (iliac adj (arter* or vein* or vessel*)) or (peripheral arter*) or (peripheral vascular) or (leg adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)) or ((lower extremit*) adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)) or ((lower limb*) adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)) or ((tibial runoff) adj (arter* or vein* or vessel*)) or (infrapopliteal)
#19 doppler ultrasonography
#20 duplex ultrasonography
#21 magnetic resonance angiograph*
#22 computed tomography
#23 echography
#24 duplex ultrasound
#25 ct angiography
#26 mr angiography
#27 mra in ti,ab(3 records)
#28 mr adj angiograph*
#29 mri angiograph*
#30 cta in ti,ab
#31 duplex ultrasound
#32 duplex ultrasound
#33 (cta in ti,ab) or (duplex ultrasound) or (mri angiograph*) or (duplex ultrasound) or (mr adj angiograph*) or (mra in ti,ab) or (mr angiography) or (ct angiography) or (duplex ultrasound) or (echography) or (duplex ultrasonography) or (computed tomography) or (doppler ultrasonography) or (magnetic resonance angiograph*)
#34 ((cta in ti,ab) or (duplex ultrasound) or (mri angiograph*) or (duplex ultrasound) or (mr adj angiograph*) or (mra in ti,ab) or (mr angiography) or (ct angiography) or (duplex ultrasound) or (echography) or (duplex ultrasonography) or (computed tomography) or (doppler ultrasonography) or (magnetic resonance angiograph*)) and ((aortoiliac) or (iliofemoral) or (femoropopliteal) or (saphenous adj (arter* or vein* or vessel*)) or (genicular adj (arter* or vein* or vessel*)) or (peroneal adj (arter* or vein* or vessel*)) or (tibial adj (arter* or vein* or vessel*)) or (popliteal adj (arter* or vein* or vessel*)) or (femoral adj (arter* or vein* or vessel*)) or (iliac adj (arter* or vein* or vessel*)) or (peripheral arter*) or (peripheral vascular) or (leg adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)) or ((lower extremit*) adj (ischaemia or ischemia or arter* or vein* or vessel* or

vascular or occlusive)) or ((lower limb*) adj (ischaemia or ischemia or arter* or vein* or vessel* or vascular or occlusive)) or ((tibial runoff) adj (arter* or vein* or vessel*)) or (infrapopliteal))

Dissertation Abstracts: Dialog

The Dissertation Abstracts database was searched from 1861 to April 2004 on 17 May 2004 and the following strategy was used. An update search was undertaken on 12 May 2005 covering the period April 2004 to May 2005.

S1 iliac(w)(arter? Or vein? Or vessel?)/ti,ab,de
s2 femoral(w)(arter? Or vein? Or vessel?)/ti,ab,de
s3 popliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s4 tibial(w)(arter? Or vein? Or vessel?)/ti,ab,de
s5 peroneal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s6 genicular(w)(arter? Or vein? Or vessel?)/ti,ab,de
s7 saphenous(w)(arter? Or vein? Or vessel?)/ti,ab,de
s8 femoropopliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s9 iliofemoral/ti,ab,de
s10 aortoiliac/ti,ab,de
s11 infrapopliteal/ti,ab,de
s12 (tibial(w)runoff)(2w)(vein? Or arter? Or vessel?)/ti,ab,de
s13 (lower(w)limb?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s14 (lower(w)extremit?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s15 leg(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s16 peripheral(w)vascular/ti,ab,de
s17 peripheral(w)arter?/ti,ab,de
s18 s1:s17
s19 doppler(2w)ultrasonograph?/ti,ab,de
s20 magnetic(w)resonance(w)angiograph?/ti,ab,de
s21 computed(2w)tomography/ti,ab,de
s22 duplex(w)ultrasound/ti,ab,de
s23 echography/ti,ab,de
s24 ct(w)angiograph?/ti,ab,de
s25 mra/ti,ab
s26 mr(w)angiograph?/ti,ab,de
s27 mri(w)angiograph?/ti,ab,de
s28 cta/ti,ab
s29 s19:s28
s30 s18 and s29

Inside Conferences: Dialog

The Inside Conferences database was searched from 1861 to April 2004 on 17 May 2004 and the following strategy was used. An update search was undertaken on 12 May 2005 covering the period May 2004 to May 2005.

S1 iliac(w)(arter? Or vein? Or vessel?)/ti,ab,de
s2 femoral(w)(arter? Or vein? Or vessel?)/ti,ab,de
s3 popliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s4 tibial(w)(arter? Or vein? Or vessel?)/ti,ab,de
s5 peroneal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s6 genicular(w)(arter? Or vein? Or vessel?)/ti,ab,de
s7 saphenous(w)(arter? Or vein? Or vessel?)/ti,ab,de
s8 femoropopliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s9 iliofemoral/ti,ab,de
s10 aortoiliac/ti,ab,de
s11 infrapopliteal/ti,ab,de
s12 (tibial(w)runoff)(2w)(vein? Or arter? Or vessel?)/ti,ab,de
s13 (lower(w)limb?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s14 (lower(w)extremit?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s15 leg(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s16 peripheral(w)vascular/ti,ab,de
s17 peripheral(w)arter?/ti,ab,de
s18 s1:s17
s19 doppler(2w)ultrasonograph?/ti,ab,de
s20 magnetic(w)resonance(w)angiograph?/ti,ab,de
s21 computed(2w)tomography/ti,ab,de
s22 duplex(w)ultrasound/ti,ab,de
s23 echography/ti,ab,de
s24 ct(w)angiograph?/ti,ab,de
s25 mra/ti,ab
s26 mr(w)angiograph?/ti,ab,de
s27 mri(w)angiograph?/ti,ab,de
s28 cta/ti,ab
s29 s19:s28
s30 s18 and s29

Pascal: Dialog

The Pascal database was searched from 1973 to 2004 July week 4 on 3 August 2004 and the following strategy was used. An update search was

undertaken on 12 May 2005 covering the period May 2004 to August 2005.

S1 iliac(w)(arter? Or vein? Or vessel?)/ti,ab,de
s2 femoral(w)(arter? Or vein? Or vessel?)/ti,ab,de
s3 popliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s4 tibial(w)(arter? Or vein? Or vessel?)/ti,ab,de
s5 peroneal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s6 genicular(w)(arter? Or vein? Or vessel?)/ti,ab,de
s7 saphenous(w)(arter? Or vein? Or vessel?)/ti,ab,de
s8 femoropopliteal(w)(arter? Or vein? Or vessel?)/ti,ab,de
s9 iliofemoral/ti,ab,de
s10 aortoiliac/ti,ab,de
s11 infrapopliteal/ti,ab,de
s12 (tibial(w)runoff)(2w)(vein? Or arter? Or vessel?)/ti,ab,de
s13 (lower(w)limb?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s14 (lower(w)extremit?)(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s15 leg(2w)(ischaemi? Or ischemi? Or arter? Or vein? Or vessel? Or vascular or occlusive)/ti,ab,de
s16 peripheral(w)vascular/ti,ab,de
s17 peripheral(w)arter?/ti,ab,de
s18 s1:s17
s19 doppler(2w)ultrasonograph?/ti,ab,de
s20 magnetic(w)resonance(w)angiograph?/ti,ab,de
s21 computed(2w)tomography/ti,ab,de
s22 duplex(w)ultrasound/ti,ab,de
s23 echography/ti,ab,de
s24 ct(w)angiograph?/ti,ab,de
s25 mra/ti,ab
s26 mr(w)angiograph?/ti,ab,de
s27 mri(w)angiograph?/ti,ab,de
s28 cta/ti,ab
s29 s19:s28
s30 s18 and s29

In addition to the literature searches to identify studies of effectiveness, searches were undertaken to inform the economic modelling. These are detailed below.

Cochrane Database of Systematic Reviews

Issue 3 2005 was searched on 1 August 2005 using the Wiley Interscience interface to identify reviews of effectiveness. The following search strategy was used.

"(lower limb*) near/2 (ischaem* or ischem*) in Record Title or (lower extremit*) near/2 (ischaem* or ischem*) in Record Title or leg* near/2 (ischaem* or ischem*) in Record Title or Peripheral arter* in Record Title or peripheral vascular disease* in Keywords in The Cochrane Database of Systematic Reviews"

MEDLINE: Ovid

The MEDLINE database was searched from 1993 to 2005 on 27 July 2005 to identify quality of life studies using the strategy below.

1. (utilit$ approach$ or health gain or hui or hui2 or hui3).ti,ab.
2. (health measurement$ scale$ or health measurement$ questionnaire$).ti,ab.
3. (standard gamble$ or categor$ scal$ or linear scal$ or linear analog$ or visual scal$ or magnitude estimat$).ti,ab.
4. (time trade off$ or rosser$ classif$ or rosser$ matrix or rosser$ distress$ or hrqol).ti,ab.
5. (index of wellbeing or quality of wellbeing or qwb).ti,ab.
6. (multiattribute$ health ind$ or multi attribute$ health ind$).ti,ab.
7. (health utilit$ index or health utilit$ indices).ti,ab.
8. (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab.
9. (health utilit$ scale$ or classification of illness state$).ti,ab.
10. health state$ utilit$.ti,ab.
11. well year$.ti,ab.
12. (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab.
13. health utilit$ scale$.ti,ab.
14. (euro qual or euro qol or eq-5d or eq5d or eq 5d or euroqual or euroqol).ti,ab.
15. (qualy or qaly or qualys or qalys or quality adjusted life year$).ti,ab.
16. willingness to pay.ti,ab.
17. (hye or hyes or health$ year$ equivalent$).ti,ab.
18. (person trade off$ or persn tradeoff$ or time tradeoff$ or time trade off$).ti,ab.
19. theory utilit$.ti,ab.
20. (sf36 or sf 36).ti,ab.
21. (short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or

shortform thirty six or short form thirtysix or short form thirty six).ti,ab.
22. (sf 6d or sf6d or short form 6d or shortform 6d or sf six$ or shortform six$ or short form six$).ti,ab.
23. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. (iliac adj (arter$ or vein$ or vessel$)).mp.
25. (femoral adj (arter$ or vein$ or vessel$)).mp.
26. (popliteal adj (arter$ or vein$ or vessel$)).mp.
27. (tibial adj (arter$ or vein$ or vessel$)).mp.
28. (peroneal adj (arter$ or vein$ or vessel$)).mp.
29. (peroneal adj (arter$ or vein$ or vessel$)).mp.
30. (peroneal adj (arter$ or vein$ or vessel$)).mp.
31. (genicular adj (arter$ or vein$ or vessel$)).mp.
32. (saphenous adj (vein$ or vessel$)).mp.
33. femoropopliteal.mp.
34. iliofemoral.mp.
35. aortoiliac.mp.
36. infrapopliteal.mp.
37. (tibial runoff adj (arter$ or vein$ or vessel$)).mp.
38. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37
39. (lower limb$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.
40. (lower extremit$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.
41. (leg adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp
42. peripheral vascular.mp.
43. peripheral arter$.mp.
44. 38 or 39 or 40 or 41 or 42 or 43
45. 23 and 44

PREMEDLINE: Ovid

The PREMEDLINE database was searched on 27 July 2005 to identify quality of life studies using the strategy below.

1. (utilit$ approach$ or health gain or hui or hui1 or hui2 or hui3).ti,ab.
2. (health measurement$ scale$ or health measurement$ questionnaire$).ti,ab.
3. (standard gamble$ or categor$ scal$ or linear scal$ or linear analog$ or visual scal$ or magnitude estimat$).ti,ab.
4. (time trade off$ or rosser$ classif$ or rosser$ matrix or rosser$ distress$ or hrqol).ti,ab.
5. (index of welbeing or quality of wellbeing or qwb).ti,ab.
6. (multiattribute$ health ind$ or multi attribute$ health ind$).ti,ab.
7. (health utilit$ index or health utilit$ indices).ti,ab.
8. (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab.
9. (health utilit$ scale$ or classification of illness state$).ti,ab.
10. health state$ utilit$.ti,ab.
11. well year$.ti,ab.
12. (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab.
13. health utilit$ scale$.ti,ab.
14. (euro qual or euro qol or eq-5d or eq5d or eq 5d or euroqual or euroqol).ti,ab.
15. (qualy or qaly or qualys or qalys or quality adusted life year$).ti,ab.
16. willingness to pay.ti,ab.
17. (hye or hyes or health$ year$ equivalent$).ti,ab.
18. (person trade off$ or person tradeoff$ or time tradeoff$ or time trade off$).ti,ab.
19. theory utilit$.ti,ab.
20. (sf36 or sf 36).ti,ab.
21. (short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab.
22. (sf 6d or sf6d or short form 6d or shortform 6d or sf six$ or shortform six$ or short form six$).ti,ab.
23. or/1-22
24. (iliac adj (arter$ or vein$ or vessel$)).mp.
25. (femoral adj (arter$ or vein$ or vessel$)).mp.
26. (popliteal adj (arter$ or vein$ or vessel$)).mp.
27. (tibial adj (arter$ or vein$ or vessel$)).mp.
28. (peroneal adj (arter$ or vein$ or vessel$)).mp.
29. (peroneal adj (arter$ or vein$ or vessel$)).mp.
30. (peroneal adj (arter$ or vein$ or vessel$)).mp.
31. (genicular adj (arter$ or vein$ or vessel$)).mp.
32. (saphenous adj (vein$ or vessel$)).mp.
33. femoropopliteal.mp.
34. iliofemoral.mp.
35. aortoiliac.mp.
36. infrapopliteal.mp.
37. (tibial runoff adj (arter$ or vein$ or vessel$)).mp.
38. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37
39. (lower limb$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.
40. (lower extremit$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.

41. (leg adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.
42. peripheral vascular.mp.
43. peripheral arter$.mp.
44. 38 or 39 or 40 or 41 or 42 or 43
45. 23 and 44

EMBASE: Ovid

The EMBASE database was searched from 1993 to 2005 on 27 July 2005 to identify quality of life studies using the strategy below.

1. (utilit$ approach$ or health gain or hui or hui1 or hui2 or hui3).ti,ab.
2. (health measurement$ scale$ or health measurement$ questionnaire$).ti,ab.
3. (standard gamble$ or categor$ scal$ or linear scal$ or linear analog$ or visual scal$ or magnitude estimat$).ti,ab.
4. (time trade off$ or rosser$ classif$ or rosser$ matrix or rosser$ distress$ or hrqol).ti,ab.
5. (index of wellbeing or quality of wellbeing or qwb).ti,ab.
6. (multiattribute$ health ind$ or multi attribute$ health ind$).ti,ab.
7. (health utilit$ index or health utilit$ indices).ti,ab.
8. (multattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab.
9. (health utilit$ scale$ or classification of illness state$).ti,ab.
10. health state$ utilit$.ti,ab.
11. well year$.ti,ab.
12. (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab.
13. health utilit$ scale$.ti,ab.
14. (euro qual or euro qol or eq-5d or eq5d or eq 5d or euroqual or euroqol).ti,ab.
15. (qualy or qaly or qualys or qalys or quality adjusted life year$).ti,ab.
16. willingness to pay.ti,ab.
17. (hye or hyes or health$ year$ equaivalent$).ti,ab.
18. (person trade off$ or person tradeoff$ or time tradeoff$ or time trade off$).ti,ab.
19. theory utilit$.ti,ab.
20. (sf36 or sf 36).ti,ab.
21. (short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or shrt form thirtysix or short form thirty six).ti,ab.
22. (sf 6d or sf6d or short form 6d or shortform 6d or sf six$ or shortform six$ or short form six$).ti,ab.
23. or/1-22
24. (iliac adj (arter$ or vein$ or vessel$)).mp.
25. (femoral adj (arter$ or vein$ or vessel$)).mp.
26. (popliteal adj (arter$ or vein$ or vessel$)).mp.
27. (tibial adj (arter$ or vein$ or vessel$)).mp.
28. (peroneal adj (arter$ or vein$ or vessel$)).mp.
29. (peroneal adj (arter$ or vein$ or vessel$)).mp.
30. (peroneal adj (arter$ or vein$ or vessel$)).mp.
31. (genicular adj (arter$ or vein$ or vessel$)).mp
32. (saphenous adj (vein$ or vessel$)).mp
33. femoropopliteal.mp.
34. iliofemoral.mp.
35. aortoiliac.mp.
36. infrapopliteal.mp.
37. (tibial runoff adj (arter$ or vein$ or vessel$)).mp.
38. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37
39. (lower limb$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.
40. (lower extremit$ adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.
41. (leg adj2 (ischaemi$ or ischemi$ or arter$ or vein$ or vessel$ or vascular or occlusive)).mp.
42. peripheral vascular.mp.
43. peripheral arter$.mp.
44. 38 or 39 or 40 or 41 or 42 or 43
45. 23 and 44

Appendix 4

QUADAS and details of criteria for scoring studies

TABLE 34 *The QUADAS tool*

1.	**Was the spectrum of patients representative of the patients who will receive the test in practice?**
Yes	Unselected, prospective, adult patients with symptoms suggestive of lower limb PAD
No	All other patient spectra including retrospectively selected patient spectra
Unclear	If insufficient details were provided to make a judgement as to whether the patient spectrum would be scored as 'yes'
2.	**Were selection criteria clearly described?**
Yes	Enough details were provided of how patients were selected so that the selection process could be replicated
No	Insufficient details were presented
Unclear	Not applicable
3.	**Was the reference standard likely to correctly classify the target condition?**
NA	Only studies with an appropriate reference standard were included
4.	**Was the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?**
Yes	The time between index test and reference standard was $\leq$1 month
No	If greater than above
Unclear	If details of the time elapsed between tests were not reported
5.	**Did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis?**
Yes	If the whole sample or a random selection of the sample received the same reference standard
No	If only a selected sample received the reference standard
Unclear	If it was not clear whether all the patients received the reference standard
6.	**Did patients receive the same reference standard regardless of the index test result?**
Yes	If all patients received the same reference standard
No	If some patients received a different reference standard
Unclear	If it was not clear whether all patients received the same reference standard
7.	**Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?**
Yes	If the index test and reference standard were independent
No	If the index test formed part of the reference standard
Unclear	If it was not clear whether the index test and reference standard were independent
8a. **8b.**	**Was the execution of the index test described in sufficient detail to permit replication of the test?** **Was the execution of the reference standard described in sufficient detail to permit its replication?**
Yes	If sufficient details of test/reference standard execution were reported so that the test/reference standard could reasonably be replicated
No	If sufficient details were not reported
Unclear	Not applicable
9a. **9b.**	**Were the index test results interpreted without knowledge of the results of the reference standard?** **Were the reference standard results interpreted without knowledge of the results of the index test?**
Yes	If the index test was interpreted without knowledge of the results of the reference standard and vice versa If one test was clearly interpreted before the results of the other test were available then this should be scored as 'yes'
No	If the person interpreting the index test was aware of the results of the reference standard or vice versa
Unclear	If no information is provided regarding whether tests were interpreted blindly

continued

TABLE 34 *The QUADAS tool (cont'd)*

10.	**Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?**
Yes	If the article states that the following information was available: description (including side) of symptoms, site of any ulceration or gangrene, presence of peripheral pulses, surgical history
No	If not as above
Unclear	If details on the availability of clinical data were not reported
11.	**Were uninterpretable/intermediate test results reported?**
Yes	If details were provided on uninterpretable/intermediate test results
No	If there appear to be some uninterpretable/intermediate test results but the results of these were not reported
Unclear	If it was not clear whether there were any uninterpretable/intermediate test results
12.	**Were withdrawals from the study explained?**
Yes	If all patients recruited into the study were accounted for
No	If there appear to be patients who were recruited into the study who were not accounted for
Unclear	If it is not clear whether any withdrawals occurred

Appendix 5

Quality checklist for the included economic evaluations

TABLE 35 *Quality checklist*

Question	Visser, 2003[128]	Visser, 2003[130]	Geitung, 1996[126]	Visser, 2003[129]	Yin, 1995[131]
1. The research question is stated	Y	Y	Y	Y	Y
2. The economic importance of the research question is stated	Y	Y	N	Y	Y
3. The viewpoint(s) of the analysis are stated and justified	Unclear	Unclear	N	N	Y
4. The rationale for choosing the alternative programmes or interventions is stated	Y	Y	Y	Y	Y
5. The alternatives being compared are clearly described	Y	Y	Y	Y	Y
6. The form of economic evaluation is stated	N	N	Y	N	Y
7. The choice of form of economic evaluation is justified in relation to the questions addressed	N	N	N	N	N
8. The source(s) of effectiveness estimates are stated	Y	Y	Y	Y	Y
9. Details of the design and results of effectiveness study are given (if based on a single study)	NA	NA	Y	NA	NA
10. Details of methods of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)	N	N	NA	N	N
11. The primary outcome measure(s) for the economic evaluation are clearly stated	Y	Y	Y	Y	Y
12. Methods to value health states and other benefits are stated	NA	Y	NA	Y	Y
13. Details of the subjects from whom valuations are obtained are given	Unclear	Unclear	Unclear	N	N
14. Productivity changes (if included) are reported separately	NA	NA	NA	N	Unclear
15. The relevance of productivity changes to the study question is discussed	Y	N	N	N	N
16. Quantities of resources are reported separately from their unit costs	N	N	Unclear	N	N
17. Methods for the estimation of quantities and unit costs are described	Unclear	Unclear	Y	Unclear	Unclear
18. Currency and price data are recorded	Y	Y	Y	Y	Unclear
19. Details of currency of price adjustments for inflation or currency conversion are given	Y	Y	N	Y	N
20. Details of any model used are given	Y	Y	NA	Y	Y
21. The choice of model used and key parameters on which it is based are justified	N	Unclear	NA	Unclear	Unclear
22. The horizon of costs and benefits is stated	Y	Y	N	Y	N
23. The discount rate is stated	Y	Y	NA	Y	Y
24. The choice of rate is justified	Unclear	Unclear	NA	Unclear	N
25. An explanation is given if costs or benefits are not discounted	NA	NA	NA	NA	NA
26. Details of statistical test and confidence intervals are given for stochastic data	N	NA	N	NA	NA
27. The approach to sensitivity analysis is given	N	Y	Y	Y	Y
28. The choice of variables for sensitivity analysis is justified	Y	Y	N	Y	Y
29. The ranges over which the variables are varied is stated	Y	Y	N	Y	Y
30. Relevant alternatives are compared	Y	Y	Y	Y	Y
31. Incremental analysis is reported	Y	N	N	Y	Y
32. Major outcomes are reported in a disaggregated as well as an aggregated form	N	N	N	N	N
33. The answer to the study question is given	Y	Y	Y	Y	Y
34. Conclusions follow from the data reported	Y	Y	Y	Y	Y
35. Conclusions are accompanied by the appropriate caveats	Y	Y	N	Y	Y
36. Generalisability issues are addressed	Y	N	N	Unclear	N

Y, yes; N, no.

