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Can blood pressure measurements taken in the physician's office avoid the 'white coat' bias?

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Objective **Obtaining an accurate blood pressure (BP) reading is vital for diagnosing hypertension. However, BP measures taken in the physician's clinic (CBP) are subject to the 'white coat' bias. Measurements taken outside the office using ambulatory (ABP) and home (HBP) monitoring are superior predictors of cardiovascular diseases compared with CBP, but ABP remains underutilized because of the effort and expense involved. Unfortunately, HBP has limitations, including questionable device validity and patient compliance. Thus, it is important to identify feasible alternative techniques to measure BP in the office that will increase the accuracy of the diagnosis.**

Methods **Auscultatory BP was measured in 249 patients in a nonclinical setting by trained technicians (NCBP); on the following day, patients were taken to their physician (CBP). They were also given an HBP monitor, and a 36 h ABP monitoring. Because ABP is considered the gold standard for prediction of cardiovascular disease, these readings were used as the criterion in a statistical model in which CBP, HBP, and NCBP were entered as predictors. The level of agreement between measurements was estimated.**

Results **Multiple regression analysis showed that HBP and NCBP ($P<0.001$) explained 94 and 87% of the variance in systolic and diastolic ABP, respectively. The agreement between NCBP and ABP was greater than that between CBP and ABP or between HBP.**

Conclusion **When ABP monitoring and HBP monitoring are not options, the NCBP at the clinic can avoid the white coat bias and therefore improve diagnosis. *Blood Press Monit* 16:231–237 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Auscultatory blood pressure (BP) taken by a physician or nurse in the clinic or office setting is the traditional basis for diagnosis of hypertension (HTN). The accuracy of the measurements is crucial because these readings will determine the treatment plan. However, BP taken in the physician's office or clinic [we will call both 'clinic blood pressure' (CBP)] may lead to a misdiagnosis: The 'white coat' bias is observed in 15–20% of diagnosed Stage I HTN patients [1–3], in which the clinic measurements are in the HTN range, but measurements taken outside the office using ambulatory blood pressure (ABP) monitoring are normal. Individuals with white coat HTN (WCHTN) are at similar risk for cardiovascular events as normotensives, and therefore many researchers and practitioners question the wisdom of drug therapy with these patients [4].

This has called the utility of office BP measurements into question. ABP is considered the 'gold standard' measure because it has been demonstrated to be a superior predictor of target organ damage and morbid events compared with CBP [5–7]. Also, ambulatory measurements minimize the white coat effect and allow a more comprehensive assessment of antihypertensive therapy, of nocturnal BP dipping status, and therefore this measure is less subject to misdiagnosis [8]. Thus, it would be desirable to use ABP rather than office measurements for diagnosis. However, ABP is not feasible for use in most practices because it is cumbersome, delays a diagnosis, is expensive, and requires repeated patient visits [9].

Some studies have found that, similar to ABP, home measurements are better predictors of target organ damage and cardiovascular mortality than clinic measurements [10]. However, as with ABP, there are limitations to the physicians' use of home blood pressure (HBP) measurements as a basis for diagnosis, including questionable device validity [11] and a low probability that the typical patient will follow a standardized protocol.

We have found that some office methods of BP measurement tend to minimize the white coat effect. For example, we found that measuring BP using an automated device in the clinic yielded values that were more

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comparable to ABP measurements than nurse-taken or physician-taken measurements [12]. Other studies have shown similar results using an automated device with the patient left alone in a quiet room [13].

In this study, we examined the effect of the setting in which BP is measured. Specifically, we tested the hypothesis that measurements taken in a plain, nonclinical room will yield BP measurements that are more similar to ABP measurements than those taken in the same clinic, but in a more typical 'medical office' patient room.

Methods

Participants

The sample was drawn from physician referrals to an outpatient HTN clinic and through advertisements. Eligible patients were referred by participating physicians at the Weill Cornell Hypertension Center of New York Presbyterian Hospital in New York City. The eligibility criteria were:

(1) age 18–80 years;
(2) patients willing, with physician's permission, to stop antihypertensive medication for the 8-week study duration;
(3) no previous cardiovascular morbid event; no major medical problem other than HTN;
(4) BMI below 32.5 kg/m^2.

