BMJ Open

Quality assessment and comparative analysis on the recommendations of current guidelines on screening and diagnosis of peripheral arterial disease: a systematic review

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To cite: Uyagu OD, Ofoegbu C, Ikhidero J, *et al*. Quality assessment and comparative analysis on the recommendations of current guidelines on screening and diagnosis of peripheral arterial disease: a systematic review. *BMJ Open* 2022;**12**:e061599. doi:10.1136/bmjopen-2022-061599

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-061599).

Received 01 February 2022
Accepted 21 August 2022

Check for updates

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ABSTRACT

Objectives There are several clinical practice guidelines available for peripheral artery disease (PAD). The paucity of strong evidence is known to give room for variations in recommendations across guidelines, with attendant confusion among clinicians in clinical practice. This study aims to conduct a quality assessment and comparative analysis on PAD screening and diagnostic recommendations in PAD management.

Selection Clinical practice guidelines written after 2010 and on or before 2020 were targeted. An exhaustive search was conducted through the major medical databases and websites of specialist international organisations of interest, and selection was made using our inclusion/exclusion criteria.

Setting Global. All guidelines written in English were included in this study.

Selected guidelines Nine guidelines were selected.

Outcomes The primary outcomes were the guidelines' quality and variations in screening and diagnostic recommendations in the selected guidelines.

Results Regarding quality, the guidelines had the lowest scores across the applicability and stakeholder involvement domains with means (SD) of 62 (9.9) and 65.3 (13), respectively. The highest score was clarity of presentation, with a mean (SD) of 86.8 (5.1). Also, the trend showed guideline quality scores improved over time. The guidelines unanimously offered to screen 'high-risk' patients, although there were some discrepancies in the appropriate age range and unavailability of strong evidence backing this recommendation. The guidelines harmoniously adopted the Ankle-Brachial Index as the initial diagnostic investigation of choice. However, concerning further diagnostic investigations and imaging, we found several discrepancies among the recommendations in the absence of strong evidence.

Conclusion Though the quality of the guidelines is shown to be improving over time, they perform poorly in stakeholder involvement and applicability domains, which could be influencing interest in research revolving around screening and diagnostic recommendations. Involving primary care providers and the public can be a possible solution.

PROSPERO registration number CRD42020219176.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This review, unlike previous studies, focused on recent peripheral arterial diseases (PAD) guidelines written after 2010 and reflects a synthesis of the current state of guideline quality and the most recent recommendations in PAD management regarding screening and diagnosis.
⇒ Complex data has been aggregated, comparatively assessed using thematic analysis and the results presented in concise and straightforward forms using texts, charts and tables.
⇒ By using rigorous systematic review methodology and a mixed qualitative and quantitative approach to the data analysis, this study has revealed the current areas of strengths and weaknesses of the quality of the PAD guidelines.
⇒ Qualitative analyses are inherently challenging to process, especially when dealing with clinical practice guidelines (CPGs) that contain large amounts of information; the process was cumbersome and time-consuming with the inevitable loss of data during the thematic classification process.
⇒ The search strategies were executed exclusively in English language labouring under the auspices that the major PAD CPGs will have an English language translation, so it is possible that some guidelines written within the study time frame were not captured due to this limitation.

INTRODUCTION

Atherosclerotic disease is an umbrella term for the world's leading cause of mortality and morbidity.[1] Peripheral artery disease (PAD) is a major component of this group of disorders after cerebrovascular and coronary artery disease, sharing the same risk factors as other atherosclerotic conditions.[2] Interestingly, according to data from the REACH (Reduction of Atherothrombosis for Continued Health) registry, it was observed that individuals with PAD do not achieve risk factor

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control as frequently as those with coronary artery disease (CAD) and cerebrovascular disease (CVD). In addition, they had higher levels of mortality comparatively.[3] The apparent explanation is that PAD is the most underdiagnosed and poorly treated atherosclerotic disease. PAD is a chronic medical disease with an asymptomatic phase of variable duration, with some individuals progressing into the symptomatic phase. Optimal management mainly involves early identification of the condition (screening and diagnosis), optimal medical management, which requires risk factor modification (through pharmacological and non-pharmacological methods), supervised exercise therapy and sometimes revascularisation.

Clinical practice guidelines (CPGs) have methodically developed statements to guide physicians and patients in making safe healthcare decisions based on the best available evidence.[4 5] Currently, there are some CPGs outlining best practices in the management of PAD. The quality of the CPGs varies between the authoring organisations and is also influenced by time as new evidence comes to light, ushering changes to guideline recommendations. As such, systematic reviews on the guidelines of particular disorders are often conducted; this study will review the quality of the guidelines available on PAD and assess the variations in their recommendations regarding the core aspects of management. A few partial reviews have been conducted on aspects of PAD guidelines in the past.[6–8] Our study encompasses all aspects of PAD. Management from screening and diagnosis, through medical management to revascularisation and follow-up. Due to the volume of findings, the paper has been split into three papers, which is the first of the series. This paper encompasses the quality assessment and critical analysis of recommendations across screening and diagnostic recommendations. Also, we have limited the publication date range for the CPGs from after the year 2010 until 2020 to get the most recent information on PAD management recommendations, unlike the previous reviews, which scanned guidelines over a wide range of time. As such, the risk of evaluating outdated information is avoided.

As outlined in our published protocol,[9] this paper aims to elucidate with diligent analysis, evaluation and crisp data presentation of the quality of the current guidelines on PAD, with recommendations on their suitability for use in clinical practice. In addition, we intend to review the long-standing debate on screening and diagnostic recommendations to ascertain the level of variation between authoring organisations. We expect that there should be greater levels of harmony with new evidence compared with older guideline reviews. Also, areas of interest where recommendations vary due to low-level evidence will be elucidated.

MATERIALS AND METHODS

A systematic search was conducted, and eligible guidelines were selected based on the attributes listed in the PICAR (Population, Intervention, Comparator, Attribute, Recommendation Characteristics) statement of our published protocol (available in online supplemental appendix 1).[9] The Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement were used as a reference to report items and results in this study.[10]

Patient and public involvement statement

Patients who are members of the Peripheral Arterial Diseases Support Group (https://www.facebook.com/groups/pad.pvd.support/members) were involved in this study's design (in modelling the research objectives). The Way to My Heart.org (https://www.thewaytomyheart.org/) founded this support group. The patient public involvement is coordinated through the group's leaders/founders (also, patients are actively involved in providing support to their fellow patients), who are advisory members to the research team. They have identified this research as a priority area for clinicians who care for patients with PAD. The group members have been informed of this study's results through their leadership. The support group will also participate in publicising the study after publication.

Search strategy

A systematic search was performed to identify relevant CPGs on PAD. One reviewer (ODU) conducted the search and extraction in line with the inclusion and exclusion criteria, and this was independently verified by a second reviewer (CO). A third reviewer (JI) was called in to resolve differing results. We developed a concept table to generate appropriate search terms (Medical Subject Headings, free-text vocabulary, key words) depending on the database's peculiarities. Databases searched included Scopus (which includes Embase and MEDLINE), TRIP and Cochrane. The search also included guideline developer websites such as NICE, SIGN, NIH, GIN and websites for national academic societies. Details of the search strategies can be found in online supplemental appendix 2 and the protocol.

Selection of guidelines

In line with our protocol, guidelines that met the following inclusion criteria were selected.

1. The guideline is a CPG developed for people with PAD.
2. The guideline covers recommendations regarding screening, non-pharmacological and pharmacological interventions, surgical and follow-up management.
3. The guidelines were written after 2010 and in or before 2020.
4. The guideline is the most recent version.
5. The guideline is available online.
6. Related or international academic organisations wrote the guideline.

Our exclusion criteria were.

1. The topic is only mentioned in the guideline.
2. The guideline is limited to a specific aspect of PAD management, such as screening, pharmacological management, etc.

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Outcomes

The primary outcome sought in this study were; Guideline Quality and Guideline recommendations on screening and diagnostic methods. Secondary outcome data included guideline characteristics; year of writing, funding source, writing language, location and website/source.

Quality assessment

In this study, the updated AGREE-II instrument was used to assess the quality of the selected guidelines. The AGREE-II instrument is a 23-item tool with international certification that evaluates the six methodological quality domains of a guideline, including scope and purpose, stakeholder involvement, the rigour of development, clarity of presentation and applicability and editorial independence.[11] As was written in the protocol, the assessment was conducted by four reviewers (as recommended by the tool's developers to minimise bias) using the instrument to assess all selected guidelines. The reviewers scored each guideline across each domain on a Likert scale of 1 through 7 (from strongly disagree to strongly agree). In addition, the reviewers gave an overall score of the guidelines on a similar Likert scale. As such, each guideline has two sets of scores: (a) the domain scores and (b) the overall score for the guideline. The details for the scoring system of the AGREE instrument are outlined in the protocol.[9]

The overall quality assessment was arrived at using the domain scores in line with the study protocol. Guidelines with four or more domains scored over 60% would be regarded as 'strongly recommended for use in practice'; if scores of most domains (four or more) ranged from 30% to 60%, the guideline was considered 'recommended for use with some modification'. Those with domain scores (four or more) less than 30% were regarded as 'not recommended for use in practice'. The overall guideline scores were used as a supporting statistic only and did not directly contribute to the grading of guideline quality. The data set for the quality appraisal is readily available in a public database.[12]

Guideline recommendations

The recommendations were extracted into a matrix in Microsoft Excel sheets. Then thematic analysis was used to organise the recommendations into themes which allowed us to summarise the information into tables for comparison. The strength of recommendations and level of evidence was extracted and displayed in the tables for each recommendation. Each guideline used its grading method, which we harmonised using our grading system for the purpose of comparison for this study (tables 1 and 2).

One reviewer performed extractions and then reviewed for completeness and consistency by another reviewer, after which comparisons were made across the guidelines.

RESULTS

Search results

The initial search identified 3149 citations. The flowchart (figure 1) shows how we systematically eliminated the guidelines by removing duplicates, previous versions and guidelines written outside the date range, screening the title and abstracts for citations not related to the topic, removing those which were not CPGs and finally eliminating those which targeted aspects of PAD. Management of special populations. In the end, we had nine CPGs, which were included in this study for analysis.[13–21]

Table 1 Harmonising recommendation strength grading system across the guidelines

Grading of recommendations										
	Grading for this study	**NICE 2012**	**VASSA 2012**	**CEVF 2013**	**AHA/ACC 2016**	**S3 2016**	**ESC 2017**	**SVS 2019**	**EVSM 2019**	**Asian Consensus 2020**
For	Strong; A	Strong words (offer, measure, advice etc).	Class I	Adopted ESC model	Class I	A	Class I	Grade 1	Class I	Adopted AHA 2016
	Moderate; B	Less confident words, eg, 'Consider'.	Class IIa		Class IIa	B	Class IIa	Grade 2	Class IIa	
	Weak; C		Class IIb		Class IIb	0	Class IIb		Class IIb	
	Ungraded: D					Consensus recommendation, insufficient evidence		Good practice statement		
Against	No benefit; N				Class III; No benefit		Class III		Class III	
	Harm; H	Do not offer.	Class III		Class III; harm					

NICE 2012; National Institute for Health and Care Excellence; Peripheral arterial disease: diagnosis and management Clinical guideline 147. VASSA 2012; Vascular Society of Southern Africa; Peripheral Arterial Disease guideline. 2012. CEVF 2013; Consensus Document on Intermittent Claudication from the Central European Vascular Forum (CEVF)—third revision (2013). AHA/ACC 2016; 2016 American Heart Association/American College of Cardiology; Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease. S3 2016; Ärzteblatt DÄG Redaktion Deutsches. The Diagnosis and Treatment of Peripheral Arterial Vascular Disease. ESC 2017; 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). SVS 2019; Joint guidelines of the Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies. Global vascular guidelines on the management of chronic limb-threatening ischaemia. ESVM 2019; European Journal of Vascular Medicine. Guideline on peripheral arterial disease. 2019. Asian Consensus; Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease. 2020.

