Marked Underestimation of Blood Pressure Control With Conventional vs. Ambulatory Measurements in an Urban, Developing Community of African Ancestry

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BACKGROUND
As groups of African descent may have higher nocturnal blood pressure (BP) for a given day BP than other ethnic groups, we ascertained whether this translates into differences in conventional (CBP) and 24-h ambulatory (ABP) BP control at a community level.

METHODS
Ambulatory 24-h, day and night BP (model 90207; SpaceLabs, Issaquah, WA) and CBP (mean of five values) control rates were determined in 689 randomly selected participants (>16 years) of African ancestry in South Africa. Target organ effects were determined from urinary microalbumin-to-creatinine ratios (ACR) and aortic pulse wave velocity (PWV, applanation tonometry).

RESULTS
Of the participants 45.7% were hypertensive and 22.6% were receiving antihypertensive medication. More participants had uncontrolled BP at night (34.0%) than during the day (22.6%, \( P < 0.0001 \)). Uncontrolled CBP was noted in 37.2% of participants, while a much lower proportion had uncontrolled ABP (24.1%) \( (P < 0.0001) \). Marked differences in the proportion of hypertensive participants with uncontrolled CBP and ABP were noted (treated: CBP = 62.2%, ABP = 33.3%, \( P < 0.0001 \); all: CBP = 81.3%, ABP = 44.4%, \( P < 0.0001 \)). These differences were accounted for by a high prevalence of isolated increases in CBP (white-coat effects) (treated = 35.9%; all = 39.4%). Indeed, after censoring data from participants with white-coat effects, similar CBP and ABP control rates were noted. Participants with white-coat effects had similar ACR and PWV values as participants with normal ABP and CBP.

CONCLUSIONS
In communities of African descent, despite worse BP control at night than during the day, a high prevalence of white-coat effects translates into a striking underestimation of BP control in hypertensives when employing CBP rather than ABP measurements.

Keywords: ambulatory blood pressure; blood pressure; community sample; hypertension; white-coat effects

Although there is a close relationship between conventional blood pressure (CBP) and cardiovascular disease,1,2 surveillance studies3–8 suggest that CBP control rates are far below acceptable standards and that these control rates may be worse in groups of African ancestry.3,4,8 Nevertheless, as outcome-driven thresholds for ambulatory BP (ABP) have only recently been reported on9 no consideration has yet been given to ABP control rates at a population level. In this regard, as compared to CBP measurements, ABP measurements have a number of advantages including the exclusion of measurements obtained during transient rises in BP in the medical environment (white-coat effects).10 Thus, in population-based studies ABP predicts cardiovascular outcomes better than CBP.11–16

Outcome-based studies have derived thresholds for ABP9 that are considerably lower (130/80 mm Hg) than thresholds for CBP (140/90 mm Hg). As thresholds for ABP control account for lower ABP values as compared to CBP values, in surveillance studies one may expect CBP control rates to closely reflect ABP control rates. However, in some populations, particularly groups of African ancestry, ABP values may be higher than other populations for a given level of CBP because of attenuated decreases in BP at night.17,18 Thus, CBP measurements in these populations may not closely reflect the extent of cardiovascular risk attributed to increases in BP. To derive a more accurate assessment of the cardiovascular risk produced by an uncontrolled BP at a community level in groups of African descent, in the present study ABP control rates were assessed and compared with CBP control rates in an urban, developing community in Africa.
**METHODS**

**Study group.** The Committee for Research on Human Subjects of the University of the Witwatersrand approved the protocol (approval number: M02-04-72 and renewed as M07-04-69). Participants gave informed, written consent. The study design has recently been described.\(^{19-23}\) Nuclear families of African descent with siblings older than 16 years of age were randomly recruited from the South West Township of Johannesburg, South Africa. Of the 1,029 participants sampled, 689 (67%) had 24-h ABP values that met with prespecified quality control criteria (longer than 20 h and >10 and 5 readings for the computation of day and night means, respectively). Of these participants 556 had CBP measurements performed at home, urinary microalbumin concentrations were determined in 411 participants with 24-h urine samples that met with prespecified quality control criteria\(^{19}\) and aortic pulse wave velocity (PWV) was determined in 595 participants. Aortic PWV could not be determined in 94 obese participants.

