Supplementary Appendix

Evaluating the prognostic performance of bedside tests used for peripheral arterial disease diagnosis in the prediction of diabetic foot ulcer healing

Contents

Figure S1

Figure S1 : Patient flow chart, showing initial criteria for Testing for Arterial disease in Diabetes (TrEAD study) followed by the patient selection and recruitment for the patients including in our study. The included patients all had active foot ulceration and the diagram highlights the number of patients who had missing data .

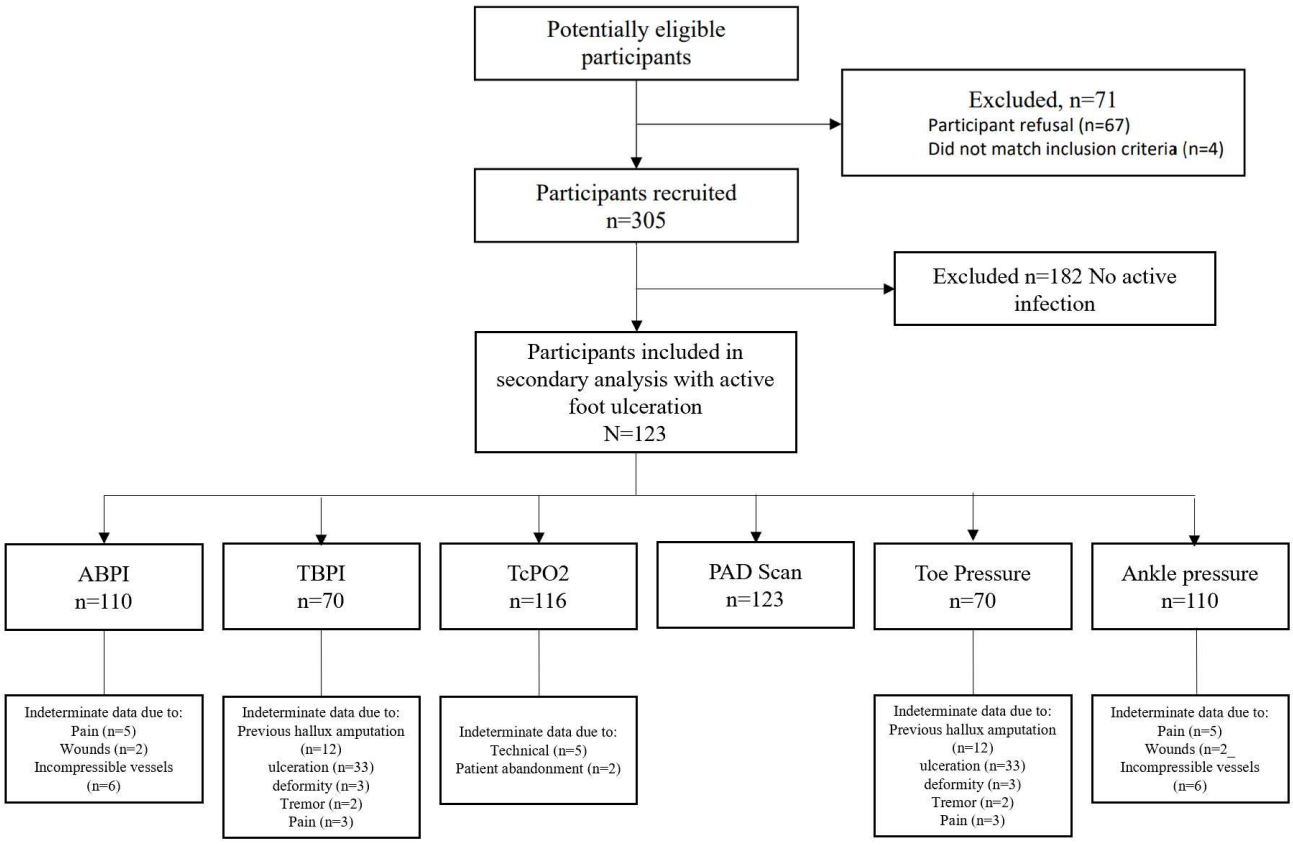


Figure S2

Figure S2 – Figure copied from Normahani et al., 'Diagnostic Accuracy of Point-of-Care Tests Used to Detect Arterial Disease in Diabetes'. Showing the flow chart for qualitative PAD-scan waveform assessment.

