Evidence overview: Automated ankle brachial pressure index measurement devices for assessing peripheral arterial disease in people with leg ulceration

This overview summarises the main issues the diagnostics advisory committee needs to consider. It should be read together with the final scope and the diagnostics assessment report.

1 Aims and scope

Leg ulcers are leg wounds that are slow to heal and usually develop on the inside of the leg, just above the ankle. When the leg ulcer is caused by a problem in the blood flow in the veins the treatment involves using compression, such as bandages or stockings. But strong compression therapy can disturb the arterial blood supply in the leg. It should not be offered to people with peripheral arterial disease (PAD), a common condition where a build-up of fatty deposits in the arteries restricts blood supply to legs.

To identify people with leg ulcers who should not have compression therapy, as part of a full clinical assessment, the ankle brachial pressure index (ABPI) is measured. Currently, this is done using a hand-held doppler ultrasound probe and a manually inflated blood pressure cuff to measure systolic pressures of the arteries in each limb (sphygmomanometer) and the ABPI is calculated manually. Lying down both for resting before the test and during the test is needed. The test can take up to an hour to complete and is often uncomfortable for people with leg ulcers. Because of the time and expertise needed for the assessment, referral to specialist services may be needed and time to assessment and treatment can be long.

Automated devices may make measuring ABPI more convenient for people with leg ulcers and free up staff time by reducing the length of time taken to

assess ABPI and any associated discomfort for the patient. They may be also easier to use. Improvement in the accuracy of detecting peripheral arterial disease could reduce time to treatment, leading to improved outcomes for people with leg ulcers.

Decision question

Are devices for automated assessment of ankle brachial pressure index a clinically and cost-effective alternative to a manual doppler test for assessing ankle brachial pressure index and peripheral arterial disease in people with leg ulcers?

Populations

People with leg ulcers who need assessment of ABPI.

Where data permits, the following subgroups may be considered:

- people with leg ulcers who need assessment of ABPI as part of their initial assessment
- people with leg ulcers or healed leg ulcers who need re-assessment of ABPI as part of monitoring
- people with diabetes, rheumatoid arthritis, systemic vasculitis, atherosclerotic disease, advanced chronic renal failure or other conditions in which arterial calcification is common
- people with sickle cell disease
- people who have had lymph nodes removed or damaged, limb amputation or other conditions where blood pressure cannot be measured on both arms or legs.

Interventions

Automated devices measuring ABPI and assessing arterial circulation using any one of the following:

- BlueDop Vascular Expert (BlueDop Medical) - doppler-based device with no cuffs
- boso ABI-system 100 (BOSCH + SOHN) - oscillometric device with 4 cuffs
- Dopplex Ability Automatic ABI System (Huntleigh Healthcare) - plethysmography-based device with 4 cuffs
- MESI ABPI MD (MESI) - oscilllometry and plethysmography-based device with 3 cuffs
- MESI mTABLET ABI (MESI) - oscilllometry and plethysmography-based device with 4 cuffs
- WatchBP Office ABI (Microlife) - oscillometric device with 2 cuffs
- WatchBP Office Vascular (Microlife) - oscillometric device with 2 cuffs

Decisions about care would be made using ABPI and any additional information provided by the devices, alongside all other information from the full clinical assessment.

Comparator

The comparator is handheld doppler probe and manual blood pressure sphygmomanometer for measuring ABPI and assessing arterial circulation.

The assessment can be done in for example community or primary care, or, if practitioners trained to do the manual doppler tests are scarce, in specialist vascular services.

Imaging (including duplex ultrasound scan, MR angiography or CT angiography) is considered the gold standard for detecting peripheral arterial disease but would not be used to assess PAD in people with leg ulcers in standard practice.

Healthcare setting

- Community (including people's homes, care homes, community hospitals, leg ulcer clinic)
- Primary care (GP practice)

- Secondary care

Further details, including descriptions of the interventions, comparator, care pathway and outcomes, are in the final scope for automated ABPI measurement devices for assessing PAD in people with leg ulceration.

2 Clinical effectiveness evidence

The external assessment group (EAG) did a systematic review to identify evidence on the clinical effectiveness and diagnostic accuracy of automated ankle brachial pressure index (ABPI) measurement devices for assessing peripheral arterial disease (PAD) in people with leg ulcers. Because there were not many studies in people with leg ulcers, the EAG also looked for evidence in people without leg ulcers. Find the methods and results on pages 14 to 57 of the diagnostics assessment report.

Overview of included studies

There were 24 studies reported in 26 publications that met the inclusion criteria for the systematic review. One of these was an ongoing study with unpublished interim results. All were observational studies. Six studies were done in the UK. Of the included studies, 15 were from elsewhere in Europe.

Only 2 studies focused on people with leg ulcers (1 on Dopplex Ability Automatic ABI System and 1 on MESI ABPI MD). Most studies included people who were referred to vascular service or had cardiovascular risk factors. Of the 24 studies, 2 studies evaluated BlueDop Vascular Expert, 4 studies boso ABI-system 100, 6 studies Dopplex Ability Automatic ABI System, 7 studies MESI ABPI MD and 4 studies WatchBP Office ABI. One study assessed both MESI ABPI MD and WatchBP Office ABI. No studies were found on MESI mTABLET ABI or WatchBP Office Vascular.

Most studies reported diagnostic accuracy data for detecting PAD. The automated device was compared with either manual doppler or a duplex ultrasound. All studies used an ABPI threshold of 0.9 for detecting PAD. The

healthcare professional assessing ABPI was most often a vascular specialist, a trained nurse or an experienced physician or technician. Two studies involved podiatrists and 1 study general practice nurses and healthcare assistants. Four studies were done in primary or community care, 16 in secondary care and 1 in both settings. Three studies were registry or survey-based studies.

Other outcomes reported included time needed to assess the ABPI, technical failures, and acceptability or experience of using the device. No studies were found on the effect of test results on clinical decision-making, time to treatment or the effects of automated assessment of ABPI on clinical outcomes. Some studies reported on results for people with diabetes. No data was available for other subgroups considered.

Find an overview of the included studies in table 4 on pages 26 to 31 of the diagnostics assessment report.

Study quality

The EAG assessed the quality of the diagnostic accuracy studies using the QUADAS-2 tool. They used QUADAS-2 with the QUADAS-C extension for the comparative accuracy study. Applicability concerns in the studies were generally low. But because of unclear reporting, the risk of bias in the studies was often unclear. In nearly half the studies it was unclear in which order the devices were used or if the healthcare professional assessing the test was unaware of the results of the automated device measurement or both. Five studies did not specify exclusion criteria. In 7 studies there was a concern over high risk of bias because they either did not let study participants rest long enough before testing or because data from more than 10% of participants were not included in the analysis. A further 7 studies did not provide enough information on the number of people included in the analysis or the length of the resting period before testing to determine the risk of bias level.

The EAG assessed the quality of the 2 observational studies that included people with leg ulcers using a Review Body for Interventional Procedures (ReBIP) checklist. The checklist assesses generalisability, sample definition and selection, description of the intervention, outcome assessment, adequacy of follow-up, and performing the analysis. The Dopplex Ability study by Welsh et al. (2016) included a representative sample, clearly defined inclusion and exclusion criteria and people at a similar stage of disease progression (in terms of leg ulcers). The MESI ABPI MD study by Green et al. (2020) did not report inclusion and exclusion criteria or enough information on if the sample was representative. Neither study provided enough information to assess whether study participants who dropped out of the study were similar to those who completed the study. But both studies collected data prospectively, delivered clearly defined interventions in an appropriate setting, and reported on important and objective outcomes.

In addition to the formal quality assessments, the EAG noted that reporting of the time needed to assess ABPI was often unclear. The studies did not consistently specify which elements of the ABPI assessment (for example resting, putting on the cuffs, measuring ABPI, calculating ABPI) were included in the estimates. Some studies provided a time estimate only for using the automated device and not the comparator.

Find details of the study quality assessments in Appendix 4 on pages 196 and 197 of the diagnostics assessment report.

BlueDop Vascular Expert

Diagnostic accuracy

One published study and an ongoing study with unpublished interim results were found comparing the performance of the BlueDop Vascular Expert with duplex ultrasound. ABPI was measured by a physician and vascular specialists (Kordzadeh et al. 2018) and in the ongoing study by [redacted]. There were some concerns over risk of bias. In the ongoing study,

[redacted]

Table 1 summarises the reported accuracy estimates for detecting PAD. The ongoing study reported [redacted] Find more details in table 6 on pages 41 to 53 of the diagnostics assessment report.

Table 1 Accuracy of BlueDop Vascular Expert to detect peripheral arterial disease in people without leg ulcers

Study	Reference device	Study population	Study size (PAD prevalence)	Sensitivity	Specificity
Kordzadeh et al. (2018)	Duplex ultrasound	People referred to vascular outpatient service	166 (not reported)	95%	90%
NCT05073510 (interim results to May 2022)	Duplex ultrasound	People with history of or suspected PAD referred for duplex ultrasound of the legs	[redacted]	[redacted]	[redacted]

Technical failures

In the ongoing BlueDop Vascular Expert study, vascular specialists recorded [redacted]

Time needed to assess ABPI

No studies that reported on time to assess ABPI were found.