**Clinical, demographic, and anthropometric measurements.** A standardized questionnaire was administered to obtain demographic and clinical data.\(^{19-23}\) From height and weight measurements, body mass index was calculated and participants were identified as being overweight if their body mass index was ≥25 kg/m\(^2\) and obese if their body mass index was ≥30 kg/m\(^2\). Standard laboratory blood tests were performed. Diabetes mellitus or abnormal blood glucose control was defined as the use of insulin or oral hypoglycemic agents or an HbA\(_{1c}\) >6.1%.\(^{24}\) Menopausal status was confirmed with measures of follicle stimulating hormone. Dyslipidemia was defined as a total cholesterol >6.5 mmol/l, low-density lipoprotein cholesterol >4.0 mmol/l, high-density lipoprotein cholesterol <1.2 mmol/l in females and <1.0 mmol/l in males. An elevated serum creatinine concentration was defined as ≥107 μmol/l for females and ≥115 μmol/l for males.

**Conventional BP.** Nurse-derived CBP was measured as previously described\(^{19}\) in the office on the same day as the 24-h ABP measurement in all participants and at home 2 weeks prior to the office visit in 556 participants. Nurse-derived in-office BP measurements were obtained between 0900 and 1200 h and nurse-derived home BP measurements were obtained between 0900 and 2100 h. The same approach was employed to determine BP in-office and at home. The average of the five readings was taken as the office or home CBP. Only 1% of visits had fewer than the planned BP recordings. The frequency of identical consecutive recordings was 0.14% for systolic BP and 1.74% for diastolic BP. The occurrence of BP values recorded as an odd number was 0.01%. Of the systolic and diastolic BP readings, 29% ended on a zero (expected = 20%).

**Ambulatory BP.** 24-h ABP monitoring was performed using SpaceLabs (Issaquah, WA) monitors (model 90207).\(^{19}\) The size of the cuff was the same as that used for CBP measurements. Monitors were programmed to measure ABP at 15-min intervals from 0600 to 2200 h and at 30-min intervals from 2200 to 0600 h. Fixed-clock time periods, identified as previously described,\(^{19}\) rather than actual in bed and out of bed periods were statistically analyzed to ensure that similar day and night time periods were selected for comparisons between individuals. Day and night periods ranged from 0900 to 1900 h and from 2300 to 0500 h, respectively. No participants reported on daytime “naps”. Intraindividual means of the ambulatory measurements were weighted by the time-interval between successive recordings.\(^{19}\) The average (± s.d.) number of BP recordings obtained was 61.2 ± 12.0 (range = 24–81) for the 24-h period, 28.9 ± 7.1 (range = 11–41) for the day and 9.4 ± 1.0 (range = 6–11) for the night.

**Urinary microalbumin excretion.** Urinary microalbumin and creatinine concentrations were determined from 24-h urine samples and expressed as the ratio between urinary microalbumin and creatinine concentrations. Microalbumin concentrations in the urine were determined using an immunoturbidimetric assay (Roche Tina-quant albumin assay; Roche Diagnostics GmbH, Mannheim, Germany) (measurement range of 3–400 mg/l or 0.046–6.08 μmol/l). The quality of urine samples was determined as previously described.\(^{23}\)

**Pulse wave velocity.** Carotid-femoral (aortic) PWV was estimated using techniques previously described.\(^{19-23}\) After participants had rested for 15 min in the supine position, arterial waveforms at the carotid and femoral pulses were recorded by applanation tonometry, each during an 8 s period using a high-fidelity SPC-301 micromanometer (Millar Instrument, Houston, TX) interfaced with a computer employing SphygmoCor, Ver 6.21 software (AtCor Medical, West Ryde, Australia). Distances from the suprasternal notch to the carotid sampling site (distance A) and from the suprasternal notch to the femoral artery (distance B) were measured. Pulse wave velocity distance was calculated as distance B minus distance A. Pulse transit time, calculated as the mean time difference between sites A and B, was determined from the average of 10 consecutive beats. Aortic PWV was calculated as the ratio of the distance in meters to the transit time in seconds.