A total of 249 participants completed the study. The mean age was 52.1 (SD = 14.9); 50.6% were women. None of the patients had received BP medication for at least 2 weeks before the study period.

Blood pressure measurement

CBP was assessed by a highly experienced clinician using the mean of three BP readings taken using a mercury column sphygmomanometer.

'Nonclinical' blood pressure (NCBP) was measured by a well trained research assistant, who used the same method and device as the physician, on the day before the clinic visit.

HBP was taken every week during the 8-week study. Patients were instructed to take their BP three times in succession using an OMRON 705IT (Omron Corporation, Kyoto, Japan) [14] digital monitor, twice a day, 3 days a week. A minimum of 40 readings was required to be included in the analysis.

ABP was measured as the 36 h mean level using a Spacelabs model 90207 ABP monitor (SpaceLabs Medical, Redmond, Washington, USA) [15]. The ABP data were edited for outliers (values greater than 220/180 and less than 70/50 were eliminated). Participants wore the monitors for a total of 36 h, including one night's sleep.

Procedure

Day 1

The BP measurements were taken in a room separate from the clinic (in a separate building from the Hypertension Center), which looked nothing like a medical office. These measurements were taken by a research assistant, a nonthreatening figure who was dressed casually compared with the physician (in his white coat), in the stereotypical medical setting. Following usual clinical practices, the research assistant took three BP readings using a mercury sphygmomanometer after the participant had rested in the seated position for 5 min, with phase 5 Korotkoff sounds used to express diastolic pressure. The average of these measurements constituted the NCBP. Patients then underwent ABP monitoring for the remainder of that day, during sleep, and during the following day until bedtime. The BP sampling interval was 15 min during the day, until 10 : 00 p.m., and 1 h between 10 : 00 p.m. and 6 :00 a.m. the next morning. After 6 : 00 a.m., the sampling interval reverted to 15 min.

Day 2

The participant, still wearing the ABP monitor, returned to the HTN Clinic and was met by a different research assistant in the waiting area, where he or she was asked to sit and relax while waiting to see the physician. Participants were then taken to the examination room where the physician took three BP measurements (using a mercury column sphygmomanometer and stethoscope, after the participant had rested in the seated position for 5 min). The average of these measurements constituted the CBP measure.

Subsequently, the patients were instructed to measure their BP three times in succession using a digital monitor, twice a day, 3 days a week. The average of these measurements constituted the HBP measure.

Statistical analysis

We used paired-sample *t*-tests to compare CBP, NCBP, and HBP against ABPs. Hierarchical multiple regression analyses were carried out to explore the relative contribution of the setting (CBP, NCBP, or HBP measurement) to predict systolic and diastolic ABP. Data are presented as standardized coefficients (β). Durbin–Watson (D–W), variance inflation factor (VIF), and tolerance (*T*) collinearity tests were performed to investigate multicollinearity among the variables entered in the regression models. Finally, to determine the level of agreement between CBP (or NCBP or HBP) and ABP, individual BP data were displayed using Bland–Altman's graphical method [16]. Following this method, the mean differences between the CBP (or NCBP or HBP) and the ABP were plotted against the average for both CBP (or NCBP or HBP) and ABP. In addition, the plots included the line for the mean difference (a statistic useful for detecting a systematic difference or bias), the 95%

confidence interval of the mean difference (or 95% CI bias, which illustrates the magnitude of the systematic difference), and the limits of agreement, which are defined as the mean difference ± 1.96 SD of the differences.

Results

Clinical and demographic characteristics

The study population consisted of 249 participants, 123 men and 126 women, mean age 52.1 ± 14.9 years. Mean BP readings taken using CBP, NCBP, HBP, and ABP are shown in Table 1. As shown in Table 1, the BP measurements taken in the clinical examination room (CBP) are higher than those taken at home, in the nonclinical room (NCBP), and also higher than the ABP means. The difference was a substantial one for diastolic BP (4.2 mmHg between CBP and ABP), but was relatively small for systolic BP (1.1 mmHg difference). The small mean differences are misleading; Fig. 1 shows the dispersion of the differences between BP measurements taken in the clinic room compared with those taken in the nonclinic room and during ambulatory monitoring. It is worth noting that, even for systolic pressure, approximately 21% of the patients exhibited elevations greater than 10 mmHg in the clinic room compared with ABP, thus placing these patients at substantial risk for being misdiagnosed as hypertensive. Approximately 25% had diastolic pressures of 10 mmHg or higher compared with ambulatory pressure when taken in the clinic room. In fact, the results showed that an equal percentage of patients exhibited systolic and diastolic elevations greater than 10 mmHg in the clinic room compared with the NCBP (approximately 21% for systolic and 25% for diastolic; see Fig. 1).