Appendix 6

Included studies evaluating tests to diagnose stenosis/occlusion

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion*

Study	Participants	Index test	Reference standard
Aly, 1998[20]	Aim of the study: Assessment of primary stenosis Number of patients: 90 (proportion male: 66%) Median age (years): 68 (range NR) Fontaine stage II: 90% Fontaine stage III: 9% Fontaine stage IV: 1% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 2.5- and 7-MHz linear array probes PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography (with DSA) Reference standard details: Uniplanar Common femoral artery puncture
Ashleigh, 1993[21]	Aim of the study: Assessment of primary stenosis Number of patients: 60 (proportion male: 63%) Mean age (years): 67 (range 34–89) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5-MHz linear array transducer PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography (with DSA) Reference standard details: None reported
Baum, 1995[22]	Aim of the study: Assessment of primary stenosis and graft stenosis Number of patients: 155 (proportion male: 63%) Mean age (years): 66 (range 27–88) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: Extremity Field strength: 1.5	Reference standard: Angiography Reference standard details: Intraoperative Hand injection directly into bypass graft Postprocedure arteriograms in patients having subcutaneous procedures
Baxter, 1993[23]	Aim of the study: Assessment of primary stenosis Number of patients: 20 (proportion male: 60%) Mean age (years): 62 (range 21–86) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5-MHz linear array probe PSVR of >1.8 indicated 50% stenosis	Reference standard: Angiography Reference standard details: 4 station cut film

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Bergamini, 1995[24]	Aim of the study: Assessment of primary stenosis Number of patients: 44 (proportion male: NR) Mean/median age (years): NR (range NR) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5-MHz Doppler transducer PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography Reference standard details: Uniplanar
Bostrom, 2001[25]	Aim of the study: Assessment of primary stenosis Number of patients: 183 (proportion male: 54%) Median age (years): 69 (range 43–88) Fontaine stage II: 52% Fontaine stage III: 27% Fontaine stage IV: 21% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 4–6-MHz linear, 2.5–5-MHz curved and 2–4-MHz vector array PSVR of 2.5 indicated 50% stenosis	Reference standard: Angiography (with DSA) Reference standard details: Uniplanar Femoral artery catheterisation
Catalano, 2004[26]	Aim of the study: Assessment of primary stenosis Number of patients: 50 (proportion male: 78%) Mean age (years): 67 (range 43–89) Fontaine stage II: 6% Fontaine stage III: 48% Fontaine stage IV: 46% Are the data from a patient subgroup? No	Index test: CTA Instrument: Volume Zoom, Siemens	Reference standard: Angiography (with DSA) Reference standard details: Transfemoral in 43 patients Left transaxillary in 7 patients
Cortell, 1996[27]	Aim of the study: Assessment of primary stenosis Number of patients: 31 (proportion male: 65%) Mean age (years): 69 (range 42–85) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: Head Field strength: 1.5 Above-knee and pelvic vessels were also imaged using 3D TOF MRA (with contrast when deemed appropriate); however, these results were not reported	Reference standard: Angiography (with DSA in 13 patients) Reference standard details: Common femoral artery puncture in 30 patients Axillary artery puncture in 1 patient
Cronberg, 2003[28]	Aim of the study: Assessment of primary stenosis Number of patients: 35 (proportion male: 46%) Mean age (years): 78 (range 50–98) Fontaine stage II: 9% Fontaine stage III: 3% Fontaine stage IV: 89% Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: 1.7-mm straight or pigtail catheter Superficial femoral or common iliac artery

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Currie, 1995[29]	Aim of the study: Assessment of primary stenosis Number of patients: 92 (proportion male: 74%) Median age (years): 64 (range 43–83) Fontaine stage II: 97% Fontaine stage III: 0% Fontaine stage IV: 3% Are the data from a patient subgroup? No	Index test 1: 2D TOF MRA Coil: NR Field strength: 1 Index test 2: Colour DUS Instrument/probe type: 5-MHz linear and 2.25- and 3.5-MHz phased array PSVR of 2.5 indicated 50% stenosis	Reference standard: Angiography Reference standard details: Biplanar Transfemoral or transbrachial routes
Davies, 1992[30]	Aim of the study: Assessment of primary stenosis Number of patients: 52 (proportion male: 75%) Median age (years): 64 (range 56–80) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: Linear 5-MHz, phased array 2.25-MHz PSVR: NR	Reference standard: Angiography Reference standard details: Biplanar
Eiberg, 2001[31]	Aim of the study: Assessment of primary stenosis Number of patients: 94 (proportion male: 55%) Median age (years): 72 (range 42–90) Fontaine stage II: 22% Fontaine stage III: 33% Fontaine stage IV: 45% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 7.5-MHz PSVR: NR	Reference standard: Angiography Reference standard details: Transfemoral arteriography
Eklof, 1998[32]	Aim of the study: Assessment of primary stenosis Number of patients: 24 (proportion male: 50%) Median age (years): 72 (range 37–97) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: Knee Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: Femoral artery puncture
El-Kayali, 2004[33]	Aim of the study: Assessment of primary stenosis Number of patients: 44 (proportion male: 66%) Mean age (years): 55 (range NR) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: DUS Instrument/probe type: 4-MHz probe (iliac segments), 7-MHz (infrainguinal segments) PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography (with DSA) Reference standard details: Uniplanar or biplanar

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Fletcher, 1990[34]	Aim of the study: Assessment of primary stenosis Number of patients: 28 (proportion male: 61%) Mean age (years): 65 (range 48–88) Fontaine stage II: 68% Fontaine stage III: 21% Fontaine stage IV: 11% Are the data from a patient subgroup? No	Index test: DUS Instrument/probe type: NR PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography Reference standard details: None reported
Grassbaugh, 2003[35]	Aim of the study: Assessment of primary stenosis Number of patients: 38 (proportion male: 53%) Mean age (years): 72 (range 44–82) Fontaine stage II: 0% Fontaine stage III: 34% Fontaine stage IV: 66% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 4–7-MHz linear array probe PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography Reference standard details: Preoperative or intraoperative Aorta, iliac or femoral artery injection
Hany, 1997[36]	Aim of the study: Assessment of primary stenosis Number of patients: 39 (proportion male: 72%) Mean age (years): 62 (range 34–81) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: Transfemorally inserted 5-F pigtail catheter
Hatsukami, 1992[37]	Aim of the study: Assessment of primary stenosis Number of patients: 29 (proportion male: 100%) Mean age (years): 63 (range 43–86) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5-MHz transducer PSVR: NR	Reference standard: Angiography Reference standard details: None reported
Heuschmid, 2003[38]	Aim of the study: Assessment of primary stenosis Number of patients: 23 (proportion male: 65%) Mean age (years): 66 (range NR) Fontaine stage II: 78% Fontaine stage III: 13% Fontaine stage IV: 9% Are the data from a patient subgroup? No	Index test: CTA Instrument: Somatom Volume Zoom (Siemens)	Reference standard: Angiography (with DSA) Reference standard details: Femoral artery puncture

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Hirai, 1998[39]	Aim of the study: Assessment of primary stenosis Number of patients: 52 (proportion male: NR) Mean/median age (years): NR (range NR) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5- or 3.5-MHz convex array (iliac), 7.5-MHz linear array (femoropopliteal) PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography Reference standard details: None reported
Hoch, 1996[40]	Aim of the study: Assessment of primary stenosis Number of patients: 45 (proportion male: 76%) Mean age (years): 65 (range NR) Fontaine stage II: 18% Fontaine stage III: 20% Fontaine stage IV: 62% Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: body (above knee), head or leg (below knee) Field strength: 1 or 1.5	Reference standard: Angiography (with DSA) Reference standard details: Femoral artery puncture
Hoch, 1999[41]	Aim of the study: Assessment of primary stenosis Number of patients: 20 (proportion male: 100%) Mean/median age (years): NR (range NR) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: body (above knee), head (below knee) Field strength: 1	Reference standard: Angiography (with DSA) Reference standard details: None reported
Hofmann, 2004[42]	Aim of the study: Assessment of primary stenosis Number of patients: 33 (proportion male: 85%) Median age (years): 70 (range 48–86) Fontaine stage II: 0% Fontaine stage III: 0% Fontaine stage IV: 100% Are the data from a patient subgroup? Diabetes mellitus	Index test: Colour DUS Instrument/probe type: 13-MHz linear array transducer PSVR: NR	Reference standard: Angiography (with DSA) and/or CE MRA[a] Reference standard details: Biplanar Ipsilateral common femoral artery puncture
Karacagil, 1996[43]	Aim of the study: Assessment of primary stenosis Number of patients: 38 (proportion male: 45%) Mean age (years): 71 (range 43–87) Fontaine stage II: 16% Fontaine stage III: 34% Fontaine stage IV: 50% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5-MHz linear array probe PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography (with DSA) Reference standard details: Uniplanar Femoral artery puncture

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Koelemay, 1997[44]	Aim of the study: Assessment of primary stenosis Number of patients: 23 (proportion male: 39%) Median age (years): 71 (range 29–85) Fontaine stage II: 9% Fontaine stage III: 52% Fontaine stage IV: 39% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 3.7- and 5.5-MHz probe PSVR: NR	Reference standard: Angiography (with DSA) Reference standard details: Biplanar Femoral artery puncture
Koelemay, 1998[45]	Aim of the study: Assessment of primary stenosis Number of patients: 120 (proportion male: 61%) Median age (years): 72 (range 27–95) Fontaine stage II: 16% Fontaine stage III: 34% Fontaine stage IV: 50% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 3.7- and 5.5-MHz PSVR: NR	Reference standard: Angiography (with DSA) Reference standard details: Biplanar Common femoral artery puncture
Kreitner, 2000[46]	Aim of the study: Unclear whether assessment of primary stenosis or graft stenosis Number of patients: 24 (proportion male: 71%) Mean age (years): 69 (range 53–84) Fontaine stage II: 0% Fontaine stage III: 0% Fontaine stage IV: 100% Are the data from a patient subgroup? Diabetes mellitus	Index test: CE MRA Coil: Head Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: 5-F pigtail catheter in distal aorta in 8 patients Femoral artery puncture in 6 patients Retrograde cross-over antegrade catheterisation of the common femoral, superficial femoral or popliteal artery in 10 patients
Lai, 1995[47]	Aim of the study: Assessment of primary stenosis Number of patients: 50 (proportion male: 0%) Mean/median age (years): NR (range NR) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 3.5- and/or 2.25-MHz and 5-MHz probe PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography (with DSA) Reference standard details: None reported
Lai, 1996[48]	Aim of the study: Assessment of primary stenosis Number of patients: 50 (proportion male: not reported) Mean/median age (years): NR (range NR) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 2.25- and/or 3.5-MHz (aortoiliac), 5-MHz (femoropopliteal) PSVR of 2.1 indicated 50% stenosis PSVR of 4.1 indicated 76% stenosis	Reference standard: Angiography (with DSA) Reference standard details: Transfemoral catheterisation

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Laissy, 1998[49]	Aim of the study: Assessment of primary stenosis Number of patients: 20 (proportion male: 85%) Mean age (years): 53 (range 42–62) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1	Reference standard: Angiography Reference standard details: Femoral or brachial artery puncture 5-F pigtail catheter in the distal aorta
Legemate, 1991[50]	Aim of the study: Assessment of primary stenosis Number of patients: 61 (proportion male: NR) Mean/median age (years): NR (range NR) Fontaine stage II: 80% Fontaine stage III: 16% Fontaine stage IV: 3% Are the data from a patient subgroup? No	Index test: DUS Instrument/probe type: 3-MHz (abdominal), 5- or 7.5-MHz (femoropopliteal) imaging or 3-MHz (abdominal), 5-MHz (femoropopliteal) single-gate pulsed-Doppler probes PSVR of 1.5 indicated 25–50% stenosis PSVR of 2.5 indicated 50–99% stenosis	Reference standard: Angiography (with DSA) Reference standard details: Common femoral artery puncture using the Seldinger technique Uniplanar recordings for superficial femoral and popliteal arteries
Lenhart, 2000[51]	Aim of the study: Assessment of primary stenosis Number of patients: 45 (proportion male: 80%) Median age (years): 63 (range 44–77) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: CE MRA Coil: Leg Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: Aortic catheterisation
Linke, 1994[52]	Aim of the study: Assessment of primary stenosis Number of patients: 25 (proportion male: 60%) Mean age (years): 68 (range 48–87) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5- and 7.5-MHz transducer PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography Reference standard details: Femoral artery puncture

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Lundin, 2000[53]	Aim of the study: Assessment of primary stenosis Number of patients: 39 (proportion male: 54%) Mean age (years): 67 (range 51–87) Fontaine stage II: 87% Fontaine stage III: 10% Fontaine stage IV: 3% Are the data from a patient subgroup? No	Index test 1: DUS Instrument/probe type: 2.5-MHz curved array/3.5- or 5-MHz linear array PSVR of 2.5 indicated 50% stenosis Index test 2: 2D TOF MRA Coil: Body Field strength: 1 Index test 3: CE MRA Coil: Body Field strength: 1	Reference standard: Angiography (with DSA) Reference standard details: Transfemoral puncture, with contrast agent injected via pigtail catheter into distal aorta in 37 patients External iliac artery approach in 2 patients
Martin, 2003[54]	Aim of the study: Assessment of primary stenosis Number of patients: 41 (proportion male: 68%) Mean age (years): 67 (range 45–84) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: CTA Instrument: Astein VR four-channel MDCT scanner	Reference standard: Angiography (with DSA) Reference standard details: Right common femoral artery approach in 25 patients Left common femoral artery approach in 15 patients Right brachial artery approach in 1 patient
McDermott, 1995[55]	Aim of the study: Assessment of primary stenosis Number of patients: 31 (proportion male: 48%) Mean/median age (years): NR (range 50–87) Fontaine stage II: 13% Fontaine stage III: 19% Fontaine stage IV: 68% Are the data from a patient subgroup? Diabetes mellitus	Index test: 2D TOF MRA Coil: Leg Field strength: 1.5	Reference standard: Angiography (with DSA in 12 patients) Reference standard details: Pigtail catheter in the distal abdominal aorta Intraoperative angiography performed in 10 patients
Meaney, 1999[9]	Aim of the study: Assessment of primary stenosis Number of patients: 20 (proportion male: 60%) Mean age (years): 65 (range 47–83) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: Pigtail catheter placed in distal aorta

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Mergelsberg, 1986[56]	Aim of the study: Assessment of primary stenosis Number of patients: 32 (proportion male: 75%) Mean/median age (years): NR (range 45–84) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: DUS Instrument/probe type: 5-MHz linear probe PSVR: NR	Reference standard: Angiography (with DSA) Reference standard details: None reported
Portugaller, 2004[57]	Aim of the study: Assessment of primary stenosis Number of patients: 50 (proportion male: 84%) Mean age (years): 68 (range 45–86) Fontaine stage II: 62% Fontaine stage III: 4% Fontaine stage IV: 34% Are the data from a patient subgroup? No	Index test: CTA Instrument: Lightspeed four-detector spiral scanner (General Electrics)	Reference standard: Angiography (with DSA) Reference standard details: Femoral puncture route in 48 patients Transbrachial approach in 2 patients
Puls, 2002[58]	Aim of the study: Assessment of primary stenosis Number of patients: 31 (proportion male: 55%) Mean age (years): 53 (range 38–75) Fontaine stage II: 97% Fontaine stage III: 3% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: CTA Instrument: Somatom Plus 4 Volume Zoom	Reference standard: Angiography (with DSA) Reference standard details: Femoral artery puncture
Rieker, 1996[59]	Aim of the study: Assessment of primary stenosis and graft stenosis Number of patients: 50 (proportion male: NR) Mean age (years): 65 (range 45–83) Fontaine stage II: 74% Fontaine stage III: 12% Fontaine stage IV: 14% Are the data from a patient subgroup? No	Index test: CTA Instrument: PQ 2000 (Picker International)	Reference standard: Angiography (with DSA) Reference standard details: Common femoral artery puncture Pigtail catheter in the infrarenal aorta or superficial femoral artery
Rieker, 1997[60]	Aim of the study: Assessment of primary stenosis Number of patients: 30 (proportion male: NR) Mean age (years): 62 (range 42–85) Fontaine stage II: 87% Fontaine stage III: 10% Fontaine stage IV: 3% Are the data from a patient subgroup? No	Index test: CTA Instrument: PQ 5000 scanner (Picker International)	Reference standard: Angiography (with DSA) Reference standard details: 5-F pigtail catheters Femoral artery route in 28 patients Transbrachial route in two patients with weak or absent femoral pulses

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Schafer, 2003[61]	Aim of the study: Assessment of primary stenosis Number of patients: 30 (proportion male: 60%) Median age (years): 68 (range 46–89) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: Catheter at aortic bifurcation
Sensier, 1996[62]	Aim of the study: Assessment of primary stenosis Number of patients: 76 (proportion male: 58%) Median age (years): 71 (range 46–84) Fontaine stage II: 88% Fontaine stage III: 0% Fontaine stage IV: 12% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 3.5- or 5-MHz probe PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography (with DSA) Reference standard details: Uniplanar, with biplanar in some aortoiliac arteries
Shaalan, 2003[63]	Aim of the study: Assessment of primary stenosis Number of patients: 132 (proportion male: 47%) Mean age (years): 65 (range NR) Fontaine stage II: 65% Fontaine stage III: 0% Fontaine stage IV: 35% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 4–7-MHz linear array transducer and probe PSVR: NR	Reference standard: Angiography Reference standard details: None reported
Snidow, 1995[64]	Aim of the study: Unclear whether assessment of primary stenosis or graft stenosis Number of patients: 42 (proportion male: 95%) Mean/median age (years): NR (range NR) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: Body Field strength: 1.5	Reference standard: Angiography Reference standard details: None reported
Snidow, 1996[65]	Aim of the study: Assessment of primary stenosis and graft stenosis Number of patients: 32 (proportion male: 97%) Mean age (years): 63 (range 43–75) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: 5-F pigtail catheter positioned at or above the level of the renal arteries, or at the aortic bifurcation

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Steffens, 1997[66]	Aim of the study: Assessment of primary stenosis Number of patients: 115 (proportion male: NR) Mean age (years): 62 (range 32–81) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: 2D PC MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: 5-F catheter positioned at the level of the first lumbar vertebra
Steffens, 2003[67]	Aim of the study: Assessment of primary stenosis Number of patients: 50 (proportion male: 58%) Mean age (years): 65 (range 35–86) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: Pigtail catheter positioned at the aortic bifurcation
Sueyoshi, 1999[68]	Aim of the study: Assessment of primary stenosis and graft stenosis Number of patients: 23 (proportion male: 87%) Mean age (years): 68 (range 52–85) Fontaine stage II: 83% Fontaine stage III: 17% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: Femoral puncture in 20 patients Brachial puncture in 3 patients Pigtail catheter positioned in the distal aorta
Timonina, 1999[69]	Aim of the study: Assessment of primary stenosis Number of patients: 36 (proportion male: 100%) Mean age (years): 54 (range 32–64) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: Body Field strength: 1.5	Reference standard: Angiography Reference standard details: Femoral artery catheterisation
Vavrik, 2004[70]	Aim of the study: Assessment of primary stenosis Number of patients: 48 (proportion male: 52%) Mean age (years): 66 (range NR) Fontaine stage II: 92% Fontaine stage III: 2% Fontaine stage IV: 6% Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: 4-F catheter positioned above the aortic bifurcation Common femoral artery puncture