**Data analysis.** For database management and statistical analysis, SAS software, Ver 9.1 (SAS Institute, Cary, NC) was employed. Data are shown as mean ± s.d. unless otherwise specified. Thresholds for ABP were defined as recently demonstrated from outcomes-based studies\(^9\) as ≥130/80 mm Hg for 24-h BP, ≥140/85 mm Hg for day BP and ≥120/70 mm Hg for night BP. As previous guidelines have advocated day thresholds of ≥135/85 mm Hg\(^{25}\) as opposed to ≥140/85 mm Hg, in secondary analysis day BP control was also assessed using a threshold of ≥135/85 mm Hg. In order to identify isolated increases in CBP (white-coat effects) and isolated increases in ABP (masked effects), ambulatory hypertension was defined as a day BP of ≥135/85 mm Hg.\(^{16}\) Proportions of participants with uncontrolled BP were compared by χ\(^2\) analysis. Multiple logistic regression analysis was used to explore the association between study factors and the presence of white coat hypertension.
Multivariate analysis of variance was used to determine the impact of uncontrolled CBP or ABP on target organ changes.

**RESULTS**

**General characteristics of the participants**

Table 1 gives the general characteristics of normotensive participants, hypertensives receiving therapy, and untreated hypertensives. Of the treated hypertensives \((n = 156)\), 67.9% \((n = 106)\) were receiving monotherapy, 88.5% \((n = 138)\) thiazide diuretic agents, 67.4% \((n = 93)\) thiazide diuretic monotherapy (hydrochlorothiazide), 18.0% \((n = 28)\) angiotensin-converting enzyme inhibitors (enalapril or perindopril), 10.3% \((n = 16)\) long acting calcium channel blockers, and 1.3% \((n = 2)\) selective \(\beta_1\)-adrenergic receptor blockers. All of these agents were taken once daily in the morning.

**Night vs. day BP control**

Irrespective of whether assessed in all participants, treated hypertensives, or all hypertensives, the proportion of participants with uncontrolled night BP was higher than the proportion with an uncontrolled day BP (Figure 1). These differences in control rates were noted in men and women, obese and non-obese, in smokers and in nonsmokers as well as for systole and diastole (data not shown). The prevalence of participants with an uncontrolled night, but normal day BP threshold, a higher prevalence of uncontrolled BP was similarly noted at night as compared to the day (% with uncontrolled BP: all participants; day = 25.4%, night = 34.0%, \(P < 0.001\): treated hypertensives; day = 30.1%, night = 48.7%, \(P < 0.005\): all hypertensives; day = 43.8%, night = 57.1%, \(P < 0.005\)).

**Proportion of participants with white-coat or masked BP effects**

A high proportion of treated hypertensives had white-coat effects and few participants had masked hypertension (Table 2).
The prevalence of white-coat hypertension was similar when evaluating systolic as compared to diastolic BP (Figure 2). As compared to the prevalence of white-coat effects determined from in-office CBP measurements (Table 2), based on home CBP measurements, a similar proportion of participants had white-coat effects (in all: 105/556 = 18.9% and in treated hypertensives: 45/135 = 33.3%). The proportions of participants with white-coat or masked hypertensive effects was similar in men and women, obese or nonobese, and in smokers and in nonsmokers (data not shown).

### Factors associated with white-coat effects

Including age, sex, treatment for hypertension, educational level, and level of employment in a multivariate model, both an older age (odds ratio = 1.03, confidence interval = 1.02–1.05, \(P < 0.0001\)) and treatment for hypertension (odds ratio = 2.11 confidence interval = 1.25–3.55, \(P < 0.005\)) were independently associated with white-coat effects. The majority of participants with white-coat effects had in-office CBP values that were <160/100 mm Hg (grade 1 hypertension). In this regard, in participants with white-coat effects, 75% of all hypertensives (\(n = 93/124\)), 71% of treated hypertensives (\(n = 40/56\)), and 77.9% of untreated hypertensives (\(n = 53/68\)) had grade I hypertension.

### Conventional vs. ambulatory BP control

Irrespective of whether assessed in all participants, treated hypertensives, or all hypertensives, the proportion of participants with an uncontrolled CBP was higher than that of participants with an uncontrolled 24-h BP (Figure 3a). These differences were noted whether or not CBP was determined

#### Table 2 | Proportion of participants who were normotensive (NT), had white-coat effects, masked hypertensive effects or had sustained increases in conventional and day blood pressure

