

# Interarm Difference in Systolic Blood Pressure in Different Ethnic Groups and Relationship to the “White Coat Effect”: A Cross-Sectional Study

Claire Lorraine Schwartz,<sup>1</sup> Christopher Clark,<sup>2</sup> Constantinos Koshariaris,<sup>1</sup> Paramjit S. Gill,<sup>3</sup> Shelia M. Greenfield,<sup>4</sup> Sayeed M. Haque,<sup>5</sup> Gurdip Heer,<sup>5</sup> Amanpreet Johal,<sup>6</sup> Ramandeep Kaur,<sup>5</sup> Jonathan Mant,<sup>7</sup> Una Martin,<sup>5</sup> Mohamed A. Mohammed,<sup>8</sup> Sally Wood,<sup>1</sup> and Richard J. McManus<sup>1</sup>

## BACKGROUND

Interarm differences (IADs)  $\geq 10$  mm Hg in systolic blood pressure (BP) are associated with greater incidence of cardiovascular disease. The effect of ethnicity and the white coat effect (WCE) on significant systolic IADs (sslADs) are not well understood.

## METHODS

Differences in BP by ethnicity for different methods of BP measurement were examined in 770 people (300 White British, 241 South Asian, 229 African-Caribbean). Repeated clinic measurements were obtained simultaneously in the right and left arm using 2 BPTu monitors and comparisons made between the first reading, mean of second and third and mean of second to sixth readings for patients with, and without known hypertension. All patients had ambulatory BP monitoring (ABPM). WCE was defined as systolic clinic BP  $\geq 10$  mm Hg higher than daytime ABPM.

## RESULTS

No significant differences were seen in the prevalence of sslAD between ethnicities whichever combinations of BP measurement were used and

regardless of hypertensive status. sslADs fell between the 1<sup>st</sup> measurement (161, 22%), 2<sup>nd</sup>/3<sup>rd</sup> (113, 16%), and 2<sup>nd</sup>–6<sup>th</sup> (78, 11%) (1<sup>st</sup> vs. 2<sup>nd</sup>/3<sup>rd</sup> and 2<sup>nd</sup>–6<sup>th</sup>,  $P < 0.001$ ). Hypertensives with a WCE were more likely to have sslADs on 1<sup>st</sup>, (odds ratio [OR] 1.73 (95% confidence interval 1.04–2.86); 2<sup>nd</sup>/3<sup>rd</sup>, (OR 3.05 (1.68–5.53); and 2<sup>nd</sup>–6<sup>th</sup> measurements, (OR 2.58 (1.22–5.44)). Nonhypertensive participants with a WCE were more likely to have a sslAD on their first measurement (OR 3.82 (1.77 to –8.25) only).

## CONCLUSIONS

sslAD prevalence does not vary with ethnicity regardless of hypertensive status but is affected by the number of readings, suggesting the influence of WCE. Multiple readings should be used to confirm sslADs.

**Keywords:** ambulatory blood pressure monitoring; blood pressure; ethnic group; hypertension; interarm blood pressure differences; simultaneous blood pressure measurement method; white coat effect.

doi:10.1093/ajh/hpx073

Differences in systolic blood pressure (BP) between right and left arms  $\geq 10$  mm Hg independently predict increased risk of cardiovascular events,<sup>1,2</sup> subclavian stenosis,<sup>3</sup> and cardiovascular or all-cause mortality.<sup>2</sup> Measuring BP in both arms is

a simple intervention that identifies the higher reading arm, which should be used for future hypertension management, and may identify patients needing investigation, or intensification of cardiovascular risk management.<sup>4</sup> Prevalence of

Correspondence: Claire Lorraine Schwartz (claire.schwartz@phc.ox.ac.uk).

Initially submitted October 21, 2016; date of first revision February 17, 2017; accepted for publication April 5, 2017; online publication May 5, 2017.

<sup>1</sup>Nuffield Department of Primary Care Health Sciences, NIHR School for Primary Care Research, University of Oxford, Radcliffe Observatory Quarter, Oxford, UK; <sup>2</sup>Primary Care Research Group, University of Exeter Medical School, Smeall Building, St Luke's Campus, Exeter, UK; <sup>3</sup>WMS—Social Science and Systems in Health, University of Warwick, Coventry, Birmingham, UK; <sup>4</sup>Institute of Applied Health Research, University of Birmingham, Edgbaston, Birmingham, UK; <sup>5</sup>Institute of Clinical Science, University of Birmingham, Edgbaston, Birmingham, UK; <sup>6</sup>NIHR Clinical Research Network: West Midlands, Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK; <sup>7</sup>Primary Care Unit, Department of Public Health and Primary Care, University of Cambridge, Strangeways Research Laboratory, Worts Causeway, Cambridge, Cambridgeshire, UK; <sup>8</sup>School of Health Studies, University of Bradford, Bradford, UK.

