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Clinical Predictors and Impact of Ambulatory Blood Pressure Monitoring in Pediatric Hypertension Referrals

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Abstract

Background—Elevated blood pressure (BP) is rising in children. Significant proportions of children have reactive hypertension or masked hypertension, making ambulatory blood pressure monitoring (ABPM) a valuable tool, although with potential economic implications. In youth referred for elevated BP, we sought clinic BP combinations that obviated the need for ABPM and to specify the economic role of ABPM.

Methods—In a retrospective pediatric referral cohort (n=170), we examine clinic systolic BP (SBP) predictors of components of ABPM hypertension and their combination. In economic analyses, we compared effectiveness and charges of three diagnostic pathways: 1. Clinic BP alone; 2. Abnormal Clinic BP prompting ABPM; or 3. Universal ABPM.

Results—ABPM hypertension occurred in 55 (32.4%) and reactive hypertension in 37 (21.8%), Average automated ($\beta=0.208$ [95%CI 0.027, 0.389], $P=0.03$) and maximum auscultatory clinic SBP ($\beta=0.160$ [95%CI 0.022, 0.299], $P=0.02$) were associated with ABPM SBP mean, but none predicted SBP load. No clinic SBP combination was associated with ABPM hypertension. Universal ABPM accrued the lowest average charge per hypertensive youth identified (\$10,948).

Conclusions—We did not identify a clinic SBP combination that predicted ABPM hypertension in youth referred for elevated BP. Universal ABPM in this context may be the most economically and clinically efficient diagnostic strategy.

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Keywords

Office blood pressure; clinic blood pressure; cost-effectiveness; cost analysis

Introduction

High blood pressure (BP) within the pediatric population appears to be on the rise, with this trend certainly influenced by the rising prevalence of obesity in US children.¹⁻³ Given the evolving influence of obesity on pediatric health and the known adverse long-term effects of hypertension, accurate and early identification of pediatric hypertension is vital. In this setting, ambulatory blood pressure monitoring (ABPM) now plays an increasingly important role as a diagnostic tool. Additionally, the Affordable Care Act of 2010 now mandates identification of elevated BP in children, possibly inciting new emphasis on universal BP screening.⁴ While this mandate contradicts the recent US Preventive Services Task Force Report questioning the utility of universal BP screening in children, the Task Force's literature review neglected at least 3 key reports detailing the longitudinal relation between BP in youth and adult cardiovascular events and early mortality.⁵⁻⁸ A more recent report detailed improvement in subclinical atherosclerosis with improving BP from a population-based metacohort of children followed into adulthood.⁹ Therefore, it is likely that BP screening in children will remain a standard practice. Rising obesity with rising BP screening may indeed add to hypertension specialist referrals, where ABPM is seeing increasing use.

True hypertension in children is uncommon while reactive (white coat) hypertension is prevalent, occurring in at least 30% of referred children.^{10, 11} Masked hypertension, where in-clinic BP is in the normal range but ABPM is elevated, is similar to sustained hypertension in its association with cardiovascular risk in adults and occurs in roughly 8% of referred children.¹¹⁻¹³ Although current pediatric guidelines still rely on height of clinic BP for diagnosis, ABPM has started to emerge as a gold standard of hypertension diagnosis for many pediatric hypertension specialists.^{14, 15} ABPM can identify reactive hypertension and masked hypertension, as well as provide added information on nocturnal BP.¹⁶ Given the pitfalls of diagnosing true hypertension from in-clinic BP alone, inadequate or inappropriate testing and therapy may be avoidable with use of ABPM. In light of the tension between the utility and high upfront costs of ABPM in the setting of rising ABPM use, this study was designed to identify combinations of in-clinic BP or other simple clinical variables associated with ABPM defined hypertension which could then be used to target ABPM use. In addition, we used the NHLBI 2011 integrated pediatric cardiovascular risk reduction guidelines in combination with actual work-up patterns and charges from our institution to model the relative outlays of using clinic BP alone, clinic BP with ABPM, and ABPM alone as referral clinic hypertension diagnostic strategies.

