Utility of ankle-brachial index (ABI)-screening for cardiovascular risk in General Practice

A literature review

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Samenvatting

Inleiding: Perifere arteriële vaatziekte (PAD) is een ondergediagnosticeerde aandoening en staat bekend om zijn associatie met totale mortaliteit en cardiovasculaire ziekte (CVD). De enkel-armindex (ABI) wordt voorgesteld als een screeningsinstrument voor PAD, hoewel het gebruik ervan voor screening controversieel is vanwege de lage sensitiviteit. Sommige richtlijnen bevelen screening aan bij hoogrisicopopulaties. Deze review beoogt de effectiviteit van screening op PAD te beoordelen door het meten van de EAI bij ongediagnosticeerde en asymptomatische personen m.b.t. mortaliteit, belangrijke cardiovasculaire gebeurtenissen (MACE) en morbiditeit als gevolg van PAD. De schadelijke gevolgen van screening en behandeling, evenals kosteneffectiviteit, worden ook beoordeeld.

Methodologie: Een literatuurreview met behulp van de Pubmed en Embase databases.

Resultaten: In de geïncludeerde systematische reviews werd geen sterk bewijs van de voordelen van screening op PAD gevonden in niet-geselecteerde of asymptomatische populaties. De United States Preventive Services Task Force (USPSTF) en andere richtlijnen bevelen momenteel geen routinematige screening naar PAD aan bij asymptomatische volwassenen, hoewel er enige consensus is om "hoogrisicopatiënten" te screenen. Toedienen van aspirine noch op beweging gebaseerde interventies toonden significante voordelen aan wat betreft totale mortaliteit, cardiovasculaire events of morbiditeit als gevolg van PAD die gedetecteerd werd bij screening. Uitgebreide cardiovasculaire screening toonde geen statistisch significante vermindering van totale mortaliteit in de DANCAVAS trial, terwijl de VIVA trial een kleine relatieve risicoreductie van totale mortaliteit liet zien zonder verschil in hazard ratio's voor CVD-gerelateerde mortaliteit.

Gegevens omtrent potentiële schadelijke effecten van screening op PAD bij asymptomatische patiënten zijn beperkt tot vals-positieve of vals-negatieve resultaten en neveneffecten van farmacologische interventies. Over de schadelijke gevolgen van aanvullend diagnostisch onderzoek werden geen gegevens gevonden.

Er werden geen directe gegevens gevonden over de kosteneffectiviteit van PAD-screening in de algemene bevolking. Verschillende computermodellen suggereren dat ABI-screening kosteneffectief is voor bepaalde populaties. De DANCAVAS en VIVA trials toonden kosteneffectiviteit voor screening op populatieniveau en interventie voor vasculaire ziekte bij Deense mannen van 65-74 jaar.

Discussie: Huidige richtlijnen adviseren screening van hoogrisicopatiënten, maar definities van deze populatie variëren en deze aanbeveling is gebaseerd op zwak bewijs. Er ontbreken ook studies over de behandeling van asymptomatische patiënten met PAD of een abnormale ABI. Behandeling op basis van fysieke activiteit heeft potentiële voordelen, maar de therapietrouw is beperkt. Data over nadelen van screening blijkt beperkt tot vals-positieve of vals-negatieve resultaten en mogelijke schade door farmacologische interventies. ABI-screening is mogelijk kosteneffectief in specifieke populaties, maar er zijn geen directe data over screening in de algemene bevolking. Deze review heeft beperkingen, zoals het ontbreken van studies over de klinische effectiviteit of schade door PAD-screening en de afhankelijkheid van computermodellen voor kosteneffectiviteit.

Conclusie: Er is geen direct bewijs en beperkt indirect bewijs gevonden voor de voordelen en schade van screening van pauci- of asymptomatische patiënten op PAD door het meten van ABI. Hoewel de beschikbare gegevens geen gunstige effecten noch schade aantonen, is het bewijs te beperkt om definitieve conclusies te trekken.

Abstract

Introduction: Peripheral arterial disease (PAD) is an underdiagnosed entity, and is well known for its association with all-cause mortality and cardiovascular disease. The ankle-brachial index (ABI) is suggested as a screening tool, although its use for screening is controversial due to low sensitivity. Some guidelines recommend screening in high-risk populations. This review aims to evaluate the effectiveness of screening for PAD by measuring ABI in undiagnosed and asymptomatic individuals in terms of mortality, major adverse cardiovascular events (MACE), and morbidity due to PAD. The harms of screening and treatment, as well as cost-effectiveness, are also evaluated.

Methodology: A literature review using the Pubmed and Embase databases.

Results: The included systematic reviews did not find strong evidence to support the benefits of screening for PAD in unselected or asymptomatic populations. The United States Preventive Services Task Force (USPSTF) and other guidelines do not currently recommend routine screening for PAD in asymptomatic adults, although there is some consensus to screen "high-risk" patients. Administration of aspirin and exercise-based interventions did not show significant benefits in terms of all-cause mortality, cardiovascular events, or morbidity from PAD after screen-detection. Comprehensive cardiovascular screening in the DANCAVAS trial showed no statistically significant reduction in all-cause mortality, whereas the VIVA trial showed a small relative risk reduction in all-cause mortality but no difference in hazard ratios for cardiovascular disease-related mortality.

Potential harms of screening for PAD in asymptomatic patients are limited to false-positive or false-negative results and harmful effects of pharmacologic interventions. No evidence was found on downstream harms due to additional diagnostic testing.

No direct data on the cost-effectiveness of PAD screening in the general population was found. Several computer models suggest that ABI screening is cost-effective in certain populations. The DANCAVAS and VIVA trials both showed cost-effectiveness for population-based screening and intervention for vascular disease in Danish men aged 65-74 years.

Discussion: Current guidelines recommend screening high-risk patients, but definitions of this population vary, and evidence supporting this recommendation is weak. There is also a lack of studies on the management of asymptomatic patients with PAD or abnormal ABI detected by screening. Exercise-based treatment has shown potential benefits but adherence is limited. The evidence on the harms of screening is limited to false-positive or false-negative results and potential harms of pharmacologic interventions. Computer models suggest that ABI screening is cost-effective in specific populations, but there is no direct data regarding screening in the general population. Our review has limitations, including the lack of studies on the clinical effectiveness or harms of PAD screening in the general population and the reliance on computer models for cost-effectiveness.

Conclusion: No direct evidence and limited indirect evidence was found for the benefits and harms of screening pauci- or asymptomatic patients for PAD by measuring ABI. Although the available evidence suggests a lack of beneficial effects as well as harms, the evidence is too limited to draw definitive conclusions.

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List of abbreviations

ABI	Ankle-Brachial Pressure Index
ACC	American College of Cardiologists
ACCF	American College of Cardiology Foundation
AHA	American Heart Association
AHT	Arterial hypertension
AMSTAR 2	A Measurement Tool to Assess the Methodological quality of Systematic Reviews, version 2
ASCVD	Atherosclerotic cardiovascular disease
CVD	Cardiovascular disease
DANCAVAS	Danish Cardiovascular Screening trial
ECQ	Edinburgh Claudication Questionnaire
MACE	Major Adverse Cardiovascular Events
MI	Myocardial infarction
PAD	Peripheral Arterial Disease
RCT	Randomized Clinical Trial
RoB 2	Risk of Bias tool, version 2
SBP	Systolic Blood Pressure
USPSTF	United States Preventive Services Task Force
WHO	World Health Organization
WTP	Willingness To Pay

Introduction

Peripheral arterial disease (PAD) is a common manifestation of systemic atherosclerosis (1,2). PAD can cause a wide range of ischemia-related symptoms in the extremities, but it can also be asymptomatic, causing it to be underdiagnosed (3,4). Even in the absence of symptoms, the presence of PAD is an independent risk factor for all-cause mortality and is associated with an elevated risk for cardiovascular disease (CVD) (4,5). Risk factors for PAD include increasing age, diabetes mellitus, chronic kidney disease and smoking (4).