<table>
<thead>
<tr>
<th>Sample number (%)</th>
<th>NT</th>
<th>White Coat</th>
<th>Masked</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants ((n = 689))</td>
<td>390 (56.6)</td>
<td>124 (18.0)</td>
<td>43 (6.2)</td>
<td>132 (19.2)</td>
</tr>
<tr>
<td>All hypertensives ((n = 315))</td>
<td>53 (16.8)</td>
<td>124 (39.4)</td>
<td>6 (1.9)</td>
<td>132 (41.9)</td>
</tr>
<tr>
<td>Treated hypertensives ((n = 156))</td>
<td>53 (34.0)</td>
<td>56 (35.9)</td>
<td>6 (3.8)</td>
<td>41 (26.3)</td>
</tr>
<tr>
<td>HT, hypertensives.</td>
<td></td>
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</tbody>
</table>

#### Figure 2 | Relationship between conventional (conv.) and day ambulatory blood pressures (BP) for either systolic BP (SBP conv. or day SBP) or diastolic BP (DBP conv. or day DBP) showing the proportion of participants with abnormal conventional and day BP thresholds. The day BP thresholds are derived from recently defined outcome-driven thresholds.\(^2\) NT, normotensive; HT, hypertensive; Mask, masked hypertensives; White Coat, white coat hypertensives.

#### Figure 3 | Comparison of the proportion of participants with an uncontrolled conventional (CBP) and uncontrolled 24-h ambulatory (24-h ABP) blood pressure (BP) in a community sample of African ancestry. (a) Data in all participants and (b) data after censoring participants with white-coat effects. Uncontrolled CBP is considered to be ≥140/90 mm Hg and uncontrolled 24-h ABP ≥130/80 mm Hg as recently defined from outcome-driven thresholds.\(^5\) *\(P < 0.0001\) compared to CBP control. HT, hypertensive.
using in-office or home (data not shown) BP measurements. Differences in CBP and 24-h BP control rates were noted in men and women, obese or nonobese, and in nonsmokers (Table 3). Similar differences in CBP and ABP control rates were noted for both systolic and diastolic BP (uncontrolled systolic CBP = 25.5%, ABP = 17.9%, \( P < 0.005 \); uncontrolled diastolic CBP = 30.3%, ABP = 19.2%, \( P < 0.0001 \)). Differences in uncontrolled CBP and ABP were abolished when data from participants with white-coat effects were censored (Figure 3b).

**Target organ changes**

Multivariate adjusted urinary microalbumin-to-creatinine ratios (ACR) and aortic PWV were increased in participants with uncontrolled 24-h and CBP values as compared to participants with controlled 24-h and CBP values (Figure 4). In contrast, participants with white-coat effects had values for indexes of target organ changes that were similar to participants with controlled 24-h and CBP values (Figure 4).

**DISCUSSION**

The main findings of the present study are that in a randomly selected community sample of African ancestry, although night was worse than day BP control, the high proportion of participants with white-coat effects translated into a marked underestimation of BP control at a community level, when CBP was employed to define BP control. In hypertensives the prevalence of an uncontrolled CBP,11–16 the extent of ABP control in the present study sample reflects cardiovascular damage more closely than does the extent of CBP control.

Table 3 | Proportion of participants with uncontrolled conventional (CBP) as compared to uncontrolled 24-h ambulatory (24-h ABP) blood pressure (BP) in important subgroups of the study sample

| Number (%) with uncontrolled | CBP (in-office) | 24-h ABP | P value*
|-----------------------------|----------------|----------|---------
| Women (n = 444)             | 156 (35.1)     | 99 (22.3) | <0.0001
| Men (n = 245)               | 100 (40.8)     | 67 (27.4) | <0.005
| Obese (n = 275)             | 133 (48.4)     | 82 (29.8) | <0.0001
| Nonobese (n = 414)          | 123 (29.7)     | 84 (20.3) | <0.005
| Smokers (n = 99)            | 40 (40.4)      | 31 (31.3) | = 0.24
| Nonsmokers (n = 590)        | 216 (36.6)     | 135 (22.9) | <0.0001

*For comparison of proportion of participants with uncontrolled CBP vs. uncontrolled 24-h ABP.

![Figure 4](https://example.com/figure4.png)
An overestimation of the prevalence of uncontrolled ABP when employing CBP measurements was particularly striking in hypertensives in whom 81.3% had an uncontrolled CBP, while 44.4% had an uncontrolled 24-h ABP. Extrapolating these figures to previous estimates of uncontrolled BP in groups of black African descent in South Africa, the previously reported age-adjusted figure of 85–93% of uncontrolled BP in all hypertensives in this group may require downward adjustments to 46–51%. This value is better than the age-adjusted prevalence of uncontrolled BP of 67% in all hypertensives of this ethnic group and in other ethnic groups in the United States and the prevalence rates of uncontrolled BP in all hypertensives in England (62%) and Italy (67%) in 1998. Therefore, the present study highlights the need for surveillance studies to adjust for estimated prevalence rates of white-coat effects.