Methods

Records from consecutive patients up to 25 years old referred to nephrology or cardiology clinics for confirmation of hypertension were examined for adequate ABPM studies

completed between October 2010 and October 2012. ABPM was performed for a 24 hour period with an oscillometric device (Spacelabs 90207 or 90217-Ultralite; Snoqualmie, WA), with readings every 20 minutes from 6am to 10pm, and readings every 60 minutes from 10pm to 6am. Patient diary was used to define sleep/wake periods when available. An adequate study was defined by the interpreting physician if all daytime hours were captured and no more than 2 hours of nighttime readings were missed. Patients on antihypertensive therapy at the time of ABPM or repeat ABPM studies were excluded. Chart review was used to collect demographic characteristics; anthropometric data; clinical BP data; medications including antihypertensive, attention deficit-hyperactivity, antipsychotic, and oral contraceptive agents; and key medical history including prematurity, cardiac, renal, or other diagnoses. Clinic BP data was collected from the single referral clinic visit immediately preceding ABPM. Clinic BP measurements were performed in seated patients on the right arm with cuff length sizes selected to cover 40% of the midarm circumference as per standard methodology.¹⁵ The bulk of patients were seen in specific Preventive Cardiology or Renal Hypertension clinics where multiple oscillometric and auscultatory BPs were performed. Some were seen by other cardiologists or nephrologists outside of these clinics and had variable numbers of BPs measured. All available auscultatory and oscillometric clinic BP data were obtained for each patient at the index visit. Departmental and institutional review boards approved this retrospective study and waived patient consent.

Clinic systolic BP (SBP) was converted to age-sex-height referenced z-score using the normative data equations from the 4th Task Force Report.¹⁵ For adults 18 years old or above, z-scores were computed using mean and standard deviation values from CDC data on normotensive adults 18-39 years old.¹⁷ Body mass was calculated as mass in kilograms divided by squared height in meters.

Our simplified definition of ABPM hypertension was adapted from the 2008 AHA Scientific Statement on pediatric ABPM as the combination of mean ambulatory SBP greater than the age-sex referenced 95th percentile and greater than 25% of SBP readings above the 95th percentile (SBP load >25%), based on ABPM standard values of Soergel et al and Wühl.¹⁶ Contrary to the AHA statement, we did not take into account the clinic blood pressure in the determination of ABPM hypertension. ABPM hypertension therefore included the categories severe ambulatory hypertension, hypertension, and masked hypertension. All others, including normal BP, reactive hypertension, and prehypertension were categorized as ABPM non-hypertensive. For adults, ages 18 years or greater, ABPM hypertension was defined per Pickering et al.¹⁸

Statistical Analysis

The primary predictors of interest were clinic SBP combinations of oscillometric and/or auscultatory BP including maximum clinic SBP, maximum automated SBP, maximum auscultatory SBP, minimum clinic SBP, mean clinic, mean automated SBP, and mean auscultatory SBP. Maximum, minimum, and mean clinic SBP were determined from a compilation of auscultatory and oscillometric BP data from the single clinic visit. All mean predictor categories required at least 2 BP measurements within the category, while minimum and maximum categories required at least 1 measurement. Clinical covariates

were age, sex, height, and clinic heart rate. Differences in clinical characteristics for the two ABPM groups were examined by Student's *t* test or χ^2 analysis as appropriate. In the primary analysis, the in-clinic SBP indices listed above were compared using Student's *t* test. Secondary analysis had two tiers. With the goal of using a stringent approach to identify predictors of ABPM hypertension, we attempted to identify predictors of both components of the 2008 AHA pediatric ABPM hypertension definition, followed by their combination. First, we employed linear regression models with ABPM mean SBP or ABPM SBP load as continuous outcomes. Due to collinearity, each primary in-clinic BP parameter was separately entered into the regression model, and adjusted for age, sex, height, and heart rate. Next, in-clinic BP predictors found significant in the linear models were separately placed into multivariable adjusted logistic regression models with ABPM hypertension or non-hypertensive as the binary outcome, again adjusted for age, sex, height, and clinic heart rate as covariates. To account for selection bias, a sensitivity analysis was performed on patients visiting one provider who orders ABPM on all children referred for hypertension. A *p* value of 0.05 was considered the threshold for statistical significance. Statistical analyses were performed with SPSS 21 (IBM; Chicago, IL).