Considering the higher risk for all-cause mortality and CVD, screening for PAD could theoretically be justified. Early detection of PAD could lead to earlier risk factor modification in patients without diagnosed atherosclerosis, to improve outcomes related to CVD (4). Patient history and clinical examination are neither sensitive nor specific enough to screen for PAD and tools such as the Edinburgh Claudication Questionnaire (ECQ) have also shown to be inadequate, especially in asymptomatic patients (2,6). Calculation of the ankle-brachial index (ABI) by comparing systolic blood pressure (SBP) at the ankle with SBP at the arm is generally considered to be an inexpensive, noninvasive and relatively simple method of diagnosing PAD.

The use of the ABI as a screening tool is currently still controversial: although it meets most of the WHO criteria for screening (7), the ABI has, among others, a low sensitivity despite a high specificity (> 80%) (4). In patients with diabetes mellitus, sensitivity is even lower because falsely high ABI values are common in this population (8,9). The USPSTF does not recommend screening for PAD in a general population (4). However, the American College of Cardiology/American Heart Association (ACC /AHA) Guideline on the Primary Prevention of Cardiovascular Disease recommends that a lowered ABI in both diabetic and nondiabetic patients should be considered as a risk factor to be taken into account when considering (pharmacological) interventions in the prevention of atherosclerotic cardiovascular disease (ASCVD) (10). Some guidelines recommend screening in high-risk populations: The Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease II recommends measurement of ABI in all patients who either have exertional leg symptoms, are aged 50-69 years in presence of a cardiovascular risk factor (especially diabetes or smoking), are aged ≥70 years regardless of risk factor status, or have a Framingham risk score of 10%-20% (11). The 2011 ACCF/AHA Focused Update of the Guideline for the Management of Patients With Peripheral Artery Disease proposed a similar approach and recommended ABI measurement to screen for PAD in a "high-risk population," defined as individuals with one or more of the following: exertional leg symptoms, nonhealing wounds, age 65 years and older or 50 years and older with a history of smoking or diabetes (12).

Another issue is whether it is feasible to implement ABI as a screening tool in general practices. In a 2012 Dutch study, the workload was considered too high without prior selection of patients to screen, and there is limited evidence on whether the necessary skills are available in primary care (1,13).

We aim to assess the value of screening patients for PAD by measuring ABI in general practices.

Clinical questions

Our main objective is to determine the effectiveness of screening for PAD by measuring ABI in undiagnosed and pauci- or asymptomatic individuals in terms of

(a) reduction in all-cause mortality

(b) reduction in major adverse cardiovascular events (MACE)

(c) morbidity due to PAD (claudication, amputation, reduction in quality of life)

We also aimed to evaluate the harms of screening, as well as treatment, on adults with PAD detected at screening or generally asymptomatic patients with PAD.

Finally, we wanted to evaluate the cost-effectiveness of such a screening initiative.

Methodology: analysis of literature regarding clinical effectiveness

Systematic reviews

Criteria

We included systematic reviews studying the effects on morbidity and mortality of screening for PAD by measuring the ankle-brachial index (ABI) in an adult population. “Systematic review” was defined, as per Cochrane, as a review which “attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question” (14).

Inclusion criteria: we included systematic reviews of observational and interventional studies in both normal and high-risk adult populations.

Exclusion criteria: we excluded studies which were not systematic reviews, studies not in English, French or Dutch, studies which did not have the effects of screening for PAD by measuring the ABI in an adult population as a subject, and studies with no full-text availability.

Search strategy

On the 1st of December 2022, we performed a literature search for systematic reviews on Pubmed and Embase using the MeSH-terms “peripheral arterial disease”, “ankle-brachial index”, “screening”, “early detection”. The exact search and search results can be found in appendix 1.

Selection of reviews

Titles and abstracts of articles found were screened for inclusion by the author. All eligible articles were then assessed on their full text. Bibliographies of the selected reviews were checked for additional articles.

Quality assessment

All selected systematic reviews were appraised for methodological quality using the validated AMSTAR 2 (“A Measurement Tool to Assess the Methodological quality of Systematic Reviews”) scoring system (15). Reviews were scored using this 16-item checklist by 1 reader, who also gathered information of each study in a table summarizing properties of all studies.

Reviews were ranked according to their respective AMSTAR 2 quality scores. We decided to use the scoring system of the authors (15), which puts priority on 7 items that are regarded as critical domains capable of affecting the validity of a study and its conclusions (table 1). Reviews with positive responses to all these critical domains and no or 1 non-critical weaknesses received “high” confidence scores, whereas more than one non-critical weakness would be cause for a “moderate” confidence score. “Low” and “critically low” confidence scores are given to reviews which had respectively one critical flaw with or without non-critical weaknesses or more than one critical flaw with or without non-critical weaknesses.

Table 1. AMSTAR 2 critical domains
Protocol registered before commencement of the review (item 2)
Adequacy of the literature search (item 4)
Justification for excluding individual studies (item 7)
Risk of bias from individual studies being included in the review (item 9)
Appropriateness of meta-analytical methods (item 11)
Consideration of risk of bias when interpreting the results of the review (item 13)
Assessment of presence and likely impact of publication bias (item 15)

Clinical studies

Criteria

We included randomized controlled trials (RCT), clinical trials, observational studies and follow-up articles studying the effects on morbidity and mortality of screening for PAD by measuring the ABI in an adult population. Meta-analyses of selected RCTs were also included.

Search strategy

We updated the evidence report published by the USPSTF in 2018 (4). On the 1st of December 2022, we performed a literature search on Pubmed and Embase using both free terms and MeSH-terms, with keywords "peripheral arterial disease", "ankle-brachial index", "screening", "early detection". The exact search and search results can be found in appendix 3.

We aimed to verify whether additional (randomized) clinical trials, observational studies or follow-up articles had been published after the USPTF systematic review published in 2018 which included studies up till 01/05/2017. Hence, only studies published from 01/05/2017 until 01/10/2022 were considered for inclusion.

We excluded studies with no full-text availability, studies not in English, French or Dutch and studies which did not have the effects of screening for PAD by measuring the ABI in an adult population as a subject.

Quality assessment

All included RCTs were appraised for methodological quality using the validated Cochrane Risk of Bias 2 Tool (RoB 2) (16). RCTs were evaluated on five domains (randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of reported result) using this validated questionnaire by 1 reader, who also gathered information of each study. The entire questionnaire can be found in appendix 4.

