Ankle-Brachial Index determination and peripheral arterial disease diagnosis by an oscillometric blood pressure device in primary care: validation and diagnostic accuracy study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001689
Article Type:	Research
Date Submitted by the Author:	19-Jun-2012
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Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Cardiovascular medicine, Public health
Keywords:	PRIMARY CARE, VASCULAR MEDICINE, PUBLIC HEALTH

Ankle-Brachial Index determination and peripheral arterial disease diagnosis by an oscillometric blood pressure device in primary care: validation and diagnostic accuracy study

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Keywords

Sensitivity and specificity, Ankle-Brachial Index, peripheral arterial disease, oscillometric device, blood pressure.

Word count - excluding title page, abstract, references, figures and tables.

2337

ABSTRACT

Objectives

To determine the level of agreement between a 'conventional' Ankle-Brachial Index (ABI) measurement (using Doppler and mercury sphygmomanometer taken by a research nurse) and a 'pragmatic' ABI measure (using an oscillometric device taken by a practice nurse) in primary care. To ascertain the utility of a pragmatic ABI measure for the diagnosis of peripheral arterial disease (PAD) in primary care.

Design

Cross-sectional validation and diagnostic accuracy study. Descriptive analyses were used to investigate the agreement between the two procedures using the Bland and Altman method to determine whether the correlation between ABI readings varied systematically. Diagnostic accuracy was assessed via sensitivity, specificity, accuracy, likelihood ratios, positive and negative predictive values, with ABI readings dichotomised and Receiver Operating Curve analysis using both univariable and multivariable logistic regression.

Setting

Primary care in metropolitan and rural Victoria, Australia between October 2009 and November 2010.

Participants

250 persons with cardiovascular disease (CVD) or at high risk (3 or more risk factors) of CVD.

Results

Despite a strong association between the two method's measurements of ABI there was poor agreement with 95% of readings within ±0.4 of the 0.9 ABI cut point. The multivariable C statistic of diagnosis of PAD was 0.89. Other diagnostic measures were sensitivity 62%,

specificity 92%, positive predictive value 67%, negative predictive value 90%, accuracy 85%, positive likelihood ratio 7.3 and the negative likelihood ratio 0.42.

Conclusions

Oscillometric ABI measures by primary care nurses on a population with a 22% prevalence of PAD lacked sufficient agreement with conventional measures to be recommended for routine determination of ABI. Their diagnostic performance suggests that a pragmatic ABI lacked sufficient sensitivity to diagnose PAD, but can reliably exclude it.

INTRODUCTION

Peripheral arterial disease (PAD) affects an estimated 27 million individuals in Europe and North America with 413,000 related hospital discharges per annum[1 2]. These figures are likely to underestimate the true impact of PAD as those with the condition disproportionally suffer from other manifestations of CVD and are therefore likely to appear in coronary artery disease or stroke statistics. As a consequence there has been a call for better detection and management of the condition[1].

One of the simplest and most useful parameters to objectively assess lower extremity arterial perfusion, and thus diagnose PAD, is the Ankle-Brachial Index (ABI). This is the lower of the left and right ABI where each ABI is the ratio of the lower limb systolic blood pressure is compared to the higher systolic brachial blood pressure recording. The ABI can be used to screen for haemodynamically significant PAD and helps to define its severity. Patients with objectively documented PAD have a four- to six-fold increase in cardiovascular mortality over healthy age-matched individuals[3]. PAD is a stronger risk marker for myocardial and stroke morbidity and mortality than those who have already had such an incident event[4]. However, only 50% of people with PAD are symptomatic which is a significant issue in the detection of PAD[5].

Between 2007 and 2009 19,500 oscillometric devices were distributed by the High Blood Pressure Research Council of Australia to physicians, mostly general practitioners (GPs). We had previously demonstrated that these devices were likely to improve blood pressure management in primary care[6]. The current study, Ankle Brachial Index Determination by oscillometric method IN General practice (ABIDING), sought to expand the utility afforded by these machines in primary care. Previous work done in those attending a specialist vascular

laboratory in the US demonstrated that patients could have their ABI reliably ascertained by such devices compared to the conventional use of a Doppler ultrasound and mercury sphygmomanometer[7]. It was therefore opportune to investigate if such measures were pragmatic in primary care where the greatest opportunity exists to identify those with undiagnosed PAD. Such persons are at very high risk for subsequent adverse cardiovascular events that can be ameliorated through management of modifiable risk factors.

The primary aim of ABIDING was to establish if there was agreement between a pragmatic ABI (measured by a practice nurse using an oscillometric blood pressure device), and a conventional ABI (measured by a research nurse using mercury sphygmomanometer and Doppler devices). A secondary aim was to ascertain diagnostic accuracy of the pragmatic approach for ascertaining PAD.

METHODS

General practitioners (GPs) and participants were recruited through the REACH Registry Victorian database. The international REACH Registry was a prospective, observational registry designed to provide long-term follow-up (36 months) of patients at high risk of atherothrombotic events. Globally 67,888 patients were involved in the REACH registry of whom 2,782 were recruited from 281 general practitioners around Australia[8 9]. Practices were eligible for ABIDING if they had previously enrolled participants in the REACH registry and had a practice nurse willing to participate or were willing to appoint a *locum tenens* nurse. Eligibility criteria for REACH are published elsewhere but can be summarised as at entry (March to June 2004) aged 45+ years, had known CVD or at least three atherosclerosis risk factors, and were physically able to attend their usual general practice[8].

Participant recruitment

All Melbourne (metropolitan) and Warrnambool (rural) Victorian study participants who had consented to follow-up, who had been identified by their GPs as alive and for whom we had a current address, were contacted by mail. If no reply was received from the participant within four weeks, a second letter was sent and then a telephone call made. Participants were seen in their usual GP's clinic between October 2009 and November 2010.

Research and practice nurses

Three experienced research nurses conducted the reference standard tests. They received standardised training from a senior research nurse who was one of the operators. Practice nurses were given training in situ by the research nurse and were observed by them. Because they worked contemporaneously the research nurse was not blinded to the practice nurses results.

'Conventional' and 'pragmatic' ABI estimation

All participants were rested supine for five minutes before measurement. Doppler blood pressure measurements (by research nurse) and automated oscillometric blood pressure measurements (by practice nurse) were performed using cuffs that had bladders >80% of the diameter of the arms and ankles measured.

Conventional measures involved Doppler blood pressure measurements in the lower limb made with a Nicolet Vascular Doppler with a 5MHz probe. The cuff was inflated to 30mmHg above systolic blood pressure and deflated slowly until a flow signal was detected over the dorsalis pedis or posterior tibial arteries. Brachial artery systolic pressure was determined similarly but utilising a stethoscope rather than a Doppler. The ABI for each lower extremity was calculated as the pedal pressure divided by the higher of the two brachial pressures. PAD is defined as an ABI <0.9 in either lower limb[10]. The mercury sphygmomanometer was calibrated by a certified laboratory.

Research nurses were trained in the measurement of ABI and were certified prior to commencement of the study. Practice nurses were simply observed and technique corrected if required. Oscillometric measurements were made by the practice nurse on all limbs using a standard automated blood pressure cuff system (OMRON HEM-907). This device is a validated blood pressure measurement device[11 12]. Oscillometric devices were new and therefore had factory calibration.

Statistical Methods

Descriptive analyses were used to investigate the agreement between the two procedures using the Bland and Altman method to determine whether measurements could be used interchangeably and if the correlation between ABI readings varied systematically[13]. Although the variability in the differences appeared to be proportional to the mean, applying a log transformation to the data did not substantially alter agreement and so raw scores are presented. Correlations between the paired readings were also calculated. Sensitivity, specificity, positive and negative predictive values, and accuracy with exact 95% confidence intervals are reported, where ABI readings taken under both conditions were dichotomised at 0.9 (reference standard). The diagnostic accuracy was evaluated using Receiver Operating Curve analysis and quantified as the area under the curve (AUC or C statistic), as determined using both univariable and multivariable logistic regression. In the multivariable model we adjusted for age, BMI, gender, and smoking status (never, former, current). The calibration of this model was validated using the Hosmer-Lemeshow statistic[14]. We examined likelihood ratios, the ratio of the expected test results in participants with PAD to those participants without. All results are reported with 95% confidence intervals. All analyses were conducted using Stata version 12.0.

Power calculations

Assuming a type 1 error of 5% ($\alpha = 0.05$) a total sample of 250 participants provided 80% power to detect systematic bias between the readings taken by the research and practice nurses if the mean difference was 0.0255[13]. Eight participants were excluded as 6 pragmatic and 2 conventional ABI readings were absent. In all other cases each patient had at least one conventional and pragmatic ABI reading (for the same leg). For a sample of 242 the difference that we could detect was 0.0257. We expected strong correlations between ABI readings taken using the different methods. Both calculations assumed a correlation between readings of 0.61 and standard deviations as reported in Benchimol *et al*[15].

RESULTS

The flow chart of the study is shown in Figure 1. The characteristics of the ABIDING population are shown in Table 1. There was no difference between those excluded and included in the analysis for any trait that we measured. We also compared in Table 1 those diagnosed with PAD vs. not using conventional ABI. Those with PAD were older (p=0.003) and more likely to be female (p=0.003). Figure 2 shows there was poor agreement between pragmatic and conventional determination of ABI with 95% of readings within ±0.4. Figure 3 shows correlation between conventional and pragmatic ABI measurements, indicating a strong association between the two measurements, despite the poor agreement. The distribution of differences between the ABI measures is shown in Figure 4. These differences were regressed on all possible confounders measured in our study, in both univariable and multivariable models. There were no significant associations, suggesting that the differences were completely random.

A 2x2 table of dichotomised conventional and pragmatic measurements is shown (Table 2). We examined the two groups comprising the 36 participants where the PAD classification differed.

There were no differences in any measured trait between those groups (data not shown). The respective pragmatic method diagnostic performance, assuming the conventional method as gold standard, was sensitivity 62% (95% CI 47-75%), specificity 92% (87-95%), positive predictive value 67% (52%-80%), negative predictive value 90% (85-94%) and accuracy 85% (80%-89%). The Likelihood ratio for a positive result (LR+) was 7.3 (95% CI 4.4-12.0) and Likelihood ratio test for a negative result (LR-) 0.42 (0.30-0.59). Area under the Receiver Operator Characteristic curves (AUC / C statistic) of pragmatic ABI against the conventional ABI <0.9 and thus PAD was 0.87 (95% CI 0.82, 0.93). The AUC from multivariable analysis (adjusting for age, gender, BMI and smoking status) for all analyses were almost identical 89% (95% CI 84%-93%).

Based on the differences in Table 1 for those with PAD vs. not we conducted a post hoc subgroup analyses on pragmatic vs. conventional ABI readings by gender, age (dichotomised as young or old) and all pairwise combinations. The agreement between reading and diagnostic criteria did not improve for any subgroup (data not shown). We also investigated (using multivariable logistic regression) whether there was any evidence that disagreements were systematic. There were no differences between in disagreement apart from current smokers were more likely to produce readings that disagreed compared to non-smokers ($p=0.025$). A subgroup analysis with current smokers removed did not alter the diagnostic criteria of the tests.

As could be expected in non-invasive testing there were no reported adverse events.

DISCUSSION

ABIDING demonstrated that use of oscillometric devices by general practice nurses to determine ABI and therefore the presence of PAD had high specificity (92%) and negative predictive value (90%), good accuracy (84%) but modest sensitivity (62%) and positive predictive value (67%). The modest sensitivity and the LR+ 7.3 indicate that this test has little value for confirming the presence of PAD. On the other hand high specificity and negative predictive value suggests that the test has some value in ruling out the disease (i.e. when the test is negative). This is in contrast to the experience in a specialist centre where their test performance (both limbs in comparison to ABIDING lower of the 2 measures) was sensitivity left/right leg 88/73% (62%), specificity 85/95% (92%), positive predictive value 65/88% (69%), negative predictive value 96/88% (90%), LR+ left/right leg 5.9/14.6 (7.9) and LR- 0.14/0.28 (0.4)[7]. A good diagnostic test has a LR+ >10 and LR- < 0.1[16]. This difference in performance to some extent may be accounted for by patient selection but is more likely due to operator expertise. In the specialist centre, the mean age was 10 years younger and 53% were female compared to only 22% in ABIDING. The respective prevalence of PAD was 32% and 22%.

ABI is a useful tool and is superior to clinical examination for identifying PAD[9]. However screening whole populations is not practical. ABI ascertainment of PAD is most effective by identifying high risk patients as we have done in ABIDING. By including high-risk and overt CVD patients we were confident that we should get a distribution of ABI scores that included PAD diagnostic scores and the outcome of the trial supports this (22% had PAD by the conventional method). Doubini *et al* found age alone (70+) a useful predictor as 12.5% of the screened population had PAD vs. only 2.5% of 50-69 years with at least 1 CVD risk factor but no established CVD (diabetes, dyslipidaemia, hypertension, or smoking)[17]. Bendermacher *et al* developed a clinical prediction model giving risk factor points per factor (age: 1 point per 5 years starting at 55 years; ever smoked: 2 points; currently smoking: 7 points; and hypertension: 3 points), showed a proportional increase of the PAD prevalence with each increasing risk profile (range: 7.0-40.6%)[18]. The overall prevalence of PAD was 18%. They found with their PREVALENT clinical prediction model (based on CVD risk factors), the GP was able to identify a high-risk population in which measurement of ABI was useful.

