Evaluating novel approaches for estimating awake and sleep blood pressure: The Better BP Study

Study Protocol & Statistical Analysis Plan

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BETTER BP STUDY

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Administrative Information

Title: Evaluating novel approaches for estimating awake and sleep blood pressure (The Better BP Study)

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Introduction

Background and Rationale

Compared with other risk factors, elevated BP is associated with more CVD events and BP is associated with more CVD events and disability-adjusted life years lost in the US and worldwide. To identify patients with hypertension and monitor their BP while taking antihypertensive medication, most US guidelines and scientific statements recommend BP be measured in the clinic setting by a trained healthcare professional. This recommendation is supported by extensive data, demonstrating that elevated BP, measured using this approach, is associated with increased risk for CVD and renal disease events. In clinical practice and research studies conducted in the US, BP is almost universally measured in the clinic with an observer present (attended clinic BP).

Several studies have found that compared with attended clinic BP, BP measured outside of the clinic is a better predictor of a person's CVD risk. The US Preventive Services Task Force (USPSTF) and the UK National Institute for Health and Care Excellence recommend that elevated BP measured in the clinic be confirmed by out-of-clinic BP measurements prior to diagnosing hypertension. ABPM is the reference standard for out-of-clinic BP assessment and making the diagnosis of hypertension. ABPM monitors are compact, worn on a belt or in a pouch, and connected to a BP cuff on the upper arm by a tube. The monitors are programmed to obtain readings using the oscillometric method, every 15 to 30 minutes, typically for 24 hours, throughout the day and night.

In some people, there is a transient BP increase that occurs in the clinic setting (i.e., white coat effect). For others, BP is lower in the clinic when compared to measurements obtained outside of the clinic environment (i.e., masked effect). White coat hypertension is defined as hypertension based on clinic-ma≥ 140 mm Hg the clinic setting (awake BP < 135/85 mm Hg). In most ABPM studies, white coat hypertension has not been associated with increased CVD risk. In contrast, masked hypertension, defined as not having hypertension based on BP measured in the clinic setting (< 140/90 mm Hg) but hypertension based on out-of-clinic measurements (awake BP ≥ 155 mm Hg) is associated with a markedly increased CVD risk. Among adults with SBP/DBP ≥ 140 mm Hg white coat hypertension. Additionally, between 15% and 30% of adults with SBP/DBP < 140/90 mm Hg, defined using attended BP measured in the clinic, have masked hypertension.

There is a diurnal pattern of BP, which normally falls to its lowest level during sleep. Nocturnal hypertension, defined by having high mean sleep BP (SBP/DBP ≥ 120/70 mm Hg) with an increased risk for CVD events, independent of BP measured in the clinic and awake BP on ABPM. Assessing sleep BP may be particularly important for African Americans, a population with high CVD risk and approximately two times higher prevalence of nocturnal hypertension compared with whites. In the Jackson Heart Study (JHS), a cohort comprised exclusively of African Americans, 60% of participants had nocturnal hypertension and the multivariable-adjusted hazard ratio for CVD events was 1.84 (95% CI: 1.00, 3.38) comparing participants with and without nocturnal hypertension. Also, a high percentage of African Americans with nocturnal hypertension do not have hypertension based on clinic BP or awake BP on ABPM.

Until recently, ABPM has been the only method that could assess sleep BP. The misdiagnosis of hypertension when BP is measured by an observer in the clinic versus by ABPM is well recognized by guidelines, scientific statements, and position papers. However, there are several challenges that have prevented the wide-spread use of ABPM in clinical practice. Recently, we conducted a nominal groups study, a qualitative research approach, with 40 physicians in Alabama and New York to identify barriers to performing ABPM. Reported barriers included need for staff training, time constraints in patient preparation, and lack of infrastructure and inaccessibility of equipment and specialists to whom providers could refer their patients for the ABPM procedure. Also, ABPM devices cost over $2,000 each, insurance companies do not commonly reimburse for indications other than white coat hypertension, and when reimbursed, the compensation is low.

Low patient tolerability for ABPM has been reported in previous studies. For example, in one study, side effects associated with ABPM ranged from 7% for bruising to 70% for the device awakening the participant during sleep. Given the real world limitations of ABPM, novel approaches are needed for measuring awake and sleep BP. An emerging method that has been proposed for estimating awake BP is to measure BP in the clinic using a fully automated oscillometric device (AOBP) without an observer being present (unattended clinic BP measurement). There are currently two validated oscillometric devices available in the US (Omron HEM-907XL and Microlife's Watch BP office) that can be programmed to measure BP automatically without an observer being present. Using these devices, the technician or healthcare provider leaves the room after a person has a BP cuff placed on their arm and they are positioned for measurements. After a minute rest, the device inflates the cuff and BP is measured. AOBP devices can obtain several BP measurements at preset (e.g., one minute) intervals. The maker of BPTru, a third device, went out of business in 2017.

Canadian studies suggest that patients with hypertension have lower unattended BP compared with attended BP. Therefore, the use of unattended clinic BP may result in a lower prevalence of white coat hypertension. In a pooled analysis of 8558 adults, the mean clinic BP was 10/7 mm Hg lower with unattended AOBP versus BP recorded by a provider in clinical practice by auscultation and a mercury sphygmometer. In the only randomized study of AOBP published to date, the difference between BP when measured observed and unobserved was small (< 5 mm Hg). In 2017, the Hypertension Canada guideline recommended unattended BP (i.e., AOBP) as the preferred method of clinic BP measurement.10 However, this recommendation was based on a Grade D level of evidence (i.e. quality of evidence is very low, based on expert opinion, no direct research evidence, and studies had very severe limitations). US guidelines do not currently recommend AOBP for use in clinic practice. Recently, in a post-hoc analysis of SPRINT data, there was no difference in clinic BP between sites that measured it unattended versus attended (manuscript under review at Hypertension, personal communication, S. Oparil). At each visit, SPRINT participants did not have both unattended and attended BP measurements; there was no randomization; information about the conduct of unattended or attended BP measurements was obtained retrospectively after study end; and no comparison to ABPM was made. There is currently equipoise as to whether unattended clinic BP provides an accurate estimate of awake BP on ABPM.

Two issues have been raised as barriers to implementing AOBP in clinical practice: the time it takes to perform this procedure and the need for dedicated space. Although AOBP takes longer than unstandardized clinic BP measurement (clinic BP taken without following guideline-recommended approaches), AOBP takes a shorter amount of time than clinic BP measurements taken following American Heart Association (AHA) recommendations. Further,

unstandardized clinic BP measurements are very common in clinical practice, generate poor estimates of BP, and interventions targeted at observers to obtain standardized clinic BP have been largely unsuccessful. Having a dedicated room to perform unattended BP has been reported as a barrier to AOBP. However, if clinic space is not available, unattended AOBP can be successfully performed while a patient is in a waiting room.

Recently, home BP monitors (HBPM) have been adapted to measure asleep BP. As described below, there are compelling preliminary data supporting this approach. Until recently, sleep BP could only be assessed by ABPM. HBPM devices have been developed that measure BP automatically during sleep. These devices have been previously validated for accuracy. Before going to sleep, a person attaches a BP cuff to their arm and turns on the HBPM device, which is programmed to take BP measurements while the person is asleep. In a prior study conducted in Japan, an HBPM device (Omron HEM-5001) was programmed to obtain BP measurements at 2am, 3am and 4am. Given that only three readings are obtained during the sleep period and that a prior study demonstrated the feasibility for measuring sleep BP, there is great potential for using these HBPM devices for accurately measuring sleep BP with less burden than ABPM. Table 3 shows the major limitations of published studies using HBPM to assess sleep BP. In the current study, we will test whether HBPM is an accurate and better tolerated approach for measuring sleep BP than ABPM.

Objectives

Primary Aim 1: To examine whether measuring unattended clinic BP with an automated device will provide a more accurate estimate of awake BP on ABPM than measuring attended clinic BP with an automated device. Hypothesis 1a: The absolute difference with awake BP will be smaller for unattended vs. attended clinic BP. Hypothesis 1b: The agreement between hypertension status using BP measured in the clinic and on ABPM while awake will be higher when clinic BP is measured unattended vs. attended. Also, the prevalence of both white coat and masked hypertension will be lower when measuring unattended clinic BP.

Primary Aim 2: To examine whether a new HBPM device provides an accurate approach for measuring sleep BP. Hypothesis 2a: Sleep BP on HBPM will provide an accurate estimate of sleep BP on ABPM. Hypothesis 2b: HBPM will be better tolerated (e.g., less awakening during sleep, pain, bruising) than ABPM.

Primary Aim 3: To compare the associations of unattended versus attending clinic BP, unattended clinic BP versus awake BP on ABPM, and sleep BP on HBPM versus ABPM with two markers of end-organ damage, left ventricular mass index (LVMI) and urinary albumin-to-creatinine ratio (ACR). Hypothesis 3a: The association with end-organ damage will be stronger for unattended vs. attended clinic BP. Hypothesis 3b: The association with end-organ damage will be similar for unattended clinic BP and awake BP. Hypothesis 3c: The association with end-organ damage will be similar for sleep BP by HBPM and ABPM.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Age 19 years or older
- Mean screening systolic blood pressure of 110 to less than 160 mm Hg **or** mean screening diastolic blood pressure of 70 to less than 100 mm Hg

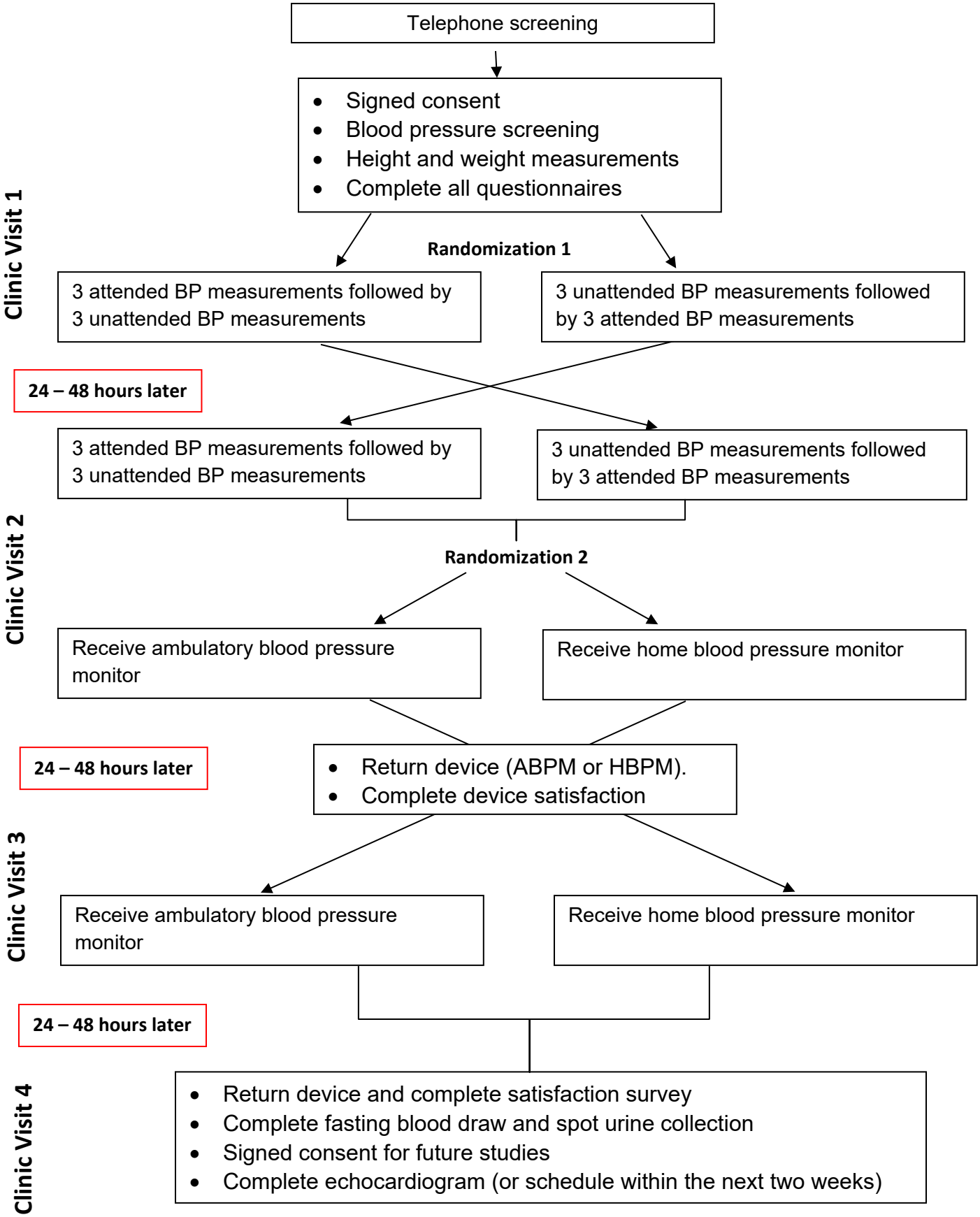
Exclusion Criteria:

- Taking antihypertensive medications
- Known to be pregnant
- History of sleep apnea
- History of cardiovascular disease, atrial fibrillation, and/or ventricular tachycardia
- High risk for sleep apnea, scoring 5 or greater on the STOP-BANG questionnaire
- Participants who work overnight shifts (11PM-7AM)
- Inability to wear the ABPM and/or HBPM devices and BP cuffs
- Completed ABPM in the past year
- No permanent residence

Sites of Recruitment: Columbia University Medical Center and University of Alabama at Birmingham

Target sample size: 315 participants with complete data.

Study Flow


Telephone screening
Signed consent
Blood pressure screening
Height and weight measurements
Complete all questionnaires
Clinic Visit 1
Randomization 1
3 attended BP measurements followed by 3 unattended BP measurements
3 unattended BP measurements followed by 3 attended BP measurements
24 – 48 hours later
3 attended BP measurements followed by 3 unattended BP measurements
3 unattended BP measurements followed by 3 attended BP measurements
Clinic Visit 2
Randomization 2
Receive ambulatory blood pressure monitor
Receive home blood pressure monitor
24 – 48 hours later
Return device (ABPM or HBPM).
Complete device satisfaction
Clinic Visit 3
Receive ambulatory blood pressure monitor
Receive home blood pressure monitor
24 – 48 hours later
Clinic Visit 4
Return device and complete satisfaction survey
Complete fasting blood draw and spot urine collection
Signed consent for future studies
Complete echocardiogram (or schedule within the next two weeks)

Recruitment Procedures

Potential participants will be recruited using flyers and contact cards placed around UAB campus and UAB primary care clinics.

There are three methods in which the participant may be contacted/contact us.

1. If the participant returns the contact card, contact the participant using their preferred method (e.g. - phone call or email).
    a. If the participant prefers to be contacted via phone, please call them during their **preferred day and time** as indicated on the contact card.
    b. If the participant prefers to be contacted via email, please refer to the draft email to schedule a screening visit to discuss the study and determine their eligibility (**Appendix 1**).

2. If the potential participant calls in to ask about the study, invite them to a screening visit to determine their eligibility (**Appendix 1**).

3. If the potential participant emails the study (bpstudy@uab.edu), use the draft email (**Appendix 1**) to schedule a screening visit to discuss the study and determine their eligibility.

Once you have confirmed the potential participant is eligible for the study, confirm that the participant will be able to attend all four study visits over a short period of time (within 1-2 weeks). Schedule their first study visit and provide them with a participant packet which will include the following:

1. ***Consent Form*** *– Ask them to read through this carefully but do not sign prior to their first visit.*
2. ***W9 Form*** *– Inform them that they will need to fill this out for compensation*
3. ***Parking decal*** *for the UAB Hypertension Research Clinic*
4. ***Directions and a parking map*** *for the UAB Hypertension Research Clinic*

Remind the participants of the following before their first study visit:

1. Please wear a loose fitting shirt or button down shirt with an undershirt so that we can properly place your blood pressure cuff on their bare skin.