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Whyman, 1992[71]	Aim of the study: Assessment of primary stenosis Number of patients: 30 (proportion male: NR) Median age (years): 65 (range 45–85) Fontaine stage II: 100% Fontaine stage III: 0% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 5-MHz transducer PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography Reference standard details: None reported
Wilson, 1997[72]	Aim of the study: Assessment of primary stenosis Number of patients: 43 (proportion male: 77%) Mean age (years): 78 (range 53–95) Fontaine stage II: 0% Fontaine stage III: 28% Fontaine stage IV: 72% Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 4–7 or 5–10-MHz linear array transducers PSVR: Not reported	Reference standard: Angiography Reference standard details: None reported
Winterer, 1999[73]	Aim of the study: Assessment of primary stenosis Number of patients: 76 (proportion male: 57%) Mean age (years): 66 (range 36–96) Fontaine stage II: 87% Fontaine stage III: 13% Fontaine stage IV: 0% Are the data from a patient subgroup? No	Index test: CE MRA Coil: Body Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: 5-F pigtail catheter in the bifurcation of the distal aorta
Yucel, 1993[74]	Aim of the study: Assessment of primary stenosis and graft stenosis Number of patients: 25 (proportion male: 60%) Mean age (years): 68 (range 37–80) Fontaine stage II: 0% Fontaine stage III: 84% Fontaine stage IV: 16% Are the data from a patient subgroup? No	Index test: 2D TOF MRA Coil: NR Field strength: 1.5	Reference standard: Angiography Reference standard details: Multistation digital or cut-film run-off studies
Zeuchner, 1994[75]	Aim of the study: Assessment of primary stenosis and graft stenosis Number of patients: 54 (proportion male: 56%) Mean age (years): 70 (range 42–86) Fontaine stage: NR Are the data from a patient subgroup? No	Index test: Colour DUS Instrument/probe type: 3.5-MHz convex, 7.5-MHz linear PSVR of 2.0 indicated 50% stenosis	Reference standard: Angiography Reference standard details: None reported

continued

TABLE 36 *Studies evaluating tests to diagnose stenosis/occlusion (cont'd)*

Study	Participants	Index test	Reference standard
Zhang, 2005[76]	Aim of the study: Assessment of primary stenosis Number of patients: 52 (proportion male: 54%) Mean age (years): 68 (range 38–92) Fontaine stage II: 46% Fontaine stage III: 12% Fontaine stage IV: 42% Are the data from a patient subgroup? No	Index test: CE MRA Coil: Head Field strength: 1.5	Reference standard: Angiography (with DSA) Reference standard details: 4- or 5-F catheter Femoral artery puncture

[a] CE MRA results are not included in this review, as the inclusion criteria specified CA as the reference standard.
NR, not reported.

Appendix 7

Data extraction of included economic evaluations

In order to facilitate data extraction the NHS EED abstract template has been used to provide critical structured abstracts. The abstracts are intended to provide users with comprehensive information about the original papers and their quality. Structured NHS EED abstracts are presented below for all economic evaluations that met the inclusion criteria of the review.

Visser and colleagues (2003)[129]

Visser K, Kuntz KM, Donaldson MC, Gazelle GS, Hunink MG. Pretreatment imaging workup for patients with intermittent claudication: a cost-effectiveness analysis. *J Vasc Interv Radiol* 2003; **14**:53–62.

This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.

Health technology
Alternative pretreatment imaging work-up procedures were studied. These were magnetic resonance angiography (MRA), duplex ultrasonography (DUS) and intra-arterial digital subtraction angiography (DSA), followed by treatment. Two alternative treatment scenarios were analysed. One was a minimally invasive scenario in which treatment was limited to angioplasty and patients with non-suitable lesions entered a supervised exercise programme. The other was a more invasive treatment scenario in which angioplasty was performed, if feasible, otherwise bypass surgery was carried out.

Disease
Cardiovascular diseases.

Type of intervention
Diagnosis and treatment.

Hypothesis/study question
The objective of this study was to assess the cost-effectiveness of MRA, DUS and intra-arterial DSA for the pretreatment imaging work-up of patients with lifestyle-limiting intermittent claudication. The comparator chosen was exercise therapy without imaging work-up. A societal perspective was adopted in the economic analysis (although this was only stated in the abstract of the study).

Economic study type
Cost–utility analysis.

Study population
The study population comprised a hypothetical cohort of 60-year-old men with a 1-year history of severe unilateral claudication, an initial ankle brachial index of 0.70 and no history of coronary artery disease.

Setting
The study setting was secondary care. It was unclear where the economic study was carried out.

Dates to which data relate
The effectiveness data were derived from studies published between 1981 and 2002. The resource-use and cost data appear to have been collected from studies published between 1998 and 2002. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published studies and several authors' assumptions.

Modelling
A decision-analytic model was developed to evaluate the cost-effectiveness of MRA, DUS and DSA. The outcomes and lifetime costs for treatment and follow-up of all possible diagnostic outcomes were calculated using a Markov model with first order Monte Carlo simulations of 100,000 hypothetical patients, and were combined with the cost and effectiveness of the pretreatment work-up. The cycle length used for the Markov model was not identified. The health states considered were severe intermittent claudication, mild intermittent claudication, critical limb ischaemia, history of angina pectoris, systemic long-term complications after intervention and death.

Outcomes assessed in the review
The outcomes assessed were:

- the sensitivity and specificity of MRA and DUS for the detection of stenosis of more than 50%
- the probabilities with MRA and DUS of uninterpretable test results and indeterminate test results
- the probabilities with MRA and DUS of results suggesting angioplasty given that the lesion is suitable for angioplasty, angioplasty given that the lesion is suitable for bypass surgery, and angioplasty given that the lesion is not suitable for invasive treatment
- the probabilities with MRA and DUS of results suggesting bypass surgery given that the lesion is suitable for bypass surgery, and bypass surgery given that the lesion is not suitable for invasive treatment
- the probability of suprainguinal disease
- the probability that a suprainguinal lesion is suitable for angioplasty
- the probability that an infrainguinal lesion is suitable for angioplasty
- the probability that lesions are suitable for invasive treatment
- the annual rate of progression of invasively untreated disease
- the annual rate of changing disease location
- the 2-year patency in patients with intermittent claudication who underwent either angioplasty or bypass surgery
- the quality of life associated with the health states mild and severe intermittent claudication, critical limb ischaemia, history of angina pectoris and systemic long-term complications after intervention.

Study designs and other criteria for inclusion in the review
The authors did not explicitly report the study designs included in the review, although they did report that several meta-analyses were included.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance, validity, extracting data
Not reported.

Number of primary studies included
Approximately 19 published studies were included in the review.

Method of combination of primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The sensitivities and specificities for MRA versus DUS to detect a stenosis of more than 50% were, respectively, 0.96 (range 0.91–0.97) and 0.96 (range 0.94–0.98) versus 0.90 (range 0.89–0.90) and 0.95 (range 0.93–0.96).

The probability of an uninterpretable result was 0.07 (range 0.05–0.10) with MRA and 0.11 (range 0.0–0.23) with DUS.

The probability of an indeterminate result was 0 with MRA and 0.089 (range 0.036–0.14) with DUS.

The probability that the results suggested angioplasty given that the lesion was suitable for angioplasty was 0.79 with MRA and 0.60 with DUS.

The probability that the results suggested angioplasty given that the lesion was suitable for bypass surgery was 0.03 with MRA and 0.08 with DUS.

The probability that the results suggested angioplasty given that the lesion was not suitable for invasive treatment was 0 with MRA and 0.09 with DUS.

The probability that the results suggested bypass surgery given that the lesion was suitable for bypass surgery was 0.97 with MRA and 0.87 with DUS.

The probability that the results suggested bypass surgery given that the lesion was suitable for angioplasty was 0.14 with MRA and 0.36 with DUS.

The probability that the results suggested bypass surgery given that the lesion was not suitable for invasive treatment was 0 with MRA and 0.09 with DUS.

The probability of suprainguinal disease was 0.56 (range 0.12–0.85).

The probability that a suprainguinal lesion was suitable for angioplasty was 0.51 (range 0.43–0.59).

The probability that an infrainguinal lesion was suitable for angioplasty was 0.18 (range 0.11–0.25).

The probability that lesions were suitable for invasive treatment was 0.95.

The annual rate of progression of invasively untreated disease was 0.20.

The annual rate of changing disease location was 0.15.

The 2-year patency in patients with intermittent claudication ranged from 0.46 for angioplasty of infrainguinal lesions occlusion to 0.95 when aortic bifurcation grafts were performed.

The health-related quality of life was:

- 0.71 in patients with severe intermittent claudication
- 0.79 in patients with mild intermittent claudication
- 0.35 in patients with critical limb ischaemia
- 0.90 in patients with history of angina pectoris
- 0.72 in patients with systemic long-term complications after intervention.

Methods used to derive estimates of effectiveness

The authors made assumptions to derive some of the effectiveness estimators.

Estimates of effectiveness and key assumptions

The authors assumed that after diagnosis with DSA, an additional angioplasty session would be required in 10% of cases, owing to incorrect referral. Moreover, 95% of patients undergoing diagnostic work-up for peripheral arterial disease would be eligible for invasive treatment after work-up.

Measure of benefits used in the economic analysis

The health benefit measure used in the economic analysis was the quality-adjusted life-years (QALYs). The health values used were obtained from the review of the literature (see the section 'Results of the review', p. 152). The time-horizon adopted was the patient's lifetime. The health benefits were discounted at a rate of 3%.

Direct costs

The direct costs included in the analysis were those of the health service and the patient. Medical costs included the costs of diagnostic tests, treatment and follow-up. The authors also included the extra costs for inefficient use of personnel, equipment and housing in the case of an incorrectly scheduled angioplasty procedure. The non-medical costs included transportation costs and patient time spent on diagnostic testing, interventions and follow-up visits. The unit costs and the resource quantities were not reported separately. The authors used Medicare reimbursement rates, which included technical and professional fees, for the costs of MRA, DUS and DSA. All other costs were derived from the literature. Discounting was necessary since the costs were incurred during the lifetime of the patient, and was undertaken at a rate of 3% per annum. All of the costs were converted to 1998 prices using the Consumer Price Index. The average costs were reported.

Indirect costs

The indirect costs were not included in the analysis.

Currency

US dollars ($).

Statistical analysis of costs

The costs were treated as point estimates (i.e. the data were deterministic).

Sensitivity analysis

All parameters were varied in a one-way sensitivity analysis within a range of plausible values. The authors also reported the cost-effectiveness of two additional diagnostic strategies in order to plan bypass surgery within the more invasive treatment scenario. One strategy was MRA in all patients followed by DSA, while the other was DUS with DSA. Two other patient cohorts were also considered. One was 40-year-old men (all other characteristics similar to the base case), while the other was 70-year-old men with a history of coronary artery disease.

Estimated benefits used in the economic analysis

The QALYs gained in the minimally invasive (more invasive) treatment scenario were:

- with no diagnostic work-up, 6.0606 (6.0606) QALYs
- with DUS, 6.1465 (6.2002) QALYs
- with MRA, 6.1487 (6.2136) QALYs
- with DSA, 6.1498 (6.2254) QALYs.

Cost results

The costs in the minimally invasive (more invasive) treatment scenario were:

- with no diagnostic work-up, $18,912 ($18,912)
- with DUS, $22,042 ($50,178)
- with MRA, $21,959 ($48,980)
- with DSA, $22,497 ($48,411).

Synthesis of costs and benefits

The cost-effectiveness was determined by excluding dominated and extended dominated strategies and then calculating the incremental cost–utility ratio (ICUR). A strategy was considered to be dominated by another strategy if the latter yielded higher QALYs at a lower cost. A strategy was considered to be extended dominated by another if the latter yielded higher QALYs at a lower ICUR. The ICUR of a strategy was calculated as the difference in QALYs compared with the next best strategy, which represented the additional costs per additional QALY gained for a strategy compared with the next best strategy.

In the minimally invasive treatment scenario for the base-case analysis, the ICUR for MRA yielded $35,000 per QALY compared with no diagnostic work-up. DSA had an ICUR of $471,000 per QALY compared with MRA. DUS was dominated by MRA.

In the more invasive treatment scenario, DSA had an ICUR of $179,000 per QALY compared with no diagnostic work-up. MRA and DUS were both dominated by DSA.

For 40-year-old men, the ICURs decreased: minimally invasive treatment scenario, $18,000 per QALY for MRA; more invasive treatment scenario, $119,000 per QALY for DSA. For 70-year-old men with a history of coronary artery disease, only the minimally invasive treatment scenario was considered and MRA had an ICUR of $95,000 per QALY.

The results from the sensitivity analyses were not sensitive to changes in the diagnostic test characteristics. If angioplasty was assumed to follow DSA immediately, it was found that the QALYs increased and costs decreased for DSA, but only the ICUR for DSA in the minimally invasive scenario changed to $195,000 per QALY. When the criteria of suitability for angioplasty were broadened for patients with intermittent claudication, the results changed in favour of DSA. When severe intermittent claudication was defined as a walking distance of less than 175 m (base case 250 m), the effectiveness increased and the costs decreased. The authors found that when they explored the cost-effectiveness of MRA and DUS in combination with DSA for planning bypass surgery, the strategy with DUS was the optimal strategy, with an ICUR of $179,000 per QALY compared with no diagnostic work-up strategy.

Authors' conclusions

The differences in costs and effectiveness among diagnostic imaging strategies for patients with intermittent claudication were slight. MRA or DUS could replace intra-arterial DSA without substantial loss in effectiveness and with a slight cost reduction.

CRD commentary

Selection of comparators

The authors evaluated MRA, DUS and DSA because they were three imaging modalities that were being widely used for the diagnostic work-up of peripheral arterial disease. You should decide whether these are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness

The authors did not report that a systematic review of the literature had been undertaken to identify relevant research and minimise biases. The authors also did not report the methods used in the review, such as the study designs to be included, the criteria used to ensure the validity of the studies, the methods used to judge relevance, and the sources searched or the search strategy to identify relevant studies. The authors did not report how estimates of effectiveness from the primary studies were combined, nor did they report whether differences between the primary studies were investigated.

The authors reported ranges for most of the model probabilities, which were then used in the sensitivity analysis. As the authors reported, the use of secondary data has its own limitations and is not always applicable to the question under study. A further limitation, as stated by the authors, was that several assumptions had to be made to keep the model tractable. However, an extensive sensitivity analysis was performed to assess the uncertainty surrounding the effectiveness parameters.

Validity of estimate of measure of benefit

The estimation of benefits was modelled. The instrument used to derive a measure of health benefit, a decision-analytic model with an

embedded Markov model, appears to have been appropriate. QALYs were used as the summary measure of benefit, which will enable comparisons of the study findings with those from different interventions. Since a lifetime horizon was considered for the estimation of health benefits, these were discounted at a rate of 3%. However, there is controversy in the health economics literature about whether health benefits should be discounted.

Validity of estimate of costs

Although the authors reported that a societal perspective was adopted, the indirect costs were not included. All of the direct costs appear to have been included in the analysis. The costs and the quantities were not reported separately, which will limit reflation exercises in other settings. The costs were derived from published sources and Medicare reimbursement rates. Hence, charges were used to proxy prices, which may not reflect the true opportunity cost of the assessed interventions. Appropriate sensitivity analyses of the costs were undertaken, and the ranges used appear to have been appropriate. The authors used the Consumer Price Index to inflate costs to 1998 prices. However, it would have been more appropriate if the authors had used healthcare inflation instead, as it is generally the case that healthcare prices rise more quickly than average prices. Since all of the costs were incurred during the lifetime of the patient, the costs were appropriately discounted. The price year was reported, which will assist any possible inflation exercises.

Other issues

The authors made appropriate comparisons with two other studies evaluating the cost-effectiveness of the pretreatment work-up for peripheral arterial disease. DUS and DSA were compared in one study, and it was concluded that DUS was not a cost-effective alternative because of its low sensitivity. The other study reported that MRA alone, or in combination with selective use of DSA, might be a cost-effective alternative compared with DSA. The issue of generalisability to other settings was partially addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively. However, in their conclusions they reported that DUS could replace DSA without substantial loss in effectiveness and with a slight cost reduction. Albeit this is true, DUS was found to be dominated by MRA in both treatment scenarios and, therefore, its use is not cost-effective and hence inefficient.

The authors reported a number of further limitations. For example, DSA and a subsequent angioplasty procedure were assumed to be scheduled in separate sessions. However, in clinical practice, DSA and angioplasty may be planned as a single session. The authors also commented that not every centre has all three diagnostic modalities at its disposal and, therefore, the comparisons considered in this study might be irrelevant in some settings.

Implications of the study

The authors suggested further research in the form of a clinical study, which should focus on the decision-making process and workflow in clinical practice. They also stated that an appropriate design for such a comparison would be a pragmatic randomised controlled trial in which patients are randomised among available imaging modalities.

Other publications of related interest

Yin D, Baum RA, Carpenter JP, Langlotz CP, Pentecost, MJ. Cost-effectiveness of MR angiography in cases of limb-threatening peripheral vascular disease. *Radiology* 1995;**194**:757–64.

Geitung JT, Wikstrom T, Zeuchner J, Gothlin JH. Cost-effectiveness of colour duplex sonography compared with angiography of the pelvis and lower limb. *Eur Radiol* 1996;**6**:481–4.

Subject index terms

Subject indexing assigned by NLM

Angiography, Digital Subtraction/ec (economics); Cost Benefit Analysis; Decision Support Techniques; Human; Intermittent Claudication/di (diagnosis); Intermittent Claudication/ec (economics); Intermittent Claudication/th (therapy); Magnetic Resonance Angiography/ec (economics); Models, Economic; Quality Adjusted Life Years; Sensitivity and Specificity; Support, Non US Gov't; Ultrasonography, Doppler, Color/ec (economics).

Country codes

The Netherlands.

Source of funding

Supported in part by the Foundation 'Vereniging Trustfolds Erasmus Universiteit Rotterdam' and by the Netherlands Organization for Scientific Research.

Copyright comments

Visser and colleagues (2003)[128]

Visser K, de Vries SO, Kitslaar PJ, van Engelshoven JM, Hunink MG. Cost-effectiveness of diagnostic imaging work-up and treatment for patients with intermittent claudication in the Netherlands. *Eur J Vasc Endovasc Surg* 2003;**25**:213–23.

This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.

Health technology
The following alternative management strategies for patients with intermittent claudication were investigated.

Magnetic resonance angiography (MRA) in all patients and subsequent angioplasty for all patients with suitable lesions, otherwise patients entered a supervised exercise programme (MRA+PTA/EX).

MRA in all patients and subsequent angioplasty for patients with suitable lesions, bypass surgery for the remainder of patients, except for those non-suitable who entered a supervised exercise programme (MRA+PTA/BS/EX).

Colour-guided duplex ultrasound (DUS) in all patients and subsequent angioplasty for patients with suitable lesions, otherwise patients entered a supervised exercise programme (DUS+PTA/EX).

Colour-guided DUS in all patients and subsequent angioplasty for patients with suitable lesions and bypass surgery for the remainder of patients, except for those non-suitable who entered a supervised exercise programme (DUS+PTA/BS/EX).

Intra-arterial digital subtraction angiography (DSA) in all patients and subsequent angioplasty for patients with suitable lesions, otherwise patients entered a supervised exercise programme (DSA+PTA/EX).

DSA in all patients and subsequent angioplasty for patients with suitable lesions and bypass surgery for the remainder of patients, except for those non-suitable who entered a supervised exercise programme (DSA + PTA/BS/EX).

A conservative strategy in which all patients entered a supervised exercise programme (Notest+EX) and were only evaluated further if critical limb ischaemia developed.

Disease
Cardiovascular diseases.

Type of intervention
Diagnosis and treatment.

Hypothesis/study question
The main objective of this study was to evaluate the cost-effectiveness of management strategies, including imaging work-up and treatment, for patients with intermittent claudication in The Netherlands. A second objective was to determine whether the results from cost-effectiveness analyses performed in the USA were generalisable to The Netherlands. The comparator chosen would appear to be the conservative strategy (since the authors stated that this was the reference strategy). A societal perspective was adopted in the economic analysis.

Economic study type
Cost–utility analysis.

Study population
The study population comprised a hypothetical cohort of previously untreated 60-year-old patients presenting with severe unilateral claudication of at least 1 year in duration, who had at least one significant lesion (>50% arterial diameter reduction) that was located predominantly suprainguinal or infrainguinal, an ankle brachial index pressure of 0.70 and no history of coronary artery disease.