If our method had been reliable it would have been readily implementable as Australian GPs have ready access to oscillometric sphygmomanometers. More than 19,500 devices were distributed on behalf of the High Blood Pressure Research Council of Australia, mostly to GPs, over the years 2007 to 2009. Practice nurses were chosen rather than GPs as this approach is also more likely to be implementable. A survey by Mohler *et al* of primary care clinicians showed that most (88%) thought ABI to be feasible in that setting[19]. However, validation studies have largely been conducted in specialist clinics in a variety of study populations rather than in the primary care setting where most of the medical contact is likely to occur[15 20-23]. The one study done in the primary care setting used an ABIgram[24]. Although the investigators demonstrated its reliability, the use of this special piece of equipment would seem to effect is acceptability as is the current situation.

Study limitations

The intervention was kept as simple as possible by using practice nurses to do single measures on a device they were familiar with but did not receive extensive further training on. While this means that this is simple to introduce into clinical practice the practice nurse performance may have been improved by more intense training and repeated limb measurements.

CONCLUSION

Oscillometric ABI measures by primary care nurses on a population with a 22% prevalence of PAD lacked sufficient agreement with conventional measures to be recommended for routine determination of ABI. This pragmatic method may be used as a screening tool in primary care but its diagnostic performance does not provide evidence sufficient for it to be used to diagnose PAD.

ACKNOWLEDGMENTS, COMPETING INTERESTS, FUNDING

Participating GPs were Drs Sam Arber, Dean Arnot, Ian Barratt, Irmgard Chia, John Chin, Eric Choo, Andrew Chow, Michael Conos, Simon Cooper, Peter Coulton, Adrian Dabscheck, Deborah Davidson, Antonio De Sousa, Hillary Donald, Peter Eizenberg, Peter Enten, Roger Fagan, Peter Ferguson, Doron Gaddie, Jon Garland, Andrew Gault, Ian Gill, Robert Gingold, Peter Goy, Judith Heale, Eva Herold, Chris Hogan, Suresh Jain, Brendan Kay, John Kirmos, Susan Kloot, Con Lahanis, Daniel Lajoie, Maryanne Lancaster, Conway Leung, Leon Lewi, John Manderson, Frank Marano, Damian Marinucci, Larry McGrath, Elizabeth McNaughton, Margaret McNiff, John Meaney, Paul Molloy, Clare Mooney, Paul O'Hanlon, James Olesen, Michael Page, John Pattison, Gary Pellizzari, Annamarie Perlesz, John Philpot, Leon Piterman, Jock Plenderleith, Mark Preston, Christopher Priest, Andy Psaradellis, Michael Quinn, Jacqueline Rounsevell, Joseph Sakowsky, Mahinda Samararatna, Victor Sammut, David Slonim, Stuart Smith, Stephen Stowe, Ian Sutherland, Edwin Turner, Peter Wexler, Andrew White, Martin Williams, Stephen Williams, Keith Wing Shing, Richard Wrennall, and Michael Ziccone.

We would also like to acknowledge the contribution of practice nurses, Dr Nyi Nyi Tun who assisted with the literature review, and research nurses Christine Mulvaney, Sue Loftus, and Anne Bruce.

This study had ethical approval from the Human Research Ethics Committee (Tasmania) Network (H0010410) and Monash University Standing Committee on Ethics in Research involving Humans (2009000860), and was registered with the Australian and New Zealand Clinical Trails Registry (ACTRN12609000744257). It was funded by the RACGP Research Foundation (Cardiovascular Research Grant) and the National Health and Medical Research

Council (Project grant 544935), and was supported by the Primary Healthcare Research, Evaluation and Development scheme. Oscillometric devices were loaned by the High Blood Pressure Research Council of Australia.

No competing interests declared.

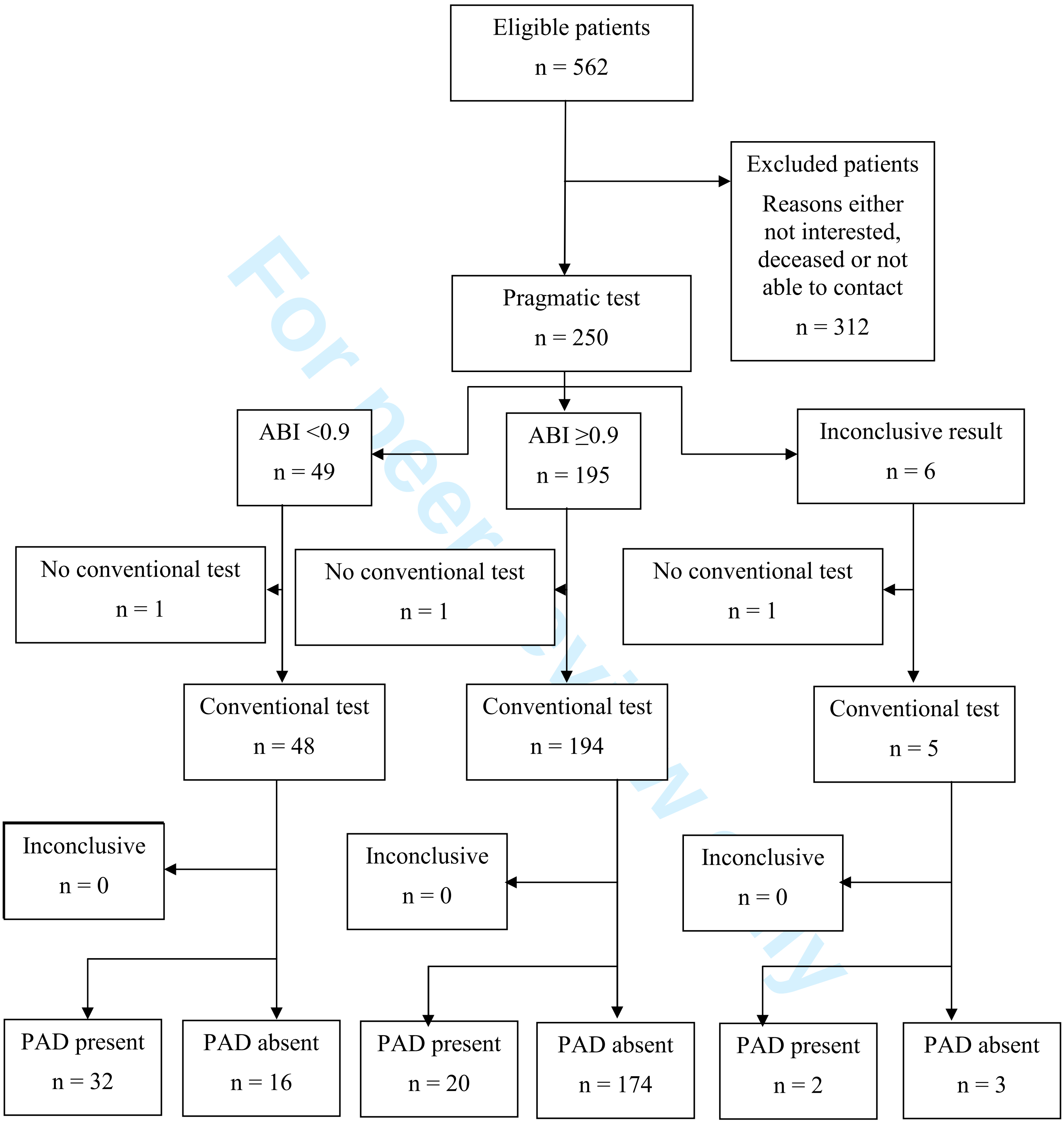

Figure 1. Flow diagram of a diagnostic accuracy in ABIDING as per STARD standard[25].

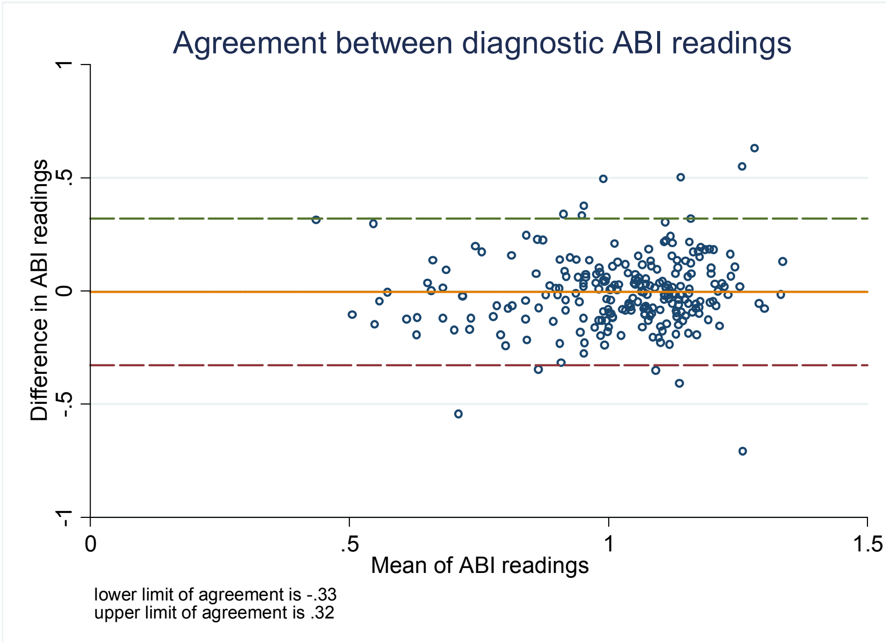

Figure 2. Agreement between pragmatic and conventional determination of ABI.

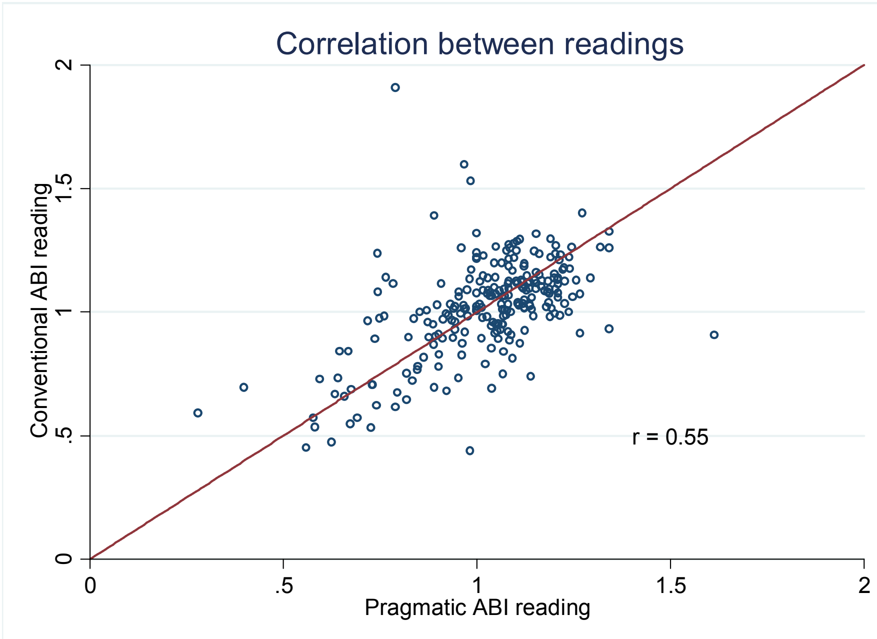

Figure 3. Correlation between pragmatic and conventional determination of ABI.

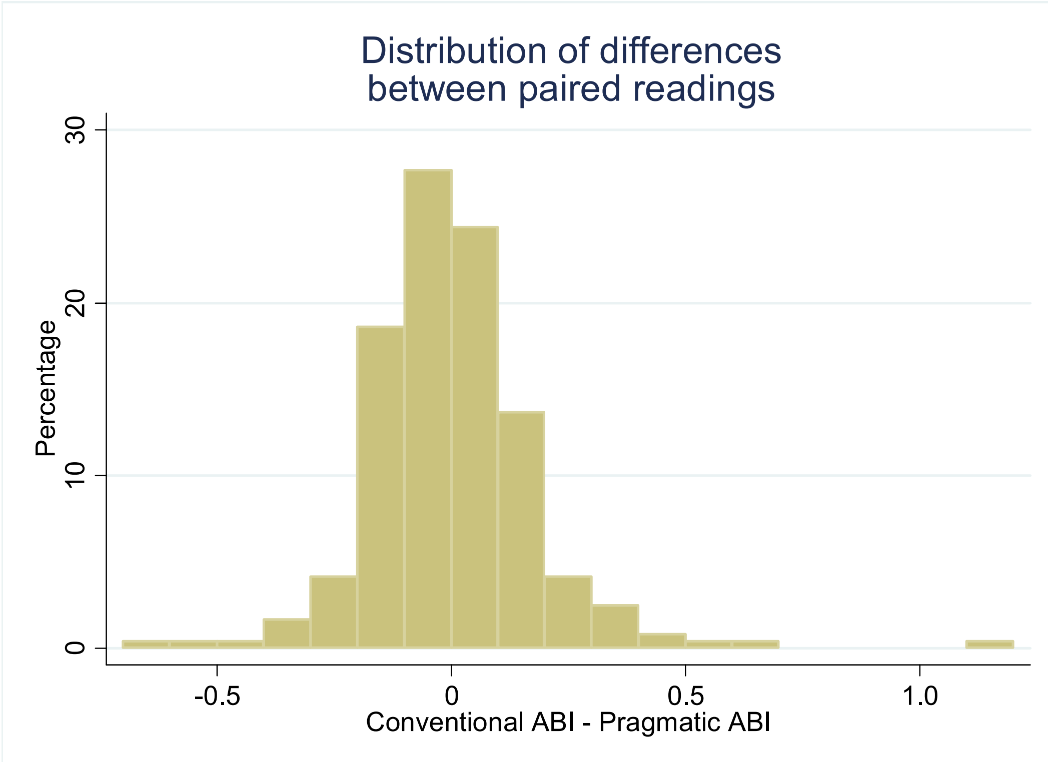

Figure 4. Distribution of the difference between the conventional ABI and the pragmatic ABI readings.