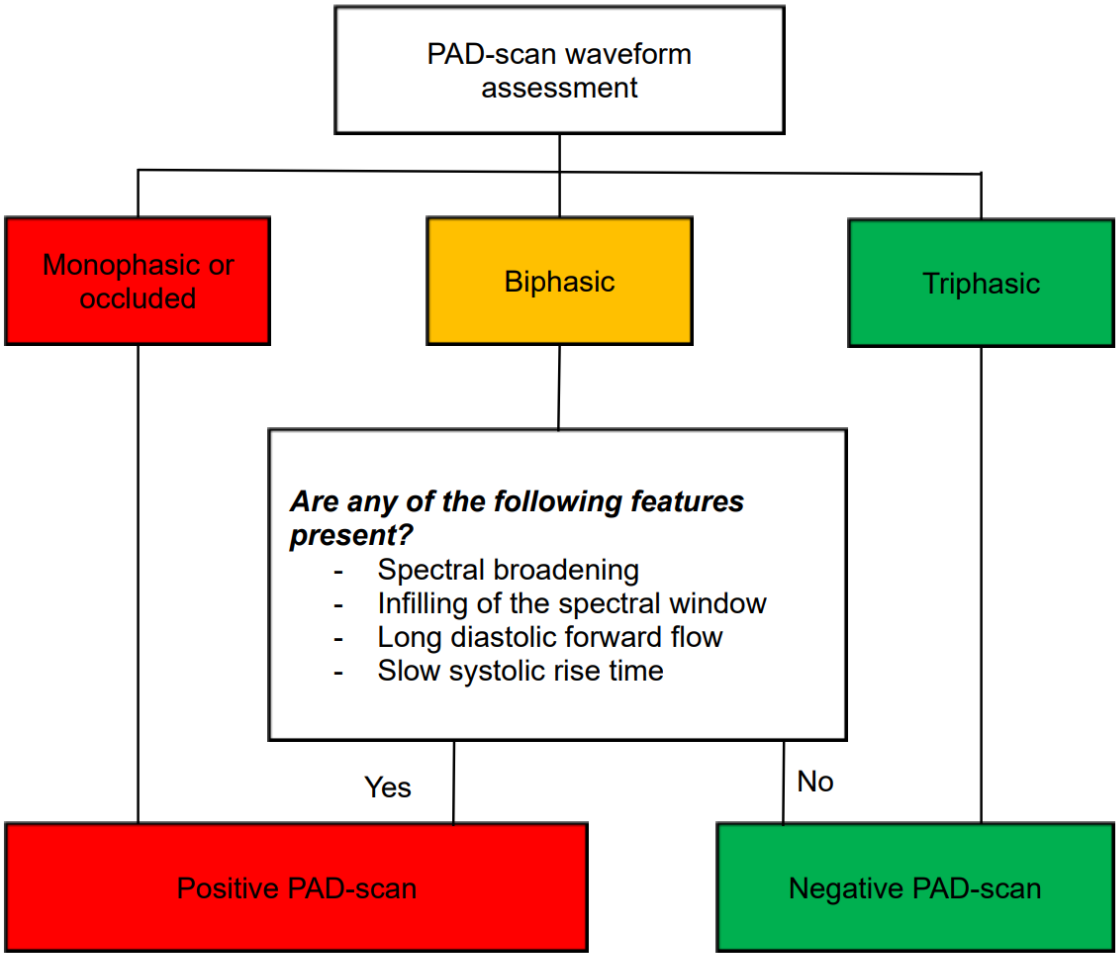
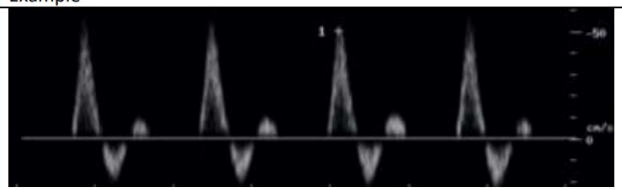
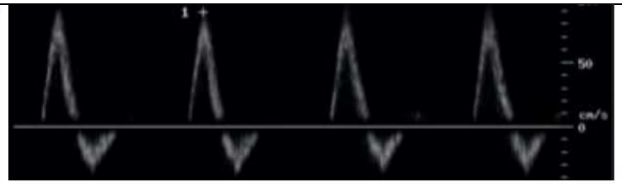
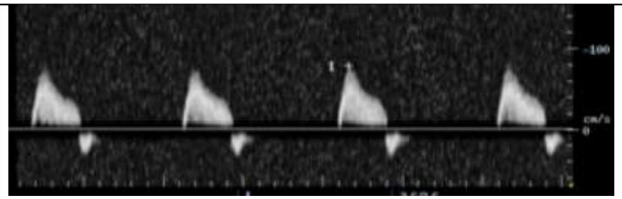
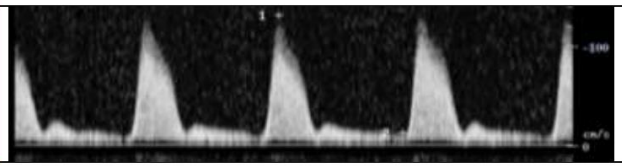


Figure S3

Figure S3 – Figure copied from Normahani et al., 'Diagnostic Accuracy of Point-of-Care Tests Used to Detect Arterial Disease in Diabetes', demonstrating normal physiological and abnormal pathological PAD-scan arterial spectral waveforms.