Economic Analysis

We compared charges and diagnostic effectiveness entailed by 3 separate clinical hypertension confirmation strategies [Figure 1]. The outcomes generated in this analysis were the proportion of children with high BP correctly identified using ABPM as the gold standard; the total charges accrued in the evaluation including clinic visit, ABPM study, laboratory testing, and imaging; and the ratio of total charges to number of high BP children identified. The superior strategy was defined as the combination of the greatest number of hypertensive children identified and the lowest charge per child identified.

In an attempt to minimize selection bias within the analysis, the distribution of BP diagnoses for each of the 3 diagnostic strategies was determined from a subset of patients randomly referred to a provider who uses ABPM for all children (*n*=58). Within each diagnostic model, actual clinic SBP z-scores determined the percent distribution of the patient subset into normal, pre-elevated, or elevated clinical categories. Actual ABPM diagnosis from the subset further determined percent distribution into ABPM normal, prehypertension, and hypertension. In-clinic BP normal, pre-elevated (between 90th and 95th percentile), and elevated (above 95th percentile) was determined from the maximum auscultatory BP z-scores.¹⁵ We elected to use maximum auscultatory BP based on linear regression modeling results and based on general consensus that auscultation is the most conservative and accurate technique. ABPM normal BP was defined as mean SBP < 95th percentile and SBP load <25%, prehypertension defined as mean SBP <95th percentile with SBP load >25%, and hypertension defined as both mean SBP >95th percentile and SBP load >25%. In-clinic BP was not used to classify ABPM categories.

The pattern of further evaluation for children with elevated BP, determined by either clinic BP or ABPM depending on diagnostic model, was guided by the NHLBI 2011 recommendations to include echocardiogram, renal ultrasound, complete blood count, renal panel, urinalysis, fasting lipids, insulin, glucose, HbA1c, ALT.¹⁴ Where the guidelines allow

for clinical discretion in secondary etiology work-up and comorbidity assessment in obese children, we used the investigation patterns and obesity prevalence that actually transpired in our cohort to determine the rates of additional workup. Polysomnography was actually performed in 20%, plasma renin and aldosterone in 20%, and combination of plasma renin, aldosterone, and urine cortisol ordered in 10%. For all children with pre-elevated BP, evaluation of target end organ damage was performed including urinalysis and echocardiogram. Roughly 80% of prehypertensive patients were obese, thus charges for laboratory co-morbidity assessment (fasting lipids, insulin, glucose, HbA1c, ALT) were included for 80% of pre-elevated BP cases. Charges incurred for the office visit, diagnostic testing, and subsequent work-up were obtained from our institution rate book. We then scaled these costs up to a hypothetical cohort of 1000 children referred for hypertension evaluation.

Results

Clinical characteristics

For the 170 patients meeting criteria for this study, the mean age was 15.6 ± 3.7 years and 34% percent were female. ABPM hypertension occurred in 55 (32.4%) comprised of 11 masked hypertension (6.5%), 12 ambulatory hypertension (7.1%), and 32 severe ambulatory hypertension (18.8%). ABPM nonhypertension was present in 115 (67.6%), including 43 normal blood pressure (25.3%), 37 reactive hypertension (21.8%), and 35 prehypertension (20.6%). There were no significant differences between ABPM hypertension versus non-hypertensive groups with respect to relevant baseline characteristics [Table 1]. By definition, the 2 groups differed substantially with regard to ABPM parameters.

In-Clinic Variable associated with ABPM outcomes

None of the in-clinic SBP indices differed between ABPM hypertension versus non-hypertensive groups [Table 2]. By multivariable adjusted linear regression, highest auscultatory clinic SBP and average automated clinic SBP were significantly associated with ABPM mean SBP, but none predicted SBP load [Table 3]. Neither highest auscultatory clinic SBP ($\beta=0.024$ [95%CI -0.013, 0.061], $P=0.20$) nor average automated SBP ($\beta=0.035$ [95%CI -0.018, 0.088], $P=0.19$) were associated with ABPM hypertension on logistic regression. Sensitivity analysis found no significant associations between in-clinic SBP indices or covariates and ABPM mean SBP, SBP load, or ABPM hypertension.