Variable	*Included*	*Excluded*[†]	*P for difference*	*Conventional ABI ≥ 0.9*	*Conventional ABI < 0.9*	*P for difference*
N	242	8		192	52	
Age in years	71.2(7.4)	72.5(7.2)	0.62	70.4(7.0)	73.9(8.3)	0.003
Male Sex (%)	167 (69.0)	5(62.5)	0.70	140(73.7)	27(52.0)	0.003
SBP (mmHg)	141.5(18.9)	153.9(20.7)	0.07	140.6(17.8)	144.5(22.4)	0.35
DBP (mmHg)	76.7(9.9)	82.1(10.6)	0.13	77.0(9.8)	75.5(10.4)	0.55
BMI (kg/h^2)	27.5(4.4)	29.3(5.9)	0.26	27.5(4.4)	27.2(4.4)	0.63
Waist	99.9(10.8)	99.1(13.0)	0.84	100.1(10.4)	99.2(12.3)	0.60
Smoking status			0.15			0.31
Never	98(40.7)	6(75.0)		81(42.9)	17(32.7)	
Former	131(54.4)	2(25.0)		100(52.9)	31(59.6)	

Current	12(5.0)	0(0.0)		8(4.2)	4(7.7)	

† 5 did not provide pragmatic ABI readings, 2 did not provide conventional ABI readings, 1 did not provide any readings.

Table 1: Characteristics of participants (included in and excluded from the analysis) and by conventional PAD status expressed as a mean (standard deviation) or N (%) as appropriate.

	PAD +ve (conventional ABI <0.9)	PAD -ve (conventional ABI ≥0.9)	Total
Test +ve (pragmatic ABI <0.9)	32	16	48
Test -ve (pragmatic ABI ≥0.9)	20	174	194
Total	52	190	242

Table 2. 2x2 table of conventional and pragmatic ABI determinations.

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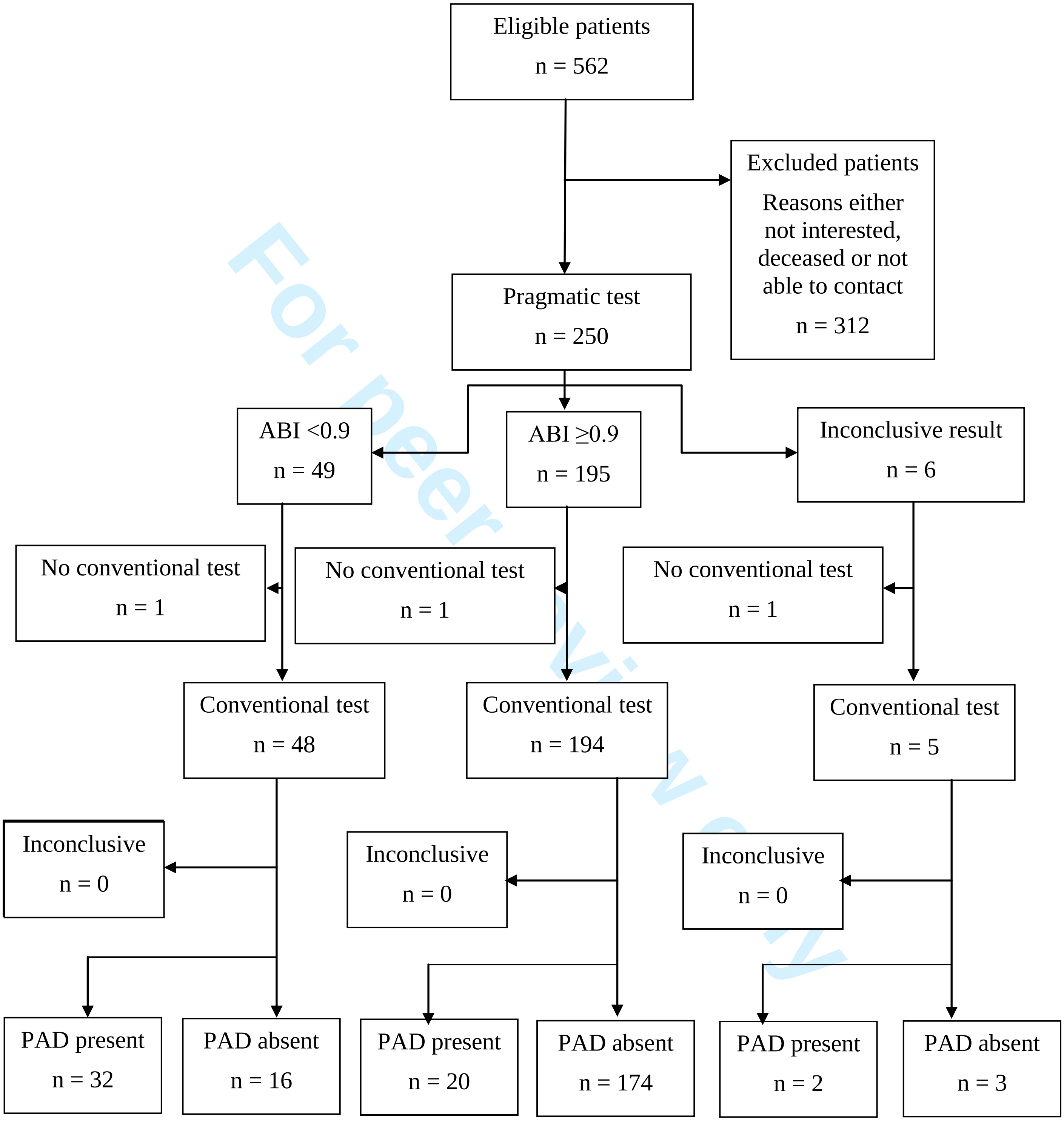

Figure 1. Flow diagram of a diagnostic accuracy in ABIDING as per STARD standard[25].

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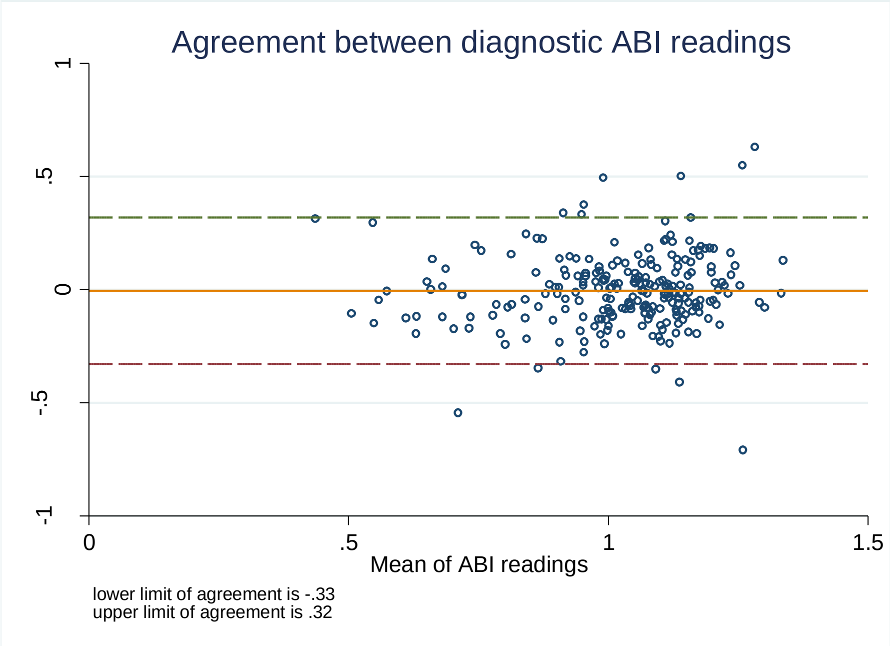
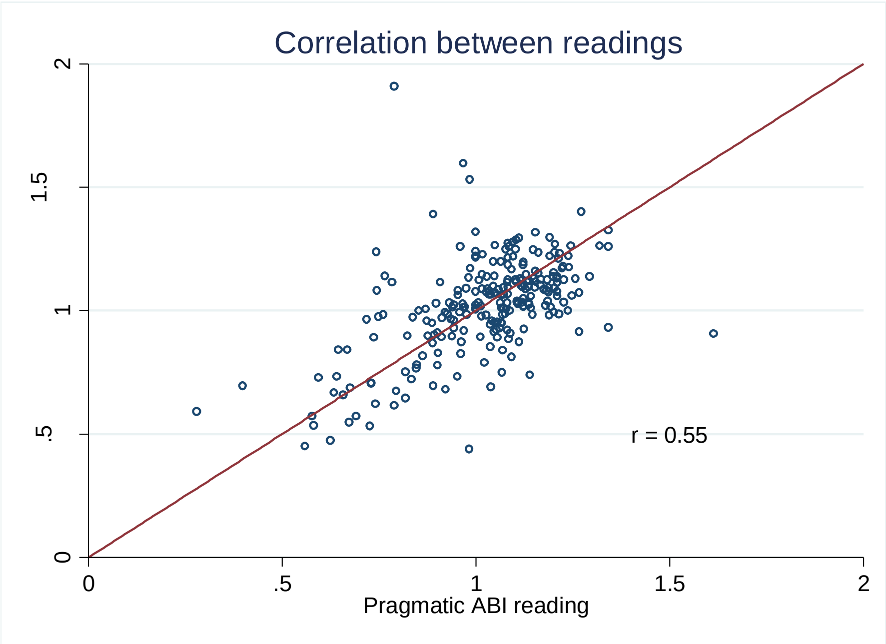


Figure 2. Agreement between pragmatic and conventional determination of ABI.



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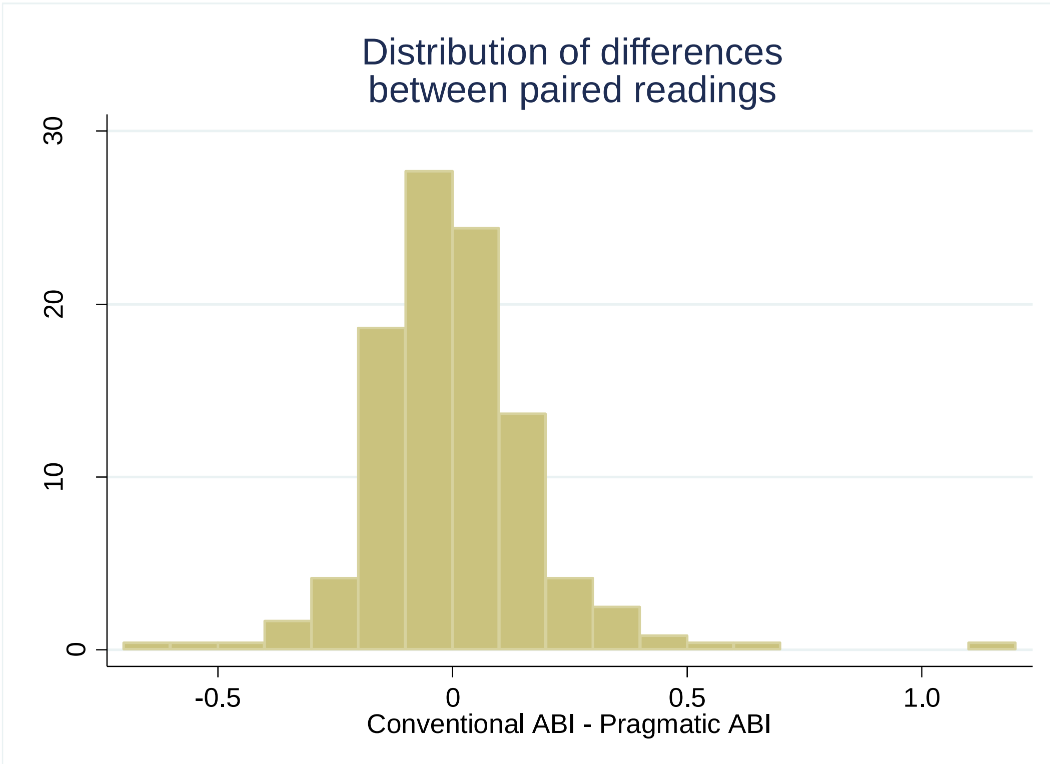

Figure 4. Distribution of the difference between the conventional ABI and the pragmatic ABI readings.

