The inter-arm blood pressure difference and peripheral vascular disease: cross-sectional study

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Background. A blood pressure (BP) difference between the upper limbs is often encountered in primary care. Knowledge of its prevalence and importance in the accurate measurement of BP is poor, representing a source of error. Current hypertension guidelines do not emphasize this.

Objectives. To establish the prevalence of an inter-arm blood pressure difference (IAD) and explore its association with other indicators of peripheral vascular disease (PVD) in a hypertensive primary care population.

Methods. This was a cross-sectional study. Primary care, one rural general practice, was the setting of the study. The methods were controlled simultaneous measurement of brachial BPs, ankle-brachial pressure index (ABPI) and tiptoe stress testing in 94 subjects.

Results. In all, 18 of 94 [19%, 95% confidence interval (CI) 11–27%] subjects had mean systolic inter-arm difference (sIAD) >10 mmHg and seven of 94 (7%, 95% CI 2–12%) had mean diastolic inter-arm difference (dIAD) >10 mmHg. Nineteen of 91 (20%, 95% CI 12–28%) had a reduced ABPI <0.9. There was negative correlation between systolic (Pearson’s correlation coefficient –0.378; P = 0.01) and diastolic (Pearson’s correlation coefficient –0.225; P = 0.05) magnitudes of IAD with ABPI. On tiptoe testing, 9/90 subjects (10%, 95% CI 4–16%) had a pressure drop >20%.

Conclusions. An IAD and asymptomatic PVD are common in a primary care hypertensive population. Magnitude of the IAD is inversely correlated with ABPI, supporting the hypotheses that IADs are causally linked to PVD, and that IAD is a useful marker for the presence of PVD. Consequently, detection of an IAD should prompt the clinician to screen subjects for other signs of vascular disease and target them for aggressive cardiovascular risk factor modification.

Keywords. Hypertension, inter-arm difference, peripheral vascular disease.

Introduction

A difference in blood pressure (BP) between the upper limbs is a relatively common finding. The vast majority of patients with hypertension are managed in primary care and the measurement of BP is the commonest procedure performed in this setting. Current guidelines for the management of hypertension recommend that “BP should initially be measured in both arms as patients may have large differences (>10 mmHg) between arms. The arm with the higher values should be used for subsequent measurements” and suggest that differences ≥20/10 mmHg warrant specialist referral or simultaneous measurement to exclude anatomical abnormality or coarctation. They do not consider the high prevalence of the inter-arm blood pressure difference (IAD) that we have previously reported, and no previous study has reported a simultaneously measured series from primary care.

An appreciation of the potential for an IAD is vital for the accurate diagnosis and consistent management of hypertension. Following our earlier study of a cohort of primary care patients, we proposed that the IAD may be a manifestation of peripheral vascular disease (PVD). Currently, non-invasive demonstration of PVD requires a reduced ankle-brachial...
pressure index (ABPI) to be detected at rest or following a simple stress test.⁶ ABPI measurement is not routinely undertaken in the general practice assessment of hypertensive patients. It is time consuming and requires specialized equipment and a degree of training, whereas bilateral brachial BP measurements can be easily made and are recommended in the assessment of new hypertensive patients.²

Subclavian artery stenosis is known to be associated with PVD⁷ but no studies have reported the relationship between the IAD and the ABPI. The demonstration of an association may imply that recognition of the IAD could provide a simple screening test in routine consultations to identify those patients most likely to have occult PVD, who would therefore benefit from further assessment and, if confirmed, aggressive primary prevention.⁸

This study was undertaken with three aims: firstly, to confirm the expected prevalence of a systolic inter-arm difference (sIAD) or a diastolic inter-arm difference (dIAD) in a hypertensive cohort of primary care patients using a simultaneous measurement technique; secondly, to explore the association of the IAD with the ABPI as the current gold standard non-invasive method of detection of PVD in primary care; and thirdly, to pilot the use of a simple stress test, the tiptoe test, in the diagnosis of PVD in primary care. This test stresses the circulation by increasing the metabolic demand of the calf muscles. Subjects with aorto-iliac PVD may have well-developed collateral arterial channels such that their resting ABPI is normal, but exercise increases the blood flow to the thigh and calf and results in a pressure drop when collateral supply is insufficient. This test has only been previously validated in secondary care in known claudicants⁹ and its value or feasibility in primary care are unknown.

