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Evaluating novel approaches for estimating awake and sleep blood pressure: design of the Better BP Study – a randomised, crossover trial

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ABSTRACT

Introduction For many people, blood pressure (BP) levels differ when measured in a medical office versus outside of the office setting. Out-of-office BP has a stronger association with cardiovascular disease (CVD) events compared with BP measured in the office. Many BP guidelines recommend measuring BP outside of the office to confirm the levels obtained in the office. Ambulatory BP monitoring (ABPM) can assess out-of-office BP but is not available in many US practices and some individuals find it uncomfortable. The aims of the Better BP Study are to (1) test if unattended office BP is closer to awake BP on ABPM compared with attended office BP, (2) assess if sleep BP assessed by home BP monitoring (HBPM) agrees with sleep BP from a full night of ABPM and (3) compare the strengths of associations of unattended versus attended office BP, unattended office BP versus awake BP on ABPM and sleep BP on HBPM versus ABPM with markers of end-organ damage.

Methods and analysis We are recruiting 630 adults not taking antihypertensive medication in Birmingham, Alabama, and New York, New York. Participants are having their office BP measured with (attended) and without (unattended) a technician present, in random order, using an automated oscillometric office BP device during each of two visits within one week. Following these visits, participants complete 24 hours of ABPM and one night of HBPM, in random order. Psychosocial factors, anthropometrics, left ventricular mass index and albumin-to-creatinine ratio are also being assessed.

Ethics and dissemination This study was approved by the University of Alabama at Birmingham and the Columbia University Medical Center Institutional Review Boards. The study results will be disseminated at scientific conferences and published in peer-reviewed journals.

Trial registration number NCT04307004.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Using a randomised controlled trial design, this study will rigorously test multiple modalities for assessing out-of-office blood pressure (BP) including automated office BP without the presence of a technician, ambulatory BP monitoring and home BP monitoring.
⇒ We will collect BP measurements from a diverse sample of participants including, but not limited to, African Americans and Hispanics, who are at elevated risk for hypertension and cardiovascular disease.
⇒ These data could provide evidence for updating guidelines on both in-office and out-of-office BP measurement.
⇒ Due to the nature of the protocol, we will be limited in capturing data on individuals with high or extremely high BP who are not currently taking antihypertensive medications.
⇒ We also will not be collecting follow-up data regarding medical diagnosis and treatment initiation for those who are identified as having hypertension based on their office and out-of-office BP measurements.

INTRODUCTION

Elevated blood pressure (BP) and hypertension are associated with more cardiovascular disease (CVD) events and disability-adjusted life years lost than any other modifiable risk factor, both in the USA and worldwide.[1 2] US guidelines and scientific statements recommend that BP be measured in the office setting by a trained healthcare professional or technician to identify individuals with hypertension.[3–5] In clinical practice and most research studies conducted in the USA, BP is measured in the office with medical staff present, an approach sometimes referred to as attended office BP measurement. It has been suggested that measuring office BP without medical staff present, unattended office BP measurement, using an automated office BP (AOBP) device, would be preferable to measuring office BP with medical staff present since the presence of an observer may lead to an alerting phenomenon that increases BP.

The US Preventive Services Task Force and the 2017 American College of Cardiology/American Heart Association BP guideline recommend measuring out-of-office BP before initiating antihypertensive treatment for most patients except those with extremely high office BP.[6] This recommendation is based on a large body of evidence demonstrating BP in many adults differs substantially when measured outside of the office versus when measured attended in the office setting and a stronger association of CVD with out-of-office BP than with attended office BP.[7–9]

Ambulatory BP monitoring (ABPM) is widely considered to be the reference standard for out-of-office BP assessment and for confirming an initial diagnosis of hypertension based on office BP.[7] A comprehensive assessment of BP requires office and out-of-office BP measurements, including while individuals are awake and asleep. ABPM devices are usually programmed to obtain BP readings every 15–30 min for 24 hours, including during sleep and can be used to identify white coat hypertension, masked hypertension and nocturnal hypertension. Prior studies have reported strong associations of awake and sleep systolic BP (SBP), assessed by ABPM, with target organ damage and CVD events.[10 11] Despite the value of ABPM for diagnosing hypertension, there are barriers to its use, including a lack of availability and poor tolerability for some individuals.[12–14]