In contrast to the 10.5% of Caucasian and Japanese participants from four population samples reported to have white-coat hypertension, in the present study using the same thresholds as this previous study, 18.0–18.5% of participants had white-coat effects. Neither education level, nor current level of occupation could account for excessive white-coat effects. The majority (71%) of participants with white-coat effects had grade I hypertension, and an older age and anti-hypertensive treatment were independently associated with white-coat effects. An equivalent proportion of participants with treated (35.9%) (who were also aware of their condition) and untreated (42.8%) (not previously diagnosed) hypertension had white-coat effects, suggesting that this effect is an alerting response either to the presence of the nurse or to the BP measurement per se and not to an awareness of the condition. We cannot attribute the white-coat response to the in-office environment as similar results were obtained with home as compared to in-office BP values.

The higher prevalence of uncontrolled night as compared to day BP in the present study is consistent with an attenuated decline in BP at night and the higher night for a given day BP value noted in groups of African as compared to European ancestry. However, alternative explanations include an inability of thiazide diuretic monotherapy, which the majority of treated hypertensives (60.0%) were receiving, to provide appropriate nocturnal BP control and that all anti-hypertensives were taken in the morning, thus providing better day as compared to night BP cover. Nevertheless, a similar proportion of treated (26.9%) and untreated (20.8%) hypertensives had an uncontrolled night and controlled day BP. Given the high prevalence of obesity in the community studied, one potential mechanism responsible for a predisposition to higher night BP values is sleep apnea. However, differences in day and night control rates were noted in both obese and nonobese participants and hence the role of obesity, and by inference sleep apnea, may not be that important. Irrespective of the mechanisms responsible for the higher prevalence of uncontrolled night as compared to day BP in the present study, current evidence suggests that 24-h ABP is more important than either day or night BP considered separately.

At a population level white-coat hypertension has been demonstrated to carry a risk for cardiovascular events that is similar to normotensives. In-keeping with a number of prior studies, in the present study white-coat effects were not associated with target organ changes. It is possible therefore that in urban, developing communities of African descent, CBP measurements may result in the treatment of, uptitration of the dose of therapy in, or the addition of further therapy in a significant number of people who are not at risk for the adverse effects of BP because they have white-coat effects. It is possible that these potentially inappropriate actions may occur in 16.9% of the community, with obvious major cost implications to the health care system. Nevertheless, of the participants who we have identified as being at risk of receiving inappropriate therapy, a significant portion of these may require additional therapy to achieve lower BP targets because of their global risk profiles (the community has a high prevalence of diabetes mellitus or an HbA1c >6.1%). However, in these cases we also assume that ABP targets should be proportionately lower. Furthermore, as white-coat hypertension is associated with a lack of nocturnal BP dipping, a recognized risk factor for cardiovascular damage, it is possible that a proportion of participants with white-coat effects in the present study may ultimately develop cardiovascular damage and hence may benefit from antihypertensive therapy. Further prospective studies are required to answer this question.

The limitations of the present study are as follows: Although we could show similar results in a number of relevant subgroups, we compared CBP and ABP control rates in one community of African ancestry. As this was a typically urban, previously disadvantaged, economically developing community, further studies are required to evaluate whether a similar high prevalence of white-coat effects characterize rural communities or economically developed communities of African ancestry. Second, although ABP has been demonstrated to be a stronger predictor of cardiovascular outcomes than CBP in a number of populations, it is possible that this may not be the case in the present study sample. However, as target organ changes were not evident in participants with white-coat effects, this possibility is unlikely.

In conclusion, the present study indicates that in a community sample with a high prevalence of white-coat effects, CBP measurement may considerably overestimate the risk related to uncontrolled ABP. Therefore, to provide a more accurate assessment of the cardiovascular risk associated with BP in surveillance studies, it may be necessary to adjust CBP control rates for the presence of white-coat effects. Further, to avoid a considerable proportion of people of African ancestry receiving unnecessary antihypertensive medication, cost-effective strategies for the identification of white-coat effects may be necessary.

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