STARD checklist for reporting of studies of diagnostic accuracy
(version January 2003)

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	In keywords
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	7
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	7, 8
	4	Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	7
	5	Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.	8
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	4
Test methods	7	The reference standard and its rationale.	
	8	Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	8
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	8
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	8
	11	Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	8
Statistical methods	12	Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	9-10
	13	Methods for calculating test reproducibility, if done.	N/A
RESULTS			
Participants	14	When study was performed, including beginning and end dates of recruitment.	8
	15	Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).	20
	16	The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).	16
Test results	17	Time-interval between the index tests and the reference standard, and any treatment administered in between.	8
	18	Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	12
	19	A cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	21
	20	Any adverse events from performing the index tests or the reference standard.	11
Estimates	21	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	10-11
	22	How indeterminate results, missing data and outliers of the index tests were handled.	12
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	N/A
	24	Estimates of test reproducibility, if done.	N/A
DISCUSSION	25	Discuss the clinical applicability of the study findings.	11

Ankle-Brachial Index determination and peripheral arterial disease diagnosis by an oscillometric blood pressure device in primary care: validation and diagnostic accuracy study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001689.R1
Article Type:	Research
Date Submitted by the Author:	24-Aug-2012
Complete List of Authors:	Nelson, Mark; University of Tasmania, Menzies Research Institute Quinn, Stephen; Flinders University, Flinders Clinical Effectiveness Winzenberg, Tamia; University of Tasmania, Menzies Research Institute Tasmania Howes, Faline; University of Tasmania, Menzies Research Institute Tasmania Shiel, Louise; Monash University, Epidemiology and Preventive Medicine Reid, Christopher; Monash University, Department of Epidemiology and Preventive Medicine (DEPM)
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Cardiovascular medicine, Public health, Diagnostics
Keywords:	PRIMARY CARE, VASCULAR MEDICINE, PUBLIC HEALTH

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Sensitivity and specificity, Ankle-Brachial Index, peripheral arterial disease, oscillometric device, blood pressure.

Word count - excluding title page, abstract, references, figures and tables.

2505

ABSTRACT

Objectives

To determine the level of agreement between a 'conventional' Ankle-Brachial Index (ABI) measurement (using Doppler and mercury sphygmomanometer taken by a research nurse) and a 'pragmatic' ABI measure (using an oscillometric device taken by a practice nurse) in primary care. To ascertain the utility of a pragmatic ABI measure for the diagnosis of peripheral arterial disease (PAD) in primary care.

Design

Cross-sectional validation and diagnostic accuracy study. Descriptive analyses were used to investigate the agreement between the two procedures using the Bland and Altman method to determine whether the correlation between ABI readings varied systematically. Diagnostic accuracy was assessed via sensitivity, specificity, accuracy, likelihood ratios, positive and negative predictive values, with ABI readings dichotomised and Receiver Operating Curve analysis using both univariable and multivariable logistic regression.

Setting

Primary care in metropolitan and rural Victoria, Australia between October 2009 and November 2010.

Participants

250 persons with cardiovascular disease (CVD) or at high risk (3 or more risk factors) of CVD.

Results

Despite a strong association between the two method's measurements of ABI there was poor agreement with 95% of readings within ±0.4 of the 0.9 ABI cut point. The multivariable C statistic of diagnosis of PAD was 0.89. Other diagnostic measures were sensitivity 62%,

specificity 92%, positive predictive value 67%, negative predictive value 90%, accuracy 85%, positive likelihood ratio 7.3 and the negative likelihood ratio 0.42.

Conclusions

Oscillometric ABI measures by primary care nurses on a population with a 22% prevalence of PAD lacked sufficient agreement with conventional measures to be recommended for routine diagnosis of PAD. This pragmatic method may however be used as a screening tool high-risk and overt CVD patients in primary care as it can reliably exclude the condition.

INTRODUCTION

Peripheral arterial disease (PAD) affects an estimated 27 million individuals in Europe and North America with 413,000 related hospital discharges per annum[1 2]. These figures are likely to underestimate the true impact of PAD as those with the condition disproportionally suffer from other manifestations of CVD and are therefore likely to appear in coronary artery disease or stroke statistics. As a consequence there has been a call for better detection and management of the condition[1].

One of the simplest and most useful parameters to objectively assess lower extremity arterial perfusion, and thus diagnose PAD, is the Ankle-Brachial Index (ABI). This is the lower of the left and right ABI where each ABI is the ratio of the lower limb systolic blood pressure compared to the higher systolic brachial blood pressure recording. The ABI can be used to screen for haemodynamic significant PAD and helps to define its severity. Patients with objectively documented PAD have a four- to six-fold increase in cardiovascular mortality over healthy age-matched individuals[3]. PAD is a stronger risk marker for myocardial and stroke morbidity and mortality than those who have already had such an incident event[4 5]. However, only 50% of people with PAD are symptomatic which is a significant issue in the detection of PAD[2].

Between 2007 and 2009 19,500 oscillometric devices were distributed by the High Blood Pressure Research Council of Australia to physicians, mostly general practitioners (GPs). We had previously demonstrated that these devices were likely to improve blood pressure management in primary care[6]. The current study, Ankle Brachial Index Determination by oscillometric method IN General practice (ABIDING), sought to expand the utility afforded by these machines in primary care. Previous work done in those attending a specialist vascular

laboratory in the US demonstrated that patients could have their ABI reliably ascertained by such devices compared to the conventional use of a Doppler ultrasound and mercury sphygmomanometer[7]. It was therefore opportune to investigate if such measures were pragmatic in primary care where the greatest opportunity exists to identify those with undiagnosed PAD. Such persons are at very high risk for subsequent adverse cardiovascular events that can be ameliorated through management of modifiable risk factors.

The primary aim of ABIDING was to establish if there was agreement between a pragmatic ABI (measured by a practice nurse using an oscillometric blood pressure device), and a conventional ABI (measured by a research nurse using mercury sphygmomanometer and Doppler devices). A secondary aim was to ascertain diagnostic accuracy of the pragmatic approach for ascertaining PAD.

METHODS

GPs and participants were recruited through the REACH Registry Victorian database. The international REACH Registry was a prospective, observational registry designed to provide long-term follow-up (36 months) of patients at high risk of atherothrombotic events. Globally 67,888 patients were involved in the REACH registry of whom 2,782 were recruited from 281 general practitioners around Australia[8 9]. Practices were eligible for ABIDING if they had previously enrolled participants in the REACH registry and had a practice nurse willing to participate or were willing to appoint a *locum tenens* nurse. Eligibility criteria for REACH are published elsewhere but can be summarised as at entry (March to June 2004) aged 45+ years, had known CVD or at least three atherosclerosis risk factors, and were physically able to attend their usual general practice[8].

Participant recruitment

All Melbourne (metropolitan) and Warrnambool (rural) Victorian study participants who had consented to follow-up, who had been identified by their GPs as alive and for whom we had a current address, were contacted by mail. If no reply was received from the participant within four weeks, a second letter was sent and then a telephone call made. Participants were seen in their usual GP's clinic between October 2009 and November 2010.

Research and practice nurses

Three experienced research nurses conducted the reference standard tests. They received standardised training from a senior research nurse who was one of the operators. Practice nurses were given training in situ by the research nurse and were observed by them. Because they worked contemporaneously the research nurse was not blinded to the practice nurses results.

'Conventional' and 'pragmatic' ABI estimation

All participants were rested supine for five minutes before measurement. Doppler blood pressure measurements (by research nurse) and automated oscillometric blood pressure measurements (by practice nurse) were performed using cuffs that had bladders >80% of the diameter of the arms and ankles measured.

Conventional measures involved Doppler blood pressure measurements in the lower limb made with a Nicolet Vascular Doppler with a 5MHz probe. The cuff was inflated to 30mmHg above systolic blood pressure and deflated slowly until a flow signal was detected over the dorsalis pedis or posterior tibial arteries. Brachial artery systolic pressure was determined similarly but utilising a stethoscope rather than a Doppler. The ABI for each lower extremity was calculated as the pedal pressure divided by the higher of the two brachial pressures. PAD is defined as an ABI <0.9 in either lower limb[10]. The mercury sphygmomanometer was calibrated by a certified laboratory.

Research nurses were trained in the measurement of ABI and were certified prior to commencement of the study. Practice nurses were simply observed and technique corrected if required. Oscillometric measurements were made by the practice nurse on all limbs using a standard automated blood pressure cuff system (OMRON HEM-907). This device is a validated blood pressure measurement device[11 12]. Oscillometric devices were new and therefore had factory calibration. Participants also completed the Edinburgh Claudication questionnaire (ECQ)[13].

Statistical Methods

Descriptive analyses were used to investigate the agreement between the two procedures using the Bland and Altman method to determine whether measurements could be used interchangeably and if the correlation between ABI readings varied systematically[14]. Although the variability in the differences appeared to be proportional to the mean, applying a log transformation to the data did not substantially alter agreement and so raw scores are presented. Correlations between the paired readings were also calculated. Sensitivity, specificity, positive and negative predictive values, and accuracy with exact 95% confidence intervals are reported, where ABI readings taken under both conditions were dichotomised at 0.9 (reference standard). The diagnostic accuracy was evaluated using Receiver Operating Curve analysis and quantified as the area under the curve (AUC or C statistic), as determined using both univariable and multivariable logistic regression. In the multivariable model we adjusted for age, BMI, gender, and smoking status (never, former, current). The calibration of this model was validated using the Hosmer-Lemeshow statistic[15]. We examined likelihood ratios, the ratio of the expected test results in participants with PAD to those participants without. All results are reported with 95% confidence intervals. All analyses were conducted using Stata version 12.0.

Power calculations

Assuming a type 1 error of 5% ($\alpha = 0.05$) a total sample of 250 participants provided 80% power to detect systematic bias between the readings taken by the research and practice nurses if the mean difference was 0.0255[14]. Eight participants were excluded as 6 pragmatic and 2 conventional ABI readings were absent. In all other cases each patient had at least one conventional and pragmatic ABI reading (for the same leg). For a sample of 242 the difference that we could detect was 0.0257. We expected strong correlations between ABI readings taken using the different methods. Both calculations assumed a correlation between readings of 0.61 and standard deviations as reported in Benchimol *et al*[16].

RESULTS

The flow chart of the study is shown in Figure 1. The characteristics of the ABIDING population are shown in Table 1. There was no difference between those excluded and included in the analysis for any trait that we measured. We also compared in Table 1 those diagnosed with PAD vs. not using conventional ABI. Those with PAD were older (p=0.003) and more likely to be female (p=0.003). Figure 2 shows there was poor agreement between pragmatic and conventional determination of ABI with 95% of readings within ±0.4. Figure 3 shows correlation between conventional and pragmatic ABI measurements, indicating a strong association between the two measurements, despite the poor agreement. The distribution of differences between the ABI measures is shown in Figure 4. These differences were regressed on all possible confounders measured in our study, in both univariable and multivariable models. There were no significant associations, suggesting that the differences were completely random.

A 2x2 table of dichotomised conventional and pragmatic measurements is shown (Table 2). We examined the two groups comprising the 36 participants where the PAD classification differed. There were no differences in any measured trait between those groups (data not shown). The respective pragmatic method diagnostic performance, assuming the conventional method as gold standard, was sensitivity 62% (95% CI 47-75%), specificity 92% (87-95%), positive predictive value 67% (52%-80%), negative predictive value 90% (85-94%) and accuracy 85% (80%-89%). The Likelihood ratio for a positive result (LR+) was 7.3 (95% CI 4.4-12.0) and Likelihood ratio test for a negative result (LR-) 0.42 (0.30-0.59). Test performance for the asymptomatic subgroup on ECQ (N = 183 PAD 18%) sensitivity 54% (95% CI 37-69%) specificity 93% (89-97%) and symptomatic (N = 18 PAD 61%) sensitivity 9% (2-41%) specificity 57% (18-90%). Area under the Receiver Operator Characteristic curves (AUC / C statistic) of pragmatic ABI against the conventional ABI <0.9 and thus PAD was 0.87 (95% CI 0.82, 0.93). The AUC from multivariable analysis (adjusting for age, gender, BMI and smoking status) for all analyses were almost identical 89% (95% CI 84%-93%).

Based on the differences in Table 1 for those with PAD vs. not we conducted a post hoc subgroup analyses on pragmatic vs. conventional ABI readings by gender, age (dichotomised as young or old) and all pairwise combinations. The agreement between reading and diagnostic criteria did not improve for any subgroup (data not shown). We also investigated (using multivariable logistic regression) whether there was any evidence that disagreements were systematic. There were no differences between in disagreement apart from current smokers were more likely to produce readings that disagreed compared to non-smokers (p=0.025). A subgroup analysis with current smokers removed did not alter the diagnostic criteria of the tests. As could be expected in non-invasive testing there were no reported adverse events.

Sensitivity analyses for excluding upper ABI cut point of 1.4 (concern regarding possible arterial incompressibility) did not affect the outcomes, and the range 0.85-0.95 gave 0.85 sensitivity 54% and specificity 95%, and 0.95 sensitivity 71% and specificity 86%.

DISCUSSION

ABIDING demonstrated that use of oscillometric devices by general practice nurses to determine ABI and therefore the presence of PAD had high specificity (92%) and negative predictive value (90%), good accuracy (84%) but modest sensitivity (62%) and positive predictive value (67%). The modest sensitivity and the LR+ 7.3 indicate that this test has little value for confirming the presence of PAD. On the other hand high specificity and negative predictive value suggests that the test has some value in ruling out the disease (i.e. when the test is negative). Looking at the symptomatic individuals as determined by ECQ showed that, though the numbers were small, the pragmatic measure had a poor performance as a diagnostic test in this high prevalence (61%) subgroup. Changing the cut point to improve sensitivity or specificity simply compromised the other measure and therefore did not improve test performance.