2. Refrain from smoking, exercise, eating food, or drinking any caffeinated beverage (including soda and tea) 30 minutes prior to your first clinic visit.

Participant Scheduling

Following telephone screening, participants who are preliminarily eligible for inclusion in the study should be scheduled within the next **2 weeks** for their screening visit with the study coordinator at the UAB Hypertension Clinic.

To access the schedule and schedule a participant, please do the following:

1. Log-in to REDCap using your log-in credentials.
2. In the left-hand column, please select ‘Calendar’.
3. Select the ‘Month’ tab at the top of the calendar.
4. Click on ‘+New’ on a day that has **less than 4 participants scheduled.**
5. Confirm with the participant that they are available on that day.
6. Ask the participant a time they would like to come in for their screening visit and enter the time in the ‘Time:’ box.
7. In the ‘Notes’ section, please enter the participant’s first and last name.
8. Using the drop-down menu next to ‘Record ID’, please select the participant’s record id number.
9. After you have entered all information, please click ‘Add Calendar Event’.

After scheduling the participant, please email or call the study coordinator to inform her of the new participant added to the schedule.

If the participant needs to re-schedule, please make the necessary change to the REDCap calendar by clicking on their calendar event and entering their new date and time. Please make sure you save both the new date and new time. Inform the study coordinator of the change to the calendar.

Summary

During the screening process, participants will complete an initial telephone screening to determine their preliminary eligibility. If eligible, they will be asked to complete a blood pressure screening in the clinic to determine if they are eligible to continue in the study.

There is a consent addendum that was prepared for the Better BP study. Participants will be consented immediately prior to initiation of this study.

Below are the steps to follow for participants who are eligible and consent for the Better BP study.

1. Participants will be randomized to have their clinic blood pressure measured unattended or attended first using a Microlife WatchBP Office AFIB device. Blood pressure will be measured three times in the non-dominant arm following a standard protocol. They will then have their blood pressure measured three times again using the opposite method (i.e. if attended first, then unattended second).

2. The following questionnaires will be administered to participants:
    a. Sociodemographic/Medical History
    b. Pittsburgh Sleep Quality Index (PSQI)

    Whenever possible, these questionnaires will be self-administered. Research coordinators can administer these questions orally for participants who would otherwise have difficulty completing questionnaires on their own.

3. Measure height, weight, and waist and neck circumference. Neck circumference is needed for the STOP-BANG sleep apnea scale.
4. Participants will then return to the clinic for the next visit in 24 to 48 hours and have their clinic blood pressure measured three times unattended and attended in the reverse order of visit 1 using the Microlife WatchBP Office AFIB device.
5. Participants will be randomized to receive either the ABPM or HBPM device at visit 2.
6. They will be fitted for the device (WatchBP O3 ABPM or WatchBP Home N) that they were randomized to receive first.
7. The staff member will explain how the participant should act when a BP measurement is taken.
8. One measurement will be taken – check to make sure the cuff inflates and deflates and that a valid reading is obtained. Watch to make sure that the participant positions their arm as instructed. If an error reading is obtained, check that the cuff is properly placed and neither too tight nor too loose, and retake the BP measurement. If three consecutive error readings are obtained, try a different device.
9. Participants will be given instructions for placing (Home N) or replacing (O3 ABPM) the device if it has to be removed.
10. Participants will be given a phone number to call if they have any questions during the monitoring period.
11. Participants will be given the appropriate (ABPM or HBPM) device log to fill out. This form captures the time a participant goes to sleep and awakens. Additionally, this form can be used to document any time when a participant removes the device and puts it back on.

12. The Actiwatch device will be fitted.
13. The next day, participants will return the device and device log, complete either the post-ABPM or post-HBPM questionnaire based on what device was worn, and be fitted for the opposite device (either O3 ABPM or Home N).
14. At the last visit, participants will return the device and device log and complete either the post-ABPM or post-HBPM questionnaire based on what device was worn.
15. Participant will complete the comparability questionnaire.
16. Participants will complete a non-fasting blood draw and spot urine.
17. Participants will complete an echocardiogram. If the echo lab does not have availability for that day, schedule their echocardiogram within the next two weeks.

Participants will return to the clinic the next day to return their ABPM/HBPM devices and actigraphy (Actiwatch) devices and the participant device log.

Upon returning the devices, the technician will:

1. Review the device log with the participant, verifying times the participant went to sleep, woke up, and took device(s) off. If the participant does not return the device log (or it is blank), be sure to fill it out at the return visit.
2. Download the data from the ABPM, HBPM, and actigraphy devices.
3. Confirm that at least 35 of planned ABPM readings are valid or all three HBPM readings are valid. If this is not the case, the participant will be offered the opportunity to complete a second ABPM or HBPM (along with actigraphy and filling out the participant device log).

For participants who have a complete ABPM (or for those who have the device picked up at their house), the participant device log will be checked for completeness, scanned and saved electronically. Next, we will administer the post-ABPM study visit form.

Upon completion of the physical exam and echocardiogram, we will then process their reimbursement. The participants will receive reimbursement through the mail.

When clinic staff will handle the return of the ABPM/HBPM:
For participants for whom the device is picked up at their house or who mail in the device, the forms/device will be delivered to the clinic staff. The staff member will check to confirm that at least 35 valid ABPM readings or 3 valid HBPM readings were obtained and that the post-ABPM questionnaire has been completed. If ≥ 35 valid ABPM readings are obtained, they will be processed as described in the manual of procedures.

Overview of Better BP Study Visits

The Better BP study involves five visits. Ideally, all five visits will occur within 24-48 hours of each other. For some participants the next visit will not occur within this timeframe; however, the next visit should be scheduled as soon as possible.

The screening visit will take approximately 10 minutes to conduct including signing of the consent form and blood pressure screening. If eligible, the participant will continue on with their first study visit.

The first study visit will take approximately 45 minutes to conduct including the initial five-minute rest prior to obtaining clinic blood. This visit includes confirming eligibility, obtaining three clinic blood pressure measurements both attended and unattended (randomized order), and completing two questionnaires (Sociodemographic/Medical History and Pittsburgh Sleep Quality Index). The visits for this study will be conducted in a separate room or, at minimum, in an area properly screened from all other activity and participants in the UAB Hypertension Research Clinic.

The second study visit will include an additional three clinic blood pressure measurements, both attended and unattended, in the reverse order of visit 1 and fitting the participant for the ABPM or HBPM device (randomized) and Actiwatch.

The third study visit will include the participant returning their device (ABPM or HBPM) and device log, confirmation that an adequate number of blood pressure readings were obtained, and completion of a post-ABPM or post-HBPM questionnaire (based on the device worn previously). The participant will then be fitted for the opposite device (either ABPM or HBPM) and receive a device log.

The fourth study visit will include the participant returning their device (ABPM or HBPM) and device log, confirmation that an adequate number of blood pressure readings were obtained, and completion of a post-ABPM or post-HBPM questionnaire (based on the device worn previously). They will also complete the comparability questionnaire. The participant will have a brief physical exam which includes a non-fasting blood draw and spot urine collection. Finally, the participant will complete an echocardiogram. Upon completion of the echocardiogram, participants will receive reimbursement through the mail.

MOP items

Initial visit

Information from this visit will be recorded on the Better BP study Visit 1 Data Collection Form.

1. **Consent participant and measure screening blood pressure to confirm participant eligibility.**
2. **Measure height, weight, and waist and neck circumference.**
3. **Take non-dominant arm circumference measurement.**
4. **Identify randomization assignment for unattended and attended clinic BP measurement.**
5. **Clinic BP measurements (unattended and attended, in randomized order).**
6. **Questionnaire administration:**
    a. **Sociodemographic/Medical History**
    b. **Pittsburg Sleep Quality Index (PSQI)**

Visit 2

Information from this visit will be recorded on the Better BP study Visit 2 Data Collection Form.

1. **Clinic BP measurements (reverse order of study visit 1).**
2. **Identify randomization assignment for ABPM and HBPM.**
3. **ABPM or HBPM fitting and guidance (based on randomization).**
4. **Actiwatch fitting and guidance.**

Visit 3

Information from this visit will be recorded on the Better BP study Visit 3 Data Collection Form.

1. **Download ABPM or HBPM and Actiwatch data and check completeness.**
2. **Review device log with participant for completeness and accuracy.**
3. **Complete post-ABPM or post-HBPM questionnaire (based on device worn).**
4. **ABPM or HBPM fitting and guidance (opposite device of visit 2).**

Visit 4

Information from this visit will be recorded on the Better BP study Visit 4 Data Collection Form.

1. **Download ABPM or HBPM and Actiwatch data and check completeness.**
2. **Review device log with participant for completeness and accuracy.**
3. **Complete post-ABPM or post-HBPM questionnaire (based on device worn).**
4. **Complete comparability questionnaire.**
5. **Brief physical exam (non-fasting blood draw and spot urine collection).**
6. **Echocardiogram**
7. **Processing of reimbursement**

Preparation for Visit 1 (Day of Appointment – before the participant arrives to the UAB Hypertension Research Clinic)

- Just prior to the scheduled appointment, the research coordinator (RC) should do the following:
  - Confirm the participant is eligible:
    - Is their screening SBP between 110-159 mm Hg or DBP between 70-99 mm Hg and SBP < 160 mm Hg and DBP < 100 mm Hg?
    - Not currently taking antihypertensive medication?
    - No history of myocardial infarction, stroke, or arrhythmias?
    - Not currently pregnant?
    - Do they have an arm available for placement of a BP cuff?
    - Arm circumference <=52 cm?
    - Can rest their arm every 30 minutes for 24 hours to allow for a BP measurement?
    - Has not had an ABPM in the past year?
    - Does not work at night (or is completing ABPM on a non-work day with a one day wait following working the night shift)?
    - Is willing to return to the clinic after both the ABPM and HBPM periods to return the devices?
    - STOP-BANG score less than 4?
    - Do you have a permanent residence?

  - Enable REDCap Mobile with the questionnaires (Sociodemographic/Medical History and PSQI).
  - Initialize the WatchBP Office AFIB device.
  - Have the WatchBP Office AFIB device set up for the correct measurement intervals [5-minute initial rest period and 1-minute interval between readings].

For participants who consent for the Better BP study at the beginning of study visit 1, please ask the participant if he/she needs to use the restroom prior to their height/weight/waist/neck measurements.

Use the Study Visit 1 Data Collection Form to record information from the first study visit.

COVID-19 Screening Procedures

Prior to the participant entering the building or exam room for **each in-person study visit**, the research coordinator should complete the following:

1. **Symptom Tracker** (remotely within 24 hours prior to the in-person visit **AND** when they arrive at their in-person visit)

2. **Temperature Check** (when they arrive at the in-person visit)

If the participant screens positive (i.e. **any of the symptoms on the symptom tracker** or have a **fever > 100.4º**), please refer them for testing at their primary care physician. If they do not have a primary care physician, please use the link below to register them for COVID-19 testing at an approved UAB site.

UAB COVID-19 Testing Registration E-form:

https://irap-apps.ad.uab.edu/covidtestrequest/

If the primary care physician oversees COVID-19 testing for the research participant, **written documentation of a negative test result** will need to be provided by the participant or physician to the research study team **within 4 days of testing** in order to proceed with research activities.

Upon completion of the e-form, a nurse from the COVID testing team will contact the research study team to register the research participant for COVID-19 testing. The COVID testing team nurse will also provide detailed instructions on the UAB testing location in addition to what to expect when they confirm the COVID-19 testing appointment. The **results of the test** will be communicated by the testing team nurse to the research subject and the research **team within 24-48 hours**.

COVID-19 testing will be billed to the participant's health insurance (without a deductible applied) OR will be covered through alternative means (such as through the CARES act funding or otherwise). **The participant will not be billed directly.**

If a participant screens positive during their study visits (i.e. after the completion of study visit 1), they have **up to 3 days** to complete their next study visit.

If they are unable to complete their next study visit within 3 days, they will be allowed to restart the study from Study Visit 1 and receive full compensation again for their completion of the study.

NOTE: If they restart the study, please create a new study ID number for them (i.e. 11XX-1) in the REDCap database. Do not delete any data from the REDCap database.

Blood Pressure Screening Procedures

Two BP measurements will be performed using the non-dominant arm, attended (i.e. – technician in the room for the resting and measurement period) following the protocol listed below.

1. Screening BP measurements
    a. Explain to the participant the following:
        i. You will have them turn off their phone and place the phone out of their view but not out of the room
        ii. Have them sit in a firm chair with a flat back
        iii. Have them place their feet flat on the floor
        iv. They should not speak until both blood pressure readings are obtained
        v. After 5 minutes of rest, you will start the blood pressure measurement device
        vi. They will have their blood pressure measured two times at a one minute interval
        vii. They should relax but not move and there should be no talking until the two blood pressure measurements are taken
    a. Connect the BP device to the cuff
    b. Position patient for their BP measurement
    c. Start the device after a 5 minute rest period and stay in the room doing other activities without talking to the participant

Following the measurements, please use the average of both measurements to determine the participant's eligibility for the study.

ELIGIBLE: Systolic BP ≥ 110 mm Hg **or** Diastolic BP ≥ 70 mm Hg

AND

Systolic BP < 160 mm Hg **and** Diastolic BP < 100 mm Hg

INELIGIBLE: Systolic BP < 110 mm Hg **and** Diastolic BP < 70 mm Hg

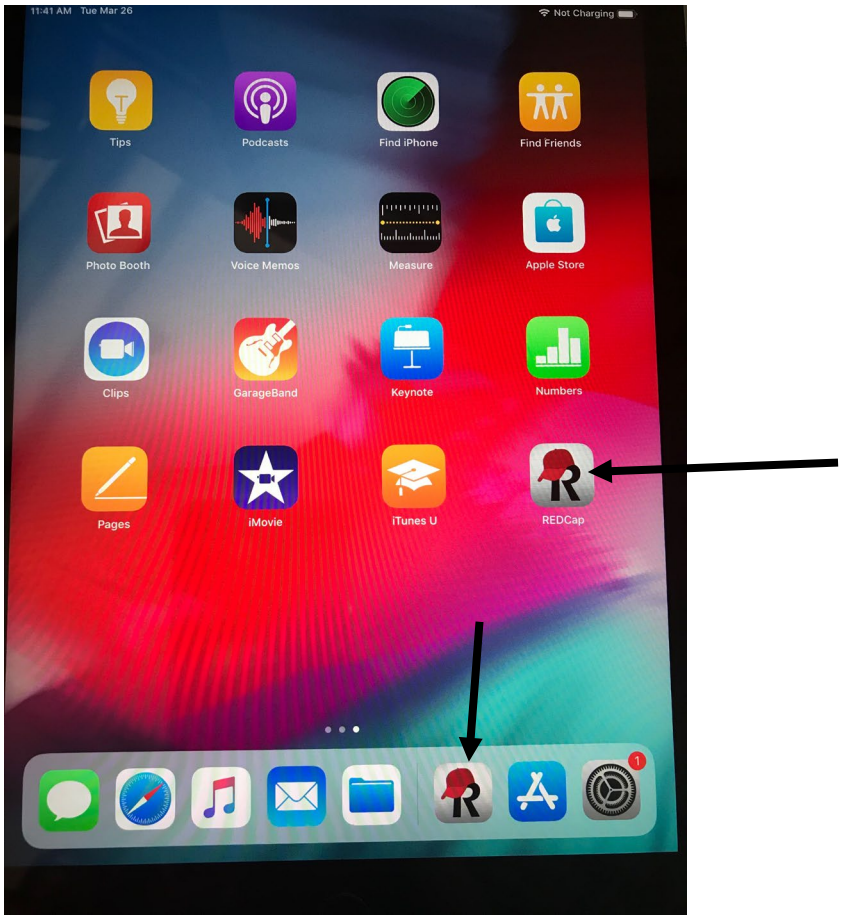
OR

Systolic BP ≥ 160 mm Hg **or** Diastolic BP ≥ 100 mm Hg

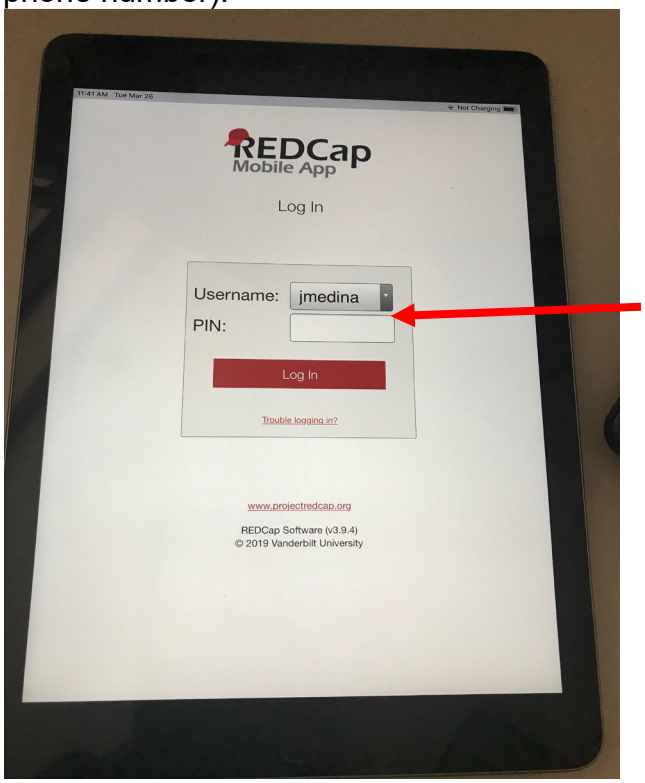
If the participant is **ineligible** based on their average blood pressure readings, please inform them that they will be allowed to re-screen in **1 month** if they would like to.