Setting
The study setting was secondary care. The economic study was carried out in The Netherlands.

Dates to which data relate
The effectiveness data were derived from studies published between 1960 and 2002. The cost data would appear to relate to data published between 1995 and 2002. The price year was 1999.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published studies.

Modelling
The authors used a model that had been developed already, which consisted of a Markov Monte Carlo model embedded in a larger decision-analytic model. The health states considered were asymptomatic or mild claudication, severe claudication, critical limb ischaemia and amputation

of the limb. Hypothetical patients were followed lifelong from the time that the initial diagnostic work-up was performed. The cycle length used in the Markov model was not clearly identified.

Outcomes assessed in the review

The outcomes assessed in the review were:

- the sensitivities for MRA and DUS to detect a stenosis of more than 50%
- the test characteristics of MRA and DUS to assess the treatment option (i.e. percentage of patients undergoing angioplasty versus bypass surgery versus lesions not suitable for invasive treatment given the test results)
- data on equivocal MRA and DUS results
- the mortality and morbidity of DSA
- the excess mortality for peripheral arterial disease (PAD)
- the mortality from vascular interventions for those patients at high and low risk
- the risk of systemic complications
- the 2-year patency in patients with intermittent claudication
- the probability of suprainguinal disease
- the suitability for angioplasty
- the rate of critical limb ischaemia
- the risk of amputation
- the relative risk of severe intermittent claudication after stopping exercise and after graft failure
- the mean annual rate of contralateral symptoms.

Study designs and other criteria for inclusion in the review

Not reported.

Sources searched to identify primary studies

Not reported.

Criteria used to ensure the validity of primary studies

Not reported.

Methods used to judge relevance, validity, extracting data

Not reported.

Number of primary studies included

Approximately 28 primary studies were included in the review (at least three of them were meta-analyses and one was a case series).

Method of combination of primary studies

Not reported.

Investigation of differences between primary studies

Not reported.

Results of the review

The sensitivities for MRA and DUS to detect a stenosis of more than 50% were, respectively, 0.98 (range 0.96–0.99) and 0.88 (range 0.84–0.91).

The probabilities that MRA and DUS results suggested angioplasty given that the lesion was suitable for angioplasty were, respectively, 0.79 and 0.60.

The probabilities that MRA and DUS results suggested angioplasty given that the lesion was suitable for bypass surgery were, respectively, 0.03 and 0.08.

The probabilities that MRA and DUS results suggested angioplasty given that the lesion was not suitable for invasive treatment were, respectively, 0 and 0.09.

The probabilities that MRA and DUS results suggested bypass surgery given that the lesion was suitable for bypass surgery were, respectively, 0.97 and 0.87.

The probabilities that MRA and DUS results suggested bypass surgery given that the lesion was suitable for angioplasty were, respectively, 0.14 and 0.36.

The probabilities that MRA and DUS results suggested bypass surgery given that the lesion was not suitable for invasive treatment were, respectively, 0 and 0.09.

The probabilities of additional work-up with DSA for equivocal MRA and DUS results were, respectively, 0.09 (range 0.06–0.14) and 0.23 (range 0.08–0.37).

The risks of major complications or death with DSA were 0.03 (range 0.02–0.05) and 3.33×10^4 (range 2.9×10^4–16.2×10^4), respectively.

The excess mortality for PAD was 3.14 (range 2.74–3.54).

The mortality from vascular interventions in high- versus low-risk patients ranged from 0.013 (range 0–0.037) versus 0.001 (range 0–0.029) when suprainguinal angioplasty with selective stent placement was performed to 0.098 (range 0.077–0.119) versus 0.147 (range 0.113–0.181)

when amputation was performed in patients aged less than 75 years old versus those aged 75 or older.

The rate of systemic complications ranged from 0.013 (range 0–0.035) when suprainguinal angioplasty with selective stent placement was performed to 0.38 (range 0.377–0.383) when amputation was performed.

The 2-year patency in patients with intermittent claudication ranged from 0.67 when suprainguinal angioplasty with selective stent placement was performed in case of occlusion to 0.95 when aortic bifurcation grafts were performed.

The probability of suprainguinal disease ranged from 0.17 (range 0.09–0.25) for subsequent interventions with prior infrainguinal disease to 0.56 (range 0.12–0.85) for the first intervention.

The suitability for angioplasty in case of claudication ranged from 0.18 for a first intervention in a patient with infrainguinal disease to 0.51 for a first intervention in a patient with suprainguinal disease.

The annual incidence rates of critical limb ischaemia for patients aged less than 65 years old and for those aged 65 or older were, respectively, 0.017 (range 0–0.039) and 0.036 (range 0–0.075).

The 5-week probabilities following graft failure of pretreatment symptoms/claudication and critical limb ischaemia were, respectively, 0.062 (range 0–0.014) and 0.242 (range 0.14–0.36).

The proportion of above-knee amputations was 0.08 (range 0.03–0.13).

The annual incidence rate of progression below-knee to above-knee amputation was 0.015 (range 0–0.07).

The relative risks of severe intermittent claudication after stopping exercise and after graft failure were, respectively, 5.81 (range 1.8–18.5) and 1.36 (range 0.96–1.92).

The mean annual rate of contralateral symptoms was 0.149.

The health-related quality of life ranged from 0.20 (range 0–0.40) in patients with above-knee amputation to 0.90 (range 0.60–1.00) in patients with angina pectoris.

Measure of benefits used in the economic analysis

The summary measure of benefit used was the number of quality-adjusted life-years (QALYs). The health values for intermittent claudication were available from patients who participated in a supervised exercise programme, with the responses to the EuroQol being transformed into time trade-off values. For all other health states, time trade-off values were used from the literature. The time-horizon considered for the estimation of health benefits was a lifetime. The health benefits were discounted at a rate of 3%.

Direct costs

The direct costs considered appear to have been those incurred by the health system and the patients. The direct medical costs were for personnel, materials, equipment, hospital admission, inpatient services and overheads. The direct non-medical costs included patient time spent on interventions and travel expenses. The costs were derived from the University Hospital Maastricht, data collected from the literature and authors' assumptions. Resource use and the costs were not reported separately. Discounting was necessary, as the costs were incurred over the lifetime of the patient, and was appropriately performed at an annual rate of 3%. The study reported the average costs. All of the costs were updated with the Consumer Price Index to 1999 prices.

Indirect costs

Friction costs (i.e. costs for productivity losses, calculated as the costs of replacement of an employee) were not included in the analysis as most patients with PAD are retired.

Currency

Euros (€). The exchange rate used was Dutch guilders 2.20 = €1.00 = US $1.06 (1999).

Statistical analysis of costs

The costs were treated as point estimates (i.e. the data were deterministic).

Sensitivity analysis

Sensitivity analyses were performed for diagnostic work-up parameters and also for the most influential parameters of treatment and follow-up, based on another analysis [de Vries *et al*., 2002, see the section 'Other publications of related interest' (p. 160) for bibliographic details]. The authors also considered a cohort of 40-year-old men and one of 70-year-old men with a history of coronary artery disease in order to assess the results for alternative populations.

Estimated benefits used in the economic analysis

The QALYs gained per patient with each management strategy were:

- 6.0606 with Notest+EX
- 6.1465 with DUS+PTA/EX
- 6.1487 with MRA+PTA/EX
- 6.1498 with DSA+PTA/EX
- 6.2002 with DUS+PTA/BS/EX
- 6.2136 with MRA+PTA/BS/EX
- 6.2254 with DSA+PTA/BS/EX.

Cost results

The cost of each management strategy was:

- Notest+EX, €6793
- DUS+PTA/EX, €8546
- MRA+PTA/EX, €8566
- DSA+PTA/EX, €8997
- DUS+PTA/BS/EX, €18,720
- MRA+PTA/BS/EX, €18,440
- DSA+PTA/BS/EX, €18,583.

Synthesis of costs and benefits

The cost-effectiveness was determined by excluding (extended) dominated strategies and then calculating the incremental cost–utility ratio (ICUR). A strategy was considered to be dominated by another strategy if the latter yielded higher QALYs at a lower cost. A strategy was considered to be extended dominated by another if the latter yielded higher QALYs at a lower ICUR. The ICUR of a strategy was calculated as the difference in QALYs compared with the next best strategy, which represented the additional costs per additional QALY gained for a strategy compared with the next best strategy.

The strategy MRA+PTA/EX had an ICUR of €20,138 per QALY compared with the Notest+EX strategy.

The strategy DSA+PTA/BS/EX had an ICUR of €130,557 per QALY compared with the MRA+PTA/EX strategy.

All other management strategies were inferior by either dominance or extended dominance.

For 40-year-old male patients, the ICURs of MRA+PTA/EX (compared with Notest+EX) and DSA+PTA/BS/EX (compared with MRA+PTA/EX) decreased (€13,000 per QALY and €98,000 per QALY, respectively). For 70-year-old patients with a history of coronary artery disease it was found that the DUS+PTA/EX strategy had an ICUR of €48,000 per QALY compared with the Notest+EX strategy, while MRA+PTA/EX had an ICUR of €75,000 per QALY compared with DUS+PTA/EX.

The results were found to be sensitive to an increase in the costs of MRA. When the number of patients with intermittent claudication having lesions suitable for angioplasty was increased, the effectiveness of all strategies increased. In addition, the costs increased for management strategies with angioplasty as the only invasive treatment option, but decreased for management strategies with both angioplasty and bypass surgery.

Authors' conclusions

For patients with severe unilateral intermittent claudication of at least 1 year in duration, non-invasive imaging modalities could replace intra-arterial DSA without an important loss in effectiveness and at a minimal cost reduction. Management strategies including angioplasty were cost-effective in The Netherlands and, although strategies including bypass surgery were more effective, their incremental costs were very high.

CRD commentary

Selection of comparators

The authors compared seven different management strategies for patients with intermittent claudication in The Netherlands and chose Notest+EX as the comparator (although no explicit justification was given for this choice). As the authors stated, medical therapy and smoking cessation were not considered as separate treatment options, but rather as a part of the general management of all patients. All these strategies appear to have covered the available diagnostic and treatment options for this group of patients. You should decide whether these are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness

The authors did not report that a systematic review of the literature had been undertaken to identify relevant research and minimise bias. They also failed to report any methodology of their review, such as the sources searched, study designs for inclusion and synthesis of the results from different studies, and whether they investigated any differences between the primary studies. Despite this, the authors included approximately 28 studies in their review, and a range of values (or an alternative value) was given for each point estimate to allow sensitivity analyses. Further, sensitivity analyses were performed for diagnostic parameters and for the most influential

parameters of treatment and follow-up, based on the results from a prior analysis.

Validity of estimate of measure of benefit

The estimation of benefit was modelled. The decision-analytic model used to derive the health benefits appears to have been appropriate. The fact that QALYs were used as the measure of benefit enables comparisons of the study results with results from different interventions. The estimated benefits were discounted, although there is controversy in the health economics literature about whether health benefits should or should not be discounted.

Validity of estimate of costs

All the categories of cost relevant to the perspective adopted appear to have been included in the analysis, although some relevant costs were omitted. Downstream induced medical costs were not considered since the treatment of PAD did not prolong life but improved the quality of life of the patient. In addition, although the stated perspective was societal, friction costs were not considered since most patients with PAD are retired. The costs and the quantities were not reported separately, which will limit reflation exercises to other settings. The costs were derived from the authors' setting, published sources and from several assumptions. Appropriate sensitivity analyses of the costs were performed. Discounting was necessary, as the costs were incurred over the lifetime of the patient, and was appropriately performed at 3% per annum. The price year was reported, which will aid any possible inflation exercises.

Other issues

The authors made appropriate comparisons of their findings with those from other US studies, finding that the ICURs for the USA were higher than those for The Netherlands. Despite this, the authors reported that the implications for both countries were the same. The issue of generalisability to other settings was addressed in the sensitivity analysis, and by the fact that the authors explicitly compared their results with those from other studies with US settings. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported a number of limitations to the study. First, they assumed that DSA would be performed for recurrent or contralateral symptoms instead of MRA or colour-guided DUS, which may not be the case in current clinical practice. However, they commented that the results would only change minimally and that the conclusions would not change. Secondly, several secondary data sources were used as input data for the parameters, with limiting assumptions having to be made.

The authors do not appear to have recommended strategies with bypass surgery, compared with angioplasty, as their additional gain in effectiveness does not justify the additional expense.

Other publications of related interest

De Vries SO, Visser K, de Vries JA, Wong JB, Donaldson MC, Hunick MGM. Intermittent claudication: cost-effectiveness of revascularisation versus exercise therapy. *Radiology* 2002;**222**:25–36.

Visser K, Kuntz KM, Donaldson MC, Gazelle GS, Hunink MG. Pretreatment imaging workup for patients with intermittent claudication: a cost-effectiveness analysis. *J Vasc Interv Radiol* 2003; **14**:53–62.

Sculpher M, Michaels J, McKenna M, Minor J. A cost–utility analysis of laser-assisted angioplasty for peripheral arterial occlusions. *Int J Technol Assess Health Care* 1996;**12**:104–25.

Subject index terms

Subject indexing assigned by NLM

Adult; Aged; Angiography, Digital Subtraction/ec (economics); Cost of Illness; Cost Benefit Analysis; Diagnostic Imaging/ec (economics); Health Care Costs; Human; Intermittent Claudication/ec (economics); Intermittent Claudication/ra (radiography); Intermittent Claudication/su (surgery); Magnetic Resonance Angiography/ec (economics); Male; Markov Chains; Models, Economic; Netherlands; Quality of Life; Support, Non U.S. Gov't; Ultrasonography, Doppler, Color/ec (economics); Vascular Surgical Procedures/ec (economics).

Country codes

The Netherlands.

Source of funding

Supported by the Netherlands Organization for Scientific Research.

Copyright comments

Visser and colleagues (2003)[130]

Visser K, Kock MC, Kuntz KM, Donaldson MC, Gazelle GS, Hunink MG. Cost-effectiveness targets

for multi-detector row CT angiography in the work-up of patients with intermittent claudication. *Radiology* 2003;**227**:647–56.

This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.

Health technology
The study investigated the use of multidetector row computed tomographic angiography (CTA) compared with gadolinium-enhanced magnetic resonance angiography (MRA) in the work-up of patients with intermittent claudication. To reflect clinical practice, the authors evaluated two treatment scenarios after initial imaging work-up. In the first scenario (minimally invasive treatment), percutaneous treatment was performed on patients in whom a lesion suitable for percutaneous treatment had been detected at imaging work-up; otherwise, patients started a supervised exercise programme. In the second scenario (more invasive treatment), bypass surgery was performed on those patients who did not have lesions that were suitable for angiography. Intra-arterial digital subtraction angiography (DSA) would be used in cases where additional work-up was required.

Disease
Cardiovascular diseases.

Type of intervention
Diagnosis and treatment.

Hypothesis/study question
The objective of the study was to determine the costs, sensitivity for the detection of significant stenoses, and proportion of equivocal multidetector row CTA results in the work-up of patients with intermittent claudication that would make this imaging examination cost-effective in comparison with gadolinium-enhanced MRA. Gadolinium-enhanced MRA was used as the comparator as it represented current practice in the authors' settings. A societal perspective was adopted in the economic analysis.

Economic study type
Cost–utility analysis.

Study population
The study population comprised hypothetical cohorts of 60-year-old men with symptoms of severe unilateral claudication for 1 year, an ankle brachial index of 0.70 and no history of coronary artery disease. All of the patients had at least one significant stenosis in the suprainguinal or infrainguinal arterial tract. Patients were excluded if they had isolated infrapopliteal disease.

Setting
The setting was secondary care. The economic study was carried out in The Netherlands.

Dates to which data relate
The effectiveness data were derived from studies published between 1961 and 2002. The healthcare use data appear to have been mainly collected from studies published between 1998 and 2000. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a review of published studies, supplemented with authors' assumptions.

Modelling
The authors used a decision-analytic model to evaluate the societal cost-effectiveness of diagnostic imaging strategies for the work-up of patients with intermittent claudication. An embedded Monte Carlo Markov model was used to include data on treatment and follow-up. A total of 100,000 patients was considered for the simulation.

Outcomes assessed in the review
The outcomes assessed were:

- the sensitivity of MRA for the detection of stenoses of more than 50%
- the probability that MRA would facilitate recommendation of angioplasty given that the lesion was suitable, the lesion was suitable for bypass surgery and the lesion was not suitable for invasive treatment
- the probability that MRA would facilitate recommendation of bypass surgery given that the lesion was suitable, the lesion was suitable for angioplasty and the lesion was not suitable for invasive treatment
- the mortality and morbidity of DSA
- the probability that additional diagnostic work-up is required after MRA
- the health-related quality of life for several health states (i.e. no or mild intermittent claudication, severe intermittent claudication, critical limb ischaemia, amputation below knee and amputation above knee)
- the proportions of suprainguinal and infrainguinal lesions that were suitable for percutaneous treatment
- the annual rate of critical limb ischaemia in patients with intermittent claudication.

Study designs and other criteria for inclusion in the review
The authors did not report the study designs included in the review. However, they did report that several published meta-analyses were included.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance, validity, extracting data
Not reported.

Number of primary studies included
Approximately 15 primary studies were included in the review.

Method of combination of primary studies
Not relevant.

Investigation of differences between primary studies
Not relevant.

Results of the review
The sensitivity of MRA for the detection of stenoses of more than 50% was 0.96.

The probabilities that MR would facilitate recommendation of angioplasty given that the lesion was suitable, the lesion was suitable for bypass surgery and the lesion was not suitable for invasive treatment were, respectively, 0.79, 0.03 and 0.

The probabilities that MR would facilitate recommendation of bypass surgery given that the lesion was suitable, the lesion was suitable for angioplasty and the lesion was not suitable for invasive treatment were, respectively, 0.97, 0.14 and 0.

The morbidity of DSA was 0.03 and the mortality was 3.3×10^4.

The probability that additional diagnostic work-up was required after MRA was 0.07.

The health-related quality of life for the different health states was:

- 0.79 for no or mild intermittent claudication
- 0.71 for severe intermittent claudication
- 0.35 for critical limb ischaemia
- 0.61 for amputation below the knee
- 0.20 for amputation above the knee.

The proportions of suprainguinal and infrainguinal lesions that were suitable for percutaneous treatment were 51% and 18%, respectively.

The annual rate of critical limb ischaemia in patients with intermittent claudication was 0.017 for patients younger than 65 years and 0.036 for patients aged 65 years and older.

Methods used to derive estimates of effectiveness
The authors supplemented the results obtained from the review of the literature with their own assumptions.

Estimates of effectiveness and key assumptions
The authors assumed the following:

- The sensitivity of DSA for the detection of stenoses of more than 50% was 1.
- The probabilities that DSA would facilitate recommendation of angioplasty given that the lesion was suitable, the lesion was suitable for bypass surgery and the lesion was not suitable for invasive treatment were, respectively, 1, 0 and 0.
- The probabilities that DSA would facilitate recommendation of bypass surgery given that the lesion was suitable, the lesion was suitable for angioplasty and the lesion was not suitable for invasive treatment were, respectively, 1, 0 and 0.
- The mortality and morbidity related risks associated with angiography were assumed to be, respectively, 0 and 0. The respective values associated with CTA were assumed to be 9.0×10^6 and 3.1×10^4.
- The probabilities of each given treatment being recommended on the basis of CTA findings were assumed to be the same as those for MRA.

Measure of benefits used in the economic analysis
The summary measure of benefits used was the number of quality-adjusted life-years (QALYs). Estimated health values were obtained from the review. The estimated health values for patients with intermittent claudication were available from a study performed with participants from

The Netherlands, which derived values from responses to the EuroQol 5D and converted them to time trade-off values. The estimated health values for patients with critical limb ischaemia and amputation were derived from a study conducted among the general public. The estimated health benefits were discounted at a rate of 3%.

Direct costs

The direct costs considered were those of the healthcare system. These included the costs of MRA and DSA, surgery, amputation, 1 year of supervised exercise, and the costs of planned but not performed angioplasty (e.g. the inefficient use of personnel, room and equipment). The unit costs of MRA, DSA and amputations were derived from Medicare reimbursement rates. All of the other unit costs were derived from the literature. In addition, the authors made several assumptions in the estimation of healthcare resource use. Resource use and the costs were not reported separately. Discounting was relevant, as the costs were incurred through the lifetime of the patient, and was appropriately applied at a rate of 3% per annum. The study reported the average costs. All of the costs were converted to 1998 prices using the Consumer Price Index.

Indirect costs

The indirect costs were not included in the analysis.

Currency

US dollars ($).

Statistical analysis of costs

The costs were treated as point estimates (i.e. the data were deterministic).