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Table 2 Harmonising level of evidence grading system across the guidelines

Grading of evidence									
Grading for this study	**NICE 2012**	**South Africa 2012**	**CEVF 2013**	**AHA 2016**	**S3 2016**	**ESC 2017**	**SVS 2019**	**EVSM 2019**	**Asian Consensus 2020**
High-level evidence, eg, multiple RCT or meta-analysis; 1	Sufficient evidence	Level A	Adopted ESC system.	Level A	Degree 1 a	Level A	Level A	Level A	Adopted AHA 2016
					Degree 1b				
					Degree 1c				
Middle level; single RCT—non-randomised studies; 2	Insufficient evidence	Level B		Level B-R	Degree 2a – 2 c	Level B	Level B	Level B	
				Level B-NR	Degree 3a – 3b				
Low level; expert opinions, case reports, etc; 3		Level C		Level C-LD	Degree 4	Level C	Level C	Level C	
				Level C-EO	Degree 5				

NICE 2012; National Institute for Health and Care Excellence; Peripheral arterial disease: diagnosis and management Clinical guideline 147. VASSA 2012; Vascular Society of Southern Africa; Peripheral Arterial Disease guideline. 2012. CEVF 2013; Consensus Document on Intermittent Claudication from the Central European Vascular Forum (CEVF)—third revision (2013). AHA/ACC 2016; 2016 American Heart Association/American College of Cardiology; Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease. S3 2016; Ärzteblatt DÄG Redaktion Deutsches. The Diagnosis and Treatment of Peripheral Arterial Vascular Disease. ESC 2017; 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). SVS 2019; Joint guidelines of the Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies. Global vascular guidelines on the management of chronic limb-threatening ischaemia. ESVM 2019; European Journal of Vascular Medicine. Guideline on peripheral arterial disease. 2019. Asian Consensus; Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease. 2020.
RCT, randomised controlled trial .

Guideline characteristics

The guidelines included are presented in table 3. They were written after 2010 and before or in 2020. Most of the guidelines (eight) were written in English, except the German guideline, which was written in German. The extended German guideline was translated into English for analysis, while a short version was already translated into English. Two guidelines did not state their source of funding (Vascular Society of Southern Africa (VASSA) and Central European Vascular Forum (CEVF)). The overall AGREE score on guideline quality ranged from 68 to 84.

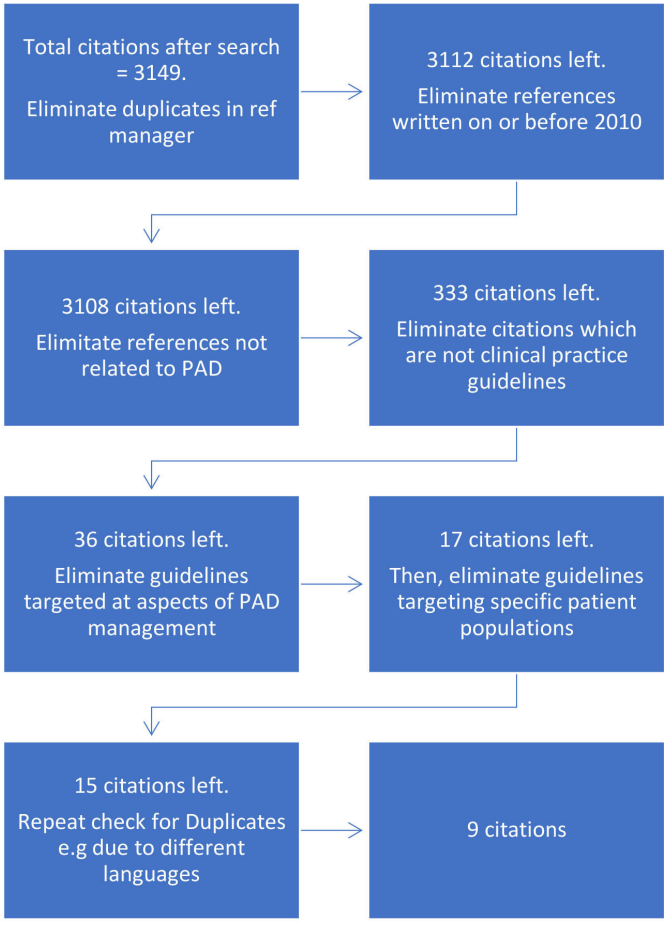

Figure 1 Flow chart of the search strategy. PAD, peripheral artery disease.

Guideline appraisal

The standardised scores for each guideline were calculated according to the formula provided by the AGREE tool developers.[10] The scores were displayed with a radar chart which allowed for easy comparison of all the guidelines included in this study across domains in figure 2. To give a general overview of the domains, Scope and Purpose; range 60–90, with a mean (SD) of 78.4 (11.4), Stakeholder Involvement; range 50–88, with a mean (SD) of 65.3 (13), Rigour of Development; range 43–82, with a mean (SD) of 70 (11.7), Clarity; range 75–94, with a mean (SD) of 86.8 (5.1), Applicability; range 46–77 with a mean (SD) of 62 (9.9), Editorial Independence; range 44–94 with a mean (SD) of 76.2 (18.6) and Overall quality; range 68–86 with a mean (SD) of 78.5 (7.2). The domains with the highest score were Clarity of presentation, Scope and purpose and Editorial independence in order of decreasing magnitude. In contrast, Applicability and Stakeholder Involvement tied domains with the lowest scores. Seven guidelines met the criteria for high-quality guidelines, while two, the CEVF and South African guidelines, were recommended for use with some modification as moderate quality guidelines.

Another area of interest was to see the performance of the guidelines over time. The line chart in figure 3 shows

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Table 3 Characteristics of included guidelines

CPG	Developing Organisation	Country	Language of publication	Date of search	Date of release	Publication site	Funding	Overall AGREE score
NICE 2012	National Health System	UK	English	2020	2012	https://www.nice.org.uk/guidance/cg147	NHS	71
VASSA 2012	One academic society	South Africa	English	2020	2012	http://www.vascularsociety.co.za/wp-content/uploads/2015/08/Peripheral-Arterial-Disease-VASSA-practice-guidelines-2012.pdf	Not stated	68
CEVF 2013	One academic society	Europe	English	2020	2013	https://www.minervamedica.it/en/journals/international-angiology/article.php?cod=R34Y2014N04A0329	Not stated	68
S3 2016	One academic society	Germany	German	2020	2016	https://www.aerzteblatt.de/int/archive/article/183158/The-diagnosis-and-treatment-of-peripheral-arterial-vascular-disease	German Society for Angiology	82
AHA/ACC 2016	Two academic societies	USA	English	2020	2016	https://www.sciencedirect.com/science/article/pii/S0735109716369029?via%3Dihub	No commercial sponsor	83
ESC 2017	Two academic societies	Europe	English	2020	2017	https://academic.oup.com/eurheartj/article/39/9/763/4095038	No commercial sponsor	82
SVS 2019	Three academic societies	Global	English	2020	2019	https://linkinghub.elsevier.com/retrieve/pii/S0741521419303210	No commercial sponsor	82
ESVM 2019	One society	Europe	English	2020	2019	https://econtent.hogrefe.com/doi/full/10.1024/0301-1526/a000834?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org	No external sponsor	86
Asian Consensus 2020		Asia	English	2020	2020	https://www.jstage.jst.go.jp/article/jat/27/8/27_53660/_article	No external sponsor	86

CPG; clinical practice guideline. NICE 2012; National Institute for Health and Care Excellence; Peripheral arterial disease: diagnosis and management Clinical guideline 147. VASSA 2012; Vascular Society of Southern Africa; Peripheral Arterial Disease guideline. 2012. CEVF 2013; Consensus Document on Intermittent Claudication from the Central European Vascular Forum (CEVF)—third revision (2013). AHA/ACC 2016; 2016 American Heart Association/American College of Cardiology; Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease. S3 2016; Ärzteblatt DÄG Redaktion Deutsches. The Diagnosis and Treatment of Peripheral Arterial Vascular Disease. ESC 2017; 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). SVS 2019; Joint guidelines of the Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies. Global vascular guidelines on the management of chronic limb-threatening ischaemia. ESVM 2019; European Journal of Vascular Medicine. Guideline on peripheral arterial disease. 2019. Asian Consensus; Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease. 2020.

the composite scores across domains for each guideline plotted over time. We can see clearly that the general trend shows the guidelines increasing in quality from 2012 through 2020.

Guideline recommendations

Screening recommendations

All included guidelines unanimously recommend screening high-risk groups, as seen in table 4 (expanded table available in online supplemental appendix 3). Recommendations against screening groups not at risk were given by the American College of Cardiology/American Heart Association (ACC/AHA) guideline and the Asian Consensus. The strength of recommendations was predominantly strong (except for the AHA guideline and Asian Consensus Statement). The evidence levels for this recommendation were predominantly moderate except for the German S3 guideline, which relied on strong evidence and European Society of Cardiology (ESC), which used weak evidence.

In those with no additional risk factors, the age range for screening recommendations with the more recent guideline written after 2016 (AHA/ACC, ESC and the Asian Consensus paper) suggest screening adults over 65 years of age, while the older guidelines (VASSA and CEVF) suggest screening for those over 70 years.

The guidelines made unanimous recommendations for using Ankle Brachial Index (ABI) as the screening tool, with the older guidelines recommending further testing in the face of normal ABI in high-risk groups. Only the CEVF guideline suggested a screening interval of 2–3 years in high-risk groups regarding a screening interval. Risk factor modification for high-risk groups is recommended by four guidelines.

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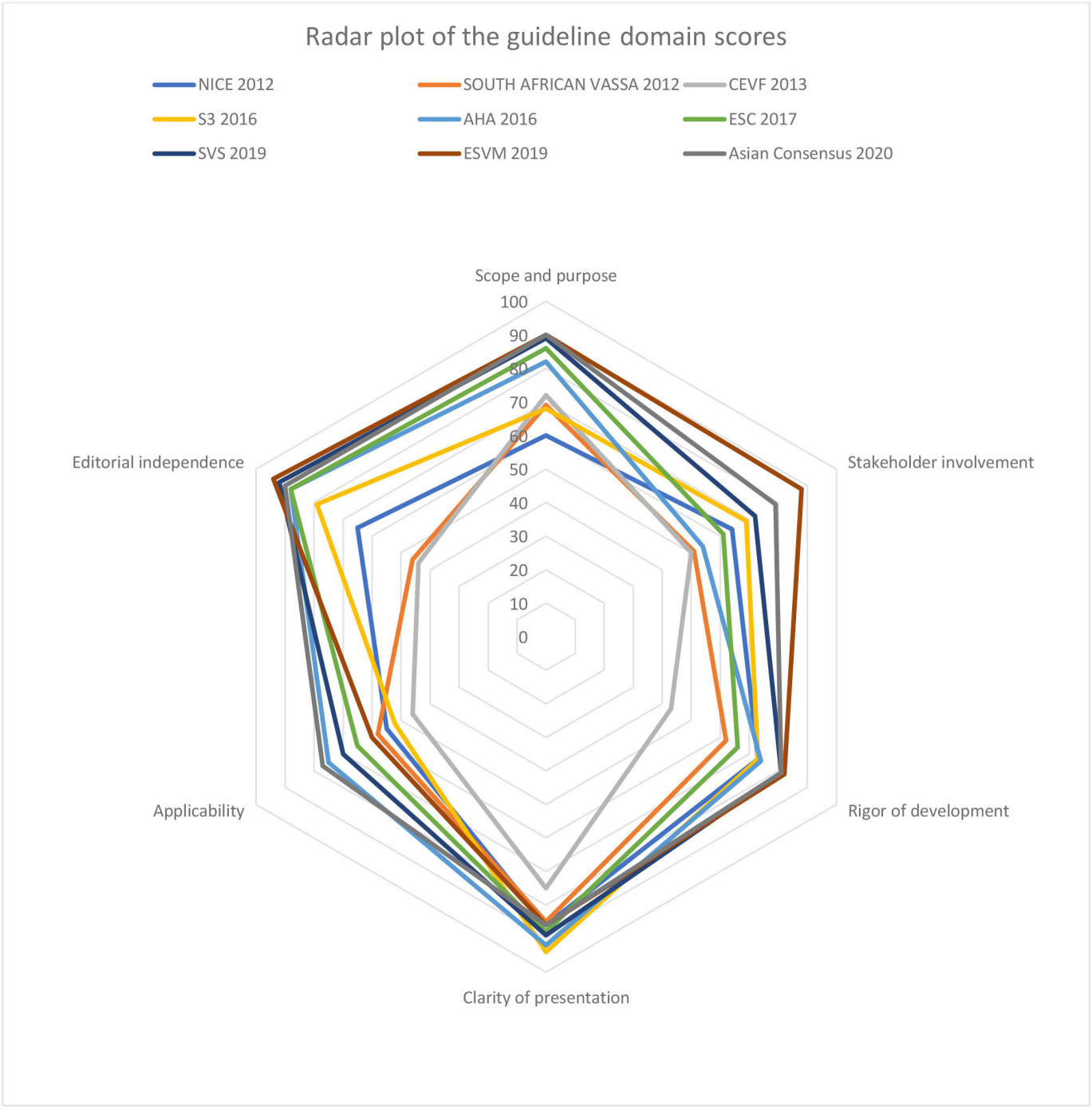