REDCAP Mobile App

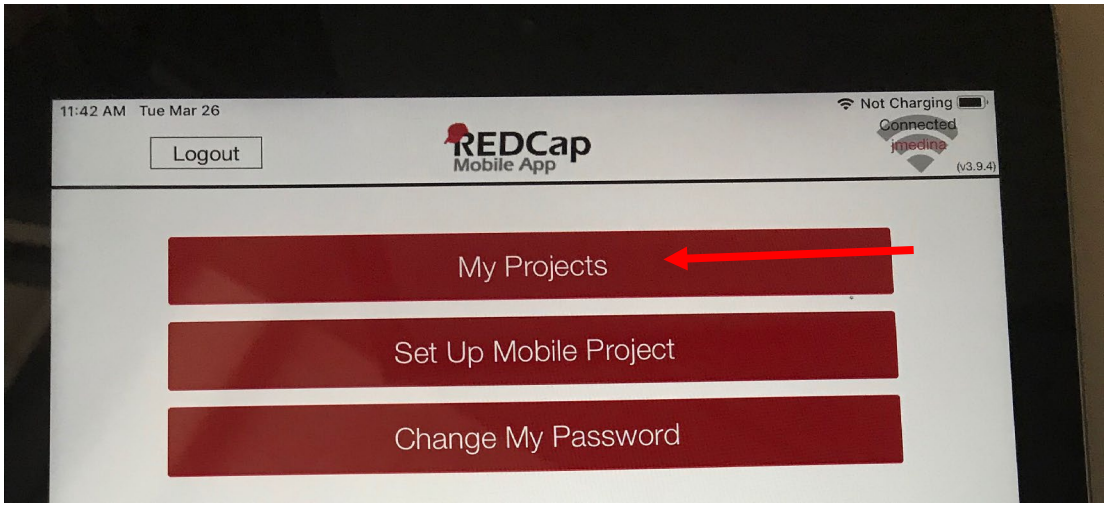
1. Open the REDCap Mobile App on the Ipad.



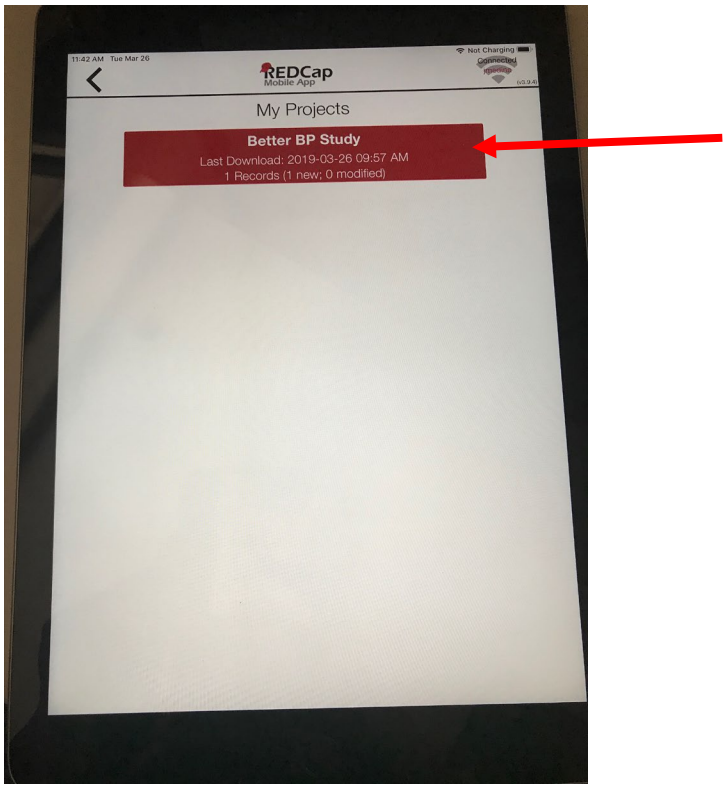
2. Select your username and enter your pin number (e.g. – last six digits of UAB phone number).



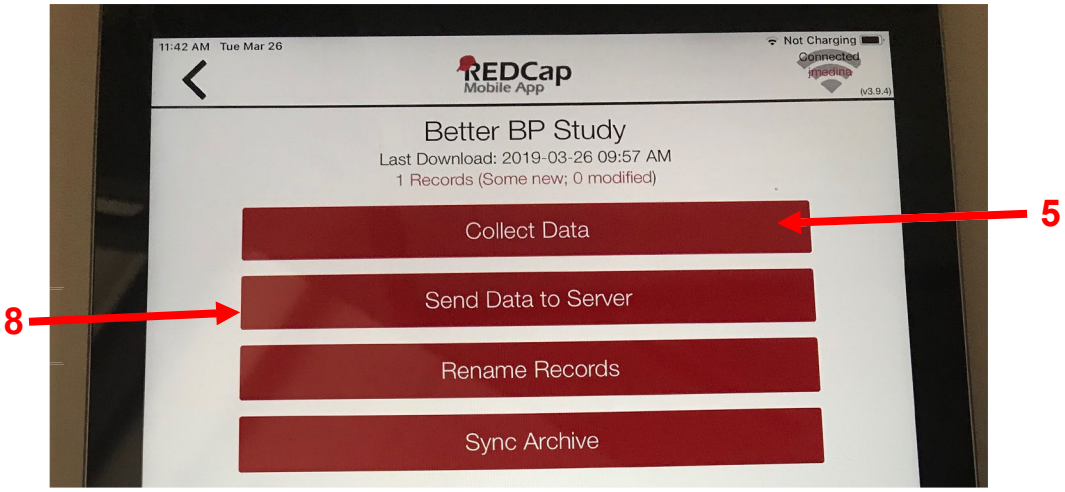
3. Select ‘My Projects’.



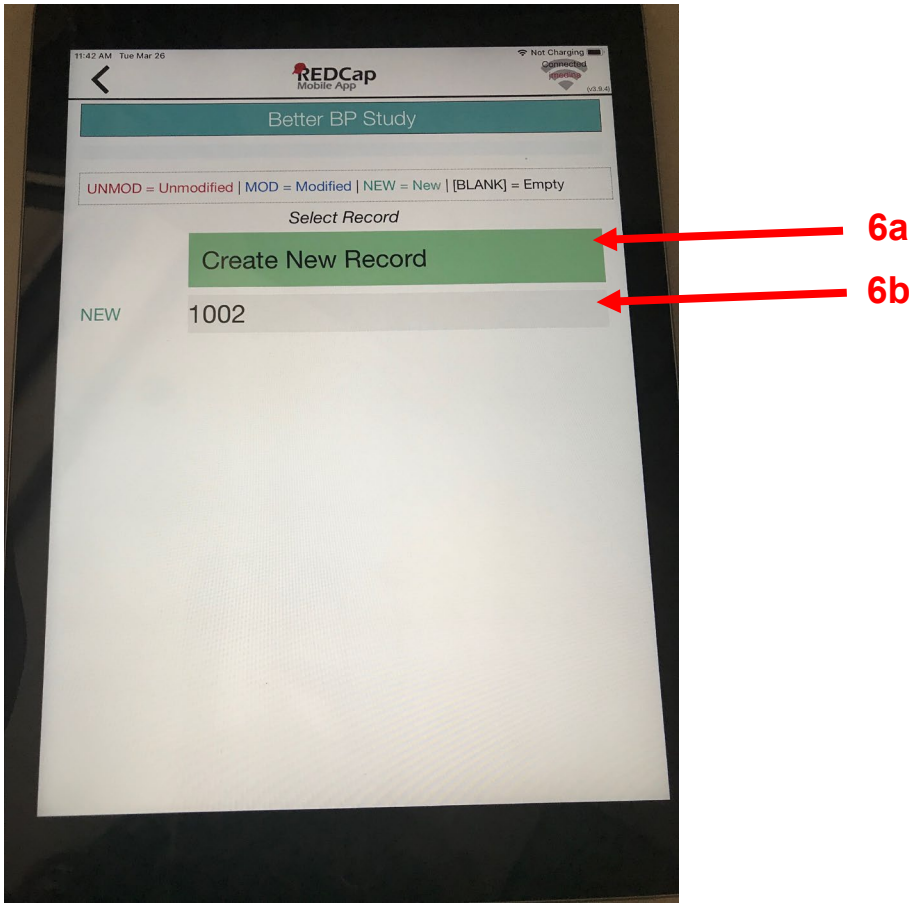
4. Select ‘Better BP Study’.



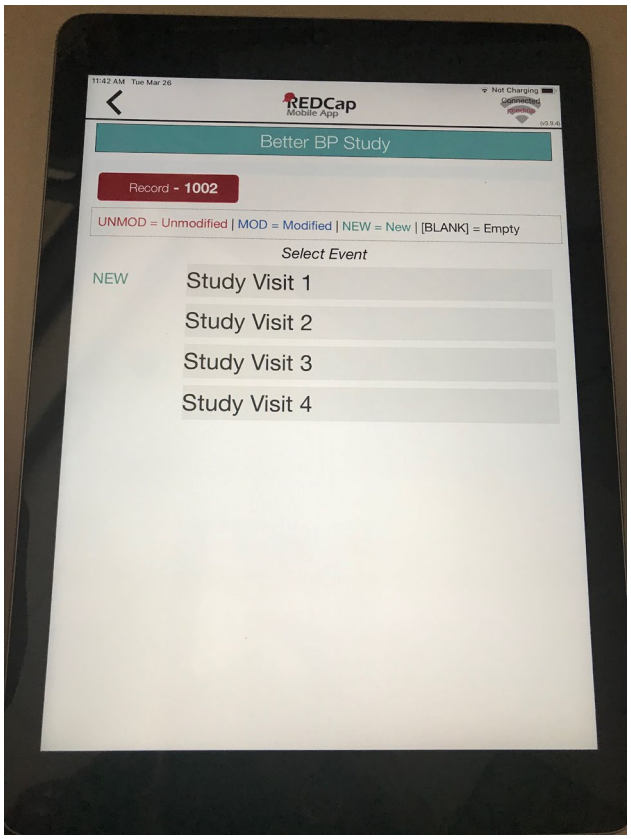
5. Select ‘Collect Data’.



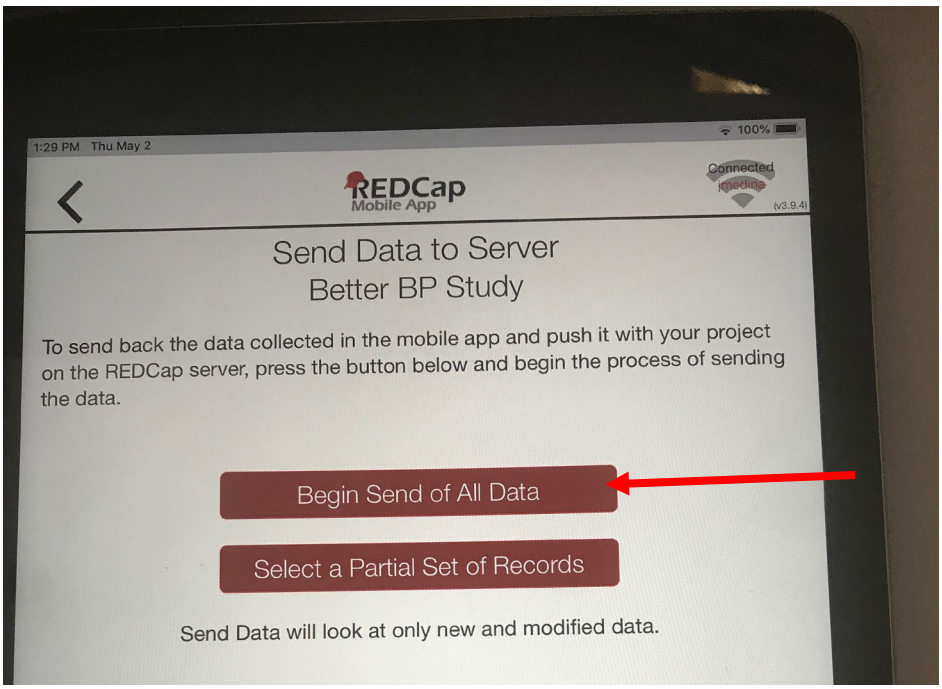
6. Select either of the following:
    a. Participant record id number
    b. If you do not see the participant's record id number, then select 'Create New Record' and enter the participant's record id number.