© The Author 2017. Published by Oxford University Press on behalf of American Journal of Hypertension, Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

patients with a significant systolic interarm difference (ssIAD) varies according to population. A U.S. systematic review, found the prevalence of ssIADs was 7.5% in primary care, 9% for hospital outpatients, and 12.1% for hospital inpatients.<sup>5</sup> A recent study using Framingham data found the prevalence of ssIADs in a community sample, free from cardiovascular disease at baseline, was 9.4%. A UK systematic review considered prevalence of ssIADs in relation to clinical predictors and found 11.2% in hypertensives, 7.4% in people with diabetes and 3.6% in the general population.<sup>6</sup> Characteristics associated with ssIADs are age,<sup>1,7–9</sup> diabetes,<sup>1</sup> higher systolic BP,<sup>1,6,8</sup> and increased body mass index (BMI).<sup>1</sup>

Some ethnic groups are at higher cardiovascular risk.<sup>10–13</sup> South Asians and African-Caribbeans have a higher incidence of diabetes than White Europeans,<sup>14</sup> and African-Caribbeans have a greater prevalence of hypertension and stroke.<sup>15,16</sup> Ethnicity may also affect the prevalence of ssIADs. Countries in the Far East appear to have a lower prevalence of patients with ssIADs than Western populations.<sup>6,8,17,18</sup> To our knowledge, there has only been one study so far to look at the effect of ethnicity on the prevalence of ssIADs.<sup>7</sup> It found a higher prevalence of ssIADs  $\geq 15$  mm Hg in African American and White Americans compared to Hispanic or Chinese Americans.

Method of measurement affects the likelihood of finding a ssIAD; single or sequential BP measurement techniques may overestimate the prevalence.<sup>6,19,20</sup>

This study, using simultaneous measurements, aimed to evaluate whether prevalence of ssIADs  $\geq 10$  mm Hg varied according to South Asian, African-Caribbean, or White British ethnicity, hypertensive status or other participant characteristic and additionally to investigate any association of prevalence with the number of readings, or the presence of a white coat effect (WCE) or white coat hypertension (WCH).

## METHODS

Blood pressure monitoring in different ethnic groups (BP-ETH), was a primary care based observational study conducted between June 2010 and December 2012. The detailed methods have been published previously<sup>21</sup> and are outlined below.

## Population

Participants were aged 40–74 years, purposefully recruited from 3 ethnic groups: White British (WB), South Asian (SA), and African-Caribbean (AC). Ethnicity was self-defined using standard UK criteria.<sup>22</sup> Respondents attended 3 research clinics at their own practice. Twenty-eight practices were recruited from the Primary-Care-Research-Network, Central England, United Kingdom, chosen to represent the required range of ethnicities. Around 40 participants were recruited from each practice, both with (HT) and without hypertension (NHT), as defined by a clinical code in the patient's record. People unable to consent, belonging to a different ethnic group or whose general practitioner felt they were unable to take part were excluded.

## Procedure

Following at least 5 minutes rest, sitting BP measurements were taken by a research nurse using 2 BPTru monitors (BpTru Medical Devices BPM-200), set to take 6 readings at 1-minute intervals and used simultaneously on both arms.<sup>23</sup> Monitors were calibrated independently to the same standard at the start of the study and the BPTru device performs an autocalibration upon activation to maintain accuracy. The research nurse remained in the room with the patient while the readings were being taken. One BPTru monitor was used consistently for the right arm and the second used for the left. This is considered to be the most accurate way of establishing an IAD.<sup>6,19,20</sup>

Participants were fitted with an ambulatory monitor (Spacelabs 90217-1Q)<sup>24</sup> on either the first or second clinic visit.

Ambulatory BP monitoring (ABPM) readings were recorded at half hourly intervals during the day and hourly overnight for a total of 24 hours. Participants' nondominant arm was used unless systolic BP was  $\geq 20$  mm Hg between the right and left arm on the first reading, which included 32 patients. In the case of these patients, the arm with the higher reading was used.

## Analysis

ssIAD for the first measurement was defined as an absolute difference  $\geq 10$  mm Hg between the right and left arm.<sup>3</sup> SSADs were further defined using absolute ssIADs of the 1<sup>st</sup> reading alone, mean of the 2<sup>nd</sup>/3<sup>rd</sup> and mean of the 2<sup>nd</sup> to 6<sup>th</sup> readings.

There is no accepted definition of the WCE or WCH therefore different analyses were undertaken based on the literature<sup>25,26</sup> using the following systolic BP definitions:

1. White coat effect (1<sup>st</sup> BP measurement):
  - a. (1<sup>st</sup> clinic measurement–mean daytime ABPM)  $\geq 10$  mm Hg
2. White coat effect (mean of 2<sup>nd</sup>/3<sup>rd</sup> BP measurements)
  - b. (Mean of 2<sup>nd</sup>/3<sup>rd</sup> clinic measurement–mean daytime ABPM)  $\geq 10$  mm Hg
3. White coat effect (2<sup>nd</sup>–6<sup>th</sup> BP measurement)
  - c. (Mean of 2<sup>nd</sup>–6<sup>th</sup> clinic measurement–mean daytime ABPM)  $\geq 10$  mm Hg

Trends between the ethnic groups for prevalence of ssIADs were tested using the Extended Mantel-Haenszel chi-squared test for linear trend.<sup>27</sup>

Univariable analyses were conducted between ssIADs and baseline characteristics stratified by diagnosed hypertension (HT) and not known to be hypertensive (NHT) patients. Chi-squared test was used when comparing binary/categorical variables. The 2 sample *t*-test was used when comparing the mean difference between 2 groups. Nonparametric tests were used for skewed variables such as BMI.<sup>27</sup>

A multivariate logistic regression model was also used where we adjusted for the following variables: ethnicity,

diabetes, age, gender, CHD, log(BMI), mean BP, medication, smoking, and deprivation score.

Differences in the proportion of patients with an absolute ssIAD, dependent on the number of measurements, were investigated using a Cochran Q test.<sup>27</sup> All BP comparisons were for measurements in the same arm.