Data from studies conducted in Canada suggest that measuring unattended office BP yields lower BP readings compared with attended measurements and are, on average, closer to the average awake BP assessed by ABPM.[15 16] In a meta-analysis of 16 studies, unattended office BP was lower than attended office BP (SBP: −10.48 mm Hg; 95% CI, −13.15 to −7.81; and diastolic BP (DBP): −4.44 mm Hg; 95% CI, −6.07 to −2.80), and was not statistically significantly different from awake BP assessed by ABPM.[17] However, there were several limitations associated with this meta-analysis. Many of the studies included did not randomise the order of BP measurement, attended office BP followed by unattended office BP versus unattended office BP followed by attended office BP. Also, the meta-analysis did not report participant-level differences between unattended office BP, attended office BP and BP assessed on ABPM.

Previously, ABPM was the only method for assessing BP while a person was sleeping. However, home BP monitoring (HBPM) devices have recently been developed that can measure BP while asleep. Prior studies suggest that compared with ABPM, HBPM devices are better tolerated as they are only worn while a person is sleeping versus a full 24 hours, and BP is measured fewer times.[18] However, few data are available comparing sleep SBP and DBP on HBPM versus ABPM.

OBJECTIVES

The overall goal of the Better BP Study is to determine the extent to which AOBP, used to measure unattended office BP, and an HBPM device that measures BP during sleep estimate BP readings obtained while awake and asleep on ABPM. The Better BP Study has three study aims. The first aim is to test whether, when following a standardised protocol, unattended office BP provides a more accurate estimate of awake SBP and DBP on ABPM than attended office BP. We hypothesise that the absolute difference between unattended office BP and awake BP on ABPM is less than the absolute difference between attended office BP and awake BP, and that the agreement between hypertension status based on office BP versus awake BP will be greater when office BP is measured unattended versus attended. The second aim is to evaluate the extent to which sleep BP obtained from a single night of HBPM agrees with sleep BP assessed by ABPM. We are also asking participants to rate the acceptability of both approaches to assessing out-of-office BP and hypothesise that HBPM will be better tolerated than ABPM. The third aim is to compare the strengths of associations of unattended versus attended office BP, unattended office BP versus awake BP on ABPM and sleep BP on HBPM versus ABPM with markers of end-organ damage, including left ventricular hypertrophy (LVH) and albuminuria. We hypothesise that the association with target-organ damage will be: (1) stronger for unattended versus attended office BP, (2) similar for unattended office and awake BP, and (3) similar for sleep BP by HBPM and ABPM.

METHODS

Brief study overview

Participants are completing four study visits that include BP measurement in an office setting, blood and urine collection, and an echocardiogram (figure 1). There is a 24-hour interval between each of the study visits as depicted in figure 1. The order in which office BP is measured at the first and second visit, unattended followed by attended or attended followed by unattended, as well as the order in which participants undergo ABPM and HBPM at the third and fourth visit is determined by 1:1:1:1 block randomisation of 4 groups with each block size consisting of either 8 (2 per condition) or 12 (3 per condition) participants. Participants are randomised to one of the following conditions: (1) unattended office BP first and attended office BP second; ABPM first and HBPM second, (2) attended office BP first and unattended office BP second; ABPM first and HBPM second, (3) unattended office BP first and attended office BP second; HBPM first and ABPM second and (4) attended office BP first and unattended office BP second; HBPM first and ABPM second. The size of the block (8 or 12 participants) is also randomised. All randomisations are conducted by study staff. At the fourth study visit, participants are providing blood and urine specimens and an echocardiogram is performed.