Figure 2 Radar chart showing the domain scores of the included guidelines. NICE 2012; National Institute for Health and Care Excellence; Peripheral arterial disease: diagnosis and management Clinical guideline 147. VASSA 2012; Vascular Society of Southern Africa; Peripheral Arterial Disease guideline. 2012. CEVF 2013; Consensus Document on Intermittent Claudication from the Central European Vascular Forum (CEVF) - 3rd revision (2013). AHA/ACC 2016; 2016 American Heart Association/ American College of Cardiology; Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease. S3 2016; Ärzteblatt DÄG Redaktion Deutsches. The Diagnosis and Treatment of Peripheral Arterial Vascular Disease. ESC 2017; 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). SVS 2019; Joint guidelines of the Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies. Global vascular guidelines on the management of chronic limb-threatening ischemia. ESVM 2019; European Journal of Vascular Medicine. Guideline on peripheral arterial disease. 2019. Asian Consensus; Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease. 2020. AHA, American Heart Association; CEVF, Central European Vascular Forum; ESC, European Society of Cardiology; ESVM, European Journal of Vascular Medicine; NICE, National Institute for Health and Care Excellence; SVS, Society for Vascular Surgery.

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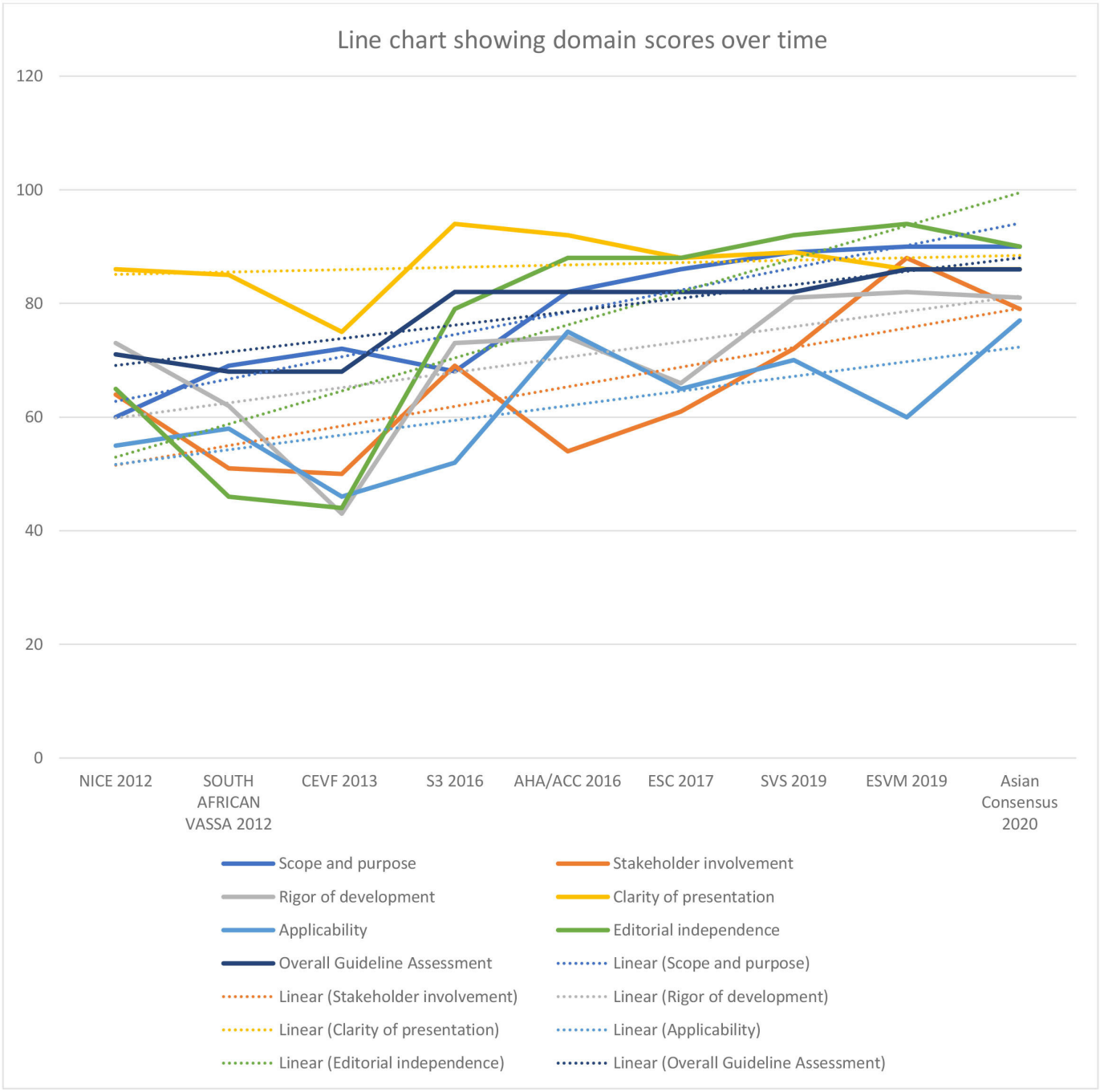

Figure 3 Time trend chart for the domain scores of the included guidelines. NICE 2012; National Institute for Health and Care Excellence; Peripheral arterial disease: diagnosis and management Clinical guideline 147. VASSA 2012; Vascular Society of Southern Africa; Peripheral Arterial Disease guideline. 2012. CEVF 2013; Consensus Document on Intermittent Claudication from the Central European Vascular Forum (CEVF) - 3rd revision (2013). AHA/ACC 2016; 2016 American Heart Association/ American College of Cardiology; Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease. S3 2016; Ärzteblatt DÄG Redaktion Deutsches. The Diagnosis and Treatment of Peripheral Arterial Vascular Disease. ESC 2017; 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). SVS 2019; Joint guidelines of the Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies. Global vascular guidelines on the management of chronic limb-threatening ischemia. ESVM 2019; European Journal of Vascular Medicine. Guideline on peripheral arterial disease. 2019. Asian Consensus; Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease. 2020. ACC, American College of Cardiology; AHA, American Heart Association; CEVF, Central European Vascular Forum; ESC, European Society of Cardiology; ESVM, European Journal of Vascular Medicine; NICE, National Institute for Health and Care Excellence; SVS, Society for Vascular Surgery; VASSA, Vascular Society of Southern Africa.

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Table 4 Summary of the screening recommendations for the included guidelines

CPG	Recommendation	Strength	Evidence	Target population	Screening test	Further testing	Intervals	Intervention for high- risk groups
NICE 2012	NR	–	–	–	–			
VASSA 2012	For	A	2	Increased risk*	ABI	Recommended†		Recommended†
CEVF 2013	For	A	2	Increased risk*	ABI	Recommended†	2–3 years	Recommended†
S3 2016	For	A	1	Increased risk	ABI			
AHA/ACC 2016	For	B	2	Increased risk	ABI			Recommended†
	Against	N	2	No risk				
ESC 2017	For	A	3	Increased risk	ABI			Recommended†
SVS 2019	NR	–	–	–				
EVSM 2019	NR	–	–	–				
Asian Consensus 2020	For	B	2	Increased risk	ABI			–
	Against	N	2	No risk				

CPG; clinical practice guideline. NICE 2012; National Institute for Health and Care Excellence; Peripheral arterial disease: diagnosis and management Clinical guideline 147. VASSA 2012; Vascular Society of Southern Africa; Peripheral Arterial Disease guideline. 2012. CEVF 2013; Consensus Document on Intermittent Claudication from the Central European Vascular Forum (CEVF)—third revision (2013). AHA/ACC 2016; 2016 American Heart Association/American College of Cardiology; Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease. S3 2016; Ärzteblatt DÄG Redaktion Deutsches. The Diagnosis and Treatment of Peripheral Arterial Vascular Disease. ESC 2017; 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). SVS 2019; Joint guidelines of the Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies. Global vascular guidelines on the management of chronic limb-threatening ischaemia. ESVM 2019; European Journal of Vascular Medicine. Guideline on peripheral arterial disease. 2019. Asian Consensus; Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease. 2020. ABI; Ankle-Brachial Index NR; no recommendations.
*View full table in online supplemental appendix for parameters that suggest increased risk according to the guideline.
†View the full table in the online supplemental appendix for details of recommendations suggested by the guideline.

Diagnostic recommendations

The guidelines unanimously decided to use the ABI as the initial testing tool with predominantly strong recommendations (except VASSA, which issued a consensus recommendation). These were based on moderate-level evidence, mostly except for the ESC and European Journal of Vascular Medicine, which used low-level evidence as shown in table 5 (expanded table available in online supplemental appendix 4). Furthermore, the guidelines recommended further testing with methods such as Exercise ABI, transcutaneous oxygen pressure (TcP02), pulse waveform, skin perfusion pressure (SPP), etc, in a wide variety of circumstances, most especially when the result of the ABI is ambivalent. The recommendations were largely ungraded, and when backed with evidence, these were with low-level evidence. Notably, the National Institute for Health and Care Excellence (NICE) guideline recommends no further testing due to insufficient evidence of their utility.

Regarding imaging, six guidelines recommended Doppler ultrasound scan (DUS) as the first-line imaging modality, with four making a strong recommendation. There was wide variation in the level of evidence used in making this recommendation. While contrast-enhanced magnetic resonance angiography (CE-MRA) and CT angiography (CTA) were unanimously recommended as additional imaging, there was variation in the circumstances in which they are to be used. Evidence levels for the recommendations for these imaging modalities ranged between middle and low. Three guidelines noted digital subtraction angiography (DSA) as the gold standard for imaging in PAD. Five guidelines unanimously agreed that this modality should be reserved for cases where the arterial networks could not be adequately visualised with the other modalities.