The same analysis was conducted checking for any differences in the prevalence of the WCE across different combinations of measurements. Post-hoc analyses were conducted using the McNemar test.<sup>27</sup> Association between ssIADs and the corresponding WCE was examined by the use of logistic regression models adjusted for baseline characteristics.

Sensitivity analyses were carried out to check the effect on WCE when using differences between clinic systolic BP and systolic ABPM of 5 and 15 mm Hg.

### Ethics and research governance approval

Ethical approval for the BP-ETH study was gained from the Black Country Research Ethics Committee, West Midlands, United Kingdom (Ref 09/H1202//114).

## RESULTS

### Baseline demographic data

Seven hundred and seventy people participated in BP-ETH of whom 300 were WB, 229 were AC, and 241 were SA (Supplementary Table 1a—Appendix). There were no significant differences in baseline characteristics between WB, AC, and SA groups, or between HT and NHT participants, although more HT participants (481) were recruited than NHT (289).

### Prevalence of IADs by ethnicity and hypertensive status

BP measurements in the right and left arms were available for 750 of the 770 participants who were grouped into HT and NHT and then subdivided into participants with a ssIAD or not. There was no systematic difference in the systolic BP of the right arm vs. that of the left (Supplementary Table 2a—Appendix); therefore, the following ssIADs are expressed as an absolute difference.

The overall prevalence of ssIADs for HT participants was 61/469 (13.0%) and 26/281 (9.3%) for NHT participants (Table 1). Overall prevalence of ssIADs in the HT was group

was higher but this difference was not found to be significant (Table 1). Association between ssIAD and ethnic group was not significant for the HT or NHT group (Table 1). There were no significant differences in the prevalence of ssIAD by ethnicity in the HT and NHT groups whichever combination of measurements was used (1<sup>st</sup>, mean of 2<sup>nd</sup>/3<sup>rd</sup>, or mean of 2<sup>nd</sup>–6<sup>th</sup>). Therefore only the sIAD using the mean of the 2<sup>nd</sup>–6<sup>th</sup> measurement is presented here as prevalence dropped the more measurements were used and this mean represented the nadir. A multivariate logistic regression model was used where we adjusted for diabetes, age, gender, CHD, log(BMI), deprivation score, and mean BP. Ethnicity remained nonsignificant in both HT and NHT patients (Table 3).

### Characteristics of participants with and without an IAD

Table 2 shows characteristics of participants with and without a ssIAD by hypertensive status. As the prevalence of ssIADs was not significantly associated with ethnicity, the 3 ethnic groups are combined for analysis of the remaining characteristics. Significantly higher mean BP was associated with a ssIAD for both HT (140.1 mm Hg [ssIAD] vs. 131.6 mm Hg [no ssIAD],  $P < 0.001$ ) and NHT groups (132.0 mm Hg [ssIAD] vs. 124.7 mm Hg [no ssIAD],  $P = 0.031$ ) (Table 2). The multivariate analysis also showed a significantly higher BP was associated with a ssIAD in both the HT and NHT groups (Table 3). Significantly higher daytime ABPM was associated with a ssIAD in the HT but not the NHT group.

As BMI was a skewed variable, this is reported as a median value with an interquartile range using the nonparametric test Wilcoxon rank sum for the  $P$  value (Table 2). Participants with a ssIAD had a significantly higher BMI in the HT group (31.0 kg/m<sup>2</sup> vs. 28.7 kg/m<sup>2</sup>,  $P = 0.025$ ); however, this significance disappeared in the multivariate analysis (Table 3). Similarly in the NHT group, where ssIAD was actually associated with a lower BMI (27.3 kg/m<sup>2</sup> vs. 29.4 kg/m<sup>2</sup>,  $P = 0.025$ ) (Table 2), the BMI no longer remained significant in the multivariate analysis (Table 3). Multivariate analysis showed that NHT participants with a ssIAD were significantly more likely to smoke, which may have affected the univariate analysis of BMI.

Difference in age between HT participants with a ssIAD and HT participants without a ssIAD was of borderline significance (58.4 vs. 60.8,  $P = 0.053$ ). This effect was not seen

**Table 1.** Incidence of sIADs by hypertensive status and ethnic group

	Prevalence of systolic interarm BP absolute difference for second to sixth measurement					
	Known hypertensive (HT)			Not known to be hypertensive (NHT)		
	≥10 mm Hg (n = 61)	<10 mm Hg (n = 408)	P value	≥10 mm Hg (n = 26)	<10 mm Hg (n = 255)	P value
Overall, No. (%)	61 (13.0)	408 (87.0)		26 (9.3)	255 (90.7)	
WB, No. (%)	17 (40)	162 (28)	0.188	10 (38)	101 (40)	0.892
SA, No. (%)	20 (29)	120 (33)		10 (38)	87 (34)	
AC, No. (%)	24 (31)	126 (39)		6 (23)	67 (26)	

Abbreviations: AC, African-Caribbean; BP, blood pressure; SA, South Asian; sIAD, Systolic Interarm Differences; WB, White British.