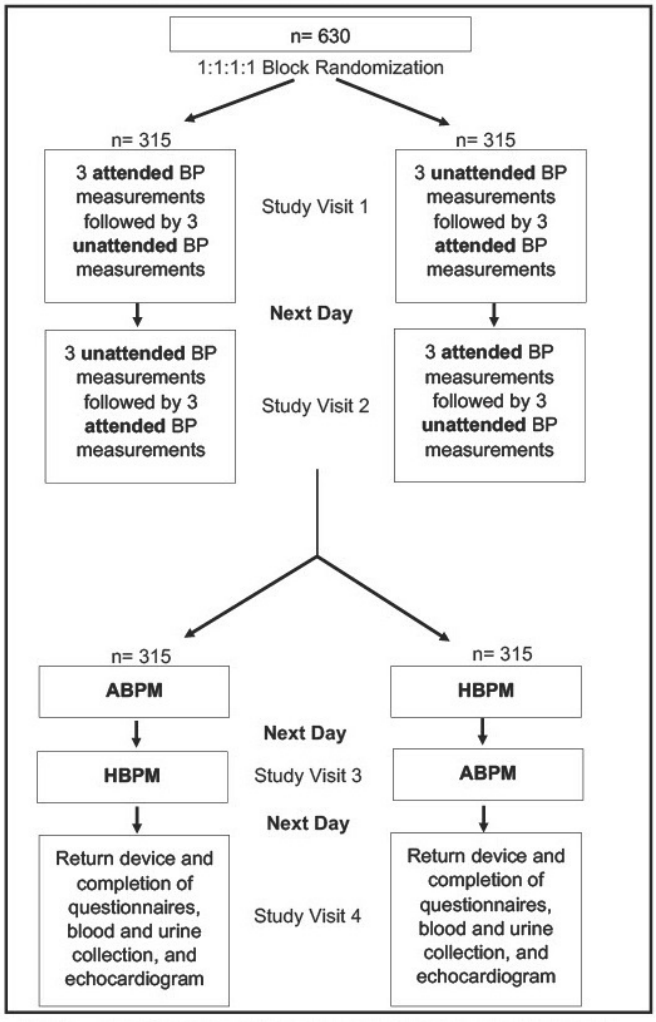

Figure 1 Study design for the Better BP study. Participants were randomised to one of the following: (1) unattended office BP first and attended office BP second; ABPM first and HBPM second, (2) attended office BP first and unattended office BP second; ABPM first and HBPM second, (3) unattended office BP first and attended office BP second; HBPM first and ABPM second and (4) attended office BP first and unattended office BP second; HBPM first and ABPM second. ABPM, ambulatory blood pressure monitoring; BP, blood pressure; HBPM, home blood pressure monitoring.

PARTICIPANTS

Eligible individuals must be ≥18 years of age and have a mean SBP of 110 to <160 mm Hg or a mean DBP of 70 to <100 mm Hg based on two consecutive BP readings conducted during an in-person screening which occurs prior to study visit 1. We also excluded individuals with mean SBP≥160 mm Hg or mean DBP≥100 mm Hg; or mean SBP<110 mm Hg and mean DBP<70 mm Hg. Inclusion and exclusion criteria are provided in box 1.

Recruitment and enrolment

The Better BP Study is being conducted at the University of Alabama at Birmingham (UAB) and at Columbia University Irving Medical Center (CUIMC) in New York City. At the UAB site, participants are being recruited from the community using flyers and at primary care clinics using contact information cards and physician referral. At the CUIMC site, participants are being recruited from the community using flyers and Columbia's RecruitMe website.[19] Overall, the study plans to recruit at least 160 non-Hispanic white, 160 non-Hispanic black and 160 Hispanic participants. The study began enrollment on 15 July 2019. The expected duration of the study is approximately 4 years.

Box 1 Inclusion and exclusion criteria for the Better BP study

Inclusion criteria

1.≥18 years of age*
2. Have a mean SBP of 110 to <160 mm Hg or a mean DBP of 70 to <100 mm Hg based on two consecutive blood pressure readings conducted during an in-person screening†

Exclusion criteria

1. Mean SBP ≥160 mm Hg or mean DBP ≥100 mm Hg; or mean SBP <110 mm Hg and mean DBP <70 mm Hg
2.Currently taking antihypertensive medication
3. Known pregnancy
4. Self-reported history of cardiovascular disease, including myocardial infarction, stroke, atrial fibrillation or ventricular tachycardia
5. History of sleep apnea or a score of 5 or greater on the STOP-BANG questionnaire[37]
6. Working second shift, overnight shift (eg, 23:00 to 7:00), or any job that would not allow the ABPM device to measure BP every 30 min for 24 hours (eg, taxi or bus drivers)
7. Completed ABPM within the past year
8. Unable to wear BP devices or cuffs
9. No permanent residence to be contacted for follow-up

*At the UAB site, individuals must be ≥19 years of age.
†Prior to study visit 1 at both sites.
ABPM, ambulatory BP monitoring; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure; STOP-BANG, **s**nore loudly, **t**ired, **o**bserved stop breathing, high blood **p**ressure, **b**ody mass index greater than 35 kg/m^2, **a**ge older than 50, **n**eck size larger than 40 cm, male **g**ender; UAB, University of Alabama at Birmingham.