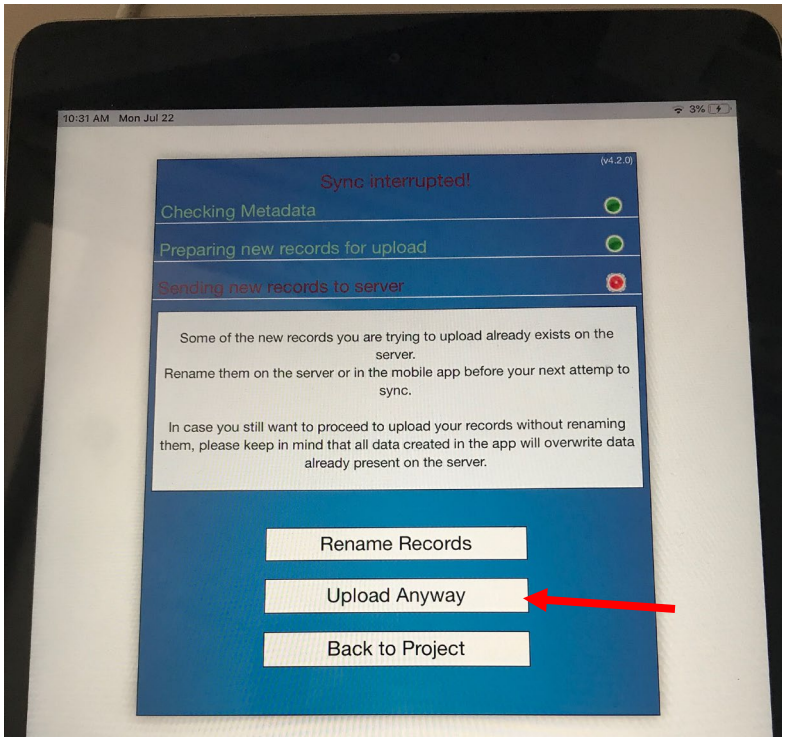


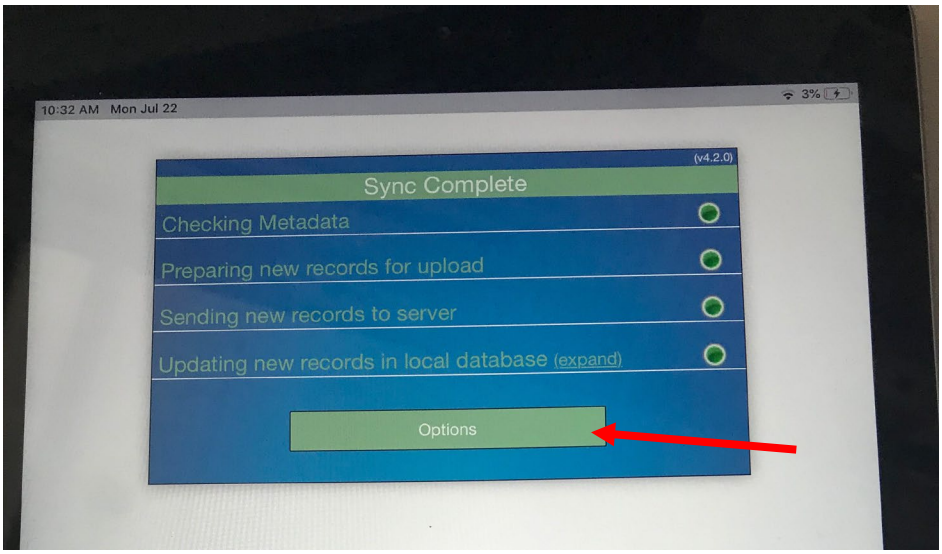
7. Select the study visit and begin entering data on the forms.



8. Once you have collected all the data, select ‘Send Data to Server’ → ‘Begin Send of All Data’ → ‘Sync Modified Records’. **NOTE: If the participant already has data in the server,** select ‘Upload Anyway’.
9. When the sync is complete, select ‘Options’ and ‘Return to Project’ to return to the Home Screen.


1:29 PM Thu May 2
100%
REDCap
Mobile App
Connected
(v3.9.4)
Send Data to Server
Better BP Study
To send back the data collected in the mobile app and push it with your project on the REDCap server, press the button below and begin the process of sending the data.
Begin Send of All Data
Select a Partial Set of Records
Send Data will look at only new and modified data.


10:31 AM Mon Jul 22
3%
(v4.2.0)
Sync interrupted!
Checking Metadata
Preparing new records for upload
Sending new records to server
Some of the new records you are trying to upload already exists on the server.
Rename them on the server or in the mobile app before your next attemp to sync.
In case you still want to proceed to upload your records without renaming them, please keep in mind that all data created in the app will overwrite data already present on the server.
Rename Records
Upload Anyway
Back to Project


10:32 AM Mon Jul 22
3%
(v4.2.0)
Sync Complete
Checking Metadata
Preparing new records for upload
Sending new records to server
Updating new records in local database (expand)
Options

E-Consent Process

If the participant indicates that they would like to complete their paperwork via electronically, **please schedule them for a Zoom conference call** to go over the consent form virtually.

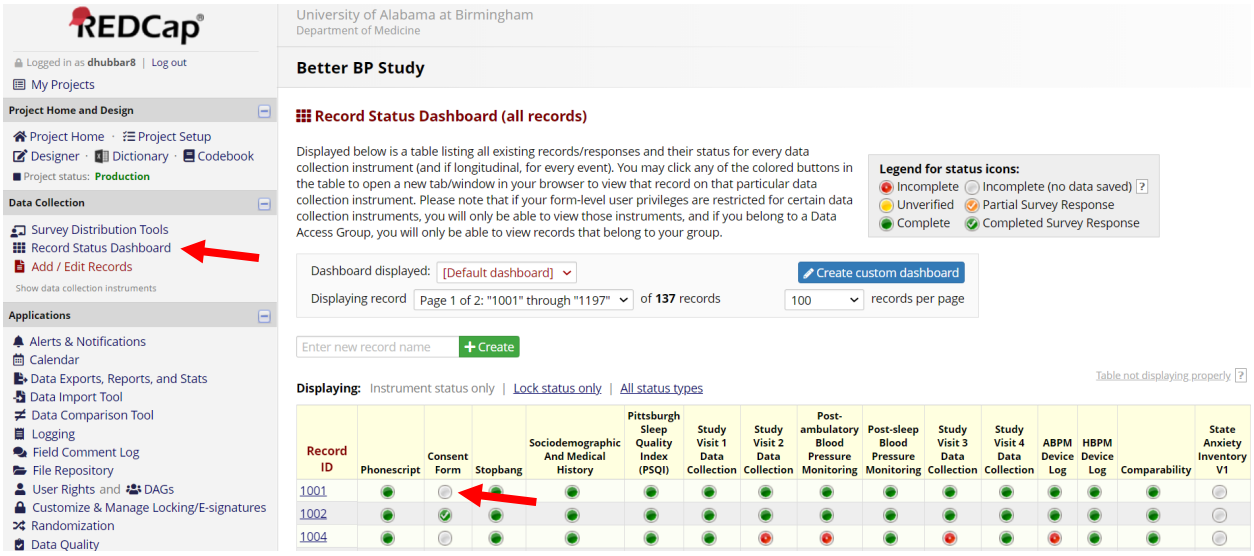
You may send them the PDF version of the consent form to review prior to their Zoom call.

Do not send the REDCap consent form until you are on the Zoom conference call with the participant, as you must observe them completing the form.

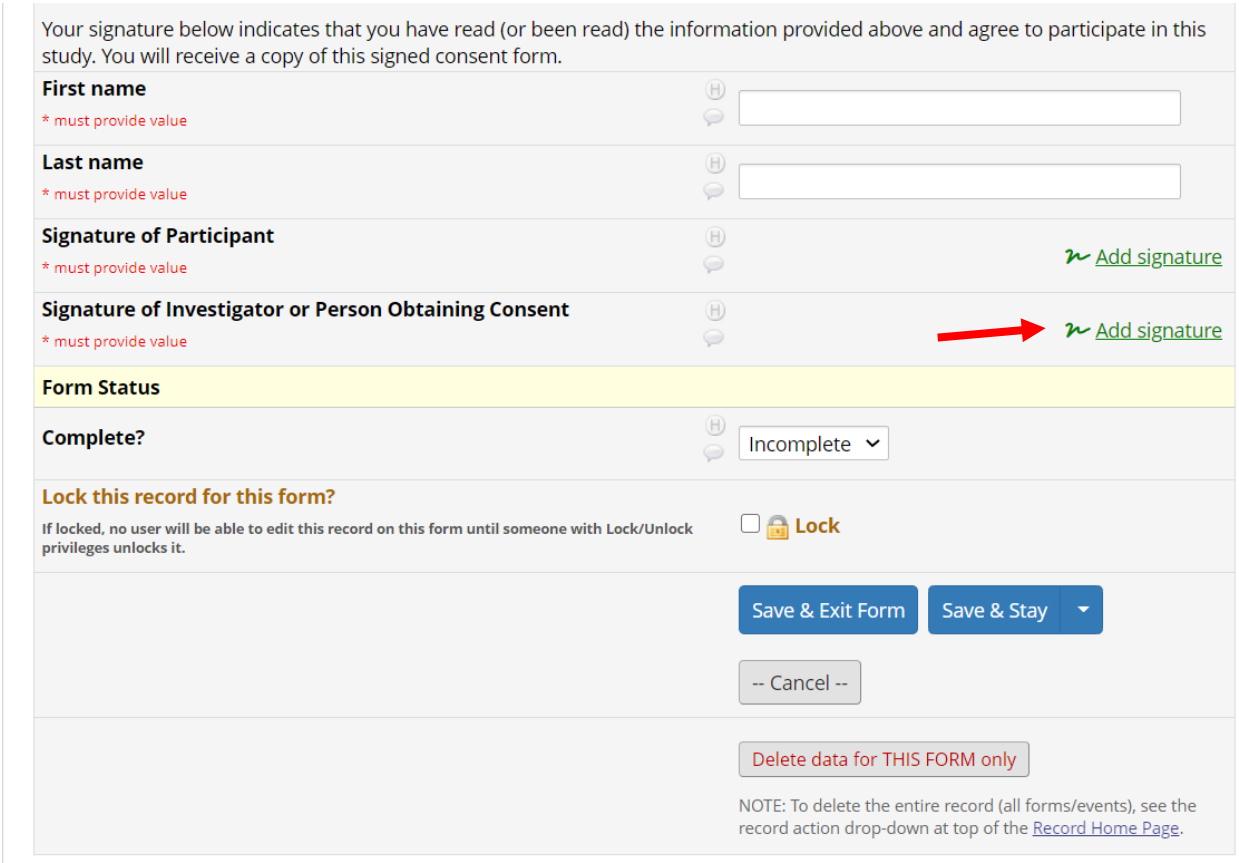
Prior to sending the REDCap consent form, please sign the portion labeled **'Signature of Person Obtaining Consent'.** You will not be able to go back and sign the consent form after the participant completes the form.

The process for sending the REDCap consent form to the participant is below.

1. **Go to the participant's REDCap chart.**
2. **Select 'Consent Form'.**

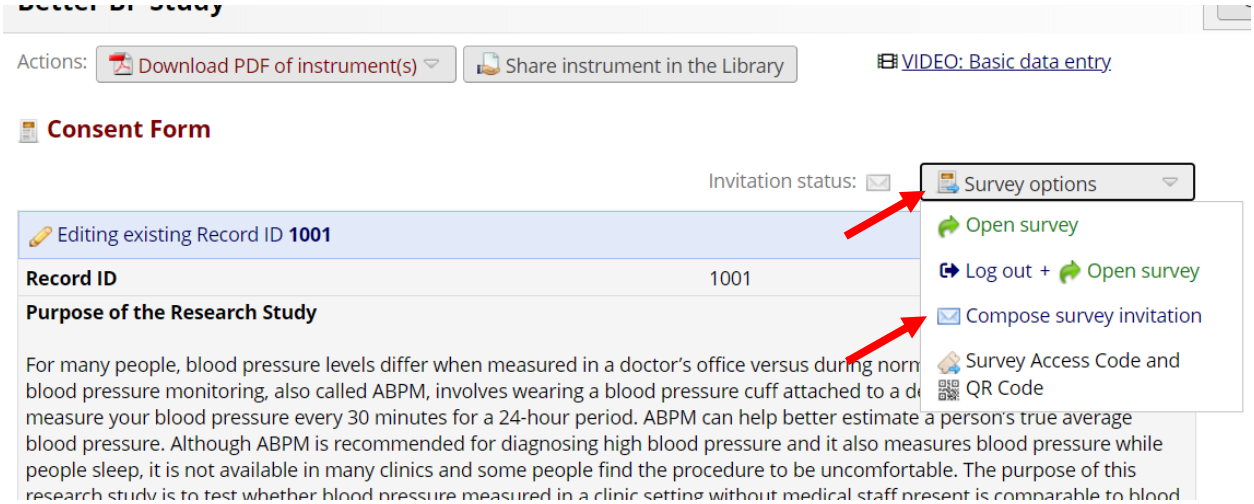


3. **Go to the bottom of the consent form and select 'Sign' in the field labeled 'Signature of Person Obtaining Consent'.**



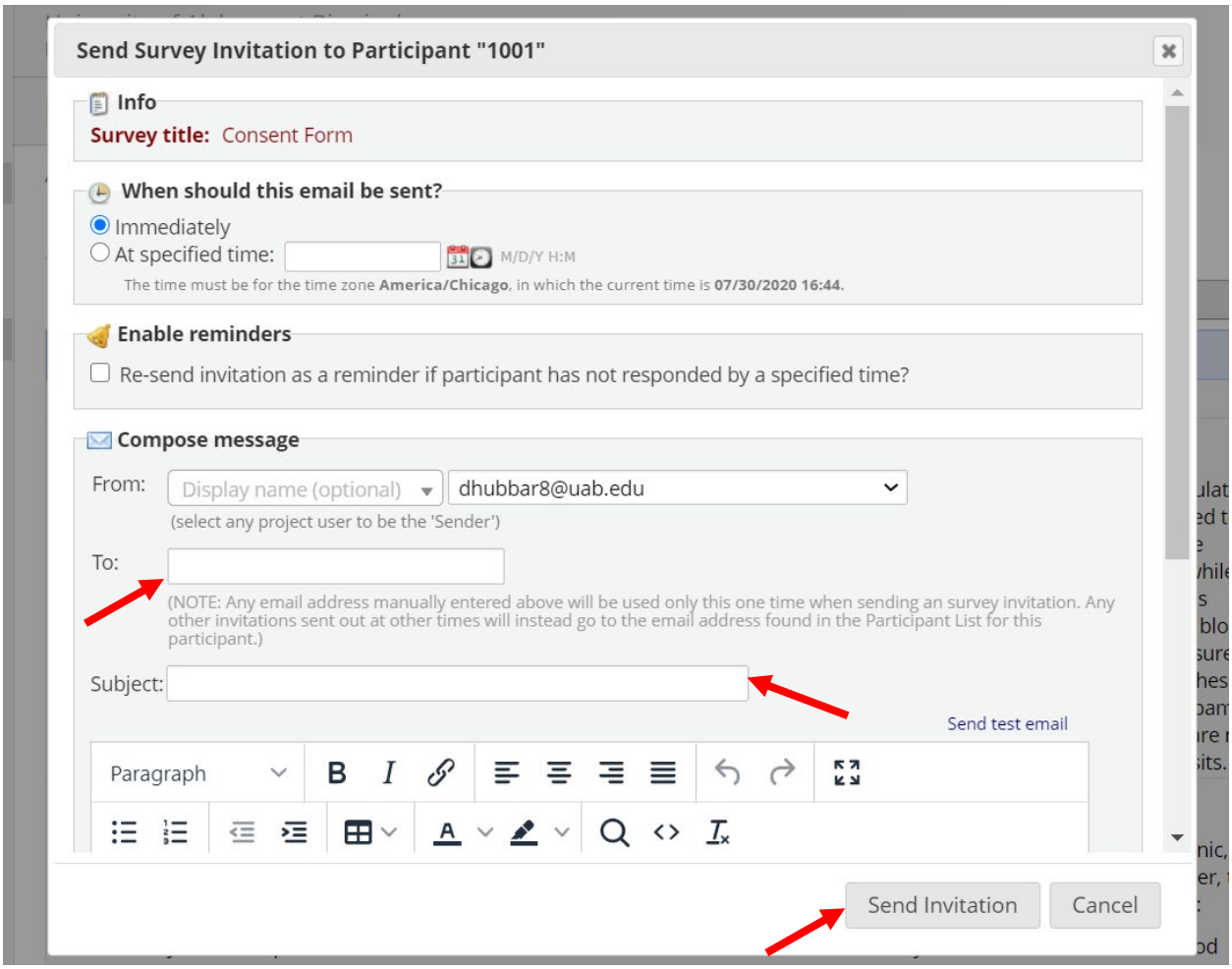
4. **Once you sign, please return to the top of the consent form and select 'Survey Options'.**

5. **Select 'Compose Survey Invitation'.**



6. **Enter the participant's email address that they provide during the Zoom call.**

7. **In the subject box, enter 'Better BP Consent Form'.**



8. **Do not edit anything in the message box. Press 'Send Invitation'.**

9. **Confirm with the participant that they have received the consent form, go through it with them, and instruct them where to sign.**

Measurements

Neck Circumference Measurement

Participants will be asked to stand with their head held erect and eyes facing forward. They will be asked to breathe normally. If the participant has long hair, please ask them to pull it up and away from their neck.