Acceptability and experience of using the device

No BlueDop Vascular Expert studies in people with leg ulcers were found.

boso ABI-system 100

Diagnostic accuracy

Four studies compared the performance of the boso ABI-system 100 with either manual doppler or duplex ultrasound. Where reported, ABPI was measured by experienced healthcare professionals (Diehm et al. 2009; Wohlfart 2011) or a trained nurse (Jarai et al. 2018). There were some concerns over risk of bias. In particular, in Wohlfart et al. (2011) the resting period before testing was too short. Table 2 summarises the results from 3 studies that reported accuracy estimates for detecting PAD.

Diehm et al. (2009), a study in people with chronic, symptomatic PAD did not report sensitivity or specificity of the device but correlation and concordance data compared with manual doppler. In this study, Pearson product-moment correlation coefficient was 0.76. The difference between the measurements was -0.02, (95% CI -0.08 to 0.04; Bland-Altman plot; using highest of ankle pressure in the leg from doppler). Find more details in table 6 on pages 41 to 53 of the diagnostics assessment report.

Table 2 Accuracy of boso ABI-system 100 to detect peripheral arterial disease in people without leg ulcers

Study	Reference device	Study population	Study size (PAD prevalence)	Sensitivity	Specificity
Homza et al. (2019)	Duplex ultrasound	People with diabetes attending a cardiovascular outpatient clinic	62 (not reported)	61%	94%
Jarai et al. (2018)	Manual doppler	People enrolled in Hungarian Hypertension Society's registry of people tested for PAD in general practice (ERV Registration Program)	397 (not reported)	77%	94%
Wohlfart et al. (2011)	Manual doppler	General population	839 (2%)	77%	98%

Two studies also determined the optimal ABPI threshold for detecting PAD with boso ABPI-system 100. Instead of 0.9, this would have been a higher threshold of 1.0 according to Homza et al. (2019) and 0.96 according to Jarai et al. (2018). Find more details in table 7 on pages 54 and 55 of the diagnostics assessment report.

Technical failures

Jarai et al. (2018) reported measurement failing in 61 of 793 (7.7%) legs using the boso ABI-system 100. In 2 of these cases, the manual doppler measurement also failed.

Time needed to assess ABPI

Both studies reporting on the time needed to assess ABPI using the boso ABI-system 100 reported that it was faster than manual doppler. Jarai et al. (2018)

reported the mean time needed was 2.1 minutes (standard deviation [SD] 0.4 minutes) using boso ABI-system 100 and 5.7 minutes (SD 0.6 minutes) using manual doppler. In Diehm 2009 the mean time needed was 3.9 minutes (SD 1.3 minutes) using boso ABI-system 100 and 11.4 minutes (SD 3.8 minutes) using manual doppler.

Acceptability and experience of using the device

No boso ABI-system 100 studies in people with leg ulcers were found.

Dopplex Ability Automatic ABI System

Diagnostic accuracy

Six studies compared the performance of the Dopplex Ability Automatic ABI System with either manual doppler or duplex ultrasound. In all studies, ABPI was measured by healthcare professionals experienced or specialised in vascular assessment. There were some concerns over risk of bias. In particular, Babaei et al. (2020) did not let the study participants rest enough before testing and in Davies et al. (2016) data from more than 10% of people was not analysed. Table 3 summarises the results from 4 studies that reported accuracy estimates for detecting PAD. In Millen et al. (2018) also reported that having diabetes had no significant effect on the accuracy. This was in a subgroup of 18 people.

The only Dopplex Ability study in people with leg ulcers included 22 people attending a community leg ulcer clinic for ABPI assessment (Welsh et al. 2016). This study did not report sensitivity and specificity but did report that 56% of Dopplex Ability readings were higher than manual doppler readings, 9% were lower and 34% were equal. Mean difference between the devices was 0.068 (standard deviation 0.175). A further study by Lewis et al. (2010) in people without leg ulcers reported a correlation between Dopplex Ability and manual doppler (r=0.89). Find more details in table 6 on pages 41 to 53 of the diagnostics assessment report.

Table 3 Accuracy of Dopplex Ability Automatic ABI System to detect peripheral arterial disease in people without leg ulcers

Study	Reference device	Study population	Study size (PAD prevalence)	Sensitivity	Specificity
Babaei et al. (2020)	Duplex ultrasound	People with diabetes and PAD symptoms	303 (2%)	20%	96%
Davies et al. (2016)	Manual doppler	People with cardiovascular risk factors	380 (6%)	70%	96%
Lewis et al. (2016)	Duplex ultrasound	People referred for arterial assessment of the legs	189 (36%)	79%	91%
Millen et al (2018)	Manual doppler	People attending non-invasive vascular assessment	66 (43%)	59%	86%

Three studies also determined the optimal ABPI threshold for detecting PAD with Dopplex Ability Automatic ABI System. Instead of 0.9, this would have been a higher threshold of 1.2 according to Babaei et al. (2020), 1.04 according to Davies et al. (2016) and 0.98 according to Lewis et al. (2018). Find more details in table 7 on pages 54 and 55 of the diagnostics assessment report.

Technical failures

Millen et al. (2018) reported that Dopplex Ability measurements in around 2% of the legs did not work. Davies et al. (2016) reported a nearly 4% technical failure rate because of legs with high blood pressure. In this study, none of the manual doppler measurements failed.

Time needed to assess ABPI

In Welsh et al. (2016), calculating ABPI with Dopplex Ability took 3-5 minutes compared with an average of 15 minutes when using manual doppler. The study did not report the duration for other elements of the assessment.

Acceptability and experience of using the device

Most of the people with leg ulcers in the study by Welsh et al. (2016) found assessing ABPI by Dopplex Ability acceptable but some said they felt discomfort when the cuff was fully inflated. Healthcare professionals found Dopplex Ability easier to use and the time taken to assess ABPI using Dopplex Ability more convenient compared with manual doppler.

MESI ABPI MD

Diagnostic accuracy

Eight studies compared the performance of MESI ABPI MD with manual doppler. Where reported, ABPI was measured by healthcare professionals specialised in vascular assessment (Boilley et al. 2020; Catillon et al. 2020; Hageman et al. 2021; Raya et al. 2019). There were some concerns over risk of bias. In Boilley et al. (2020), all measurements were done by 1 person who took the manual doppler measurements after MESI ABPI MD measurements. In Span et al. (2016) and Varetto et al. (2019), data from more than 10% of people was not analysed. Table 4 summarises the results from 5 studies that reported accuracy estimates for detecting PAD and the pooled estimate from EAG's meta-analysis. One of these 5 studies, Raya et al. evaluated both MESI ABPI MD and WatchBP Office ABI. In this study, MESI ABPI MD was more accurate (see also table 5). Hageman et al. (2021) also reported results in a subgroup of 61 people with diabetes. In this group, both sensitivity (68%) and specificity (95%) were lower than in the study overall.

The only MESI ABPI MD study in people with leg ulcers included 145 people who had ABPI at GP clinics (Green et al. 2020). This study reported 17% of

MESI ABPI MD readings were accurate compared with manual doppler as the reference device. Two further studies in people without leg ulcers reported on the correlation between MESI ABPI MD and manual doppler. A study of 185 people attending a vascular consultation (Varetto et al. 2019) reported a correlation (Kendall's Tau 0.63) and a small mean difference between the measurements 0.07 (95% CI 0.05 to 0.09; Bland-Altman plot). A study of 43 people attending a doppler appointment (Catillon et al. 2020) found nearly no correlation between the measurements by the 2 devices (r=0.2). Find more details in figure 2 on page 36, figure 3 on page 37, and table 6 on pages 41 to 53 of the diagnostics assessment report.

Table 4 Accuracy of MESI ABPI MD to detect peripheral arterial disease in people without leg ulcers

Study	Reference device	Study population	Study size (PAD prevalence)	Sensitivity	Specificity
Boilley et al. (2020)	Manual doppler	People with with suspected PAD because of exercise-related leg symptoms	102 (80%)	66%	85%
Hageman et al. (2021)	Manual doppler	People referred for ABPI assessment	201 (31%)	74%	97%
Raya et al. (2019)	Manual doppler	People attending primary care centre	202 (6%)	63%	98%
Span et al. (2016)	Manual doppler	People with PAD symptoms	136 (10%)	57%	99%
Zebari et al. (2022)	Manual doppler	People attending vascular surgery outpatient clinic	153 (52%)	75%	67%
Pooled estimate	Manual doppler	Not applicable	742 (33%) from 5 studies	67% (95% CI 59% to 74%)	94% (95% CI 83% to 98%)

Four studies also determined the optimal ABPI threshold for detecting PAD with MESI ABPI MD. Instead of 0.9, this would have been a higher threshold of 1.0 for people with and 1.2 for people without diabetes according to Hageman et al. (2021), 1.16 according to Raya et al. (2019), and 1.0 according to Span et al. (2016) and Zebari et al. (2022). Find more details in table 7 on pages 54 and 55 of the diagnostics assessment report.