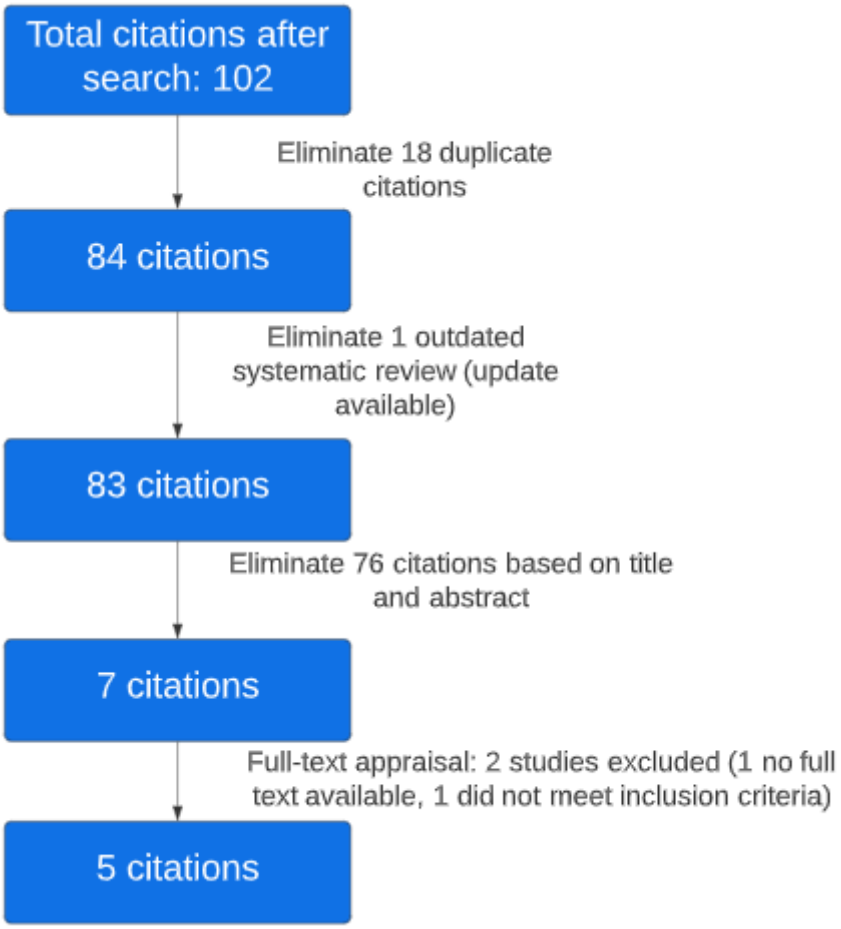
Study selection

Systematic reviews

Search results

The search strategy described above yielded 102 results (33 via Pubmed, 69 via Embase), 18 of which were duplicate results. Hence, a total of 84 articles was found (appendix 1), which were screened for inclusion based on title and abstract. One systematic review by the USPSTF (17) was excluded, as an updated USPSTF systematic review was published on a later date (4). Seventy-six reviews did not meet

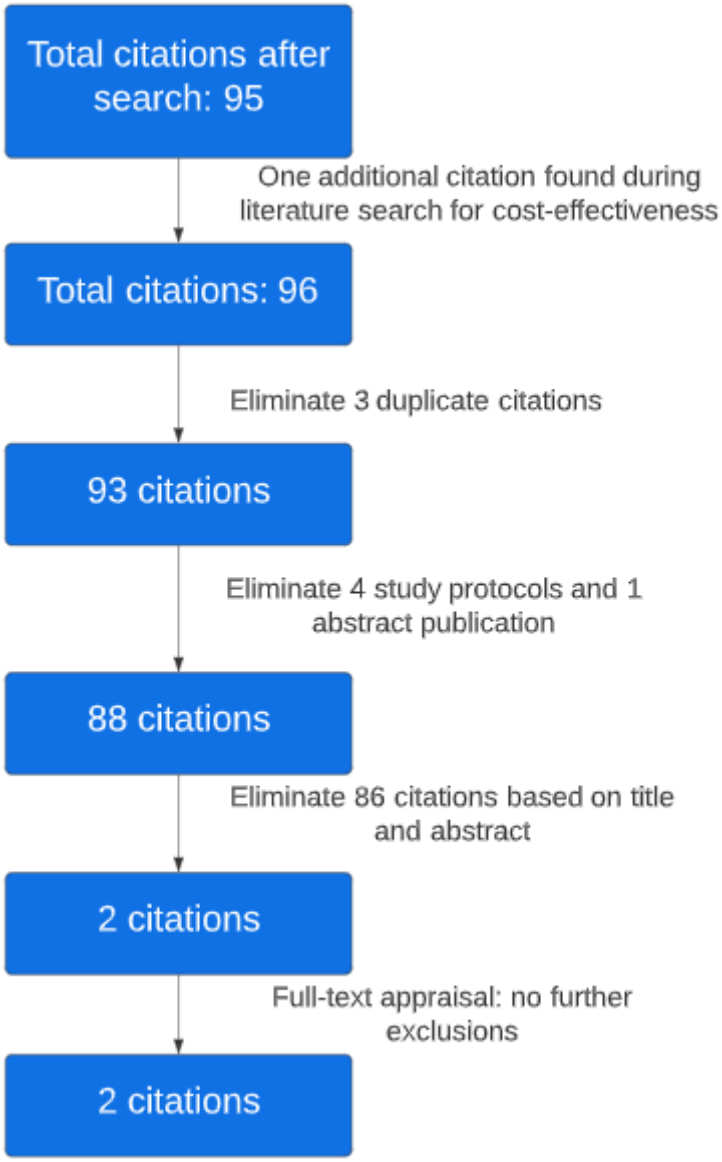
inclusion criteria. For one review (18), we were unable to retrieve the full text (only a conference abstract was available). One other was excluded, as it did not meet inclusion criteria. The remaining 5 reviews were appraised based on full text. All were included in our review (appendix 2).



Clinical studies

Search results

The search strategy described above yielded 95 results (appendix 3) which were screened by title and abstract. One additional study (19) was found during the literature search to determine cost-effectiveness (see below). Four articles were excluded as they only included study protocols or designs, one was only a published abstract of another search result. Three results were duplicates. Eighty-six studies did not meet inclusion criteria. The remaining two studies (20,21) were appraised based on full text and included in our review.



Analysis of literature regarding cost-effectiveness

Methodology

Criteria

We included RCTs, clinical trials, observational studies, reviews, systematic reviews, meta-analyses, follow-up articles and computer simulations evaluating the cost-effectiveness of screening for PAD by measuring the ABI in an adult pauci-or asymptomatic population.

Search strategy

On the 1st of December 2022, we performed a literature search in the PubMed and Embase databases for cost-effectiveness studies using both free term and MeSH-terms “peripheral arterial disease”,

"ankle-brachial index", "screening", "early detection", "economics" and "cost-effectiveness". The exact search strategy and results can be found in appendix 6.

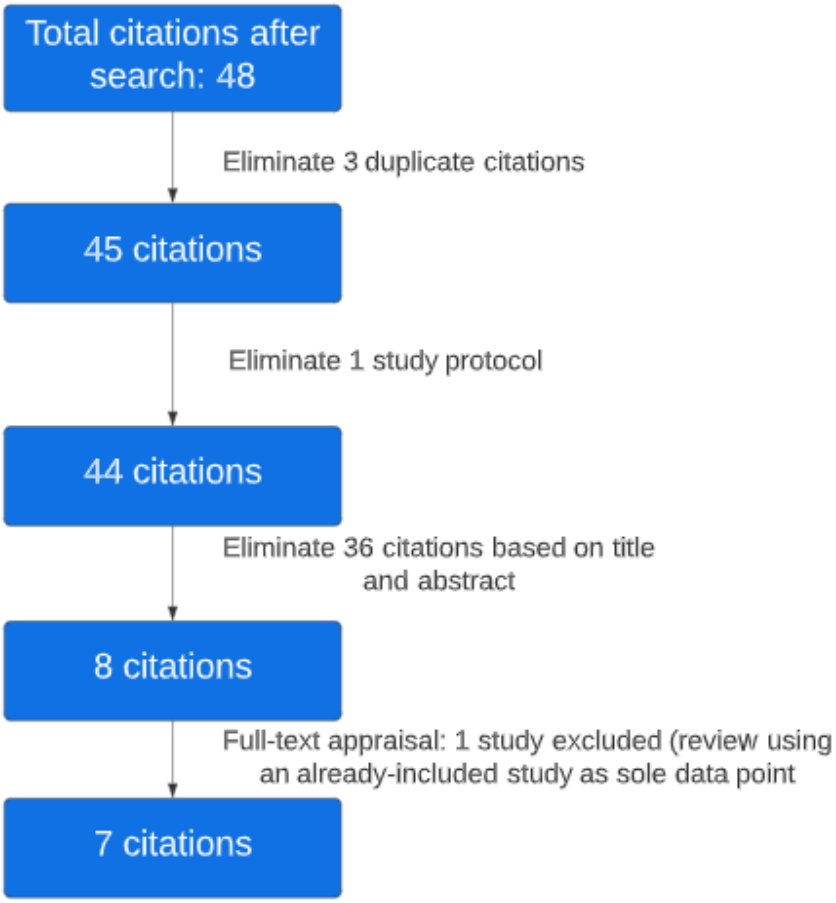
We excluded studies with no full-text availability, studies not in English, French or Dutch and studies which did not have the cost-effectiveness of screening for PAD by measuring the ABI in an adult population as a subject.