Finally, our results showed that 17.7% of the 249 participants had WCHTN when we used CBP to make the WCHTN diagnosis (systolic CBP ≥ 140 mmHg or diastolic CBP ≥ 90 mmHg, and systolic ABP ≤ 140 mmHg and diastolic ABP ≤ 90 mmHg). However, when we used the nonclinical measurement to make the WCHTN diagnosis (NCBP ≥ 140 mmHg or diastolic NCBP ≥ 90 mmHg, and systolic ABP ≤ 140 mmHg and diastolic ABP ≤ 90 mmHg), only 6% of the patients had WCHTN.

Table 1 Mean (± SD) ambulatory blood pressure (mmHg) values compared with 'nonclinical' blood pressure and home blood pressure (*P* values related to the ambulatory blood pressure)

	Mean blood pressure (SD)			
Blood pressure measurement	Systolic blood pressure	*P*	Diastolic blood pressure	*P*
NCBP	133.7 (20.32)	NS	79.7 (11.76)	NS
HBP	132.3 (16.07)	0.04*	81.4 (10.10)	0.001**
CBP	135.0 (21.11)	0.07	83.8 (11.69)	0.0001***
ABP (reference)	133.9 (18.05)	–	79.6 (11.87)	–

ABP, ambulatory blood pressure; CBP, clinical blood pressure; HBP, home blood pressure; NCBP, 'nonclinical' blood pressure.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.

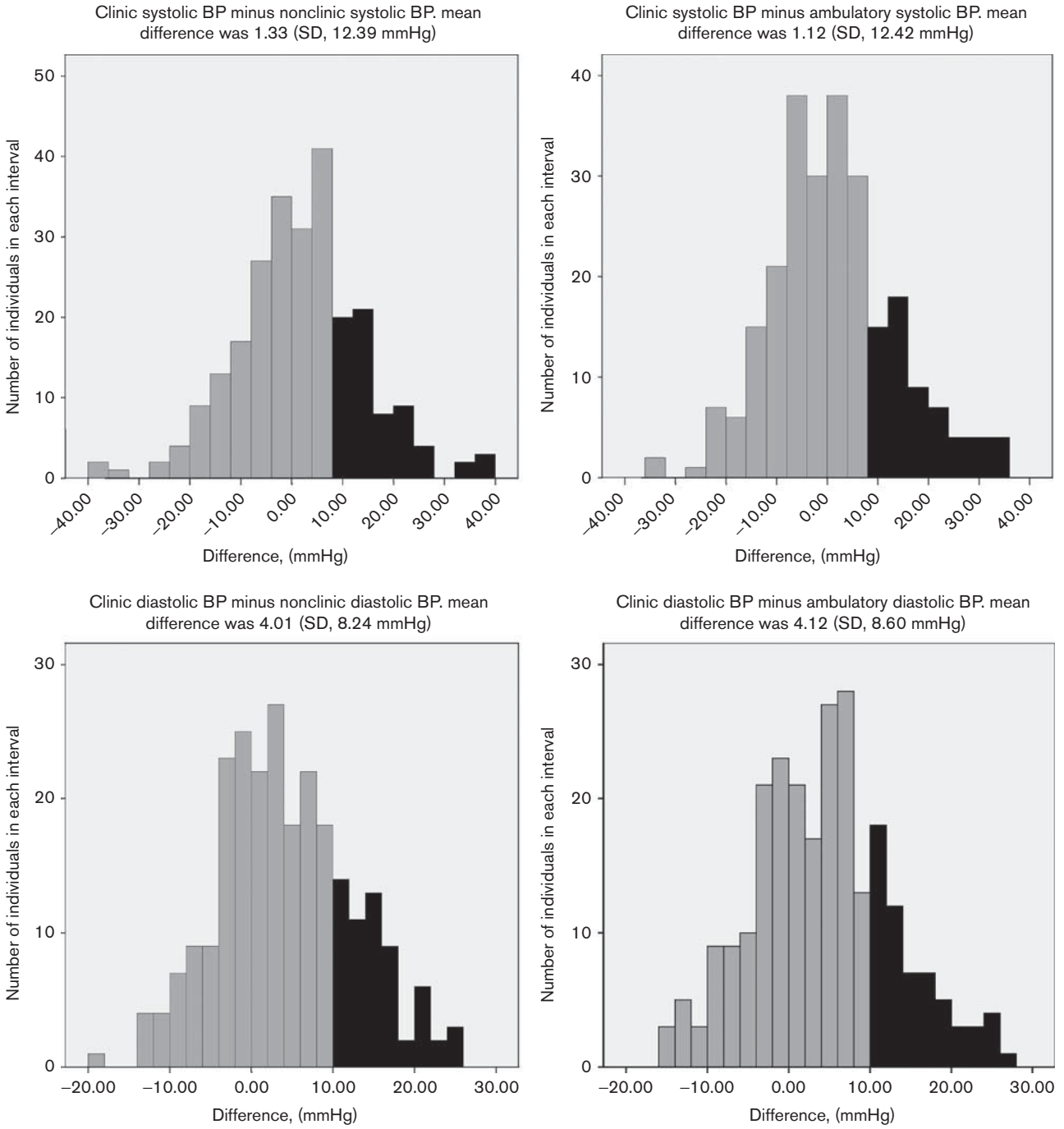
'Nonclinical' room blood pressure as a predictor of ambulatory blood pressure