Technical failures

Four studies reported on technical failures using MESI ABPI MD. In these studies, the rate of failed measurements ranged from around 9% to 19% of the legs. In the study that also provided details of measurement failures using manual doppler (Varetto et al. 2019), the failure rate using MESI ABPI MD was 19% compared to 11% using manual doppler. In 1 study (Hageman et al. 2021), more measurements failed in legs with PAD (28%) compared to legs without PAD (7%). Another study reported that all failures were in people with critical limb ischaemia and incompressible arteries. One study (Zebari et al. 2022) noted that of the reported 28 error codes in 306 legs, only 6 were considered technical failures.

Time needed to assess ABPI

Five studies provided some data on time needed to assess ABPI. Green et al. (2020) reported that ABPI reading including full clinical assessment with MESI ABPI MD took between 10-40 minutes but did not provide information on the time it took with manual doppler. Four studies (Catillon et al. 2020, Raya et al. 2019, Span et al. 2016, Varetto et al. 2019) suggested assessing ABPI using MESI ABPI MD was slightly faster compared with manual doppler. With MESI ABPI MD, the assessment took between around 2 and 11 minutes. With the manual doppler, it took around 5 to 14 minutes. It was not clear what elements of assessing ABPI were included in these estimates.

Acceptability and experience of using the device

In the study by Green et al. (2020), healthcare professionals at the GP clinics using MESI ABPI MD found that the initial setting up of the software was complex and took a long time. But they found the device simple and fast to use, felt it was accurate and thought printouts of the assessment were useful. They also felt that using the device helped improve clinical management of leg ulcers. Half of the healthcare professionals involved in the study said they would continue using the MESI ABPI MD device but pointed out that additional resources such as staff, time and funding would be needed.

WatchBP Office ABI

Diagnostic accuracy

Five studies compared the performance of WatchBP Office ABI with manual doppler test. Where reported, ABPI was measured by experienced healthcare professionals (Raya et al. 2019; Sinski et al. 2013) or a trained nurse (Rodriguez-Roca et al. 2014). There were some concerns over risk of bias. In particular, Rodriguez-Roca et al. (2014) did not let the study participants rest long enough before testing. Table 5 summarises the results from 4 studies that reported accuracy estimates for detecting PAD and the pooled estimate from EAG's meta-analysis.

Kollias et al. (2011) reported that the mean difference between ABPI measurements using WatchBP Office ABI and manual doppler was similar in in people with (subgroup of 42 people) and without diabetes. A further study of 322 people without PAD attending primary care (Rodriguez-Roca et al. 2014) reported a correlation between the measurements (r=0.7) and a small mean difference between the measurements -0.03 (limits of agreement -0.21 to 0.15; Bland-Altman plot). Find more details in figures 4 and 5 on page 38, and table 6 on pages 41 to 53 of the diagnostics assessment report.

Table 5 Accuracy of WatchBP Office ABI to detect peripheral arterial disease in people without leg ulcers

Study	Reference device	Study population	Study size (PAD prevalence)	Sensitivity	Specificity
Kollias et al. (2011)	Manual doppler	People with cardiovascular risk factors attending a hypertension or diabetes outpatient clinic	93 (17%)	83%	97%
Raya et al. (2019)	Manual doppler	People attending primary care centre	202 (6%)	44%	98%
Sinski et al. (2013)	Manual doppler	People with coronary artery disease	80 (40%)	46%	98%
Verma et al. (2022)	Manual doppler	Construction workers described as a high-risk population	200 (6%)	50%	100%
Pooled estimate	Manual doppler	Not applicable	575 (13%) from 4 studies	53% (95% CI 37% to 69%)	98% (95% CI 96% to 99%)

Two studies also determined the optimal ABPI threshold for detecting PAD with WatchBP Office ABI. Instead of 0.9, this would have been a higher threshold of 0.97 according to Kollias et al. (2011) and 1.12 according to Raya et al. (2019). Find more details in table 7 on pages 54 and 55 of the diagnostics assessment report.

Technical failures

Three studies provided data on technical failures using WatchBP ABI. Technical failures were reported in 2.5% of study participants (Sinski et al. 2013), and 1.6% of legs (Kollias et al. 2011). In Kollias et al. (2011) more errors were observed in legs with PAD (35.2%) than in legs without PAD

(5.7%). Raya et al. (2019) reported that ABPI measurement did not work in 13% of study participants using WatchBP Office ABI compared with 4% using manual doppler.

Time needed to assess ABPI

Two studies reported on the time needed to assess ABPI. Kollias et al. (2011) reported mean time needed was 5.8 minutes (SD 0.3 minutes) using WatchBP Office ABI and 9.3 minutes (SD 2.2 minutes) using manual doppler. In the other study (Raya et al. 2019), measuring ABPI took slightly longer using WatchBP Office ABI (mean 14.4 minutes) compared with manual doppler (mean 12.1 minutes). This was because time was spent on identifying the arm with the highest systolic blood pressure.

Acceptability and experience of using the device

No WatchBP Office ABI studies in people with leg ulcers were found.

3 Cost effectiveness evidence

The external assessment group (EAG) did a search to identify existing economic evaluations of devices for automated assessment of ankle brachial pressure index (ABPI) for diagnosing peripheral arterial disease (PAD) in people with leg ulcers. The EAG also constructed a de novo economic model to assess the cost effectiveness of using automated devices for measuring ABPI in adults with leg ulcers.

Systematic review of cost-effectiveness evidence

The EAG did not identify any published economic studies for automated devices for assessing PAD in people with leg ulcers.

The EAG conducted additional literature searches for economic evaluations for diagnosis of PAD and treatment/management of leg ulcers to inform their model structure. They identified 1 study (Itoga et al. 2018) that was relevant to the use of ABPI for screening peripheral arterial disease in the general

population and 8 relevant studies for treatment/management of people with leg ulcers.

Economic analysis

The EAG developed a de novo economic model to assess the cost effectiveness of automated ABPI devices to detect PAD in adults with leg ulcers presenting to a leg ulcer clinic in the community. The base case assumes sufficient skills are available to assess the condition.

The population in the economic model was based Callam et al. (1987), which is a large study reporting the prevalence of arterial insufficiency, alongside the age and sex profile of leg ulcer patients in UK clinical practice. The cohort consisted of 600 people with chronic leg ulceration with an average age of 70 and 30.46% female. The EAG's clinical expert confirmed that the demographics of the cohort included in the model were consistent with those that would be seen in current practice.

The model compares the cost-effectiveness of 7 automated devices compared with manual doppler testing using an ABPI threshold of 0.9.

A linked evidence approach was used to quantify the potential consequences of test accuracy for ulcer healing times, risk of requiring invasive PAD treatment and subsequent outcomes because no direct evidence was identified.