Quality assessment

All selected systematic reviews were appraised for methodological quality using the validated AMSTAR 2 scoring system (15) described earlier. The included cost-effectiveness studies (RCTs and computer simulations) were appraised using the checklist of Drummond and Jefferson (22).

Study selection

The search strategy described above yielded 48 results (appendix 6), which were screened for inclusion based on title and abstract. Three duplicate articles were identified. One article was excluded as it was a study protocol. Thirty-five studies did not meet inclusion criteria. The remaining 8 were appraised based on their full text. One study (7) was excluded, as it was a review using an already included study as its sole data point (23). The remaining 7 studies were included in our review.



Results: clinical effectiveness

Out of five included systematic reviews, one (24) had a “low” confidence score using the AMSTAR 2 score system. One (4) scored “moderate”, the other systematic reviews scored “high”. Both included RCTs scored “low risk of bias” on all domains using the RoB 2 tool (appendix 5). A more detailed overview of the included systematic reviews and meta-analyses can be found in appendix 2.

1. Does screening for PAD by ABI-measurement reduce all-cause mortality, cardiovascular events or morbidity from PAD?

Few studies have been conducted to compare mortality, morbidity from PAD or cardiovascular events in screened and nonscreened populations. Most guidelines base their decision making regarding screening on other data such as disease morbidity and mortality (25). We searched for studies that made direct comparisons between screened and nonscreened individuals.

The systematic reviews that were included did not find compelling evidence to support the benefits of PAD screening in populations that are unselected or asymptomatic. The USPSTF does not currently recommend PAD screening, considering the lack of direct evidence of its utility this intervention in asymptomatic adults (4). Alahdab et al. also found insufficient evidence to support the benefit of routine ABI screening or aggressive treatment of patients with abnormal ABI, although PAD is associated with significant morbidity and mortality (25). An analysis of current guidelines by Uyagu et al. revealed a consensus to screen "high-risk" patients, although differences in the definition of this population were found across guidelines, as well as a lack of strong evidence to support this recommendation (26). There is also no consensus among the recommendations concerning further diagnostic testing following screening (26). Ferket et al. and Chen et al. also found conflicting guidelines: while some guidelines recommended screening for asymptomatic PAD, others found insufficient evidence or recommended against screening (24,27).

The USPSTF evidence report by Guirguis-Blake et al. (4) found 4 RCTs studying the benefits of treating asymptomatic patients with PAD or an abnormal ABI detected by screening. Two RCTs examined aspirin (28,29), two others examined the benefits of lifestyle interventions and exercise programs (30,31). None of the other systematic reviews we included found additional relevant data on this clinical question. Our own search for clinical studies yielded 2 additional results from the VIVA and DANCAVAS trials (20,21).

The aspirin trials, both in diabetics (28) and in the general population (29), , did not show any significant difference between the aspirin and control groups in terms of all-cause mortality, cardiovascular

events, or morbidity from PAD (such as intermittent claudication, need for revascularization, or amputation) after screen-detection.

Exercise-based treatment may have limited efficacy in improving disability, although the variability in outcome measures in the Collins et al. and Fowler et al. studies does not allow for definite conclusions, and neither study examined the effects on PAD progression or cardiovascular event rates (30,31). It should be noted that the Fowler et al. study included patients with intermittent claudication, whereas Collins et al. strictly excluded patients with symptoms of intermittent claudication (30,31).

The DANCAVAS trial showed no statistically significant reduction in all-cause mortality at 5 years (p= 0.06) after invitation to undergo comprehensive cardiovascular screening (including ABI measurement) in men aged 65 to 74 years, based on an intention-to-screen analysis (21).

The VIVA trial, a large RCT assessing the benefits of a multimodality screening program for abdominal aortic aneurysm, PAD, and hypertension in men aged 65-74 years, found a small relative risk reduction of 7% for all-cause mortality in the screened versus the nonscreened group (20). Re-analysis suggests the PAD focus represents 1.71 percentage points (19). However, no difference was found in hazard ratios for cardiovascular disease-related mortality (20,32).

Table 2. Summary of clinical trials studying clinical effectiveness of PAD-screening

Study	**Population**	**Intervention**	**Effectiveness**	**% PAD detected**
Lindholt et al. (19)	Men aged 65 to 74 years	Screening for PAD	1.71% decrease in relative mortality, suggesting PAD screening is responsible for one fourth of the reported overall 7% relative mortality risk reduction observed with combined screening for abdominal aortic aneurysm, PAD, and AHT	PAD (ABI <0.9 or >1.4) diagnosed in 2052 out of 18 749 participants: 10.9% (10.5 to 11.4) (33)
Belch et al. (28)	People with diabetes mellitus with asymptomatic PAD.	Aspirin or antioxidant treatment	Neither aspirin nor antioxidant treatment showed any statistically significant benefits on cardiovascular events or cardiovascular mortality	Proportion of PAD detected not stated in article

Fowkes et al. (29)	Patients aged 50 to 75 years without clinical CVD, with PAD detected by screening	Aspirin treatment	No decrease in major cardiovascular events	Of 28980 participants screened, 4914 (17%) had a low ABI (≤0.95)
Collins et al. (30)	Adults with an ABI of 0.50-0.89 and no symptoms of intermittent claudication	A 12-week risk-factor management education intervention	Significant increase in both ABI and stair-climbing ability, but no notable difference in adjusted mean walking distance benefits.	Proportion not stated in article
Fowler et al. (31)	Men aged 65 to 79 years with early PAD identified through screening using ECQ and ABI.	A smoking cessation and physical activity program	Improvement in the maximum walking distance rate at 12 months, with a higher percentage of improvement observed in the intervention group compared to the control group (23% versus 15%; $\chi 2$ = 9.74, df = 2, p = 0.008).	PAD diagnosed through ABI or ECQ in 928 out of 7987 men (11.6%).
Lindholt et al. (21)	Men aged 65 to 74 years	Invitation for comprehensive cardiovascular screening (including ABI)	No significant risk reduction for all-cause mortality (HR 0.95; 95% CI [0.90-1.00]), stroke (HR 0.93; 95% CI [0.86-0.99]), myocardial infarction (HR 0.91; 95% CI [0.81-1.03]), aortic dissection (HR 0.95; 95% CI [0.61-1.49]), and aortic rupture (HR 0.81; 95% CI [0.49-1.35]).	PAD (ABI 0.9 or less) diagnosed in 1147 out of 16768 participants: 11.0% (34)

2. What are the harms of screening for PAD by ABI-measurement or of treatment of screen-detected PAD or abnormal ABI?

The ABI test is a noninvasive physical examination and is harmless in itself. The DANCAVAS trial did not find any harmful effect of screening on quality of life (21). Evidence of harm from screening in asymptomatic patients is limited to false-positive or false-negative results and harmful effects of pharmacologic interventions (4,25).

