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[Diagnostic Test Accuracy Review]

Ankle brachial index for the diagnosis of lower limb peripheral arterial disease

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ABSTRACT

Background

Peripheral arterial disease (PAD) of the lower limb is common, with prevalence of both symptomatic and asymptomatic disease estimated at 13% in the over 50 age group. Symptomatic PAD affects about 5% of individuals in Western populations between the ages of 55 and 74 years. The most common initial symptom of PAD is muscle pain on exercise that is relieved by rest and is attributed to reduced lower limb blood flow due to atherosclerotic disease (intermittent claudication). The ankle brachial index (ABI) is widely used by a variety of healthcare professionals, including specialist nurses, physicians, surgeons and podiatrists working in primary and secondary care settings, to assess signs and symptoms of PAD. As the ABI test is non-invasive and inexpensive and is in widespread clinical use, a systematic review of its diagnostic accuracy in people presenting with leg pain suggestive of PAD is highly relevant to routine clinical practice.

Objectives

To estimate the diagnostic accuracy of the ankle brachial index (ABI) - also known as the ankle brachial pressure index (ABPI) - for the diagnosis of peripheral arterial disease in people who experience leg pain on walking that is alleviated by rest.

Search methods

We carried out searches of the following databases in August 2013: MEDLINE (Ovid SP), Embase (Ovid SP), the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO), Latin American and Caribbean Health Sciences (LILACS) (Bireme), Database of Abstracts of Reviews of Effects and the Health Technology Assessment Database in *The Cochrane Library*, the Institute for Scientific Information (ISI) Conference Proceedings Citation Index - Science, the British Library Zetoc Conference search and Medion.

Selection criteria

We included cross-sectional studies of ABI in which duplex ultrasonography or angiography was used as the reference standard. We also included cross-sectional or diagnostic test accuracy (DTA) cohort studies consisting of both prospective and retrospective studies.

Participants were adults presenting with leg pain on walking that was relieved by rest, who were tested in primary care settings or secondary care settings (hospital outpatients only) and who did not have signs or symptoms of critical limb ischaemia (rest pain, ischaemic ulcers or gangrene).

The index test was ABI, also called the ankle brachial pressure index (ABPI) or the Ankle Arm Index (AAI), which was performed with a hand-held doppler or oscillometry device to detect ankle vessels. We included data collected via sphygmomanometers (both manual and aneroid) and digital equipment.

Data collection and analysis

Two review authors independently replicated data extraction by using a standard form, which included an assessment of study quality, and resolved disagreements by discussion. Two review authors extracted participant-level data when available to populate 2×2 contingency tables (true positives, true negatives, false positives and false negatives).

After a pilot phase involving two review authors working independently, we used the methodological quality assessment tool the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2), which incorporated our review question - along with a flow diagram to aid reviewers' understanding of the conduct of the study when necessary and an assessment of risk of bias and applicability judgements.

Main results

We screened 17,055 records identified through searches of databases. We obtained 746 full-text articles and assessed them for relevance. We scrutinised 49 studies to establish their eligibility for inclusion in the review and excluded 48, primarily because participants were not patients presenting solely with exertional leg pain, investigators used no reference standard or investigators used neither angiography nor duplex ultrasonography as the reference standard. We excluded most studies for more than one reason.

Only one study met the eligibility criteria and provided limb-level accuracy data from just 85 participants (158 legs). This prospective study compared the manual doppler method of obtaining an ABI (performed by untrained personnel) with the automated oscillometric method. Limb-level data, as reported by the study, indicated that the accuracy of the ABI in detecting significant arterial disease on angiography is superior when stenosis is present in the femoropopliteal vessels, with sensitivity of 97% (95% confidence interval (CI) 93% to 99%) and specificity of 89% (95% CI 67% to 95%) for oscillometric ABI, and sensitivity of 95% (95% CI 89% to 97%) and specificity of 56% (95% CI 33% to 70%) for doppler ABI. The ABI threshold was not reported. Investigators attributed the lower specificity for doppler to the fact that a tibial or dorsalis pedis pulse could not be detected by doppler in 12 of 27 legs with normal vessels or non-significant lesions. The superiority of the oscillometric (automated) method for obtaining an ABI reading over the manual method with a doppler probe used by inexperienced operators may be a clinically important finding.

Authors' conclusions

Evidence about the accuracy of the ankle brachial index for the diagnosis of PAD in people with leg pain on exercise that is alleviated by rest is sparse. The single study included in our review provided only limb-level data from a few participants. Well-designed cross-sectional studies are required to evaluate the accuracy of ABI in patients presenting with early symptoms of peripheral arterial disease in all healthcare settings. Another systematic review of existing studies assessing the use of ABI in alternative patient groups, including asymptomatic, high-risk patients, is required.

PLAIN LANGUAGE SUMMARY

Ankle brachial index for the diagnosis of lower limb peripheral arterial disease

Peripheral arterial disease (PAD) of the legs affects 13% of people over 50 years of age. Sometimes PAD is "silent" and people are unaware they have it, but PAD can cause pain in the legs, especially with walking, and this type of symptomatic PAD affects about 5% of people in the Western world between the ages of 55 and 74 years. In PAD, fatty deposits (atherosclerosis) and blood clots cause the arteries to narrow and block. This leads to poor blood flow to the muscles during exercise, causing the classical symptom of muscle pain during walking that goes away after rest (intermittent claudication). In severe cases of PAD, symptoms of rest pain, ulceration and gangrene may develop and, if untreated, can lead to lower limb amputation. People with PAD are also at higher risk for cardiovascular disease and stroke.

The ankle brachial index (ABI) is a test that is used to facilitate diagnosis of PAD. This test uses a device for measuring blood pressure with an inflatable cuff, and blood pressure measurements are taken at the upper arm and the ankle. The equipment can be manual or digital with automatic electronic calculation of blood pressure. The ABI is widely used for assessment of PAD by specialist nurses, physicians, surgeons and podiatrists working in hospitals. Dividing blood pressure recorded at the ankle by that recorded at the arm produces a ratio. Ratios of 0.90 to 1.30 are considered normal for adults, and ratios less than 0.8 indicate that PAD is present. Lower readings (< 0.7) suggest that the disease is severe and people might develop ulcers and gangrene. People with mild to moderate PAD can

arrive at a diagnosis by several routes when using the ABI: during routine diabetic foot checks in general practice, in community health clinic or hospital settings, as a screening test for PAD in people who have no symptoms and during assessment of people presenting with exertional leg pain suggestive of PAD. Once a diagnosis of PAD is established, treatment will include prescribed secondary prevention therapy and lifestyle advice (exercise, smoking cessation, diet, weight), and for those with impaired quality of life, treatment may include supervised exercise therapy, or revascularisation, which commonly involves endovascular treatment rather than surgery.

In hospitals, other tests may be used to diagnose PAD. Duplex ultrasound (DUS) shows blood flow in the arteries and is non-invasive, but only an experienced radiologist can achieve useful images. Hospital staff can use other tests to image the blood vessels, namely, computerised tomography angiography (CTA), magnetic resonance angiography (MRA) and catheter angiography.

The ABI test is non-invasive and inexpensive and is widely used clinically; therefore, we have reviewed all available reports obtained from a wide search of databases of medical literature to estimate its accuracy in identifying PAD in people who experience pain on walking that goes away after rest. Two review authors independently assessed studies that met inclusion criteria of the review, including use of a cross-sectional study design; enrolment of participants with pain on walking that got better with rest; and use of duplex ultrasonography or angiography to check that results of the ABI test were accurate. One study met our criteria and provided data from 85 participants (158 limbs). Investigators compared the manual doppler method of measuring ABI with the automated method. Researchers provided only data for legs as opposed to data for patients; we were therefore unable to recalculate the analysis at the whole-participant level.

In conclusion, we found little evidence about the accuracy of the ankle brachial index for diagnosing PAD in people presenting with exertional leg pain. The study included in our review had some flaws, and well-designed cross-sectional studies are needed to measure the accuracy of the ABI for diagnosing PAD in patients with early symptoms.

BACKGROUND

Peripheral arterial disease (PAD) of the lower limbs is common, with prevalence of both symptomatic and asymptomatic disease estimated at 13% in the over 50 age group (Hirsch 2001). Symptomatic PAD affects about 5% of individuals in Western populations between the ages of 55 and 74 years (Khan 2007). The most common initial symptom of PAD is muscle pain on exercise that is relieved by rest and is attributed to reduced lower limb blood flow due to atherosclerotic disease (intermittent claudication; IC). Patients with more severe PAD may develop rest pain, ulceration and gangrene (critical limb ischaemia; CLI), which, if untreated, can lead to lower limb amputation (Hooi 2007; Twine 2009). The presence of PAD has been shown to be a marker of underlying cardiovascular disease.

A simple, non-invasive test known as the ankle brachial index (ABI) - or the ankle brachial pressure index (ABPI) - can detect PAD. Healthcare providers can use the ABI to screen asymptomatic patients at increased risk of developing PAD, for example, people with diabetes, and to assess people presenting with leg pain suggestive of PAD. Clinicians can use a low ABI, even in the absence of symptoms, to identify people who are at increased risk of cardiac and cerebrovascular disease (Ankle Brachial Index Collaboration 2008; SIGN 2007).

Dividing the highest ankle pressure (obtained in the posterior tibial, dorsalis pedis and, when required, peroneal arteries) by

the highest systolic arm pressure yields the ABI ratio. Classically, healthcare providers have used a doppler probe to detect signals within the arteries, but recently designed oscillometric and photoplethysmographic devices are now available. Current guidelines do not endorse the use of these newer devices but recommend the hand-held doppler technique (NICE 2012). Ratios of 0.90 to 1.30 are normal for adults, ratios less than 0.9 are indicative of arterial stenosis and ratios less than 0.5 are associated with CLI (Bhasin 2007; MacLeod-Roberts 1995; NICE 2012). Individuals with aorto-iliac disease may have normal ABI at rest and low values after exercise. An 'exercise-ABI' test can detect this and can be performed during secondary care.

