



This document is intended to replace pages xiv, xix, 2, 12, and 92 of the original EAG assessment report for Automated measurement of ankle brachial pressure index for assessing the presence of peripheral arterial disease in people with leg ulceration, which contained a few inaccuracies or typographical errors identified by the consultees and commentators involved in the consultation phase of this assessment.

The amended pages follow in order of page number below.

## Scientific Summary

### Background

Peripheral artery disease (PAD) is a highly prevalent atherosclerotic condition characterised by the narrowing of the peripheral arteries resulting in restriction of blood supply to the affected limb. Although PAD is frequently asymptomatic, it can cause complications that can range from intermittent claudication (pain on walking which is relieved by rest) to critical limb ischaemia. Up to one-quarter of people with symptomatic PAD may require intervention and amputation may be necessary if it is left untreated. Leg ulcers are defined as wounds that occur below the knee and either on or above the ankle (malleolus). Compression treatment (bandages or stockings) is recommended to treat venous leg ulcers and there is a robust evidence base to support its effectiveness. However, compression therapy should be avoided in people with leg wounds and symptoms of arterial insufficiency as compression may cause damage by impairing the arterial supply to the ulcerated leg. To improve PAD diagnosis and decide the most suitable treatment, people with leg ulcers are assessed using ankle-brachial pressure index (ABPI) measurements. Ankle brachial pressure index is usually measured using a sphygmomanometer and manual Doppler device, which requires expertise from the relevant operator/healthcare professional. The procedure can be protracted and unpleasant for those with leg ulcers. Automated devices may be advantageous in reducing the length of time taken to assess ABPI and, thereby, any associated discomfort for the patient. In addition, automated devices may potentially be more accurate than manual processes in detecting PAD, thus conferring additional benefits such as reduced time to treatment and improved outcomes for people with leg ulcers.

### Objectives

The specific objectives of this assessment were to:

- Determine the diagnostic performance and clinical utility of automated devices available in UK clinical practice (BlueDop Vascular Expert [BlueDop Medical], boson ABI-system 100 [BOSCH + SOHN], WatchBP Office ABI [Microlife], WatchBP Office Vascular [Microlife]), MESI ABPI MD [MESI], MESI mTABLET ABI (MESI), Dopplex Ability Automatic ABI System [Huntleigh Healthcare]) for assessing the presence of PAD in people with leg ulcers.

- Considerable clinical heterogeneity - in terms of characteristics of the patient population, setting, and testing procedures - across studies that focused on people without leg ulcers;
- Suboptimal agreement between readings of the automated devices and those of the manual Doppler with a systematic tendency toward higher automated readings;
- Use of manual Doppler as the reference standard for detection of PAD;
- Variation in the prevalence of PAD across studies;
- Limited data on the performance of the automated devices in relevant subgroups of patients (e.g., diabetes patients);
- Uncertainty about the optimal threshold for automated ABPI measurement;
- Uncertainty about the potential role of automated devices in clinical practice (screening tool, alternative/adjuvant tool to current manual Doppler);
- Lack of data on the impact of the routine use of automated devices on health outcomes (e.g., the consequences of a delayed diagnosis because of false negative results);
- No data on the WatchBP Office Vascular and MESI mTABLET ABI devices

With regard to the economic modelling, we identified the following areas of uncertainties that complement those identified for the review of clinical effectiveness evidence and raise doubt about the robustness of the cost-effectiveness results:

- A lack of data regarding the impact of different tests on patient-relevant outcomes such as ulcer healing.
- It is unclear whether automated tests could achieve tangible benefits in terms of a reduced time to compression therapy in patients with venous disease. Any benefits would rely on a lack of skills to complete manual Doppler assessment in the community, and it is unclear how widespread such a skill shortage might be.
- Uncertainty around whether inaccurate test results might be identified during clinical evaluation of patients during a testing appointment, and thus the extent to which inaccurate results would be acted upon in clinical practice (i.e., if tests would lead to inappropriate compression of arterial ulcers [false negatives], or delayed time to compression [false positives]).
- Limited data regarding the costs and outcomes specifically for mixed ulcer disease

## **Chapter 2. Background and definition of the decision problem**

### **2.1 Description of the health problem**

#### ***Peripheral artery disease***

Peripheral artery disease (PAD) is a common atherosclerotic condition caused by narrowing or blockage of the arteries by fatty deposits (known as atheroma), which results in a reduction of blood supply to the affected limb. PAD is associated with an increased risk of vascular complications such as myocardial infarction and stroke. Early treatment is known to reduce mortality and morbidity.<sup>1</sup> Although PAD is frequently asymptomatic, it can cause complications that can range from intermittent claudication (pain on walking which is relieved by rest) to critical limb ischaemia. Manifestations of critical limb ischaemia include ulceration and gangrene. People with critical limb ischaemia are at high risk of limb amputation and premature death.<sup>2-4</sup>