A multiple regression analysis showed that both systolic and diastolic HBP and NCBP were significantly associated with ABP ($r > 0.70$); together, they explained 94 and 87% of the variance in systolic and diastolic BP, respectively (see Table 2). Importantly, neither systolic nor diastolic BPs taken in the clinical room remained in the model as a significant predictor of ABP. It is noteworthy that, with regard to the relations between BP measures and systolic ABP, systolic CBP was entered at Step 1, explaining 65.6% of the variance of systolic ABP. After entering systolic HBP at Step 2, the total variance explained increased significantly [$\Delta R^2 = 0.05$, $\Delta F_{(1,246)} = 43.02$, $P < 0.001$]; furthermore, after entering systolic NCBP at Step 3 also the total variance explained increased significantly [$\Delta R^2 = 0.23$, $\Delta F_{(1,245)} = 1020{,}02$, $P < 0.001$]. Hence, the final model was considered significant [$F_{(3,248)} = 1358.04$, $P < 0.001$]. Related to diastolic ABP models, diastolic CBP was entered at Step 1, explaining 54.4% of the variance of diastolic ABP. After entering diastolic HBP at Step 2, the total variance explained increased significantly [$\Delta R^2 = 0.09$, $\Delta F_{(1,246)} = 61.50$, $P < 0.001$], and finally after entering diastolic NCBP at Step 3 also the total variance explained increased significantly [$\Delta R^2 = 0.24$, $\Delta F_{(1,245)} = 481.29$, $P < 0.001$]. Thus, the model reached significance [$F_{(3,248)} = 582.48$, $P < 0.001$; see Table 2].

Agreement between 'nonclinical' room blood pressure and ambulatory blood pressure

Figures 2–4 show the Bland–Altman plots of BP differences (CBP vs. ABP, NCBP vs. ABP, and HBP vs. ABP, respectively) against the mean averages for both measurement methods for systolic and diastolic readings. Also included in the graphs are bias (the mean difference), 95% CI bias, and the limits of agreement (1.96 SD bias). For systolic pressure, the Bland–Altman plots were similar for the agreement between CBP and ABP and the agreement between HBP and ABP. Thus, the mean difference between systolic CBP and ABP was 1.14 mmHg (bias), the SD of the difference was 12.4 mmHg (precision or random scatter), and the limits of agreement (± 2 SD) were −23.2 and 25.5 mmHg, whereas the mean difference between systolic HBP and ABP was −1.57 mmHg (bias), the SD of the difference was 12.9 mmHg, and the limits of agreement were −26.8 and 23.7 mmHg. All these limits of agreements were wider than those between NCBP and ABP. Thus, the mean difference between systolic NCBP and ABP was −0.18 mmHg (bias), the SD of the difference was 5.2 mmHg, and the limits of agreement were −10.5 and 10.1 mmHg. That is, 95% of the systolic CBP or HBP were not more than approximately 23–27 mmHg lower or