These findings were in contrast to the experience in a specialist centre where their test performance (both limbs in comparison to ABIDING lower of the 2 measures) was sensitivity left/right leg 88/73% (62%), specificity 85/95% (92%), positive predictive value 65/88% (69%), negative predictive value 96/88% (90%), LR+ left/right leg 5.9/14.6 (7.9) and LR- 0.14/0.28 (0.4)[4]. A good diagnostic test has a LR+ >10 and LR- < 0.1[17]. This difference in performance to some extent may be accounted for by patient selection but is more likely due to operator expertise. In the specialist centre, the mean age was 10 years younger and 53% were female compared to only 22% in ABIDING. The respective prevalence of PAD was 32% and 22%. In other studies reporting being conducted in primary care Mehlsen *et al* enrolled 1258 consecutive general practice patients for an oscillometric determination of ABI, with those with an ABI <0.9 referred for a Doppler measure in a vascular unit[18]. Hence all 'negatives' including false negatives did not have a gold standard measure and therefore this was not a true measure of test performance in primary care. Nicholai *et al* and Aboyens had similar limitations[19 20]. Verberk and colleagues conducted a systematic review of automated oscillometric devices including a subgroup analysis on devices developed for arm BP measurement[21]. Only one of the 18 studies identified was conducted in primary care and that with an ABIgram and not a simple BP arm device[22]. Although the investigators demonstrated its reliability, the use of this special piece of equipment would seem to effect is acceptability as is the current situation.ABI is a valid and reliable clinical measure although an indirect one. The true gold standard would be an intravascular perfusion study. Both methods have been compared to the true gold standard in 85 patients with claudication undergoing angiography[23]. The oscillometric method showed 97% sensitivity, 89% specificity, 98% positive predictive value, and 86% negative predictive value. The Doppler method showed 95% sensitivity, 56% specificity, 91% positive predictive value, and 68% negative predictive value. This study suggests that the oscillometric method had greater diagnostic accuracy but the test was performed by physicians not specifically trained to use the Doppler probe. This said ABI is a practical tool and is superior to clinical examination for identifying PAD[20]. However screening whole populations is not always practical. ABI ascertainment of PAD is most effective by identifying high risk patients as we have done in ABIDING. By including high-risk and overt CVD patients we were confident that we should get a distribution of ABI scores that included PAD diagnostic scores and the outcome of the study supports this (22% had PAD by the conventional method).

If our method had been reliable it would have been readily implementable as Australian GPs have ready access to oscillometric sphygmomanometers. More than 19,500 devices were distributed on behalf of the High Blood Pressure Research Council of Australia, mostly to GPs, over the years 2007 to 2009. Practice nurses were chosen rather than GPs as this approach is also more likely to be implementable. A survey by Mohler *et al* of primary care clinicians showed that most (88%) thought ABI to be feasible in that setting[23].

Study limitations

The intervention was kept as simple as possible by using practice nurses to do single measures on a device they were familiar with but did not receive extensive further training on. While this means that this is simple to introduce into clinical practice the practice nurse performance may have been improved by more intense training and repeated limb measurements.

CONCLUSION

Oscillometric ABI measures by primary care nurses on a population with a 22% prevalence of PAD lacked sufficient agreement with conventional measures to be recommended for routine diagnosis of PAD. This pragmatic method may however be used as a screening tool in high-risk primary care patients as it can reliably exclude the condition.

ACKNOWLEDGMENTS, COMPETING INTERESTS, FUNDING

Participating GPs were Drs Sam Arber, Dean Arnot, Ian Barratt, Irmgard Chia, John Chin, Eric Choo, Andrew Chow, Michael Conos, Simon Cooper, Peter Coulton, Adrian Dabscheck, Deborah Davidson, Antonio De Sousa, Hillary Donald, Peter Eizenberg, Peter Enten, Roger Fagan, Peter Ferguson, Doron Gaddie, Jon Garland, Andrew Gault, Ian Gill, Robert Gingold, Peter Goy, Judith Heale, Eva Herold, Chris Hogan, Suresh Jain, Brendan Kay, John Kirmos, Susan Kloot, Con Lahanis, Daniel Lajoie, Maryanne Lancaster, Conway Leung, Leon Lewi, John Manderson, Frank Marano, Damian Marinucci, Larry McGrath, Elizabeth McNaughton, Margaret McNiff, John Meaney, Paul Molloy, Clare Mooney, Paul O'Hanlon, James Olesen, Michael Page, John Pattison, Gary Pellizzari, Annamarie Perlesz, John Philpot, Leon Piterman, Jock Plenderleith, Mark Preston, Christopher Priest, Andy Psaradellis, Michael Quinn, Jacqueline Rounsevell, Joseph Sakowsky, Mahinda Samararatna, Victor Sammut, David Slonim, Stuart Smith, Stephen Stowe, Ian Sutherland, Edwin Turner, Peter Wexler, Andrew White, Martin Williams, Stephen Williams, Keith Wing Shing, Richard Wrennall, and Michael Ziccone.

We would also like to acknowledge the contribution of practice nurses, Dr Nyi Nyi Tun who assisted with the literature review, and research nurses Christine Mulvaney, Sue Loftus, and Anne Bruce.

This study had ethical approval from the Human Research Ethics Committee (Tasmania) Network (H0010410) and Monash University Standing Committee on Ethics in Research involving Humans (2009000860), and was registered with the Australian and New Zealand Clinical Trails Registry (ACTRN12609000744257). It was funded by the RACGP Research Foundation (Cardiovascular Research Grant) and the National Health and Medical Research

Council (Project grant 544935), and was supported by the Primary Healthcare Research, Evaluation and Development scheme. Oscillometric devices were loaned by the High Blood Pressure Research Council of Australia.

No competing interests declared.

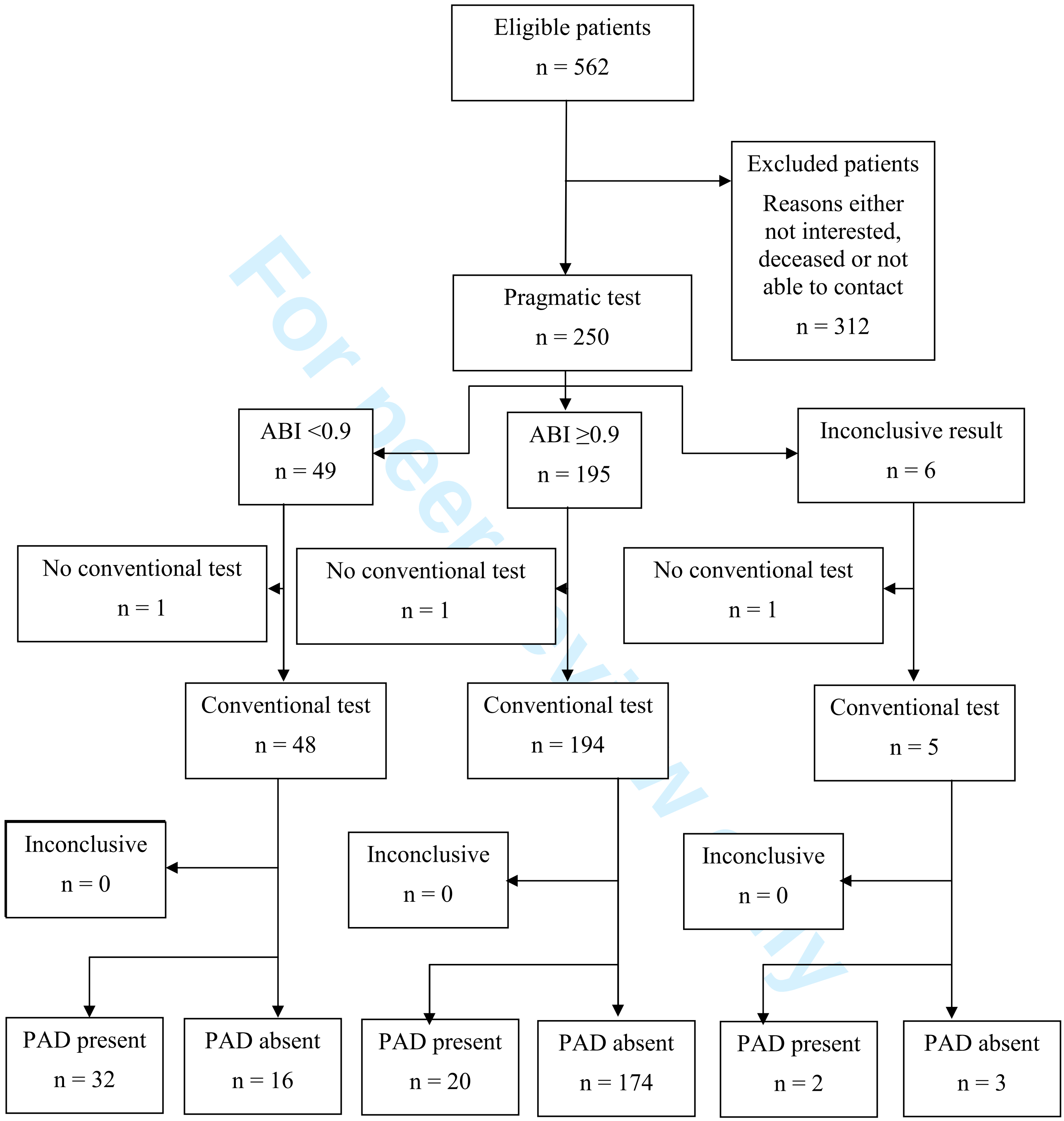

Figure 1. Flow diagram of a diagnostic accuracy in ABIDING as per STARD standard[25].

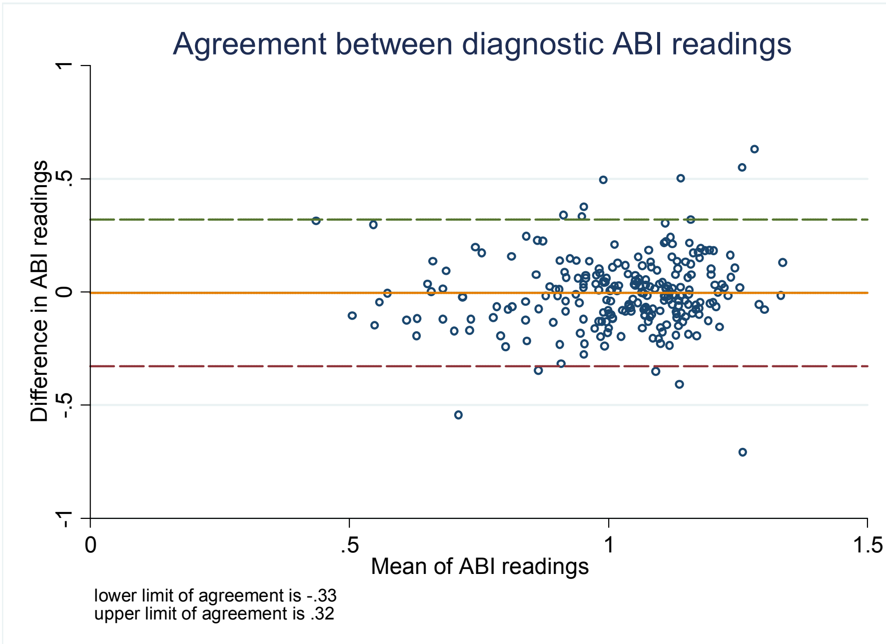

Figure 2. Agreement between pragmatic and conventional determination of ABI.

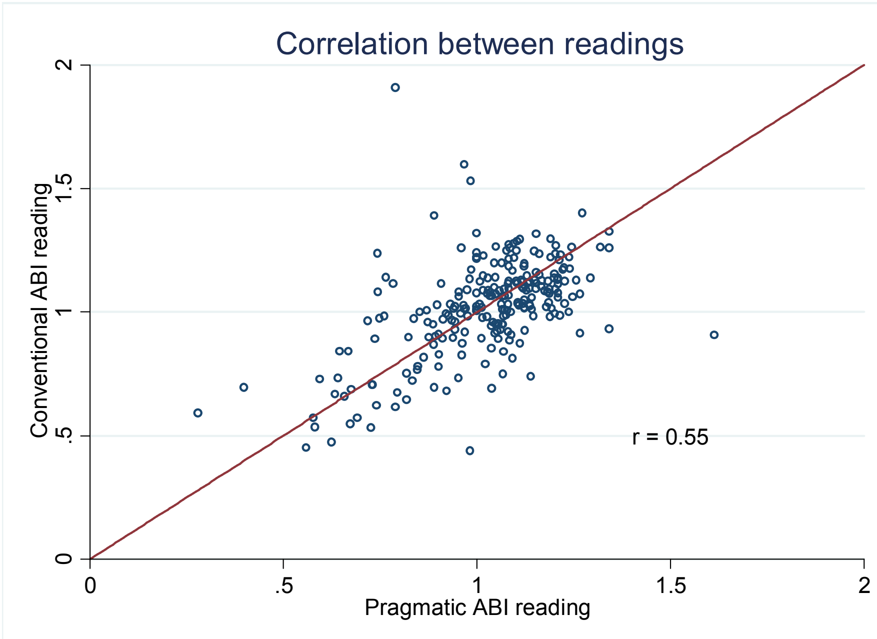

Figure 3. Correlation between pragmatic and conventional determination of ABI.