#### ***Leg ulcers***

Leg ulcers are defined as wounds that occur below the knee and either on or above the ankle (malleolus). Most leg ulcers (about 70%) are venous leg ulcers caused by blood accumulating in the legs due to problems in the veins, which tend to be chronic and recurring;<sup>5</sup> about 10% of leg ulcers are caused by peripheral arterial disease and about 20% are mixed aetiology leg ulcers (both arterial and venous).<sup>5-8</sup> Outbreaks of ulceration can last from weeks to years and ulcers can extend to a surface area greater than 25cm<sup>2</sup>.<sup>9-11</sup>

Compression therapy (bandages or stockings) has historically been used to treat venous leg ulcers and there is a large evidence base to support its effectiveness.<sup>12</sup> However, using compression to treat ulcers may cause damage by impairing the arterial supply to the ulcerated leg. As compression therapy is unsuitable for people with PAD,<sup>13, 14</sup> it is recommended that people with leg ulcers are screened for arterial disease using the ankle-brachial pressure index (ABPI).<sup>12, 13</sup>

## **2.2 Incidence and/ or prevalence**

### ***Peripheral artery disease***

Global prevalence of PAD of 10-15% has been estimated<sup>3, 15, 16</sup> and increases with age, especially in those aged in their 60s and 70s.<sup>2, 17-20</sup> The incidence of PAD is similar between and review every 6 months. Changes in symptoms or skin problems related to the compression hosiery should prompt a reassessment, including a vascular assessment of arterial supply.

The SIGN Guideline 120 for management of chronic venous leg ulcers indicated that patients should be offered the strongest compression that maintains patient concordance. The guideline was withdrawn in August 2020 and is currently being refreshed.<sup>29</sup>

### ***Model parameters – Transition probabilities for Markov model.***

At the end of the decision tree phase of the model, the surviving cohort enter the Markov model. Patients with venous ulcers enter the healed / unhealed states depending on whether their ulcer healed by week 24. Patients with arterial disease, are assumed to have CLI, due to the presence of an arterial ulcer (Fontaine Stage 4) and enter the CLI state where they receive invasive treatment (angioplasty or bypass surgery). Patients with mixed ulcers follow a pathway according to disease severity defined using the Fontaine stages of disease.

#### *Venous ulcers*

Those who are unhealed at 24 weeks entered the “unhealed” model state, but can continue to transition to the healed state over the longer term, following long-term follow up data from the EVRA RCT.<sup>99</sup> Data from the per protocol analysis for deferred ablation show that 87.2% (170/195) of venous ulcer patients have achieved healing of the primary index ulcer by one year.

The proportion of the cohort with a healed ulcer are then subject to an ongoing risk of recurrence. Two sources were deemed potentially relevant for parameterising venous ulcer recurrence risk, with long term data available from both the ESCHAR and EVRA long-term follow up studies. The ESCHAR study showed a recurrence rate of 56% for the compression only arm of the trial at 4 years follow-up.<sup>100</sup> Data from the deferred intervention arm of the EVRA study showed that 38 /154 (24.7%) of those followed up at 1 year had a recurrence of the primary ulcer.<sup>93</sup> Long term follow-up data showed that 2- and 3-year cumulative recurrence rates were 0.239 (95% CI: 0.1852, 0.3053) and 0.2995 (95% CI: 0.2392, 0.3710) respectively, converting to six monthly probabilities of ulcer recurrence of 3.5% and 5.5% in years 2 and 3 respectively.<sup>99</sup> Four-year data were also available, but the numbers at risk were small (N=32) and considered insufficient to populate the model. 3-year recurrence probabilities are then extrapolated over the remaining lifetime horizon of the model. The data from EVRA are applied in the base case analysis because 1) it provides a consistent source to populate multiple model parameters, 2) data are obtained from a large UK sample, and 3) granular data across multiple timepoints, including confidence intervals to derive distributions for the probabilistic analysis are available for several parameters.

The probability of healing for a recurrent ulcer was also obtained from the EVRA long-term follow up data. The probability of healing and subsequent recurrence risks for second and subsequent recurrences were assumed equal to the first given a lack of data beyond the first venous ulcer recurrence. This is likely to be a conservative estimate of future long-term