Methods

Potential subjects, from a total list of 1700 patients, were all hypertensives being treated and followed up by CEC. A power calculation suggested a sample size of 102 would have a 90% power to detect a 20% frequency of the IAD (P < 0.05). Subjects who did not meet the predefined exclusion criteria (Box 1) were invited to a single assessment session and non-responders received a telephone reminder. Assessment sessions took place from October 2002 to December 2003.

Measurements were made at the assessment session by a nurse trained in ankle-brachial pressure measurement. The following were recorded: age, gender, height and weight, body mass index (BMI), smoking status, previous and family history of cardiovascular disease (CVD) or cerebrovascular disease or diabetes. Lipid profile, glucose, renal function and an electrocardiogram were obtained unless data less than 3 years old existed. Patients rested seated for 5 minutes before recording commenced, and then four pairs of simultaneous arm BP measurements were recorded without pause using a pair of automated sphygmomanometers with standard cuffs (Omron model 711). Cuffs were changed to the opposite arms after the first two pairs of readings were taken, and then the cuffs were swapped to the opposite arms and two further pairs of readings obtained, to eliminate any equipment bias, in a modification of a previously used technique.¹⁰¹¹ The order of machine allocation was randomized.

Subjects then rested on a couch for 5 minutes. Doppler pressures were measured at the dorsalis pedis and posterior tibial arteries of both lower limbs using a hand-held Doppler monitor (Dopplex II FD2—Huntleigh Healthcare) with an 8-MHz vascular probe. Order of measurement was again randomized. Subjects performed the tiptoe test⁹ by standing and rising onto tiptoes repeatedly for 30 seconds without pause. Ankle Doppler pressures were then measured again within 1 minute.

Data were stored on an Excel spreadsheet and analysed using SPSS for Windows v11.5. Mean arm pressures were calculated to derive the sIAD and dIAD. The ABPI was calculated for both legs using the higher mean arm systolic BP.¹² The lower ABPI of the two (representing the more severe lower limb PVD) was recorded for each subject.¹³ Reductions in pressure for the tiptoe stress test were expressed as percentage falls for each artery and the largest reduction was recorded. Associations between the IAD, ABPI and tiptoe pressure reduction were tested for significance using Pearson’s correlation coefficient. Predefined cut-offs of 5, 7 and 10 mmHg dIAD and 10 and 20 mmHg sIAD were compared for associations with ABPI values and their sensitivities and specificities calculated.

Results

One hundred and thirty-one subjects were invited and 95 (70%; 40 male) attended. Attendees and non-attendees did not differ in respect of demographic data, lipid levels, glucose, renal function, previous medical history, pretreatment or current BP levels or

Box 1 Exclusion criteria

- Hemiparesis, limb abnormality or significant limb injury (known to affect IAD)
- History of vascular surgery (as looking for occult PVD)
- Known atrial fibrillation (reduced accuracy of automated BP measurements)
- Physically unable to comply with study protocol
- Psychologically unable to comply with study protocol
- No longer registered with the practice (i.e. deceased or moved away)
previously sequentially measured IADs. One subject was excluded from the analysis as no paired BP readings were successfully obtained. Findings for the remaining 94 subjects are summarized in Tables 1 and 2.

Eighteen subjects [19%, 95% confidence interval (CI) 11–27%] had a sIAD $\geq 10$ mmHg (Fig. 1) and 7 (7%, 95% CI 2–12%) had a dIAD $\geq 10$ mmHg. There was no association of sIAD or dIAD with age, gender, height, biochemical variables, Framingham score or personal or family medical histories. BMI scores were significantly higher for subjects with a sIAD $\geq 10$ mmHg than without (28.4 versus 31.8; difference 3.4, 95% CI 1.0–5.7%; $P < 0.01$) but there was no such difference with dIAD. There was no correlation of IAD and absolute BP values.

Individual pairs of BP recordings showed a significant decline over time in absolute BP values from first to fourth pairs. The sIAD and dIAD varied between the first and fourth recordings but there was no significant trend (Figs 2 and 3).