DISCUSSION

Overall, nine guidelines were identified and analysed in this study. In line with the study objectives, the quality of the guidelines was appraised using the AGREE tool, with the results summarised in table 3 and figures 1 and 2. This study found low scores across the applicability and stakeholder involvement domains. The low scores in applicability can be explained by the fact that most of the analysed guidelines did not mention monitoring or auditing criteria. Also, there was an ambiguous representation of the facilitators and barriers to implementing the guideline recommendations. Furthermore, aside from the CEVF guidelines, we observed that general practitioners (GPs), patients and public involvement were poorly represented in the guideline development committees, resulting in low stakeholder involvement scores. This is particularly of interest, given that PAD is a largely underdiagnosed and highly prevalent condition, especially among patients seen in primary care where they can and should be identified.[22] Improved GP and public involvement will improve the adoption of guideline recommendations, ultimately translating into improved patient care through early identification, which will impact a public health scale

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Table 5 Summary of the diagnostic recommendations across the included guidelines

	ABI			Further testing			Imaging												Screening for AAA.			Screening for CAD		
							DUS			CE-MRA			CTA			DSA								
CPG	Rec.	Str.	Evid.	Rec.	Str.	Evid.	Rec.	Str.	Evid.	Rec.	Str.	Evid.	Rec.	Str.	Evid.	Rec.	Str.	Evid.	Rec.	Str.	Evid.	Rec.	Str.	Evid.
NICE 2012	For	A	2	Against	4		First line	A	1–3	Second line	A	1–2	For; third line	A	1–2	–			–			–		
VASSA 2012	For	CR		For	4		First line	4		For*	A	2	For			Gold standard	A	2	–			–		
CEVF 2013	For	A	2	For	4		For	4		For			For			–			For	4		For	D	
S3 2016	For	A	2	For	4		First line	A	1	For			For			Gold standard	4		–			–		
AHA 2016	For	A	2	For	A–B	2–3	For	A	2	For	A	2	For	A	2	Gold standard	A-B	2–3	For	B	2	N	D	
ESC 2017	For	A	3	For	4		First line	A	3	For	A	3	For	A	3				–			–		
SVS 2019	For	A	2	For	A–B	2–3	First line	B	2	For	B	2	For	B	2	For	4		–					
ESVM 2019	For	A	2–3	For	I–IIb	2–3	First line	A	2	For	A	2	For	A	2	For	A	2	–			–		
Asian Consensus 2020	For			For	A–B	2–3	For	A	2	For	A	2	For	A	2	First line in CLI	A	3	For	IIa	B-NR	Against	H	3

CPG; clinical practice guideline. NICE 2012; National Institute for Health and Care Excellence; Peripheral arterial disease: diagnosis and management Clinical guideline 147. VASSA 2012; Vascular Society of Southern Africa; Peripheral Arterial Disease guideline. 2012. CEVF 2013; Consensus Document on Intermittent Claudication from the Central European Vascular Forum (CEVF)—third revision (2013). AHA/ACC 2016; 2016 American Heart Association/American College of Cardiology; Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease. S3 2016; Ärzteblatt DÄG Redaktion Deutsches. The Diagnosis and Treatment of Peripheral Arterial Vascular Disease. ESC 2017; 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). SVS 2019; Joint guidelines of the Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies. Global vascular guidelines on the management of chronic limb-threatening ischaemia. ESVM 2019; European Journal of Vascular Medicine. Guideline on peripheral arterial disease. 2019. Asian Consensus; Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease. 2020. Rec.; recommendations. Str.; strength of recommendations. Evid.; evidence. DUS; Doppler ultrasound scan. CE-MRA; contrast-enhanced magnetic resonance angiography. CTA; CT angiography. DSA; digital subtraction angiography. AAA; aortic abdominal aneurysm. CAD; coronary artery disease. CLI; critical limb ischaemia.

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given the high prevalence of people living with PAD. A 2016 estimate placed age-standardised rates at 1930 (95% CI: 1702 - 2202) per 100 000 for women and 1658 (95% UI: 1457 to 1900) per 100 000 for men.[23] Furthermore, we noticed an improvement in the guidelines across time in all domains in our study (figure 3), and this effect was present when we compared scores in this study to those done previously. The rigour of development scores particularly exemplifies this. The line chart in figure 3 clearly shows the rigour improving in the guidelines as they get more recent, just as observed in previous PAD guideline quality assessments. Unsurprisingly, we noticed better scores across the domains in this review compared with the previous studies.[6–8] Hence we can confidently say that the PAD guidelines are improving over time which is encouraging.

With regards to the recommendations on screening, we observed increased harmony across the guidelines of interest (over the study period) as opposed to the heterogeneity in the recommendations found in previous reviews, which included much older guidelines. Despite the underlying deficiency in high-quality evidence, that is, randomised controlled trials (RCTs) specifically designed to compare screening versus non-screening for PAD are still lacking across the guidelines. However, there is a general harmony in the recommendation to screen 'high risk' patients. The best evidence supporting screening comes from the VIVA study,[24] where combined screening for aortic abdominal aneurysm (AAA), PAD and hypertension was offered to men aged 65–74. The PAD research community continues to anticipate an RCT to address this topic confidently. In addressing the high-risk group, there was some conflict regarding age and general silence on the contribution of gender, which is well known to influence cardiovascular risk.[25] Furthermore, in this study, we observed that just one guideline proffered a recommendation on screening intervals for PAD, further highlighting the gaps created by the absence of clear evidence.

In this paper, we also reviewed the recommendations for diagnosing PAD. We found no discrepancy in using ABI in conjunction with clinical history and physical examination for the initial diagnosis of PAD, as solid evidence exists for this recommendation. However, there is ample evidence to show that there are occasions when ABI readings are difficult to rely on, for example, in conditions associated with hardened arteries such as diabetes.[26] In such settings, other methods were made across the guidelines for using such methods as Exercise ABI, Toe-Brachial Index (TBI), TcP02, pulse waveform, SPP, among others. There is sparse evidence backing these recommendations with attendant variations in the circumstances in which they should be used. Six guidelines strongly support the use of TBI in situations where there may be arterial hardening, such as diabetes, based on moderate-level evidence. Additionally, we noticed the more recent guidelines (written after 2016) relied on weak-to-moderate level evidence as opposed to the older ones, which relied more on consensus. So, while more evidence is finding its way into the guidelines clarifying this topic, we look forward to more extensive studies being conducted to enhance clarity. Furthermore, as with the recommendations on screening, these areas are of research interest to primary care physicians who are poorly represented in the PAD guideline writing groups could explain the apparent lack of interest in these topics.

The guidelines agreed that imaging is reserved for patients with confirmed PAD via initial testing methods, for whom revascularisation is being considered. The available imaging techniques suggested in the guidelines were uniform, including DUS, CTA, CE-MRA and DSA. It is widely acknowledged that place of practice, availability of enabling equipment, local policies and healthcare funding modalities offer some variation in the sequence/circumstances in which each modality should be chosen. For these reasons, rather than based on solid evidence, the majority (six guidelines) recommended that DUS be used as the first-line imaging of choice because it is readily available and offers the least risk to the patients (table 5). Conversely, most guidelines also agreed that DSA should be reserved for cases where the arterial architecture remains ambiguous despite imaging with the other modalities due to elevated risk levels associated with its use.

And finally, regarding screening for other arterial diseases in other vascular beds, most of the guidelines were silent. Perhaps there appears to be no additional benefit to be obtained from this. Three guidelines, CEVF, AHA and the Asian Consensus, did make recommendations. All three guidelines recommended screening for AAA via ultrasound scan, two of them, AHA and the Asian Consensus, relied on evidence that shows that PAD is a strong independent risk factor for AAA. However, the CEVF guideline recommends screening for CAD based on consensus recommendations. In contrast, the AHA and Asian Consensus cautioned against screening for arterial disease in other vascular beds, stating that current evidence does not justify the benefit, especially since patients with PAD should be placed on best medical therapy (BMT). Current evidence has established that people living with PAD have higher rates of atherosclerotic arterial disease in other arterial beds (CAD, CVD, renal artery disease).[27] So long as there is no need for vascularisation, the treatment for all these conditions remains BMT, including risk factor optimisation that the patient with PAD already benefits from. Justifying screening for these conditions will require evidence showing that revascularising asymptomatic forms of these diseases will result in better mortality and morbidity rates, which is currently unavailable.

There were some obvious limitations to this study. First, this review used thematic qualitative analysis in synthesising guideline recommendations for comparison. Given the large volume of information contained in the guidelines, some loss of vital information was inevitable during data analysis. Extensive efforts were made to minimise

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these losses by using consistent rigorous and systematic approaches while organising the data into themes for comparation. Second, during the literature search for relevant CPGs, we exclusively conducted our search strategies in English. As such, it is not impossible that some relevant guidelines written during this period were not captured in this study.

CONCLUSION

The quality of PAD guidelines have been improving consistently over time. Nonetheless, future guideline writers/updates should consider focusing on the guideline applicability and stakeholder involvement domains. There is less variation in screening recommendations in the recent guidelines, but a dearth of evidence persists, which could be solved with better stakeholder involvement among guideline writing committees. Finally, more research is needed to provide better evidence and thus improve guideline recommendations on imaging options for PAD.

ETHICS APPROVAL STATEMENT

Being a systematic review that does not involve human subjects or other sensitive data, there was no need to seek ethical approval.

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Contributors ODU was responsible for the initial concept, design and is responsible for the overall content as guarantor of the study. All authors, ODU, CO, JI, OE, EC, AA and OO, participated in the concept and design, extraction, analysis and interpretation of the data, critical revision of the manuscript and approval of the final version to be published.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. The data generated in this study are publicly available at http://doi.org/10.11922/sciencedb.01479.

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REFERENCES

1 Herrington W, Lacey B, Sherliker P, *et al*. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. *Circ Res* 2016;118:535–46.
2 Barquera S, Pedroza-Tobías A, Medina C, *et al*. Global overview of the epidemiology of atherosclerotic cardiovascular disease. *Arch Med Res* 2015;46:328–38.
3 Cacoub PP, Abola MTB, Baumgartner I, *et al*. Cardiovascular risk factor control and outcomes in peripheral artery disease patients in the reduction of atherothrombosis for continued health (reach) registry. *Atherosclerosis* 2009;204:e86–92.
4 Medicine I of, Guidelines C to A the PHS on CP. *Clinical practice guidelines: directions for a new program*. National Academies Press, 1990.
5 Murad MH. Clinical practice guidelines: a primer on development and dissemination. *Mayo Clin Proc* 2017;92:423–33.
6 Ferket BS, Spronk S, Colkesen EB, *et al*. Systematic review of guidelines on peripheral artery disease screening. *Am J Med* 2012;125:198–208.
7 Barriocanal AM, López A, Monreal M, *et al*. Quality assessment of peripheral artery disease clinical guidelines. *J Vasc Surg* 2016;63:1091–8.
8 Chen Q, Li L, Chen Q, *et al*. Critical appraisal of international guidelines for the screening and treatment of asymptomatic peripheral artery disease: a systematic review. *BMC Cardiovasc Disord* 2019;19:17.
9 Uyagu OD, Ofoegbu C, Ikhidero J, *et al*. Quality assessment and comparative analysis on the recommendations of current guidelines on the management of peripheral arterial disease: a systematic review protocol. *BMJ Open* 2021;11:e047980.
10 Moher D, Liberati A, Tetzlaff J, *et al*. Reprint—preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Phys Ther* 2009;89:873–80.
11 Brouwers MC, Kho ME, Browman GP, *et al*. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010;182:E839–42.
12 Uyagu OD, Ofoegbu C, Ikhidero J, *et al*. Quality assessment and comparative analysis on the recommendations of current guidelines on the management of peripheral arterial disease: a systematic review protocol. *BMJ Open* 2021;11:e047980.
13 NICE. Overview | Peripheral arterial disease: diagnosis and management | Guidance [online]. Available: https://www.nice.org.uk/guidance/cg147 [Accessed 6 Dec 2021].
14 Layden J, Michaels J, Bermingham S, *et al*. Diagnosis and management of lower limb peripheral arterial disease: summary of NICE guidance. *BMJ* 2012;345:e4947.
15 Andreozzi GM, Kalodiki E, L Gašpar L, *et al*. Consensus Document on Intermittent Claudication from the Central European Vascular Forum (C.E.V.F.)-3rd revision (2013) with the sharing of the Mediterranean League of Angiology and Vascular Surgery, and the North Africa and Middle East Chapter of International Union of Angiology. *Int Angiol* 2014;33:329–47.
16 Ärzteblatt DÄG Redaktion Deutsches. The diagnosis and treatment of peripheral arterial vascular disease [online]. Available: https://www.aerzteblatt.de/int/archive/article?id=183158 [Accessed 6 Dec 2021].
17 Gerhard-Herman MD, Gornik HL, Barrett C. AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American heart association Task force on clinical practice guidelines. *J Am Coll Cardiol* 20162017;69:e71–126.