Sensitivity analysis

Sensitivity analyses were performed. In these analyses:

- the thresholds (i.e. the willingness to pay for an extra QALY) were varied
- two different patient cohorts (40-year-old men with characteristics similar to those in the base case and 70-year-old men with a history of coronary artery disease and other characteristics similar to those in the base case) were considered
- quality of life with no or mild intermittent claudication was varied
- the costs of revascularisation were varied (by 50% and 150% of the baseline estimates).

Estimated benefits used in the economic analysis

In the minimally invasive treatment scenario, MRA yielded 6.1487 QALYs and CTA yielded 6.1490 QALYs.

In the more invasive treatment scenario, MRA yielded 6.2137 QALYs and CTA yielded 6.2151 QALYs.

Cost results

In the minimally invasive treatment scenario, MRA cost $21,942 and CTA cost $21,965.

In the more invasive treatment scenario, MRA cost $48,965 and CTA cost $49,102.

Synthesis of costs and benefits

In the minimally invasive treatment scenario, using a societal willingness to pay of $100,000 per QALY, CTA was equivalent to MRA in terms of cost-effectiveness if the cost of the modality was $420, the sensitivity for the detection of significant stenoses was 90%, and 20% of the patients required additional work-up because of equivocal CTA results.

In the more invasive treatment scenario, using a societal willingness to pay of $100,000 per QALY, CTA was equivalent to MRA in terms of cost-effectiveness if the cost of the modality was $673, the sensitivity for the detection of significant stenoses was 95%, and 20% of the patients required additional work-up because of equivocal CTA results.

These target values did not change substantially when the societal willingness to pay was varied. For the younger cohort the target criterion for the cost of CTA was more lenient, whereas for the older cohort the target criterion was stricter.

There was an inverse relationship between health-related quality of life and the estimated costs of CTA.

Authors' conclusions

Multidetector row CTA, compared with currently used imaging modalities such as MRA, has the potential to be cost-effective in the evaluation of patients with intermittent claudication.

CRD commentary

Selection of comparators

Gadolinium-enhanced MRA was used as the comparator as it represented current practice in the authors' settings. You should decide whether this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken to identify relevant research and minimise biases. The authors also failed to describe much of the methodology used in their review, such as the sources searched, the study designs for inclusion and the methods used to judge the validity of the studies. The authors also supplemented the results from the review of the literature with their own assumptions. The authors did not report whether these had been derived from expert opinion or were based on the literature. However, they did perform sensitivity analyses on the effectiveness parameters used in the model.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using a decision-analytic model, which appears to have been appropriate for the research question posed. The fact that QALYs were used as the summary measure of benefit enables comparisons with the findings from other interventions. The benefits were discounted at a rate of 3%. However, there is controversy in the health economics literature about the discounting of health benefits.

Validity of estimate of costs
Although the authors reported that the costs were estimated from a societal perspective, the indirect costs were not included. It was also unclear whether all the relevant costs were included in the analysis, as the authors did not report what resources were included for each treatment modality. The costs and the quantities were not reported separately, which will limit the transferability of the authors' results to other settings. The costs were derived from Medicare reimbursement rates and from published sources. Appropriate sensitivity analyses of the costs, using ranges that appear to have been appropriate, were performed. Although all of the costs were converted to 1998 prices using the Consumer Price Index, it would have been more appropriate had these been converted using the health section of the Consumer Price Index as, generally, healthcare cost inflation is higher than for the economy in general. Medicare reimbursement rates were used to proxy prices, consequently these cost estimates might not represent the actual costs of the treatment provided. The price year was reported, which will aid any possible inflation exercises.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies, although they did point out that the cost of a contrast material-enhanced CTA examination was estimated to be $237, which was below the target cost they found. The issue of generalisability to other settings was partially addressed in the sensitivity analysis since different age groups were evaluated. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported a number of further limitations. First, they used several data sources and made a number of assumptions to keep the model tractable. Secondly, they assumed that MRA and CTA were clinically interchangeable, an assumption that may not be realistic. Thirdly, the model did not consider regional healthcare circumstances such as the expertise of the radiologists and the availability of the equipment. Fourthly, to determine the cost-effectiveness of CTA it might have been better had these comparisons been made through a randomised controlled trial. Finally, the authors based the societal willingness to pay for one additional QALY on an assumption.

Implications of the study
The authors reported that the role of new imaging modalities that have shown fairly good preliminary results could be assessed by performing a pragmatic randomised controlled trial in which the new modality is compared with the imaging modality currently in use.

Other publications of related interest
Visser K, Hunink MG. Peripheral arterial disease: gadolinium enhanced MR angiography versus colour guided duplex US – a meta-analysis. *Radiology* 2000;**216**:67–77.

Visser K, Kuntz KM, Donaldson MC, Gazelle GS, Hunick MGM. Pretreatment imaging workup for patients with intermittent claudication: a cost-effectiveness analysis. *J Vasc Interv Radiol* 2003;**14**:53–62.

De Vries SO, Visser K, de Vries JA, Wong JB, Donaldson MC, Hunick MGM. Intermittent claudication: cost-effectiveness of revascularisation versus exercise therapy. *Radiology* 2002; **222**:25–36.

Subject index terms
Subject indexing assigned by NLM
Angiography, Digital Subtraction/ec (economics); Angiography, Digital Subtraction/mt (methods);

Contrast Media; Cost Benefit Analysis; Costs and Cost Analysis; Decision Trees; Gadolinium; Human; Intermittent Claudication/ec (economics); Intermittent Claudication/ra (radiography); Intermittent Claudication/th (therapy); Magnetic Resonance Angiography/ec (economics); Quality Adjusted Life Years; Sensitivity and Specificity; Support, Non US Gov't; Tomography, X Ray Computed/ec (economics); Tomography, X Ray Computed/mt (methods).

Country codes
The Netherlands.

Source of funding
Supported in part by the Netherlands Organization for Scientific Research.

Copyright comments

Geitung and colleagues (1996)[126]

Geitung JT, Wikstrom T, Zeuchner J, Gothlin JH. Cost-effectiveness of colour duplex sonography compared with angiography of the pelvis and lower limb. *Eur Radiol* 1996;**6**:481–4.

This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.

Health technology
Use of colour duplex sonography (CDS) as a preoperative examination in aorta, pelvis and lower limb. The CDS examinations were performed with a Toshiba SSA 270A ultrasound scanner, with 7.5-MHz linear, or 3.5-MHz convex, scanner probes (3.5 MHz for most of the pelvic arteries). Documentation of CDS was performed on colour prints.

Disease
Techniques and equipment; cardiovascular diseases.

Type of intervention
Diagnosis and treatment.

Hypothesis/study question
The aim of the study was to assess the cost-effectiveness of the use of CDS compared with angiography as a preoperative examination in aorta, pelvis and lower limb. The strategy of using angiography, as the gold standard, was regarded as the comparator. Angiography was performed with a conventional technique in a standardised manner, comprising images of the distal abdominal aorta, pelvic and peripheral vessels down to ankle level. Documentation of the angiograms was performed on conventional films.

Economic study type
Cost-effectiveness analysis.

Study population
Patients referred for preoperative angiography of the lower limb.

Setting
Hospital. The economic analysis was carried out in Sweden.

Dates to which data relate
Effectiveness and resource-use data corresponded to patients examined between January and September 1991. The price year was 1993.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was performed on the patient sample (n = 122) in 1993 at the study hospital. It was reported as having been conducted both retrospectively and prospectively.

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of a total of 53 patients with a mean age of 69.4 (range 42–86) years.

Study design
This was a diagnostic cohort study, carried out in a single centre. The duration of the follow-up was not reported. Regarding the loss to follow-up, it was reported that the records of four patients were not available when the review was performed (they could not be retrieved from the archive). The results were confirmed at surgery. Both angiograms and CDS were either performed by, or controlled by, experienced radiologists (consultant level). An experienced vascular surgeon and an experienced vascular radiologist reviewed all clinical and radiological data. They reviewed the records together and reached complete consensus in all cases.

Analysis of effectiveness
The principle used in the analysis of effectiveness was treatment completers only. The form for recording the clinical efficacy and radiological results included:

- comparisons of the methods' efficacy in detecting occlusions and stenoses
- evaluation of possible discrepancies between the two methods
- a clinical evaluation of whether or not the methods were adequate for planning surgery.

Effectiveness results
The effectiveness results were as follows:

- If surgery had been performed solely on the basis of the ultrasonographic diagnosis, repeat surgery would have been necessary in nine patients.
- In a further three patients, necessary surgery would not have been performed.
- Two patients would have been overtreated (unnecessary surgery instead of percutaneous transluminal balloon angioplasty).
- There were discrepancies between the findings at angiography and CDS in 33 of 49 patients.
- CDS overlooked ten occlusions, 14 stenoses greater then 50% and 22 stenoses less than 50%.
- The clinical review showed neither of the two diagnostic methods to be sufficient for preoperative planning in 32 of the patients.
- Angiography alone was adequate in 15 cases.

Clinical conclusions
CDS as a preoperative investigation for aorta, pelvic and lower limb vascular diseases had low sensitivity for aortic aneurysms and for occlusions and stenoses in the pelvic region. This has been reported elsewhere in studies on the efficacy and accuracy of ultrasonography.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only individual clinical outcomes were reported, as shown in the effectiveness results.

Direct costs
Costs were not discounted owing to the short time-frame of the cost analysis. Some quantities were reported separately from the costs. Cost items were reported separately. Cost analysis covered the costs of CDS and angiographic examinations (wages, material and contrast medium, overheads, capital costs, patient preparation and idle time), surgical procedures (hospital stay, surgery, anaesthesiology, intensive care, and services from the departments of clinical physiology, clinical chemistry and radiology). The costs of the two diagnostic methods and the consequences of inappropriate treatment were assessed. The perspective adopted in the cost analysis appears to have been that of the hospital (Department of Surgery). The cost analysis appears to have been conducted both retrospectively (based on the hospital's price list) and prospectively. The source of the cost data for the two methods was the prices at the radiology department of the study hospital. The cost of hospitalisation with surgery was based upon the diagnosis related group (DRG) prices and the hospital's accounting. The cost analysis was based on true costs. The price year was 1993.

Indirect costs
Indirect costs were not considered.

Currency
Swedish kroner (Sek).

Statistical analysis of costs Sensitivity analysis
The result of a threshold analysis was reported, but the parameters modified and the areas of uncertainty investigated were not identified.

Estimated benefits used in the economic analysis
See effectiveness results above.

Cost results
The total cost savings from performing CDS instead of angiography in 122 patients would total Sek 514,000. The additional costs from utilising only CDS would total Sek 1,303,000, resulting in net costs of Sek 789,000. It was reported that, on the basis of 49 patients, the boundary of the sensitivity analysis was at 2.7 reoperations.

Synthesis of costs and benefits
Costs and benefits were not combined.

Authors' conclusions
The present investigation concludes that, with current techniques, CDS of the aorta and arteries of the pelvis and lower limb is not cost-effective as a preoperative examination because of its low sensitivity in the pelvic region.

CRD commentary
Selection of comparators
A justification was given for the choice of the comparator. It was the gold standard in the

context in question at the time of the study. You, as a database user, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The study design was appropriate in answering the question, but had a number of limitations associated with the retrospective analysis, the lack of power calculations to determine sample size and the fact that the effectiveness analysis was based on treatment completers only. The study sample is likely to have been representative of the study population, but more information could have been provided regarding the inclusion and exclusion criteria adopted in the study.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was therefore one of cost–consequences design.

Validity of estimate of costs
The validity of the cost results was enhanced by the following features of the cost analysis: some quantities were reported separately from the costs; adequate details of methods of cost estimation were given; the price year was specified; the perspective adopted in the cost analysis was explicitly reported; and the cost analysis was based on actual costs. However, the following limitations exist: statistical analysis was not performed on resource-use and cost data; the variables modified and ranges used for the threshold sensitivity analysis were not identified in the paper; the effects of the two diagnostic procedures on indirect costs (productivity loss) were not addressed; and the cost results may not be generalisable outside the study setting.

Other issues
Given the limitations of the study design and the lack of extensive sensitivity analysis and statistical analysis of costs, some degree of caution should be exercised in interpreting the study results. The issue of generalisability to other settings or countries was not addressed, although appropriate comparisons were made with other studies. The issue of whether the study sample was representative of the study population was not fully addressed; it was only reported that all the patients studied had severe vascular disease with atherosclerosis and tortuous pelvic arteries.

Implications of the study
The results of the study suggest that, at present, angiography must be regarded as the most cost-effective preoperative examination. Awareness of this may stimulate technical improvements in CDS that may make angiography unnecessary in the future.

Subject index terms
Subject indexing assigned by NLM
Adult; Aged; Aged,-80-and-over; Angioplasty,-Balloon/ec (economics); Aorta/us (ultrasonography); Aortography/ec (economics); Arterial-Occlusive-Diseases/su (surgery); Arterial-Occlusive-Diseases/th (therapy); Cost-Benefit-Analysis; Diagnostic-Errors; Health-Care-Costs; Middle-Age; Preoperative-Care; Prospective-Studies; Reoperation/ec (economics); Sweden; Angiography/ec (economics); Arterial-Occlusive-Diseases/ra (radiography); Arterial-Occlusive-Diseases/us (ultrasonography); Leg/bs (blood-supply); Pelvis/bs (blood-supply); Ultrasonography,-Doppler,-Color/ec (economics); Comparative-Study; Female; Human; Male.

Country codes
Sweden.

Source of funding
None stated.

Yin and colleagues (1995)[131]

Yin D, Baum RA, Carpenter JP, Langlotz CP, Pentecost MJ. Cost-effectiveness of MR angiography in cases of limb-threatening peripheral vascular disease. *Radiology* 1995;**194**:757–64

This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.

Health technology
The health intervention examined in the study was magnetic resonance angiography (MRA), used as the diagnostic imaging procedure in the preoperative evaluation of patients with limb-threatening peripheral vascular disease (PVD).

Disease
Type of intervention
Diagnosis.

Hypothesis/study question
The main objective of the study was to examine the cost-effectiveness of MRA in comparison with

conventional angiography in the preoperative management of patients with limb-threatening PVD. A secondary aim of the analysis was to determine the threshold of diagnostic accuracy that MRA should reach for it to be a cost-effective option relative to conventional angiography. MRA had several advantages over standard angiography, but its economic implications were unclear. A combined approach based on MRA used as the primary imaging modality plus conventional angiography performed only in patients with contraindication to resonance was also evaluated in comparison with conventional angiography alone. A societal perspective was adopted in the study.

Economic study type
Cost–utility analysis.

Study population
The study population comprised a hypothetical cohort of patients undergoing angiography for the preoperative evaluation of limb-threatening PVD.

Setting
The setting was hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1981 and 1994. No dates were reported for resource-use data. The price year might have been 1992.

Source of effectiveness data
The effectiveness evidence came from a synthesis of previously completed studies and authors' assumptions.

Modelling
A decision-tree model was constructed to determine the costs and benefits of conventional versus MRA in a cohort of patients undergoing the preoperative work-up before surgical treatment for limb-threatening PVD. The structure of the tree was reported. Patients initially could receive MRA or conventional angiography and, based on the results of the tests (positive inflow lesion, negative inflow lesion or non-informative), could undergo another test. Then an outflow angiographic (MRA or CA) evaluation was performed in order to find a suitable target vessel. Again the test could be positive (suitable target vessel present), negative (suitable target vessel absent) or non-informative (in this case another test was performed). If a target vessel was identified patients underwent surgical bypass grafting. Bypass graft could be successful or unsuccessful (in this case patients returned to undergo re-evaluation and surgical procedures). Patients without a suitable target vessel underwent amputation. All patients underwent at least two tests, an inflow and outflow evaluation. However, it is not clear from the model whether these two evaluations were undertaken at the same time (i.e. one appointment). The time-horizon was not explicitly reported.

Outcomes assessed in the review
The outcomes estimated from the literature were as follows: sensitivity and specificity of MRA and conventional angiography in inflow evaluation, sensitivity of MRA and conventional angiography in outflow evaluation, percentage of patients with suitable target vessels, percentages of non-diagnostic MR angiograms in inflow and outflow evaluations, and quality of life values (derived using the Quality of Well-Being Scale) after amputation and after bypass graft.

Study designs and other criteria for inclusion in the review
It was not stated whether a systematic review of the literature had been undertaken. The design of the primary studies was not reported. However, the results in terms of sensitivity and specificity of MRA and conventional angiography were reported for all the included studies, together with the number of patients and the number of segments (when available).

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance, validity, extracting data
Not stated.

Number of primary studies included
The effectiveness evidence came from 14 studies.

Method of combination of primary studies
Primary estimates appear to have been combined using narrative methods. In some cases, the authors selected the best estimate.

Investigation of differences between primary studies
Not stated.

Results of the review

The sensitivity and specificity of MRA in inflow evaluation were 92% (range 92–95%) and 88% (range 88–92%), respectively.

The sensitivity and specificity of conventional angiography in inflow evaluation were both 97% (range 95–99%).

The sensitivity in outflow evaluation was 98% (range 95–100%) for MRA and 83% (range 75–88%) for conventional angiography.

The percentage of patients with suitable target vessels was 86% (range 70–100%).

The percentage of non-diagnostic MR angiograms was 2% (range 0–10%) in both inflow and outflow evaluations.

The values of quality of life were 0.484 (range 0.3–0.7) after amputation and 0.939 (range 0.9–1) after bypass graft.

Methods used to derive estimates of effectiveness

The authors made some assumptions in order to derive some estimators.

Estimates of effectiveness and key assumptions

The percentage of patients with clinically important stenosis was 80% (range 50–100%). The disutility value associated with conventional angiography relative to MRA was 0.0015 owing to a higher risk of complications. Other disutility values were 0.005 for blind surgical exploration and 0.02 for repeated surgical procedures. The rate of graft failure if a substantial stenosis was missed was 100% (range 90–100%). The rate of graft failure if an artificial stenosis was assumed was 30% (range 10–60%).

Measure of benefits used in the economic analysis

The summary benefit measure used in the economic evaluation was the number of quality-adjusted life-years (QALYs), which were derived from the decision model. Utility weights were based on authors' assumptions, as reported above. An annual 5% discount rate was applied to QALYs.

Direct costs

Discounting was relevant as costs were incurred over a long time-frame and, appropriately, a 5% annual rate was applied. Unit costs were not presented separately from quantities of resources used and a detailed breakdown of cost items was not provided. The health services included in the economic evaluation were professional fees (surgeon, radiologist and anaesthesiologist) and hospital costs associated with angiography, bypass grafting and amputation. The cost/resource boundary of the third party payer was adopted in the analysis of direct costs. Costs were derived from Medicare sources, while resource-use data were mainly based on authors' assumptions. The price year appears to have been 1992.

Indirect costs

Indirect costs in the form of productivity losses were included in the analysis as the perspective of society was adopted. Lost income was based on US national average daily earnings and the number of workdays lost due to the diagnostic and surgical procedures. Resource-use data were mainly based on authors' assumptions. Unit costs were not reported. Discounting was relevant and a 5% annual rate was applied as costs were incurred over a long time-frame. The price year was 1992.

Currency

US dollars ($).

Statistical analysis of costs

Costs were treated deterministically in the base case.

Sensitivity analysis

Univariate sensitivity analyses were carried out on each major model input to investigate the impact of data variability on the estimated cost–utility ratios. A threshold analysis was also performed to identify the sensitivity/specificity values of MRA that would produce a cost per QALY below the threshold value of $30,000.

Estimated benefits used in the economic analysis

The estimated quality of life value was 0.8680 with MRA and 0.8636 with conventional angiography.

Assuming that the benefits lasted for 2 years, in a cohort of 1000 patients, the estimated QALYs saved with MRA over conventional angiography would be 8.5 (or 0.0085 per patient).

Cost results

The estimated costs of patient management were $19,671 with MRA and $19,451 with conventional angiography.

In a cohort of 1000 subjects, the additional costs associated with MRA relative to conventional angiography would be $220,000 (or $220 per patient).

Synthesis of costs and benefits

An incremental cost–utility ratio was calculated to combine costs and QALYs of the two diagnostic strategies. Under base-case assumptions, the incremental cost per QALY saved with MRA over conventional angiography was $25,895.

The results of the univariate sensitivity analysis showed that the cost–utility ratio was sensitive to variations in the sensitivity of MRA for inflow lesions, sensitivity of conventional angiography for inflow lesions and sensitivity of conventional angiography for target vessels.

The cost–utility ratio varied from a negative value (which suggested that MRA saved QALYs and costs) to a maximum of $78,166 per QALY. However, in the vast majority of cases the incremental cost per QALY for MRA compared with conventional angiography was lower than $50,000.

The threshold analysis showed that, when the sensitivity and specificity of conventional therapy were 95%, MRA would have to have at least 90% sensitivity and 85% specificity for it to be cost-effective (cost per QALY below the threshold of $30,000) in comparison with conventional angiography; when the sensitivity and specificity of conventional therapy were 100%, MRA would have to have at least 95% sensitivity and 86% specificity to be cost-effective.