Economic Analysis

Strategy 1 using in-clinic maximum auscultatory BP $>95^{\text{th}}$ percentile alone for diagnosis identified 40% of true hypertensive children. A theoretical cohort of 1000 referred children would accrue \$1.86 million in charges and charges per hypertensive child identified would be \$27,012. Strategy 2 identified 70% of hypertensive patients. More precisely, of the 48% of patients with in-clinic maximum auscultatory BP $>90^{\text{th}}$ percentile, ABPM found hypertension in 28%, prehypertension in 16%, and normal blood pressure in 56%. Of the 52% of children classified as normal due to in-clinic maximum auscultatory BP less than 90^{th} percentile, 11% actually had hypertension on ABPM. Strategy 2 would accrue charges of \$1.33 million for every 1,000 children referred, with charges per identified child

averaging \$11,035. Strategy 3 using universal ABPM identified 100% of hypertensive children by definition. Every 1,000 patients referred would accrue charges totaling \$1.88 million, with charge per hypertensive child identified of \$10,948. We performed a sensitivity analysis theoretically fixing the proportion of WCH to 35% within our economic models for consistency with previous reports.^{10, 11} We found strategy 1 accrued total charges of \$1.86 million per 1,000 patients referred with a charge per hypertensive child identified of \$11,990. Diagnostic strategy 2 accrued total charges of \$1.59 million with an average charge per hypertensive child identified of \$7,454. And finally, strategy 3 accrued total charges of \$2.22 million with a charge per hypertensive child identified of \$8,180.

Discussion

The utilization of ABPM must balance its superior ability to discern normal BP, reactive hypertension, and hypertension against its cost.¹⁶ In the presented analyses, in-clinic SBP indices were associated with the height of ABPM mean SBP, but none were associated with the ABPM load, which in turn prevented any in-clinic SBP index from predicting categorical ABPM hypertension. No other clinical variables increased the likelihood of ABPM hypertension, beyond being referred itself. The results were robust to sensitivity analysis accounting for selection bias. The economic analysis based on the combination of NHLBI 2011 recommendations and our actual investigation patterns found that universal ABPM for all children referred accrued more cost than using clinic BP followed by ABPM. But ABPM also correctly identified more hypertensive children, resulting in the lowest average charges per child identified. In sensitivity analyses, strategy 2 had the lowest average charge per hypertensive patient identified, although still inappropriately identifying some hypertensive children. This illustrates that as accuracy of clinic blood pressure to identify ABPM hypertension improves, economic attractiveness of strategy 2 improves in parallel. However, diagnostic strategy 2 still fails to identify masked hypertension. While validating clinical intuitions that in-clinic BPs are related to ABPM BPs, our work support the use of ABPM in all referred children regardless of in-clinic BP or other variables.

Our results are broadly consistent with previous reports on the relation between in-clinic and ambulatory BP. Investigators have previously found height of single, average clinic, or home BPs were directly associated with mean daytime ambulatory BPs in referral patients.^{19, 20} Our results extend these findings to include prediction of the ABPM mean SBP for the entire period, in agreement with prior report of correlation between a single office SBP with 24-hour ABPM SBP.²¹ But to our knowledge, the presented work is the first to study the association between in-clinic SBP and ABPM hypertension as a category.

Previous work has modeled ABPM to be cost-effective in identifying hypertension in both adults and children.^{10, 22} The present results extend the previous findings by using a broader model, which accounted for a more extensive clinical work-up advised by the recent NHLBI 2011 guidelines, including in prehypertension, and accounting for masked hypertension children. We also analyzed an 'intermediate' diagnostic strategy of clinic BP followed by ABPM in high clinic BP children. This work therefore broadens the inferences previously drawn to suggest the clinical and economic superiority of ABPM even in the absence of

referral clinic BP. However, the superiority of universal ABPM may depend on the prevalence of reactive hypertension.

Given the rise in prevalence of abnormal blood pressures in children, which is explained partly by the parallel rise in childhood obesity, BMI is certainly an important variable in hypertension diagnosis.^{2, 3} Indeed, obese patients have a higher prevalence of hypertension, and may have higher rates of both white coat hypertension and masked hypertension.²³⁻²⁵ BMI (z-score) is also associated with clinic SBPs and ambulatory SBP.²⁵ Intriguingly, BMI did not differ significantly here between the ABPM hypertensive versus non-hypertensive groups. Given this lack of difference and absence of general consensus on adjusting BP categories for body adiposity given the potentially mediating role as noted, we chose not to adjust for BMI as a covariate. Also, we were unable to confirm heart rate as a predictor of hypertension category. We had hoped to use heart rate as an index of anxiety, as nervous children may have higher heart rates.^{26, 27} This association may have been obscured by the association between obesity or poor lifestyle habits with higher heart rates.^{28, 29}