The ABPI could be calculated for 90 subjects (four could not tolerate tight cuffs on their legs). ABPIs ranged from 1.45 to 0.49 (mean 1.03) with 19 subjects (20%, 95% CI 12–28%) having an ABPI <0.9 and 12 subjects (13%, 95% CI 6–20%) <0.85. In 11 subjects (12%, 95% CI 5–19%), one or more ankle signals could not be detected. There was an inverse correlation between both the sIAD and dIAD ($r = –0.378$, $P = 0.01$ and $r = –0.225$, $P < 0.05$, respectively) and ABPI. Analysis of $2 \times 2$ tables for cut-offs of dIAD $\geq 5$, 7 and 10 mmHg showed a significant association of dIAD $\geq 7$ and 10 mmHg with an ABPI <0.9. Similarly, for sIAD cut-offs of $\geq 10$ and 20 mmHg, there was a significant association of sIAD $\geq 10$ mmHg with ABPI <0.9 and of sIAD $\geq 10$ and 20 mmHg with ABPI $\leq 0.85$. Sensitivities of the IAD for detecting a reduced ABPI ranged from 25% (sIAD $\geq 20$ mmHg and ABPI $\leq 0.85$) to 53% (dIAD $\geq 7$ mmHg and ABPI <0.9); specificities ranged from 73% (dIAD $\geq 7$ mmHg and ABPI < 0.9) to 97% (sIAD $\geq 20$ mmHg and ABPI $\leq 0.85$). Likelihood ratios (LRs) for a positive test ranged from 2.0 (dIAD $\geq 7$ mmHg and ABPI <0.9) to 8.3 (sIAD $\geq 20$ mmHg and ABPI $\leq 0.85$) (Table 3).

Eighty-nine subjects completed the tiptoe stress test. Reductions in systolic ankle pressures following the test ranged from –13 to 90 mmHg (mean 17.3; 95% CI 14.0–20.6%) or from –8 to 41% (mean 9.6%, 95% CI 7.9–11.5%). The percentage tiptoe reduction was inversely correlated with the ABPI ($r = –0.257; P < 0.05$). Nine (10%, 95% CI 4–16%) showed a drop $\geq 20$% and in total 23 (25%, 95% CI 16–34%) subjects showed either a tiptoe drop $\geq 20$% or an ABPI < 0.9. Mean ABPI in subjects with a $\geq 20$% tiptoe drop was significantly lower than in those without [(0.83 versus 1.05; difference 0.22 (95% CI 0.10–0.34; $P < 0.001$)].

There was no correlation between the percentage tiptoe drop and IAD. The maximum and percentage tiptoe drops were higher for diabetic than for non-diabetic subjects [27.7 versus 16.4 mmHg; difference 11.3 mmHg (95% CI 0.34–23.0%; $P < 0.05$) and 15.3% versus 9.1% difference 6.2% (95% CI 11.9–0.4%; $P < 0.05$)].

**Discussion**

This study confirms, using a simultaneous measurement technique, that an IAD is a common finding in a hypertensive population in primary care. The higher prevalences compared with the general population of two recognized measures of PVD, the ABPI and the tiptoe ankle pressure drop, observed in this group

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### Table 1 Baseline characteristics of 94 subjects in study (continuous data)