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18 Aboyans V, Ricco J-B, Bartelink M-LEL, *et al*. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J* 2018;39:763–816.
19 Conte MS, Bradbury AW, Kolh P, *et al*. Global vascular guidelines on the management of chronic limb-threatening ischemia. *J Vasc Surg* 2019;69:3S-125S.e40
20 Frank U, Nikol S, Belch J, *et al*. ESVM guideline on peripheral arterial disease. *Vasa* 2019;48:1–79.
21 Abola MTB, Golledge J, Miyata T, *et al*. Asia-pacific consensus statement on the management of peripheral artery disease: a report from the Asian Pacific Society of atherosclerosis and vascular disease Asia-Pacific peripheral artery disease consensus statement project committee. *J Atheroscler Thromb* 2020;27:809–907.
22 Si S, Golledge J, Norman P, *et al*. Prevalence and outcomes of undiagnosed peripheral arterial disease among high risk patients in Australia: an Australian REACH sub-study. *Heart Lung Circ* 2019;28:939–45.
23 Johnson CO, Nguyen M, Zipkin B, *et al*. Abstract p135: prevalence of peripheral vascular disease: results of the global burden of disease 2016 study. *Circulation* 2018;137:AP135.
24 Lindholt JS, Søgaard R. Population screening and intervention for vascular disease in Danish men (VIVA): a randomised controlled trial. *Lancet* 2017;390:2256–65.
25 O'Neil A, Scovelle AJ, Milner AJ, *et al*. Gender/sex as a social determinant of cardiovascular risk. *Circulation* 2018;137:854–64.
26 Trevethan R. Subjecting the ankle-brachial index to timely scrutiny: is it time to say goodbye to the ABI? *Scand J Clin Lab Invest* 2018;78:94–101.
27 Agnelli G, Belch JJF, Baumgartner I, *et al*. Morbidity and mortality associated with atherosclerotic peripheral artery disease: a systematic review. *Atherosclerosis* 2020;293:94–100.

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Quality assessment and comparative analysis on the recommendations of current guidelines on the management of peripheral arterial disease: a systematic review protocol

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To cite: Uyagu OD, Ofoegbu C, Ikhidero J, *et al*. Quality assessment and comparative analysis on the recommendations of current guidelines on the management of peripheral arterial disease: a systematic review protocol. *BMJ Open* 2021;**11**:e047980. doi:10.1136/bmjopen-2020-047980

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-047980).

Received 15 December 2020
Accepted 16 August 2021

Check for updates

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ABSTRACT

Introduction Peripheral arterial disease (PAD) is the third leading atherosclerotic arterial disease. There is evidence that there is a high variation in the quality and recommendations of clinical practice guidelines for PAD, leading to the possibility of confusion among clinicians and patients. This study aims to conduct a quality assessment and comparative analysis of the clinical practice guidelines on PAD written between 2010 and 2020.

Method and analysis We aim to perform a systematic review of clinical practice guidelines written between 2010 and 2020. A search for guidelines will be conducted through medical databases Scope, Pubmed, TRIP, Guideline Clearinghouses and specialist international organisations' specific websites. Guidelines that meet the inclusion criteria will be extracted from the search result. The Appraisal of Guidelines for Research and Evaluation II (AGREE-II instrument) will assess the quality of the selected guidelines. The recommendations, level of evidence and other relevant information will be extracted in a datasheet for qualitative analysis. The score for each guideline's quality will be represented using charts and central tendency measures for comparison. The summary of recommendations will also be represented in tables for easy comparison for similarities and variations across sections. Finally, the level of evidence on which the recommendations are based will also be noted along with other significant characteristics such as the authors' financial relationship to the biomedical community. We aim to point out deficiencies present in current guidelines and elucidate areas where recommendations are made with low-level evidence. The results will enable the scientific community to design future research to fill in PAD management knowledge gaps.

Ethics and dissemination No ethical approval was sought. Dissemination will be via journal articles and conference presentations.

PROSPERO registration number CRD42020219176.

Strengths and limitations of this study

- This review will be exhaustive, critically appraising all aspects of clinical practice guidelines (CPGs) for peripheral arterial disease (PAD), from the quality, through screening and diagnosis, to all aspects of treatment (pharmacological and non-pharmacological), and to our knowledge, previous reviews have only reviewed aspects of the CPGs, so this will be the first all-encompassing review.
- In the previous reviews, Ferket and colleagues focused on reviewing recommendations on screening across the PAD guidelines, Barriocanal and colleagues focused on reviewing the quality of PAD CPGs and, finally, Chen *et al* reviewed guideline quality and recommendations across screening and pharmacological aspects of PAD management; however, this review will not be limited in that regard and as such will include quality assessment, and recommendations across screening, diagnosis and investigative evaluations, pharmacological and non-pharmacological interventions.
- Our review will focus on the most recently written CPGs, that is, those written within the last 10 years with an expectation that the more recent advancements revealed through clinical trials and improved standards for writing CPGs should reflect in this work when compared with the previous reviews.
- This study, being a systematic review that will not involve patient recruitment and using a qualitative methodology, will be cost-effective, furthermore, since a qualitative approach is to be used for the CPG recommendation synthesis is that the underlying reasons for variations can be explored in detail with the potential of exposing knowledge gaps in PAD and atherosclerosis management.
- Qualitative analysis is inherently difficult to analyse and summarise especially as there is so much information contained in the CPGs, as such, distilling all that information into useful summaries will be a daunting task, with the potential loss of vital information that may be difficult to prevent and also, given the large amount of information in the CPGs, data extraction will be a time-consuming process.

INTRODUCTION AND BACKGROUND

Atherosclerotic vascular diseases remain the world's leading cause of mortality today despite dramatic declines in trend over the

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last few decades.[1] Epidemiological data show that behind ischaemic heart disease and stroke, peripheral arterial disease (PAD) is the third most common atherosclerotic arterial disease.[2–5]

Despite its significant contribution to morbidity and mortality globally, there had been a paucity in the number of randomised clinical trials and high-quality systematic reviews of randomised clinical trials on PAD with consequent low-quality recommendations in practical guidelines. Over time, the results of high-powered RCT have been published with others on the way, which we expect to influence the more recent clinical practice guidelines (CPGs). Also, several recommendations in available guidelines were reached via expert consensus.[6] It is no surprise that reviews of existing guidelines have revealed variations in PAD treatment recommendations in the past.[7 8]

CPGs are methodically developed statements aimed at guiding physicians and patients in making safe healthcare decisions based on the best available evidence.[9 10] The last 30 years have witnessed a skyrocketing in developing CPGs,[11] calling into question quality issues; consequently, several reputable organisations have continued to improve the standards for CPG developments.[12–14] Ideal CPG recommendations are based on strong evidence.[15] However, high-level evidence is often unavailable for specific situations for several reasons, giving room for introducing various forms of bias with consequent variations in recommendations across various CPG developers for the same clinical scenario.[16]

Literature search reveals high interest among academics in reviewing CPG's quality for their specialty areas with numerous studies on the topic. Interestingly, very few reviews have been conducted regarding the CPGs available for PAD. Also, to our knowledge, the available reviews focused on aspects of the PAD guidelines such as reviews on screening recommendations,[17] reviewing the quality of the CPGs and reviewing the pharmacologic recommendations.[18 19] In this study, we aim to conduct a more exhaustive review of the most recent guidelines (written in the last 10 years).

In 2012, a systemic review was conducted on eight guidelines published between 2003 and 2011, comparing their quality and recommendations for PAD screening. The study results revealed that the majority of the guidelines favoured screening for PAD. However, three guidelines did not advocate for PAD screening due to the absence of appropriate clinical trials. The studies were considered inappropriate because the available clinical trials were conducted on individuals with established PAD and were unsuitable to be the basis for clinical advice for the general population. The guidelines' quality was also assessed using the Appraisal of Guidelines for Research and Evaluation II (AGREE-II) tool, with results revealing a range between 33% and 81%.[17]

Further work was done on this topic by another team of researchers who reviewed seven guidelines written between 2006 and 2012. The study focused on the quality of the guidelines using the AGREE-II instrument. Their results revealed a significant variation similar to the 2012 study with a range of 45%–72%. The reviewed CPGs were found to have high scores in clarity and editorial independence but with low scores in applicability and rigour of development. In their recommendations, they stated that only one CPG could be recommended for use without modification.[19]

The most recent review assessed CPGs written between 2000 and 2017. This study was a more exhaustive review. They assessed the guideline quality using the AGREE-II instrument and the recommendations across screening and pharmacological management. The result revealed a quality range between 39% and 73%, similar to the earlier reviews. However, this work found the CPGs to have low scores in the rigour of development (similar to the previous study) and editorial independence (unlike the previous study where they scored high marks). This difference may be because Chen and colleagues reviewed more CPGs. It was also observed that just two of the CPGs reached the standard for conflict of interest from the Institute of medicine. Regarding the screening recommendations, 8 guidelines out of 14 recommended screening (at different strengths) while the others stated insufficient evidence or were against it. Treatment recommendations also showed conflicts concerning target values for lipid-lowering and antiplatelet therapy.[18]

In summarising these findings, the PAD guidelines show considerable variation in quality and variations in their recommendations. The paucity of high-quality research could explain these variations for the specific topics for which recommendations are needed, prompting the need for reliance on lower strengths of evidence such as expert consensus or research conducted on established disease participants. Clearly, there is a knowledge gap that can easily be filled with the right form of interest from the research community.

The rationale for the study

Systematic reviews of CPGs are used to systematically identify, assess and summarise the current state of guidance on a clinical topic. Well-written systemic reviews that adhere to a rigorous methodological approach and use transparent reporting to identify knowledge gaps where improvement in current recommendations can be achieved.[20]

The previous reviews on the CPGs for PAD have revealed a wide variation in the quality and variations in screening and pharmacologic management recommendations.[17–19] However, these reviews were restricted in their comparators, focusing on aspects of the CPGs rather than performing a more holistic review.

Furthermore, the previous reviews included CPGs written over a wide range of time. Advancements in treatment options of atherosclerotic diseases have advanced considerably in the last decade, with consequent paradigm shift occurring after the results of relatively recent randomised clinical trials. We expect that this will be

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reflected in more recent CPGs compared with their older counterparts.

The findings of this review will be compared with those of the previous reviews. Significant areas of interest, such as changes in overall quality over time and changes in the strength of pharmacological management recommendations, will be made manifest. Also, a nouvelle comparison of non-pharmacological management will be conducted across the guidelines.

Aim

A quality assessment and comparative analysis of the CPGs on PAD written between 2010 and 2020 to assess the quality of the CPGs and identify the gaps in evidence as reflected by the nature of their recommendations.

Objectives

1. To compare the quality of the CPGs on PAD written between 2010 and 2020 using the AGREE-II instrument.
2. To compare the recommendations for screening for PAD across CPGs on PAD written between 2010 and 2020.
3. To summarise the recommendations for pharmacologic management across CPGs on PAD written between 2010 and 2020.
4. To critically appraise the non-pharmacologic recommendations across CPGs on PAD written between 2010 and 2020.
5. To collate and contrast the follow-up recommendations across CPGs on PADs written between 2010 and 2020.

METHODOLOGY

Patient and public involvement statement

Patients who are members of the Peripheral Arterial Diseases Support Group (https://www.facebook.com/groups/pad.pvd.support/members) were involved in this study's design (in modelling the research objectives) and will be involved in the study when it commences. The Way to My Heart.org (https://www.thewaytomyheart.org/) founded this support group. The patient public involvement will be coordinated through the group's leaders/founders (also patients themselves are actively involved in providing support to their fellow patients) who are advisory members to the research team. They have identified this research as a priority area for clinicians who provide care to patients living with PAD. The group members will be informed of this study's results through their group page on Facebook in a newsletter suitable for a non-specialist audience. The patients and public will also be sought in the development of an appropriate method of dissemination.