Fig. 1



Histogram showing the differences between blood pressure (BP) measurements taken in the clinic room compared with those taken in the nonclinic room, as well as those taken during ambulatory monitoring.

24–25 mmHg higher than systolic ABP, whereas 95% of systolic NCBP were not more than approximately 10 mmHg lower or 10 mmHg higher than systolic ABP.

Similarly, for diastolic pressure, the Bland–Altman plots were similar for the agreement between CBP and ABP and the agreement between HBP and ABP. The mean difference between diastolic CBP and ABP was 4.13 mmHg, the SD of the difference was 8.6 mmHg, and the limits of agreement were −12.7 and 21 mmHg, whereas the mean difference between HBP and ABP was 1.79 mmHg, the SD of the difference was 8.5 mmHg, and

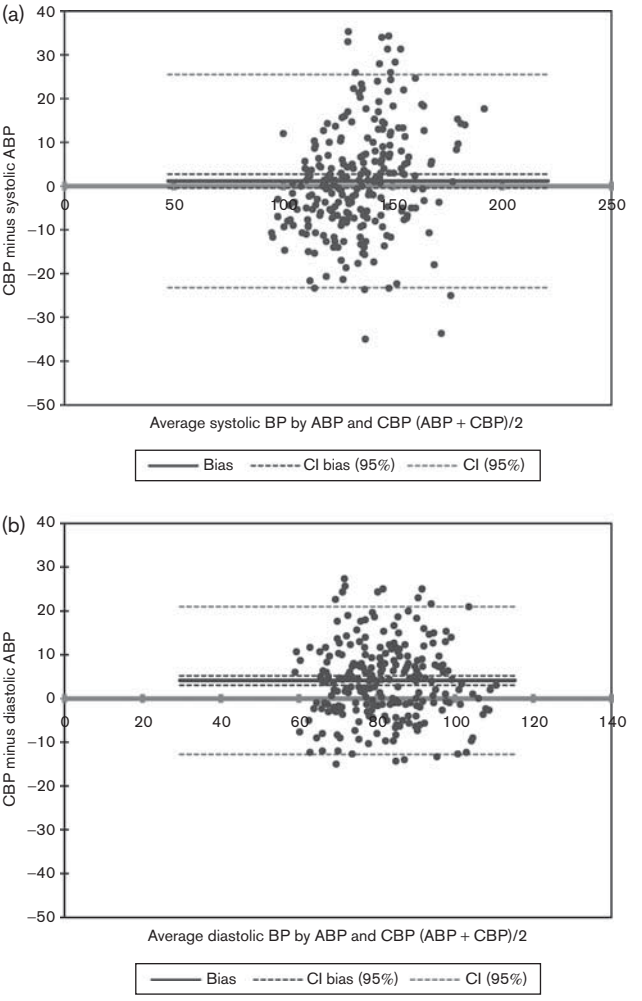
Table 2 Prediction of systolic and diastolic ambulatory blood pressure by clinical, 'nonclinical' and home blood pressure measurements

	R^2	ΔR^2	t	β	P
Dependent variable: systolic ABP					
Step 1	0.65***	0.65***			
Systolic CBP			21.69	0.81	0.0001***
Step 2	0.70***	0.05***			
Systolic CBP			12.53	0.59	0.0001***
Systolic HBP			6.55	0.31	0.0001***
Step 3	0.94***	0.23***			
Systolic CBP			0.44	0.01	0.65
Systolic HBP			3.73	0.08	0.0001***
Systolic NCBP			31.93	0.90	0.0001***
Dependent variable: diastolic ABP					
Step 1	0.54***	0.54***			
Diastolic CBP			17.17	0.73	0.0001***
Step 2	0.63***	0.09***			
Diastolic CBP			9.33	0.47	0.0001***
Diastolic HBP			7.84	0.40	0.0001***
Step 3	0.87***	0.24***			
Diastolic CBP			1.25	0.04	0.21
Diastolic HBP			3.15	0.10	0.002**
Diastolic NCBP			21.93	0.82	0.0001***