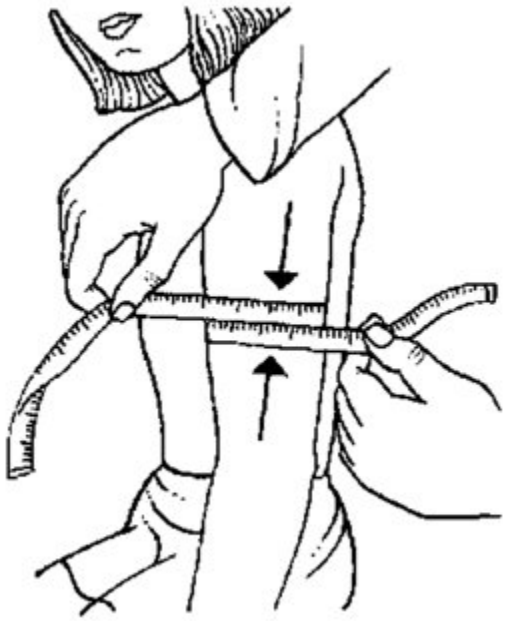
A flexible tape measure (AdvoCare) will be used to measure neck circumference at the level of the cricothyroid membrane (thyroid cartilage or Adam's apple).

Neck circumference should be recorded to the nearest 0.1 centimeter.

Arm Circumference Measurement (non-dominant arm)

The participant should remove his/her upper garment, or clear the upper arm area so that an unencumbered measurement may be made. The technician should:

- Have the participant stand, with the non-dominant arm hanging and bending the elbow so that the forearm is horizontal (parallel) to the floor.
- Measure their arm length from the acromion (bony protuberance at the shoulder) to the olecranon (tip of the elbow), using the AdvoCare anthropometric tape.
- Mark the midpoint on the dorsal surface of the arm.
- Have the participant relax their arm alongside of the body.
- Draw the tape snugly around the arm at the midpoint mark. **Note: Tape should be horizontal and should not indent the skin.**
- Noting the arm circumference indicated by the tape to the nearest tenth of a centimeter, use the criteria above for determining cuff size. **Note: If > 52 cm, the participant will be excluded from the study.**



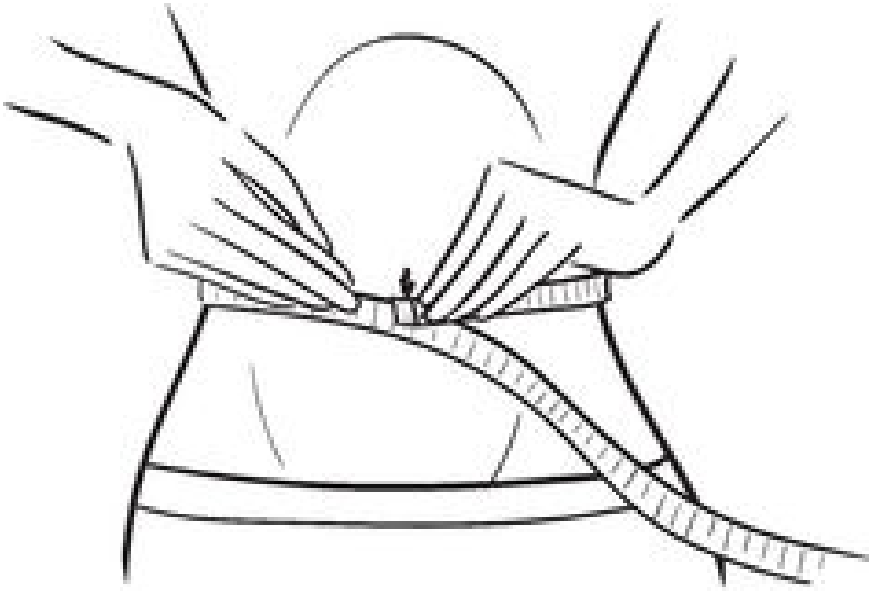
1. Select the appropriate cuff for WatchBP Office AFIB device (see Table below).
2. Fit participant with the following sized cuff:

Cuff Size	WatchBP Office AFIB
Small adult	17-21.9 cm
Medium adult	22-32 cm
Large adult	32.1-42 cm
Extra-large	42.1-52 cm

3. The research coordinator will select the appropriate cuff size, based on arm circumference (see Table above).

Waist Circumference Measurement

- Have the participant stand erect with the abdomen relaxed, arms at the sides and feet together.
- Draw the tape snugly around the midpoint between the lower rib margin and the iliac crest (or 2 inches below the belly button). Note: Tape should be horizontal and should not indent the skin. **Note: Tape should be horizontal and should not indent the skin.**



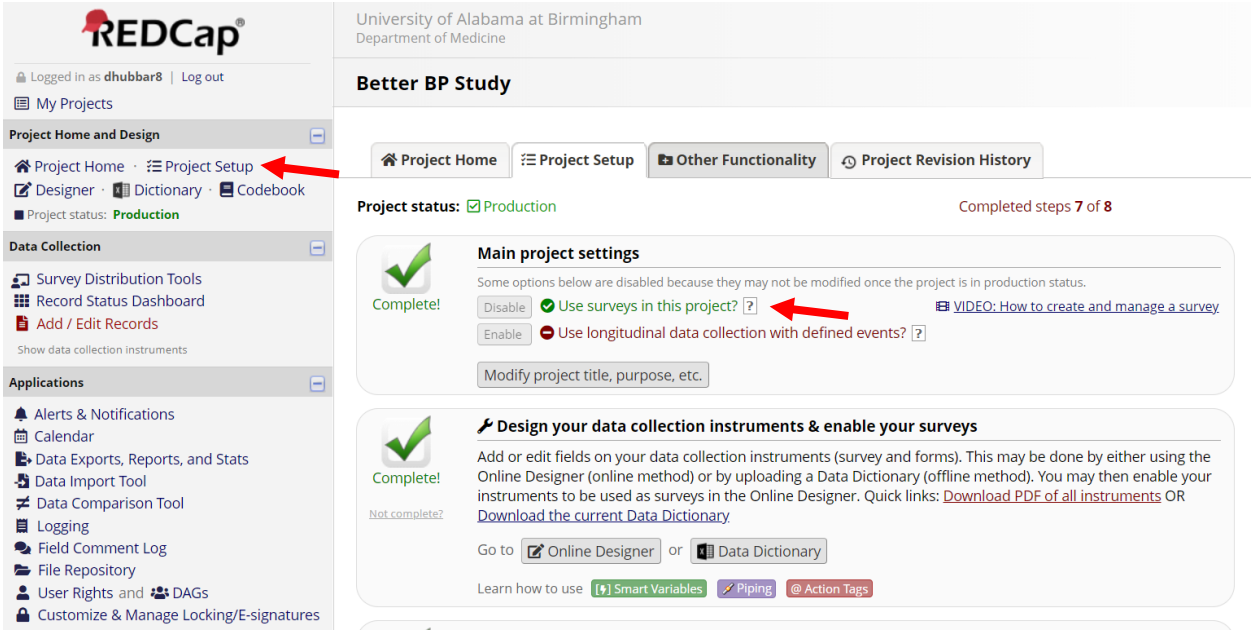
Questionnaire administration

Whenever possible, these questionnaires will be self-administered. Participants have the option to complete these surveys in-person or electronically. Research coordinators can administer these questions orally for participants who would otherwise have difficulty completing questionnaires on their own.

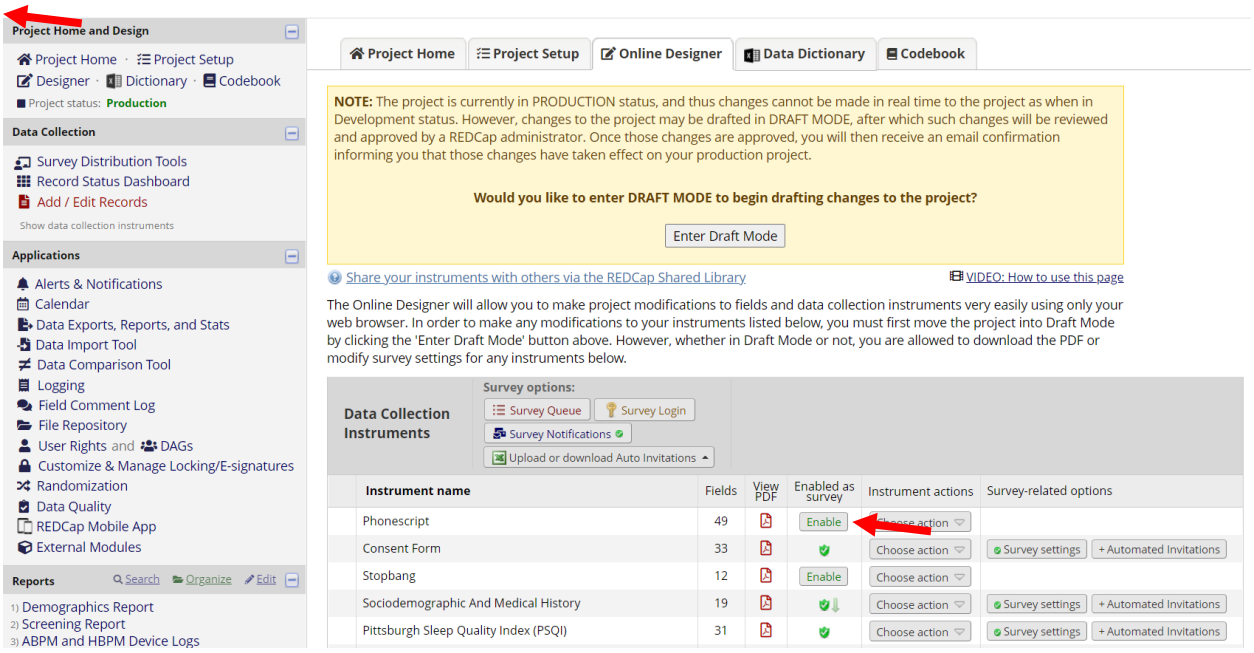
a. **Sociodemographic/Medical History**
b. **PSQI**
c. **Post-ABPM questionnaire (following ABPM period)**
d. **Post-HBPM questionnaire (following HBPM period)**
e. **Comparability questionnaire (following both ABPM and HBPM period)**

Electronic questionnaire set-up

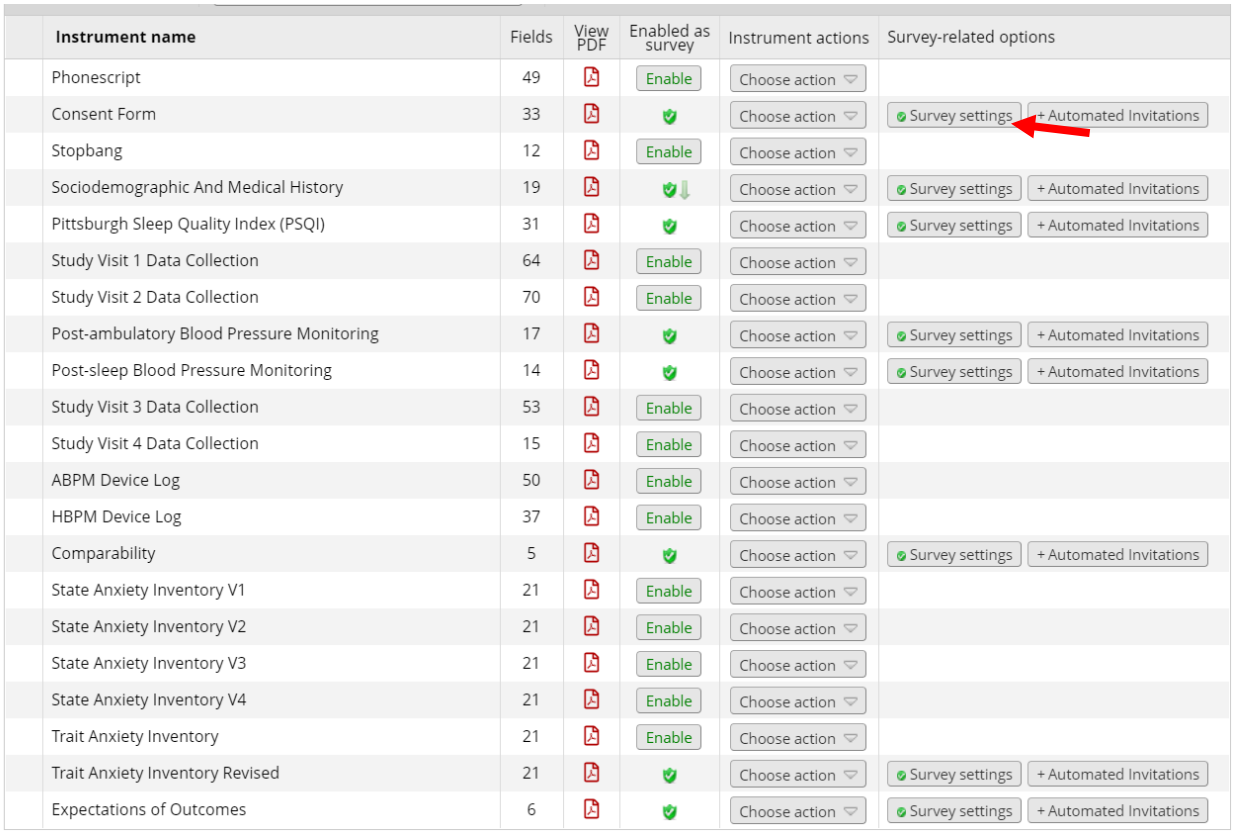
1. **Before you get started, go to the 'Project Set-Up' tab and make sure 'Use surveys in this project?' is enabled.**



2. **Go to the 'Designer' tab and click 'Enable' for all of the forms that you would like to be able to send participants as a survey. A green checkmark will appear once it is enabled.**

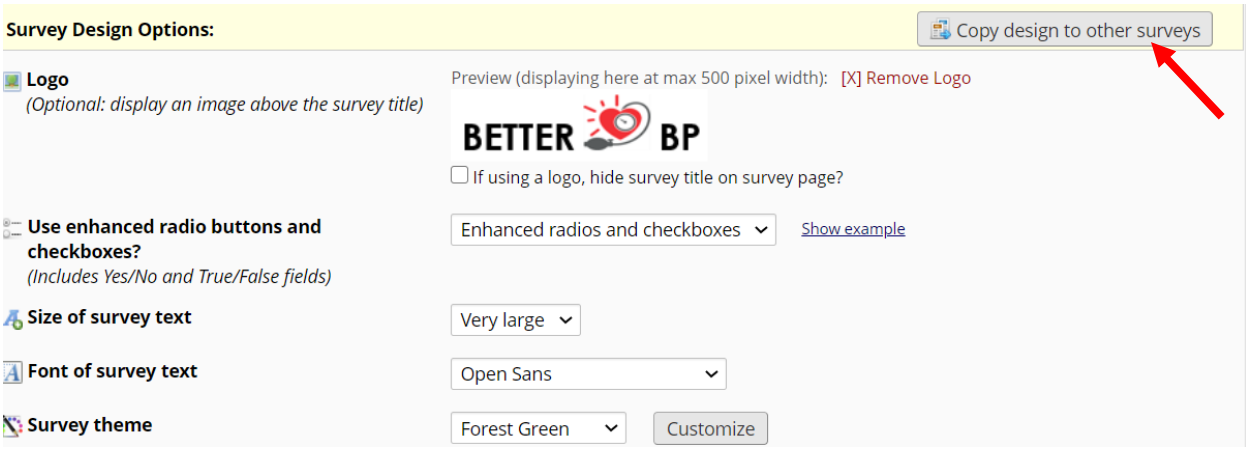


3. **To change the survey settings (i.e. appearance, wording, and other functionalities), please select 'Survey settings'.**