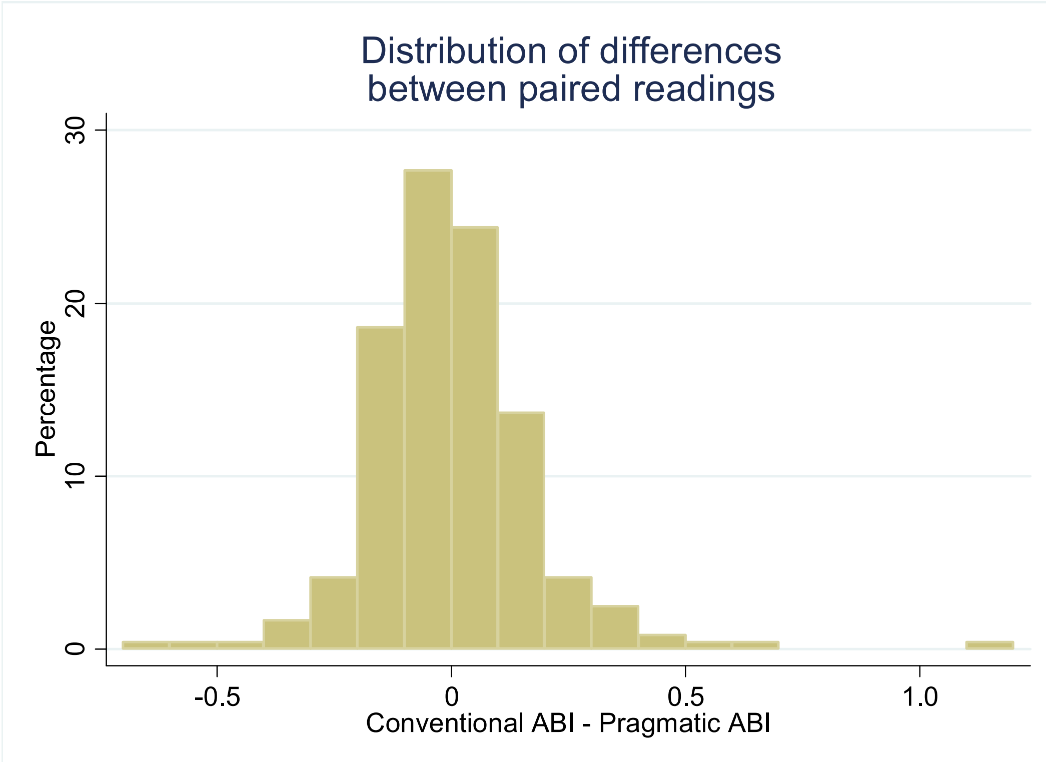

Figure 4. Distribution of the difference between the conventional ABI and the pragmatic ABI readings.

Variable	*Included*	*Conventional ABI ≥ 0.9*	*Conventional ABI < 0.9*	*P for difference*
N	242	192	52	
Age in years	71.2(7.4)	70.4(7.0)	73.9(8.3)	0.003
Male Sex (%)	167 (69.0)	140(73.7)	27(52.0)	0.003
SBP (mmHg)	141.5(18.9)	140.6(17.8)	144.5(22.4)	0.35
DBP (mmHg)	76.7(9.9)	77.0(9.8)	75.5(10.4)	0.55
BMI (kg/h^2)	27.5(4.4)	27.5(4.4)	27.2(4.4)	0.63
Waist	99.9(10.8)	100.1(10.4)	99.2(12.3)	0.60
Smoking status				0.31
Never	98(40.7)	81(42.9)	17(32.7)	
Former	131(54.4)	100(52.9)	31(59.6)	
Current	12(5.0)	8(4.2)	4(7.7)	

Table 1: Characteristics of participants by conventional PAD status expressed as a mean (standard deviation) or N (%) as appropriate.

	PAD +ve (conventional ABI <0.9)	PAD -ve (conventional ABI ≥0.9)	Total
Test +ve (pragmatic ABI <0.9)	32	16	48
Test -ve (pragmatic ABI ≥0.9)	20	174	194
Total	52	190	242

Table 2. 2x2 table of conventional and pragmatic ABI determinations.

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Word count - excluding title page, abstract, references, figures and tables.

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Primary care in metropolitan and rural Victoria, Australia between October 2009 and November 2010.

Participants

250 persons with cardiovascular disease (CVD) or at high risk (3 or more risk factors) of CVD.

Results

Despite a strong association between the two method's measurements of ABI there was poor agreement with 95% of readings within ±0.4 of the 0.9 ABI cut point. The multivariable C statistic of diagnosis of PAD was 0.89. Other diagnostic measures were sensitivity 62%,

specificity 92%, positive predictive value 67%, negative predictive value 90%, accuracy 85%, positive likelihood ratio 7.3 and the negative likelihood ratio 0.42.

Conclusions

Oscillometric ABI measures by primary care nurses on a population with a 22% prevalence of PAD lacked sufficient agreement with conventional measures to be recommended for routine diagnosis of PAD. This pragmatic method may however be used as a screening tool high-risk and overt CVD patients in primary care as it can reliably exclude the condition.~~determination of ABI. Their diagnostic performance suggests that a pragmatic ABI lacked sufficient sensitivity to diagnose PAD, but can reliably exclude it.~~

INTRODUCTION

Peripheral arterial disease (PAD) affects an estimated 27 million individuals in Europe and North America with 413,000 related hospital discharges per annum[1 2]. These figures are likely to underestimate the true impact of PAD as those with the condition disproportionally suffer from other manifestations of CVD and are therefore likely to appear in coronary artery disease or stroke statistics. As a consequence there has been a call for better detection and management of the condition[1].

One of the simplest and most useful parameters to objectively assess lower extremity arterial perfusion, and thus diagnose PAD, is the Ankle-Brachial Index (ABI). This is the lower of the left and right ABI where each ABI is the ratio of the lower limb systolic blood pressure ~~is~~ compared to the higher systolic brachial blood pressure recording. The ABI can be used to screen for ~~haemodynamically~~haemodynamic significant PAD and helps to define its severity. Patients with objectively documented PAD have a four- to six-fold increase in cardiovascular mortality over healthy age-matched individuals[3]. PAD is a stronger risk marker for myocardial and stroke morbidity and mortality than those who have already had such an incident event[4 5]. However, only 50% of people with PAD are symptomatic which is a significant issue in the detection of PAD[2].

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Between 2007 and 2009 19,500 oscillometric devices were distributed by the High Blood Pressure Research Council of Australia to physicians, mostly general practitioners (GPs). We had previously demonstrated that these devices were likely to improve blood pressure management in primary care[6]. The current study, Ankle Brachial Index Determination by oscillometric method IN General practice (ABIDING), sought to expand the utility afforded by these machines in primary care. Previous work done in those attending a specialist vascular

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laboratory in the US demonstrated that patients could have their ABI reliably ascertained by such devices compared to the conventional use of a Doppler ultrasound and mercury sphygmomanometer[47]. It was therefore opportune to investigate if such measures were pragmatic in primary care where the greatest opportunity exists to identify those with undiagnosed PAD. Such persons are at very high risk for subsequent adverse cardiovascular events that can be ameliorated through management of modifiable risk factors.

The primary aim of ABIDING was to establish if there was agreement between a pragmatic ABI (measured by a practice nurse using an oscillometric blood pressure device), and a conventional ABI (measured by a research nurse using mercury sphygmomanometer and Doppler devices). A secondary aim was to ascertain diagnostic accuracy of the pragmatic approach for ascertaining PAD.

METHODS

General practitioners (GPs) and participants were recruited through the REACH Registry Victorian database. The international REACH Registry was a prospective, observational registry designed to provide long-term follow-up (36 months) of patients at high risk of atherothrombotic events. Globally 67,888 patients were involved in the REACH registry of whom 2,782 were recruited from 281 general practitioners around Australia[8 9]. Practices were eligible for ABIDING if they had previously enrolled participants in the REACH registry and had a practice nurse willing to participate or were willing to appoint a *locum tenens* nurse. Eligibility criteria for REACH are published elsewhere but can be summarised as at entry (March to June 2004) aged 45+ years, had known CVD or at least three atherosclerosis risk factors, and were physically able to attend their usual general practice[58].

Participant recruitment

All Melbourne (metropolitan) and Warrnambool (rural) Victorian study participants who had consented to follow-up, who had been identified by their GPs as alive and for whom we had a current address, were contacted by mail. If no reply was received from the participant within four weeks, a second letter was sent and then a telephone call made. Participants were seen in their usual GP's clinic between October 2009 and November 2010.

Research and practice nurses

Three experienced research nurses conducted the reference standard tests. They received standardised training from a senior research nurse who was one of the operators. Practice nurses were given training in situ by the research nurse and were observed by them. Because they worked contemporaneously the research nurse was not blinded to the practice nurses results.

'Conventional' and 'pragmatic' ABI estimation

All participants were rested supine for five minutes before measurement. Doppler blood pressure measurements (by research nurse) and automated oscillometric blood pressure measurements (by practice nurse) were performed using cuffs that had bladders >80% of the diameter of the arms and ankles measured.

Conventional measures involved Doppler blood pressure measurements in the lower limb made with a Nicolet Vascular Doppler with a 5MHz probe. The cuff was inflated to 30mmHg above systolic blood pressure and deflated slowly until a flow signal was detected over the dorsalis pedis or posterior tibial arteries. Brachial artery systolic pressure was determined similarly but utilising a stethoscope rather than a Doppler. The ABI for each lower extremity was calculated as the pedal pressure divided by the higher of the two brachial pressures. PAD is defined as an ABI <0.9 in either lower limb[610]. The mercury sphygmomanometer was calibrated by a certified laboratory.

Research nurses were trained in the measurement of ABI and were certified prior to commencement of the study. Practice nurses were simply observed and technique corrected if required. Oscillometric measurements were made by the practice nurse on all limbs using a standard automated blood pressure cuff system (OMRON HEM-907). This device is a validated blood pressure measurement device[11 12]. Oscillometric devices were new and therefore had factory calibration. Participants also completed the Edinburgh Claudication questionnaire (ECQ)[13].

Statistical Methods

Descriptive analyses were used to investigate the agreement between the two procedures using the Bland and Altman method to determine whether measurements could be used interchangeably and if the correlation between ABI readings varied systematically[~~7~~14]. Although the variability in the differences appeared to be proportional to the mean, applying a log transformation to the data did not substantially alter agreement and so raw scores are presented. Correlations between the paired readings were also calculated. Sensitivity, specificity, positive and negative predictive values, and accuracy with exact 95% confidence intervals are reported, where ABI readings taken under both conditions were dichotomised at 0.9 (reference standard). The diagnostic accuracy was evaluated using Receiver Operating Curve analysis and quantified as the area under the curve (AUC or C statistic), as determined using both univariable and multivariable logistic regression. In the multivariable model we adjusted for age, BMI, gender, and smoking status (never, former, current). The calibration of this model was validated using the Hosmer-Lemeshow statistic[~~8~~15]. We examined likelihood ratios, the ratio of the expected test results in participants with PAD to those participants without. All results are reported with 95% confidence intervals. All analyses were conducted using Stata version 12.0.

Power calculations

Assuming a type 1 error of 5% ($\alpha = 0.05$) a total sample of 250 participants provided 80% power to detect systematic bias between the readings taken by the research and practice nurses if the mean difference was 0.0255[7][14]. Eight participants were excluded as 6 pragmatic and 2 conventional ABI readings were absent. In all other cases each patient had at least one conventional and pragmatic ABI reading (for the same leg). For a sample of 242 the difference that we could detect was 0.0257. We expected strong correlations between ABI readings taken using the different methods. Both calculations assumed a correlation between readings of 0.61 and standard deviations as reported in Benchimol *et al*[9][16].

RESULTS

The flow chart of the study is shown in Figure 1. The characteristics of the ABIDING population are shown in Table 1. There was no difference between those excluded and included in the analysis for any trait that we measured. We also compared in Table 1 those diagnosed with PAD vs. not using conventional ABI. Those with PAD were older (p=0.003) and more likely to be female (p=0.003). Figure 2 shows there was poor agreement between pragmatic and conventional determination of ABI with 95% of readings within ±0.4. Figure 3 shows correlation between conventional and pragmatic ABI measurements, indicating a strong association between the two measurements, despite the poor agreement. The distribution of differences between the ABI measures is shown in Figure 4. These differences were regressed on all possible confounders measured in our study, in both univariable and multivariable models. There were no significant associations, suggesting that the differences were completely random.

A 2x2 table of dichotomised conventional and pragmatic measurements is shown (Table 2). We examined the two groups comprising the 36 participants where the PAD classification differed. There were no differences in any measured trait between those groups (data not shown). The respective pragmatic method diagnostic performance, assuming the conventional method as gold standard, was sensitivity 62% (95% CI 47-75%), specificity 92% (87-95%), positive predictive value 67% (52%-80%), negative predictive value 90% (85-94%) and accuracy 85% (80%-89%). The Likelihood ratio for a positive result (LR+) was 7.3 (95% CI 4.4-12.0) and Likelihood ratio test for a negative result (LR-) 0.42 (0.30-0.59). Test performance for the asymptomatic subgroup on ECQ (N = 183 PAD 18%) sensitivity 54% (95% CI 37-69%) specificity 93% (89-97%) and symptomatic (N = 18 PAD 61%) sensitivity 9% (2-41%) specificity 57% (18-90%). Area under the Receiver Operator Characteristic curves (AUC / C statistic) of pragmatic ABI against the conventional ABI <0.9 and thus PAD was 0.87 (95% CI 0.82, 0.93). The AUC from multivariable analysis (adjusting for age, gender, BMI and smoking status) for all analyses were almost identical 89% (95% CI 84%-93%).

Based on the differences in Table 1 for those with PAD vs. not we conducted a post hoc subgroup analyses on pragmatic vs. conventional ABI readings by gender, age (dichotomised as young or old) and all pairwise combinations. The agreement between reading and diagnostic criteria did not improve for any subgroup (data not shown). We also investigated (using multivariable logistic regression) whether there was any evidence that disagreements were systematic. There were no differences between in disagreement apart from current smokers were more likely to produce readings that disagreed compared to non-smokers (p=0.025). A subgroup analysis with current smokers removed did not alter the diagnostic criteria of the tests.