**Table 2.** Showing demographic and health differences between those patients with an interarm BP difference and those without for the HT and NHT groups

Variable	Systolic interarm BP absolute difference for second to sixth measurement					
	Known hypertensive (HT)			Not known to be hypertensive (NHT)		
	≥10 mm Hg (n = 61) <sup>a</sup>	<10 mm Hg (n = 408) <sup>a</sup>	P value	≥10 mm Hg (n = 26) <sup>a</sup>	<10 mm Hg (n = 255) <sup>a</sup>	P value
Age (years)	58.4 (8.9)	60.8 (8.8)	0.053	54.8 (9.1)	53.9 (9.4)	0.669
Men	26 (43%)	208 (51%)	0.223	11 (42%)	121 (47%)	0.617
Mean blood Pressure <sup>a</sup>	(n = 52)	(n = 386)	<0.001	(n = 24)	(n = 239)	0.02
SD	143.7 (19.6)	134.1 (17.6)		135.3 (15.8)	126.4 (17.2)	
BMI <sup>b</sup> (kg/m <sup>2</sup> )	31.0 (26.7–34.3)	28.7 (25.5–32.1)	0.0254	27.3 (24.9–30.6)	29.4 (26.5–33.5)	0.025
Coronary heart disease	5 (8%)	53 (13%)	0.403	2 (8%)	9 (4%)	0.270
Diabetes	16 (27%)	94 (23%)	0.536	1 (4%)	16 (6%)	0.519
Mean deprivation score <sup>c</sup>	(n = 60)	(n = 384)	0.572	(n = 21)	(n = 236)	0.79
SD	44.1 (17.55)	42.8 (17.58)		41.3 (19.18)	42.3 (17.11)	
Mean daytime ABPM <sup>a</sup>	(n = 47)	(n = 341)	0.003	(n = 22)	(n = 209)	0.19
SD	139.5 (15.8)	132.8 (14.3)		133.2 (15.0)	129.3 (12.8)	
Taking antihypertensive medication (Y)	58 (95%)	396 (97%)	0.308	1 (4%)	15 (6%)	1.00
Smoking (Y)	6 (10%)	60 (15%)	0.207	10 (38%)	28 (11%)	0.001

Abbreviations: ABPM, ambulatory blood pressure monitoring BP, blood pressure.

<sup>a</sup>Number of participants unless otherwise stated.<sup>b</sup>mm Hg.<sup>c</sup>BMI, body mass index, reported as a median value with (interquartile range).<sup>d</sup>Index of multiple deprivation 2007.**Table 3.** Multivariable analysis showing the likelihood of a sslAD for the HT and NHT groups

Variables	Known hypertensive (HT) (n = 437) (OR)	Not known to be hypertensive (NHT) (n = 262) (OR)
WB <sup>a</sup>	1	1
SA	1.9 (0.851–4.333)	1.2 (0.386–3.916)
AC	1.7 (0.777–3.919)	0.8 (0.226–2.963)
Diabetes	1.2 (0.597–2.483)	0.5 (0.0524–5.495)
Age	1.0 (0.940–1.011)	1.0 (0.936–1.058)
Sex (Men)	0.8 (0.446–1.527)	0.8 (0.324–2.128)
CHD	0.6 (0.177–2.169)	1.4 (0.0663–29.91)
BMI <sup>b</sup> (log transformed)	2.6 (0.580–11.46)	0.2 (0.0141–3.170)
Mean blood pressure	1.03*** (1.010–1.043)	1.03** (1.006–1.064)
On medication	0.8 (0.158–4.160)	0.8 (0.0410–15.17)
Smoker	0.9 (0.333–2.184)	5.4*** (1.887–15.21)
IMD <sup>c</sup>	1.0 (0.988–1.004)	1.0 (1.000–1.003)

Abbreviations: AC, African-Caribbean; CHD, coronary heart disease; OR, odds ratio; SA, South Asian; sslAD, significant systolic interarm differences; WB, White British.

<sup>a</sup>Reference category \*\*\*P < 0.01 \*\*P < 0.05.<sup>b</sup>Body mass index.<sup>c</sup>Index of multiple deprivation 2007.

in the NHT group and the effect was no longer significant when other variables were accounted for in the multivariate analysis (Table 3). There were no other significant differences between participants with and without sslAD (Table 2).

### Changes in interarm BP differences between the 1<sup>st</sup> reading, 2<sup>nd</sup> and 3<sup>rd</sup> reading, and 2–6<sup>th</sup> reading

Out of 469 HT participants, 449 had all 6 BP readings available on both arms. The number of participants with a



ssIAD fell as more pairs of readings were included in the calculation of mean BP (Supplementary Table 3a—Appendix): 101 (22%) for the 1<sup>st</sup> measurement, 69 (15%) for the mean of the 2<sup>nd</sup>/3<sup>rd</sup> measurements, and 54 (12%) for the mean of the 2<sup>nd</sup>–6<sup>th</sup> measurements. Post-hoc analysis revealed a significant difference ( $P < 0.001$ ) between the number of participants with a ssIAD on the 1<sup>st</sup> pair of readings vs. the number with a ssIAD on the mean of the 2<sup>nd</sup>/3<sup>rd</sup> and the 2<sup>nd</sup>–6<sup>th</sup> pairs of readings, with a smaller nonsignificant difference between the latter 2 measurement methods (Supplementary Table 3a—Appendix). NHT (271/281) patients showed a similar pattern (Supplementary Table 3a—Appendix).

This effect was mirrored by the decline in the prevalence of a WCE; numbers of HT participants with a WCE on the 1<sup>st</sup> measurement was 128 (35%), 89 (25%) for the mean of the 2<sup>nd</sup>/3<sup>rd</sup>, and 66 (18%) for 2<sup>nd</sup>–6<sup>th</sup> BP readings (1<sup>st</sup> vs. 2<sup>nd</sup>/3<sup>rd</sup>  $P < 0.001$ ; 1<sup>st</sup> vs. 2<sup>nd</sup>–6<sup>th</sup> reading  $P < 0.001$ ) (Supplementary Table 4a—Appendix). This decline was also seen in the NHT participants (Supplementary Table 4a—Appendix).