Guideline identification

A systematic search will be conducted, and eligible guidelines selected based on the attributes listed in table 1. These selected guidelines will be comparatively assessed across quality and recommendations. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement will be used as a reference to report items and results in this review.[21]

Table 1 Population, Clinical Indication, Comparators, Attributes of Eligible guidelines, Recommendation characteristics (PICAR) statement

	Study-specific criteria
Population/clinical condition	Adults 18 and above, with peripheral arterial disease
Intervention	All forms of management.
Comparators	No comparator. All aspects of PAD management will be taken into consideration in the comparisons
Attributes of eligible CPGs	Language; no restriction
	Time range; published from 2010 to 2020
	Publishing region; global
	Versions; latest versions only
	Development process; explicitly evidence-based
	System of rating evidence; must be available and stated clearly
	Scope; to cover all aspects of PAD management
	Recommendations; must be available and clearly stated
Recommendation characteristics	Recommendations covering screening, diagnosis, pharmacological and non-pharmacological management are of interest.
	Levels of confidence; an explicit level of confidence must accompany each recommendation
	Locating recommendations; within the CPG's texts, tables, algorithms and or decision paths

CPG, clinical practice guideline; PAD, peripheral arterial disease.

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One reviewer will perform the search and extraction for recommendations, which will be validated by another reviewer. A third reviewer will be consulted to resolve disagreements if they arise. The AGREE-II instrument will be used to assess the quality of the selected guidelines by four reviewers. One reviewer will extract the recommendations, and another reviewer will validate this.

Search strategy

A systematic search will be performed to identify relevant CPGs on PAD. A concept table will be used to generate appropriate search terms (MeSH, Free text vocabulary, Key Words) depending on the database's peculiarities.

The searches will be conducted on the following databases:

1	Medical databases	PubMed
		Scopus (which includes Embase and MEDLINE)
		TRIP
		Cochrane
2	Guideline developer website	NICE
		SIGN
		National Library of Medicine—National Institute of Health (USA)
		Canadian Medical Association Infobase
		NewZealand Guidelines Group
		Guidelines International Network
		National Guidelines Clearinghouse
3	Expert contributions/ websites of specific societies	

Example: A draft of the search strategy for PubMed via MEDLINE.

1. Arterial Disease, Peripheral.
2. Arterial Diseases, Peripheral.
3. Disease, Peripheral Arterial.
4. Diseases, Peripheral Arterial.
5. Peripheral Arterial Diseases.
6. Peripheral Artery Disease.
7. Artery Disease, Peripheral.
8. Artery Diseases, Peripheral.
9. Disease, Peripheral Artery.
10. Diseases, Peripheral Artery.
11. Peripheral Artery Diseases.
12. Peripheral Arterial Disease [MeSH].
13. Intermittent Claudication [MeSH].
14. Limb Ischemia.
15. 1 OR 2OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14.
16. Screening.
17. Treatment.
18. Management.
19. Diagnosis.
20. Pharmacological.
21. Diagnosis[MeSH Terms].
22. Therapy[MeSH Terms].
23. 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22.
24. Guidelines.
25. Guideline.
26. Standards.
27. Practice guideline[MeSH Major Topic]
28. 24 OR 25 OR 26 OR 27.
29. Quality.
30. Recommendations.
31. Quality improvements[MeSH Terms]).
32. 29 0R 30 OR 31.
33. 15 AND 23 AND 28 AND 32.

The search was conducted on 11 December 2020. Result: 7014 references.

Guideline selection

The extracted references will be searched through the title and abstract for guidelines that meet the inclusion and exclusion criteria outlined below. This selection will be done by the lead researcher and verified by another researcher. Conflicts of ideas will be resolved by consensus by taking a third researcher's opinion to minimise selection bias risk.

Inclusion criteria

1. The guideline is developed for people with PAD.
2. The guideline covers recommendations regarding screening, non-pharmacological and pharmacological interventions.
3. The guidelines were written between 2010 and 2020.
4. The guideline is the most recent version.
5. The guideline is available online.
6. Related or international academic organisations wrote the guideline.

Exclusion criteria

1. The topic is only mentioned in the guideline.
2. The guideline is limited to a specific aspect of PAD management, such as screening, pharmacologic management, etc.

Outcomes: the outcomes in this study are

1. Guideline quality.
2. Guideline recommendations.

Quality assessment

Instrument

The updated AGREE-II instrument (online supplemental appendix 1) will be used to assess the quality of the selected guidelines.[22] The AGREE-II instrument is a 23-item tool with international certification that evaluates

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Table 2 Example of domain scoring for scope and purpose

	Item 1	Item 2	Item 3	Total
Appraiser 1	5	6	6	**17**
Appraiser 2	6	6	7	**19**
Appraiser 3	2	4	3	**9**
Appraiser 4	3	3	2	**8**
Total	**16**	**19**	**18**	**53**

the six domains of methodological quality of a guideline, including scope and purpose, stakeholder involvement, rigour of development, clarity of presentation and applicability and editorial independence.[23] The assessment will be conducted by four reviewers (as recommended by the developers of the tool to minimise bias) using the instrument to assess all selected guidelines. The reviewers will score each guideline across each domain on a Likert scale of 1 through 7 (from strongly disagree to strongly agree).

In addition, the reviewers will give an overall score of the guidelines on a similar Likert scale. As such, each guideline will have two sets of scores: (1) the domain scores and (2) the overall score for the guideline.

Scoring

Domain scores are calculated by summing up all the individual items' scores in a domain and scaling the total percentage of that domain's maximum possible score. The example on scoring below was extracted from the user manual.

To give an example, if four appraisers give the following scores for domain 1 (dummy scores are generated for scope and purpose in table 2):

Maximum possible score=7 (strongly agree) × 3 (items) × 4 (appraisers)=84.

Minimum possible score=1 (strongly disagree) × 3 (items) × 4 (appraisers)=12.

The scaled domain score will be:

$$\frac{\text{Obtained maximum score}-\text{Minimum possible score}}{\text{Maximum possible score}-\text{Minimum possible score}}$$

$$\frac{53-12}{84-12} \times 100 = \frac{41}{72} \times 100 = 57\%$$

Interpreting domain scores

There are no fixed cut-offs for high-quality or low-quality guidelines set by the instrument developers. The scores of the domains will be compared against each other between the guidelines. The overall assessment will be arrived at using the domain scores, and for this purpose, we have decided to set out cut-offs in line with the study conducted by Chen and colleagues because of its practicability.[18] If most (four or more) domains scored over 60%, a guideline would be regarded as 'strongly recommended for use in practice'; if scores of most domains (four or more) ranged 30%–60%, the guideline would be regarded as 'recommended for use with some modification'; if most of the domains (four or more) scored less than 30%, the guideline would be regarded as 'not recommended for use in practice.'

Interpreting the overall guideline scores

This will be used as an additional matrix for assessing the guideline as a supporting statistic. It will not provide any direct contribution for the final assessment into high-quality or low-quality guidelines.

Data extraction and management for quality scores

The data from each appraiser for the AGREE instrument will be entered into an initial excel sheet for upload into SPSS V.22 for analysis. The four appraisers' scores will be aggregated within the SPSS datasheet in line with the formula highlighted above. The final scores, which will be used to generate the recommendation for using the guidelines, will be presented in the Results sections. The preliminary datasheet templates are attached below (see online supplemental appendix 2).

Guideline recommendations

Recommendations extraction

A recommendation matrix will be developed based on the focus areas of the data synthesis in line with the research objectives. The recommendations will be extracted across screening, pharmacological and non-pharmacological treatment modalities for comparative assessment. Systematic methodology will be employed to harmonise specific details of the guidelines, which may vary due to differences in terminology or differences in interventions/comparators. For example, recommendations will be harmonised into themes (thematic analysis), which can then be coded and entered into the software/datasheet.

Particular interest will be paid to the level of evidence on which the recommendations are based. A preliminary review of some guidelines shows variations in the grading system for the level of evidence. The evidence grading schemes for each guideline will be harmonised and standardised to enhance the data synthesis process. Evidence categories will be developed using an iterative process of refinement through discussions within the review team.

Other characteristics of interest, such as the data aimed at evaluating the financial relationship between guideline producers and the biomedical industry, and others outlined in the PICAR statement, will be extracted. A preliminary version of what the data extraction sheet will appear like is attached below, highlighting all the variables that will be extracted (see online supplemental appendix 3). As the study progresses, the datasheet is bound to evolve to fit the study's objectives better.

Recommendation data management

The recommendation data will be extracted using Nvivo software for qualitative data extraction and management. The extracted information will be summarised through qualitative/thematic analysis. The variables of interest are listed in table 3.

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Table 3 List of variables

S/no	Name of variable	Definition
1	Guideline name	Title of the published guideline.
2	Guideline organisation/society	The name of the organisation responsible for the publication of the guideline
3	Year	Year of publication
4	Funding	Source of funding for guideline production.
5	Country	The country where the guideline was produced
6	Target users	Endusers of the guideline
7	Guideline writers	The authors
8	Evidence grading system	The system used to grade the evidence on which the recommendations are made
9	Recommendations	The recommendations that were made in the guidelines for specific clinical scenarios.
10	Level of evidence	The strength of the evidence used in making a particular recommendation
11	Strength of recommendation	The level of confidence in the accuracy of the recommendation
12	Domain 1	First domain of the AGREE-II instrument; scope and purpose
13.	Domain 2	Second domain of the AGREE-II instrument; stakeholder involvement
14	Domain 3	Third domain of the AGREE-II instrument; rigour of development
15	Domain 4	Fourth domain of the AGREE-II instrument; clarity of presentation
16	Domain 5	Fifth domain of the AGREE-II instrument; applicability
17	Domain 6	Sixth domain of the AGREE-II instrument; editorial independence
18	Overall score	The appraisers overall score for the guideline
19	Cumulative scores for domains 1–6	The aggregate of the scores from the four reviewers
20	Cumulative of the overall score	The aggregate of the overall scores from the four reviewers
21	Final guideline recommendation	The final recommendation for the guideline based on the overall percentage score.

AGREE II, Appraisal of Guidelines for Research and Evaluation II.

RESULTS

1. Flowchart of search strategy.
2. Results of quality assessment using AGREE-II represented by bar charts/histograms, also +overall recommendations.
3. A tabular summary of screening recommendations for PAD.
4. A tabular summary of non-pharmacological recommendations for PAD.
5. A tabular summary of pharmacological recommendations for PAD.
6. Additional relevant information on the guidelines.

The study is proposed to be completed within a period of 26 weeks, with dedicated attention from all participants. The activity breakdown and allotted time for each activity are shown in table 4.

Significance of the study

This study's significant finding will be identifying low-grade recommendations in the available guidelines (recommendations based on low-level evidence). The only way to remedy this situation is for researchers to conduct appropriate-sized randomised controlled trials tailored to answering the recommendations' problems. These shortcomings will be highlighted in the results and discussions, paving the way for improved PAD CPGs in the future.

The results of this study will also serve as a guide for future CPG writers to pay attention to all aspects of CPG development, especially domains where they performed poorly in the quality assessment using the AGREE-II instrument.

Table 4 Timeline

1	Title adoption	Done
2	Develop protocol	4weeks
3	Study search	2weeks
4	Study selection	2 weeks
5	Data extraction—AGREE-II+recommendation extraction	8 weeks
6	Data analysis	2 weeks
7	Write up and discussion	4 weeks
8	Review and discussion	4 weeks
Total		**26 weeks**

AGREE II, Appraisal of Guidelines for Research and Evaluation II.

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Ethics and dissemination

Because this is a systematic review and no human subjects, we do not see the need to seek ethical approval.