This study has limitations. First, as a retrospective cohort study, prospective and causal inference cannot be made. Second, given the inclusion of only referral patients undergoing ABPM, selection bias exists regarding the indications for the ABPM studies. The subset analysis on studies ordered by a provider who used ABPM on all patients was concordant with the general findings albeit with limited statistical power. Clinic blood pressure data may be variable in technique and protocol across two specialties clinics and multiple clinic sites. Existing BP-focused training programs and the use of multiple in-clinic blood pressures were relied upon to minimize this variability, but ultimately the presented data reflects the real world clinic setting and should be interpreted in that context. Reports document the possibility of regression to the mean accounting for inflated white coat hypertension or masked hypertension diagnosis.²¹ Again, multiple clinic BP indices and averages were included to mitigate clinic BP outliers. There is also a possibility that very severe hypertension patients didn't come to clinic at all and were triaged and managed as inpatients. The study is limited to specialty clinics within a pediatric referral center, reflected by characteristics of the study population, which impedes generalizability of this data to the general population or to blood pressure screening. As a referral center, we do not have complete capture of BPs from primary care settings prior to the child's referral. This may be an issue for future studies, especially in light of high variability in measurement techniques and accuracy in the community setting.

Previous work has identified high daytime ABPM means to be clinically significant in adolescents with nighttime being normal. We did not examine this possibility in this work as the current consensus as defined by the AHA guidelines focus on the 24 hour means and loads and we have adhered to the spirit of these criteria. Future work may explore this important area. In economic analysis based on the 2011 NHLBI guidelines, the main drivers of total charges for hypertension evaluation were echocardiogram and renal US, and thus any strategy to minimize their use may appear economically more attractive. And finally, two years of consecutive years of ABPM studies from our single institution may have limited power to detect significant predictors of ABPM parameters. However the results may be considered hypothesis generating for future larger studies

In summary, our data suggest that all patients referred to pediatric centers for elevated BP may benefit from diagnostic ABPM, as SBPs from a single clinic visit have poor association with subsequent ABPM diagnosis and thus poor ability to appropriately target confirmatory ABPM testing. In addition, consistent with previous findings, ABPM as the initial diagnostic test for all referral patients may be the most economically efficient diagnostic strategy, although possibly dependent on specific WCH rates. Future work is needed in larger prospective cohorts to further examine clinic predictors of ABPM diagnosis and to determine the utility of ABPM in primary care settings.

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Abbreviations

ABPM	ambulatory blood pressure monitoring
BP	blood pressure
SBP	systolic blood pressure

Figure 1.

Schematic of clinic diagnostic pathways created for economic analysis. Pathway 1: Clinic BP values alone stratify into normal, pre-elevated, or elevated BP diagnostic categories; Pathway 2: Clinic BP followed by confirmatory ABPM for clinic BP >90th percentile, employing clinic BP then ABPM to stratify; Pathway 3: ABPM alone stratifies into normal, prehypertension, or hypertension. Work-up 1 evaluation for elevated BP includes a) Imaging: echocardiogram and renal ultrasound; b) Laboratory tests: CBC, renal panel, urinalysis, fasting lipids, insulin, glucose, HbA1c, ALT. Work-up 2 evaluation for pre-elevated BP includes echocardiogram & urinalysis. CBP, clinic blood pressure; HTN, hypertension; PreHTN, prehypertension.

Table 1

Study Population.