### Association of the WCE and interarm BP difference

The relationship between the WCE and ssIAD was investigated using a logistic regression model and adjusted for baseline characteristics. Resulting odds ratios show that in the HT group there was a significant association between the WCE and ssIAD for the 1<sup>st</sup> measurement, 2<sup>nd</sup>/3<sup>rd</sup>, and 2<sup>nd</sup>–6<sup>th</sup> measurement (Table 4).

In the NHT group, the odds ratio was significant for the association between WCH and ssIAD for the first reading (4.06, 95% confidence interval, 1.83, 9.00) (Table 4) but no significant differences were found in the association of WCH and ssIAD between the mean of the 2<sup>nd</sup>/3<sup>rd</sup> and the 2<sup>nd</sup>–6<sup>th</sup> readings (Table 4).

Sensitivity analyses using definitions of a 5 mm Hg and 15 mm Hg difference between clinic systolic BP and the systolic mean daytime ABPM showed a similar pattern of results (Supplementary Tables 5a and 6a—Appendix).

## DISCUSSION

### Summary

In this community-based study, ethnicity had no significant impact on the prevalence of ssIAD. The HT group had a greater prevalence of ssIADs overall but the difference between the HT and the NHT groups was not significant. However, the prevalence of ssIADs significantly increased

with increasing BP regardless of hypertensive status. NHT Participants with a ssIAD were more likely to be a smoker, but there did not appear to be the same association for BMI and age. There was no systematic difference in systolic BP between the right and the left arm, which was in keeping with the results of a recent meta-analysis.<sup>28</sup>

Calculating ssIAD with increasing numbers of repeated measurements significantly reduced the prevalence of a ssIAD and this appeared to be associated with the WCE, especially for HT participants. For NHT participants, the association between a ssIAD and WCH was present on the first measurement but not thereafter.

### Strengths and Limitations

The main strength of this study was that it was large, community-based, and recruited approximately equal numbers of patients from each of 3 ethnic groups. It included patients with a diagnosis of hypertension, those with no known diagnosis and did not exclude patients with comorbidities. Measurements were taken in a Primary Care setting, which is where most office BP is taken and provides the most generalizable comparison of the WCE.<sup>29</sup> The study used 6 BP measurements, allowing for analysis of ssIADs over several consecutive readings, and measurements were taken simultaneously with a validated monitor which is widely acknowledged as the most accurate way to measure IAD.<sup>19,30,31</sup> There is a theoretical bias arising from the use of different monitors on each arm, which could not be helped as the BPTru monitor takes readings automatically at 1-minute intervals precluding switching of monitors between arms. However, the monitors were all calibrated prior to the start of the study and autocalibrate each time when activated therefore reducing the likelihood of monitors on different arms being in a different state of calibration.<sup>23</sup> The number of patients with ssIADs was relatively small which affected power to assess associations and differences between groups. Only systolic BP was assessed therefore any associated or independent effects on IAD between diastolic BP are unknown.

The current study did not include Far Eastern ethnicities such as Chinese, who may have significantly lower incidence of ssIADs than Western groups.<sup>6</sup> Despite the range of ethnicities, there was only 1 area of the UK studied, which does not take into account potential effects different environments may have.

The population here came from more deprived areas in comparison with the rest of the UK. While we do not know what association deprivation would have with the prevalence

**Table 4.** ORs for ssIADs when the WCE is present in HT and NHT groups

	ORs for ssIAD when WCE is present in HT group	ORs for ssIAD when WCE is present in NHT group
First pair of readings	2.12 (95% CI: 1.24–3.62; $P = 0.006$ , $n = 370$ )	4.06 (95% CI: 1.83–9.00; $P = 0.001$ , $n = 220$ )
Mean of the 2 <sup>nd</sup> and 3 <sup>rd</sup> pair of readings	3.69 (95% CI: 1.96–6.93; $P < 0.001$ , $n = 373$ )	1.07 (95% CI: 0.41–2.79; $P = 0.888$ , $n = 226$ )
Mean of the 2 <sup>nd</sup> –6 <sup>th</sup> pair of readings	3.48 (95% CI: 1.56, 7.71; $P = 0.002$ , $n = 364$ )	1.68 (95% CI: 0.451–6.32; $P = 0.436$ ; $n = 219$ )

Logistic regression model was used and adjusted for gender, ethnicity, logarithm of BMI, age, CHD, daytime ABPM, diabetes, smoking, medication, and IMD. Abbreviations: CI, confidence interval; HT, known hypertensive; IMD, index of multiple deprivation; NHT, not known to be hypertensive; OR, odds ratio; ssIAD, significant systolic interarm differences; WCE, white coat effect.

of ssIADs, hypertension is more prevalent in deprived settings so a concomitant trend to increased prevalence of ssIADs with deprivation might be predicted.<sup>32</sup>

In this study, the definition of a clinically significant systolic IAD was defined as  $\geq 10$  mm Hg. Current European hypertension guidelines suggest a ssIAD  $> 10$  mm Hg between arms carries an increase in cardiovascular risk<sup>33</sup> and although the UK guidelines suggest a difference in systolic BP  $\geq 20$  mm Hg is indicative of vascular disease, they only specify a ssIAD  $< 10$  mm Hg as normal.<sup>4</sup> Although a ssIAD  $\geq 10$  mm Hg may show less specificity for peripheral artery disease than that of 15 mm Hg, it is more sensitive<sup>34</sup> and, in addition, it is in keeping with the definition used in many current studies.<sup>1,3,5,35</sup> Using this definition meant that our work could be compared to the current literature more easily and was clinically relevant.