A wide variety of healthcare professionals, including specialist nurses, physicians, surgeons and podiatrists working in primary and secondary care settings, frequently use the ABI to assess PAD. These providers normally check foot and leg pulses of people presenting with leg pain suggestive of PAD before performing an ABI to determine their presence or absence. Once PAD is diagnosed, first-line management of the condition consists of cardiac risk factor management, which includes lifestyle advice, smoking cessation, statin and antiplatelet therapy, blood pressure control and screening for and treatment of diabetes (Bhasin 2007; Heald 2006). Supervised exercise programmes can lead to symptomatic improvement, and healthcare providers can perform arterial revascularisation, in the form of angioplasty or less commonly

surgery, to treat those with incapacitating disease and significantly impaired quality of life (Cassar 2003; Chang 2011; de Backer 2012; Fokkenrood 2013; Lane 2014; NICE 2012; Rutherford 1997). Physicians may prescribe naftidrofuryl oxalate for patients in whom supervised exercise therapy has not been found to be effective and who do not wish to be referred for revascularisation (NICE 2012).

In secondary care, hospital staff may use a variety of non-invasive imaging tests for patients with suspected PAD in whom revascularisation may be considered, including non-invasive duplex ultrasonography, computerised tomography angiography (CTA) or magnetic resonance angiography (MRA). The National Institute for Health and Care Excellence suggests duplex ultrasonography as the first-line approach for imaging PAD, and CTA or contrast-enhanced MRA for those who need further imaging (NICE 2012).

The ABI test is non-invasive and inexpensive and is in widespread clinical use; a systematic review of its diagnostic accuracy in people presenting with leg pain suggestive of PAD is highly relevant to routine clinical practice.

Target condition being diagnosed

Presence or absence of peripheral arterial disease of the lower limb.

Index test(s)

Healthcare providers use the ankle brachial index (ABI) to diagnose peripheral arterial disease (PAD), by dividing highest systolic pressure measured in the arteries at the ankle (dorsalis pedis and posterior tibial arteries, or peroneal if the others are non-detectable) by highest systolic blood pressure at the arm (brachial artery).

Physicians can calculate an ankle brachial ratio in several ways. UK clinical guidelines recommend that the patient is rested in a supine position and that blood pressure is taken by using a sphygmomanometer with an appropriately sized cuff at the brachial artery and the posterior tibial, dorsalis pedis and, when possible, peroneal arteries. A doppler probe detects audible systolic pressure (Aboyans 2012; McDermott 2000; NICE 2012).

For each leg, the healthcare professional calculates the ABI by dividing the highest ankle pressure by the highest pressure reading taken from the arm (McDermott 2000). MacLeod-Roberts 1995 presents a classification of ABI values.

In this review, we use the threshold of less than 0.90 to distinguish between positive (< 0.90) and negative (\geq 0.90) test results. Clinicians commonly use this threshold in clinical practice, and is cited in current guidelines (NICE 2012).

The position of the patient at the time blood pressure is taken is important: For each inch that the ankle is positioned below the

heart, care providers have noted a 1 mmHg increase in systolic ankle blood pressure (MacLeod-Roberts 1995).

False negatives commonly occur in people who have calcification of the ankle artery wall, which creates incompressibility and an artificially high reading. This may occur in some patients with diabetes (Bhasin 2007; MacLeod-Roberts 1995).

Several automated blood pressure machines are available, and all are eligible for inclusion in the review.

Clinical pathway

Healthcare providers may follow several clinical pathways to diagnose mild to moderate PAD by using the ABI: They may measure the ABI in primary care to diagnose PAD in members of the general population who report symptoms of exertional leg pain. They sometimes use ABI in addition to routine diabetic foot checks in primary care, community health settings or hospital settings as a screening test for PAD in people who have no symptoms but are at high risk. Once a diagnosis of PAD is established, healthcare staff will prescribe secondary prevention therapy and will give lifestyle advice (exercise, smoking cessation, diet, weight); for those who have impaired quality of life, they may offer supervised exercise therapy, or revascularisation, which commonly involves endovascular treatment rather than surgery.

Role of index test(s)

Practitioners use the ABI test in healthcare settings to identify PAD in people who have suggestive symptoms, and can use this test to screen those at increased risk for PAD. An ABI < 0.90 is predictive of increased risk of cardiovascular disease (Ankle Brachial Index Collaboration 2008). This review aimed to include studies evaluating the diagnostic test accuracy of the ABI used in primary and secondary (outpatient only) care settings by a range of healthcare professionals, to evaluate people presenting with leg pain on exercise that is relieved by rest, which is suggestive of underlying PAD.

Alternative test(s)

Uses of the ABI in clinical practice are diverse, and care providers do not need to consider standard alternative tests.

Rationale

The success of management strategies for PAD depends upon the quality of the diagnostic process, which involves careful assessment of underlying pathology through diagnostic tests that possess a high level of accuracy.

OBJECTIVES

To estimate the diagnostic accuracy of the ankle brachial index (ABI) - also known as the ankle brachial pressure index (ABPI) - for the diagnosis of peripheral arterial disease in people who experience leg pain on walking that is alleviated by rest.

Secondary objectives

We also intended to investigate the effect of sources of heterogeneity on diagnostic accuracy, specifically, study setting, previous tests, types of equipment used, types of reference standards applied, different groups of patients examined (people with type 1 or type 2 diabetes and suspected aorto-iliac disease) and duration of symptoms, by including them as co-variables in the meta-analysis, if sufficient studies provided relevant data. It was our intention that we would examine graphically other potential sources of heterogeneity for signs that they were a cause of heterogeneity.

METHODS

Criteria for considering studies for this review

Types of studies

We included studies of ABI that used duplex ultrasonography or angiography as the reference standard. We included cross-sectional or diagnostic test accuracy (DTA) cohort studies examining both prospective and retrospective studies. These studies had to report that all participants received a reference standard; investigators had to present cross-tabulated results of the index test and the reference standard (2x2 table), or had to report sufficient information to allow the 2x2 table data to be back-calculated.

Participants

Adults with leg pain on walking relieved by rest, who are tested in primary care settings or secondary care settings (hospital outpatients only) and do not have signs or symptoms of critical limb ischaemia (rest pain, ischaemic ulcers or gangrene). We excluded from the review patients who were free of exertional leg pain, as well as those with CLI.

Index tests

Ankle brachial index (ABI), also called ankle brachial pressure index (ABPI). We included data collected by sphygmomanometers (both manual and aneroid) as well as by digital equipment that

used manual or automatic inflation. We included studies that used hand-held doppler or oscillometry to detect ankle vessels.

Target conditions

Peripheral arterial disease of the lower limbs.

Reference standards

We included studies that used duplex ultrasonography or angiography as the reference standard test, and we noted instances in which different reference standards were used to verify the presence or absence of disease in the same study population.

Search methods for identification of studies

We applied no restrictions in terms of date, language of publication or publication status of studies. We used no diagnostic method search filters.

Electronic searches

We applied no restrictions in terms of language of publication or publication status.

We searched the following databases.

- MEDLINE Ovid (1946 to July week 5 2013).
- Embase (Ovid SP) (1980 to 2013 week 32).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO (12 August 2013).
- Latin American and Caribbean Health Sciences (LILACS) (Bireme) (13 August 2013).
- Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment Database (HTA), in *The Cochrane Library* (2013, Issue 7).
- Institute for Scientific Information (ISI) Conference Proceedings Citation Index - Science (14 August 2013).
- British Library Zetoc Conference search (29 August 2013).

We used the search strategies shown in [Appendix 1](#); [Appendix 2](#); [Appendix 3](#); [Appendix 4](#); [Appendix 5](#); [Appendix 6](#) and [Appendix 7](#).

We also searched MEDION (www.mediondatabase.nl/) using the 'Systematic Reviews of Diagnostic Studies' search filter (29 August 2013) ([Appendix 8](#)).

Searching other resources

We reviewed the bibliographies of review articles identified by searches for potentially relevant studies.

Data collection and analysis

Selection of studies

One review author (FC) screened titles and abstracts retrieved by the electronic searches, and a second review author (AA) checked a random sample of 10% of the studies. We obtained full papers for potentially eligible studies, including those identified by non-electronic means. Two review authors (FC, AA) independently applied exclusion criteria to the full papers and resolved disagreements by discussion. We used a flow diagram to show results of the decision-making process.

Data extraction and management

Two review authors (FC, AA) independently used a standard form to replicate data extraction; this form included an assessment of study quality. Review authors corroborated their data extraction and quality assessment decisions and resolved disagreements by discussion. Review authors intended to extract participant-level data to populate 2×2 contingency tables - true positives (TPs), true negatives (TNs), false positives (FPs) and false negatives (FNs) - as reported. We also extracted details of test threshold(s) used for interpretation of results.

We collected data on mortality, adverse events, the nature of the equipment used (manual or automated) and the number of technical failures.

Assessment of methodological quality

After a pilot phase involving two review authors working independently, we used the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) (Whiting 2011), which incorporated our review question, a flow diagram to aid reviewers' understanding of the conduct of the study when necessary and an assessment of risk of bias and applicability judgements. We presented review-specific signalling questions and appropriate items concerning the applicability of primary studies relative to the review, together with guidance about ratings, in Appendix 9. We resolved disagreements by discussion.