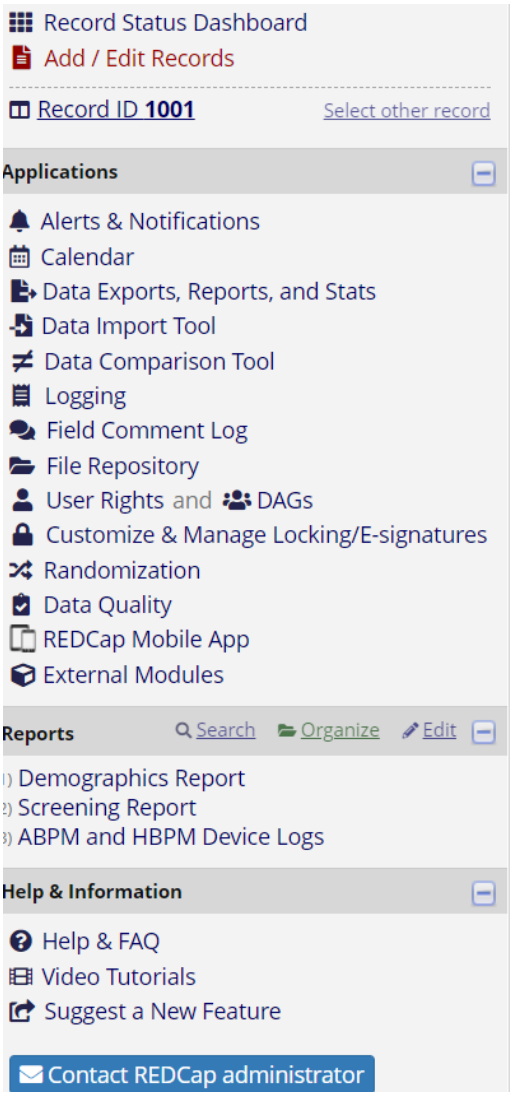
Instrument name	Fields	View PDF	Enabled as survey	Instrument actions	Survey-related options
Phonescript	49		Enable	Choose action	
Consent Form	33			Choose action	Survey settings + Automated Invitations
Stopbang	12		Enable	Choose action	
Sociodemographic And Medical History	19			Choose action	Survey settings + Automated Invitations
Pittsburgh Sleep Quality Index (PSQI)	31			Choose action	Survey settings + Automated Invitations
Study Visit 1 Data Collection	64		Enable	Choose action	
Study Visit 2 Data Collection	70		Enable	Choose action	
Post-ambulatory Blood Pressure Monitoring	17			Choose action	Survey settings + Automated Invitations
Post-sleep Blood Pressure Monitoring	14			Choose action	Survey settings + Automated Invitations
Study Visit 3 Data Collection	53		Enable	Choose action	
Study Visit 4 Data Collection	15		Enable	Choose action	
ABPM Device Log	50		Enable	Choose action	
HBPM Device Log	37		Enable	Choose action	
Comparability	5			Choose action	Survey settings + Automated Invitations
State Anxiety Inventory V1	21		Enable	Choose action	
State Anxiety Inventory V2	21		Enable	Choose action	
State Anxiety Inventory V3	21		Enable	Choose action	
State Anxiety Inventory V4	21		Enable	Choose action	
Trait Anxiety Inventory	21		Enable	Choose action	
Trait Anxiety Inventory Revised	21			Choose action	Survey settings + Automated Invitations
Expectations of Outcomes	6			Choose action	Survey settings + Automated Invitations

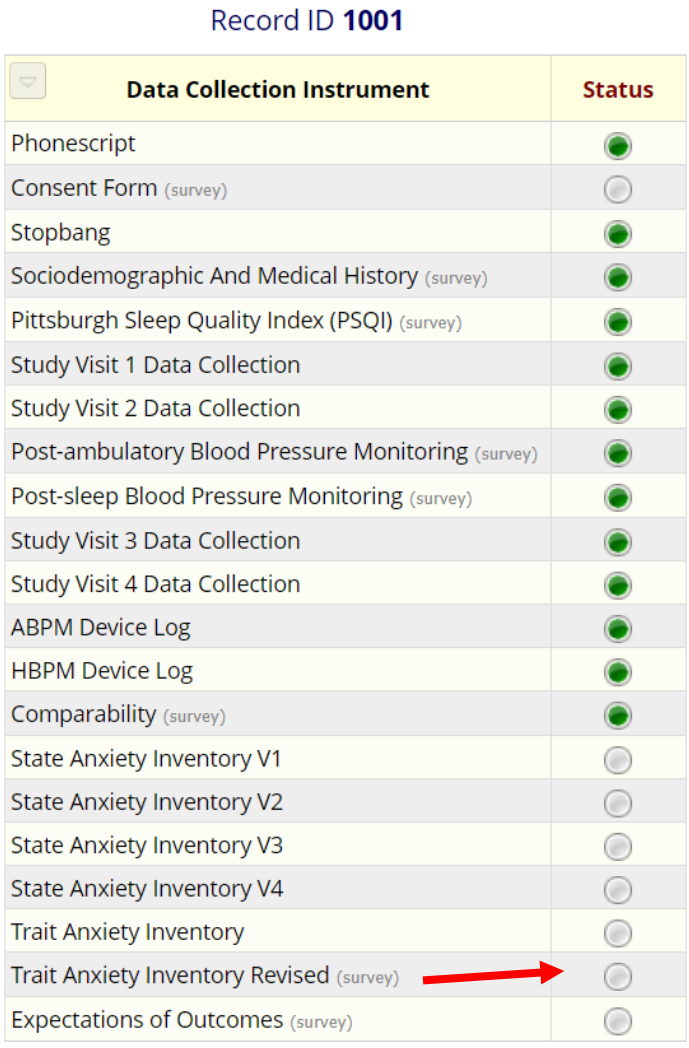
4. **To apply your changes to all surveys, select 'Copy design to other surveys'.**



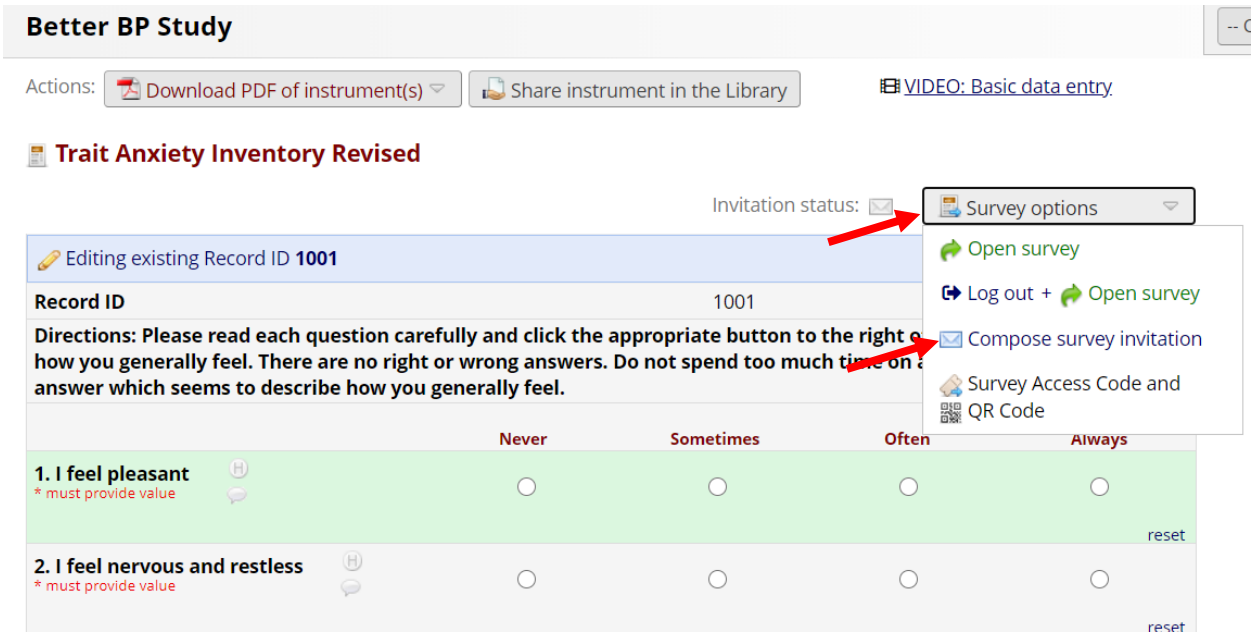
Electronic questionnaire administration

1. **Go to the participant's record and select the survey form you would like to send.**





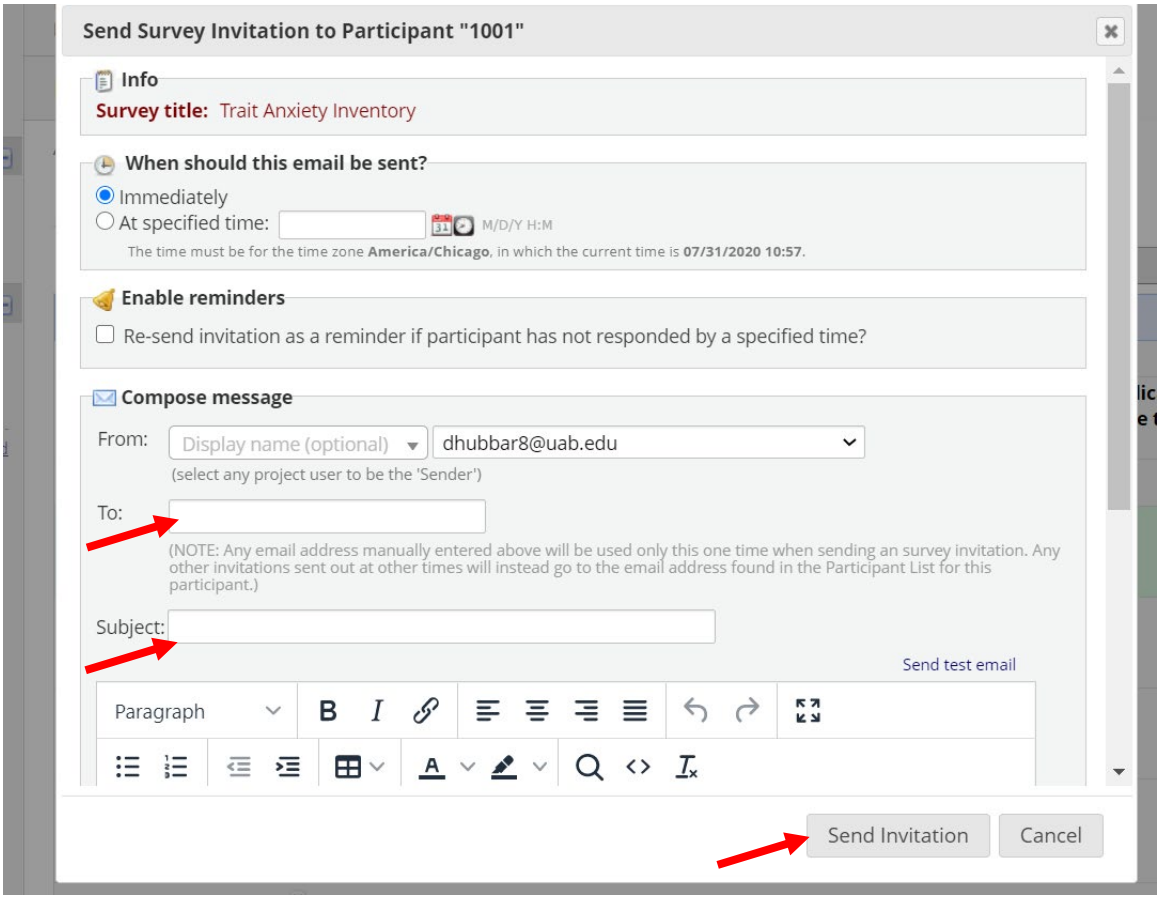
2. **Select ‘Survey Options’ then ‘Compose Survey Invitation’.**



3. **Enter the participant's email address provided on the screening form.**

4. **In the subject box, enter 'Better BP' + title of the survey.**

5. **Do not edit anything in the message box. Press 'Send Invitation'.**
   ***Note – if you need to test the email, press 'Send test email'.**



Clinic BP Measurements

Three BP measurements will be performed in the non-dominant arm, both attended (i.e. – technician in the room for the resting and measurement period) and unattended (i.e. – technician starts the device and leaves the room during the measurement period), based on the participant's randomization order following the protocol listed below.

2. Unattended BP measurements
    a. Explain to participant the steps involved in obtaining unattended BP measurements:
        i. You will have them turn off their phone and place the phone out of their view but not out of the room
        ii. Have them sit in a firm chair with a flat back
        iii. Have them place their feet flat on the floor
        iv. They should not speak until all three blood pressure readings are obtained
        v. You will start the blood pressure measurement device
        vi. You will leave the room for 10 minutes
        vii. After 5 minutes, they will have their blood pressure measured
        viii. They will have their blood pressure measured two more times at one minute intervals
        ix. They should relax but not move or talk until you return to the room
    b. Connect the BP device to the cuff
    c. Position patient for their BP measurement
    d. Start the device for a 5 minute waiting period
    e. Leave the room for 10 minutes

3. Attended BP measurements

    d. Explain to participant the steps involved in obtaining unattended BP measurements:

        i. You will have them turn off their phone and place the phone out of their view but not out of the room

        ii. Have them sit in a firm chair with a flat back

        iii. Have them place their feet flat on the floor

        iv. They should not speak until all three blood pressure readings are obtained

        v. You will start the blood pressure measurement device

        vi. After 5 minutes, they will have their blood pressure measured

        vii. They will have their blood pressure measured two more times at one minute intervals

        viii. They should relax but not move and there should be no talking until the three blood pressure measurements are taken

    e. Connect the BP device to the cuff

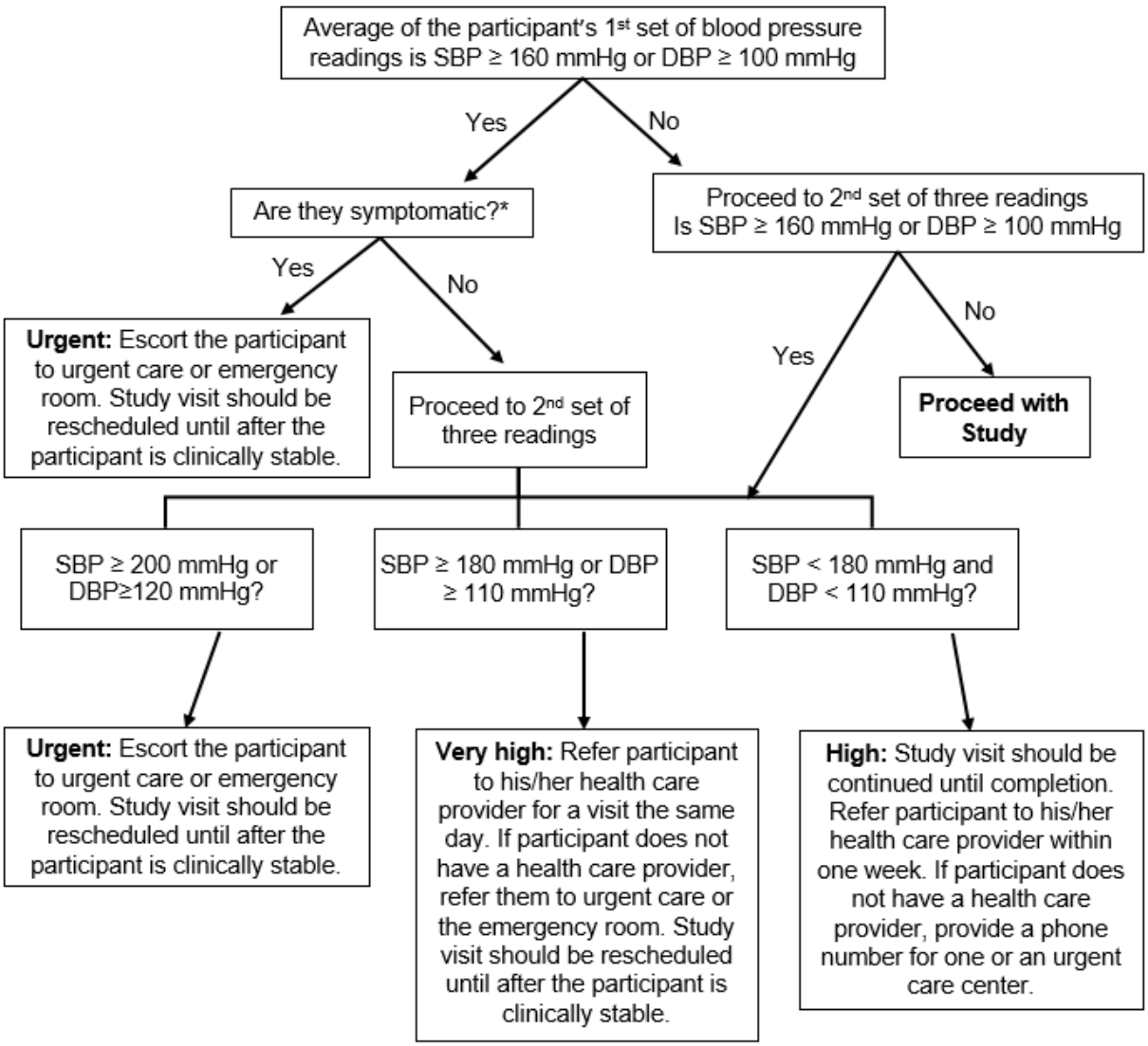
    f. Position patient for their BP measurement

    g. Start the device for a 5 minute waiting period and stay in the room doing other activities without talking to the participant

If the participant asks about his/her clinic blood pressure, the technician should tell the participant that the readings will be given to him/her in a report approximately 7 days following their final study visit if they have provided consent to receive their results.