As there is no accepted definition of the WCE or WCH, a pragmatic definition for the study was developed using an arbitrary level of the clinic-ambulatory difference ( $\geq 10$  mm Hg).<sup>4</sup> Differences between clinic and ambulatory BP are potentially subject to bias, principally from variation in the clinic BP due to operator error, hypertensive status and activities, and environment of the patient.<sup>36</sup> However, given the controlled nature of the research measurements, such errors would be expected to be minimized in this study.

### Comparison with existing literature

The prevalence of ssIADs in the HT and NHT groups was 13.0% and 9.3%, respectively. In the NHT group, this appeared to be high for a general population.<sup>6</sup>

A recent systematic review, analysing prevalence of ssIADs from 16 studies, found a prevalence of 3.6%. However, the population group included 2 studies of Far Eastern origin which had a much lower prevalence than studies of Western origin and therefore reduced the pooled prevalence.<sup>6</sup> There was a higher prevalence in a hypertensive population (11.2%) and when studies causing statistical heterogeneity were removed, the prevalence of ssIADs in a Western, hypertensive population was 13.3%, almost identical to the prevalence found here.<sup>6</sup> Similar to the current study, the multiethnic study of atherosclerosis (MESA) also reported no significant differences in ssIADs between African American and White non-Hispanic groups.<sup>7</sup> However, there was a significantly lower prevalence of ssIADs in Hispanic and Chinese Americans suggesting that Hispanic and Far Eastern ethnicities may be less predisposed to ssIADs than Western populations.

A higher BMI has been previously reported<sup>1,7,8</sup> as being associated with a ssIAD and is likely to relate to patients with ssIADs having a higher cardiovascular risk.<sup>1</sup> However, another study<sup>9</sup> found that age was the only significant predictor for ssIADs. Neither age nor BMI was found to have a significant association here with a ssIAD in the HT or NHT group. However, BMI was higher in the HT group so this may have been compounded by the fact that the number of patients with a ssIAD was small. The NHT group had a significant association between smoking and ssIAD, which is in keeping with the link between ssIADs and a greater cardiovascular risk. However, the link between

smoking and ssIADs is varied with some studies showing some association<sup>7</sup> but others showing no significance.<sup>1</sup> The number of participants in this study who smoked was very small and is likely to affect the significance of any associations here.

Results here are in agreement with that found in the Framingham Heart Study, a study in a Japanese population and a recent large meta-analysis of 16 IAD studies showing that those patients with a  $\geq 10$  mm Hg difference between arms had significantly higher systolic BP compared to those without.<sup>1,6,8</sup> This is likely to be an effect of the absolute IAD increasing as absolute BP increases and may in part explain why patients with a ssIAD appear to be at higher risk of a cardiovascular event.<sup>1</sup>

Systolic BP decreased over the 6 clinic measurements, and the prevalence of ssIAD followed the same pattern. This pattern has been seen in other studies<sup>35,37,38</sup> and a study by Martin *et al.* suggested that the effect may be associated with the WCE,<sup>30</sup> although they used sequential measurements to estimate IAD which can overestimate its prevalence.<sup>19</sup>

A significant association was found here between WCH and ssIAD on the first reading for participants in the NHT group and between the WCE and ssIADs for all BP measurements used in the HT patients.

For HT patients, the strongest association between the WCE and ssIAD was using the mean of 2<sup>nd</sup>/3<sup>rd</sup> readings which may be explained by HT participants having a stronger, more persistent WCE than those with no diagnosis. There is closer agreement between clinic and ambulatory BP when a patient's BP is closer to normal levels.<sup>33,36,38–40</sup> This suggests that the increase in prevalence of ssIADs in response to higher BP levels may be linked to the WCE.

### Implications for practice

There appears to be little difference in the prevalence of ssIADs between SA and AC cohorts compared to a WB population. However, those with higher mean clinic BP were more likely to have a ssIAD regardless of hypertensive status. European guidelines recommend simultaneous measurement to exclude clinical ssIADs.<sup>33</sup> A much greater effect was seen in terms of the number of measurements used; hence, health professionals should not rely on single BP measurements to identify ssIADs.

This study and others<sup>19</sup> have shown that the prevalence of a ssIAD continues to fall when greater numbers of pairs of readings are taken into account. Therefore, if a ssIAD is detected on the first measurement, we propose that BP should be taken simultaneously at least 3 times in both arms with the mean IAD calculated for the 2<sup>nd</sup> and 3<sup>rd</sup> readings in order to more accurately estimate a “true” IAD.

### SUPPLEMENTARY MATERIAL

Supplementary data are available at *American Journal of Hypertension* online.

## ACKNOWLEDGMENTS

Mr Roger Holder, previously Head of Statistics at Primary Care Clinical Sciences, University of Birmingham, and Jamie Coleman, Consultant Clinical Pharmacologist at University Hospital Birmingham, were original co-applicants who assisted in the design of the BP-ETH study before moving on to other projects. Hardeep Sandhar (database developer) and Kirandeep Jheeta (data manager) gave important support and developed the data strategy. Sabina Yasin helped with initial research clinics. Mr David Yeomans served as Patient and Public Involvement (PPI) representative on the steering group and has given helpful advice throughout. The authors would like to acknowledge their contribution to this work. We would like to acknowledge the input of participating patients, practices, and the NIHR Clinical Research network, without whom this research would not be possible. This article presents independent research funded by the National Institute for Health Research (NIHR) under the Research for Patient Benefit Program and through RM's NIHR Professorship. The views expressed in this publication are those of the authors and not necessarily those of the National Health Service, the NIHR or the Department of Health. NIHR Research for Patient Benefit (grant references PB-PG-1207-15042 and NIHR-RP-R2-12-015). C.S. and C.K. are supported by NIHR Oxford CLAHRC. C.C. is supported by an NIHR Clinical Lectureship.