A recent evaluation of the diagnostic performance of the ABI in lower extremity PAD found a false-positive rate of 34.4% and a false-negative rate of 27.5% (35).

Studies evaluating the harms of pharmacological interventions are limited to the two aspirin studies by Belch et al. and Fowkes et al. already mentioned (28,29). Neither saw a statistically significant increase of major hemorrhage (28,29). No evidence was found on the harms of other pharmacological interventions.

No evidence was found on downstream harms due to additional diagnostic testing (4,25).

Results: cost-effectiveness

The only included systematic review (25) received a "high" confidence score using AMSTAR 2 score system (as mentioned above, appendix 2). An overview of our quality appraisal of the included cost-effectiveness studies using the checklist of Drummond and Jefferson can be found in appendix 7.

No studies were found that provided direct data on the cost-effectiveness of PAD screening in the general population. Alahdab et al. found no reliable studies of cost-effectiveness (25). The VIVA study found that population-based screening and intervention for abdominal aortic aneurysm, peripheral artery disease, and hypertension were cost-effective in Danish men aged 65-74 years (36). The DANCAVAS trial, in which Danish men aged 65-74 years were invited to multimodality screening for vascular disease, also showed cost-effectiveness for such a strategy (37).

Specifically for PAD screening, only computer models could be found: a Markov model based on data from the VIVA study showed ABI screening was cost-effective in Danish men aged 65-74 years (19). A discrete event simulation model from 2022 found ABI screening to be a cost-effective strategy for asymptomatic 50-year-old patients (38). Similarly, a 2014 Markov model suggests that one-time screening of a high-risk population at age 55 years with ABI followed by antiplatelet therapy may be cost-effective in the Dutch healthcare system (23). Another Markov model evaluating the cost-effectiveness of initiating medical therapy after a positive ankle-brachial index (ABI) screening test in 65-year-old patients suggests cost-effectiveness under favorable drug adherence assumptions (39).

Table 3. Summary of studies on cost-effectiveness of PAD-screening

Study	**Cost-effectiveness assessment**
Alahdab et al. (25)	No reliable studies of cost-effectiveness were found.
Søgaard et al. (36)	Comprehensive vascular screening appears to be cost-effective.
Søgaard R et al. (37)	Comprehensive screening for CVD is overall cost effective at conventional thresholds for willingness to pay. There is, however, a need to define the screening target group.
Lindholt et al. (19)	At conventional thresholds for cost effectiveness, it is probable that screening will be deemed cost effective.
Kamenský et al. (38)	ABI screening appears to be a cost-effective strategy for asymptomatic patients aged 50 years when compared to the no-screening option.
Vaidyah et al. (23)	There is an 88% probability of PAD screening being cost effective at the Willingness To Pay (WTP) threshold of 40000 Euros.
Itoga et al. (39)	Screening in higher-risk populations under favorable assumptions about medication adherence results in cost effectiveness, but limitations in the primary data preclude definitive conclusions.

Discussion

1. Clinical effectiveness

Relevant studies have been summarized in table 2. Currently, there are no studies on the effectiveness of screening for PAD by measuring ABI as a single measure to reduce PAD- or CVD-related morbidity or mortality in a broad (pauci- or asymptomatic) population. Although there is a consensus in current guidelines that “high-risk” patients should be screened, definitions of this population vary across guidelines, and the evidence supporting this recommendation is weak (26).

Two large multimodality trials of cardiovascular screening were reviewed: the DANCAVAS and VIVA trials. The DANCAVAS trial found no benefit on 5-year overall survival after invitation to undergo comprehensive cardiovascular screening (21). However, the trial only assessed the benefit of inviting for screening and not the screening itself, with only 62.6% of invited men undergoing screening (21). In addition, the trial targeted a limited population (men aged 65 to 74 years).

The VIVA trial showed a modest 7% relative risk reduction for all-cause mortality in the screened versus the nonscreened group of a multimodal screening program followed by relevant interventions (diet

and exercise recommendations, as well as antihypertensive, lipid-lowering and antiplatelet therapy) for abdominal aortic aneurysm, PAD, and hypertension in men aged 65-74 years (20). A subanalysis suggested that the PAD focus accounted for 1.71 percentage points (19), but no difference was found in hazard ratios for cardiovascular disease-related mortality or any other specific cause of death (20,32). As the reduction in overall mortality is diffuse, the risk of a “random high” should be considered (32).

There is also a severe lack of trials on management of asymptomatic patients with PAD or abnormal ABI detected by screening. Two RCTs studying the effects of aspirin treatment in this population (28,29) were found, but none showed clinical benefit, either in diabetics (28) or in the general population (29). No studies on other pharmacotherapeutic treatment options were found.

Exercise-based treatment for asymptomatic patients with PAD or abnormal ABI detected by screening has been shown to be potentially beneficial, but adherence is very limited in the long term: 82% at 12 weeks in the trial by Collins et al. versus 16.5% at 1 year of follow-up in the trial by Fowler et al. (30,31). However, it should be noted that Fowler et al. did not screen exclusively by measuring ABI, but also used the Edinburgh Claudication Questionnaire (ECQ), meaning symptomatic patients were also included in the trial, which may affect adherence to physical exercise (31). Collins et al. conducted a pilot study, in which only 50 patients were randomized. While a significant increase in ABI and stair-climbing ability was shown, there was no benefit in adjusted mean walking distance (30).

Regarding the harms of screening for PAD in asymptomatic patients, the evidence is limited to false-positive or false-negative results and harmful effects of pharmacologic interventions (4,25). Both false-positive and false-negative rates are very high, 34.4% and 27.5%, respectively (35). Although downstream harms due to additional diagnostic testing might be expected, none of the included articles found direct evidence to support this idea (4,25). However, the 2016 AHA /ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease recommends against angiography in asymptomatic PAD patients and classifies this procedure as "harmful" (40).

None of the abovementioned aspirin trials showed a statistically significant increase in major hemorrhage (28,29). No evidence was found on the harms of other pharmacologic interventions, despite known potential side effects of both antihypertensive agents (e.g. hypotension, syncope, acute kidney injury) (41) and lipid-lowering agents (e.g. myopathy, renal and liver dysfunction) (42).

2. Cost-effectiveness

Relevant studies were summarized in Table 3. No studies were found that provided direct data on the cost-effectiveness of PAD screening by measuring ABI in the general (asymptomatic) population. Specific to PAD screening, only computer models on cost effectiveness in specific populations could be found. All four included models (19, 23, 36, 37) concluded that ABI screening is a cost-effective strategy in specific populations.

The VIVA and DANCAVAS studies of multimodal cardiovascular screening found population-based screening and intervention (36) and invitation to multimodal screening for vascular disease to be cost-effective in Danish men aged 65-74 years, respectively, to be cost-effective (37).

3. Study limitations

Our study has several limitations. There is a substantial lack of studies on the clinical effectiveness or harms of PAD screening in the general population. Also, the populations studied as well as subsequent interventions after diagnosis of PAD or an abnormal ABI vary widely.

No studies were found that provided direct data on the cost effectiveness of PAD screening by measuring ABI in the general (asymptomatic) population. Specifically for PAD screening, only computer models of cost effectiveness in specific populations could be found. However, using only these computer models to evaluate the cost-effectiveness of PAD screening may be too positive, especially given the lack of evidence for clinical effectiveness (43).

4. Future research

Further studies of population screening for PAD using methods such as ABI as a single measure are needed to evaluate the potential benefits, cost-effectiveness, and harms.

Conclusion

No direct evidence and limited indirect evidence was found for the benefits and harms of screening pauci or asymptomatic patients for PAD by measuring ABI. Although the available evidence suggests a lack of beneficial effects as well as harms, the evidence is too limited to draw definitive conclusions.