Statistical analysis and data synthesis

We intended to use 2×2 contingency tables populated with participant-level data, rather than data on limbs, to estimate sensitivity and specificity for each study. When data were adequate, we intended to perform a bivariate random-effects meta-analysis of sensitivity and specificity. We anticipated that we would use these estimates to create receiver operating characteristic (ROC) and forest plots. As an ABI less than 0.90 is the accepted threshold used in clinical practice, we had planned to restrict the meta-analysis to studies that used this threshold, so that our estimates of sensitivity

and specificity would be derived directly from that threshold. We intended to add items investigated for heterogeneity as co-variables to the bivariate model.

However, available data are based on limbs as the unit of analysis. If two datapoints were obtained from the same participant (one from each leg), these datapoints will tend to be more similar to each other than datapoints from different patients, thus changing the variance in data. However, estimating within-study variance is a key part of meta-analysis, and current methods do not allow for studies in which a participant may contribute data from more than one potential disease site. If studies do not provide participant-level data, we have no correct way to estimate within-study variance, and so meta-analysis, whether bivariate or based on hierarchical summary receiver operating characteristic (HSROC) models (Harbord 2007), or univariate meta-analysis for sensitivity and specificity, is not an option.

We intended to perform all analyses in R 7.1 (cran.r-project.org) and SAS 9.3 (www.sas.com).

Investigations of heterogeneity

Our planned investigations into the effect of sources of heterogeneity on diagnostic accuracy focussed on patient groups (e.g. type 1 and type 2 diabetes, suspected aorto-iliac disease), duration of symptoms, previous tests and types of equipment (automatic or manual) by including them as co-variables in the meta-analyses. We intended to examine other potential sources of heterogeneity graphically for signs that they were the source of heterogeneity. We planned to group estimates in plots according to items considered potential sources of heterogeneity, as detailed above, and to present these as forest and ROC plots for visual assessment of heterogeneity.

If we found sufficient studies, we planned to investigate heterogeneity by adding items as co-variables to the meta-analysis model, from a bivariate or univariate analysis, depending on results of the main analysis. However, we recognised the likelihood of having too few studies to perform meta-regression with all items listed as potential sources of heterogeneity, and under these circumstances, we planned to limit ourselves to visual inspection of ROC and forest plots. We understand that some items are investigated better with individual participant data, as they are patient-specific, rather than study-specific, for example, duration of symptoms, and we planned to interpret any aggregate results cautiously.

Sensitivity analyses

We intended to conduct several sensitivity analyses to compare the diagnostic accuracy of ABI in those with and without diabetes, in those with and without coronary heart disease, in smokers versus non smokers and when manual versus automated methods are used to measure the ABI.

Assessment of reporting bias

(Deeks 2005).

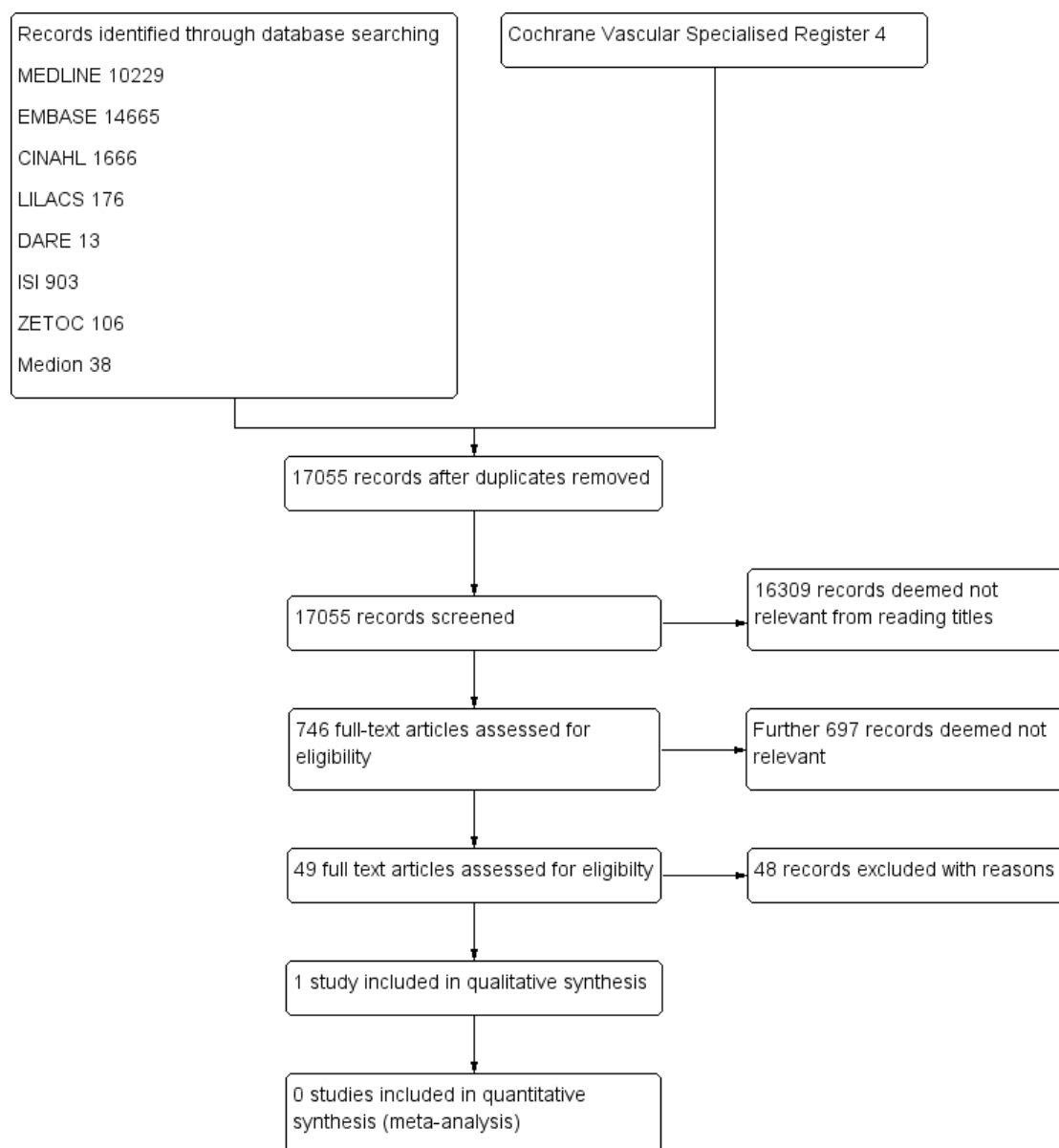
Methods for dealing with publication bias in reviews of diagnostic accuracy studies are relatively underdeveloped. Consequently, we interpreted our results cautiously, and with awareness of the likelihood of publication bias, rather than by using funnel plots, which can be challenging to interpret in this context. We planned to consider using a funnel plot of the log of the diagnostic odds ratio (lnDOR), provided we found low heterogeneity in the lnDOR

RESULTS

Results of the search

See [Figure 1](#).

Figure 1. Study flow diagram.



We screened 17,055 records identified through searches of databases. We obtained and assessed for relevance 746 full-text articles. A second review author (AA) checked a 10% random sample of these articles and reached 100% agreement with the first review author (FC). We scrutinised 49 studies to establish their eligibility for inclusion in the review.

We included only one study (Vega 2011) with a total of 85 participants and have described it in the [Characteristics of included studies](#) table.

We have listed the 48 studies excluded from the review, along with

reasons for exclusion, in the [Characteristics of excluded studies](#) table. We excluded studies primarily because participants were not patients presenting solely with exertional leg pain, investigators used no reference standard or the reference standard used was neither angiography nor duplex ultrasonography. We have provided more than one reason for exclusion of most studies.

Methodological quality of included studies

See [Figure 2](#); [Figure 3](#).

Figure 2. Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies.

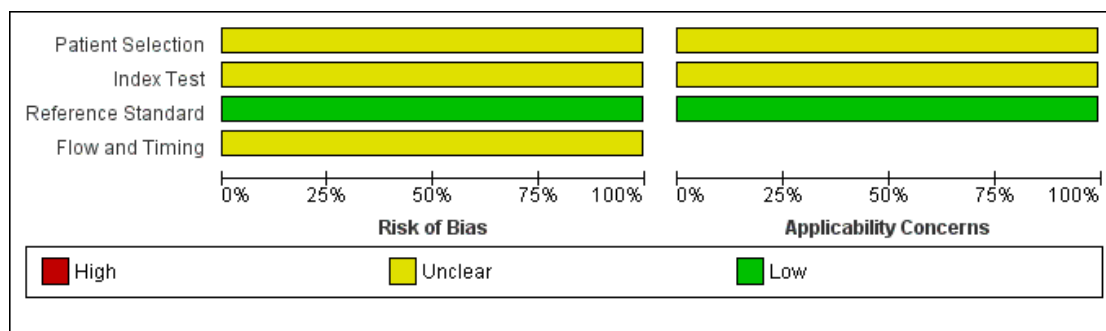
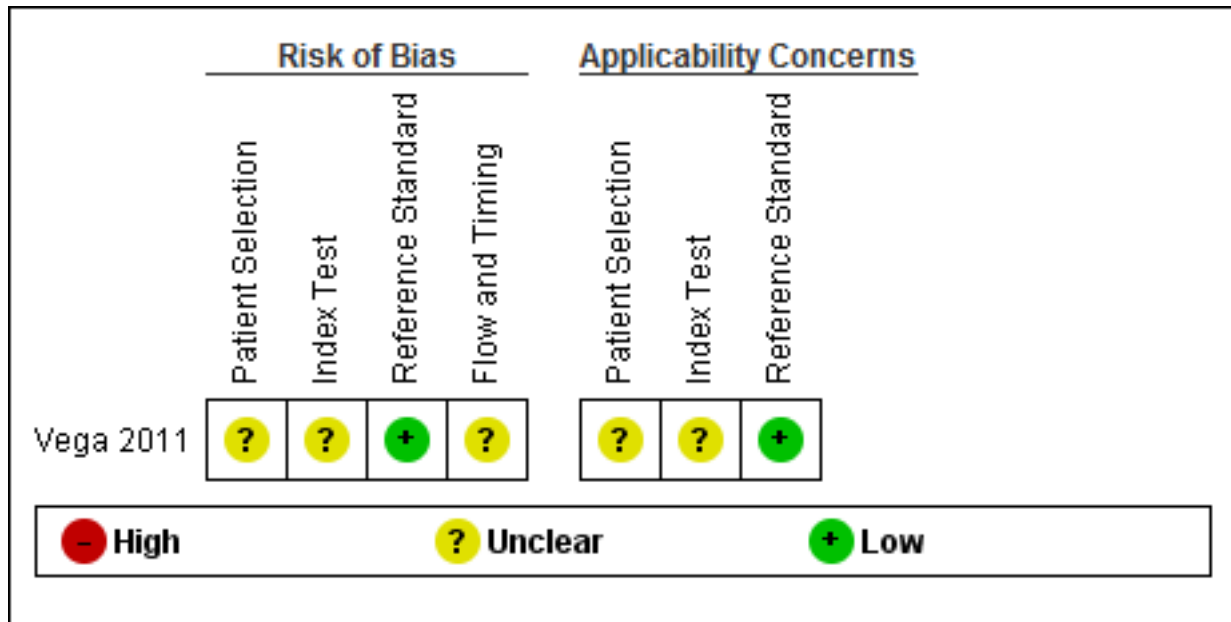