## DISCLOSURE

RM Has received BP monitoring equipment from Omron and Lloyds Pharmacies. The other authors declare no conflict of interest.

## REFERENCES

- Weinberg I, Gona P, O'Donnell CJ, Jaff MR, Murabito JM. The systolic blood pressure difference between arms and cardiovascular disease in the Framingham Heart Study. *Am J Med* 2014; 127:209–215.
- Clark CE, Taylor RS, Shore AC, Campbell JL. The difference in blood pressure readings between arms and survival: primary care cohort study. *BMJ* 2012; 344:e1327.
- Clark CE, Taylor RS, Shore AC, Ukoumunne OC, Campbell JL. Association of a difference in systolic blood pressure between arms with vascular disease and mortality: a systematic review and meta-analysis. *Lancet* 2012; 379:905–914.
- NICE. Hypertension: Clinical Management of Primary Hypertension in Adults London 2011. London: National Clinical Guideline Centre, The Royal College of Physicians.
- Singh S, Sethi A, Singh M, Khosla S. Prevalence of simultaneously measured interarm systolic blood pressure difference and its clinical and demographic predictors: a systemic review and meta-analysis. *Blood Press Monit* 2015; 20:178–185.
- Clark CE, Taylor RS, Shore A, Campbell J. Prevalence of systolic inter-arm differences in blood pressure for different primary care populations: systematic review and meta-analysis. *Br J Gen Pract* 2016; 66:e297–e308.
- Aboyans V, Kamineni A, Allison MA, McDermott MM, Crouse JR, Ni H, Szklo M, Criqui MH. The epidemiology of subclavian stenosis and its association with markers of subclinical atherosclerosis: the Multi-Ethnic Study of Atherosclerosis (MESA). *Atherosclerosis* 2010; 211:266–270.
- Kimura A, Hashimoto J, Watabe D, Takahashi H, Ohkubo T, Kikuya M, Imai Y. Patient characteristics and factors associated with inter-arm difference of blood pressure measurements in a general population in Ohasama, Japan. *J Hypertens* 2004; 22:2277–2283.
- Fotherby MD, Panayiotou B, Potter JF. Age-related differences in simultaneous interarm blood pressure measurements. *Postgrad Med J* 1993; 69:194–196.
- Joshi P, Islam S, Pais P, Reddy S, Dorairaj P, Kazmi K, Pandey MR, Haque S, Mendis S, Rangarajan S, Yusuf S. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA* 2007; 297:286–294.
- Lip GY, Barnett AH, Bradbury A, Cappuccio FP, Gill PS, Hughes E, Imray C, Jolly K, Patel K. Ethnicity and cardiovascular disease prevention in the United Kingdom: a practical approach to management. *J Hum Hypertens* 2007; 21:183–211.
- Anand SS, Yusuf S, Vuksan V, Devanese S, Teo KK, Montague PA, Kelemen L, Yi C, Lonn E, Gerstein H, Hegele RA, McQueen M. Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic groups in Canada: the Study of Health Assessment and Risk in Ethnic groups (SHARE). *Lancet* 2000; 356:279–284.
- Mensah GA, Mokdad AH, Ford ES, Greenlund KJ, Croft JB. State of disparities in cardiovascular health in the United States. *Circulation* 2005; 111:1233–1241.
- Cappuccio FP, Cook DG, Atkinson RW, Strazzullo P. Prevalence, detection, and management of cardiovascular risk factors in different ethnic groups in south London. *Heart* 1997; 78:555–563.
- Chiu M, Austin PC, Manuel DG, Tu JV. Comparison of cardiovascular risk profiles among ethnic groups using population health surveys between 1996 and 2007. *CMAJ* 2010; 182:E301–E310.
- Howard VJ. Reasons underlying racial differences in stroke incidence and mortality. *Stroke* 2013; 44:S126–S128.
- Sheng CS, Liu M, Zeng WF, Huang QF, Li Y, Wang JG. Four-limb blood pressure as predictors of mortality in elderly Chinese. *Hypertension* 2013; 61:1155–1160.
- Kim KB, Oh MK, Kim HG, Ki JH, Lee SH, Kim SM. Inter-arm differences in simultaneous blood pressure measurements in ambulatory patients without cardiovascular diseases. *Korean J Fam Med* 2013; 34:98–106.
- Verberk WJ, Kessels AG, Thien T. Blood pressure measurement method and inter-arm differences: a meta-analysis. *Am J Hypertens* 2011; 24:1201–1208.
- Lane D, Beevers M, Barnes N, Bourne J, John A, Malins S, Beevers DG. Inter-arm differences in blood pressure: when are they clinically significant? *J Hypertens* 2002; 20:1089–1095.
- Wood S, Martin U, Gill P, Greenfield SM, Haque MS, Mant J, Mohammed MA, Heer G, Johal A, Kaur R, Schwartz C, McManus RJ. Blood pressure in different ethnic groups (BP-Eth): a mixed methods study. *BMJ Open* 2012; 2:e001598.
- McKenzie K, Crowcroft N. Ethnicity, race, and culture: guidelines for research, audit, and publication. *BMJ* 1996; 312:1094.
- Wright JM, Mattu GS, Perry Jr TL, Gelferc ME, Strange KD, Zorn A, Chen Y. Validation of a new algorithm for the BPM-100 electronic oscillometric office blood pressure monitor. *Blood Press Monit* 2001; 6:161–165.
- Baumgart P, Kamp J. Accuracy of the SpaceLabs Medical 90217 ambulatory blood pressure monitor. *Blood Press Monit* 1998; 3:303–307.
- Lerman CE, Brody DS, Hui T, Lazaro C, Smith DG, Blum MJ. The white-coat hypertension response: prevalence and predictors. *J Gen Intern Med* 1989; 4:226–231.
- Rasmussen SL, Torp-Pedersen C, Borch-Johnsen K, Ibsen H. Normal values for ambulatory blood pressure and differences between casual blood pressure and ambulatory blood pressure: results from a Danish population survey. *J Hypertens* 1998; 16:1415–1424.
- Altman DG. *Practical Statistics for Medical Research*. Chapman & Hall: London, 1991.
- Joshi S, Christopher C, Campbell J. What is the normal inter-arm difference? It depends on left or right handedness: systematic review and meta-analysis. *J Hypertens* 2016; 34(e-Suppl 2):e359.
- NHS England. 2016/17 General Medical Services (GMS) contract Quality and Outcomes Framework (QOF) Guidance for GMS contract 2016/17. London: NHS Employers, 2016.
- Martin U, Holder R, Hodgkinson J, McManus R. Inter-arm blood pressure differences compared with ambulatory monitoring: a manifestation of the 'white-coat' effect? *Br J Gen Pract* 2013; 63:e97–103.