Procedures

The manual of operations and procedures for the study and the consent forms at UAB and CUIMC are available from the investigators on request after study completion.

Office BP measurements

Both unattended and attended office BP are being measured using the Microlife WatchBP Office AFIB automated BP device (Microlife USA). The device is programmed to have a 5 min rest period followed by three consecutive BP readings taken at 1 min intervals. All office BP measurements are obtained using the participant's non-dominant arm, unless this is not feasible, in which case their dominant arm is used for office BP measurements. Prior to having their BP measured, participants are asked to place their feet flat on the ground (levelled), uncross their legs, sit with their back flat against the chair,

place their arm in a resting position on a hard surface at heart level, and remain still and quiet until all BP readings are obtained. The research coordinator sets up the device and leaves the room for 10 min in order to obtain the unattended office BP or remains in the room for the attended office BP measurements. When the research coordinator remains in the room, he/she instructs the participant not to talk during the 5 min rest period or while their BP is being measured.

ABPM and HBPM

ABPM is being conducted using the Microlife WatchBP O3 ambulatory monitor (Microlife USA), which is programmed to obtain a BP reading every 30 min. Sleep HBPM is being conducted using a Microlife WatchBP Home Nighttime device (Microlife USA) that is programmed to take three SBP and DBP readings at 2, 3 and 4 hours after going to sleep. For both ABPM and HBPM, participants are given a device log to indicate the time they went to bed, the time they woke up the next morning, and any times they removed the device. The Microlife WatchBP O3 ambulatory monitor and the Microlife WatchBP Home Nighttime device have previously been validated.[20]

Actigraphy

Participants are wearing a wrist activity monitor, Philips Respironics Actiwatch 2 Device (Philips USA), on the same arm as the BP cuff from study visit 2 to study visit 4 (ie, when ABPM and sleep HBPM are being conducted) and are being instructed to press a button on the device when they are going to sleep and when they wake up in the morning. The device has a light sensor and records the amount of physical movement (activity count) and light in 1 min epochs. The data are being uploaded and stored in a database using the Actiware software (Philips USA), which also generates preliminary estimates of sleep onset and wake-up times. A trained technician reviews and can adjust these software-generated times based on the actigram, an on-screen graphic showing both the activity count and the level of light on a minute-by-minute basis and the participant's self-reported sleep/wake times. Once sleep/wake times are finalised, the software computes a number of sleep-related parameters; for example, sleep duration, wake after sleep onset and a sleep fragmentation index. The sleep/wake times are also used to differentiate sleep from awake BP readings on ABPM for the calculation of mean awake and mean sleep SBP and DBP and measures of absolute and relative nocturnal BP dipping.

Blood and urine collection

At study visit 4, each participant is providing blood and urine samples for measurement of serum creatinine, a complete lipid panel, haemoglobin A1C and urine albumin and creatinine. Samples collected at the UAB site are being frozen and shipped to CUIMC. All specimens are being analysed at the CUIMC Center for Advanced Laboratory Medicine Lab. Participants are providing 7 mL of blood and at least 3 mL of urine to be stored for future studies.

Echocardiogram

A 2D echocardiogram is obtained prior to or following the fourth study visit using the Philips IE33 or a Philips EPIQ 7 ultrasound system (Philips USA) according to the 2015 recommendations of the American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging.[21]

Other covariates

Self-administered questionnaires are being completed to assess each participant's sociodemographic characteristics including age, race/ethnicity, sex, education level, income, medical history, current smoking status, physical activity level, alcohol consumption, stress, anxiety and sleep quality (table 1). Height, weight, and waist and neck circumferences are measured during study visit 1, following a standard protocol.