A standard automated blood pressure measurement monitor (Microlife WatchBP Office AFIB) and a specific protocol for the measurement of blood pressure will be utilized.

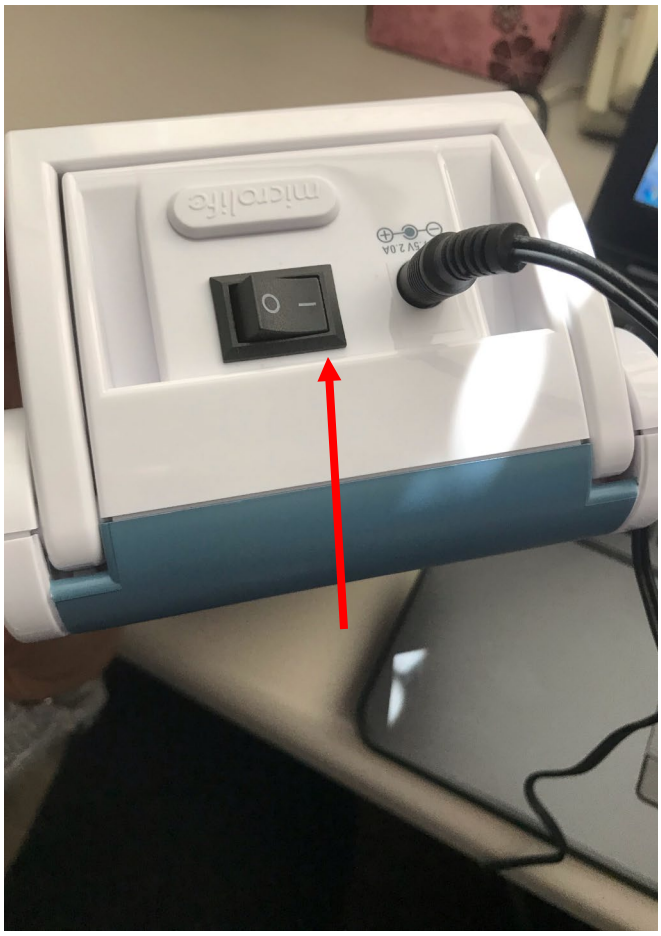
Blood Pressure Safety Protocol



*Symptoms include chest pain or discomfort, shortness of breath, back pain or discomfort, numbness/weakness, change in vision and/or difficulty speaking.

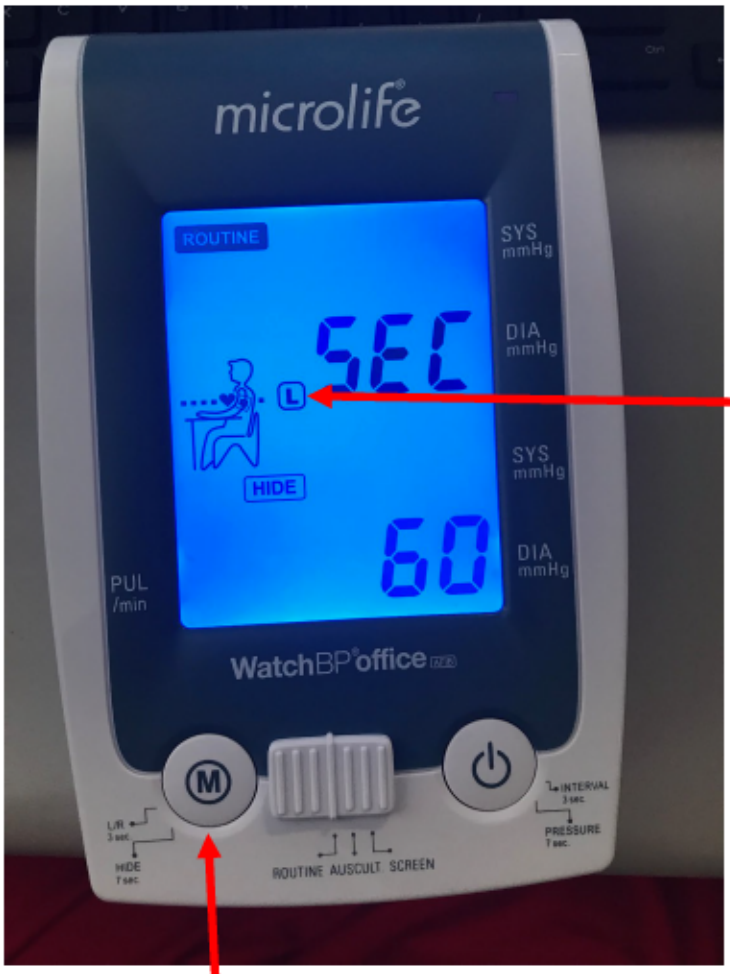
WatchBP Office AFIB Initializing Procedures

1. Plug the adapter in the wall and plug into the back of the device.
2. On the top of the clinic device is the **on/off** switch. Turn the clinic device on by switching the **on/off** button.

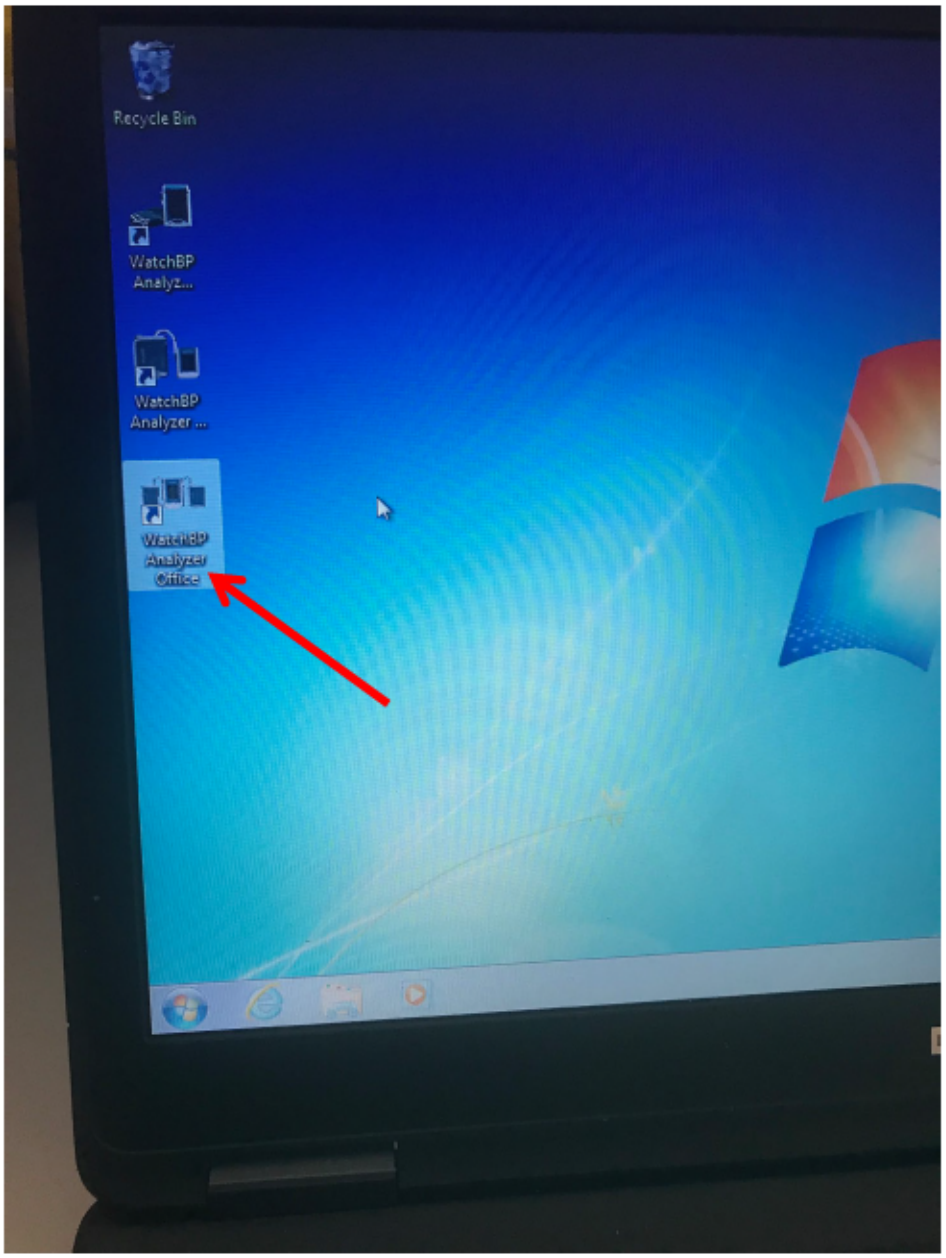


3. Press the circular **on/off** button on the lower right of the device to power up the device.
4. Make sure the slider on the front of the device between the 'M' and on/off button is all the way to the left on 'Routine'.
5. Press and hold the **on/off** button for 3 seconds until the device lights up blue, 'Sec' appears, and a flashing number appears. This will allow you to set the interval between readings and the rest period.
6. Next, the resting period time will begin to flash. Press the 'M' button until the '300' appears on the device. This will set the resting period to 5-minutes. Press the **on/off** button to confirm the resting period.

7. Press the 'M' button until the '60' appears on the device. This will set the interval between measurements to 1-minute. Press the **on/off** button to confirm this interval (see **3** in the Figure below).

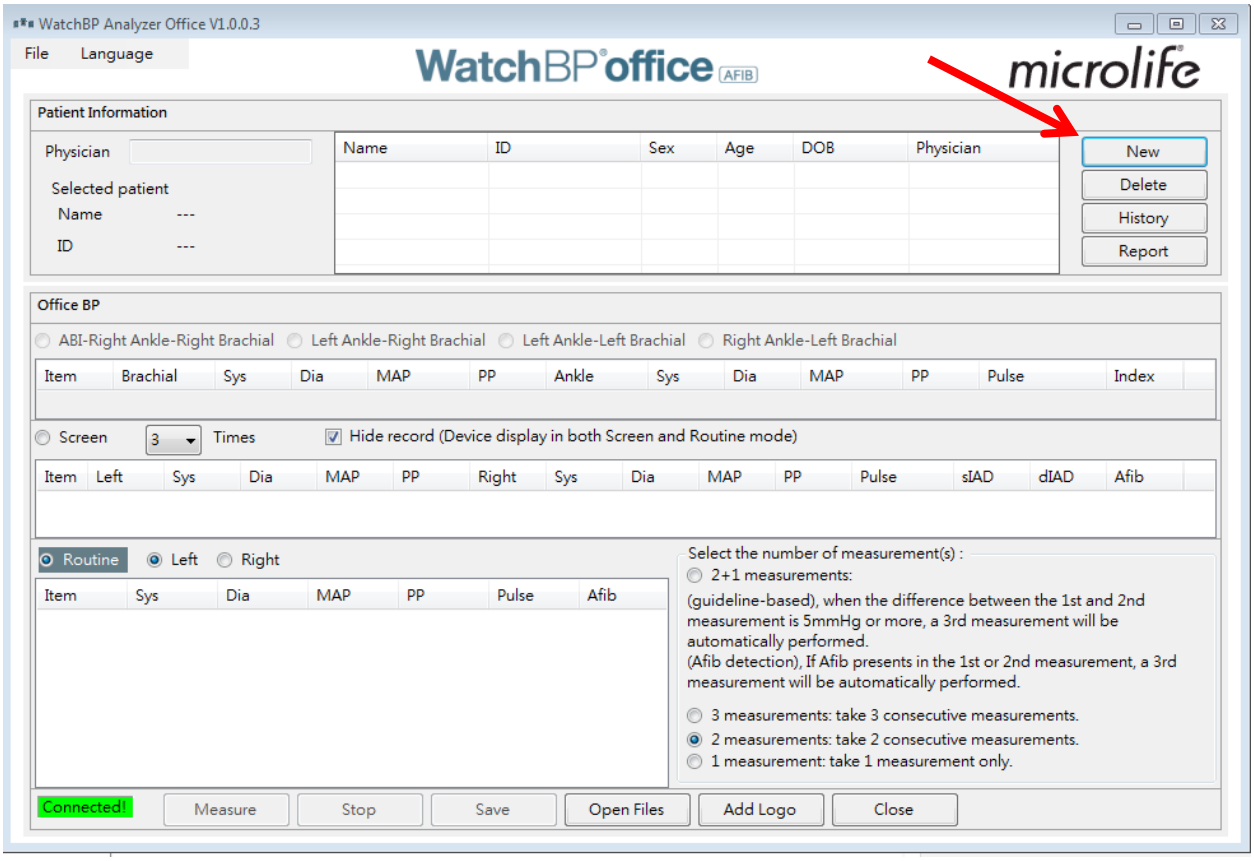


8. To switch the arm that is being measured (Left or Right; whichever is the participant's non-dominant arm), press and hold the **M** button for 3 seconds.
9. To hide the blood pressure readings, press and hold the **M** button for 7 seconds.
10. Connect the clinic device to the computer using the USB to micro-USB computer cable.
11. Launch WatchBP Analyzer Office software.