Waveform	Example	Description
Triphasic		Normal 'triphasic' waveform.
Biphasic (with no adverse features)		Normal 'biphasic' waveform.
Biphasic (with adverse features)		Abnormal 'biphasic' waveform with spectral broadening.
		Abnormal 'biphasic' waveform with spectral broadening, infilling of the spectral window and long diastolic forward flow.

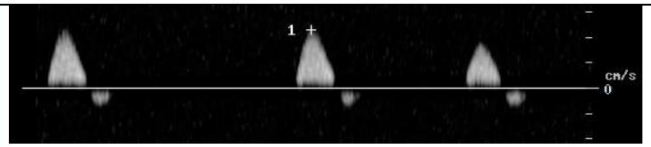
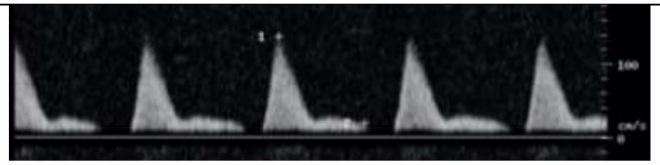
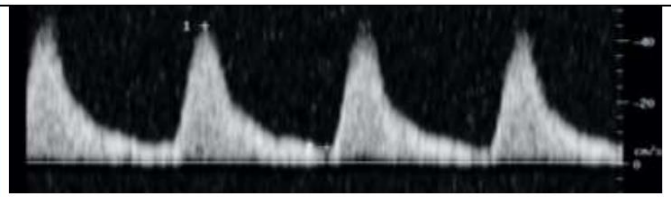
		Abnormal 'biphasic waveform with slow systolic rise time, spectral broadening and infilling of the spectral window.
		Abnormal 'biphasic' waveform with spectral broadening, long diastolic forward flow and infilling of the spectral window.
Monophasic		Abnormal 'monophasic' waveform.
		Abnormal 'monophasic' waveform.
		Abnormal 'monophasic' waveform.

Table S1

Table S1		
Index/Reference	Test	Procedure / diagnostic cut off
Index	PAD-scan	**Procedure** The PAD-scan was performed using a portable ultrasound system (Mindray M7; Shenzhen, China) with a linear 6-14Hz transducer. The anterior tibial posterior tibial artery were first visualised at the ankle, using B-mode imaging and colour Doppler, in transverse and then longitudinal 17 planes. Arterial spectral waveforms were then sampled from the centre of each vessel using a Doppler angle of <60. Waveforms were optimised for interpretation by adjusting sample volume, sample size, **Primary cut-off** The presence of an occlusion, venous like slow flow, monophasic waveform or a biphasic waveform with adverse features in either vessel scanned was considered diagnostic of PAD (figure S1). Adverse features (assessed qualitatively) were defined as slow systolic rise time, spectral broadening, infilling of the spectral window and long forward flow (figure S2).

		Secondary cut-off Monophasic waveform in either vessel. A monophasic or any biphasic waveform in either vessel.
Index	ABPI	**Procedure** ABPI measurements were performed using a sphygmomanometer cuff placed at the ankle and a handheld audible Doppler device (Dopplex D900 Audio only Doppler, Huntleigh Healthcare Ltd., Cardiff) to measure dorsalis pedis and posterior tibial artery systolic pressure. Brachial artery pressures from both arms were taken and the highest reading used to calculate the ABPI. **Primary cut-off** ABPI values ≤0.9 in either vessel. **Secondary cut-off** ABPI value ≤0.9 or >1.3 in either vessel.
Index	TBPI	**Procedure** TBPI assessment were performed after the patient was rested in the supine position for at least 10 minutes. Measurements were made using the Huntleigh toe pressure kit (Huntleigh Healthcare Ltd., Cardiff) employing an infrared sensor placed on the hallux and

		both index fingers. The highest upper limb reading was used to calculate the TBPI. **Primary cut-off** TBPI values of <0.75 in either vessel **Secondary cut off** N/A
Index	TcPO2	**Procedure** TcPO2 measurements were taken using the Periflux System 5000 (Perimed, Sweden) following at least a 20-minute period of acclimatisation in the resting supine position with the room temperature maintained between 23°C and 25°C. Dry skin was removed and the skin cleansed before 18 fixing transducers using double-sided adhesive rings and contact liquid. The machine was calibrated prior to every patient assessment. Re-membraning of electrodes was carried out on a weekly basis. Measurements were taken centrally (at the sternum, or the deltoid in the presence of a sternotomy scar) and on the dorsum of the foot using an automated machine equipped with Clark electrodes. Electrodes were kept on for 15 minutes prior to taking readings. Foot TcPO2 measurements were performed away from bony prominences, wounds, superficial vessels, callused skin, oedematous