Model structure

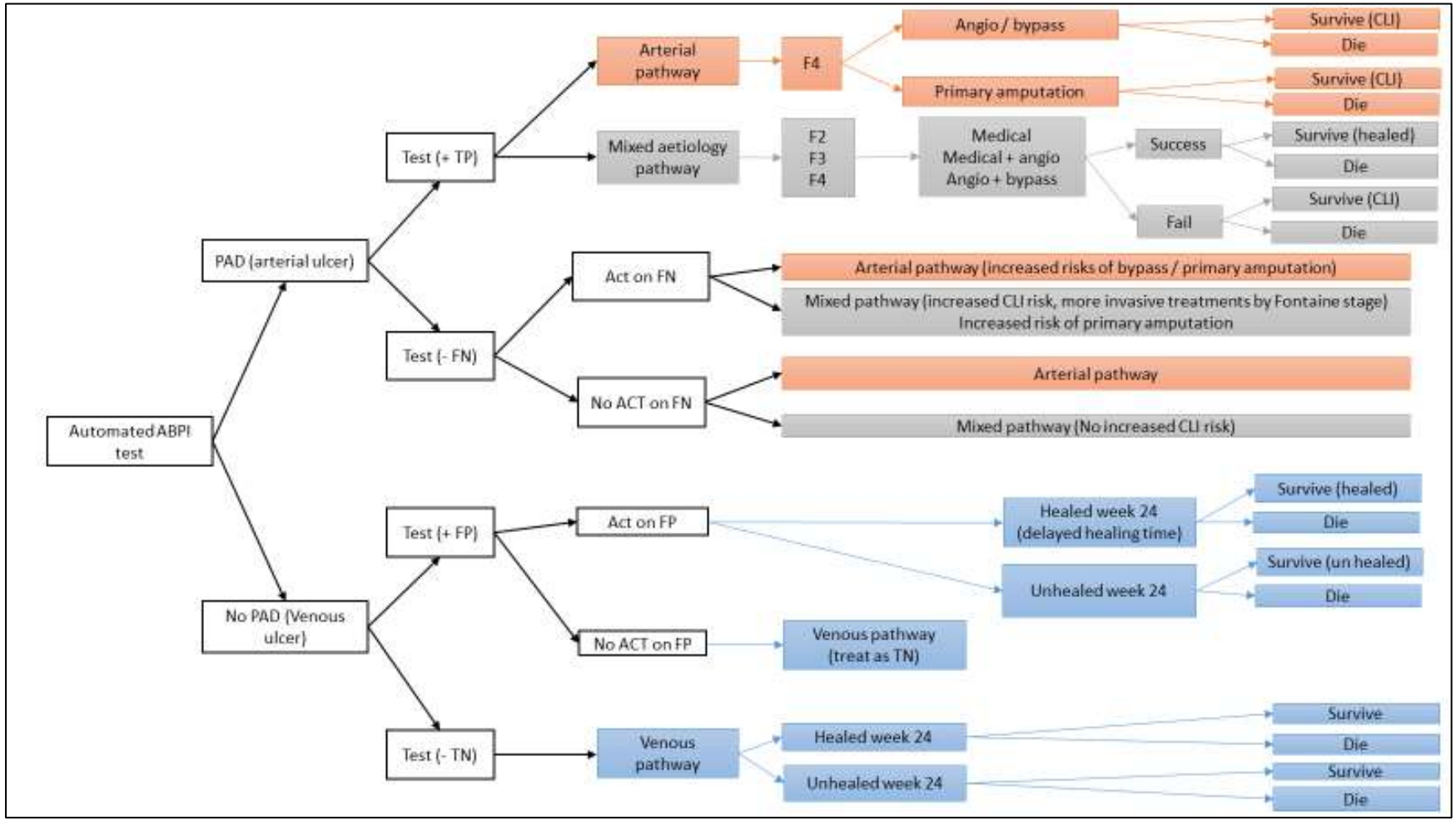
The EAG developed a two-stage model (decision tree followed by Markov cohort state transition). The model structure was informed by an assessment of existing leg ulcer economic evaluation models and was developed to be consistent with the recommendations of the National Wound Care Strategy Programme (NWCSP) on the management of leg ulcers.

The initial diagnostic stage is modelled using a decision-tree, which captures the costs and consequences of diagnostic accuracy (sensitivity and specificity) of the automated ABPI measurement devices compared with manual doppler testing (see figure 1). The time horizon for the initial diagnostic decision tree phase was 24 weeks after the initial presentation with a leg ulcer. During this time period in the model, the following is assumed to occur (based on clinical expert feedback):

- testing for ABPI
- identification of false positive and false negative testing errors in clinical practice
- people assigned to the correct treatment pathways (arterial, mixed, venous)
- urgent PAD referrals from the community are acted upon and appropriate surgical management is initiated where appropriate.

Following this, the surviving cohort are assigned to separate Markov models which model either the venous, mixed (both arterial and venous aetiology) or arterial disease pathway according to underlying PAD prevalence. This allows different input parameters and treatment pathways to be modelled depending on the underlying cause of the ulcer. Arterial disease was defined using Fontaine stage (summary of stages provided in table 11 of the diagnostic assessment report). Those with purely arterial disease are assumed to be stage 4 because of the presence of an ulcer. For mixed disease, the cohort is assumed to be a mix of Fontaine stages 2 to 4. A lifetime time horizon with a 6-month cycle length was applied in the Markov model.

Figure 1 Diagnostic phase, simplified decision tree model pathway



Arterial ulcers

In the model, those correctly identified as having PAD are referred to vascular services for further assessment and treatment in accordance with NWCSP recommendations. Those with purely arterial disease are assumed to have critical limb ischemia (CLI) (due to being classified as Fontaine stage 4), and therefore need surgical treatment to restore blood flow (angioplasty or surgical bypass). A small proportion also needs primary amputation. This cohort of people receives their first arterial treatment within the decision tree phase of the model because it is assumed they would have an urgent referral due to the presence of an ulcer and positive ABPI test.

Those with a false negative result, that is those people who have PAD but the test incorrectly indicates that they do not, are assumed to have multiple signs of arterial disease (due to being Fontaine stage 4) and therefore it is assumed that a holistic assessment of their condition would identify a false negative result promptly and inappropriate compression would not be applied and so would be unlikely to lead to long-term negative consequences.

At the end of the diagnostic phase, people who remained alive would enter the Markov model (shown in figure 2) in either the:

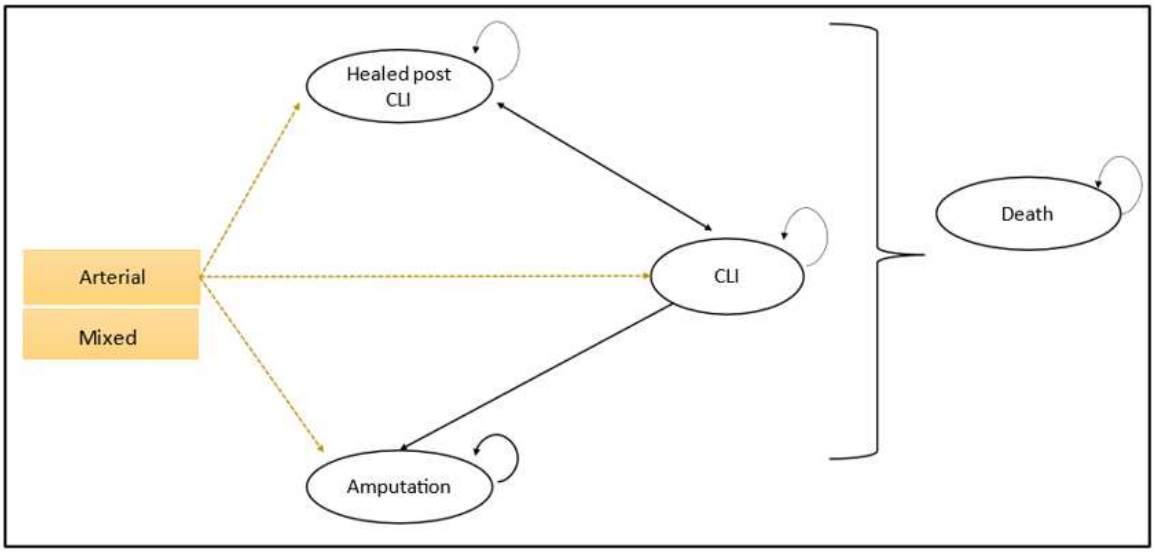
- “healed post critical limb ischemia (CLI)” state if initial surgery from the decision tree phase was successful. People who are in this health state are at risk of recurrence and can re-enter the CLI state during subsequent cycles (further ulcer recurrences are assumed to be CLI).
- “CLI” state if initial surgery was unsuccessful at restoring blood flow and further treatment needed. People in this health state receive angioplasty or bypass procedure. People with unhealing ulcers can re-cycle through this health state and receive subsequent treatments that increase in intensity up to bypass and amputation. For example, those who have failed angioplasty are assumed to require bypass, and those who have failed bypass require a repeat surgery or amputation. All of those who have failed

to achieve successful outcomes in the first 4 cycles of treatment are assumed to require amputation.

- "Amputation" state if primary amputation was required or if subsequent treatment has been unsuccessful.

People can enter the "death" state from all other model health states, with an excess risk of mortality applied for underlying arterial disease in all model states. Further additional risks of death are applied in the CLI state.

Figure 2 Markov model structure: arterial and mixed ulcers



Mixed aetiology ulcers

For those with mixed aetiology ulcers, the EAG assumed that initial treatments and patient outcomes modelled in the first 24 weeks would depend on the severity of the underlying arterial disease (classified using Fontaine system). The mixed ulcer population was assumed to include Fontaine stages 2 to 4 because people in stage 1 would typically have a higher ABPI than 0.9. The EAG clinical expert view was that the arterial component of the ulcer would take priority in UK clinical practice and therefore in most cases strong compression would not be applied. The model structure for the mixed cohort

is very similar to the arterial cohort for this reason, however, the EAG clinical expert noted that it is more difficult to detect arterial disease amongst people with mixed aetiology ulcers, especially for those with less severe arterial disease. Therefore, false negative test mistakes may be more likely to be missed in clinical practice for mixed aetiology compared with arterial disease.

The EAG explored the implications of a false negative (FN) test for mixed ulcers using a survey with clinical experts. The majority thought that a FN test leading to inappropriate compression, could feasibly lead to delayed ulcer healing, increased risks of requiring invasive treatment (angioplasty or bypass) and potentially increased risk of ultimately requiring limb amputation. These outcomes and risks were included in the mixed model. In the base case it was assumed that all false negative results for mixed ulcers would be acted upon and the implications of this would depend on severity and include:

- Mild disease (Fontaine stage 2) – would likely experience extreme pain and return within one week at which point the error would be identified. Therefore most would have no long-lasting medical consequences and would be managed medically with eventual surgery for the venous disease.
- Moderate disease (Fontaine stage 3) – would be more likely to require escalation of treatment to more invasive procedures. Whilst highly uncertain, the EAG's clinical expert estimated around 70% would require escalation to bypass with the remaining having no longer term implications.
- Severe disease (Fontaine stage 4) – would require escalation to bypass procedure and an additional 2.5% require primary amputation.