ABP, ambulatory blood pressure; CBP, clinic blood pressure; HBP, home blood pressure; NCBP, nonclinical blood pressure.
**$P<0.01$.
***$P<0.001$.

the limits of agreement were −14.9 and 18.5 mmHg. Again, these limits of agreements were wider than those between diastolic NCBP and ABP. Thus, the mean difference between diastolic NCBP and ABP was 0.12 mmHg, the SD of the difference was 4.3 mmHg, and the limits of agreement were −8.4 and 8.7 mmHg. That is, 95% of diastolic CBP or HBP were not more than approximately 13–15 mmHg lower or 18–21 mmHg higher than diastolic ABP, whereas 95% of the diastolic NCBP were not more than approximately 8 mmHg lower or 9 mmHg higher than the diastolic ABP.

Fig. 2



For systolic (a) and diastolic (b) blood pressure, the averages of ambulatory blood pressure (ABP) and clinic blood pressure (CBP) are plotted against the differences between CBP and ABP. CI, confidence interval.

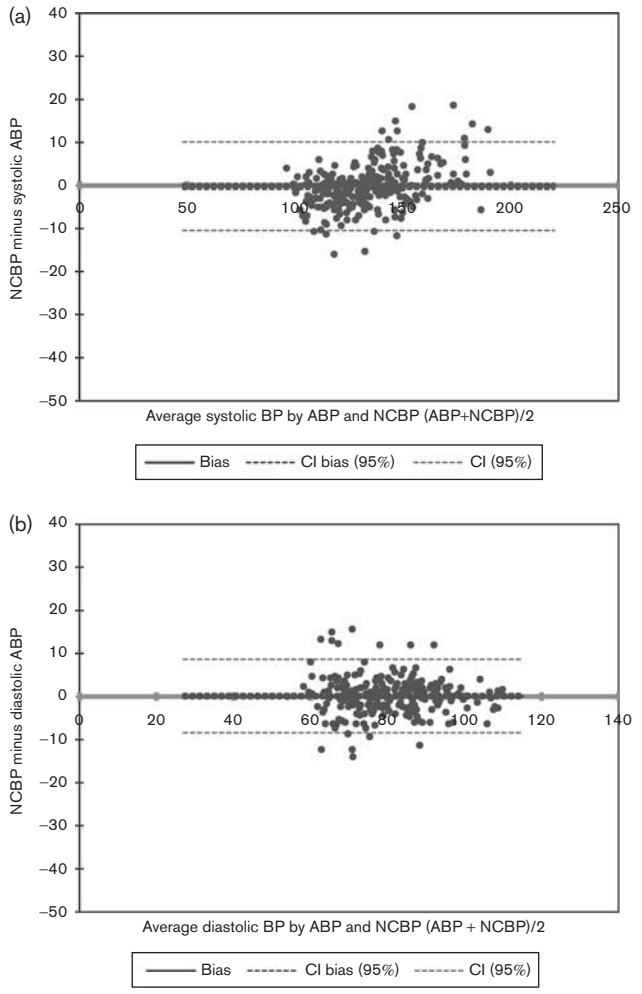
Discussion

As predicted, the BP measurements taken in the clinical examination room were higher than those taken in the nonclinical room (systolic, $P = 0.09$; diastolic, $P = 0.001$). The CBP measurements were also significantly higher than the ABP measures, systolic HBP was significantly lower than ABP, and was (along with NCBP) a significant predictor of ABP. Thus, the measurements taken in a nonclinical room at the doctor's office were a stronger predictor of ABP than of BP measured in a clinic examination room. Indeed, CBP failed to emerge as a significant predictor of ABP after accounting for HBP and NCBP measurements. Moreover, the limits of agreement between the NCBP and ABP were narrower than the limits of agreement between the CBP and ABP or between HBP and ABP, indicating that the agreement between the NCBP and ABP was greater than those between the CBP and ABP or between the HBP, and, therefore, ABP can be better estimated from the NCBP than from CBP or HBP. Similar findings have been observed in several previous studies where CBP measurements were higher than ABP measurements [13,17], and were higher than BP measurements taken by a trained nurse [12,18].