31. van der Hoeven NV, Lodestijn S, Nanninga S, van Montfrans GA, van den Born BJ. Simultaneous compared with sequential blood pressure measurement results in smaller inter-arm blood pressure differences. *J Clin Hypertens (Greenwich)* 2013; 15:839–844.
32. NHS England. Health Survey for England—Health, Social Care and Lifestyles 2011 <<http://digital.nhs.uk/catalogue/PUB09300/HSE2011-Ch3-Hypertension.pdf>> 2016. Access 26 September 2016.
33. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F, Redon J, Dominiczak A, Narkiewicz K, Nilsson PM, Burnier M, Viigimaa M, Ambrosioni E, Caulfield M, Coca A, Olsen MH, Schmieder RE, Tsioufis C, van de Borne P, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Clement DL, Coca A, Gillebert TC, Tendera M, Rosei EA, Ambrosioni E, Anker SD, Bauersachs J, Hitij JB, Caulfield M, De Buyzere M, De Geest S, Derumeaux GA, Erdine S, Farsang C, Funck-Brentano C, Gerc V, Germano G, Gielen S, Haller H, Hoes AW, Jordan J, Kahan T, Komajda M, Lovic D, Mahrholdt H, Olsen MH, Ostergren J, Parati G, Perk J, Polonia J, Popescu BA, Reiner Z, Rydén L, Sirenko Y, Stanton A, Struijker-Boudier H, Tsioufis C, van de Borne P, Vlachopoulos C, Volpe M, Wood DA. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013; 34:2159–2219.
34. English JA, Carell ES, Guidera SA, Tripp HF. Angiographic prevalence and clinical predictors of left subclavian stenosis in patients undergoing diagnostic cardiac catheterization. *Catheter Cardiovasc Interv* 2001; 54:8–11.
35. Sun H, Li P, Su H, Wang J, Hu W, Li J, Liu Y, Cheng X. The detection rates of inter-arm systolic blood pressure difference vary with blood pressure levels in hypertensive patients under antihypertensive therapy. *Int J Cardiol* 2014; 172:e419–e420.
36. Head GA, Mihailidou AS, Duggan KA, Beilin LJ, Berry N, Brown MA, Bune AJ, Cowley D, Chalmers JP, Howe PR, Hodgson J, Ludbrook J, Mangoni AA, McGrath BP, Nelson MR, Sharman JE, Stowasser M; Ambulatory Blood Pressure Working Group of the High Blood Pressure Research Council of Australia. Definition of ambulatory blood pressure targets for diagnosis and treatment of hypertension in relation to clinic blood pressure: prospective cohort study. *BMJ* 2010; 340:c1104.
37. Lohmann FW, Eckert S, Verberk WJ. Interarm differences in blood pressure should be determined by measuring both arms simultaneously with an automatic oscillometric device. *Blood Press Monit* 2011; 16:37–42.
38. Eguchi K, Yacoub M, Jhalani J, Gerin W, Schwartz JE, Pickering TG. Consistency of blood pressure differences between the left and right arms. *Arch Intern Med* 2007; 167:388–393.
39. Staessen JA, O'Brien E, Amery AK, Atkins N, Baumgart P, De Cort P, Degaute JP, Dolenc P, De Gaudemaris R, Enström I. Ambulatory blood pressure in normotensive and hypertensive subjects: results from an international database. *J Hypertens Suppl* 1994;12:S13–S22.
40. Thomas O, Shipman KE, Day K, Thomas M, Martin U, Dasgupta I. Prevalence and determinants of white coat effect in a large UK hypertension clinic population. *J Hum Hypertens* 2016; 30:386–391.