Outcomes

BP measures

For the primary analysis, we will estimate the average office SBP and DBP measured unattended or attended using the first three measurements obtained at study visits 1 and 2. Through randomisation, 50% of participants should have their first three office SBP and DBP measurements obtained unattended at study visit 1 and attended at study visit 2, while 50% should have their first three office SBP and DBP measurements attended at study visit 1 and unattended at study visit 2. For a sensitivity analysis, the analysis will be repeated using the unattended and attended measurements collected at study visit 1 and study visit 2, separately. Additionally, we will do an analysis using unattended and attended BP measurements from both visits. Awake and sleep SBP and DBP on ABPM are being defined as the mean of all SBP and DBP readings while participants are awake and asleep, respectively, as determined from the actigraphy data in conjunction with the self-reported sleep and wake times from the device log. Sleep SBP and DBP on HBPM is being defined as the mean of the three SBP and DBP measurements.

Office hypertension and BP phenotypes

Office hypertension is being defined as attended office SBP≥130 mm Hg or DBP≥80 mm Hg or unattended office SBP≥130 mm Hg or DBP≥80 mm Hg.[4 22–24] The definitions of white coat hypertension, masked hypertension and nocturnal hypertension are provided in table 2.[4 24–27]

Echocardiographic and other measures

Left ventricular mass (LVM) is determined using the ASE formula.[21] LVM index (LVMI) is defined as LVM divided by body surface area (g/m^2). LVH is defined as an LVMI≥96 g/m^2 in females and LVMI≥116 g/m^2 in males.[21] Albuminuria is defined as having an albumin-to-creatinine ratio≥30 mg/g.

Table 1 Survey measures being collected by self-administered questionnaires in the Better BP Study

Survey measures	Number of items	When assessed	Description
Eligibility Screening form	8	Prescreening	Demographics and medical history including age, pregnancy, blood pressure measurements, cardiovascular diseases, ability to wear devices and work shifts to determine eligibility.
STOP-BANG Questionnaire*	8	Screening visit	Risk for sleep apnea.
State-Trait Anxiety Inventory Form Y1 (State Anxiety)	20	Study visits 1–4	Includes statements that evaluate how respondents feel 'right now, at this moment'.
Sociodemographic, Medical History and Health Behaviors Questionnaire	14	Study visit 1	Date of birth, race/ethnicity, sex, education completed, household income, marital status, smoking status, physical activity, alcohol consumption, and medical history.
Pittsburgh Sleep Quality Index (PSQI) Questionnaire	10	Study visit 1	Sleep quality and disturbances during the past month.
Post-ABPM Questionnaire	14	Study visit 3 or 4†	Experience while wearing ABPM including questions about device satisfaction and sleep experience.
Post-HBPM Questionnaire	13	Study visit 3 or 4†	Experience while wearing HBPM including questions about device satisfaction and sleep experience.
State-Trait Anxiety Inventory Form Y2 (Trait Anxiety)	13	Study visit 4	Includes statements that evaluate how respondents feel 'in general'.
Expectation of Outcomes Questionnaire	5	Study visit 4	State levels with a physician present.
Comparability Questionnaire	3	Study visit 4	Participant preferences for wearing ABPM versus HBPM.

*Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. Chest. 2016 Mar;149(3):631–8. doi: 10.1378/chest.15–0903. Epub 2016 Jan 12. PMID: 26378880.
†Based on randomization order.
ABPM, ambulatory blood pressure monitor; HBPM, home blood pressure monitor; STOP-BANG, **s**nore loudly, **t**ired, **o**bserved stop breathing, high blood **p**ressure, **b**ody mass index greater than 35 kg/m^2, **a**ge older than 50, **n**eck size larger than 40 cm, male **g**ender.

Tolerability of ABPM and HBPM

Tolerability of ABPM and HBPM is being evaluated using a 15-item questionnaire that includes items assessing comfort with wearing the devices and disturbances experienced during ABPM and HBPM.[14] There are also questions on pain, skin irritation and bruising resulting from wearing the devices. Eight of the questions are answered with a Likert-type scale (eg, did you find the monitor interfered with your normal sleeping pattern? With response options of 0 'not at all', 5 'somewhat',

Table 2 Outcome definitions for office, white coat, masked and nocturnal hypertension