Both NCBP and HBP were better predictors of ABP than CBP. However, we still recommend NCBP over HBP, because although HBP is less expensive than ABP, it is also complicated for the patient and compliance may be poor [11]. Thus, when ABP is not possible, NCBP levels taken by a research assistant under unusual clinic room conditions can be representative of ABP levels.

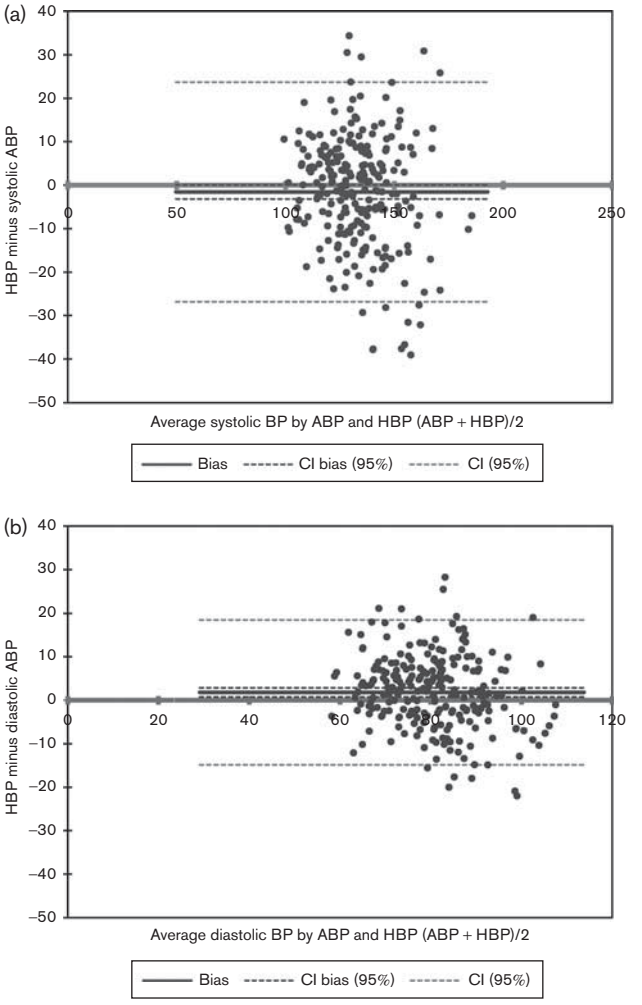
This study has important implications for the question of accurate HTN diagnosis and for avoiding unnecessary drug therapy in patients who do not have persistent HTN. In fact, a variety of factors are likely to contribute to the white coat response when BP is recorded in the office of a physician using a mercury or aneroid

Fig. 3



For systolic (a) and diastolic (b) blood pressure, the averages of ambulatory blood pressure (ABP) and nonclinical blood pressure (NCBP) are plotted against the differences between NCBP and ABP. CI, confidence interval.

Fig. 4



For systolic (a) and diastolic (b) blood pressure, the averages of ambulatory blood pressure (ABP) and home blood pressure (HBP) are plotted against the differences between HBP and ABP. CI, confidence interval.

sphygmomanometer. Data from several studies show that the individual who takes the BP measurement and the manner in which it is taken have a substantial effect on the measurement [19]. Ogedegbe *et al.* [20] have reported that both anxiety and the BP response may be a conditioned response to a specific set of stimuli, notably, those that tend to appear in the milieu of the examination room and the presence of the physician. Our data suggest that much of the white coat effect can be eliminated when a nonclinical room is used to take readings (approximately there are 11% minus the number of patients with WCHTN when we used NCBP vs. CBP measurements to make the diagnosis). This result has important implication for the drug therapy of these patients.

Recommendation

The sum of our studies, including these results, suggests that BP readings should be taken in a nonclinical room, by a technician or nurse rather than the physician, using a validated automated device, with the patient alone in the room while the measurements are taken.

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Conflicts of interest

There are no conflicts of interest.

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