As could be expected in non-invasive testing there were no reported adverse events.

Sensitivity analyses for excluding upper ABI cut point of 1.4 (concern regarding possible arterial incompressibility) did not affect the outcomes, and the range 0.85-0.95 gave 0.85 sensitivity 54% and specificity 95%, and 0.95 sensitivity 71% and specificity 86%.

DISCUSSION

ABIDING demonstrated that use of oscillometric devices by general practice nurses to determine ABI and therefore the presence of PAD had high specificity (92%) and negative predictive value (90%), good accuracy (84%) but modest sensitivity (62%) and positive predictive value (67%). The modest sensitivity and the LR+ 7.3 indicate that this test has little value for confirming the presence of PAD. On the other hand high specificity and negative predictive value suggests that the test has some value in ruling out the disease (i.e. when the test is negative). Looking at the symptomatic individuals as determined by ECQ showed that, though the numbers were small, the pragmatic measure had a poor performance as a diagnostic test in this high prevalence (61%) subgroup. Changing the cut point to improve sensitivity or specificity simply compromised the other measure and therefore did not improve test performance.

~~This is~~These findings were in contrast to the experience in a specialist centre where their test performance (both limbs in comparison to ABIDING lower of the 2 measures) was sensitivity left/right leg 88/73% (62%), specificity 85/95% (92%), positive predictive value 65/88% (69%), negative predictive value 96/88% (90%), LR+ left/right leg 5.9/14.6 (7.9) and LR- 0.14/0.28 (0.4)[4]. A good diagnostic test has a LR+ >10 and LR- < 0.1[~~10~~17]. This difference in performance to some extent may be accounted for by patient selection but is more likely due to operator expertise. In the specialist centre, the mean age was 10 years younger and 53% were female compared to only 22% in ABIDING. The respective prevalence of PAD was 32% and 22%. In other studies reporting being conducted in primary care Mehlsen *et al* enrolled 1258 consecutive general practice patients for an oscillometric determination of ABI, with those with an ABI <0.9 referred for a Doppler measure in a vascular unit[18]. Hence all 'negatives' including false negatives did not have a gold standard measure and therefore this was not a true measure of test performance in primary care. Nicholai *et al* and Aboyens had similar limitations[19 20]. Verberk and colleagues conducted a systematic review of automated oscillometric devices including a subgroup analysis on devices developed for arm BP measurement[21]. Only one of the 18 studies identified was conducted in primary care and that with an ABIgram and not a simple BP arm device[22]. Although the investigators demonstrated its reliability, the use of this special piece of equipment would seem to effect is acceptability as is the current situation.

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ABI is a valid and reliable clinical measure although an indirect one. The true gold standard would be an intravascular perfusion study. Both methods have been compared to the true gold standard in 85 patients with claudication undergoing angiography[23]. The oscillometric method showed 97% sensitivity, 89% specificity, 98% positive predictive value, and 86% negative predictive value. The Doppler method showed 95% sensitivity, 56% specificity, 91% positive predictive value, and 68% negative predictive value. This study suggests that the oscillometric method had greater diagnostic accuracy but the test was performed by physicians not specifically trained to use the Doppler probe. This said ABI is a ~~useful~~ practical tool and is superior to clinical examination for identifying PAD~~[11]~~[20]. However screening whole populations is not always practical. ABI ascertainment of PAD is most effective by identifying high risk patients as we have done in ABIDING. By including high-risk and overt CVD patients we were confident that we should get a distribution of ABI scores that included PAD diagnostic scores and the outcome of the ~~trial~~ study supports this (22% had PAD by the conventional method). ~~Doubini *et al* found age alone (70+) a useful predictor as 12.5% of the screened population had~~

PAD vs. only 2.5% of 50-69 years with at least 1 CVD risk factor but no established CVD (diabetes, dyslipidaemia, hypertension, or smoking)[12]. Bendermacher *et al* developed a clinical prediction model giving risk factor points per factor (age: 1 point per 5 years starting at 55 years; ever smoked: 2 points; currently smoking: 7 points; and hypertension: 3 points), showed a proportional increase of the PAD prevalence with each increasing risk profile (range: 7.0-40.6%)[13]. The overall prevalence of PAD was 18%. They found with their PREVALENT clinical prediction model (based on CVD risk factors), the GP was able to identify a high-risk population in which measurement of ABI was useful.

If our method had been reliable it would have been readily implementable as Australian GPs have ready access to oscillometric sphygmomanometers. _More than 19,500 devices were distributed on behalf of the High Blood Pressure Research Council of Australia, mostly to GPs, over the years 2007 to 2009. Practice nurses were chosen rather than GPs as this approach is also more likely to be implementable. A survey by Mohler *et al* of primary care clinicians showed that most (88%) thought ABI to be feasible in that setting[1423]. However, validation studies have largely been conducted in specialist clinics in a variety of study populations rather than in the primary care setting where most of the medical contact is likely to occur[15-20-239 15-18]. The one study done in the primary care setting used an ABIgram. Although the investigators demonstrated its reliability, the use of this special piece of equipment would seem to effect is acceptability as is the current situation.

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Study limitations

The intervention was kept as simple as possible by using practice nurses to do single measures on a device they were familiar with but did not receive extensive further training on. While this means that this is simple to introduce into clinical practice the practice nurse performance may have been improved by more intense training and repeated limb measurements.

CONCLUSION

Oscillometric ABI measures by primary care nurses on a population with a 22% prevalence of PAD lacked sufficient agreement with conventional measures to be recommended for routine determination diagnosis of ABIPAD. This pragmatic method may however be used as a screening tool in high-risk primary care patients primary care but its diagnostic performance does not provide evidence sufficient for it to be used to diagnose PADas it can reliably exclude the condition.

ACKNOWLEDGMENTS, COMPETING INTERESTS, FUNDING

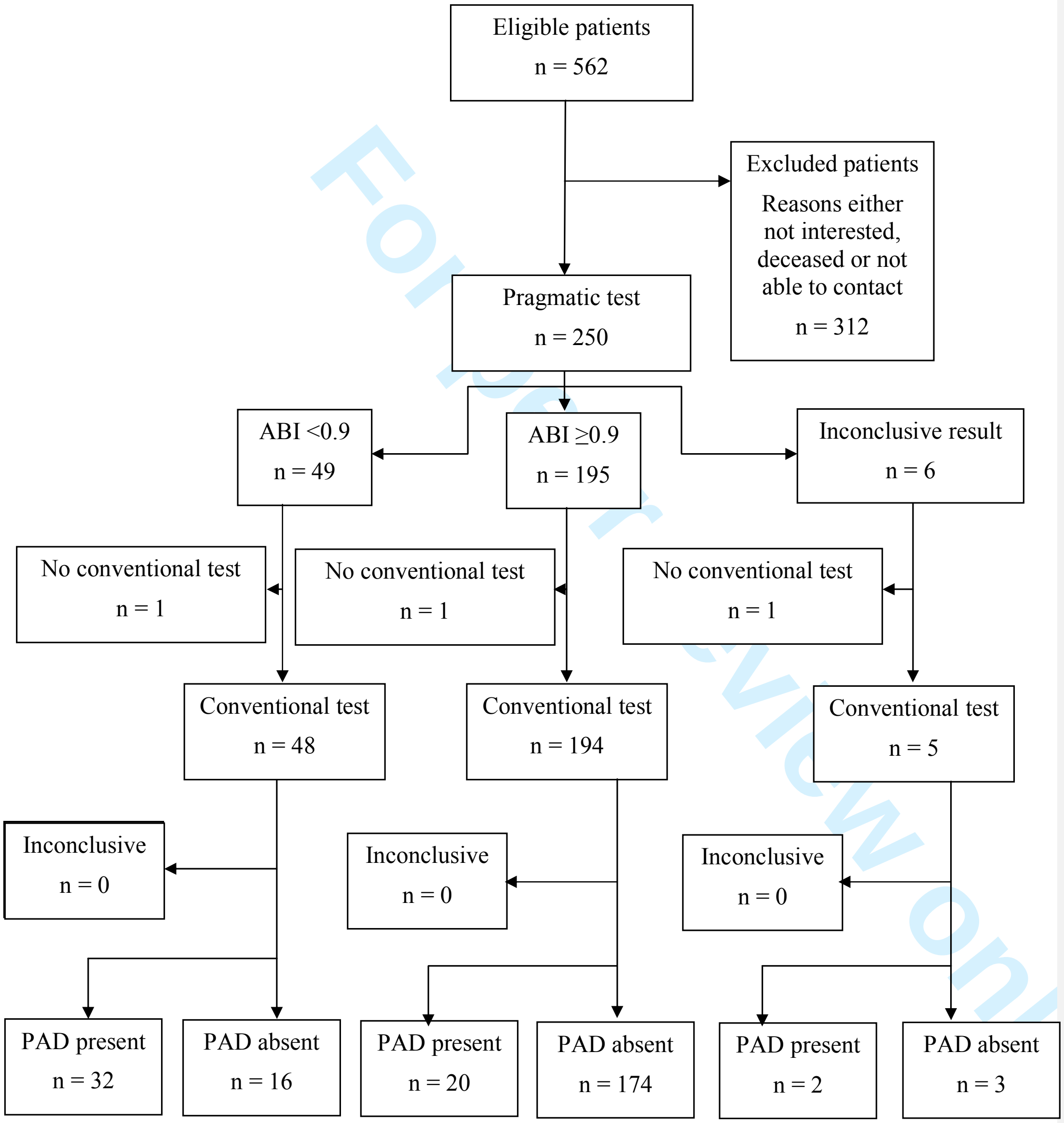
Participating GPs were Drs Sam Arber, Dean Arnot, Ian Barratt, Irmgard Chia, John Chin, Eric Choo, Andrew Chow, Michael Conos, Simon Cooper, Peter Coulton, Adrian Dabscheck, Deborah Davidson, Antonio De Sousa, Hillary Donald, Peter Eizenberg, Peter Enten, Roger Fagan, Peter Ferguson, Doron Gaddie, Jon Garland, Andrew Gault, Ian Gill, Robert Gingold, Peter Goy, Judith Heale, Eva Herold, Chris Hogan, Suresh Jain, Brendan Kay, John Kirmos, Susan Kloot, Con Lahanis, Daniel Lajoie, Maryanne Lancaster, Conway Leung, Leon Lewi, John Manderson, Frank Marano, Damian Marinucci, Larry McGrath, Elizabeth McNaughton, Margaret McNiff, John Meaney, Paul Molloy, Clare Mooney, Paul O'Hanlon, James Olesen, Michael Page, John Pattison, Gary Pellizzari, Annamarie Perlesz, John Philpot, Leon Piterman, Jock Plenderleith, Mark Preston, Christopher Priest, Andy Psaradellis, Michael Quinn, Jacqueline Rounsevell, Joseph Sakowsky, Mahinda Samararatna, Victor Sammut, David Slonim, Stuart Smith, Stephen Stowe, Ian Sutherland, Edwin Turner, Peter Wexler, Andrew White, Martin Williams, Stephen Williams, Keith Wing Shing, Richard Wrennall, and Michael Ziccone.

We would also like to acknowledge the contribution of practice nurses, Dr Nyi Nyi Tun who assisted with the literature review, and research nurses Christine Mulvaney, Sue Loftus, and Anne Bruce.

This study had ethical approval from the Human Research Ethics Committee (Tasmania) Network (H0010410) and Monash University Standing Committee on Ethics in Research involving Humans (2009000860), and was registered with the Australian and New Zealand Clinical Trails Registry (ACTRN12609000744257). It was funded by the RACGP Research Foundation (Cardiovascular Research Grant) and the National Health and Medical Research

Council (Project grant 544935), and was supported by the Primary Healthcare Research, Evaluation and Development scheme. Oscillometric devices were loaned by the High Blood Pressure Research Council of Australia.

No competing interests declared.


Eligible patients
n = 562
Excluded patients
Reasons either not interested, deceased or not able to contact
n = 312
Pragmatic test
n = 250
ABI <0.9
n = 49
ABI ≥0.9
n = 195
Inconclusive result
n = 6
No conventional test
n = 1
No conventional test
n = 1
No conventional test
n = 1
Conventional test
n = 48
Conventional test
n = 194
Conventional test
n = 5
Inconclusive
n = 0
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n = 0
Inconclusive
n = 0
PAD present
n = 32
PAD absent
n = 16
PAD present
n = 20
PAD absent
n = 174
PAD present
n = 2
PAD absent
n = 3

Figure 1. Flow diagram of a diagnostic accuracy in ABIDING as per STARD standard[20][25] _ENREF_20..

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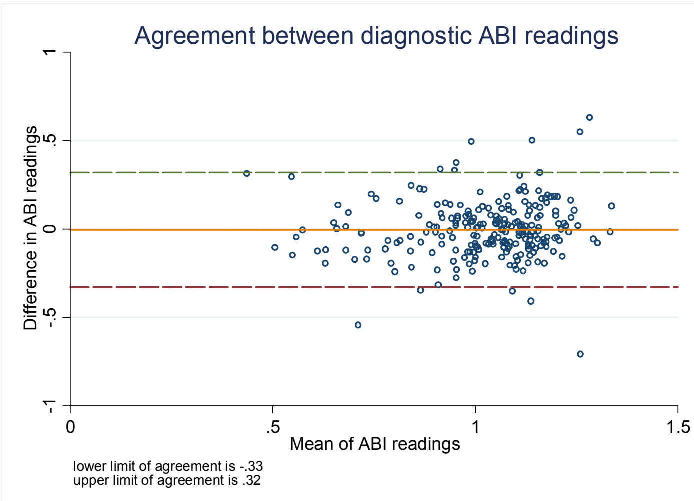

Figure 2. Agreement between pragmatic and conventional determination of ABI.