Under base-case assumptions, the incremental cost per additional QALY saved with the combined approach (MRA plus conventional angiography) relative to conventional angiography alone was $29,305.

Authors' conclusions

The authors concluded that MRA proved to be a cost-effective alternative to conventional angiography as a preoperative diagnostic tool in patients undergoing surgery for limb-threatening PVD.

CRD commentary

Selection of comparators

The choice of comparator was appropriate as conventional angiography represented the traditional diagnostic procedure in the authors' setting. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness

The effectiveness evidence was mainly derived from published studies, but it was unclear whether a systematic review of the literature had been undertaken. No information on the design of the primary studies was provided. Therefore, it is not possible to comment on the validity of the sources used. Primary estimates were combined using narrative methods and the authors did not investigate possible differences among the published studies. Some assumptions were also made and the issue of uncertainty was investigated in the sensitivity analysis. The authors acknowledged that some key estimates were derived from a limited number of studies. In addition, some data were obtained from studies with short-term follow-up, which led to some uncertainty in the long-term results of the analysis.

Validity of estimate of measure of benefit

The use of QALYs as a summary benefit measure was appropriate as it captured the impact of the interventions on quality of life and survival. Discounting was applied, as recommended in US guidelines. The method used to derive utility values was reported. The impact of variations in quality of life values was investigated in the sensitivity analysis. QALYs can be readily compared with the benefits of other healthcare interventions.

Validity of estimate of costs

The authors explicitly reported the perspective adopted in the study and all relevant costs were included in the economic evaluation. The source of data was reported, but a detailed breakdown of cost categories was not provided. Therefore, it could be difficult to replicate the cost analysis. Costs were treated deterministically in the base case, but sensitivity analyses were conducted to examine the issue of variability in economic data. The price year was reported, which will simplify reflation exercises in other settings. The authors noted some limitations of using Medicare charges as source of cost data.

Other issues

The authors compared their findings with those from other studies and reported that similar results were observed. The authors noted that the cost-effectiveness of MRA might have been underestimated owing to the use of conservative assumptions. The issue of the generalisability of the study results to other settings was not explicitly addressed. However, several sensitivity analyses were carried out on key model inputs, which had a positive impact on the external validity of the analysis. The authors acknowledged some limitations to the validity of their analysis, such as the use of assumptions and the fact that the decision model did not consider angioplasty as an alternative reconstructive procedure.

Implications of the study

The authors stress that further research should be carried out in order better to determine the quality of life associated with patients undergoing amputation and bypass procedures. The availability of data based on prospective trials could provide an opportunity to replicate the analysis in order to corroborate the current findings.

Other publications of related interest

Owen RS, Baum RA, Carpenter JP, Holland GA, Cope C. Symptomatic peripheral vascular disease: selection of imaging parameters and clinical evaluation with MR angiography. *Radiology* 1993;**187**:627–35.

Arfvidisson B, Karlsson J, Dahllof A, Lundholm K, Sullivan M. The impact of intermittent claudication on quality of life evaluated by the sickness impact profile technique. *Eur J Clin Invest* 1993;**23**:741–5.

Subject index terms

Subject indexing assigned by NLM

Angiography/ec (economics); blood Vessel Prosthesis; Comparative Study; Cost Benefit analysis; Costs and Cost analysis; Decision Support Techniques; Humans; Magnetic Resonance Angiography/ec (economics); Outcome Assessment (Health Care); Peripheral Vascular Diseases/di (diagnosis); Peripheral Vascular Diseases/ec (economics); Peripheral Vascular Diseases/su (surgery); Preoperative Care; Quality of Life; Sensitivity and Specificity; Treatment Outcome.

Country codes

USA.

Source of funding

None stated.

Copyright comments

Appendix 8

Parameter distributions used in the probabilistic sensitivity analysis for baseline analysis (1-year time-horizon model)

TABLE 37 *Parameter distributions used in PSA for baseline analysis (1-year time-horizon model)*

Description of the parameters used	Distributions
Probability of inaccurate amputation with CA	Beta, integer parameters only, $n = 5$, $r = 3$; expected value: 0.6
Probability of inaccurate amputation with MRA	Beta, integer parameters only, $n = 3$, $r = 1$; expected value: 0.333333333
Probability of inaccurate amputation with DUS	Beta, integer parameters only, $n = 4001$, $r = 1$; expected value: 0.000249938
Probability of having amputation after CA	Dirichlet, alphas list = list(5;61;33); expected value: 0.050505051; 0.616161616; 0.333333333
Probability of having amputation after MRA	Dirichlet, alphas list = list(3;67;29); expected value: 0.03030303; 0.676767677; 0.292929293
Probability of having amputation after DUS	Dirichlet, alphas list = list(4;18;15); expected value: 0.108108108; 0.486486486; 0.405405405
Probability of having bypass after CA	Dirichlet, alphas list = list(61;5;33); expected value: 0.616161616; 0.050505051; 0.333333333
Probability of having bypass after MRA	Dirichlet, alphas list = list(67;3;29); expected value: 0.676767677; 0.03030303; 0.292929293
Probability of having bypass after DUS	Dirichlet, alphas list = list(18;4;15); expected value: 0.486486486; 0.108108108; 0.405405405
Probability of having PTA after CA	Dirichlet, alphas list = list(33;5;61); expected value: 0.333333333; 0.050505051; 0.616161616
Probability of having PTA after MRA	Dirichlet, alphas list = list(29;3;67); expected value: 0.292929293; 0.03030303; 0.676767677
Probability of having PTA after DUS	Dirichlet, alphas list = list(15;4;18); expected value: 0.405405405; 0.108108108; 0.486486486
Probability of modifying incorrect amputation after CA	Dirichlet, alphas list = list(1001;2001;1;1); expected value: 0.33322237; 0.666111851; 0.000332889; 0.000332889
Probability of modifying incorrect amputation after MRA	Dirichlet, alphas list = list(1001;1;1;1); expected value: 0.997011952; 0.000996016; 0.000996016; 0.000996016
Probability of modifying incorrect amputation with DUS	Dirichlet, alphas list = list(1001;1;1;1); expected value: 0.997011952; 0.000996016; 0.000996016; 0.000996016
Probability of changing from incorrect amputation to bypass with CA	Dirichlet, alphas list = list(2001;1001;1;1); expected value: 0.666111851; 0.33322237; 0.000332889; 0.000332889
Probability of changing from incorrect amputation to bypass with MRA	Dirichlet, alphas list = list(1;1001;1;1); expected value: 0.000996016; 0.997011952; 0.000996016; 0.000996016
Probability of changing from incorrect amputation to bypass after DUS	Dirichlet, alphas list = list(1;1001;1;1); expected value: 0.000996016; 0.997011952; 0.000996016; 0.000996016
Probability of changing from incorrect amputation to PTA after CA	Dirichlet, alphas list = list(1;1001;2001;1); expected value: 0.000332889; 0.33322237; 0.666111851; 0.000332889
Probability of changing from incorrect amputation to PTA after MRA	Dirichlet, alphas list = list(1;1001;1;1); expected value: 0.000996016; 0.997011952; 0.000996016; 0.000996016
Probability of changing from incorrect amputation to PTA after DUS	Dirichlet, alphas list = list(1;1001;1;1); expected value: 0.000996016; 0.997011952; 0.000996016; 0.000996016

continued

TABLE 37 *Parameter distributions used in PSA for baseline analysis (1-year time-horizon model) (cont'd)*

Description of the parameters used	Distributions
Probability of changing from incorrect amputation to medical management after CA	Dirichlet, alphas list = list(1;1001;2001;1); expected value: 0.000332889; 0.33322237; 0.666111851; 0.000332889
Probability of changing from incorrect amputation to medical management after MRA	Dirichlet, alphas list = list(1;1001;1;1); expected value: 0.000996016; 0.997011952; 0.000996016; 0.000996016
Probability of changing from incorrect amputation to medical management after DUS	Dirichlet, alphas list = list(1;1001;1;1); expected value: 0.000996016; 0.997011952; 0.000996016; 0.000996016
Probability of changing from incorrect bypass to amputation after CA	Dirichlet, alphas list = list(1;2001;1;1); expected value: 0.000499002; 0.998502994; 0.000499002; 0.000499002
Probability of changing from incorrect bypass to amputation after MRA	Dirichlet, alphas list = list(1;2001;5001;1); expected value: 0.000142776; 0.285693889; 0.71402056; 0.000142776
Probability of changing from incorrect bypass to amputation after DUS	Dirichlet, alphas list = list(1;11001;2001;1); expected value: 0.000076899; 0.845970471; 0.153875731; 0.000076899
Probability of modifying incorrect bypass after CA	Dirichlet, alphas list = list(2001;1;1;1); expected value: 0.998502994; 0.000499002; 0.000499002; 0.000499002
Probability of modifying incorrect bypass after MRA	Dirichlet, alphas list = list(2001;1;5001;1); expected value: 0.285693889; 0.000142776; 0.71402056; 0.000142776
Probability of modifying incorrect bypass after DUS	Dirichlet, alphas list = list(11001;1;2001;1); expected value: 0.845970471; 0.000076899; 0.153875731; 0.000076899
Probability of changing from incorrect bypass to PTA after CA	Dirichlet, alphas list = list(1;1;2001;1); expected value: 0.000499002; 0.000499002; 0.998502994; 0.000499002
Probability of changing from incorrect bypass to PTA after MRA	Dirichlet, alphas list = list(5001;1;2001;1); expected value: 0.71402056; 0.000142776; 0.285693889; 0.000142776
Probability of changing from incorrect bypass to PTA after DUS	Dirichlet, alphas list = list(2001;1;11001;1); expected value: 0.153875731; 0.000076899; 0.845970471; 0.000076899
Probability of changing from incorrect bypass to medical management after CA	Dirichlet, alphas list = list(1;1;2001;1); expected value: 0.000499002; 0.000499002; 0.998502994; 0.000499002
Probability of changing from incorrect bypass to medical management after MRA	Dirichlet, alphas list = list(1;1;2001;5001); expected value: 0.000142776; 0.000142776; 0.285693889; 0.71402056
Probability of changing from incorrect bypass to medical management after DUS	Dirichlet, alphas list = list(1;1;11001;2001); expected value: 0.000076899; 0.000076899; 0.845970471; 0.153875731
Probability of changing from incorrect PTA to amputation after CA	Dirichlet, alphas list = list(1;1001;2001;1); expected value: 0.000332889; 0.33322237; 0.666111851; 0.000332889
Probability of changing from incorrect PTA to amputation after MRA	Dirichlet, alphas list = list(1;1001;1001;1); expected value: 0.000499002; 0.499500998; 0.499500998; 0.000499002
Probability of changing from incorrect PTA to amputation after DUS	Dirichlet, alphas list = list(1;3001;1;1001); expected value: 0.00024975; 0.7495005; 0.00024975; 0.25
Probability of changing from incorrect PTA to bypass after CA	Dirichlet, alphas list = list(1001;1;2001;1); expected value: 0.33322237; 0.000332889; 0.666111851; 0.000332889
Probability of changing from incorrect PTA to bypass after MRA	Dirichlet, alphas list = list(1001;1;1001;1); expected value: 0.499500998; 0.000499002; 0.499500998; 0.000499002
Probability of changing from incorrect PTA to bypass after DUS	Dirichlet, alphas list = list(3001;1;1;1001); expected value: 0.7495005; 0.00024975; 0.00024975; 0.25
Probability of modifying incorrect PTA after CA	Dirichlet, alphas list = list(2001;1;1001;1); expected value: 0.666111851; 0.000332889; 0.33322237; 0.000332889
Probability of modifying incorrect PTA after MRA	Dirichlet, alphas list = list(1001;1;1001;1); expected value: 0.499500998; 0.000499002; 0.499500998; 0.000499002
Probability of modifying incorrect PTA after DUS	Dirichlet, alphas list = list(1;1;3001;1001); expected value: 0.00024975; 0.00024975; 0.7495005; 0.25
Probability of changing from PTA to medical management after CA	Dirichlet, alphas list = list(1;1;1001;2001); expected value: 0.000332889; 0.000332889; 0.33322237; 0.666111851

continued

TABLE 37 *Parameter distributions used in PSA for baseline analysis (1-year time-horizon model) (cont'd)*

Description of the parameters used	Distributions
Probability of changing from PTA to medical management after MRA	Dirichlet, alphas list = list(1;1;1001;1001); expected value: 0.000499002; 0.000499002; 0.499500998; 0.499500998
Probability of modifying from PTA to medical management after DUS	Dirichlet, alphas list = list(1001;1;3001;1); expected value: 0.25; 0.00024975; 0.7495005; 0.00024975
Probability of inaccurate bypass with CA	Beta, integer parameters only, $n = 61$, $r = 2$; expected value: 0.032786885
Probability of inaccurate bypass with MRA	Beta, integer parameters only, $n = 67$, $r = 7$; expected value: 0.104477612
Probability of inaccurate bypass with DUS	Beta, integer parameters only, $n = 18$, $r = 2$; expected value: 0.111111111
Probability of inaccurate PTA with CA	Beta, integer parameters only, $n = 33$, $r = 3$; expected value: 0.09090909
Probability of inaccurate PTA with MRA	Beta, integer parameters only, $n = 29$, $r = 2$; expected value: 0.068965517
Probability of inaccurate PTA with DUS	Beta, integer parameters only, $n = 15$, $r = 1$; expected value: 0.066666667
Probability of having positive test (i.e. 50% or more of stenosis) with 2D TOF MRA	Beta, real-numbered parameters, alpha = (0.468 ^ 2)*(1-0.468)/(0.0097 ^ 2), beta = 0.468*(1-0.468)/(0.0097 ^ 2)-(0.468 ^ 2)*(1-0.468)/(0.0097 ^ 2); expected value: 0.468
Probability of having positive test (i.e. 50% or more of stenosis) with CE MRA	Beta, real-numbered parameters, alpha = 0.271 ^ 2*(1-0.271)/(0.0064 ^ 2), beta = 0.271*(1-0.271)/(0.0064 ^ 2)-0.271 ^ 2*(1-0.271)/(0.0064 ^ 2); expected value: 0.271
Probability of having positive test (i.e. 50% or more of stenosis) with DUS	Beta, real-numbered parameters, alpha = 0.222 ^ 2*(1-0.222)/(0.0055 ^ 2), beta = 0.222*(1-0.222)/(0.0055 ^ 2)-0.222 ^ 2*(1-0.222)/(0.0055 ^ 2); expected value: 0.222
Probability of having positive test (i.e. 50% or more of stenosis) with CA	Beta, real-numbered parameters, alpha = 0.279 ^ 2*(1-0.279)/(0.0039 ^ 2), beta = 0.279*(1-0.279)/(0.0039 ^ 2)-0.279 ^ 2*(1-0.279)/(0.0039 ^ 2); expected value: 0.279
Negative predictive value after 2D TOF MRA	Beta, real-numbered parameters, alpha = 0.881 ^ 2*(1-0.881)/(0.0087 ^ 2), beta = 0.881*(1-0.881)/(0.0087 ^ 2)-0.881 ^ 2*(1-0.881)/(0.0087 ^ 2); expected value: 0.881
Negative predictive value after CE MRA	Beta, real-numbered parameters, alpha = 0.983 ^ 2*(1-0.983)/(0.0023 ^ 2), beta = 0.983*(1-0.983)/(0.0023 ^ 2)-0.983 ^ 2*(1-0.983)/(0.0023 ^ 2); expected value: 0.983
Negative predictive value after DUS	Beta, real-numbered parameters, alpha = 0.969 ^ 2*(1-0.969)/(0.0028 ^ 2), beta = 0.969*(1-0.969)/(0.0028 ^ 2)-0.969 ^ 2*(1-0.969)/(0.0028 ^ 2); expected value: 0.969
Cost of CA (includes capital equipment)	Gamma, alpha = (536.80 ^ 2)/(178.1814 ^ 2), lambda = 536.80/(178.1814 ^ 2); expected value: 536.8
Costs of complications with CA	Gamma, alpha = (5740.35 ^ 2)/(1305.3197 ^ 2), lambda = 5740.35/(1305.3197 ^ 2); expected value: 5740.35
Costs of MRA (includes capital equipment)	Gamma, alpha = (462 ^ 2)/(13.2487 ^ 2), lambda = 462/(13.2487 ^ 2); expected value: 462
Cost of DUS	Gamma, alpha = (92.49 ^ 2)/(15.6747 ^ 2), lambda = 92.49/(15.6747 ^ 2); expected value: 92.49
Cost of primary amputation	Gamma, alpha = (6435.36 ^ 2)/(230.334 ^ 2), lambda = 6435.36/(230.334 ^ 2); expected value: 6435.36
Costs of changing from incorrect amputation to bypass	Gamma, alpha = (5943.65 ^ 2)/(245.7685 ^ 2), lambda = 5943.65/(245.7685 ^ 2); expected value: 5943.65
Cost of amputation revision, readmission	Gamma, alpha = (6232.81 ^ 2)/(2219.6125 ^ 2), lambda = 6232.81/(2219.6125 ^ 2); expected value: 6232.81

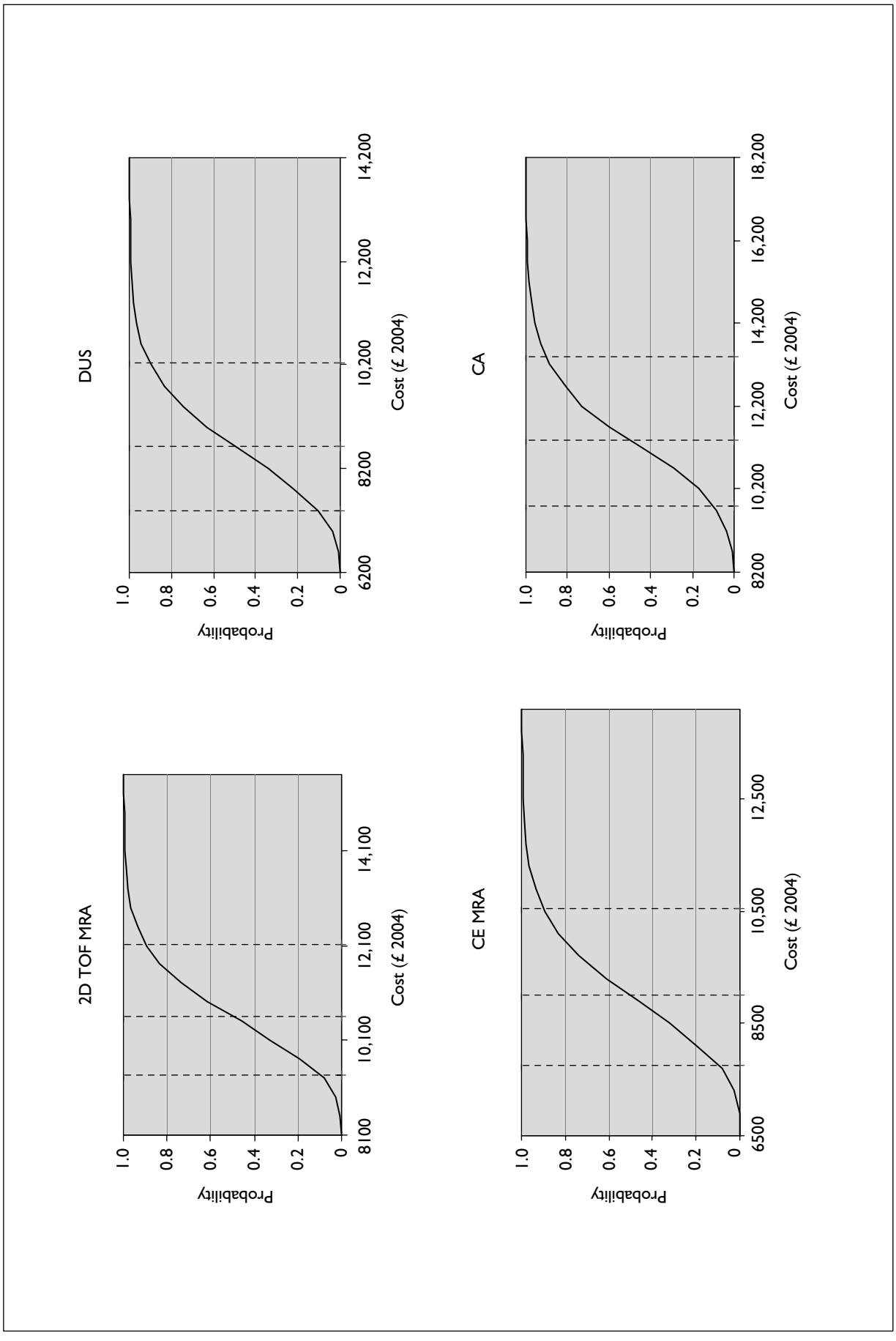
continued

TABLE 37 *Parameter distributions used in PSA for baseline analysis (1-year time-horizon model) (cont'd)*