	ABPM non-Hypertensive (n=115)	ABPM Hypertension (n=55)	<i>p</i> value
Age (years)	15.9 ± 3.4	15.0 ± 4.2	0.14
Males/Females	76/39	36/19	0.94
Height (cm)	166.2 ± 13.5	163.5 ± 17.8	0.29
Height z score	0.33 ± 1.10	0.47 ± 0.91	0.39
Weight (kg)	78.3 ± 26.8	71.0 ± 24.57	0.09
Weight z score	1.47 ± 1.19	1.37 ± 1.02	0.64
BMI (kg m ⁻²)	27.7 ± 7.7	25.8 ± 6.1	0.11
BMI z score	1.29 ± 1.12	1.20 ± 0.93	0.64
Clinic Heart rate	84.1 ± 17.9	82.8 ± 15.7	0.66
ABPM Average Systolic BP	121.5 ± 6.8	134.7 ± 7.0	P<0.001
ABPM Average Diastolic BP	67.3 ± 6.7	74.0 ± 8.5	P<0.001
ABPM Systolic BP Load	20.7% ± 13.5	66.6% ± 17.8	P<0.001
ABPM Systolic BP Dip	7.7% ± 7.0	9.4% ± 5.0	0.12
Prematurity (%)	17 (15%)	6 (11%)	0.53
Significant Medications (%)	29 (25%)	16 (29%)	0.59
Significant Cardiac Disease (%)	1 (1%)	1 (2%)	0.13
Significant Renal Disease (%)	5 (4%)	1 (2%)	0.62
Diabetes (%)	2 (2%)	2 (4%)	0.45
Genetic Syndrome (%)	10 (9%)	4 (7%)	0.75

Data presented as Mean ± standard deviation or proportion as listed.

Table 2

Univariate Comparison of In-Clinic SBP Indices.

Clinic SBP Indices (mm Hg)	n	ABPM non-Hypertensive (n=115)	ABPM Hypertension (n=55)	p value
<i>With at least 1 clinic BP measured within category:</i>				
Highest clinic SBP	114	137.2 ± 12.5	138.9 ± 12.3	0.43
Highest automated SBP	109	136.2 ± 12.1	137.6 ± 13.0	0.49
Highest auscultatory SBP	85	128.2 ± 12.2	130.3 ± 12.0	0.38
<i>With >1 clinic BP measured within category:</i>				
Average clinic SBP	101	130.4 ± 10.3	130.8 ± 11.0	0.82
Average automated SBP	66	130.9 ± 10.3	133.5 ± 12.1	0.30
Average auscultatory SBP	46	127.4 ± 12.0	127.1 ± 12.1	0.93
Lowest clinic SBP	101	123.6 ± 11.9	124.2 ± 11.6	0.78

Data presented as mean ± standard deviation. Highest clinic SBP, average clinic SBP, and lowest clinic SBP categories are combinations of both auscultatory and oscillometric BP data.

Table 3

Results of Linear Regression Models for outcomes A) ABPM Mean SBP and B) SBP Load.

<u>Clinic SBP Indices (mm Hg)</u>	<u>n</u>	<u>A) ABPM Mean SBP (mm Hg)</u>		<u>B) ABPM SBP Load (%)</u>	
		<u>Regression Coefficient (95% CI)</u>	<u>p value</u>	<u>Regression Coefficient (95% CI)</u>	<u>p value</u>
<i>With at least 1 clinic BP measured within category:</i>					
Highest clinic SBP	157	0.117 (0.0, 0.235)	0.05	0.3 (0.0, 0.7)	0.09
Highest automated SBP	152	0.104 (-0.016, 0.224)	0.09	0.4 (0.0, 0.7)	0.06
Highest auscultatory SBP	117	0.160 (0.022, 0.299)	0.02	0.4 (0.0, 0.8)	0.07
<i>With >1 clinic BP measured within category:</i>					
Average clinic SBP	135	0.102 (-0.052, 0.255)	0.19	0.3 (-0.2, 0.8)	0.20
Average automated SBP	87	0.208 (0.027, 0.389)	0.03	0.5 (-0.1, 1.0)	0.12
Average auscultatory SBP	69	0.073 (-0.124, 0.269)	0.46	0.0 (-0.6, 0.6)	0.98
Lowest clinic SBP	135	0.096 (-0.038, 0.231)	0.16	0.3 (-0.1, 0.7)	0.18

Adjusted for age, sex, height, and clinic heart rate. Regression coefficient indicates mmHg higher or % higher increment in ABPM outcome for each 1mmHg higher in clinic SBP parameter.

Table 4

Results of Logistic regression models.

		ABPM Hypertension vs. Non-Hypertensive	
Clinic SBP Indices (mm Hg)	n	Regression Coefficient (95% CI)	p Value
With at least 1 clinic BP measured within category:			
Highest auscultatory SBP	117	0.024 (-0.013,0.061)	0.20
With >1 clinic BP measured within category:			
Average automated SBP	87	0.035 (-0.018,0.088)	0.19

Adjusted for age, sex, height, and clinic heart rate.