Figure 3. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study.



The [Characteristics of included studies](#) table incorporates the methodological quality assessment. In [Vega 2011](#), the risk of bias was generally 'low', but some items had 'unclear' risk of bias; we explain these below. QUADAS-2 quality assessment items are grouped into four domains: patient selection, index test, reference standard and flow and timing.

The risk of bias arising from patient selection was unclear ([Vega 2011](#)). Although a consecutive sample of patients was reported, inappropriate exclusions may not have been avoided. Investigators included patients who had 'suspected advanced PAD'; consequently, the patient population may have been affected by disease spectrum bias.

Investigators described the execution of ABI tests well but did not state the ABI threshold used ([Vega 2011](#)); this led to a classification of "unclear risk of bias".

[Vega 2011](#) did not report the time between ABI and angiography assessments, which might have led to misclassification due to progression of the disease to a more advanced state (disease progression bias).

We have presented in the [Characteristics of included studies](#) table details of the execution of index and reference standard tests used by [Vega 2011](#).

Findings

The one included study ([Vega 2011](#)) did not report accuracy data at the participant level; therefore, we were unable to calculate estimates of sensitivity or specificity for individual participants. The

accuracy estimates reported in the narrative synthesis below are those calculated and reported by [Vega 2011](#). See also [Summary of findings](#).

Vega 2011

This prospective study compared the manual doppler method of obtaining an ABI with the automated oscillometric method ([Vega 2011](#)). In total, researchers recruited into the study 85 patients (76 men and nine women) with a mean (standard deviation) age of 68 (11) years, who were referred for angiography with 'symptoms of intermittent claudication'. Study participants had several comorbidities, including diabetes (52%), hypertension (76%), hypercholesterolaemia (43.5%), ischaemic heart disease (30%), percutaneous coronary intervention (12%), coronary surgery (6%), previous stroke (22%), carotid revascularisation (2.4%) and aortic aneurysm (6%), and included current smokers (32%) and previous smokers (46%).

Doctors with no specialist training performed ABI measurements, and researchers conducted the study in a hospital catheterisation laboratory in Spain. Investigators performed manual doppler ABI by using an 8 MHz doppler probe (Dopplex II MD2/SD, ArjoHuntleigh Inc., Addison, Illinois) model and a sphygmomanometer with cuffs of appropriate size. They obtained automated ABI measurements by using automated oscillometric equipment: Omron M4-1 (Omron Healthcare Europe BV, Hoofddorp, The Netherlands). The threshold for a positive test result was a significant lesion of > 50% occlusion detected by catheter angiogra-

phy (the reference standard). Researchers defined non-significant PAD as < 50% obstruction.

According to [Vega 2011](#), the reported accuracy of automated oscillometric ABI was not statistically significantly different from that of the manual doppler method, with reported sensitivity of 97% (95% confidence interval (CI) 93% to 99%) and specificity of 89% (95% CI 67% to 95%) for oscillometric ABI, compared with sensitivity of 95% (95% CI 89% to 97%) and specificity of 56% (95% CI 33% to 70%) for the manual doppler ABI. The reason for the lower specificity for the doppler was that the doppler could not detect a tibial or dorsalis pedis pulse in 12 legs with normal vessels or non-significant lesions, among a total of 27 legs. How-

ever, with the automated method, investigators could not measure blood pressure in 70 legs, 69 of which were found to have severe angiographic lesions. The superiority of the automated oscillometric method for obtaining an ABI reading over the manual method in which inexperienced operators used a doppler probe may be a clinically important finding.

Researchers reported accuracy estimates with 'limbs' as the unit of analysis, and as participant-level data are not available, we were unable to reproduce accuracy estimates. The number of significant lesions (occlusions > 50%) detected by angiography in this study population was 131 (83%).

Summary of findings

Accuracy of the ankle brachial index (ABI) in diagnosing symptomatic peripheral arterial disease (PAD)				
Population:	People with intermittent claudication			
Setting	Primary and secondary care settings (hospital outpatients)			
Index test	Ankle brachial index			
Importance	The success of management strategies for PAD depends upon the quality of the diagnostic process, which involves careful assessment of the underlying pathology with diagnostic tests that possess a high level of accuracy, to allow detection and measurement of an arterial stenosis and its distribution in the blood vessels			
Reference standard	Duplex ultrasonography or angiography			
Studies	Cross-sectional or diagnostic cohort study			
Test/subgroup	Sensitivity	Specificity	No. of participants (studies)	Quality (QUADAS-2) ^a and comments
Cut-off ABI ratio positivity				
Mild PAD: 0.7 to 0.9				
Moderate PAD: 0.41 to 0.69				
Automated ABI:	97% (95% CI 93% to 99%)	89% (95% CI 67% to 95%)	85 (n = 158 legs) (1 study)	Unclear risk of bias: Vega 2011 may have included patients with severe PAD (stenosis > 50%); the threshold was not reported; time between conduct of the index test and use of the reference standard is not reported One study, no pooled analysis, sensitivity and specificity data for limb level - not for participant level, as reported by study authors
Manual ABI:	95% (95% CI 89% to 97%)	56% (95% CI 33% to 70%)		

^aQUADAS-2 is a tool used for assessment of the quality of diagnostic accuracy studies. This tool comprises four domains: patient selection, index test, reference standard and flow and timing. Each domain is assessed in terms of risk of bias; the first three domains are also assessed in terms of concerns regarding applicability.

ABI: ankle brachial index.

PAD: peripheral arterial disease.

DISCUSSION

The ankle brachial index (ABI) test is cheap and non-invasive, which makes it potentially valuable in health care. Unfortunately, evidence for the accuracy of the ABI test for the detection of peripheral arterial disease (PAD) in people presenting with leg pain on exercise that is alleviated by rest is sparse. We included in this review only one study, which evaluated automated versus manual ABI equipment, and provided limb-level data from a total of 85 participants.

The main findings of the review are the following: (1) Although both ABI tests demonstrated high levels of sensitivity, the results came from a single small study in which participants with critical limb ischaemia (CLI) may have been included, and researchers reported no threshold for the ABI; (2) investigators reported no statistically significant differences in accuracy between automated and manual ABI equipment in this small group of participants, although automated ABI was associated with a greater number of technical failures than the hand-held doppler, and these technical failures occurred in participants with severe angiographic lesions; and (3) in light of recruitment of patients from those already referred for angiography, it seems likely that participants included in the review may have had worse PAD than those recruited directly from a primary healthcare setting, and we would not extrapolate these findings to all patients presenting in primary care.

More than half of the participants in this study had received a diagnosis of diabetes mellitus, but we were unable to produce evidence to support the advice given in clinical guidelines (NICE 2012) that the use of ABI in assessment of PAD among people with diabetes is less reliable than among those who do not have diabetes mellitus, because data were not available for such an analysis. The single included study (Vega 2011) excluded patients with an ABI > 1.4, but investigators excluded only two patients for this reason and did not reveal whether these patients had diabetes.

The review excluded 48 studies, most of which were cross-sectional studies evaluating the accuracy of ABI or comparing different ABI techniques in the diagnosis of PAD. Unfortunately, these studies usually included patients other than those presenting with exertional leg pain, and many did not use the reference standard of duplex ultrasonography or angiography. These shortcomings are important findings of this review, and in the recommendations for research section below, we make specific suggestions to inform the design of future DTA studies of ABI for the diagnosis of PAD in people with exertional leg pain.

Summary of main results

This review found a very small amount of evidence indicating that the ABI test is accurate in the diagnosis of symptomatic PAD among people with intermittent claudication (IC). The one included study suggests that automated equipment may be more

accurate than manual methods when used by individuals with no specialist training. The accuracy of manual doppler varies with operator skill, and so trained individuals may obtain more accurate results with this method. The small number of participants who took part in the study led to our cautious interpretation of the data.

Strengths and weaknesses of the review

We identified only one study for inclusion. We restricted the inclusion criteria for this review to patients with leg pain on walking relieved by rest and use of duplex ultrasonography or angiography as the reference standard; this contributed to the exclusion of a large number of studies.