		and inflamed areas. Foot measurements were then repeated after 3 minutes of 30° leg elevation supported by a wedge. **Primary cut-off** TcPO2 readings of <40mmHg at resting supin position in the foot electrode **Secondary cut off** TcPO2 drop of >10mmHg on foot elevation TcPO2 regional perfusion index (RPIl limb TcPO2 values normalised to central values of <0.6

Table S1_Table copied from Normahani et al., 'Diagnostic Accuracy of Point-of-Care Tests Used to Detect Arterial Disease in Diabetes'. details of index test procedure and diagnostic cut off values.

Table S2

Table S2 – tabulated results comparing each modality of bedside tests and the positive and negative results at different measurements. These results were used to analyse the positive and negative likelihood ratios.

	Not Healed	Healed
PAD-scan		
Mono, or absent, or any bi		
Positive	45	39
Negative	13	26
Mono or any bi with adverse features		
Positive	53	49
Negative	5	16
Mono or absent		
Positive	54	60
Negative	4	5
ABPI (n=110)		
<=0.9 or absent signal in both vessels		
Positive	19	22
Negative	30	39
<=0.7 or absent signal in		

both vessels Positive Negative	 14 35	 16 45
<=0.5 or absent signal in both vessels Positive Negative	 11 38	 12 49
Ankle pressure (n=110)		
<=90 mmHg or absent signal in both vessels Positive Negative	 46 3	 59 2
<=70mmHg or absent signal in both vessels Positive Negative	 43 6	 57 4
<=50mmHg or absent signal in both vessels Positive Negative	 42 7	 57 4

	Not Healed	Healed
TBPI (n=70)		
<=0.8		
Positive	19	23
Negative	5	23
<=0.6		
Positive	13	13
Negative	11	33
<=0.4		
Positive	6	7
Negative	18	39
TCPO2 (n= 116)		
TcPO2 at rest (<=80mmHg)		
Positive	54	58
Negative	2	2
TcPO2 at rest (<=60mmHg)		
Positive	44	43
Negative	12	17
TCPO2 at rest (<=40mmHg)		
Positive	24	18
Negative	32	42
TCPO2 at rest (<=20mmHg)		
Positive	5	2
Negative	51	58

Toe pressure (n=70)		
<=80mmHg		
Positive	21	37
Negative	3	9
<=60mmHg		
Positive	17	28
Negative	7	18
<=40mmHg		
Positive	11	23
Negative	13	23
<=20mmHg		
Positive	6	18
Negative	18	28

Table S3 – STARD Checklist

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	1
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	3
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	4
	4	Study objectives and hypotheses	4
METHODS			
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	5

Participants	**6**	Eligibility criteria	5
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	5
	8	Where and when potentially eligible participants were identified (setting, location and dates)	5
	9	Whether participants formed a consecutive, random or convenience series	5
Test methods	**10a**	Index test, in sufficient detail to allow replication	5 & Table S1
	10b	Reference standard, in sufficient detail to allow replication	5,6 & Table S1
	11	Rationale for choosing the reference standard (if alternatives exist)	5, 6
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	5, 6 & Table S1
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	5, 6 & 7
	13a	Whether clinical information and reference standard results were available	5, 6 & 7

		to the performers/readers of the index test	
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	5, 6 & 7
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy	5, 6 & 7
	15	How indeterminate index test or reference standard results were handled	5, 6 & 7
	16	How missing data on the index test and reference standard were handled	5, 6 & 7
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	5, 6 & 7
	18	Intended sample size and how it was determined	5, 6 , 7 & Figure S3
RESULTS			
Participants	**19**	Flow of participants, using a diagram	Figure S3
	20	Baseline demographic and clinical characteristics of participants	5 & Figure S3
	21a	Distribution of severity of disease in those with the target condition	5-7
	21b	Distribution of alternative diagnoses in those without the target condition	5-7
	22	Time interval and any clinical interventions between index test and reference standard	5

Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	9-15
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	9-15
	25	Any adverse events from performing the index test or the reference standard	8-15
DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	16-18
	27	Implications for practice, including the intended use and clinical role of the index test	16-18
OTHER INFORMATION			
	28	Registration number and name of registry	1
	29	Where the full study protocol can be accessed	N/A
	30	Sources of funding and other support; role of funders	19