We aim to disseminate this work through a journal publication and conference presentation. The work will also be disseminated through our Patient and Public Initiative Network.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

1 Herrington W, Lacey B, Sherliker P, *et al*. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. *Circ Res* 2016;118:535–46.
2 Chun D-I, Kim S, Kim J, *et al*. Epidemiology and burden of diabetic foot ulcer and peripheral arterial disease in Korea. *J Clin Med* 2019;8. doi:10.3390/jcm8050748. [Epub ahead of print: 25 05 2019].
3 Bediako-Bowan AA, Adjei GO, Clegg-Lamptey JN, *et al*. The burden and characteristics of peripheral arterial disease in patients undergoing amputation in Korle BU teaching Hospital, Accra, Ghana. *Ghana Med J* 2017;51:108–14.
4 Marrett E, DiBonaventura MdaCosta, Zhang Q. Burden of peripheral arterial disease in Europe and the United States: a patient survey. *Health Qual Life Outcomes* 2013;11:175.
5 Bakhai A. The burden of coronary, cerebrovascular and peripheral arterial disease. *Pharmacoeconomics* 2004;22 Suppl 4:11–18.
6 Behrendt C-A, Rieß H, Härter M, *et al*. [Guideline recommendations and quality indicators for invasive treatment of peripheral arterial disease in Germany : The IDOMENEO study for quality improvement and research in vascular medicine]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2018;61:218–23.
7 Hussain MA, Al-Omran M, Creager MA. Antithrombotic therapy for peripheral artery disease: recent advances. *J Am Coll Cardiol* 2018;29;71:2450–67.
8 Khariton Y, Patel KK, Chan PS, *et al*. Guideline-directed statin intensification in patients with new or worsening symptoms of peripheral artery disease. *Clin Cardiol* 2018;41:1414–22.
9 Murad MH. Clinical practice guidelines: a primer on development and dissemination. *Mayo Clin Proc* 2017;92:423–33.
10 Field MJ, Lohr KN. *Clinical practice guidelines: directions for a new program*. Washington: National Academies Press, 1990. http://scholar.googleusercontent.com/scholar?q=cache:VPqWGZMXHyYJ:scholar.google.com/&hl=en&as_sdt=0,5
11 Genuis SJ. The proliferation of clinical practice guidelines: professional development or Medicine-by-Numbers? *J Am Board Fam Pract* 2005;18:419–25.
12 Qaseem A*et al*. Guidelines international network: toward international standards for clinical practice guidelines. *Ann Intern Med* 2012;156:525–31.
13 Afshari A, De Hert S. Pitfalls of clinical practice guidelines in the era of broken science: Let's raise the standards. *Eur J Anaesthesiol* 2018;35:903–6.
14 Hollon SD, Teachman BA. Advantages of developing clinical practice guidelines using international standards. *Psychotherapy* 2019;56:340–6.
15 Culleton B. Evidence-based decision-making 4: development and limitations of clinical practice guidelines. *Methods Mol Biol Clifton NJ* 2015;1281:443–53.
16 Turner T, Misso M, Harris C, *et al*. Development of evidence-based clinical practice guidelines (CpGs): comparing approaches. *Implementation Sci* 2008;3:45.
17 Ferket BS, Spronk S, Colkesen EB, *et al*. Systematic review of guidelines on peripheral artery disease screening. *Am J Med* 2012;125:198–208.
18 Chen Q, Li L, Chen Q, Li Y, *et al*. Critical appraisal of international guidelines for the screening and treatment of asymptomatic peripheral artery disease: a systematic review. *BMC Cardiovasc Disord* 2019;19:17.
19 Barriocanal AM, López A, Monreal M, *et al*. Quality assessment of peripheral artery disease clinical guidelines. *J Vasc Surg* 2016;63:1091–8.
20 Johnston A, Kelly SE, Hsieh S-C, *et al*. Systematic reviews of clinical practice guidelines: a methodological guide. *J Clin Epidemiol* 2019;108:64–76.
21 Moher D, Liberati A, Tetzlaff J, *et al*. Reprint—preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Phys Ther* 2009;89:873–80.
22 Brouwers MC, Kho ME, Browman GP, *et al*. Agree II: advancing Guideline development, reporting and evaluation in health care. *Can Med Assoc J* 2010;182:E839–42.
23 Brouwers MC, Kerkvliet K, Spithoff K, *et al*. The agree reporting checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 2016:i1152.

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Pubmed

Research Question;

Is there a significant variation in the quality and treatment recommendations of recent clinical practice guidelines on peripheral arterial disease?

Concept table

	P	I	C	0
	Adults + Elderly Peripheral Artery Disease	Screening Non-pharmacological Pharmacological	None	Quality Recommendations
Concepts	Peripheral Artery disease. Chronic limb ischemia. Critical limb ischemia.	Treatment/Management	Guideline	Recommendations Quality
Free Text Terms	Arterial Disease, Peripheral. (tw) Arterial Diseases, Peripheral. (tw) Disease, Peripheral Arterial. (tw) Diseases, Peripheral Arterial. (tw) Peripheral Arterial Diseases. (tw) Peripheral Artery Disease. (tw) Artery Disease, Peripheral. (tw) Artery Diseases, Peripheral. (tw) Disease, Peripheral Artery. (tw)	Screening (tw). Treatment (tw). Management (tw). Diagnosis (tw). Pharmacological (tw)	Clinical (tw) practice (tw). Guideline (tw). Standards (tw).	Quality (tw) Standards (tw) Recommendations (tw)

	Diseases, Peripheral Artery. (tw) Peripheral Artery Diseases. (tw) Limb Ischemia (tw). Chronic (tw). Acute (tw).			
Controlled Vocabulary/MeSH	Peripheral Arterial Disease (mh) Intermittent claudication (mh). Lower extremity, ischemia (mh).	Diagnosis (mh). Therapy (mh).	Practice Guidelines as Topic / standards* (mh)	Quality Improvements. (mh) Quality Indicators. (mh)

((((((((((((((((((((((((((((((((Arterial Disease, Peripheral) OR (Arterial Diseases, Peripheral)) OR (Disease, Peripheral Arterial)) OR (Diseases, Peripheral Arterial)) OR (Peripheral Arterial Diseases)) OR (Peripheral Artery Disease)) OR (Artery Disease, Peripheral)) OR (Artery Diseases, Peripheral)) OR (Disease, Peripheral Artery)) OR (Diseases, Peripheral Artery)) OR (Peripheral Artery Diseases)) OR (Peripheral Arterial Disease[MeSH Terms])))) OR (intermittent claudication[MeSH Terms])) OR (limb ischemia)) AND (screening)) OR (treatment)) OR (management)) OR (diagnosis)) OR (pharmacological)) OR (Diagnosis[MeSH Terms])) OR (therapy[MeSH Terms])) AND (guidelines)) OR (guideline)) OR (standards)) OR (practice guideline[MeSH Major Topic])) AND (Quality)) OR (recommendations)) OR (quality improvements[MeSH Terms])

Example search 11/12/2020; 7014

1. Arterial Disease, Peripheral
2. Arterial Diseases, Peripheral
3. Disease, Peripheral Arterial
4. Diseases, Peripheral Arterial
5. Peripheral Arterial Diseases
6. Peripheral Artery Disease
7. Artery Disease, Peripheral
8. Artery Diseases, Peripheral
9. Disease, Peripheral Artery
10. Diseases, Peripheral Artery
11. Peripheral Artery Diseases
12. Peripheral Arterial Disease [MeSH]
13. Intermittent Claudication [MeSH]

14. Limb Ischemia
15. 1 OR 2OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. Screening.
17. Treatment.
18. Management.
19. Diagnosis
20. Pharmacological
21. Diagnosis[MeSH Terms]
22. Therapy[MeSH Terms]
23. 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22
24. Guidelines.
25. Guideline
26. Standards
27. Practice guideline[MeSH Major Topic]
28. 24 OR 25 OR 26 OR 27
29. Quality
30. Recommendations
31. Quality improvements[MeSH Terms])
32. 29 0R 30 OR 31
33. 15 AND 23 AND 28 AND 32

Search conducted on 11/12/2020. Result; 7014 references

DETAILS OF SYSTEMATIC SEARCH STRATEGY (20/12/2020 – 30/12/2020)

Scopus SEARCH = 942

TITLE-ABS-KEY ("Arterial disease, Peripheral" OR "Arterial diseases, Peripheral" OR "Disease, Peripheral arterial" OR "Peripheral Arterial Diseases" OR "Peripheral artery disease" OR "Artery Disease, peripheral" OR "Artery Diseases, Peripheral" OR "Disease, Peripheral Artery" OR "Diseases, Peripheral Artery" OR "Peripheral Artery Diseases" OR "Limb Ischemia" OR "Chronic limb ischemia" OR "Arterial occlusive disease" OR "Artery occlusive disease" OR "Arterial occlusive diseases" OR "Artery occlusive diseases" OR "Intermittent Claudication" AND treatment OR management OR screening OR diagnosis OR therapy AND "Clinical Practice Guideline" OR "Clinical Practice Guidelines" OR guideline OR guidelines OR guide OR standard OR standards OR "Practice Guideline" OR "Practice Guidelines" OR recommendations) AND (LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010)) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "NURS") OR LIMIT-TO (SUBJAREA , "NEUR") OR LIMIT-TO (SUBJAREA , "IMMU")) AND (LIMIT-TO (PUBSTAGE , "final")) AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (SRCTYPE , "j")) AND (EXCLUDE (PUBYEAR , 2010)) AND (EXCLUDE (SUBJAREA , "BIOC") OR EXCLUDE (SUBJAREA , "PHAR") OR EXCLUDE (SUBJAREA , "ENGI") OR EXCLUDE (SUBJAREA , "IMMU") OR EXCLUDE (SUBJAREA , "CENG") OR EXCLUDE (SUBJAREA , "SOCI") OR EXCLUDE (SUBJAREA , "ENVI") OR EXCLUDE (SUBJAREA , "AGRI") OR EXCLUDE (SUBJAREA , "MATE") OR EXCLUDE (SUBJAREA , "BUSI") OR EXCLUDE (SUBJAREA , "COMP") OR EXCLUDE (SUBJAREA , "MATH") OR EXCLUDE (SUBJAREA , "PHYS") OR EXCLUDE (SUBJAREA , "PSYC")) AND (EXCLUDE (EXACTKEYWORD , "Peripheral Occlusive Artery Disease"))

Pubmed Search = 1723

Search: ((((((((((((((((((((("Peripheral arterial disease"[MeSH Terms]) OR ("Peripheral arterial disease"[Text Word])) OR ("Arterial Disease, Peripheral"[Title/Abstract])) OR ("Arterial Diseases, Peripheral"[Title/Abstract])) OR ("Disease, Peripheral Arterial"[Title/Abstract])) OR ("Diseases, Peripheral Arterial"[Title/Abstract])) OR ("Peripheral Arterial Diseases"[Title/Abstract])) OR ("Peripheral Artery Disease"[Title/Abstract])) OR ("Artery Disease, Peripheral"[Title/Abstract])) OR ("Artery Diseases, Peripheral"[Title/Abstract])) OR ("Disease, Peripheral Artery"[Title/Abstract])) OR ("Diseases, Peripheral Artery"[Title/Abstract])) OR ("Peripheral Artery Diseases"[Title/Abstract])) OR ("limb ischemia")) OR (intermittent claudication[MeSH Terms])) OR (intermittent claudication[Text Word])) AND (therapy[MeSH Subheading])) OR (therapeutics[MeSH Terms])) OR (treatment[Text Word])) OR (treatment[Text Word])) OR (disease management[MeSH Terms])) AND (practice guideline[Publication Type])) OR (practice guidelines as topic[MeSH Terms])) OR (clinical practice guideline) Filters: Practice Guideline, in the last 10 years, Humans, Adult: 19+ years

TRIP database Search = 366;

(Peripheral, Arterial, Artery, Disease, Diseases, Guidelines, Guideline) (""Peripheral arterial disease" OR "Clinical practice guidelines" OR 'Peripheral artery disease" OR "Extremity Ischemia"") from:2010 to:2020. Filter; Guideline documents.