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Appendices

Appendix 1 - Systematic reviews: search strategy and results

On the 1st of December 2022, we performed a literature search on Pubmed and Embase using the MeSH-terms “peripheral arterial disease”, “ankle-brachial index”, “screening”, “early detection” and as publication type “systematic review”. The exact search strategies are described below.

Search strategy

1. Pubmed

("peripheral artery disease"[All Fields] OR "ankle-brachial index"[All Fields]) AND ("screening"[All Fields] OR "early detection"[All Fields]) AND ("systematic review"[Publication Type])

2. Embase

(('peripheral arterial disease'/exp OR 'peripheral arterial disease' OR 'ankle brachial index':ab,ti) AND (screening:ab,ti OR 'early detection':ab,ti) AND 'systematic review'/de)

Search results

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Appendix 2 - Systematic reviews: overview of included studies

First author (year) Meta-analysis (MA) + or – AMSTAR2-score	Clinical question	Design of included studies and search period	Interventions / Comparators	Population studied	Outcomes	Important results	Important conclusions
"Screening for Peripheral Artery Disease…" **Guirguis-Blake JM (2018) (1)** **MA –** **Moderate (did not account for risk of bias in individual studies when interpreting/discussing the results of the review)**	1. Does screening for PAD with ABI in adults without symptoms lead to a reduction in CVD or PAD-related morbidity/mortality? 2. How accurate is ABI as a screening tool for PAD in adults without symptoms of PAD? 3. What are possible harms of ABI screening for PAD in pauci- or asymptomatic adults? 4. Does treatment of adults with no symptoms who have screen-detected PAD or abnormal ABI lead to better health outcomes? 5. What are the potential harms of treating asymptomatic adults with abnormal ABI?	- Studies included in Lin, et al (2) - RCTs, nonrandomized controlled intervention studies and systematic reviews published between January 2012 and May 2, 2017	- Screening versus no screening by measuring resting ABI - Treatment: pharmacologic or lifestyle interventions to reduce CVD risk	Screen-detected patients or generally asymptomatic adults without known CVD	- Cardiovascular morbidity (myocardial infarction (MI) and CVA); - PAD morbidity, including ambulation impairment or amputation; - mortality; - health-related quality of life; - diagnostic accuracy of resting ABI ; - adverse outcomes related to the ABI test; - serious treatment-related adverse events	1. No RCTs focused on screening for PAD using ABI alone on a population level were found 2. Evidence regarding the accuracy of ABI as a screening test for PAD in asymptomatic adults is limited, relying on a single study published in 2008, showing low sensitivity and high specificity 3. Evidence on potential harms of screening for PAD using ABI is limited to the rates of false-positive and false-negative results reported in the above-mentioned 2008 study 4. A. Two RCTs investigating the effectiveness of aspirin found no significant differences between the aspirin and control groups for cardiovascular outcomes, fatal CVD events, or all-cause mortality 4. B: Two trials were conducted to assess the effectiveness of exercise-based treatment for	The evidence regarding the advantages of screening for PAD using ABI in unselected or asymptomatic populations is scarce and indirect. The available research indicates low sensitivity and a lack of beneficial impact on health outcomes, although these studies have significant limitations. The US Preventive Services Task Force (USPSTF) has determined that the current evidence is inadequate to evaluate the benefits and harms of screening for PAD and CVD risk using ABI in asymptomatic adults.

						screen-detected PAD. Variations in outcome measures preclude definitive conclusions; however, the evidence suggests that this form of treatment may have limited effectiveness. 5. Evidence on harms of treatment is limited to the aspirin trials, which show increased risk of major bleeding. However, the wide confidence intervals and rarity of events preclude drawing definitive conclusions	
"A systematic review for the screening for…" **Alahdab F (2015) (3)** **MA –** **High**	1. Does using ABI screening in asymptomatic adults reduce cardiovascular or PAD morbidity (such as ambulation impairment or amputation) or mortality? 2. Does treatment of individuals with PAD detected through screening lead to improved morbidity? 3. Is screening with ABI both safe and cost-effective?	All studies, regardless of their design, language, size, or duration of follow-up, were considered for inclusion. A search was performed from 2005 to March 2010, and an update was conducted in June 2014.	- Screening versus no screening using ABI - (intense) treatment vs less intense or no treatment of screen-detected PAD	Asymptomatic indivuals	- yield of screening and the benefits and harms of screening, as well as subsequent treatment (in terms of death, amputation, development of symptoms, and quality of life) - cost-effectiveness of screening	1. No studies directly compared the impact of screening for PAD on morbidity or mortality between a population that was screened versus a population that was not screened. 2. There is no strong evidence suggesting significant benefits of aggressive treatment of individuals with an abnormal ABI. 3. A. No studies were found regarding the adverse effects of treating PAD-patients detected through ABI screening. 3. B. No reliable cost-effectiveness studies found	Current available evidence does not show benefit of routine ABI screening.
" Systematic review of guidelines on	1. Does screening for PAD in people without	Guidelines in English published between	Screening for asymptomatic PAD and/or	Asymptomatic adults	- PAD progression	1. Available evidence is insufficient to support the	Due to the differing recommendations found in current guidelines, the

peripheral artery disease screening." **Ferket B (2012) (4)** **MA –** **High**	symptoms prevent the progression of PAD? 2. Does screening for PAD in people without symptoms prevent cardiovascular events? 3. If screening for PAD in people without symptoms is beneficial, which screening tool should be used?	January 1, 2003 and January 20, 2011	treatment for asymptomatic PAD vs no screening/no treatment		- Cardiovascular events	justification of PAD screening, as interventions to prevent PAD progression in asymptomatic individuals such as exercise and smoking cessation are recommended regardless 2. No guidelines were found providing guidance on how to incorporate both ABI outcomes and conventional cardiovascular risk factors into a multivariable risk model. 3. Guidelines supporting screening for PAD recommend using the ABI, either alone or in conjunction with a screening questionnaire or physical examination.	value of PAD screening is uncertain. This is likely a result of the lack of evidence supporting the benefits of early PAD detection over traditional risk assessment and expectant management.
"Critical appraisal of international guidelines for the screening …" Chen Q (2019) (5) **MA –** **Low (no accounting for risk of bias in individual studies, no protocol registered before review)**	1. Should asymptomatic individuals undergo PAD screening? If so, what test(s) should be used? 2. Which approach is recommended for asymptomatic PAD?	Guidelines in English between January 1st, 2000 to December 31th, 2017	Screening and/or treatment for asymptomatic PAD (including but not limited to exercise, pharmacological treatment, surgical treatment); versus no screening or expectant approach	Asymptomatic individuals	Guidelines' quality and variations in screening and diagnostic recommendations	Out of 14 guidelines, 8 recommend PAD screening with varying levels of support, while the others either found insufficient evidence or recommend against screening. There were conflicting recommendations regarding the target values for lipid-lowering and regarding antiplatelet therapy. Other preventive measures included smoking cessation, healthy diet, and treatment of hypertension and diabetes.	Recommendations on both screening and treatment are conflicting.

"Quality assessment and comparative analysis on the recommendations of current guidelines on …" Uyagu O (2022) (6) **MA –** **High**	Should asymptomatic individuals undergo PAD screening? If yes, which screening tool should be used and which population should be screened? If an abnormal ABI is detected, should further diagnostic testing be conducted and should additional screening be done in other vascular areas?	Clinical practice guidelines written after 2010 and on or before 2020	Screening versus not screening for PAD	Adults	Primary outcomes were the guidelines' quality and variations in screening and diagnostic recommendations in the selected guidelines	Guidelines are in agreement on screening "high-risk" patients for PAD, but there were differences in age range and a lack of strong evidence to support this recommendation. The guidelines unanimously recommend the ABI as the initial screening test. However, differences exist in recommendations for further diagnostic testing and imaging due to insufficient evidence. Most guidelines provide no recommendations for screening for arterial diseases in other vascular beds.	Although guidelines suggest screening individuals at high risk for PAD, there is a lack of evidence to support this practice.