People with false negative results may also be subject to consequences of delayed healing time due to a lack of clinical uncertainty around wound treatment. This is detailed further in table 8.

Prior to assigning people to the Markov model, people with mixed disease are first split according to severity (Fontaine stage 2, 3 or 4). This, the initial treatment received (medical management for stage 2, angioplasty and/or

bypass for stage 3 and 4), and the success of that initial treatment is used to assign people to the following health states in the mixed Markov model: those with successful treatment enter the “healed” state, failed treatment in the “CLI” state and those who have a primary amputation, or amputation following failed bypass surgery enter the “amputation” state. The Markov model structure used for mixed ulcers is the same as that used for arterial ulcers (see figure 2) but with different transition probabilities applied.

Venous ulcers

People in the model who are accurately detected as having a venous ulcer are treated with strong compression and follow-up patient management in line with current guidelines.

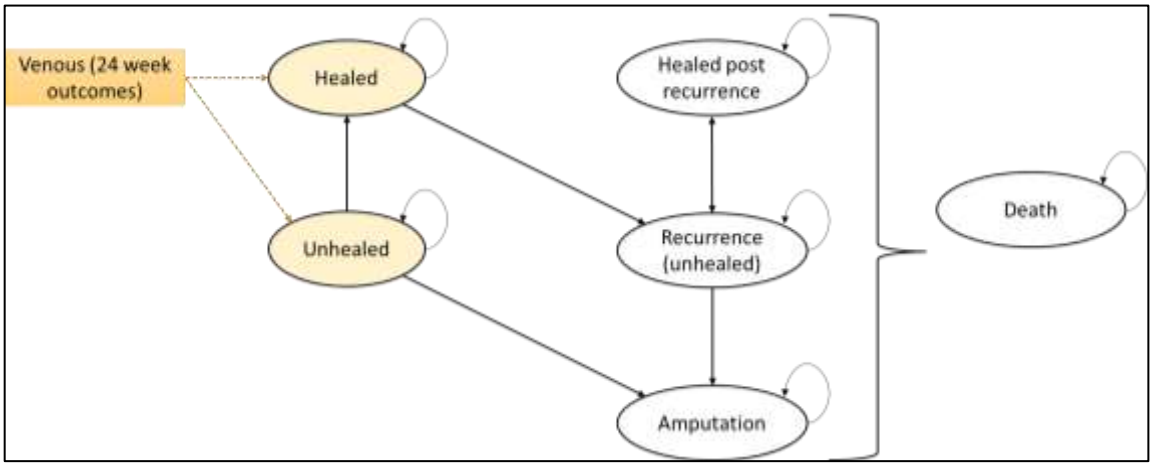
People who are incorrectly diagnosed as having arterial disease (a false positive result) are assumed to have compression withheld and therefore experience a delay to healing until the false positive is identified via review. All clinical experts agreed that it would not lead to amputation of a venous ulcer because amputation in clinical practice is extremely rare.

People with correctly diagnosed venous ulcers enter the venous Markov model following the diagnostic decision tree model at the end of the 24-week period in either the healed or unhealed ulcer state (see figure 3).

Unhealed ulcers can continue to heal in subsequent model cycles and a small proportion may remain unhealed longer term. Once an ulcer heals, it can remain healed or experience a recurrence. In the base case it is assumed that amputation does not occur for venous ulcers but this health state was included to allow the EAG to conduct scenario analysis. The EAG included multiple rounds of healing and recurrence in the model to reflect the chronic recurrent nature of venous ulcers.

Mortality for those with venous ulcers was assumed to be equal to that of the UK age and sex-adjusted general population mortality risk and is not dependent on whether an ulcer heals.

Figure 3 Markov model structure: venous ulcers



Model inputs

Prevalence of peripheral arterial disease

The EAG based the prevalence of arterial disease (including both arterial aetiology and mixed aetiology) in the model (22%, 75% of whom have mixed disease) on Callam et al. (1987). This was used to maintain consistency with the modelled cohort age and sex profile, and because the studies included in the review were mostly in patients without leg ulceration.

Diagnostic accuracy of the technologies

Diagnostic accuracy for automated ABPI devices and manual doppler tests was informed by the results from the diagnostic accuracy review (see tables 1 to 5). Diagnostic accuracy of manual doppler was assumed to be perfect in the EAG base case. All but 3 of the included studies in the review treated manual doppler as the reference standard and where available this is used in the base case analysis. However, there were no comparisons of diagnostic accuracy with manual doppler for the BlueDop Vascular Expert device, so it

was assumed that diagnostic accuracy of manual doppler and duplex ultrasound were equivalent for this analysis.

The EAG noted study populations in the included studies were highly heterogeneous and therefore they had serious concerns about the validity of pooling diagnostic accuracy results so used single studies to populate diagnostic accuracy data for each technology. The EAG assessed the studies shown in table 6 as being most suitable to populate diagnostic accuracy in the base case analysis. All studies used for the base case analysis used manual doppler for the reference standard with the exception of the study used for BlueDop Vascular Expert which used duplex ultrasound.

Table 6 Diagnostic accuracy data used in the model base case

Device	Study details	Sensitivity	Specificity
BlueDop Vascular Expert	Kordzadeh et al (2017): • 166 people referred to vascular outpatient service • PAD prevalence not reported • ABPI by physician and vascular specialist (BlueDop), senior vascular scientist (duplex ultrasound)	95%	90%
boso ABI-system 100	Jarai et al. (2018): • 397 people enrolled in Hungarian hypertension ERV registration program • PAD prevalence not reported • ABPI by trained nurse	77%	94%
Dopplex Ability Automatic ABI System	Davies et al. (2016): • 380 people with cardiovascular risk factors • PAD prevalence 6% • ABPI by nurse with significant experience of vascular assessment of legs	70%	96%
MESI ABPI MD	Hageman et al. (2021): • 201 people referred for ABPI assessment • PAD prevalence 31% • Device user not reported	74%	97%
WatchBP Office ABI	Kollias et al. (2011): • 93 people with cardiovascular risk factors attending a hypertension or diabetes outpatient clinic • PAD prevalence 17% • Device user not reported	83%	97%

No studies were identified for WatchBP Office Vascular or MESI mTABLET ABI so the EAG assumed these devices were equivalent to WatchBP Office ABI and MESI ABPI MD respectively.

The EAG also conducted several scenario analyses which vary sensitivity and specificity parameters using high and low values as well as pooled data and optimal cut off data where available. They also conducted subgroup analysis using data specific to people with diabetes.

Initial treatments for PAD in decision tree model

The base case model assumes treatment for moderate to severe PAD (F3 and F4) would include angioplasty and/or bypass with the split based on data from the national vascular registry. Mild PAD (F2) was assumed to be treated with medical management. The EAG clinical expert opinion was that primary amputation would only occur in people with severe disease (F4) and in the model base case was assumed to be required for 5% of people with severe arterial disease, and 0% of people with mixed disease regardless of severity.

Treatment success was based on the national vascular registry annual report. It was not reported by severity so the EAG estimated treatment success by severity using data on the proportion of procedures that were elective or non-elective

Further detail on treatment outcome parameters used in the arterial and mixed decision tree models are available in table 14 on pages 86 to 87 of the diagnostic assessment report.

Ulcer healing probabilities

For arterial ulcers, the model assumes that all ulcers remained unhealed at 24 weeks. For venous ulcers healing probabilities were obtained from the delayed ablation arm of the UK EVRA RCT, per protocol analysis, showing a 24-week healing probability of 0.826 (0.768 to 0.876) (Gohel et al. 2019). For mixed-aetiology ulcers, healing probabilities were from Humphreys et al, (2007) which was a prospective study of leg ulcer patients, treated with modified compression and assessed for revascularisation at 3 months if no improvement or worsening symptoms. Within 36 weeks the ulcer healing

probability was 0.676. Further details on healing probabilities are provided in table 16 on pages 95 to 96 of the diagnostic assessment report.

Ulcer healing times

Average healing time in the intervention arm for an ulcer that ultimately heals at 24 weeks was estimated in the model as a function of baseline healing time (based on manual doppler from the literature), adjusted for time gains due to potential early diagnosis and time delays due to inaccurate diagnosis.

The EAG assumed there are no time gains in healing of ulcers from the use of automated tests in the base case model because the clinical experts advised that the appropriate skills in community leg ulcer clinics or vascular services would likely be available and therefore referrals to outpatient vascular services purely for ABPI assessment would be unusual and use of automated tests would be unlikely to lead to more efficient triage of people to community of vascular services.