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>94</td>
<td>69.6</td>
<td>9.7</td>
<td>44.5</td>
<td>91.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>94</td>
<td>29.1</td>
<td>4.7</td>
<td>19.6</td>
<td>40.1</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>91</td>
<td>96.5</td>
<td>26.6</td>
<td>54.0</td>
<td>190.0</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>94</td>
<td>5.6</td>
<td>1.1</td>
<td>3.5</td>
<td>8.6</td>
</tr>
<tr>
<td>High density lipoprotein (mmol/l)</td>
<td>81</td>
<td>1.0</td>
<td>0.2</td>
<td>0.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>88</td>
<td>6.0</td>
<td>2.6</td>
<td>2.8</td>
<td>21.4</td>
</tr>
<tr>
<td>10-year coronary heart disease risk</td>
<td>81</td>
<td>24.2</td>
<td>11.3</td>
<td>7.0</td>
<td>57.0</td>
</tr>
<tr>
<td>Mean right systolic BP (mmHg)</td>
<td>94</td>
<td>155.7</td>
<td>18.0</td>
<td>118.5</td>
<td>216.3</td>
</tr>
<tr>
<td>Mean left systolic BP (mmHg)</td>
<td>94</td>
<td>152.6</td>
<td>17.2</td>
<td>119.0</td>
<td>210.8</td>
</tr>
<tr>
<td>Mean right diastolic BP (mmHg)</td>
<td>94</td>
<td>85.9</td>
<td>10.8</td>
<td>62.5</td>
<td>111.3</td>
</tr>
<tr>
<td>Mean left diastolic BP (mmHg)</td>
<td>94</td>
<td>84.3</td>
<td>11.2</td>
<td>55.8</td>
<td>111.5</td>
</tr>
<tr>
<td>Mean sIAD (mmHg)</td>
<td>94</td>
<td>3.1</td>
<td>7.0</td>
<td>– 12.3</td>
<td>22.3</td>
</tr>
<tr>
<td>Mean dIAD (mmHg)</td>
<td>94</td>
<td>1.6</td>
<td>5.6</td>
<td>– 10.0</td>
<td>19.0</td>
</tr>
<tr>
<td>Mean absolute sIAD (mmHg)</td>
<td>94</td>
<td>5.9</td>
<td>4.9</td>
<td>0</td>
<td>22.3</td>
</tr>
<tr>
<td>Mean absolute dIAD (mmHg)</td>
<td>94</td>
<td>4.6</td>
<td>3.6</td>
<td>0</td>
<td>19.0</td>
</tr>
<tr>
<td>Minimum ABPI</td>
<td>90</td>
<td>1.0</td>
<td>0.2</td>
<td>0.5</td>
<td>1.4</td>
</tr>
<tr>
<td>Maximum mean tip toe test reduction</td>
<td>89</td>
<td>17.3</td>
<td>15.9</td>
<td>– 13.0</td>
<td>90.0</td>
</tr>
<tr>
<td>Percent tip toe test reduction</td>
<td>89</td>
<td>9.6</td>
<td>8.8</td>
<td>– 8.3</td>
<td>40.9</td>
</tr>
</tbody>
</table>
of hypertensive subjects suggest that asymptomatic or undiagnosed PVD is also frequently present in this population. The inverse correlations between the magnitudes of the IADs and the ABPI in this study support the hypothesis that the IAD is a proxy marker for PVD in this population. We therefore suggest that the presence of an IAD may predict an increased likelihood of PVD which would justify further investigation to confirm PVD and indicate the need for aggressive risk factor management.

This study was only conducted in one surgery in rural Mid Devon, England; an area with virtually no ethnic minority representation. The prevalence of hypertensive patients treated at the surgery (14.3%), from whom this study population was derived, was comparable with recently reported English national surveys (13.7% for women and 11.7% for men). While the lack of ethnic minority representation in the sample may limit the generalizability of the observations made, it is of clear relevance to the white indigenous population.

The simultaneous measurement technique with two automated sphygmomanometers prevents the erroneous diagnosis of a BP difference due to short-term fluctuations between measurements and avoids intra-observer bias. From our systematic review, studies using a simultaneous technique have reported lower prevalence rates for the IAD than those using sequential measurements. The prevalence reported here is similar to the expected prevalence from previous sequential measurements during the consultation, suggesting that these differences are constant and reproducible. The absence of a significant decline in measured IAD with repeated measurements supports this and suggests that the IAD, like the ABPI, is not a function of absolute BP values.
The prevalences of 19% sIAD $\geq 10$ mmHg and 7% dIAD $\geq 10$ mmHg are lower than those which we and others have previously reported from primary care. However, they are consistent with the best estimates [19.6% sIAD $\geq 10$ mmHg (95% CI 18.0–21.3%) and 8.1% dIAD $\geq 10$ mmHg (95% CI 6.9–9.2%)] which we have reported from the most methodologically robust studies. A higher prevalence of an IAD than previously reported was anticipated since an IAD has been shown to occur more frequently in hypertensive than normotensive subjects in earlier studies of selected populations and upper limb vascular disease is associated with hypertension. However, this is both the first series of hypertensive patients and the first report using simultaneous measurements from primary care, so no direct comparisons can be made.