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Appendix 3 - Clinical studies

On the 1st of December 2022, we performed a literature search on Pubmed and Embase using both free terms and MeSH-terms, with keywords “peripheral arterial disease”, “ankle-brachial index”, “screening”, “early detection”. We searched for clinical trials, randomized controlled trials and observational studies published after 01/05/2017, in either English, Dutch or French.

The exact search and search results can be found below.

Search strategy

1. Pubmed

("Peripheral Arterial Disease"[MeSH Terms] OR "Ankle Brachial Index"[MeSH Terms] OR "peripheral artery disease"[All Fields] OR "ankle-brachial index"[All Fields]) AND ("Mass Screening"[MeSH Terms] OR “screening"[All Fields] OR "early detection"[All Fields]) AND ("randomized controlled trial"[Publication Type] OR "clinical trial"[Publication Type] OR "observational study"[Publication Type]) AND (2017/5/1:2022/12/1[pdat]) AND ("English"[Language] OR "Dutch"[Language] OR "French"[Language])

2. Embase

('peripheral arterial disease'/exp OR 'peripheral arterial disease':ab,ti OR 'ankle brachial index'/exp OR 'ankle brachial index':ab,ti) AND ('mass screening':ab,ti OR 'screening':ab,ti OR 'early detection':ab,ti) AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND (2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py OR 2022:py) AND [01-05-2017]/sd NOT [01-12-2022]/sd AND ([dutch]/lim OR [english]/lim OR [french]/lim)

Search results

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Appendix 4 - Version 2 of the Cochrane risk-of-bias assessment tool (RoB 2)

Based on Sterne et al. (16).

Bias domain and signalling question*	**Response options**		
	Lower risk of bias	Higher risk of bias	Other
Bias arising from the randomisation process			
1.1 Was the allocation sequence random?	Y/PY	N/PN	NI
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y/PY	N/PN	NI
1.3 Did baseline differences between intervention groups suggest a problem with the randomisation process?	N/PN	Y/PY	NI
Risk-of-bias judgment (low/high/some concerns)			
Optional: What is the predicted direction of bias arising from the randomisation process?			
Bias due to deviations from intended interventions			
2.1 Were participants aware of their assigned intervention during the trial?	N/PN	Y/PY	NI
2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	N/PN	Y/PY	NI
2.3 If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	N/PN	Y/PY	NA/NI
2.4 If Y/PY/NI to 2.3: Were these deviations likely to have affected the outcome?	N/PN	Y/PY	NA/NI
2.5 If Y/PY to 2.4: Were these deviations from intended intervention balanced between groups?	Y/PY	N/PN	NA/NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y/PY	N/PN	NI
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	N/PN	Y/PY	NA/NI
Risk-of-bias judgment (low/high/some concerns)			
Optional: What is the predicted direction of bias due to deviations from intended interventions?			
Bias due to missing outcome data			
3.1 Were data for this outcome available for all, or nearly all, participants randomised?	Y/PY	N/PN	NI
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Y/PY	N/PN	NA
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/PN	Y/PY	NA/NI

3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N/PN	Y/PY	NA/NI
Risk-of-bias judgment (low/high/some concerns)			
Optional: What is the predicted direction of bias due to missing outcome data?			
Bias in measurement of the outcome			
4.1 Was the method of measuring the outcome inappropriate?	N/PN	Y/PY	NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N/PN	Y/PY	NI
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	N/PN	Y/PY	NI
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N/PN	Y/PY	NA/NI
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	N/PN	Y/PY	NA/NI
Risk-of-bias judgment (low/high/some concerns)			
Optional: What is the predicted direction of bias in measurement of the outcome?			
Bias in selection of the reported result			
5.1 Were the data that produced this result analysed in accordance with a prespecified analysis plan that was finalised before unblinded outcome data were available for analysis?	Y/PY	N/PN	NI
Is the numerical result being assessed likely to have been selected, on the basis of the results, from:			
5.2 ... multiple eligible outcome measurements (eg, scales, definitions, time points) within the outcome domain?	N/PN	Y/PY	NI
5.3 ... multiple eligible analyses of the data?	N/PN	Y/PY	NI
Risk-of-bias judgment (low/high/some concerns)			
Optional: What is the predicted direction bias due to selection of the reported results?			
Overall bias			
Risk-of-bias judgment (low/high/some concerns)			
Optional: What is the overall predicted direction of bias for this outcome?			
Y=yes; PY=probably yes; PN=probably no; N=no; NA=not applicable; NI=no information. *Signalling questions for bias due to deviations from intended interventions relate to the effect of assignment to intervention.			

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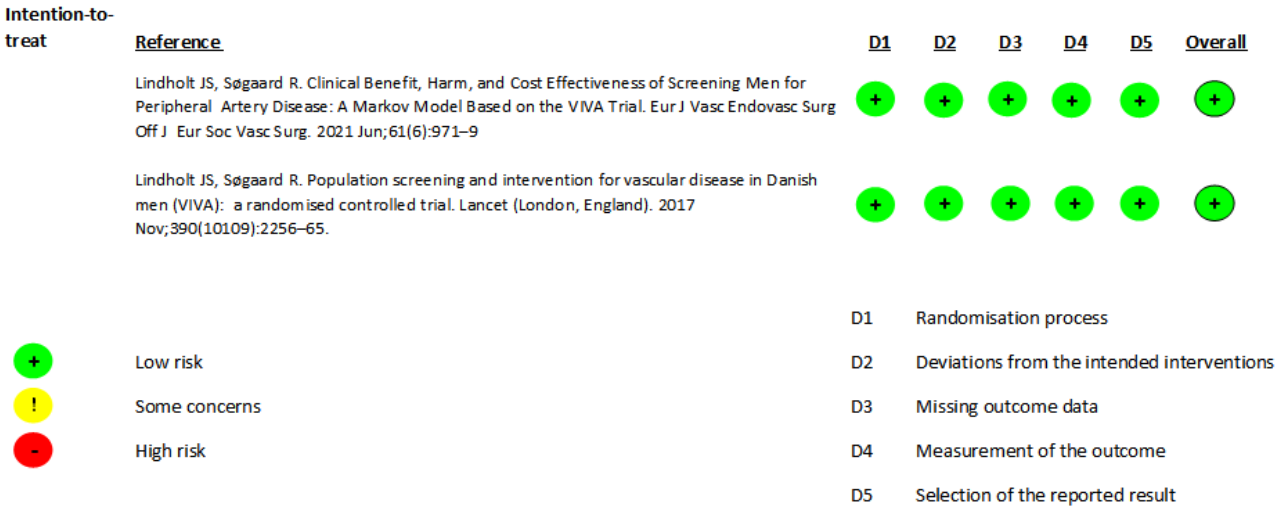
Appendix 5 – Assessment of risk of bias using the Cochrane RoB 2 tool



Appendix 6 – Cost-effectiveness studies

On the 1st of December 2022, we performed a literature search in the PubMed and Embase databases for cost-effectiveness studies using both free term and MeSH-terms “peripheral arterial disease”, “ankle-brachial index”, “screening”, “early detection”, “economics” and “cost-effectiveness”. The exact search strategy and results can be found below.

We excluded studies with no full-text availability, studies not in English, French or Dutch.