However, they noted there may be a very small number of settings where automated devices could lead to more efficient referrals; for example, some small rural GP practices or district nurses who may not have been trained in manual doppler assessment. This is reflected in a scenario analysis where people with correctly diagnosed venous ulcers (true negative) diagnosed with an automated test can be referred directly to community leg ulcer services for treatment rather than to outpatient vascular clinics. Time gains are based on the difference in waiting times for vascular services compared with community leg ulcer clinics. The EAG assumed a maximum plausible time gain of 16 weeks (based on clinical expert suggestion that waiting times for community leg ulcer clinics may be as low as 2 weeks and people in England are guaranteed to receive a non-urgent outpatient consultation within 18 weeks so this could be considered the maximum usual waiting time). Alternative time gain scenarios (6, 8 and 12 weeks), were also explored in an addendum to the diagnostics assessment report.

Time delays due to inaccurate test results with an automated test were based on a survey of 4 clinical experts. Both time gains and delays remain highly uncertain and the EAG presented 3 alternative base cases based on pessimistic, moderate and optimistic assumptions to as well as a range of scenario analyses to explore the impact of this uncertainty. The assumptions made in each base case is detailed in table 8. Delays in healing for venous ulcers incorrectly diagnosed as arterial ulcers (false positive) vary from no delay to no venous ulcers healing by 24 weeks. For arterial and mixed ulcers, delay to healing and risk of treatment escalation from a false negative result varies from no delay or treatment escalation to a delay of 116 days in healing and all false negative results requiring non-elective surgery.

Transition probabilities for Markov model

Venous ulcers

The probability of unhealed ulcers healing in the longer term (post 24 weeks) is based on the EVRA RCT which showed 87.2% of venous ulcers have healed by 1 year. This study was also used to populate ulcer recurrence rates in the model (1 year probability of recurrence 24.7%). Amputation was assumed not to occur for venous ulcers based on clinical expert opinion. Probability of death for venous ulcers was assumed to be in line with general population mortality. For full details on transition probabilities used for venous ulcers see table 18 on pages 102 to 103 of the diagnostics assessment report.

Arterial/mixed ulcers

The transition probabilities for people with arterial/mixed leg ulcers are presented in table 19 on pages 107 to 109 of the diagnostic assessment report.

Multiple 6-monthly transition probabilities were applied to model healing based on treatment specific success rates following angioplasty and bypass weighted according to procedure type (elective/emergency). Risk of amputation from CLI (13.4% 6-month probability) was obtained from NICE

CG147 which was based on ACC/AHA 2005 practice guidelines. Recurrence was assumed equal to the transition between symptomatic PAD and CLI from Sigvant et al. 2016 (2.3% 6-monthly probability).

The EAG noted that transitions to death state for those with arterial or mixed disease were uncertain in the model, and likely to be patient and risk-factor dependent. Mortality risks from PAD health states include all-cause general population mortality, excess risks for PAD patients generally (HR 1.98), excess risk for CLI (HR 3.026), and in-hospital mortality risks for CLI related procedures (angioplasty, bypass, and amputation). A higher risk of death following amputation was modelled for the first 6 months following the procedure. The EAG used UK general population data, matched for sex and age, to estimate patients' survival in the economic model (Office for National Statistics national life tables for the UK).

Costs

The following costs are considered in the model (all valued in 2020/21 GBP):

Diagnostic test costs

The total cost of testing was calculated by the EAG using a micro-costing approach based on the following:

- Staff costs (1 band 5 community nurse to conduct test)
- Equipment costs (devices, cuffs, software), 8 tests per day throughput
- Consumables (printed results, ultrasound gel)
- Repeat test costs (error rate from clinical evidence, assumed maximum 1 retest due to error or zero reading)

A breakdown of resource use and cost for each test in the base case analysis is presented in table 20 on pages 112 to 114 of the diagnostic assessment report. Table 7 summarises the total cost per test of the devices included in the model. Scenario analyses were conducted around the costs of testing to explore uncertainty around different staff levels completing the test, the

number of tests per day and proportions of tests that need to re-run because of technical failures.

Table 7 Cost of testing in the base case

Devices	Cost per test (fixed cost per unit)
Manual doppler	£20.48 (£341)
BlueDop Vascular Expert	[redacted] (£4,995)
Boso ABI-system 100	£7.86 (£3,187)
Dopplex Ability Automatic ABI System	£10.79 (£3,937)
MESI ABPI MD	£7.45 (£2,499)
MESI mTABLET ABI	£10.01 (£2,847)
WatchBP Office ABI	£17.09 (£2,145)
WatchBP Office Vascular	£17.11 (£2,445)

Treatment or management costs

Data on treatment or management costs for health states included in the models were obtained from published studies, and were re-costed using the appropriate national average unit costs for 2020/21, including PSSRU for primary care and hospital staff time, NHS reference costs for procedures and the British National Formulary, BNF for drug treatments. Health state costs applied in the model are presented in table 22 on pages 120 to 124 of the diagnostics assessment report.

Health-related quality of life

The utility values for healed and unhealed venous ulcers in the model are based on Iglesias et al. (2005), a large UK study, reporting an economic evaluation of the VenUS1 trial. The EAG used data from this study because it reported EQ-5D utility data classified by healed or unhealed status.

For mixed ulcers, where the ulcer was treated with compression (i.e., primarily venous), the EAG assumed that the utility of the healed, unhealed and recurrence states would be equivalent to those with venous ulcers.

The EAG based utility values for arterial ulcers on Forbes et al. (2010), which reported baseline EQ-5D data for UK CLI patients needing angioplasty or surgery (n=417). The EAG explored using utility values from other published studies such as Pisa et al. (2012) but advised this did not have any substantial effect on the model results. Table 23 on page 126 of the diagnostics assessment report summarises the utility values used in the model.

Summary of key original base-case assumptions

The following assumptions were applied in the original base-case analysis, as summarised on pages 129 to 130 of the diagnostics assessment report:

- It is assumed that the data from the diagnostic accuracy studies (which cover a heterogenous population without leg ulcers) is transferable to people with leg ulcers (the modelled population).
- Manual doppler in the model is assumed to be 100% accurate.
- The model uses a linked evidence approach informed heavily by expert opinion to describe the impact of the tests on health outcomes. In particular impact of inaccurate test results on delayed ulcer healing time/need for invasive surgery, and potential time gains in diagnosis and treatment of venous ulcers from use of automated devices is uncertain.
- People with PAD are split into those with arterial and those with mixed ulcers. The Fontaine system is used to describe severity of the underlying PAD. This is not used universally in clinical practice but was deemed a useful approach for for classifying severity of disease in the model and therefore the consequences of inappropriate compression.
- It is assumed that primary amputation is rare, and that limb salvage is attempted using bypass and / or revascularization wherever possible, though it is more likely to be required for an inappropriately compressed arterial ulcer.
- It is assumed that any test errors would be identified within 24 weeks and patients would receive appropriate treatment for their condition within this time (i.e., compression applied to a patient with an initial FP result, and

appropriate surgical management of an inappropriately compressed patients due to a FN result).

- It is assumed that the proportion of the cohort with arterial (or mixed) disease who have a recurrence after 6 months incur the same costs and utilities regardless of the number of previous cycles in the critical limb ischemia state.
- Costs and utilities applied to healed states are assumed the same regardless of whether it is the primary ulcer that healed or an ulcer that has healed following recurrence. Risk of recurrence also stays constant regardless of the number of previous recurrences.
- The model assumes that for the proportion of the cohort with mixed ulceration, that clinical management prioritises the arterial component of disease first.
- It is assumed that people with venous ulcer disease have similar mortality risks to the general population, and that amputation does not take place in modern clinical practice for venous disease.

Base case results

The EAG presented 3 possible alternative base cases, according to moderate, optimistic, and pessimistic assumptions for automated ABPI testing because of a lack of data. Table 8 outlines the assumptions for 3 proposed base cases. The EAG considered that the moderate set of assumptions could be plausible, but further evidence is required on several key parameters before a definitive base case analysis could be determined.

The EAG presents probabilistic base-case results for each of the 7 automated ABPI devices compared with manual doppler as well as fully incremental analysis. Using moderate and pessimistic base case assumptions, results in all automated ABPI devices being more costly and less effective when with manual doppler (tables 9 and 10). However, using optimistic base case assumptions results in all automated ABPI devices becoming less costly and

more effective than manual doppler (table 11). For further details see table 25 of the diagnostic assessment report.