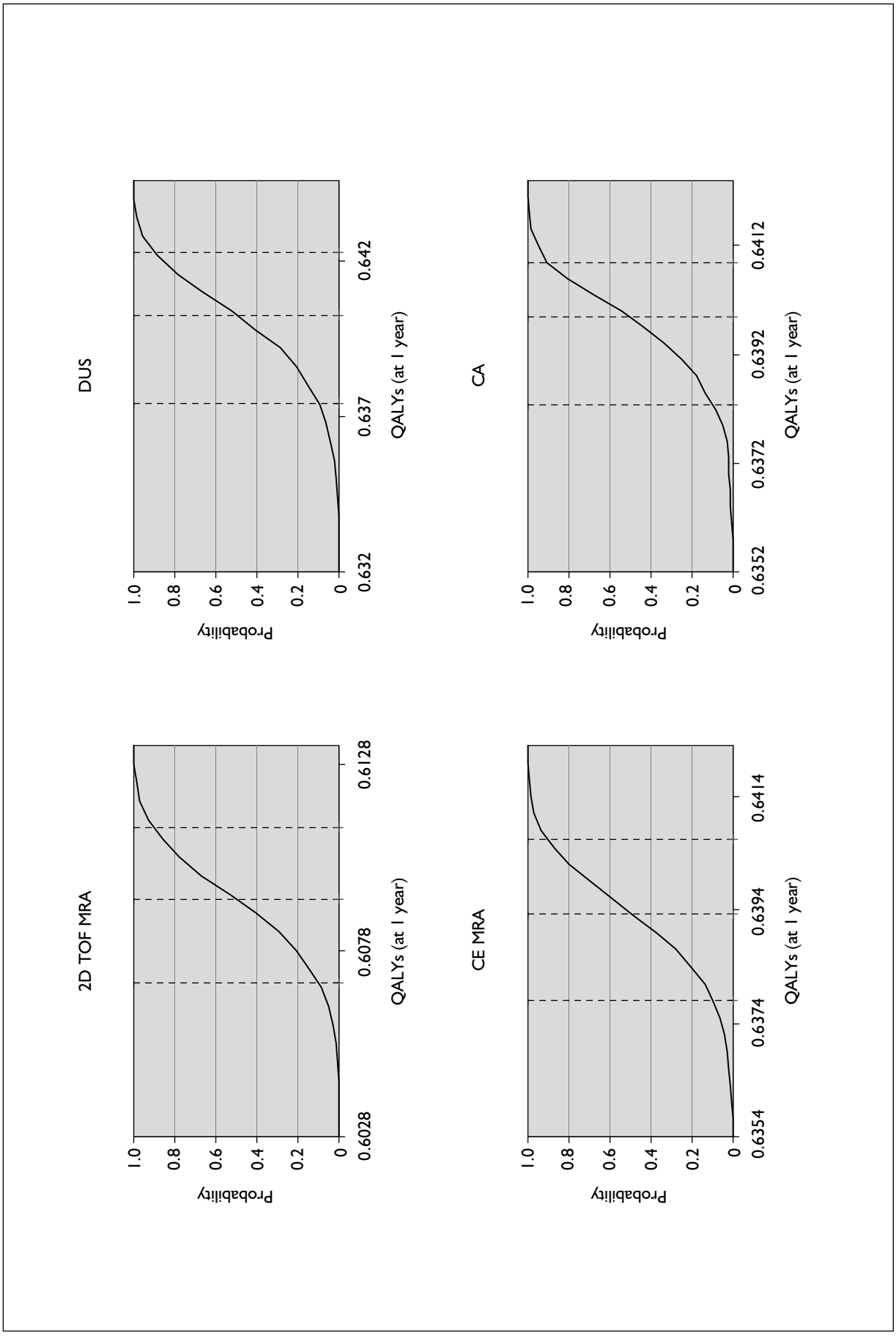
Description of the parameters used	Distributions
Cost of primary bypass	Gamma, alpha = (4965.55 ^ 2)/(193.9938 ^ 2), lambda = 4965.55/(193.9938 ^ 2); expected value: 4965.55
Cost of changing from incorrect bypass to amputation	Gamma, alpha = (4965.55 ^ 2)/(193.9938 ^ 2), lambda = 4965.55/(193.9938 ^ 2); expected value: 4965.55
Cost of changing from incorrect bypass to PTA	Gamma, alpha = (2355.46 ^ 2)/(11.0515 ^ 2), lambda = 2355.46/(11.0515 ^ 2); expected value: 2355.46
Cost of bypass revision, readmission	Gamma, alpha = (4965.55 ^ 2)/(193.9938 ^ 2), lambda = 4965.55/(193.9938 ^ 2); expected value: 4965.55
Costs of primary PTA	Gamma, alpha = (1178.27 ^ 2)/(48.7386 ^ 2), lambda = 1178.27/(48.7386 ^ 2); expected value: 1178.27
Cost of changing from incorrect PTA to bypass	Gamma, alpha = (5502.21 ^ 2)/(222.4012 ^ 2), lambda = 5502.21/(222.4012 ^ 2); expected value: 5502.21
Cost of changing from incorrect PTA to amputation	Gamma, alpha = (7141.67 ^ 2)/(267.7218 ^ 2), lambda = 7141.67/(267.7218 ^ 2); expected value: 7141.67
Cost of changing from incorrect PTA to MM	Gamma, alpha = (245.36 ^ 2)/(62.592 ^ 2), lambda = 245.36/(62.592 ^ 2); expected value: 245.36
Cost of PTA revision, readmission	Gamma, alpha = (1178.27 ^ 2)/(48.7386 ^ 2), lambda = 1178.27/(48.7386 ^ 2); expected value: 1178.27
Cost of mortality from vascular interventions	Gamma, alpha = (9906.04 ^ 2)/(3567.3456 ^ 2), lambda = 9906.04/(3567.3456 ^ 2); expected value: 9906.04
Long term costs of limited mobility independent patient	Gamma, alpha = (771.45 ^ 2)/(393.3202 ^ 2), lambda = 771.45/(393.3202 ^ 2); expected value: 771.45
Long term costs of limited mobility dependent patient	Gamma, alpha = (7290.35 ^ 2)/(2932.9266 ^ 2), lambda = 7290.35/(2932.9266 ^ 2); expected value: 7290.35
Long term costs of being in a wheelchair	Gamma, alpha = (13169.81 ^ 2)/(908.9147 ^ 2), lambda = 13169.81/(908.9147 ^ 2); expected value: 13169.81
Long term costs of being bedridden	Gamma, alpha = (22150.2 ^ 2)/(3672.9206 ^ 2), lambda = 22150.2/(3672.9206 ^ 2); expected value: 22150.2
Probability of complications with CA	Triangular, Min = 0.2, Likeliest = 0.3, Max = 0.5; expected value: 0.333333333
Cost per outpatient visit (i.e. to the vascular surgeon)	Gamma, alpha = (144 ^ 2)/(15.3265 ^ 2), lambda = 144/(15.3265 ^ 2); expected value: 144
Cost of medical management per year	Gamma, alpha = (14.66 ^ 2)/(4.2699 ^ 2), lambda = 14.66/(4.2699 ^ 2); expected value: 14.66

Appendix 9

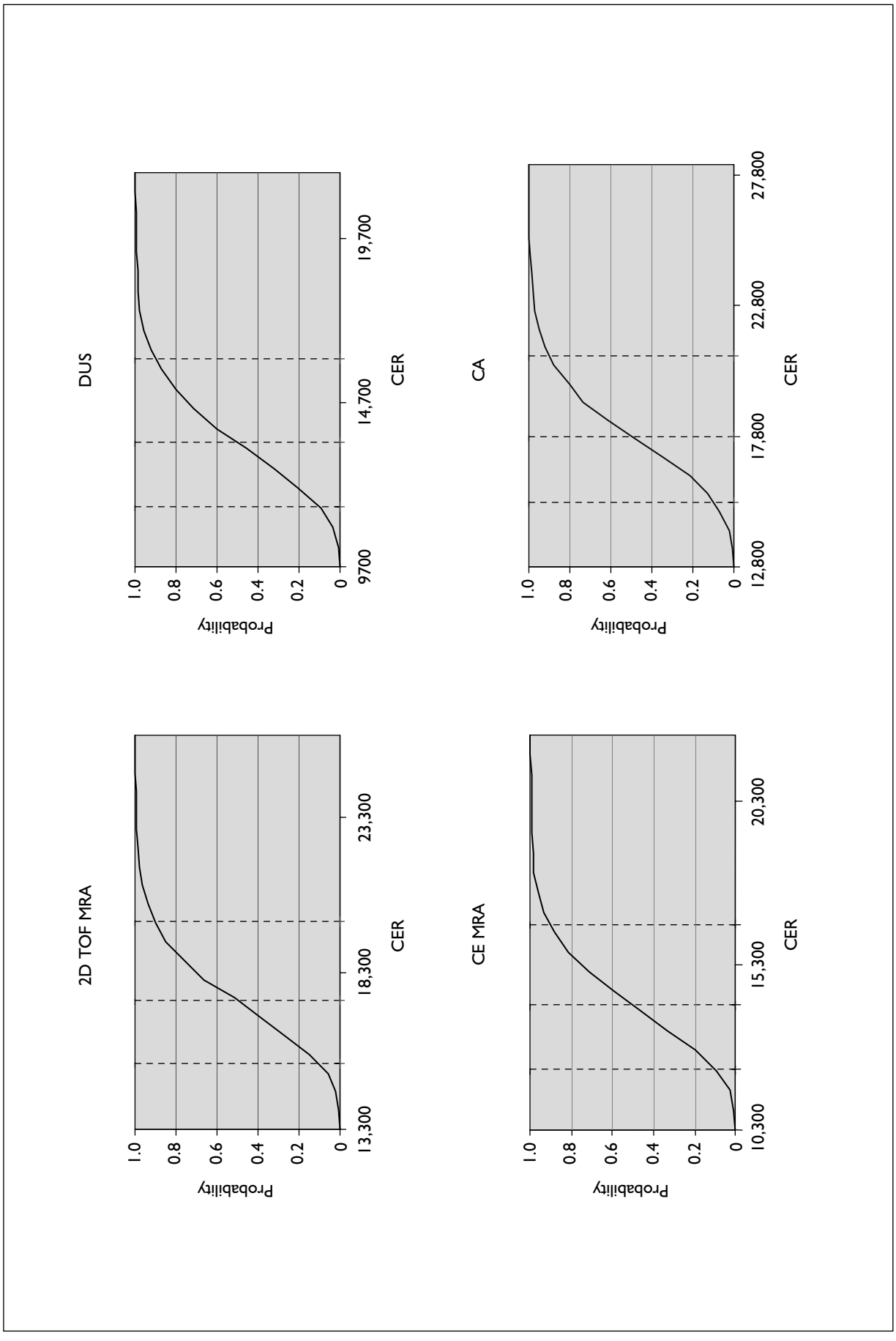
Cumulative probabilities for the distributions of costs, effectiveness and cost-effectiveness



FIGURES 32–35 *Cumulative probabilities for distribution of costs (10/50/90%) (base case, 1-year time-horizon)*



FIGURES 36–39 *Cumulative probabilities for the distribution of effectiveness (10/50/90%) (base case, 1-year time-horizon)*



FIGURES 40–43 *Cumulative probabilities for the cost-effectiveness ratios (10/50/90%) (base case, 1-year time-horizon)*

Appendix 10

Cost-effectiveness analysis for 1-year time-horizon model: endarterectomy considered as a PTA procedure

TABLE 38 *Cost-effectiveness results for endarterectomy as a PTA procedure (1-year time-horizon model)*

		Mean	SD	Minimum	Median	Maximum
2D TOF MRA	Cost (£ 2004)	10,690	1145	8393	10552	15075
	QALYs	0.609	0.002	0.601	0.609	0.614
	CER	17,559	1,886	13,756	17,331	24,840
CE MRA	Cost (£ 2004)	9,039	1,163	6,662	8,899	13,486
	QALYs	0.64	0.001	0.634	0.64	0.642
	CER	14,134	1,819	10,409	13,913	21,093
DUS	Cost (£ 2004)	8,724	1,170	6,366	8,610	13,426
	QALYs	0.64	0.002	0.632	0.64	0.645
	CER	13,629	1,833	9,892	13,463	21,025
CA	Cost (£ 2004)	11,459	1,358	8,456	11,354	16,824
	QALYs	0.64	0.001	0.635	0.64	0.643
	CER	17,901	2,122	13,242	17,739	26,386

TABLE 39 *Incremental cost-effectiveness results for endarterectomy as a PTA procedure (1-year time-horizon model)*

Strategy	Cost	Incremental cost	Effectiveness	Incremental effectiveness	C/E	Incremental C/E (ICER)
DUS	8,723.75	–	0.640124	–	13,628.22	–
CE MRA	9,039.433	315.6833	0.639564	–0.00056	14,133.74	Dominated
2D TOF MRA	10,689.74	1,965.99	0.608814	–0.03131	17,558.31	Dominated
CA	11,458.95	2,735.203	0.640113	–1.1E-05	17,901.46	Dominated

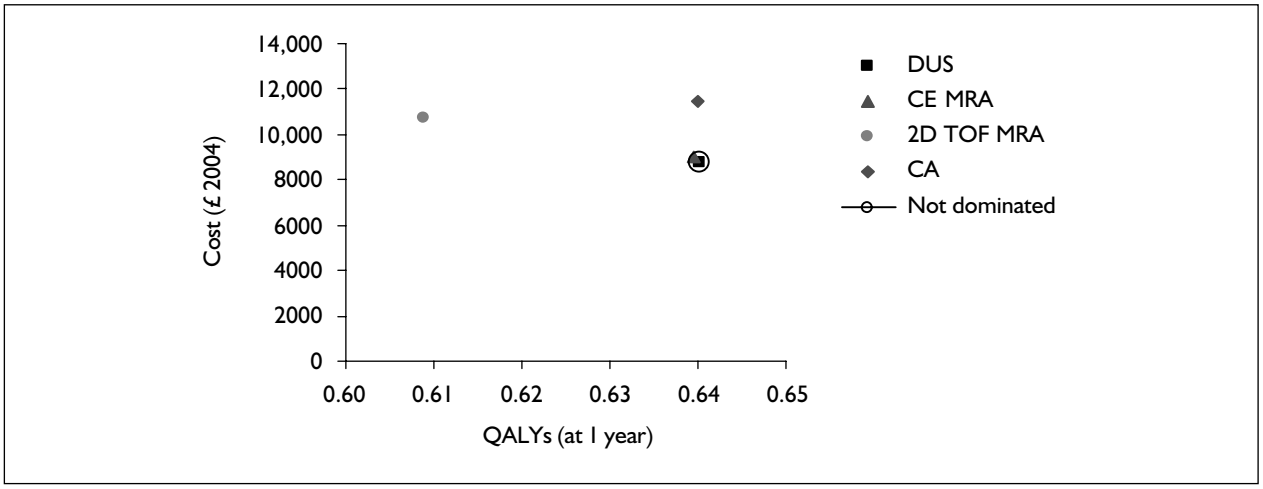


FIGURE 44 *Cost-effectiveness plane for endarterectomy as a PTA procedure (1-year time-horizon model)*

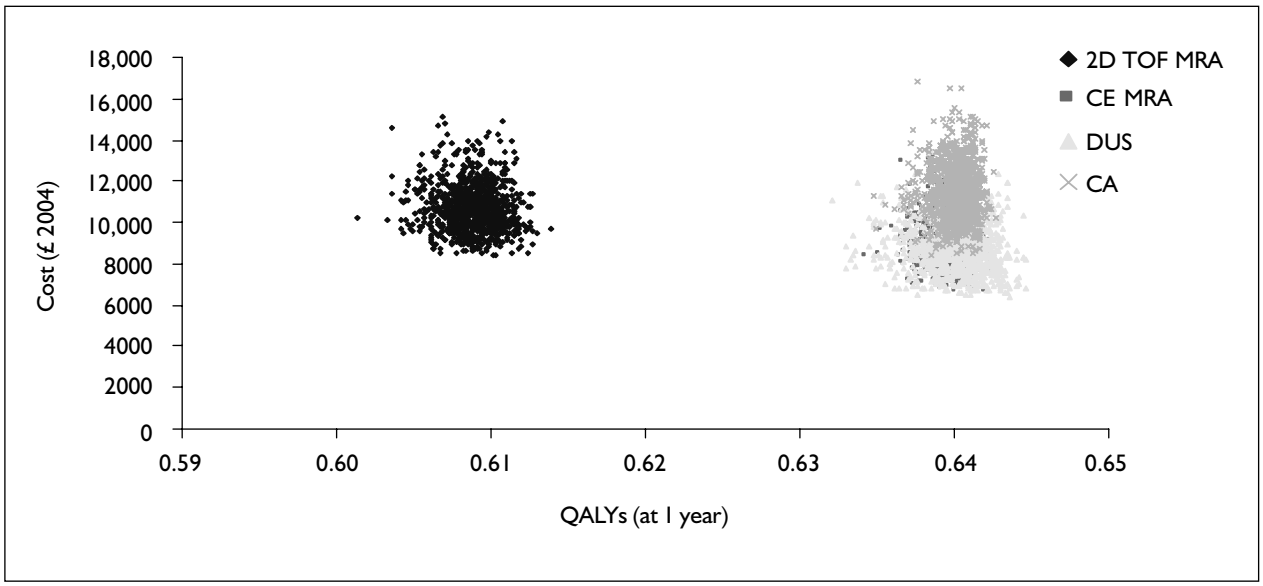


FIGURE 45 *Scatterplot for PSA for endarterectomy as a PTA procedure (1-year time-horizon model)*

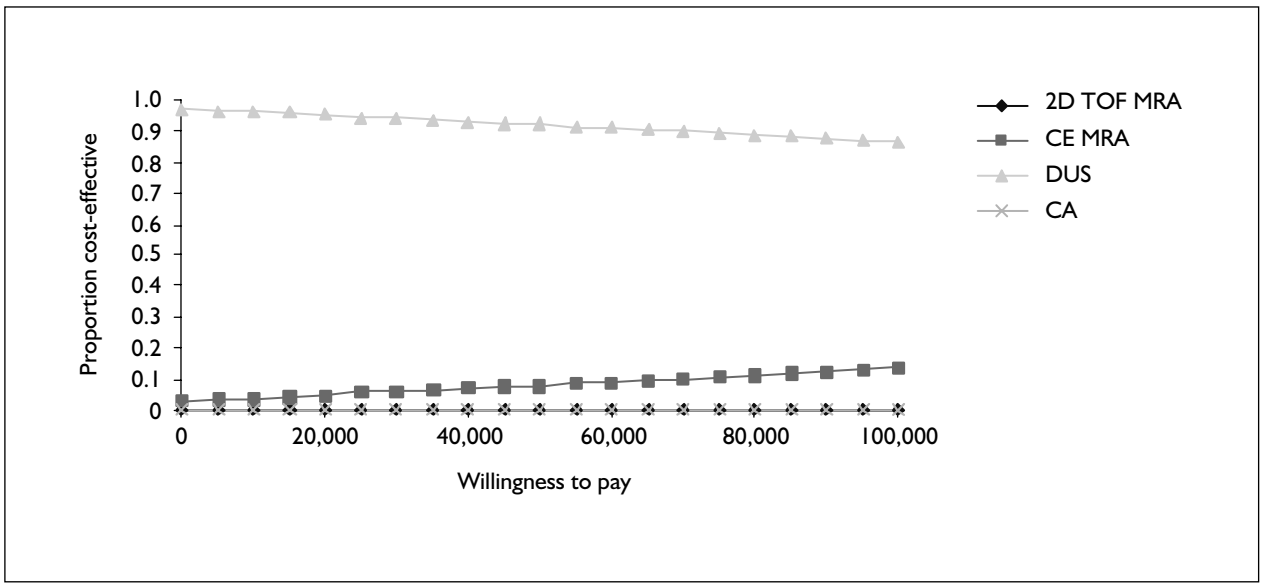


FIGURE 46 *CEACs of the alternative diagnostic preoperative tests for endarterectomy as a PTA procedure (1-year time-horizon model)*

Appendix 11

Cost-effectiveness analysis for adjustment of Dirichlet distribution-10 (1-year time-horizon model)

TABLE 40 *Cost-effectiveness results for adjustment of Dirichlet distribution-10 (1-year time-horizon model)*

		Mean	SD	Minimum	Median	Maximum
2D TOF MRA	Cost (£ 2004)	10,715	1,160	8,317	10,581	16,377
	QALYs	0.609	0.001	0.604	0.609	0.613
	CER	17,588	1,910	13,612	17,364	26,994
CE MRA	Cost (£ 2004)	9,125	1,182	6,807	8,977	14,856
	QALYs	0.639	0.001	0.635	0.639	0.642
	CER	14,274	1,850	10,668	14,053	23,248
DUS	Cost (£ 2004)	8,755	1,197	6,222	8,612	14,715
	QALYs	0.64	0.002	0.631	0.64	0.644
	CER	13,679	1,874	9,687	13,444	23,033
CA	Cost (£ 2004)	11,501	1,437	7,976	11,357	19,208
	QALYs	0.64	0.001	0.634	0.64	0.642
	CER	17,977	2,245	12,465	17,738	29,990