	Office BP					
Outcome	**Attended measurements**	**Unattended measurements**		**Awake BP**		**Sleep BP***
Office hypertension	SBP≥130 mm Hg or DBP≥80 mm Hg	SBP≥130 mm Hg or DBP≥80 mm Hg	†	N/A	†	N/A
White coat hypertension	SBP≥130 mm Hg or DBP≥80 mm Hg	SBP≥130 mm Hg or DBP≥80 mm Hg	and	SBP<130 mm Hg and DBP<80 mm Hg	†	N/A
Masked hypertension	SBP<130 mm Hg and DBP<80 mm Hg	SBP< 130 mm Hg and DBP< 80 mm Hg	and	SBP≥130 mm Hg or DBP≥80 mm Hg	†	N/A
Nocturnal hypertension	N/A	N/A	†	N/A	†	SBP ≥ 110 mm Hg or DBP ≥ 65 mm Hg

*The same threshold is used for ambulatory blood pressure monitoring and home blood pressure monitoring.
†No conjunction (and/or).
BP, blood pressure; DBP, diastolic blood pressure; N/A, not applicable; SBP, systolic blood pressure.

10 'extremely'). The remaining seven questions have response options of 'yes' or 'no' (eg, 'did you experience pain from wearing the monitor?').

Definition of complete BP assessments

We will define a complete office BP assessment by three unattended and three attended office SBP and DBP measurements at visits 1 and 2. We will require 70% of planned SBP and DBP readings (n=34 or more of 48 readings) and 20+ awake SBP and DBP readings, and 7+ sleep SBP and DBP readings for an ABPM assessment to be considered complete. We will require two or three SBP and DBP readings for a sleep HBPM recording to be complete.

Statistical analysis

A statistician masked to participants' randomisation assignments will analyse the data using uninformative codes to represent randomisation assignments. Assignments will be unmasked only after completion of the statistical analyses. Our primary approach to missing data is to collect complete data. We will examine missing data and use multiple imputation, as appropriate. Characteristics of participants at study visit 1 will be summarised by randomisation assignment.

For aim 1, scatterplots will be assembled to show the relation between unattended office SBP, attended office SBP and awake SBP assessed by ABPM. For each pair of SBP measures, intraclass correlation coefficients will be calculated. The statistical significance of the difference in the correlation coefficients will be calculated using the Fisher r-to-z transformation accounting for the correlation between SBP measures. We will also generate Bland-Altman plots showing the differences between unattended and attended SBP, separately, versus awake SBP assessed by ABPM. The absolute differences of mean attended office SBP and unattended office SBP from awake SBP assessed by ABPM will be calculated. Next, we will determine whether the absolute difference between unattended office SBP and awake SBP is different than the absolute difference between attended office SBP and awake SBP by calculating if the difference in differences (ie, absolute difference of unattended office SBP minus awake SBP minus absolute difference of attended office SBP minus awake SBP) is different than zero using a multilevel mixed models. Next, a two-way ANOVA will be conducted treating SBP as a repeated measures outcome, with indicator variables for (1) whether SBP was measured unattended versus attended, (2) visit and (3) the order effect. These analyses will be repeated for DBP. The overall agreement and agreement above that expected by chance (ie, the Kappa statistic) will be calculated between (1) attended and unattended office hypertension, (2) attended office hypertension and awake hypertension and (3) unattended office hypertension and awake hypertension.

For aim 2, we will calculate the mean sleep SBP and DBP assessed by HBPM and ABPM, separately. The statistical significance of differences in mean sleep SBP and DBP assessed by HBPM versus ABPM will be determined using multilevel mixed models. In addition, the mean absolute differences between SBP and DBP, separately, assessed by HBPM versus ABPM will be reported and a Bland-Altman plot generated. We will also calculate the overall agreement and Kappa statistic between nocturnal hypertension when sleep BP is assessed by HBPM and ABPM. We will report tolerability scores for ABPM and HBPM, separately, and test for differences in mean tolerability using multilevel mixed models.