Table 8 Assumptions for 3 alternative base cases

Parameter	Pessimistic	Moderate	Optimistic
• Time gains due to quicker diagnosis and treatment (venous ulcers only)	• 0 days	• 0 days	• 16 weeks
• Time delay for a false positive result (venous ulcers incorrectly diagnosed as arterial)	• No healing by 24 weeks for false positive results	• 63 days to recognise • 118 days to healing	• No delay
• Time delay and risk of treatment escalation for a false negative result (mixed or arterial ulcers incorrectly diagnosed as venous)	• Arterial ulcers: FN not recognised, all require non-elective surgery, and a relative risk of primary amputation (RR=2) is applied • Mixed ulcers: 17 days to recognise FN and 116 days to healing. All FN require non-elective surgery	• Arterial ulcers: FN recognised so 0 days delay to healing and no treatment escalation • Mixed ulcers: 17 days to recognise FN and 116 days delay to healing • 70% of people with moderate (F3) disease and FN require escalation to bypass. All people with severe (F4) disease and FN require escalation to bypass and 2.5% with FN require escalation to primary amputation.	• All FNs identified in routine practice so no delay to healing or treatment escalation for mixed or arterial ulcers

Table 9 Moderate base case

	Total costs (£)	Total QALYs	Incremental costs (£) vs manual doppler	Incremental QALYs vs manual doppler	ICER (£) vs manual doppler	ICER (£) ranked
Manual doppler	£11,713	8.046	-	-	--	-
BlueDop Vascular Expert	£11,930	8.043	£217	-0.003	Dominated	Dominated
WatchBP Office ABI	£12,037	8.042	£325	-0.004	Dominated	Dominated
WatchBP Office Vascular	£12,037	8.042	£325	-0.004	Dominated	Dominated
boso ABI-system 100	£12,149	8.041	£436	-0.005	Dominated	Dominated
MESI ABPI MD	£12,189	8.040	£476	-0.005	Dominated	Dominated
MESI mTABLET ABI	£12,191	8.040	£478	-0.005	Dominated	Dominated
Dopplex Ability Automatic ABI System	£12,262	8.040	£549	-0.006	Dominated	Dominated

Table 10 Pessimistic base case

	Total costs (£)	Total QALYs	Incremental costs (£) vs manual doppler	Incremental QALYs vs manual doppler	ICER (£) vs manual doppler	ICER (£) ranked
Manual doppler	£11,680	8.042	-	-	--	-
BlueDop Vascular Expert	£12,136	8.035	£456	-0.007	Dominated	Dominated
WatchBP Office ABI	£12,216	8.035	£535	-0.007	Dominated	Dominated
WatchBP Office Vascular	£12,216	8.035	£535	-0.007	Dominated	Dominated
boso ABI-system 100	£12,449	8.032	£769	-0.010	Dominated	Dominated
MESI ABPI MD	£12,462	8.033	£782	-0.009	Dominated	Dominated
MESI mTABLET ABI	£12,465	8.033	£785	-0.009	Dominated	Dominated
Dopplex Ability Automatic ABI System	£12,591	8.031	£910	-0.011	Dominated	Dominated

Table 11 Optimistic base case

	Total costs (£)	Total QALYs	Incremental costs (£) vs manual doppler	Incremental QALYs vs manual doppler	ICER (£) vs manual doppler	ICER (£) ranked
MESI ABPI MD	£10,977	8.072	-£802	0.019	Dominant	
MESI mTABLET ABI	£10,980	8.072	-£799	0.019	Dominant	Dominated
Dopplex Ability Automatic ABI System	£10,987	8.071	-£792	0.018	Dominant	Dominated
WatchBP Office ABI	£10,988	8.072	-£791	0.019	Dominant	Dominated
WatchBP Office Vascular	£10,988	8.072	-£791	0.019	Dominant	Dominated
boso ABI-system 100	£11,008	8.071	-£771	0.018	Dominant	Dominated
BlueDop Vascular Expert	£11,048	8.070	-£731	0.017	Dominant	Dominated
Manual doppler	£11,779	8.053	-	-	--	Dominated

Sensitivity analysis

The EAG also did deterministic scenario analyses on the moderate base case (n=28) to explore the impact of various assumptions and alternative parameter sources on results which are briefly summarised below (see page 136 of the diagnostic assessment report for more details).

- One-way changes to parameters that contribute to the pessimistic and optimistic base cases (time gains and impact of inaccurate results) explored in scenarios 1 to 7. Additional scenarios on time gains were also presented in an addendum to the diagnostics assessment report.
- Diagnostic accuracy data varied in scenarios 8 to 12 using alternative sources, meta-analysis results and subgroup data.
- PAD prevalence varied in scenario 13.
- Diagnostic test costs (exploring variation in healthcare professionals conducting the test, time taken to complete each test, high and low estimates of test throughput, and cost implications of technical failures) in scenarios 14 to 21.
- Impact of positive test results requiring duplex ultrasound and outpatient consultation to confirm result in scenario 22
- Mortality data for arterial disease based around health state rather than procedure specific risks in scenarios 23 and 24.
- Assuming no patients have primary amputation in scenario 25.
- Assuming false negative results lead to all arterial procedures being non-elective and hence having poorer outcomes in scenario 26.
- Reduction in time horizon of the model and undiscounted ICERs presented in scenarios 27 and 28.

Results of scenario analyses are shown in table 26 on pages 138 to 152 of the diagnostic assessment report. In almost all scenario analyses the automated ABPI devices remained more costly and less effective compared with manual doppler. The magnitude of additional costs and QALY losses for automated tests largely depended on the sensitivity of the automated ABPI

devices. The only scenarios where these results changed were scenarios 1 (time gain in healing of 16 weeks for venous ulcers) and 4 (equivalent to the optimistic base case) which resulted in the automated ABPI devices becoming cheaper and more effective than manual doppler. Additional scenarios were conducted by the EAG further exploring the impact of improvements in venous ulcer healing time in an addendum to the diagnostics assessment report. These scenarios estimated that when the time gain for venous ulcer healing was above 3 weeks, BlueDop Vascular Expert is estimated to be more cost-effective than manual doppler (highest net monetary benefit). All automated devices are estimated to be more cost-effective than manual doppler when the time gain is increased to more than 7 weeks (for further details see Table 2 in the addendum to the diagnostics assessment report).

Cost-effectiveness acceptability curves are shown in figures 13 to 15 on pages 135 and 136 of the diagnostic assessment report. For moderate and pessimistic base cases the probability of manual doppler being the most cost-effective intervention at a £20,000 threshold is estimated to be over 99%. In the optimistic base case MESI ABPI MD was the most cost-effective intervention in 51% of iterations and manual doppler was estimated to be most cost-effective in less than 1% of iterations.

4 Summary

Clinical effectiveness

The EAG's review found only 2 studies that focused on people with leg ulcers. Neither study provided sensitivity or specificity estimates but both reported automated devices gave generally higher readings than manual doppler. The EAG expanded their search and also identified evidence in people without leg ulcers. Most included studies included people who were referred to vascular service or had cardiovascular risk factors. No studies were found on MESI mTABLET ABI or WatchBP Office Vascular.

Most studies reported on diagnostic accuracy to detect peripheral arterial disease (PAD). In general, using manual doppler as the reference standard, the automated devices had good specificity but only moderate sensitivity, so they missed some people with PAD. In the studies that reported on the agreement between the measurements from the automated devices and manual doppler, the automated device often overestimated ABPI values. This happened particularly when the ABPI values were lower. Some studies suggested that using a higher ABPI threshold than 0.9 would be more optimal for the automated devices and would improve the sensitivity. Based on 2 studies in people with diabetes and 4 studies which reported diabetes subgroups, with the exception of Babaei et al. (2020) who reported a very low sensitivity (20%) for Dopplex Ability Automatic ABI System, there was no clear indication the automated devices were much more or much less accurate for people with diabetes. No data on other subgroups was available.

Technical failure rates were generally below 10% but some studies found that the ABPI measurement worked less often in people with PAD. Some of these studies reported failure rates over 20%.

Nearly all studies that provided information about the time needed to assess ABPI, suggested assessing ABPI using an automated device was slightly faster compared with manual doppler. But mostly only a few minutes were gained, and it was not clear which elements of the assessment (for example resting, putting on the cuffs, measuring ABPI, calculating ABPI) were included in the estimates. The healthcare professionals measuring ABPI were experienced or specialised. A larger time saving may be expected if ABPI is measured by a healthcare professional who less frequently uses manual doppler.

The EAG found data on acceptability and experience of using the device from the 2 studies that included people with leg ulcers. Most of the people with leg ulcers found assessing ABPI by Dopplex Ability Automatic ABI System acceptable but some said they felt discomfort when the cuff was fully inflated.

The healthcare professionals in both this and the MESI ABPI MD study said the automated device was easier and faster to use than a manual doppler.

No studies were found on the effect of test results on clinical decision-making, time to treatment or the effects of automated assessment of ABPI on clinical outcomes.

Cost effectiveness

Uncertainties in the diagnostic accuracy evidence base and the association between test results and treatment meant that it was difficult for the EAG to draw firm conclusions about cost-effectiveness. No evidence was identified to inform parameters on potential time gains for venous ulcer healing due to the use of automated devices or on the consequences of inaccurate ABPI results. Consequently the EAG used clinical expert opinion to populate these parameters in the model and proposed 3 alternative base cases according to moderate, optimistic, and pessimistic assumptions for automated testing.