Vega 2011 included some patients with 'suspected advanced PAD' and did not present data for these participants separately. This may have led to higher estimates of accuracy than would be observed in a population that was strictly recruited on the basis of leg pain alone. In addition, researchers did not report the ABI threshold. Vega 2011 reported accuracy data at limb level only; therefore we were unable to calculate estimates of sensitivity and specificity for individual participants. We attempted to contact the study authors to obtain participant-level data, but we received no response.

Applicability of findings to the review question

The patient population recruited to the included study suggests that the findings may not answer the review question. Investigators recruited the study population from patients referred for angiography for peripheral arterial intermittent claudication or suspected advanced PAD (Vega 2011). The percentage of people with symptoms of IC and the percentage with more advanced PAD remain unclear, but it is likely that researchers included in this population people with critical limb ischaemia. Use of angiography as the reference standard by which to verify results of the ABI (index) test may mean that the spectrum of disease is worse than in the general population seeking a diagnosis for PAD, as angiography is an invasive test conducted in hospital vascular departments. Authors of the included study themselves cautioned that their findings should not be extrapolated to the general population because of the high prevalence of PAD reported among study participants (Vega 2011).

Authors of another systematic review evaluating the accuracy of ABI for PAD suggest that accuracy is dependent on the purpose of the examination; they found ABI to be highly accurate when used to detect serious stenosis (> 50%) (Dachun 2013). The American Heart Association (AHA) Scientific Statement on measurement and interpretation of the ABI reports that areas under the receiver operating characteristic (ROC) curve are higher for ABI measured by doppler than for ABI measured by oscillometric methods (Aboyans 2012). This narrative review provides evidence on the overall diagnostic ability of the ABI in a variety of populations

and settings based on four studies that did not meet the eligibility criteria for the current review (Aboyan 2012).

AUTHORS' CONCLUSIONS

Implications for practice

This review found little evidence on the value of the ankle brachial index (ABI) for detection of lower limb peripheral arterial disease (PAD) in patients with exertional leg pain. The paucity of studies assessing the accuracy of ABI in patients with leg pain and the small number of participants enrolled in only one included study mean that robust conclusions cannot be reached.

It is often written that the ABI is not a useful test for detecting PAD in those with diabetes (Bhasin 2007; MacLeod-Roberts 1995) because incompressibility of calcified vessels produces false results. In the included study, the co-morbidities of participants who were withdrawn, or in whom ABI measurement was not possible, are not reported, and uncertainty exists about the influence that any underlying disease may have on the accuracy of ABI in the diagnosis of PAD.

Implications for research

Well-designed primary studies are needed to evaluate the diagnostic accuracy of ABI in patients presenting specifically with exertional leg pain in both primary and secondary (outpatient) healthcare settings. Further systematic review of existing studies assessing the use of ABI in alternative patient groups, including high-risk patients without leg pain and patients with atypical leg pain, is required. Additional primary studies will likely be required in these populations, including patients not previously diagnosed

with PAD and asymptomatic patients with co-morbidities such as diabetes mellitus.

We suggest that duplex ultrasonography is a more appropriate reference standard for a population of patients who present for assessment for the first time, as it is non-invasive in nature and may be available outside the hospital setting. We recommend that this single reference standard should be used to validate the presence or absence of disease in the ABI test result for each individual patient.

A comparison of the accuracy between the manual doppler probe ABI and automated oscillometric ABI measurements has cost implications, deserves further consideration, and should include patients with co-morbidities such as diabetes mellitus and should be performed by trained healthcare professionals.

Moreover, study authors must be careful about how they analyse their data, in particular, they need to account for participants contributing data from both legs and must provide participant-level data to facilitate meta-analyses in updates of this, and other, systematic reviews.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Vega 2011

Study characteristics			
Patient sampling	The sample of patients was reported to be consecutive.		
Patient characteristics and setting	85 patients (158 legs) referred to the catheterisation laboratory for angiography for peripheral arterial intermittent claudication or suspected advanced PAD and over 30 years of age were included		
Index tests	Doppler ABI measurement was performed with an 8 MHz doppler probe (Dopplex II MD2/SD, Huntleigh model) (ArjoHuntleigh Inc., Addison, Illinois), and a sphygmomanometry with cuffs of appropriate size. The oscillometer used was an Omron M4-1 (Omron Healthcare Europe BV, Hoofddorp, The Netherlands). The ABI was calculated as the ratio of peak systolic pressure at the ankle and arms. Patients with non-compressible arteries with ABI > 1.4 were excluded. If the oscillometric method still gave an error reading after 3 serial attempts with rehabilitation of cuff pressures, pressure was assumed to be < 60 mmHg and a '0 index' was assigned if it was not possible to detect flow with the doppler method (DM) The ABI threshold was not prospectively stated.		
Target condition and reference standard(s)	Haemodynamically significant or severe PAD was defined as stenosis with > 50% obstruction, and non-significant PAD as < 50% obstruction. Severity was determined simultaneously by visual comparison between healthy and diseased segments and by use of the Quantitative Coronary Angiography (QCA) programme. Reference standard was the angiography digital subtraction technique with sequential images		
Flow and timing	We excluded 12 legs for a variety of reasons: 6 cases because of amputation, 4 because of painful ulcers, which ruled out examination, and 2 because ABI was > 1.4 The time between the conduct of the index test and use of the reference standard is not reported		
Comparative			
Notes	Only 131 (83%) limbs had verification from angiography. Contacted study author to request participant-level data and received no response		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		

Vega 2011 (Continued)

Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	Unclear
DOMAIN 2: Index Test ABI			
If a threshold was used, was it pre-specified?	No		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Were all patients included in the analysis?	No		
		Unclear	

ABI: ankle brachial index.

DM: doppler method.

PAD: peripheral arterial disease.

QCA: quantitative coronary angiography.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Akhtar 2009	Study did not use duplex ultrasonography nor angiography as reference standard. Case-control study comparing different techniques for measurement of the ABI (hand-held doppler ABI vs palpatory ABI) in healthy, high-risk asymptomatic and known PAD patients

(Continued)

Alnaeb 2007	Study population not defined as presenting with exertional leg pain. Patients with diabetes, recruited from hospital vascular clinic, and control patients from an orthopaedic outpatient clinic used to compare ABI and photoplethysmography with duplex ultrasonography
Alnaeb 2008	Study population not defined as presenting with exertional leg pain. PAD and non-PAD patients recruited from vascular outpatient clinic for comparison of ABI and photoplethysmography with duplex ultrasonography
Armstrong 2010	Study did not use duplex ultrasonography nor angiography as reference standard. Study comparing physical examination with ABI in people suspected of having or at high risk for PAD
Baxter 1993	Study population not selected owing to exertional leg pain. Patients with lower limb claudication, rest pain or cellulitis assessed with ABI, colour doppler ultrasonography and arteriography. Separate data for claudication population sought from study author, who replied that data were not available
Beckman 2005	Study did not use duplex ultrasonography nor angiography as reference standard. Comparison of 2 different types of ABI (oscillometric and continuous wave doppler ultrasonography) in participants referred to lab for evaluation of PAD
Benchimol 2009	Study did not use duplex ultrasonography nor angiography as reference standard. Comparison of ABI measuring methods (automated vs doppler ultrasonography) in participants recruited by physicians in preventive medicine attending annual check-up
Beutner 2012	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared 2 different ABI measurement methods in healthy participants and in participants with confirmed lower limb PAD before revascularisation
Bogomolov 2012	Study did not use duplex ultrasonography nor angiography as reference standard. Unclear whether study population was selected for exertional leg pain. Study performed ABI and doppler examination in people with and without diabetes
Cacoub 2005	Comparison of 2 types of ABI measurements (stethoflux and continuous wave doppler) in patients recruited consecutively from vascular laboratory
Carmo 2009	Study did not use duplex ultrasonography nor angiography as reference standard. Comparison of ABI measured by stethoscope and doppler in people referred to haemodynamic laboratory of Fekicio Rocho Hospital for peripheral, renal, coronary and cerebral vascular territory diagnostic and interventional angiographic examinations
Clairotte 2009	Unclear whether study population selected because of exertional leg pain. Study assessed oscillometric ABI vs doppler ABI in patients referred to physiology department for doppler ultrasound examination of PAD. Two-dimensional ultrasound measurement reported but not used as reference standard
Cortez-Cooper 2003	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared automated device with manual method for assessment of ABI in normotensive and hypertensive participants
Eason 2005	Study did not use duplex ultrasonography nor angiography as reference standard. Study in asymptomatic PAD population (patients with symptomatic PAD were excluded). PAD assessed via ABI and the San Diego