TABLE 41 *Incremental cost-effectiveness results for adjustment of Dirichlet distribution-10 (1-year time-horizon model)*

Strategy	Cost	Incremental cost	Effectiveness	Incremental effectiveness	C/E	Incremental C/E (ICER)
DUS	8,755.34	–	0.64007	–	13,678.72	–
CE MRA	9,125.48	370.1395	0.639307	–0.00076	14,274.01	Dominated
2D TOF MRA	10,715.27	1,959.932	0.609275	–0.0308	17,586.91	Dominated
CA	11,500.98	2,745.643	0.639772	–0.0003	17,976.7	Dominated

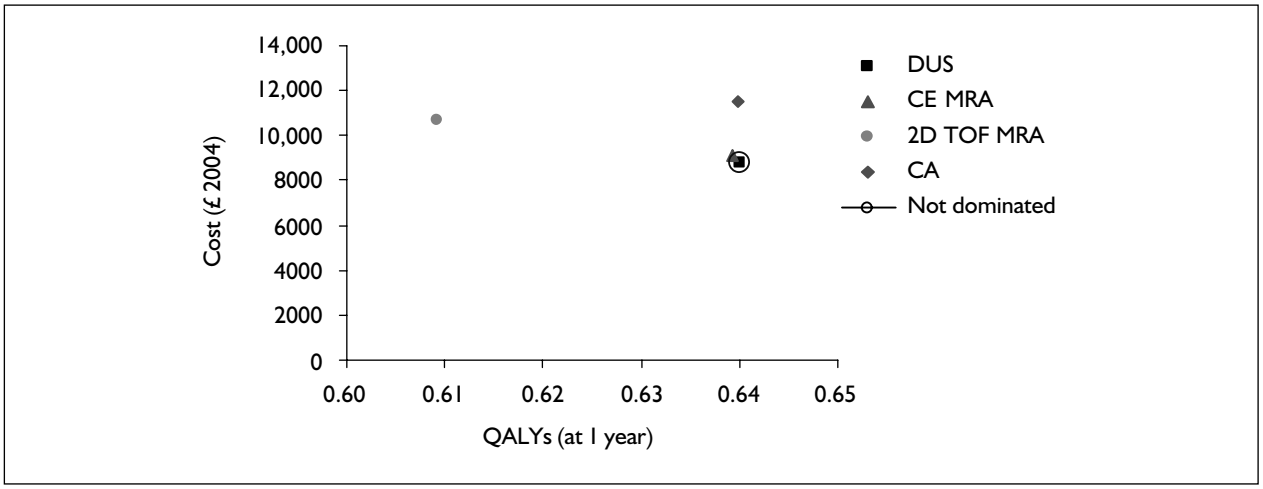


FIGURE 47 *Cost-effectiveness plane for adjustment of Dirichlet distribution-10 (1-year time-horizon model)*

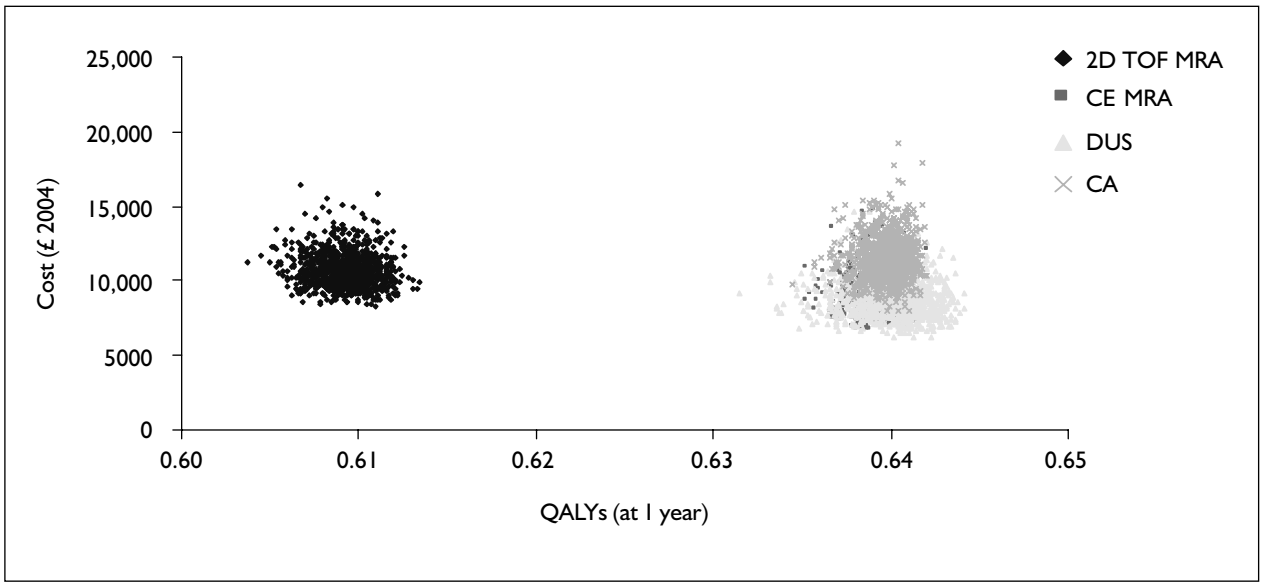


FIGURE 48 *Scatterplot for PSA for adjustment of Dirichlet distribution-10 (1-year time-horizon model)*

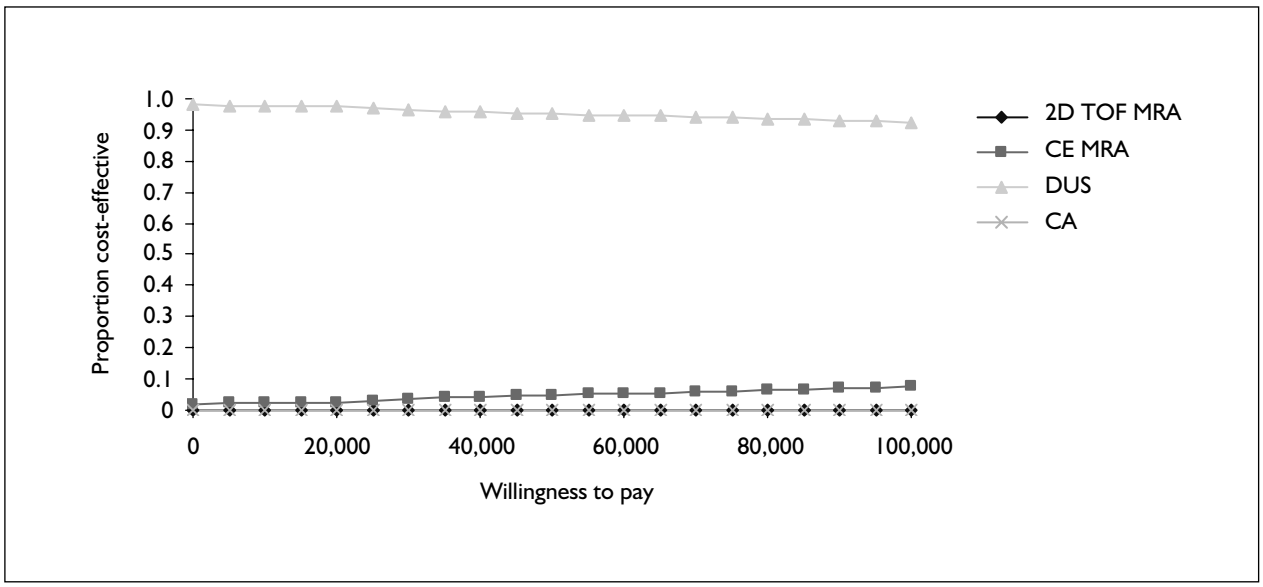


FIGURE 49 *CEACs of the alternative diagnostic preoperative tests for adjustment of Dirichlet distribution-10 (1-year time-horizon model)*

Health Technology Assessment Programme

Prioritisation Strategy Group

Members

HTA Commissioning Board

Members

Current and past membership details of all HTA 'committees' are available from the HTA website (www.hta.ac.uk)

Diagnostic Technologies & Screening Panel

Members

Chair,
Dr Ron Zimmern, Director of the Public Health Genetics Unit, Strangeways Research Laboratories, Cambridge

Ms Norma Armston, Freelance Consumer Advocate, Bolton

Professor Max Bachmann, Professor of Health Care Interfaces, Department of Health Policy and Practice, University of East Anglia

Professor Rudy Bilous Professor of Clinical Medicine & Consultant Physician, The Academic Centre, South Tees Hospitals NHS Trust

Ms Dea Birkett, Service User Representative, London

Dr Paul Cockcroft, Consultant Medical Microbiologist and Clinical Director of Pathology, Department of Clinical Microbiology, St Mary's Hospital, Portsmouth

Professor Adrian K Dixon, Professor of Radiology, University Department of Radiology, University of Cambridge Clinical School

Dr David Elliman, Consultant in Community Child Health, Islington PCT & Great Ormond Street Hospital, London

Professor Glyn Elwyn, Research Chair, Centre for Health Sciences Research, Cardiff University, Department of General Practice, Cardiff

Professor Paul Glasziou, Director, Centre for Evidence-Based Practice, University of Oxford

Dr Jennifer J Kurinczuk, Consultant Clinical Epidemiologist, National Perinatal Epidemiology Unit, Oxford

Dr Susanne M Ludgate, Clinical Director, Medicines & Healthcare Products Regulatory Agency, London

Mr Stephen Pilling, Director, Centre for Outcomes, Research & Effectiveness, Joint Director, National Collaborating Centre for Mental Health, University College London

Mrs Una Rennard, Service User Representative, Oxford

Dr Phil Shackley, Senior Lecturer in Health Economics, Academic Vascular Unit, University of Sheffield

Dr Margaret Somerville, Director of Public Health Learning, Peninsula Medical School, University of Plymouth

Dr Graham Taylor, Scientific Director & Senior Lecturer, Regional DNA Laboratory, The Leeds Teaching Hospitals

Professor Lindsay Wilson Turnbull, Scientific Director, Centre for MR Investigations & YCR Professor of Radiology, University of Hull

Professor Martin J Whittle, Clinical Co-director, National Co-ordinating Centre for Women's and Childhealth

Dr Dennis Wright, Consultant Biochemist & Clinical Director, The North West London Hospitals NHS Trust, Middlesex

Pharmaceuticals Panel

Members

Chair,
Professor Robin Ferner, Consultant Physician and Director, West Midlands Centre for Adverse Drug Reactions, City Hospital NHS Trust, Birmingham

Ms Anne Baileff, Consultant Nurse in First Contact Care, Southampton City Primary Care Trust, University of Southampton

Professor Imti Choonara, Professor in Child Health, Academic Division of Child Health, University of Nottingham

Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford

Mrs Barbara Greggains, Non-Executive Director, Greggains Management Ltd

Dr Bill Gutteridge, Medical Adviser, National Specialist Commissioning Advisory Group (NSCAG), London

Mrs Sharon Hart, Consultant Pharmaceutical Adviser, Reading

Dr Jonathan Karnon, Senior Research Fellow, Health Economics and Decision Science, University of Sheffield

Dr Yoon Loke, Senior Lecturer in Clinical Pharmacology, University of East Anglia

Ms Barbara Meredith, Lay Member, Epsom

Dr Andrew Prentice, Senior Lecturer and Consultant Obstetrician & Gynaecologist, Department of Obstetrics & Gynaecology, University of Cambridge

Dr Frances Rotblat, CPMP Delegate, Medicines & Healthcare Products Regulatory Agency, London

Dr Martin Shelly, General Practitioner, Leeds

Mrs Katrina Simister, Assistant Director New Medicines, National Prescribing Centre, Liverpool

Dr Richard Tiner, Medical Director, Medical Department, Association of the British Pharmaceutical Industry, London

Therapeutic Procedures Panel

Members

Chair,
Professor Bruce Campbell, Consultant Vascular and General Surgeon, Department of Surgery, Royal Devon & Exeter Hospital

Dr Mahmood Adil, Deputy Regional Director of Public Health, Department of Health, Manchester

Dr Aileen Clarke, Consultant in Public Health, Public Health Resource Unit, Oxford

Professor Matthew Cooke, Professor of Emergency Medicine, Warwick Emergency Care and Rehabilitation, University of Warwick

Mr Mark Emberton, Senior Lecturer in Oncological Urology, Institute of Urology, University College Hospital

Professor Paul Gregg, Professor of Orthopaedic Surgical Science, Department of General Practice and Primary Care, South Tees Hospital NHS Trust, Middlesbrough

Ms Maryann L Hardy, Lecturer, Division of Radiography, University of Bradford

Dr Simon de Lusignan, Senior Lecturer, Primary Care Informatics, Department of Community Health Sciences, St George's Hospital Medical School, London

Dr Peter Martin, Consultant Neurologist, Addenbrooke's Hospital, Cambridge

Professor Neil McIntosh, Edward Clark Professor of Child Life & Health, Department of Child Life & Health, University of Edinburgh

Professor Jim Neilson, Professor of Obstetrics and Gynaecology, Department of Obstetrics and Gynaecology, University of Liverpool

Dr John C Pounsford, Consultant Physician, Directorate of Medical Services, North Bristol NHS Trust

Dr Karen Roberts, Nurse Consultant, Queen Elizabeth Hospital, Gateshead

Dr Vimal Sharma, Consultant Psychiatrist/Hon. Senior Lecturer, Mental Health Resource Centre, Cheshire and Wirral Partnership NHS Trust, Wallasey

Professor Scott Weich, Professor of Psychiatry, Division of Health in the Community, University of Warwick

Disease Prevention Panel

Members

Chair,
Dr Edmund Jessop, Medical Adviser, National Specialist Commissioning Advisory Group (NSCAG), London

Mrs Sheila Clark, Chief Executive, St James's Hospital, Portsmouth

Mr Richard Copeland, Lead Pharmacist: Clinical Economy/Interface, Wansbeck General Hospital, Northumberland

Dr Elizabeth Fellow-Smith, Medical Director, West London Mental Health Trust, Middlesex

Mr Ian Flack, Director PPI Forum Support, Council of Ethnic Minority Voluntary Sector Organisations, Stratford

Dr John Jackson, General Practitioner, Newcastle upon Tyne

Mrs Veronica James, Chief Officer, Horsham District Age Concern, Horsham

Professor Mike Kelly, Director, Centre for Public Health Excellence, National Institute for Health and Clinical Excellence, London

Professor Yi Mien Koh, Director of Public Health and Medical Director, London NHS (North West London Strategic Health Authority), London

Ms Jeanett Martin, Director of Clinical Leadership & Quality, Lewisham PCT, London

Dr Chris McCall, General Practitioner, Dorset

Dr David Pencheon, Director, Eastern Region Public Health Observatory, Cambridge

Dr Ken Stein, Senior Clinical Lecturer in Public Health, Director, Peninsula Technology Assessment Group, University of Exeter, Exeter

Dr Carol Tannahill, Director, Glasgow Centre for Population Health, Glasgow

Professor Margaret Thorogood, Professor of Epidemiology, University of Warwick, Coventry

Dr Ewan Wilkinson, Consultant in Public Health, Royal Liverpool University Hospital, Liverpool

Expert Advisory Network

Members

Professor Douglas Altman, Professor of Statistics in Medicine, Centre for Statistics in Medicine, University of Oxford

Professor John Bond, Director, Centre for Health Services Research, University of Newcastle upon Tyne, School of Population & Health Sciences, Newcastle upon Tyne

Professor Andrew Bradbury, Professor of Vascular Surgery, Solihull Hospital, Birmingham

Mr Shaun Brogan, Chief Executive, Ridgeway Primary Care Group, Aylesbury

Mrs Stella Burnside OBE, Chief Executive, Regulation and Improvement Authority, Belfast

Ms Tracy Bury, Project Manager, World Confederation for Physical Therapy, London

Professor Iain T Cameron, Professor of Obstetrics and Gynaecology and Head of the School of Medicine, University of Southampton

Dr Christine Clark, Medical Writer & Consultant Pharmacist, Rossendale

Professor Collette Clifford, Professor of Nursing & Head of Research, School of Health Sciences, University of Birmingham, Edgbaston, Birmingham

Professor Barry Cookson, Director, Laboratory of Healthcare Associated Infection, Health Protection Agency, London

Dr Carl Counsell, Clinical Senior Lecturer in Neurology, Department of Medicine & Therapeutics, University of Aberdeen

Professor Howard Cuckle, Professor of Reproductive Epidemiology, Department of Paediatrics, Obstetrics & Gynaecology, University of Leeds

Dr Katherine Darton, Information Unit, MIND – The Mental Health Charity, London

Professor Carol Dezateux, Professor of Paediatric Epidemiology, London

Dr Keith Dodd, Consultant Paediatrician, Derby

Mr John Dunning, Consultant Cardiothoracic Surgeon, Cardiothoracic Surgical Unit, Papworth Hospital NHS Trust, Cambridge

Mr Jonothan Earnshaw, Consultant Vascular Surgeon, Gloucestershire Royal Hospital, Gloucester

Professor Martin Eccles, Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle upon Tyne

Professor Pam Enderby, Professor of Community Rehabilitation, Institute of General Practice and Primary Care, University of Sheffield

Professor Gene Feder, Professor of Primary Care Research & Development, Centre for Health Sciences, Barts & The London Queen Mary's School of Medicine & Dentistry, London

Mr Leonard R Fenwick, Chief Executive, Newcastle upon Tyne Hospitals NHS Trust

Mrs Gillian Fletcher, Antenatal Teacher & Tutor and President, National Childbirth Trust, Henfield

Professor Jayne Franklyn, Professor of Medicine, Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, Birmingham

Dr Neville Goodman, Consultant Anaesthetist, Southmead Hospital, Bristol

Professor Robert E Hawkins, CRC Professor and Director of Medical Oncology, Christie CRC Research Centre, Christie Hospital NHS Trust, Manchester

Professor Allen Hutchinson, Director of Public Health & Deputy Dean of ScHARR, Department of Public Health, University of Sheffield

Professor Peter Jones, Professor of Psychiatry, University of Cambridge, Cambridge

Professor Stan Kaye, Cancer Research UK Professor of Medical Oncology, Section of Medicine, Royal Marsden Hospital & Institute of Cancer Research, Surrey

Dr Duncan Keeley, General Practitioner (Dr Burch & Ptnrs), The Health Centre, Thame

Dr Donna Lamping, Research Degrees Programme Director & Reader in Psychology, Health Services Research Unit, London School of Hygiene and Tropical Medicine, London

Mr George Levvy, Chief Executive, Motor Neurone Disease Association, Northampton

Professor James Lindesay, Professor of Psychiatry for the Elderly, University of Leicester, Leicester General Hospital

Professor Julian Little, Professor of Human Genome Epidemiology, Department of Epidemiology & Community Medicine, University of Ottawa

Professor Rajan Madhok, Consultant in Public Health, South Manchester Primary Care Trust, Manchester

Professor Alexander Markham, Director, Molecular Medicine Unit, St James's University Hospital, Leeds

Professor Alistaire McGuire, Professor of Health Economics, London School of Economics

Dr Peter Moore, Freelance Science Writer, Ashtead

Dr Andrew Mortimore, Public Health Director, Southampton City Primary Care Trust, Southampton

Dr Sue Moss, Associate Director, Cancer Screening Evaluation Unit, Institute of Cancer Research, Sutton

Mrs Julietta Patnick, Director, NHS Cancer Screening Programmes, Sheffield

Professor Robert Peveler, Professor of Liaison Psychiatry, Royal South Hants Hospital, Southampton

Professor Chris Price, Visiting Professor in Clinical Biochemistry, University of Oxford

Professor William Rosenberg, Professor of Hepatology and Consultant Physician, University of Southampton, Southampton

Professor Peter Sandercock, Professor of Medical Neurology, Department of Clinical Neurosciences, University of Edinburgh

Dr Susan Schonfield, Consultant in Public Health, Hillingdon PCT, Middlesex

Dr Eamonn Sheridan, Consultant in Clinical Genetics, Genetics Department, St James's University Hospital, Leeds

Professor Sarah Stewart-Brown, Professor of Public Health, University of Warwick, Division of Health in the Community Warwick Medical School, LWMS, Coventry

Professor Ala Szczepura, Professor of Health Service Research, Centre for Health Services Studies, University of Warwick

Dr Ross Taylor, Senior Lecturer, Department of General Practice and Primary Care, University of Aberdeen

Mrs Joan Webster, Consumer member, HTA – Expert Advisory Network

Feedback

The HTA Programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (http://www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@hta.ac.uk
http://www.hta.ac.uk

ISSN 1366-5278