Manual doppler was assumed to be a perfect reference standard in the model and diagnostic accuracy was based on single studies for all devices in the model due to either insufficient study numbers or heterogeneity between studies meaning pooled results may be unreliable.

In probabilistic pairwise analyses, automated ABPI devices were more costly and less effective compared with manual doppler testing in both moderate and pessimistic base cases. Where time gains in venous ulcer healing of more than 3 weeks for BlueDop Vascular Expert, and between 5 and 7 weeks for other automated devices were considered, the automated devices became less costly and more effective than manual doppler. In these scenarios, the EAG compared automated devices being used for ABPI assessment versus manual devices. These scenarios did not consider, for example, no assessment of ABPI being undertaken in the standard care arm due to a lack of sufficient skills being available. The EAG noted caution when interpreting these scenarios due to substantial uncertainties remaining around this and

other input parameters such as the impact of inaccurate test results on clinical outcomes.

No existing economic evaluations of devices for automated assessment of ABPI were identified with which to compare the results of the analysis.

The EAG ran a number of scenario analyses, and the majority estimated that the automated tests would remain more costly and less effective than manual doppler unless a time gain in healing for venous ulcers could be realised. The EAG concluded that it is unlikely that the automated tests would generate QALY gains or cost savings unless a high proportion of inaccurate results could be reliably identified in clinical practice through holistic patient assessment, and automated tests could deliver improvements in patient referral and therefore quicker treatment.

5 Issues for consideration

Clinical effectiveness

Automated devices had generally good specificity but only moderate sensitivity to detect peripheral arterial disease (PAD) meaning they may miss people with PAD. Additionally, all the diagnostic accuracy studies identified were in people without leg ulcers and the generalisability of the data to the leg ulcer population is uncertain. The performance of automated devices could be worse in people with leg ulcers because ABPI assessment may be more challenging. For example, people may find it painful to wear blood pressure cuffs on their legs and/or find it difficult to lay still during the measurements.

The automated devices seemed to overestimate ABPI in both people with and without leg ulcers and particularly when ABPI values were lower. Some studies suggest that using a higher ABPI threshold than the commonly used 0.9 would help improve the performance of the devices but the EAG notes that this would need to be prospectively validated in people with leg ulcers in non-specialised settings.

Most studies used manual doppler as the reference standard. Manual doppler is used to measure ABPI in clinical practice but it is not a perfect test and will also miss some cases of PAD. The EAG noted that in all studies, the healthcare professionals using the devices were specialised, experienced or trained professionals. It is unclear if measurements performed by less experienced or specialised professionals would produce the same findings.

In the Green et al. (2020) study that included people with leg ulcers, healthcare professionals at GP clinics felt that using the automated devices (MESI ABPI MD) improved clinical management of leg ulcers. But there was no data on whether using the automated devices allowed for faster access to assessment and the most effective and safe treatment.

Lack of evidence on clinical outcomes associated with using the automated devices leads to substantial uncertainty about whether in practice incorrect test results would be identified by the full clinical assessment for ulcer treatment planning. So, it is unclear how using automated devices would affect clinical outcomes.

Cost effectiveness

The EAG calculated pooled diagnostic accuracy results for 2 devices (MESI ABPI MD and WatchBP Office ABI) but cautioned about using these in the model because of the study differences. So, instead of pooled estimates the base case used estimates from single studies for all devices. Pooling the studies reduced the sensitivity for both devices in comparison to the single study selected by the EAG for use in the base case.

Manual doppler was used as the comparator in the model and was assumed to be a perfect reference standard. Where possible the study selected by the EAG used to populate diagnostic accuracy data for the base case compared the automated device with manual doppler. However, this was not possible for the BlueDop Vascular Expert device because studies identified only compared

against duplex ultrasound and therefore this was assumed equivalent to manual doppler for the purposes of modelling.

The base case in the model assumed that there was no time gain in healing of venous ulcers from using automated devices (i.e. that sufficient skills exist in the community to assess ABPI with manual doppler) and so the automated devices were dominated. The EAG conducted additional scenarios in an addendum to the report which showed that when time gains above 3 weeks were considered, one automated device (BlueDop Vascular Expert) became more cost-effective than manual doppler. When time gains over 5 to 7 weeks were considered, all other automated devices also became more cost-effective than manual doppler. Scenarios in which time gains in healing were considered still included the costs of manual doppler assessment being undertaken in the standard care arm.

In most scenarios any savings from slightly cheaper tests were quickly offset by risks and costs associated with withholding compression or inappropriately applying compression. There is substantial uncertainty in the model results because no data on the consequences of inaccurate test results on clinical decisions and outcomes were identified. These parameters in the model are populated using clinical expert opinion.

6 Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

People with sickle cell disease are prone to leg ulcers. Sickle cell disease is more common in people with an African or Caribbean family background.

The risk of cardiovascular disease, including peripheral arterial disease, is greater in men, people from South Asian family background and in areas of socio-economic deprivation. The risk increases with age. People with diabetes

have an increased risk of cardiovascular disease, including peripheral arterial disease.

Some people with leg ulcers may find it difficult to lie flat, in particular for the length of time it may take to rest before and do a manual doppler test. Swelling of the leg, obesity or complex ulceration may make it difficult or painful to wear blood pressure cuffs. If the automated devices can make doing the test more comfortable or quicker they may have particular benefit for these groups. But the tests may not be suitable or work accurately for people who have had lymph nodes removed or damaged (and are at risk of lymphoedema), limb amputation or other conditions where blood pressure cannot be measured on both arms or legs.

7 Implementation

User training

According to clinical experts and companies, extensive training is not needed to use the automated devices.

User skills and expertise

There are concerns about nurses becoming less skilled in using manual dopplers if the use of automated devices becomes more common. Because less expertise may be needed to use the automated devices, people who are less experienced not just in measuring ABPI but also the rest of the ulcer assessment may be expected to do the assessments and make treatment decisions.

8 Authors

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Glossary

Ankle brachial pressure index (ABPI)

Ankle brachial pressure index is measured to diagnose peripheral arterial disease. To calculate ABPI, the highest ankle pressure in a leg is divided by the highest of the 2 arm pressures. When arterial supply is healthy, the pressures are almost the same.

The NICE clinical knowledge summary on interpretation of ABPI suggests that the values are typically interpreted as:

- between 0.8 and 1.3 suggests no evidence of significant arterial disease
- between 0.5 and 0.79 suggests there are signs of arterial disease
- less than 0.5 suggests severe arterial disease

This may vary in practice. For example instead of 0.8 to 1.3, ABPI values between 0.85 or 0.9 to 1.25 are considered to suggest no sign of arterial disease. ABPI ranges used to assess arterial disease may vary for the different automated devices. In some people with diabetes, rheumatoid arthritis, systemic vasculitis, atherosclerotic disease, and advanced chronic renal failure, ABPI results may misleadingly appear normal or high because arteries have been hardened by calcium build up (arterial calcification) and are difficult to compress.

Full clinical assessment for ulcer treatment planning

Within 14 days of initial presentation, people with leg ulcers should be offered a full clinical assessment that covers their general health, the ulcer, and their leg (National Wound Care Strategy Programme [NWCSP]). Experts noted that achieving this within 14 days is a challenge, and time to this appointment can be substantially longer in some parts of the UK. In areas where practitioners trained to do the manual doppler tests are scarce, referrals may need to be made to specialist vascular services to do this assessment. This assessment

aims to identify underlying causes of the ulcer and to inform suitable treatment (NWCSP). The assessment includes vascular assessment of arterial supply using ABPI.

Doppler-based device

Doppler-based devices detect blood flow using a doppler ultrasound probe. The devices also provide doppler waveform signals in an audible form or as a visual output. The pattern of these signals can help understand the quality of the blood flow in the legs.

Oscillometric device

Oscillometric devices detect blood flow by assessing oscillations in the blood vessel wall. Because they do not use doppler ultrasound, they do not give out doppler waveform signals. But some devices provide alternative outputs such as information on pulse waveforms and oscillation profile that aim to provide information to the about the quality of the blood flow in the legs.

Plethysmography-based device

Plethysmography-based devices detect blood flow by assessing changes in blood volume. Because they do not use doppler ultrasound, they do not give out doppler waveform signals. But some devices provide alternative outputs such as information on pulse waveforms that aim to provide information to the about the quality of the blood flow in the legs.

Sickle cell disease

Sickle cell disease is the name for a group of inherited health conditions that affect the red blood cells. People with sickle cell disease produce unusually shaped red blood cells that can cause problems because they do not live as long as healthy blood cells and can block blood vessels. Sickle cell disease is a serious and lifelong health condition.

Vascular services

The Vascular Society of Great Britain and Ireland's provision of services for people with vascular disease 2021 document describes vascular service as a team of healthcare professionals who manage disorders of arteries, veins and lymphatics. Specialist vascular services are often also asked to assess people with leg ulceration.