Search strategy

1. Pubmed

((("Peripheral Arterial Disease"[MeSH Terms] OR "ankle brachial index"[MeSH Terms] OR "peripheral artery disease"[All Fields] OR "ankle brachial index"[All Fields]) AND ("Mass Screening"[MeSH Terms] OR "screening"[All Fields] OR "early detection"[All Fields]) AND ("economics"[All Fields] OR "cost-effectiveness"[All Fields])) OR "ankle brachial index/economics"[MeSH Terms]) AND ("English"[Language] OR "Dutch"[Language] OR "French"[Language])

2. Embase

('peripheral arterial disease'/exp OR 'peripheral arterial disease':ab,ti OR 'ankle brachial index'/exp OR 'ankle brachial index':ab,ti) AND ('mass screening':ab,ti OR 'screening':ab,ti OR 'early detection':ab,ti) AND 'cost effectiveness analysis':ab,ti AND ([dutch]/lim OR [english]/lim OR [french]/lim)

Search results

1. Søgaard R, Diederichsen ACP, Rasmussen LM, Lambrechtsen J, Steffensen FH, Frost L, et al. Cost effectiveness of population screening vs. no screening for cardiovascular disease: the Danish Cardiovascular Screening trial (DANCAVAS). Eur Heart J. 2022 Nov;43(41):4392–402.
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Appendix 7 – quality appraisal of cost-effectiveness studies

We performed quality appraisal of the included cost-effectiveness studies using the checklist of Drummond and Jefferson (1).

Criteria	Søgaard R, Lindholt JS (2)	Lindholt JS, Søgaard R (3)	Søgaard R et al. (4)	Vaidya et al. (5)	Kamenský et al. (6)	Itoga et al. (7)
	Study design					
The research question is stated	✓	✓	✓	✓	✓	✓
The economic importance of the research question is stated	✓	✓	✓	✓	✓	✓
The viewpoint(s) of the analysis are clearly stated and justified	✓	✓	✓	✓	✓	✓
The rationale for choosing alternative programmes or interventions compared is stated	✓	✓	✓	✓	✓	✓
The alternatives being compared are clearly described	✓	✓	✓	✓	✓	✓
The form of economic evaluation used is stated	✓	✓	✓	✓	✓	✓
The choice of form of economic evaluation is justified in relation to the question addressed	✓	✓	✓	✓	✓	✓
	Data collection					
The source(s) of effectiveness estimates used are stated	✓	✓	✓	✓	✓	✓
Details of the design and results of the effectiveness study are given (if based on a single study)	✓	✓	✓	NA	✓	✓
Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies)	NA	NA	NA	✗	NA	NA
The primary outcome measure(s) for the economic evaluation are clearly stated	✓	✓	✓	✓	✓	✓
Methods to value benefits are stated	✗	✗	✗	✗	✗	✗

Criteria	Søgaard R, Lindholt JS (2)	Lindholt JS, Søgaard R (3)	Søgaard R et al. (4)	Vaidya et al. (5)	Kamenský et al. (6)	Itoga et al. (7)
Details of the subjects from whom valuations were obtained are given	NA	NA	NA	NA	NA	NA
Productivity changes (if included) are reported separately	NA	NA	NA	NA	NA	NA
The relevance of productivity changes to the study question is discussed	NA	NA	NA	NA	NA	NA
Quantities of resource use are reported separately from their unit costs	✓	✓	✓	✗	✓	✓
Methods for the estimation of quantities and unit costs are described	✓	✓	✓	✗	✓	✓
Currency and price date are recorded	✓	✓	✓	✓	✓	✓
Details of currency of price adjustments for inflation or currency conversion are given	✓	✓	✗	✓	NA	✓
Details of any model used are given	NA	✓	NA	✓	✓	✓
The choice of model used and the key parameters on which it is based are justified	NA	✓	NA	✓	✓	✓
	Analysis and interpretation of results					
Time horizon of costs and benefits is stated	✓	✓	✓	✓	✓	✓
The discount rate(s) is stated	✗	✓	✓	✗	✓	✓
The choice of discount rate(s) is justified	NA	✗	✓	NA	✗	✗
An explanation is given if costs and benefits are not discounted	✗	NA	NA	✗	NA	NA
Details of statistical tests and confidence intervals are given for stochastic data	✓	✓	✓	✗	✗	✗
The approach to sensitivity analysis is given	✓	✓	✓	✓	✓	✓
The choice of variables for sensitivity analysis is justified	✓	✓	✓	✓	✓	✓
The ranges over which the variables are varied are justified	✓	✓	✓	✓	✓	✓

Criteria	Søgaard R, Lindholt JS (2)	Lindholt JS, Søgaard R (3)	Søgaard R et al. (4)	Vaidya et al. (5)	Kamenský et al. (6)	Itoga et al. (7)
Relevant alternatives are compared	✓	✓	✓	✓	✓	✓
Incremental analysis is reported	✓	✓	✓	✓	✓	✓
Major outcomes are presented in a disaggregated as well as an aggregated form	✓	✓	✓	✓	✓	✓
The answer to the study question is given	✓	✓	✓	✓	✓	✓
Conclusions follow from the data reported	✓	✓	✓	✓	✓	✓
Conclusions are accompanied by the appropriate caveats	✓	✓	✓	✓	✓	✓

✓, included; ✗, missing; attempted, missing but attempted; NA, not applicable; partial, partially included.

Only full articles were critically assessed.

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Ethical committee

Is de enkel-arm index bruikbaar als screeningstool voor cardiovasculair risico in de huisartsenpraktijk?

Dossiernr.:	MP018615
Masterproef:	Masterproef I HAIO, 2020 – 2023
Faculteit/opleiding:	Faculteit Geneeskunde - Master in de huisartsgeneeskunde
Studiefase:	eerste fase
Academiejaar:	2021-2022
Korte omschrijving / abstract:	De enkel-arm-index (EAI) is breed aanvaard als onderzoek voor de initiële diagnostiek van perifere vaatziekten (PAD). Er is echter ook een sterk verband tussen perifeer vaatlijden en andere cardiovasculaire aandoeningen (CVD), aangezien deze beide beïnvloed worden door systemische atheromatose. Momenteel voorzien de richtlijnen echter geen screening van de EAI bij populaties met hoog risico op cardiovasculaire aandoeningen. Met dit onderzoek willen we graag nagaan of dit toch nuttig zou zijn, en of dit haalbaar is in de huisartsenpraktijk.
Toegepaste technieken:	Review
Gewenste taal van communicatie:	nl
Promotor:	Professor Bert Vaes (u0087897)
Organisatie:	KU Leuven
Dienst:	Academisch Centrum voor Huisartsgeneeskunde
Discipline:	Masterproef
Extra groepsleden:	Wim De Mol wim.demol@student.kuleuven.be r0449384

De verstrekte informatie toont aan dat het onderzoek in het kader van de masterproef een zuivere literatuurstudie betreft en dat er op geen enkele wijze gebruik wordt gemaakt van proefdieren, proefpersonen of menselijk lichaamsmateriaal.

Dit type onderzoek vereist geen goedkeuring van een gemachtigde commissie voor medische ethiek.

Onder voorbehoud van de volledigheid en correctheid van de door u verstrekte gegevens, krijgt u hierbij het akkoord om het onderzoek in het kader van de masterproef te starten. Deze mail dient als bewijs van goedkeuring mocht u uw onderzoek wensen te publiceren.

Wij willen u erop attent maken dat u zelf verantwoordelijk blijft voor uw onderzoek. Bovendien doet elke wijziging aan de door u verstrekte gegevens omtrent de onderzoeksopzet deze goedkeuring vervallen. U dient in dat geval een amendement te maken aan uw huidig dossier.