GUIDELINE DATABASES

1. Guidelines International Network Library

https://guidelines.ebmportal.com/

Phrase Search for “Peripheral arterial disease" Found = 6

2. National guideline clearing house through Alliance for the implementation of clinical practice guidelines

https://aicpg.org/ngc-summaries/

Phrase Search for “Peripheral arterial disease” Found = 3

3. Canadian Medical association clinical practice guideline infobase

https://joulecma.ca/cpg/homepage

Phrase Search for “Peripheral arterial disease” Found = 4

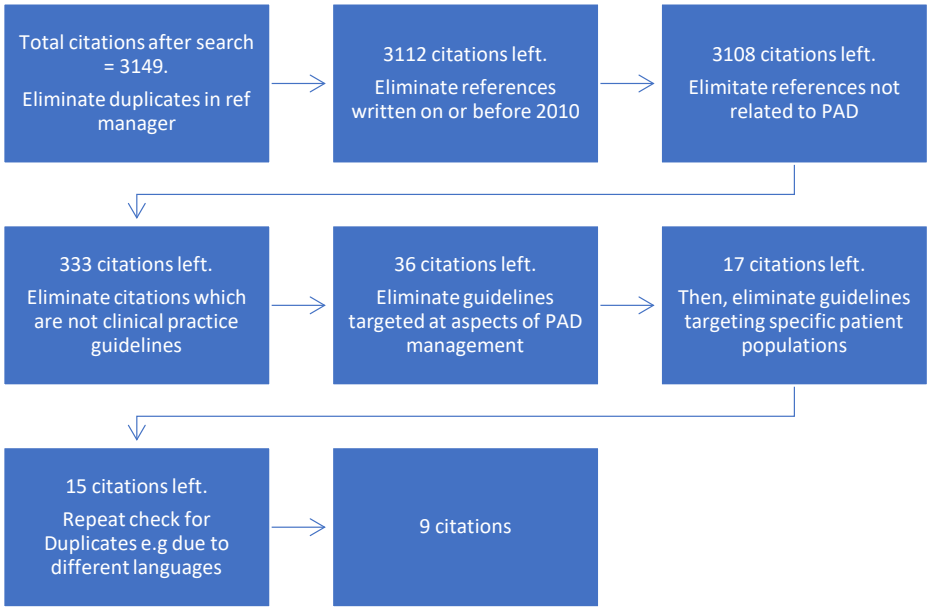
4. NICE

https://www.evidence.nhs.uk/

Phrase Search for “Peripheral arterial disease” Found = 105

Total citations = 3148

Scopus	942
Pubmed	1723
TRIP	366
Guidelines international network Library	6
National guideline clearing house through Alliance for the implementation of clinical practice guidelines	3
Canadian Medical association clinical practice guideline infobase	2
NICE	105
Targeted Internet search from expert recommendations	1
TOTAL	3148



	NICE 2012	South Africa 2012	CEVF 2013	S3 2016	ACC/AHA 2016		ESC 2017	SVS 2019	ESVM 2019	ASIAN Consensus 2020	
Recommendation	-	For	For	For	For	Against	For	-	-	For	Against
Strength of recommendation	-	I	I	A	IIA	III; No Benefit	I	-	-	IIA	III; No Benefit
Level of evidence	-	B	B	I	B-NR	B-NR	C	-	-	B-NR	B-NR
Target Population	-	Patients at risk; 1. Age < 50 years with diabetes mellitus and one additional risk factor (e.g., smoking, dyslipidaemia and hypertension) 2. Age 50 – 69 years with history of smoking and diabetes 3. Age 70 years or more 4. Leg symptoms with exertional symptoms (suggestive of claudication) or rest pain (ischaemic foot	In individuals whom; 1. Show arterial wall changes 2. Subjects > 70 years 3. Aged 60-69 with history of smoking or DM 4. <50 with DM +other atherosclerotic risk factors 5. >50 with metabolic syndrome	High Risk group (Not specified)	In Patients at increased risk of PAD; 1.Age >65 yn 2.Age 50–64 y, with risk factors for atherosclerosis (e.g., diabetes mellitus, history of smoking, hyperlipidemia, hypertension) or family history of PAD. 3.Age <50 y, with diabetes	In Patients not at an increased risk of PAD	1.Men and Women aged >65. 2.Men and Women aged <65 classified at high CV risk according to Esc guidelines 3.Men and Women >50 with family history of LEAD	-	-	Adopted AHA 2016	In Patients not at an increased risk of PAD

		pain) 5. Abnormal lower extremity pulse examination 6. Known atherosclerotic coronary, renal and carotid disease			mellitus and 1 additional risk factor for atherosclerosis. 4.Individuals with known atherosclerotic disease in another vascular bed (e.g., coronary, carotid, subclavian, renal, mesenteric artery stenosis, or AAA)						
Screening Test	-	ABI	ABI	ABI	ABI		ABI	-	-		ABI
Further testing	-	A more comprehensive workup of patients with PAD, considering the multiple risk factors for atherosclerosis and the polyvascular nature of the disease	Exercise ABI can be useful if ABI is normal in at risk individuals.	-	None		None	-	-		None

Intervention	-	- known to decrease their increased risk of myocardial infarction, stroke, and death. - Smoking cessation, lipid lowering drugs, and hypertensive medication.	- Interventions known to decrease their increased risk of myocardial infarction, stroke, and death. - Smoking cessation, lipid lowering drugs, diabetes, and hypertensive medication.	-	- Statins; improves cardiovascular outcomes - No benefit from SAPT.		Modification of risk factors to CVD. No benefit from SAPT.	-	-		-
Screening Intervals	-	Not stated	2-3 years	-	-	-	-	-	-		-

Item		NICE 2012			South Africa 2012			CEVR 2013			S3 2016		
		Recommendation	**Strength**	**Evidence**	**Recommendation**	**Strength**	**Evidence**	**Recommendation**	**Strength**	**Evidence**	**Recommendation**	**Strength**	**Evidence**
Initial Testing with ABI		Recommended for Initial diagnosis	Strong	Moderate	For	-	-	Recommended for initial diagnosis	I	B	Recommended for initial diagnosis	A	I
Further Testing for Diabetics		Against use of Pulse Oximetry. Insufficient evidence for TBI and doppler wave form analysis.		Insufficient evidence	-			*Toe systolic pressure suggested*	-	-	TBI For diabetics with an ABI >1.3		CR
Other Further testing		-	-		*Exercise ABI for claudicants. Toe pressure measurements and transcutaneous oxygen measurements in selected patients*		-	Exercise ABI for symptomatic patients with Normal ABI.	I	B	TBI and Pausatility index if ABI is implausible		CR
								Transcutaenous oxygen pressure for severe claudicants	-	-	Oscillography and light reflection rheography in conditions like media sclerosis or acral circulatory disorders		CR
											Stress test -Walking distance in Claudicants and for diagnosis in atypical complaints		CR
Imaging for diagnosis of anatomical location and severity of stenosis when revascularization is considered.	**DUS**	First - line	Strong	High - Low	First-Line			*All patients with Moderate – Severe/CLI*	-	-	First-Line	A	I
	CE-MRA	Second - line	Strong	High - Moderate	Useful in Aorto-Iliac Disease	I	A	*For patients with severe -CLI*	-	-	Inconclusive DUS. Interdisciplinary decision with regards to therapy		CR
	CTA	Third – line (If CE-MRA is not tolerated)	Strong	High - Moderate	Second-line (First line in Aorto-iliac disease)	IIa	B	*For patients with severe -CLI*	-	-	Inconclusive DUS. Interdisciplinary decision with regards to therapy		CR
	DSA				Gold standard. Reserved for prior to surgical intervention	I	B				Gold standard. Inconclusive DUS. Interdisciplinary decision with regards to therapy		CR
Screening Duplex USS scan for AAA, SAoA		-						*Screening with Doppler of the Supra-aortic arteries and abdominal aorta*	-	-			
Screening for CAD								*Always perform ECG and Echo*	-	-			

Item		ACC/AHA 2013			ESC 2017			SVS 2019		
		Recommendation	Strength	Evidence	Recommendation	Strength	Evidence	Recommendation	Strength	Evidence
Initial Testing with ABI		Recommended for Initial Diagnosis.	I	B-NR	Recommended for Initial Diagnosis.	I	C	Recommended for Initial Diagnosis.	I	B
Further Testing for Diabetics		-	-		-	-	-			
Other Further testing		TBI recommended when ABI >1.4	I	B-NR	TBI or Doppler wave form analysis or pulse volume recordings indicated for incompressible arteries or ABI > 1.4			TP and TBI in all patients with suspected CTLI and tissue loss	I	B
		Exercise ABI for non-joint leg related symptoms and normal or borderline ABI + Assessing functional status	I + IIa	B-NR + B-NR				Consider PVR, TcPO2 or SPP when ankle or toe pressure indices cannot be assesed	II	C
		TBI with waveform, TcPO2, SPP; For normal/borderline ABI with non-healing wounds or gangrene	IIa	B-NR						
Imaging for diagnosis of anatomical location and severity of stenosis when revascularization is considered.	DUS	An option for first line; individualized decision	I	B-NR	First Line Imaging for confirmation of LEAD	I	C	First line Imaging	II	B
					An option for anatomic categorization	I	C			
	CE-MRA	An option for first line; individualized decision	I	B-NR	An option for anatomic categorization	I	C	Option for second line imaging	II	B
	CTA	An option for first line; individualized decision	I	B-NR	An option for anatomic categorization	I	C	Option for second line imaging	II	B
	DSA (IA)	Gold standard. For confirmation when first line is inconclusive.	I	B-NR	-	-	-	Should be done for all patients with suspected CTLI	Good practice statement	
		First line in CLI	I	C-EO						
		Life limiting claudication with minimal response to BMT	IIa	C-EO						
		Should not be performed in asymptomatic PAD	III; Harm	B-R						
Screening Duplex USS scan for AAA, SAoA		Is Reasonable	IIa	B-NR	-	-	-	-	-	-
Screening for CAD		*Not recommended*	-	-	-	-	-	-	-	-

Item		ESVM 2019			Asian Consensus 2020		
		Recommendation	Strength	Evidence	Recommendation	Strength	Evidence
Initial Testing with ABI		ABI as appropriate initial test	I	B - C	Recommended for Diagnosis of PAD		
Further Testing for Diabetics		In diabetes mellitus and in all those with an ABI > 1.3, toe pressure measurements and calculation of the toe-brachial Index are recommended to detect PAD	I	B			
Other Further testing		Exercise ABI is useful in atypical presentations and ambiguous ABI at rest result	I	B	TBI, where available, should be measured to diagnose patients with suspected PAD when the ABI is greater than 1.40	I	B-NR
		In the presence of implausible ABI values, complementary methods such as TBI and calculation of pulsatility index are to be employed	II	B	Patients with exertional non-joint-related leg symptoms and normal or borderline resting ABI (> 0.90 and ≤ 1.40) should undergo exercise treadmill ABI testing to evaluate for PAD.	I	B-NR
		In the case of incompressible ankle arteries, in medial calcific sclerosis, acral circulatory disorders or ABI > 1.30, alternative methods such as the toe-brachial index, Doppler frequency analysis, oscillography or LRR or pulse volume recording may be considered	IIb	C	In patients with normal (1.00 – 1.40) or borderline (0.91 – 0.99) ABI in the setting of nonhealing wounds or gangrene, it is reasonable to diagnose CLI by using TBI with waveforms, transcutaneous oxygen pressure (TcPO2), or skin perfusion pressure (SPP).	IIa	B-NR
Imaging for diagnosis of anatomical location and severity of stenosis when revascularization is considered.	DUS	Method of choice for primary diagnosis and initial evaluation of the arterial architecture	I	B	DUS, CTA, or MRA of the lower extremities is useful to assess anatomic location and severity of stenosis for patients with symptomatic PAD in whom revascularization is considered.	I	B-NR
	CE-MRA	Additional diagnostic procedures –MRA, computed tomographic angiography CTA or DSA are recommended only if CCDS fails to sufficiently reveal the underlying pathology, and if proceeding to elective	I	B			
	CTA						
	DSA (IA)				First line in CLI	I	C-EO

		surgical revascularization					
		It is recommended that when findings are inconclusive, a second imaging method must be applied prior to invasive procedures. Individual risk profile and the diagnostic precision of the additional method must be considered in selecting the further diagnostical procedure.	I	B	Invasive angiography is reasonable for patients with lifestyle-limiting intermittent claudication with an inadequate response to GDMT for whom revascularization is being considered	IIa	C-EO
					Should not be performed in asymptomatic PAD	III; Harm	B-R
Screening Duplex USS scan for AAA, SAoA		-			Is Reasonable	IIa	B-NR
Screening for CAD		-			Not recommended	III;Harm	C-EO