(Continued)

	claudication questionnaire
Ena 2011	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared ABI measured with upper arm automated blood pressure device vs ABI measured by hand-held doppler in diabetic patients attending screening for PAD
Espeland 2008	Study did not use duplex ultrasonography nor angiography as reference standard. Population not presenting with exertional leg pain. Study compared different systolic blood pressure protocols for measuring ABI in a trial population of overweight/obese volunteers with type 2 diabetes
Feigelson 1994	Study population not identified as presenting with exertional leg pain. Participants were a population-based cohort of adults screened for large-vessel PAD
Fronek 1999	Index test was upper thigh/brachial index measurement rather than ankle/brachial index measurement. Study performed in patients referred to the Veterans' Administration Vascular Laboratory with suspected arterial occlusive disease of lower extremities
Guo 2008	Population not identified as presenting with exertional leg pain to primary care or outpatient clinic. Participants recruited from cardiology hospital ward
Heidrich 1998	Index test involved measurement of BP in upper limb digital arteries. Study population consisted of people with primary or secondary Raynaud's disease or digital occlusions
Hoyer 2012	Index test was new portable photoplethysmography device for diagnosing ABI; reference standard was strain-gauge plethysmography
Hriljac 2004	Study did not report the use of duplex ultrasonography nor angiography as reference standard. Unclear whether study population referred for exertional leg pain, Study assessed the added diagnostic utility of measuring ABI and pulse volume waveforms at rest and after exercise in patients referred to vascular laboratory by 'non-vascular' specialists
Johansson 2002	Study did not use duplex ultrasonography nor angiography as reference standard. Population not identified as presenting with exertional leg pain. Study compared pulse oximetric method for assessment of toe pressure ABI with traditional ankle doppler pressure ABI in people with diabetes drawn from the case records of primary healthcare clinics
Klein 2003	Study population not identified as presenting with exertional leg pain. Participants were patients considered for fibula free flap transplantation or those who had undergone this procedure. Patients with a history of intermittent claudication were excluded
Kollias 2011	Study did not use duplex ultrasonography nor angiography as reference standard. Study investigated automated vs manual doppler method in patients with CVD risk factors attending hypertension or diabetes clinic
Korno 2009	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared automated oscillometric ABI vs hand-held doppler ABI in patients admitted for surgical treatment or for evaluation of venous disease to the department of vascular surgery, including participants with intermittent claudication or critical ischaemia

(Continued)

Kurtoglu 2009	Study population not identified as presenting with exertional leg pain. Participants were patients with extremity injury or with suspicion of peripheral artery injury admitted to trauma and emergency medicine department
Lijmer 1996	Patients referred by general practitioner for claudication or critical ischaemia - separate ABI data for patients with IC requested from study authors but no reply received
MacDougall 2008	Study did not use duplex ultrasonography nor angiography as reference standard. Study investigated oscillometric ABI vs doppler ABI in 3 groups of patients: normal volunteers, patients with significant CV risk profiles and patients suspected of having PAD who were referred to a vascular lab
Manzano 2006	Study did not use duplex ultrasonography nor angiography as reference standard. Study population was not defined as people presenting with exertional leg pain. Study compared ABI vs Edinburgh Claudication Questionnaire in patients without typical intermittent claudication or known atherosclerotic disease
McLafferty 1997	Study population consisted of people who had undergone previous revascularisation procedures
Mehlsen 2008	Paper reports 2 studies, neither of which used duplex ultrasonography nor angiography as reference standard <ul style="list-style-type: none">• Study compared measurement of blood pressures at ankle and toe levels with oscillometry with mercury strain gauge plethysmography in patients with possible PAD referred to vascular unit• Study compared low ABI measurement using oscillometry with mercury strain gauge plethysmography in patients attending primary care clinics for any reason
Nam 2010	Index test was ABI measured using photoplethysmography (currently not an endorsed method for the assessment of ABI)
Nexoe 2012	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared ABI measured in GP surgery vs ABI measured by experienced staff of Department of Nuclear Medicine in people presenting to GP surgery
Niazi 2006	Uncertain whether study population was recruited with exertional leg pain. Population recruited from a retrospective sample of people who had undergone an angiogram and ABI measurement; no indication for angiography given. Study authors contacted for further information but did not reply
Oksala 2010	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared different methods of calculating ABI from BP measurements in people 50 to 69 years of age with ≥ 1 cardiovascular risk factor; > 70 years of age; with claudication defined as pain in the calf during exercise
Paez 2010	Study population was not defined as presenting with exertional leg pain. Patients with ≥ 1 cardiovascular risk factor were recruited from the Heart Institute of Bucaramanga (Colombia)
Parmeswarin 2005	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared ABI with pulse oximetry test in patients with type 2 diabetes without known lower extremity arterial disease or symptoms of LEAD (typical IC or rest pain)
Potier 2008	Study did not use duplex ultrasonography nor angiography as reference standard. Study compared doppler ABI and oscillometric measured ABI in diabetic and non-diabetic patients

(Continued)

Premalatha 2002	Study population was not defined as presenting with exertional leg pain. Participants were diabetic hospital inpatients with severe foot infection
Premanath 2010	Study did not use duplex ultrasonography nor angiography as reference standard. Study population was not defined as presenting with exertional leg pain. Study compared different methods of measuring ABI in patients with diabetes attending a clinic, irrespective of their symptoms
Ramos 2011	Study did not use duplex ultrasonography nor angiography as reference standard. Study population was not defined as presenting with exertional leg pain. Study used ABI < 0.9 as an outcome to develop a predictive risk score for low ABI in people recruited from a primary healthcare setting, irrespective of symptoms
Schroder 2006	Study population was not defined as presenting with exertional leg pain. Participants were patients presenting at outpatient clinic with suspected vascular disease; < 40% had intermittent claudication (data not presented separately in paper, and study authors unable to provide data when contacted)
Stoffers 1996	Unclear whether duplex ultrasonography or angiography was used as reference standard. Participants selected from Limburg POAD study with ABI < 0.95, typical IC complaints or leg complaints less typical of IC but with ≥ 1 foot pulse missing. Study compared ABI measurements with diagnostic conclusions of vascular laboratory from “sophisticated ultrasound measurements”. Pressure measurements at rest and after treadmill walking test; technician interpreted acoustic and audiospectrum pulsewave signals from posterior tibial and dorsalis pedis arteries. No separate 2 x 2 data for the 22 patients in the total population who had IC. Contacted study author, who replied that data were not available
Vinyoles 2007	Study did not use duplex ultrasonography nor angiography as reference standard. Study population was not defined as presenting with exertional leg pain. Study compared oscillometry ABI vs ABI measured with doppler ultrasound probe
Williams 2005	Study population was not defined as presenting with exertional leg pain. Study evaluated ABI and other methods of screening for lower limb PAD in diabetic and non-diabetic participants with and without arterial disease and neuropathy
Wohlfahrt 2011	Study did not use duplex ultrasonography nor angiography as reference standard. Study population was not defined as presenting with exertional leg pain. Study compared doppler ABI vs oscillometric ABI in randomly selected general population sample
Zhang 2010	Study population was not defined as presenting with exertional leg pain. Study assessed lower limb PAD using ABI and duplex ultrasonography in diabetic individuals recruited from a secondary care setting, irrespective of symptoms

ABI: ankle brachial index.

CV: cardiovascular.

DTA: diagnostic test accuracy.

IC: intermittent claudication.

PAD: peripheral arterial disease.

DATA

This review has no data.

APPENDICES

Appendix I. MEDLINE search strategy

Database: Ovid MEDLINE(R) <1946 to July Week 5 2013>

Search Strategy:

-
- 1 Ankle Brachial Index/ (1231)
 - 2 Oscillometry/ [Methods] (1841)
 - 3 Blood Pressure Determination/ (16515)
 - 4 Laser-Doppler Flowmetry/ (7317)
 - 5 oscillometr\$.ti,ab. (1745)
 - 6 (doppler adj2 (ultrasound or flow\$ or method or device)).ti,ab. (24957)
 - 7 ABI.ti,ab. (4022)
 - 8 ABPI.ti,ab. (309)
 - 9 AAI.ti,ab. (1016)
 - 10 (ankle adj4 index).ti,ab. (3997)
 - 11 (arm adj4 index).ti,ab. (877)
 - 12 (brachial adj4 (index or pressure)).ti,ab. (4836)
 - 13 (systolic adj5 ratio).ti,ab. (2833)
 - 14 (pressure adj5 ratio).ti,ab. (5088)
 - 15 (BP adj5 ratio).ti,ab. (618)
 - 16 (four and limbs and pressure).ti,ab. (309)
 - 17 or/1-16 (63464)
 - 18 (anterior tibial or dorsalis pedis or posterior tibial).ti,ab. (6189)
 - 19 (ankle or arm or elbow or calf).ti,ab. (172149)
 - 20 (lower and upper and (extremity\$ or limb)).ti,ab. (9791)
 - 21 or/18-20 (185143)
 - 22 (systolic or pressure).ti,ab. (588700)
 - 23 21 and 22 (11891)
 - 24 17 or 23 (71623)
 - 25 exp Peripheral Vascular Diseases/di [Diagnosis] (8148)
 - 26 Arterial Occlusive Diseases/di [Diagnosis] (4178)
 - 27 exp Arteriosclerosis/di [Diagnosis] (13998)
 - 28 exp Atherosclerosis/di [Diagnosis] (2178)
 - 29 exp Peripheral Arterial Disease/di [Diagnosis] (498)
 - 30 Intermittent Claudication/di [Diagnosis] (994)
 - 31 (atherosclero* or arteriosclero* or PVD or PAOD or PAD).ti,ab. (130870)
 - 32 (arter\$ adj4 (\$occlus\$ or steno\$ or obstruct\$ or lesio\$ or block\$ or obliter\$)).ti,ab. (76067)
 - 33 (vascular adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (20139)
 - 34 (vein* adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (8880)
 - 35 (veno* adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (9793)
 - 36 (peripher* adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (12782)
 - 37 (peripheral adj3 dis*).ti,ab. (28626)
 - 38 arteriopathic.ti,ab. (152)
 - 39 (claudic* or hinken* or IC).ti,ab. (53144)

- 40 CLL.ti,ab. (1175)
- 41 dysvascular*.ti,ab. (144)
- 42 (leg adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. (484)
- 43 (limb adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. (1330)
- 44 (lower adj3 extrem* adj4 (obstruct* or occlus* or steno* or block* or obliter*)).ti,ab. (1345)
- 45 or/25-44 (320767)
- 46 24 and 45 (10229)

Appendix 2. Embase search strategy

Database: Embase <1980 to 2013 Week 32>

Search Strategy:

-
- 1 ankle brachial index/ (4434)
 - 2 oscillometry/ (6310)
 - 3 blood pressure measurement/ (34214)
 - 4 laser Doppler flowmetry/ (8539)
 - 5 oscillometr\$.ti,ab. (2398)
 - 6 (doppler adj2 (ultrasound or flow\$ or method or device)).ti,ab. (31994)
 - 7 ABI.ti,ab. (6940)
 - 8 ABPI.ti,ab. (455)
 - 9 AAI.ti,ab. (1452)
 - 10 (ankle adj4 index).ti,ab. (5541)
 - 11 (arm adj4 index).ti,ab. (1137)
 - 12 (brachial adj4 (index or pressure)).ti,ab. (6690)
 - 13 (systolic adj5 ratio).ti,ab. (3654)
 - 14 (pressure adj5 ratio).ti,ab. (6524)
 - 15 (BP adj5 ratio).ti,ab. (895)
 - 16 (four and limbs and pressure).ti,ab. (389)
 - 17 or/1-16 (98837)
 - 18 (anterior tibial or dorsalis pedis or posterior tibial).ti,ab. (7231)
 - 19 (ankle or arm or elbow or calf).ti,ab. (210874)
 - 20 (lower and upper and (extremit\$ or limb)).ti,ab. (14215)
 - 21 or/18-20 (228282)
 - 22 (systolic or pressure).ti,ab. (736050)
 - 23 21 and 22 (15587)
 - 24 17 or 23 (109336)
 - 25 peripheral vascular disease/di [Diagnosis] (2054)
 - 26 artery disease/di [Diagnosis] (1691)
 - 27 arteriolosclerosis/di [Diagnosis] (32)
 - 28 arteriosclerosis/di [Diagnosis] (2186)
 - 29 atherosclerosis/di [Diagnosis] (5485)
 - 30 atherosclerotic plaque/di [Diagnosis] (2755)
 - 31 peripheral occlusive artery disease/di [Diagnosis] (3610)
 - 32 artery occlusion/di [Diagnosis] (2700)
 - 33 intermittent claudication/di [Diagnosis] (870)
 - 34 (atherosclero* or arteriosclero* or PVD or PAOD or PAD).ti,ab. (168115)
 - 35 (arter\$ adj4 (\$occlus\$ or steno\$ or obstruct\$ or lesio\$ or block\$ or obliter\$)).ti,ab. (96829)
 - 36 (vascular adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (25100)
 - 37 (vein* adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (11516)
 - 38 (veno* adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (11947)
 - 39 (peripher* adj4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)).ti,ab. (16599)
 - 40 (peripheral adj3 dis*).ti,ab. (37189)

- 41 arteriopathic.ti,ab. (183)
 42 (claudic* or hinken* or IC).ti,ab. (43148)
 43 CLI.ti,ab. (1795)
 44 dysvascular*.ti,ab. (165)
 45 (leg adj4 (obstruct* or occlus* or steno* or block* or obliter*)),ti,ab. (585)
 46 (limb adj4 (obstruct* or occlus* or steno* or block* or obliter*)),ti,ab. (1808)
 47 (lower adj3 extrem* adj4 (obstruct* or occlus* or steno* or block* or obliter*)),ti,ab. (1656)
 48 or/25-47 (372990)
 49 24 and 48 (14665)

Appendix 3. CINAHL search strategy

S40	S22 AND S39	1,666
S39	S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39	44,201
S38	TI ((limb N4 (obstruct* or occlus* or steno* or block* or obliter*))) OR AB ((limb N4 (obstruct* or occlus* or steno* or block* or obliter*))))	159
S37	TI ((leg N4 (obstruct* or occlus* or steno* or block* or obliter*))) OR AB ((leg N4 (obstruct* or occlus* or steno* or block* or obliter*))))	70
S36	TI dysvascular* OR AB dysvascular	75
S35	TI CLI OR AB CLI	123
S34	TI (claudic* or hinken* or IC) OR AB (claudic* or hinken* or IC)	3,907
S33	TI arteriopathic OR AB arteriopathic	9
S32	TI peripheral N3 dis* OR AB peripheral N3 dis*	4,086
S31	TI ((peripher* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))) OR AB ((peripher* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))))	1,159
S30	TI ((veno* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))) OR AB ((veno* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))))	656
S29	TI ((vein* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))) OR AB ((vein* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))))	696

(Continued)

S28	TI ((vascular N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))) OR AB ((vascular N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))))	1,251
S27	TI ((arter* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))) OR AB ((arter* N4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*))))	6,063
S26	TI (atherosclero* or arteriosclero* or PVD or PAOD or PAD) OR AB (atherosclero* or arteriosclero* or PVD or PAOD or PAD)	11,796
S25	(MH "Atherosclerosis") OR (MH "Intermittent Claudication/DI")	3,829
S24	(MH "Arterial Occlusive Diseases+") OR (MH "Arteriosclerosis+/DI")	24,816
S23	(MH "Peripheral Vascular Diseases+/DI")	1,760
S22	S15 OR S21	12,571
S21	S19 AND S20	2,069
S20	TI (systolic or pressure) OR AB (systolic or pressure)	69,646
S19	S16 OR S17 OR S18	31,950
S18	TI ((lower and upper and (extremit* or limb))) OR AB ((lower and upper and (extremit* or limb)))	2,062
S17	TI (ankle or arm or elbow or calf) OR AB (ankle or arm or elbow or calf)	28,839
S16	TI (anterior tibial or dorsalis pedis or posterior tibial) OR AB (anterior tibial or dorsalis pedis or posterior tibial)	1,839
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	11,160
S14	TI (four and limbs and pressure) OR AB (four and limbs and pressure)	23
S13	TI BP N5 ratio OR AB BP N5 ratio	105
S12	TI pressure N5 ratio OR AB pressure N5 ratio	653
S11	TI systolic N5 ratio OR AB systolic N5 ratio	340

(Continued)

S10	TI ((brachial N4 (index or pressure))) OR AB ((brachial N4 (index or pressure)))	953
S9	TI arm N4 index OR AB arm N4 index	210
S8	TI ankle N4 index OR AB ankle N4 index	871
S7	TI AAI OR AB AAI	236
S6	TI ABPI OR AB ABPI	83
S5	TI ABI OR AB ABI	743
S4	TI ((doppler N2 (ultrasound or flow* or method or device))) OR AB ((doppler N2 (ultrasound or flow* or method or device)))	2,041
S3	TI oscillometr* OR AB oscillometr*	337
S2	MH Blood Pressure Determination	5,576
S1	MH Ankle Brachial Index	1,194

Appendix 4. LILACS search strategy

Database :	LILACS 13 August 2013 http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/
Search on :	((ankle OR arm or brachial) AND index) OR ((ultrasound OR flow\$ OR method OR device) AND doppler) OR abi OR abpi OR aai [Words] and atherosclero\$ OR arteriosclero\$ OR pvd OR paod OR pad OR cli OR ((occlus\$ OR steno\$ OR obstruct\$ OR lesion\$ OR block\$ OR obliter\$) and leg or limb) OR claudic\$ [Words] or (ankle brachial index or Oscillometry or Blood Pressure Determination or Laser-Doppler Flowmetry) AND (Atherosclerosis OR (Peripheral Arterial Disease)) [Subject descriptor]
Total of references :	176

Appendix 5. DARE (Database of Abstracts of Reviews of Effects) and the Health Technology Assessment Database (HTA) in *The Cochrane Library*

#1	MeSH descriptor: [Arteriosclerosis] explode all trees and with qualifiers: [Diagnosis - DI]	408
#2	MeSH descriptor: [Arteriolosclerosis] explode all trees and with qualifiers: [Diagnosis - DI]	0
#3	MeSH descriptor: [Arteriosclerosis Obliterans] explode all trees and with qualifiers: [Diagnosis - DI]	3
#4	MeSH descriptor: [Atherosclerosis] explode all trees and with qualifiers: [Diagnosis - DI]	45
#5	MeSH descriptor: [Arterial Occlusive Diseases] explode all trees and with qualifiers: [Diagnosis - DI]	563
#6	MeSH descriptor: [Intermittent Claudication] explode all trees and with qualifiers: [Diagnosis - DI]	44
#7	MeSH descriptor: [Ischemia] explode all trees and with qualifiers: [Diagnosis - DI]	48
#8	MeSH descriptor: [Peripheral Vascular Diseases] explode all trees and with qualifiers: [Diagnosis - DI]	254
#9	MeSH descriptor: [Vascular Diseases] explode all trees and with qualifiers: [Diagnosis - DI]	4377
#10	MeSH descriptor: [Leg] explode all trees and with qualifiers: [Blood supply - BS]	1090
#11	MeSH descriptor: [Femoral Artery] explode all trees	736
#12	MeSH descriptor: [Popliteal Artery] explode all trees	259
#13	MeSH descriptor: [Iliac Artery] explode all trees	152
#14	MeSH descriptor: [Tibial Arteries] explode all trees	29
#15	(atherosclero* or arteriosclero* or PVD or PAOD or PAD)	17613
#16	(arter*) near (*occlus* or steno* or obstruct* or lesio* or block* or obliter*)	4961
#17	(vascular) near (*occlus* or steno* or obstruct* or lesio* or block* or obliter*)	1416

(Continued)