The ABPI results revealed that 20% of this hypertensive population had evidence of asymptomatic PVD when assessed using a diagnostic cut-off of 0.9. The prevalence of symptomatic PVD (defined as intermittent claudication) is around 2% in men and 1% in women, but asymptomatic PVD prevalences are two- to seven-fold higher, and from their large Scottish primary care cohort study, Leng et al. reported a very similar baseline prevalence of 18.2% with an ABPI $\leq 0.9$. The diagnosis of PVD is important as it implies a heightened risk of cardiovascular (CV) events and therefore merits aggressive targeting of primary prevention.

The tiptoe test also provided evidence of occult peripheral arterial insufficiency, and in combination with the ABPI suggested an overall 25% prevalence of asymptomatic PVD in this study population.

The study showed an inverse association between absolute values of the ABPI and IAD, confirming the suggestions of previous selective studies and supporting the hypothesis that the presence of an IAD may be an indicator of occult PVD.

From the finding that 19% of patients had a sIAD $\geq 10$ mmHg, this study shows that in nearly one in 10 consultations for BP measurements (i.e. half of the time if the lower arm is measured by chance), a hypertensive patient could have their systolic BP underestimated by 10 mmHg or more, if the presence of a IAD has not been specifically excluded. It has been estimated that a reduction of BP of this magnitude could prevent > 4000 fatal and non-fatal coronary events and > 6000 fatal and non-fatal strokes each year in England; thus, the risks to effective management of high BP of missing an IAD are evident, and should be better emphasized in current guidelines. The importance of standardizing readings to the higher arm for consistency is also demonstrated. Similarly, when measuring the ABPI, the variation between arms has also been observed and shown to affect the diagnosis of PVD in 2–6% of cases.

The fact that one in five patients in this study have evidence of PVD, as defined by an ABPI < 0.9, emphasizes the high prevalence of asymptomatic PVD in primary care and is in keeping with previously reported figures. The accurate measurement of ABPI requires time, experience and training, and although it is an independent indicator of risk, the ABPI has a low sensitivity as a predictor of CV events. We propose that detection of an IAD may be a more pragmatic means of identifying subjects who should be investigated for further signs of PVD in the carotid, coronary, renal and lower limb vessels. The correlation between ABPI and sIAD and dIAD values supports this view. Both the sIAD and dIAD, as has been shown in predicting subclavian stenosis, showed a low sensitivity for detecting a reduced ABPI but a high specificity, suggesting that the presence of an IAD may indicate an increased likelihood of PVD. This was most evident for a sIAD $\geq 20$ mmHg which showed an LR of 8.3 for an ABPI $\leq 0.85$. This magnitude of LR can generate a moderate shift in pretest to post-test probability, for example using the 20% starting probability of PVD in this population, an LR of 8.3 for a sIAD $\geq 20$ mmHg suggests a post-test probability of 66%, which would clearly justify further investigation for PVD. Detection of asymptomatic PVD is important as the overall risk of CV events or death is as high in asymptomatic primary care patients as in claudics.

The tiptoe test is a simple stress test. It is useful for identifying aorto-iliac disease where good collateral vessels maintain the ABPI at rest. It has been validated in claudics in secondary care against treadmill testing as a gold standard and is well suited to use in primary care since it is a submaximal exercise test achievable for most patients without limitation.