For aim 3, we will calculate the correlation coefficients for attended and unattended office SBP and DBP, awake SBP and DBP and sleep SBP and DBP assessed by ABPM and HBPM with LVMI. The association between each BP measure and LVMI will be estimated using linear regression. An initial model will include adjustment for age, race/ethnicity, sex and study site (UAB or CUIMC). A second model will include further adjustment for education, body mass index, smoking, physical activity, alcohol consumption, sleep quality, diabetes, estimated glomerular filtration rate and 10-year predicted atherosclerotic cardiovascular disease risk. We will also model the association of each BP measure with the outcome of LVH using Poisson regression with the same covariates as mentioned above. The correlation coefficients and regression models for each BP measure will also be generated for the outcomes of albumin-to-creatinine ratio as a continuous outcome and albuminuria as a binary outcome. The statistical significance of the difference in the correlation coefficients will be calculated using the Fisher r-to-z transformation and test for dependent correlations.[21 28]

Sample size estimation

Sample size and minimum detectable difference calculations were based on 80% statistical power and a two-sided alpha level of 5%. Based on the results of these calculations as described below, we plan to enrol 630 participants in the proposed study and the detectable differences assume that 600 (~95%) participants will have complete data. Estimates of complete data are based on our prior studies.[29 30] For aim 1, we will have 80% statistical power to detect a difference between the absolute value of the difference between unattended office SBP and awake SBP on ABPM versus the absolute value of the difference between attended office SBP and awake SBP on ABPM of 1.5 and 1.2 mm Hg assuming an SD of 15 mm Hg for each SBP measurement and correlations between the two SBP measures of 0.5 and 0.7, respectively.[31–35] For DBP and assuming an SD of 10 mm Hg, the detectable difference is 1.3 mm Hg and 1.1 mm Hg for correlations between the two DBP measures of 0.5 and 0.7, respectively. In a subgroup of 160 participants (eg, race subgroups) and correlations of 0.5 and 0.7, we can detect an absolute difference with awake BP assessed by ABPM and unattended versus attended clinic BP of 3.1 and 2.4 mm Hg for SBP and 2.7 mm Hg and 2.2 for DBP. For aim 2, we assumed an SD of sleep SBP of 15 mm Hg and sleep DBP

Table 3 Minimal detectable correlation coefficients between blood pressure measurements and LVMI

Correlation between BP measurements*	Correlation coefficient between BP measurements and LVMI		
	0.30	0.50	0.60
	Minimal detectable difference		
0.5 (N=600)	0.11	0.09	0.08
0.7 (N=600)	0.08	0.07	0.07
0.5 (N=160)	0.18	0.15	0.13
0.7 (N=160)	0.14	0.12	0.11

80% power; two-tailed α=0.05.
*BP measurements could include attended and unattended systolic BP or sleep systolic BP on ambulatory BP monitoring and home BP monitoring.
BP, blood pressure; LVMI, left ventricular mass index.

of 10 mm Hg on ABPM and HBPM, a correlation between sleep SBP (alternatively, DBP) on ABPM with HBPM of 0.5.[36] Under these assumptions, we will have 80% statistical power to detect an absolute mean difference equal to or greater than 2.1 mm Hg for SBP or 1.4 mm Hg for DBP comparing sleep BP assessed by ABPM versus HBPM. For aim 3, the minimum detectable difference in correlation coefficients depends on the correlation between attended and unattended office BP and the correlation of attended office BP with LVMI, as displayed in table 3.

Ethics and dissemination

Informed consent

Each individual who expresses interest in participating in the study receives information about its aims and procedures. They are being informed of the associated risks and the freedom to withdraw at any time. We are obtaining a signature from each individual on an informed consent document and HIPAA forms prior to initiating any study procedures. A research coordinator is cosigning the informed consent document.

Ethics review and dissemination

This study is being conducted in compliance with the UAB and the CUIMC Institutional Review Boards. Results of the study will be disseminated at scientific meetings and in peer-reviewed scientific journals.

Additional potential limitations of the study design

A potential limitation includes the exclusion of individuals taking antihypertensive medication. Although ABPM can also be used to monitor on-treatment BP for people with hypertension and who are taking antihypertensive medication, this is a less common recommendation. Another potential limitation is that ABPM instead of HBPM is assumed to be a reference standard for measuring awake BP. We have chosen to use ABPM rather than HBPM to assess awake BP because it is widely considered the reference standard for out-of-office BP assessment and confirming hypertension status. Further, conducting HBPM to assess awake BP was not practical for the proposed study because it requires up to 7 days of measurements, which will confound the ability to assess the tolerability of the HBPM device for assessing sleep BP, based on a single night.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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Data availability statement Data are available upon reasonable request. This is not a clinical trial therefore no data will be shared except with sponsors as requested.

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