#18	(vein*) near (*occlus* or steno* or obstruct* or lesio* or block* or obliter*)	747
#19	(veno*) near (*occlus* or steno* or obstruct* or lesio* or block* or obliter*)	1004
#20	(peripher*) near (*occlus* or steno* or obstruct* or lesio* or block* or obliter*)	1380
#21	peripheral near/3 dis*	3353
#22	arteriopathic	17
#23	(claudic* or hinken*)	1469
#24	(isch* or CLI)	17265
#25	dysvascular*	26
#26	leg near/4 (obstruct* or occlus* or steno* or block* or obliter*)	187
#27	limb near/4 (obstruct* or occlus* or steno* or block* or obliter*)	241
#28	(lower near/3 extrem*) near/4 (obstruct* or occlus* or steno* or block* or obliter*)	146
#29	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28	42501
#30	MeSH descriptor: [Ankle Brachial Index] explode all trees	68
#31	MeSH descriptor: [Oscillometry] explode all trees and with qualifiers: [Methods - MT]	31
#32	MeSH descriptor: [Blood Pressure Determination] this term only and with qualifiers: [Methods - MT]	301
#33	MeSH descriptor: [Laser-Doppler Flowmetry] this term only and with qualifiers: [Methods - MT]	63
#34	oscillometr*:ti,ab,kw (Word variations have been searched)	304
#35	(doppler near/2 (ultrasound or flow* or method or device)):ti, ab,kw (Word variations have been searched)	2211

(Continued)

#36	ABI or ABPI or AAI:ti,ab,kw (Word variations have been searched)	321
#37	ankle near/4 index:ti,ab,kw (Word variations have been searched)	458
#38	arm near/4 index:ti,ab,kw (Word variations have been searched)	114
#39	(brachial near/4 (index or pressure)):ti,ab,kw (Word variations have been searched)	847
#40	systolic near/5 ratio:ti,ab,kw (Word variations have been searched)	247
#41	pressure near/5 ratio:ti,ab,kw (Word variations have been searched)	505
#42	pressure near/5 ratio:ti,ab,kw (Word variations have been searched)	505
#43	BP near/5 ratio:ti,ab,kw (Word variations have been searched)	71
#44	BP near/5 ratio:ti,ab,kw (Word variations have been searched)	71
#45	four and limbs and pressure:ti,ab,kw (Word variations have been searched)	135
#46	#30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45	4577
#47	anterior tibial or “dorsalis pedis” or “posterior tibial”:ti,ab,kw (Word variations have been searched)	226
#48	ankle or arm or elbow or calf:ti,ab,kw (Word variations have been searched)	25464
#49	(lower and upper and (extremit* or limb)):ti,ab,kw (Word variations have been searched)	792
#50	#47 or #48 or #49	26142
#51	systolic or pressure:ti,ab,kw (Word variations have been searched)	67765
#52	#50 and #51	2741
#53	#46 or #52	6726

(Continued)

#54	#29 and #53 in Other Reviews and Technology Assessments	13
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Appendix 6. ISI Conference Proceedings Citation Index

Topic=(ABI or ABPI or AAI or (ankle NEAR/4 index) or (arm NEAR/4 index) or (brachial NEAR/4 (index or pressure)) or (systolic NEAR/4 ratio) or (pressure NEAR/3 ratio) or (BP NEAR/3 ratio) or Oscillometr* or Blood Pressure Determination or Laser-Doppler Flowmetry or (doppler NEAR/2 (ultrasound or flow* or method or device))) AND Topic=(Claudicat* or IC or CLI or atherosclero* or arteriosclero* or PVD or PAOD or PAD or (arter* NEAR/4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)) or (vascular NEAR/4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)) or (vein* NEAR/4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)) or (veno* NEAR/4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)) or (peripher* NEAR/4 (occlus* or steno* or obstruct* or lesio* or block* or obliter*)) or (peripheral NEAR/3 dis*) or dysvascular* or (leg NEAR/4 (obstruct* or occlus* or steno* or block* or obliter*)) or (limb NEAR/4 (obstruct* or occlus* or steno* or block* or obliter*)) or (lower NEAR/4 (obstruct* or occlus* or steno* or block* or obliter*)))

Refined by: Document Types=(PROCEEDINGS PAPER OR MEETING ABSTRACT)

Timespan=All years. Databases=CPCI-S, CCR-EXPANDED, IC.

Results: 903

Appendix 7. ZETOC Conference search

ABI in title 87

ABPI in title 5

“brachial index” in title 14

Appendix 8. Medion search

ABI in title 36

ABPI in title 0

Brachial in title 2

Appendix 9. Quality Assessment Checklist (QUADAS-2)

Domains, signalling questions (SQ) and applicability	Rating criteria
Domain 1: Patient selection	
A. Risk of bias	Describe the methods of patient selection given in the report:
SQ 1: Was a consecutive or random sample of patients enrolled?	Yes: it is reported that a consecutive or a random sample was included Unclear: the precise method of sampling is not reported
SQ 2: Did the study avoid inappropriate exclusions?	Yes: the study included all symptomatic outpatients (in primary or secondary care) without previous ABI test results No: the study included patients who had received an ABI test before, or were asymptomatic Unclear: the ABI test history of the patients in the study was not reported

(Continued)

B. Concerns regarding applicability	Give the paper's description of the inclusion/exclusion criteria, including setting, prior tests and symptoms
Domain 2: Index test	
A. Risk of bias	Give the paper's description of the index test and how it was conducted and interpreted, including the background of the person who carried out the test
SQ 1: Were index test results interpreted without knowledge of results of the reference standard?	<p>Yes: it is stated that the index tests were interpreted in a blind manner (i.e. without knowledge of results of the reference standard), or the index test was always performed and interpreted before the reference standard</p> <p>No: the results of the reference standard were known to the reader of the index test</p> <p>Unclear: it is not reported whether the index test was conducted without knowledge of results of the index test, or whether the index test was completed before the reference standard</p>
SQ 2: If a threshold was used, was it prespecified?	<p>Yes: value for an abnormal test result is < 0.90, and this is clearly stated in the Methods section or elsewhere in the report</p> <p>No: values for a normal or abnormal test results are not reported (prespecified)</p> <p>Unclear: it is not clear at what point in time values for normal and abnormal test results were decided</p>
SQ 3: Was the person conducting the test (measuring the ABI) trained to do so?	<p>Yes: it is stated that the person conducting the test was trained in ABI measurement</p> <p>No: it is clearly reported that the person conducting the test was not trained in ABI measurement</p> <p>Unclear: the expertise and background of the individuals conducting the index test are unclear</p>
B. Concerns regarding applicability?	<p>High: the index test was conducted using hand-held Dopplers as opposed to a stethoscope or other equipment not widely available</p> <p>Low: the index test was not conducted using hand-held Dopplers, and the equipment was standard (as outlined in the protocol)</p> <p>Unclear: information about the equipment used to conduct the test is not presented</p>
Domain 3: Reference standard	
A. Risk of bias	Give the reported definition of the reference standard and how it was conducted and interpreted
SQ 1: Is the reference standard likely to correctly classify the target condition?	<p>Yes: it is reported that duplex ultrasonography or angiography test results were interpreted by trained operatives</p> <p>No: it is reported that the duplex ultrasonography or angiography test results were not interpreted by trained operatives</p>

(Continued)

	Unclear: it is not clear whether those individuals who interpreted the duplex ultrasonography or angiography test results were trained
SQ 2: Were the reference standard test results interpreted without knowledge of the index test results?	Yes: the person classifying the reference standard test results was unaware of the ABI test results No: the person classifying the reference standard test results was aware of the ABI test results Unclear: not reported
SQ 3: Was the person conducting the reference standard test (duplex ultrasonography) trained?	Yes: it is stated that the person conducting the reference standard test was trained in the interpretation of duplex ultrasonography No: it is clear that the person conducting the reference standard test was not trained in the interpretation of duplex ultrasonography Unclear: the expertise and background of the reference standard test readers are unclear
Domain 4: Flow and timing	
A. Risk of bias	Describe the reasons why any patients recruited into the study did not contribute to the 2 × 2 table (i.e. patients who did not undergo the reference standard and/or the index test) referring to the flow diagram Give the time interval between the ABI and the reference standard tests
SQ 1: Was there an appropriate interval between the index test and the reference standard?	Yes: the index and reference standard tests were all conducted within 2 weeks of each other No: some of the reference standard test results were not conducted within 2 weeks of each other Unclear: no information about the relative timing of the tests is provided
SQ 2: Did all the patients receive the same reference standard?	Yes: a complete set of reference standard test results is available for all study patients No: the same reference standard test results are not available for all patients Unclear: insufficient information is available to make a judgement about the availability of reference standard
SQ 3: Were all patients included in the final analysis?	Yes: all patients enrolled contributed to the 2 × 2 table No: not all patients enrolled contributed to the 2 × 2 table Unclear: it is not clear whether patients were recruited but not included in the study report of the 2 × 2 table

CONTRIBUTIONS OF AUTHORS

The whole review team has contributed to the development of the protocol. KW developed the search strategy. FC and AA applied the eligibility criteria and extracted data from studies. FC completed RevMan. FMC assumed responsibility for plans for the analysis. All review authors contributed to the final report of the review.

DECLARATIONS OF INTEREST

FC: none known.

KW: none known.

AA: none known.

FMC: none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The reference standard in our protocol was duplex ultrasonography, and patients were required to have their peripheral arterial disease (PAD) categorised as 1, 2 or 3 on the basis of the Rutherford index ([Rutherford 1997](#)), or as stage II on the basis of the Fontaine classification system ([Fontaine 1954](#)). None of the studies that we considered for inclusion in the review met these criteria. After discussion between the review authors and Cochrane Vascular editorial base, it was agreed that we should deviate from the protocol to include studies that had used angiography as the reference standard and to include studies in which participants presented with exertional leg pain, with or without subsequent categorisation by [Fontaine 1954](#) or [Rutherford 1997](#).

We were not able to search the Cochrane Register of Diagnostic Test Accuracy Studies.