### Table 3

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Chi-square</th>
<th>$P$</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>dIAD $\geq 7$ mmHg and ABPI $&lt; 0.9$</td>
<td>4.59</td>
<td>&lt;0.05</td>
<td>53</td>
<td>73</td>
<td>2.0</td>
</tr>
<tr>
<td>dIAD $\geq 10$ mmHg and ABPI $&lt; 0.9$</td>
<td>4.46</td>
<td>&lt;0.05</td>
<td>26</td>
<td>92</td>
<td>3.3</td>
</tr>
<tr>
<td>sIAD $\geq 10$ mmHg and ABPI $&lt; 0.9$</td>
<td>4.27</td>
<td>&lt;0.05</td>
<td>37</td>
<td>85</td>
<td>2.5</td>
</tr>
<tr>
<td>sIAD $\geq 10$ mmHg and ABPI $\leq 0.85$</td>
<td>4.06</td>
<td>&lt;0.05</td>
<td>42</td>
<td>90</td>
<td>4.2</td>
</tr>
<tr>
<td>sIAD $\geq 20$ mmHg and ABPI $\leq 0.85$</td>
<td>9.98</td>
<td>&lt;0.01</td>
<td>25</td>
<td>97</td>
<td>8.3</td>
</tr>
</tbody>
</table>
due to exhaustion, angina or other symptoms; measurement of ankle Doppler pressures is straightforward, and no other apparatus is required. Its use has not been previously reported in a primary care population. In normal individuals, the ankle pressure is elevated during exercise but it falls in peripheral arterial insufficiency, and a 20% drop is indicative of significant arterial disease. In this study, the percentage tip-toe drop was inversely correlated with the ABPI and the mean ABPI was significantly reduced in the presence of a 20% drop. This drop was seen in 10% of subjects, half of whom would not have been diagnosed with PVD on the resting ABPI alone. Therefore, this study shows that the test can be utilized in primary care and could provide additional information when PVD is strongly suspected if the resting ABPI is not diagnostic. The results did not show a correlation with the IAD; however, the tip-toe test aims to identify individuals with well-established PVD (as evidenced by development of collateral vessels), and is an exercise test, whereas the IAD may be an early marker of asymptomatic PVD as proximal vessels are affected earlier, and we have not examined the effect of exercise on the IAD. The marked pressure drops in tip-toe tests in diabetics are in keeping with the knowledge that these are a particularly high-risk group for PVD and suggest that this test may aid diagnosis.

It is concluded that IAD should be excluded in all new hypertensive patients for the accurate diagnosis, clinical assessment and consistent management of their BP. These prevalence findings are supported by a number of previous studies and should be incorporated into future guidelines for the management of hypertension.

The study findings support the proposal that detection of an IAD may provide a simple method of detecting patients at increased risk of CVD events. Further measurements on a large cohort of hypertensive patients should be undertaken to further define estimates of sensitivity and specificity of a defined IAD for predicting PVD, to discover whether the IAD could indeed identify subjects who should be more intensively investigated with ABPI measurement and therefore if PVD is confirmed managed aggressively with drugs and lifestyle interventions for primary prevention of CV events. Further work is also needed to confirm the proposal that the aetiology of the IAD is a manifestation of PVD.

The study has piloted the use of the tip-toe stress test in primary care and shown that it can be easily used and has the potential to make a contribution to the diagnosis of asymptomatic PVD over and above that made by the resting ABPI alone. This work needs to be extended to a larger sample of primary care subjects and compared to known risk factors for PVD to discover whether it can make an independent contribution to vascular risk assessment.

Conclusions

An IAD is common in a primary care hypertensive population; therefore, its presence should be documented for the accurate measurement and management of hypertension. Underestimation of systolic BP by \( \geq 10 \) mmHg could fail to prevent \( > 4000 \) fatal and non-fatal coronary events and \( > 6000 \) fatal and non-fatal strokes each year in England. Asymptomatic PVD, as defined by a reduced ABPI, is also common in a primary care hypertensive population. The IAD detected in routine consultations is reproducible in a controlled setting and shows an inverse correlation with the ABPI. These findings support the hypothesis that an IAD is a manifestation of asymptomatic PVD.

Detection of a sIAD of \( \geq 10 \) mmHg may identify hypertensive patients at increased risk of CV events, who would benefit from further investigation for PVD and ought to be targeted with aggressive management of their CV risk factors. Such an approach would facilitate more effective targeting of finite resources in primary prevention strategies.

Acknowledgements

The data were collected by Sarah Holmes, RGN.

Declaration

Funding: Plymouth teaching Primary Care Trust; the Peninsula Medical School; Mid Devon Research Group to CEC; GlaxoSmithKline to Sarah Holmes, RGN.

Ethical approval: North and East Devon Research Ethics Committee approved the study.

Conflicts of interest: None.

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