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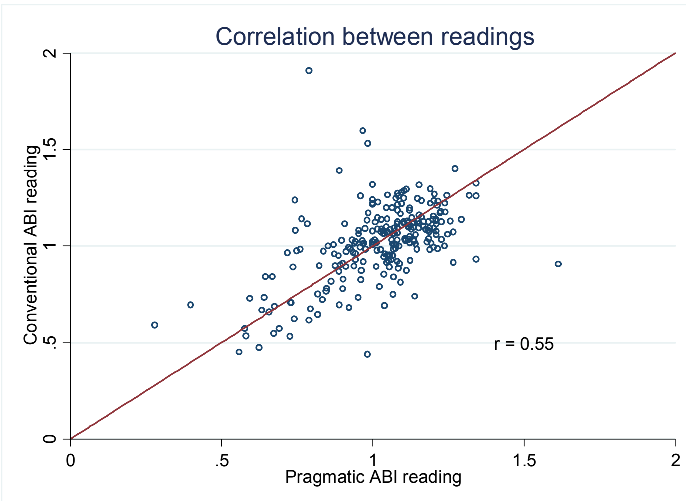

Figure 3. Correlation between pragmatic and conventional determination of ABI.

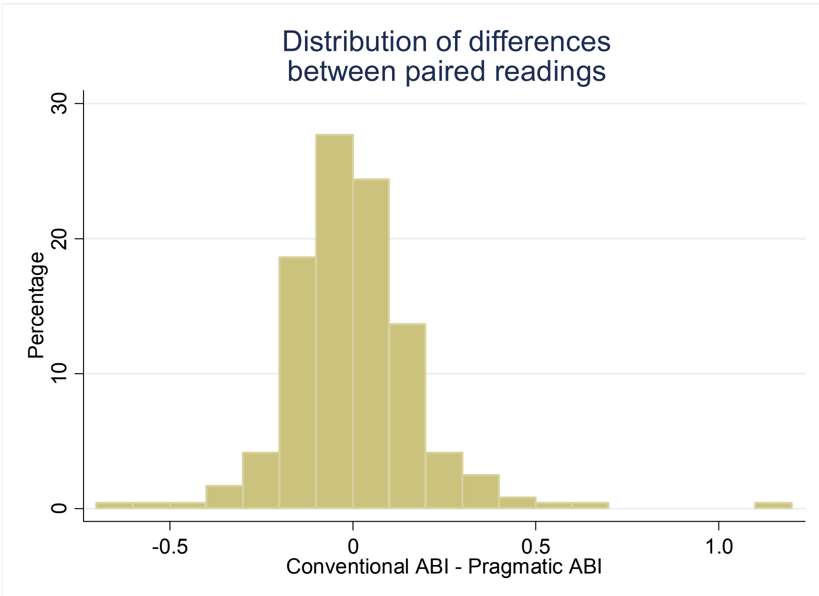

Figure 4. Distribution of the difference between the conventional ABI and the pragmatic ABI readings.

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Variable	*Included*	*Conventional ABI ≥ 0.9*	*Conventional ABI < 0.9*	*P for difference*
N	242	192	52	
Age in years	71.2(7.4)	70.4(7.0)	73.9(8.3)	0.003
Male Sex (%)	167 (69.0)	140(73.7)	27(52.0)	0.003
SBP (mmHg)	141.5(18.9)	140.6(17.8)	144.5(22.4)	0.35
DBP (mmHg)	76.7(9.9)	77.0(9.8)	75.5(10.4)	0.55
BMI (kg/h^2)	27.5(4.4)	27.5(4.4)	27.2(4.4)	0.63
Waist	99.9(10.8)	100.1(10.4)	99.2(12.3)	0.60
Smoking status				0.31
Never	98(40.7)	81(42.9)	17(32.7)	
Former	131(54.4)	100(52.9)	31(59.6)	
Current	12(5.0)	8(4.2)	4(7.7)	

Table 1: Characteristics of participants ~~(included in and excluded from the analysis) and~~ by conventional PAD status expressed as a mean (standard deviation) or N (%) as appropriate.

24

	PAD +ve (conventional ABI <0.9)	PAD -ve (conventional ABI ≥0.9)	Total
Test +ve (pragmatic ABI <0.9)	32	16	48
Test -ve (pragmatic ABI ≥0.9)	20	174	194
Total	52	190	242

Table 2. 2x2 table of conventional and pragmatic ABI determinations.

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STARD checklist for reporting of studies of diagnostic accuracy
(version January 2003)

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	In keywords
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	7
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	7, 8
	4	Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	7
	5	Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.	8
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	4
Test methods	7	The reference standard and its rationale.	
	8	Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	8
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	8
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	8
	11	Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	8
Statistical methods	12	Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	9-10
	13	Methods for calculating test reproducibility, if done.	N/A
RESULTS			
Participants	14	When study was performed, including beginning and end dates of recruitment.	8
	15	Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).	20
	16	The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).	16
Test results	17	Time-interval between the index tests and the reference standard, and any treatment administered in between.	8
	18	Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	12
	19	A cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	21
	20	Any adverse events from performing the index tests or the reference standard.	11
Estimates	21	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	10-11
	22	How indeterminate results, missing data and outliers of the index tests were handled.	12
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	N/A
	24	Estimates of test reproducibility, if done.	N/A
DISCUSSION	25	Discuss the clinical applicability of the study findings.	11

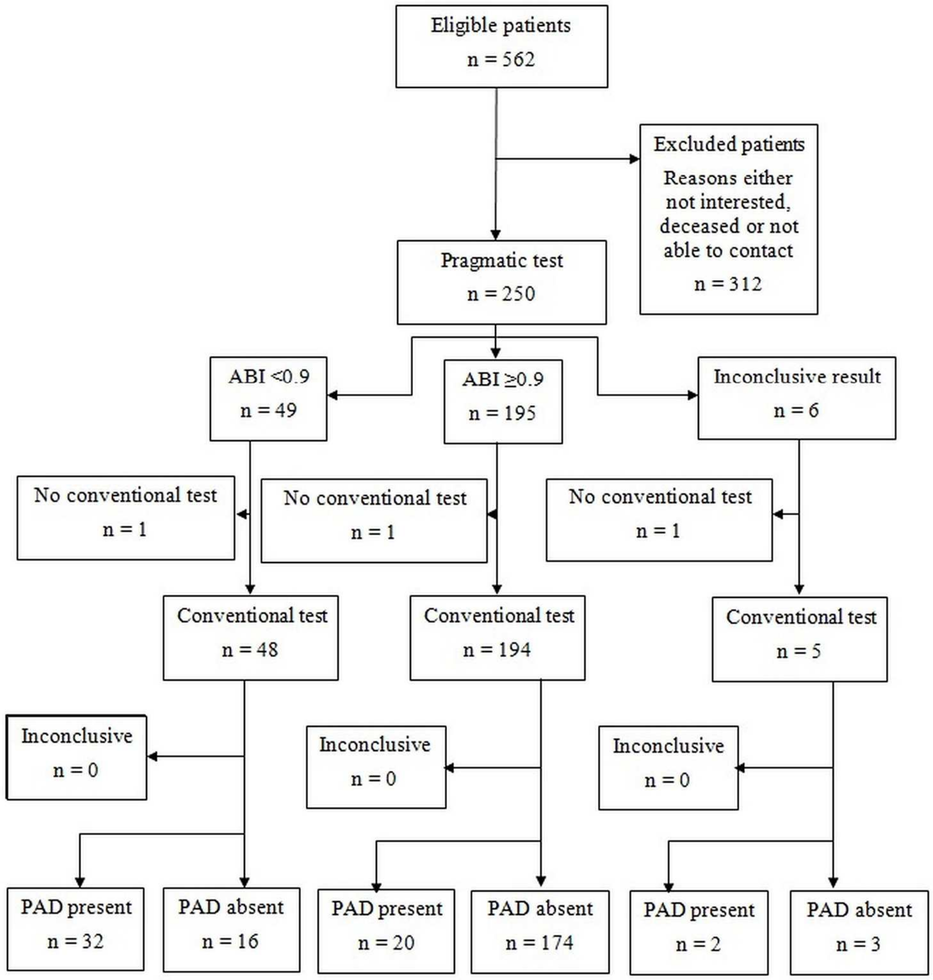

Figure 1. Flow diagram of a diagnostic accuracy in ABIDING as per STARD standard[25].

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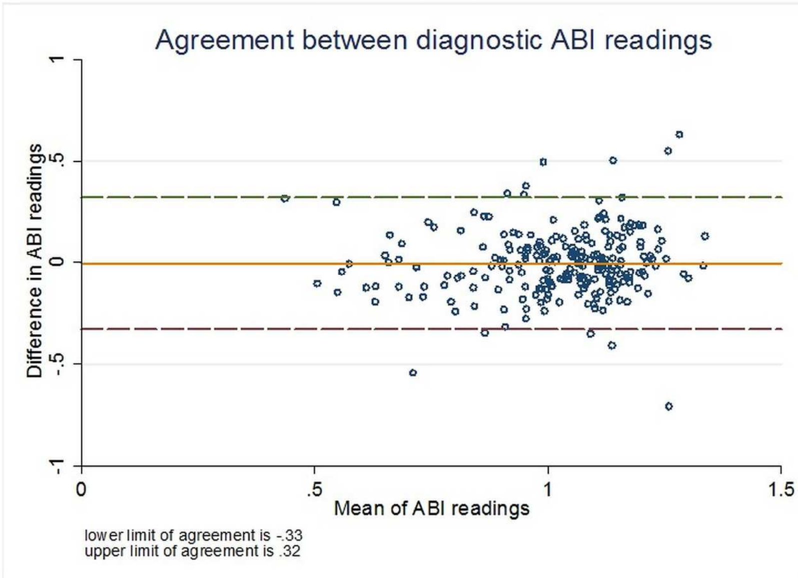

Figure 2. Agreement between pragmatic and conventional determination of ABI.

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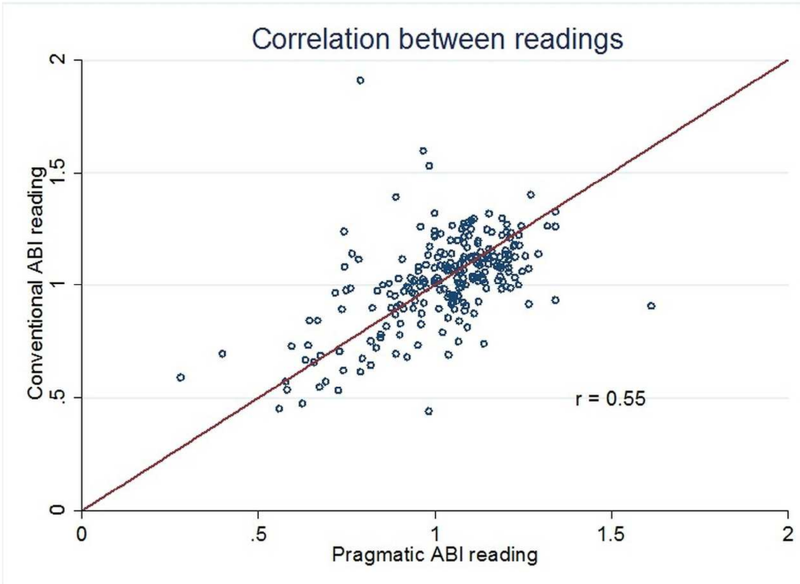

Figure 3. Correlation between pragmatic and conventional determination of ABI.

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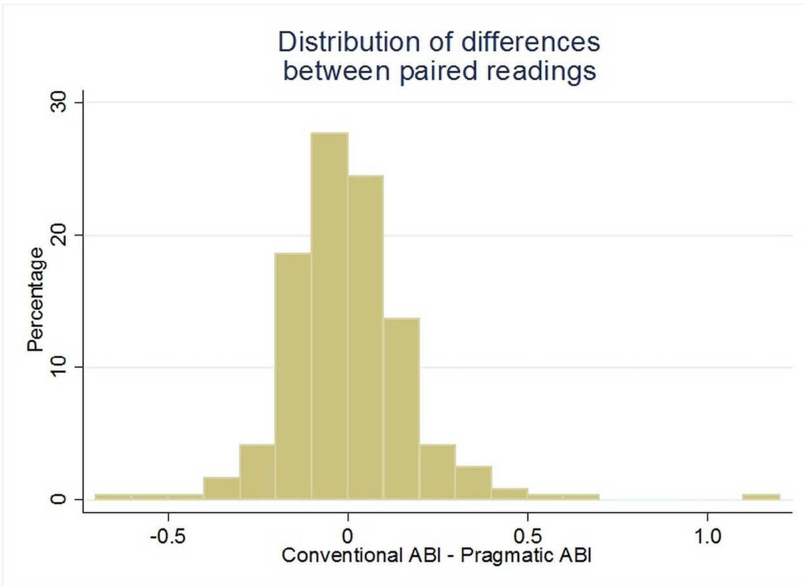

Figure 4. Distribution of the difference between the conventional ABI and the pragmatic ABI readings.

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