12. Select 'WatchBP Office AFIB' (see below).

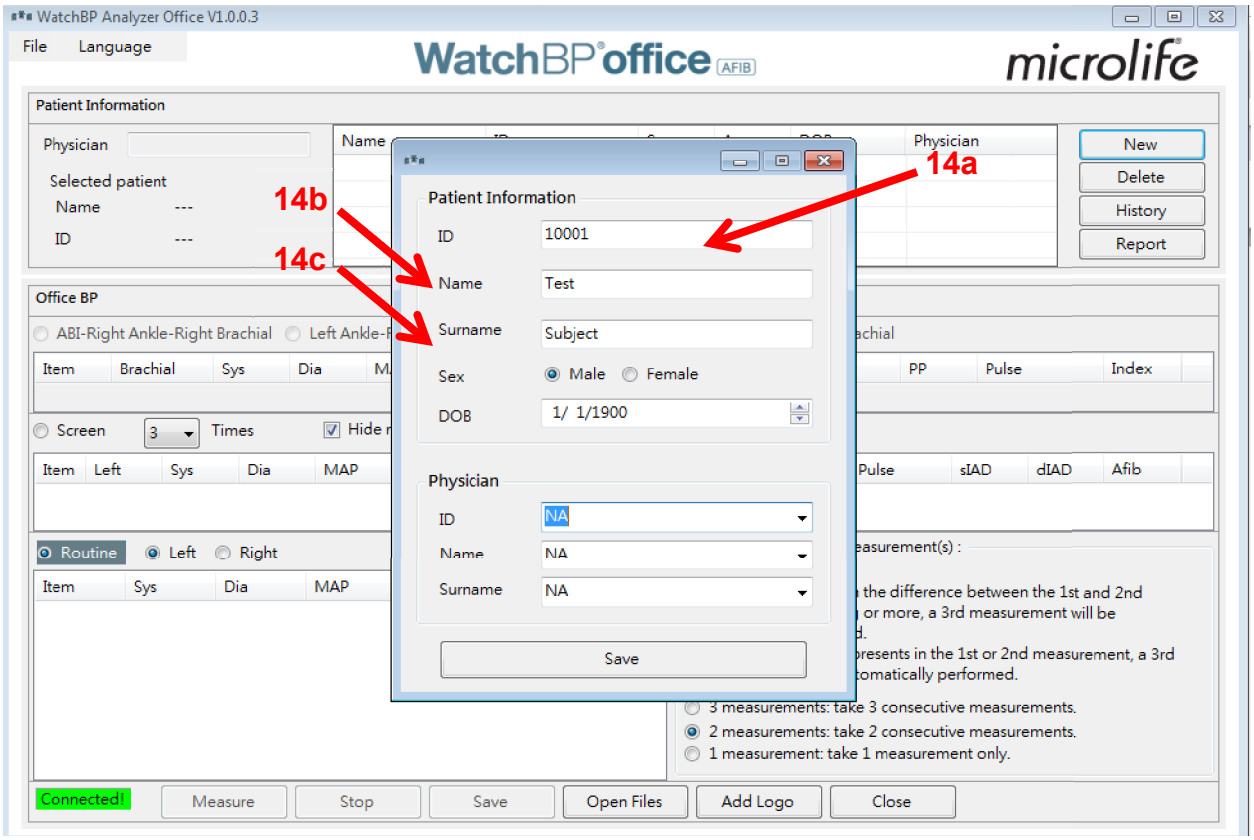
13. Create a new patient entry by selecting ‘New’.



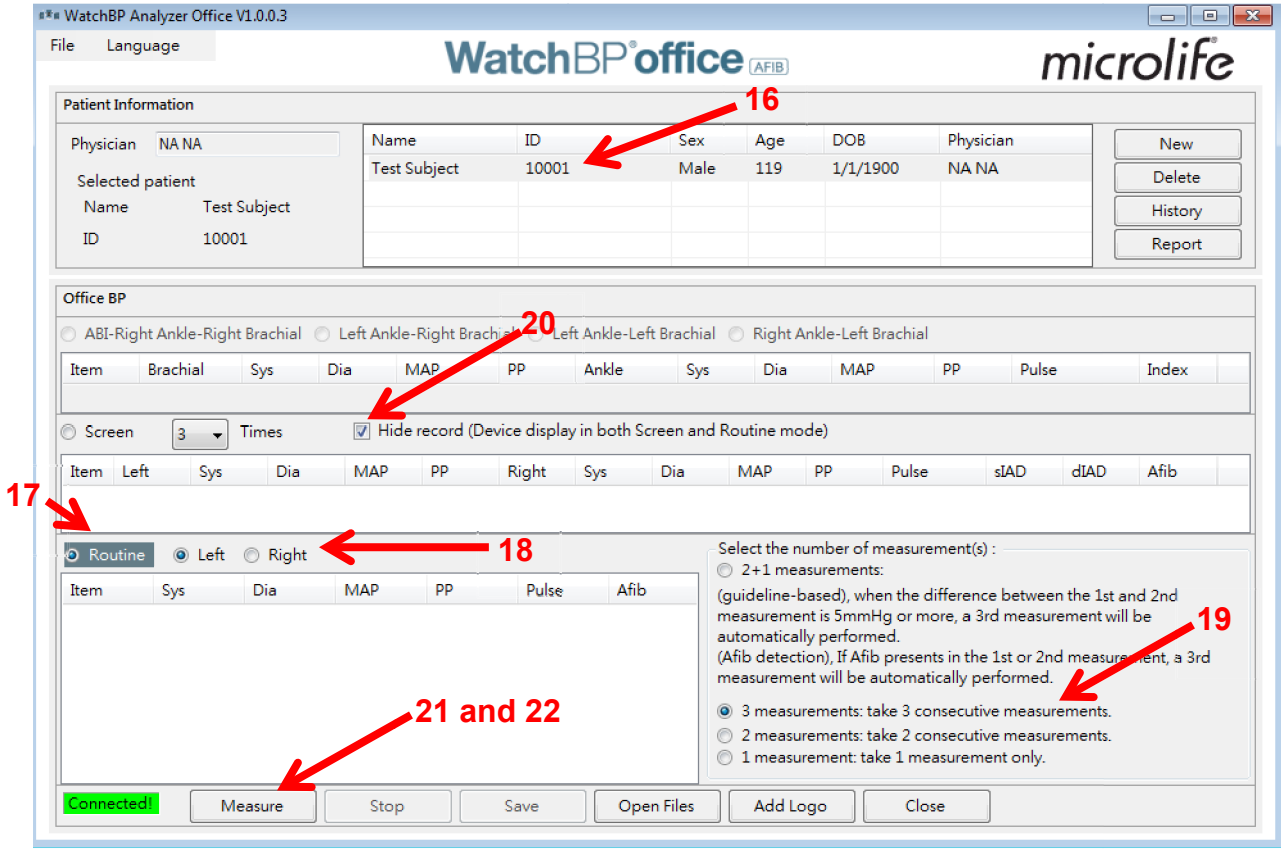
14. Enter the participant's information in window. The Participant ID number will be entered three times in the following text fields: ID number, Last Name and First Name. **Do not enter participant name and Date of Birth and Gender.**

    Enter 'NA' for Physician ID, Name, and Surname.

    a. *Participant ID number (required – enter participant ID)*
    b. *Last name (required – enter participant ID)*
    c. *First name (required – enter participant ID)*
    d. *Date of Birth (Leave as pre-filled value 1/1/1900)*
    e. *Gender (Leave as 'Male')*



15. Select ‘Save’ once you enter their information.
16. Select the participant id number you created **(see screen grab below)**.
17. Select ‘Routine’ measurements.
18. Select the arm (**Left/Right**) the participant will have their clinic blood pressure measured. This should be their **non-dominant arm** unless there is some reason it is not possible to use their non-dominant arm. **This should be notated on the Study Visit 1 Form.**
19. Under ‘Select the number of measurement(s):’ select ‘3 measurements: take 3 consecutive measurements’.
20. Select ‘Hide Record (Device display in both Screen and Routine mode)’. This ensures that participant will not be able to see their blood pressure readings.



21. If taking attended clinic blood pressure, press ‘Measure’ and remain in the room, but do not talk or interact with the participant. Make sure the 5-minute rest period has begun by looking at the countdown on the device.
22. If taking unattended clinic blood pressure, press ‘Measure’ and look at the device to make sure the 5-minute has begun by looking at the countdown on the device. Once countdown has started, remind the participant to rest, not talk or move until three blood pressure measurements are taken, then exit the room and return in 10-minutes.

ABPM Procedures

Use the Better BP Study Visit 2 and Study Visit 3 Data Collection Forms to record information from the second and third study visit.

Testing the ABPM Device and Fitting Participant with Equipment

1. The appropriate cuff size should be ready (see arm circumference measurement on Study Visit Form 1 to verify correct size). Place the cuff on the participant's non-dominant arm. **If the non-dominant arm cannot be used, use the participant's dominant arm (**this will require using a bladder positioned for the other arm)**.** The cuff must be placed against the skin (not over any clothing). Locate the brachial artery by palpation and mark the skin with a small dot, using a black pen. (The brachial artery is usually found just medial and superior to the cubital fossa, posterior to the biceps muscle and slightly toward the body.) For brachial artery palpation, fingertips or thumb may be used. Refer to the **Participant Instructions**.
2. The research coordinator will explain to the participant that the cuff will feel tight during the first measurement. The participant will be instructed that the ABPM will inflate the cuff to a pressure between 170 and 180 mmHg, but this will only occur on the first reading. Each subsequent reading will go only 20 mmHg higher than the previous systolic reading. The research coordinator will instruct the participant that a tone will go off during the daytime to alert them that a reading is about to occur.
3. During recordings, the participant is instructed to: (1) remain as still as possible, (2) keep his/her arm relaxed at his/her side or at heart level as if in a sling or resting on a table or armrest, and (3) refrain from talking The research coordinator should demonstrate the appropriate arm positioning to the study participant.
4. Next, a blood pressure reading should be taken using the ABPM device to confirm it is working properly. The research coordinator will press the **On/Off** button and place the device in

'Ambulatory' mode. The purpose of taking an initial reading is to make sure the cuff inflates and deflates as expected. Once one successful reading is acquired, proceed to the next step. If the cuff does not inflate and then deflate, then check that batteries are properly inserted and if so, initialize a new ABPM device for use. Also, if three readings are attempted and all result in errors, then a new ABPM device will be initialized for use. If either of the above occurs, the research coordinator will email Paul Muntner (pmuntner@uab.edu) to inform them of a non-functioning device.

5. Final fitting of the ABPM device: the non-latex red tubing should go around the back of the participant's neck and come down the dominant side of his/her body. Usually, it is placed underneath the participant's clothing, coming out at the waist or between two button holes of the shirt. The pouch with the ABPM device can be 1) placed in a jacket pocket, 2) hooked onto a belt (using the loop on the back of the pouch), or 3) worn with a shoulder strap connected by 2 black plastic tabs to the inside edges of the pouch.

6. The research coordinator will explain how the ABPM device works to the participant, noting that every 30 minutes the ABPM device will automatically make a BP measurement.

7. The research coordinator will show the participant the phone number for the research team. This is located inside the **Participant Instructions** that will be provided to them. Therefore, the participant can call with any questions or concerns about any of the equipment. Also, the research coordinator will show the participant the number to call for the research coordinator during regular business hours. For after hours' calls, participants will be provided with a cell phone number for one of the study staff members familiar with the study.

8. The participant will be informed that if an ABPM measurement fails, usually because of motion (including driving), talking, or because the arm is not relaxed, the device will attempt another measurement 2 minutes later. If this repeat attempt fails, no further attempts will be made until the next scheduled reading 30 minutes later.

9. The participant will then be told that in the very unlikely event the cuff does not deflate after a reading, the **On/Off** circular button on the ABPM device should be pressed (shown in picture above). The cuff should automatically deflate. If the cuff still does not deflate, the participant should turn off the device. To do so, they will hold the **On/Off** circular button for three seconds. Once the cuff has deflated, the participant can push the **On/Off** circular button to turn the device back on. Then, they can resume wearing the device as before (i.e., they can place the device back in the pouch) and their blood pressure should be measured every 30 minutes.

10. At this time, the research coordinator should tell the participant that the ABPM device will continue to obtain recordings during sleep. The participant is told that the device is programmed so that during the daytime, the ABPM device will emit a tone immediately before each BP measurement to signal that the cuff is about to be inflated; however, during the participant's usual sleep hours, this tone is turned off.

11. The research coordinator will then ask the participant to avoid getting the ABPM device wet, but mention that there is no personal danger to the participant if the ABPM device does get wet. The research coordinator will ask the participant to keep the equipment dry at all times. We prefer that participants not shower, swim, or go to the gym during the 24 hours they are wearing the ABPM device. However, if this is absolutely not possible, then the equipment should be removed before showering, swimming or engaging in vigorous activity. Each time the participant removes equipment he/she should log the time the equipment was removed as well as the time it was put back on **(see ABPM Device Log; Appendix 2).**

12. The research coordinator will show the participant how to remove and put back on the ABPM device.

13. To remove ABPM device, the research coordinator instructs the participant to pull the

Velcro flap away from his/her body and slide the cuff down off his/her arm.

14. The participant is told to gently pull the white tubing over his/her head and away from his/her body.

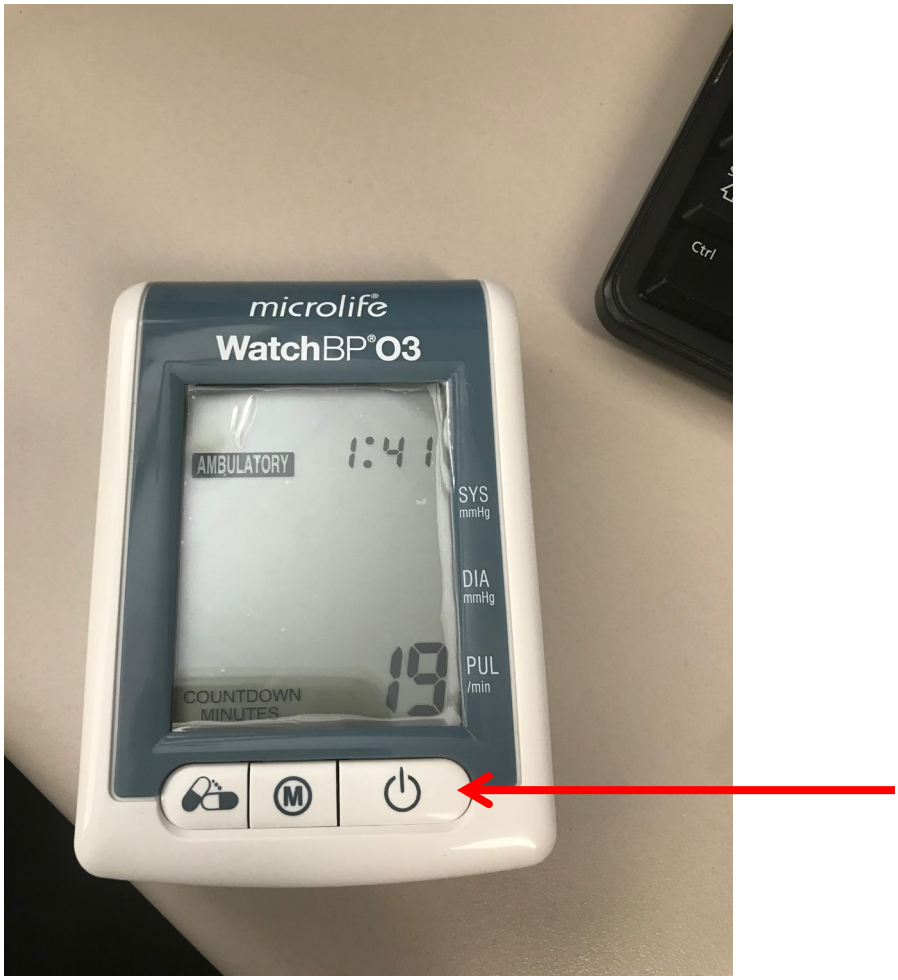
15. To put the ABPM device back on, the participant is instructed to place the cuff on his/her non-dominant arm, lead the white tubing behind his/her neck and let it rest by his/her opposite side. The arrow on the bottom of the cuff should be pointing down and situated over the brachial artery, about 1 inch above the bend in the elbow. If the participant does not know where the brachial artery is located, the research coordinator will offer to mark it with a pen (if this has not already been done) so that the participant can be assured the cuff is situated properly.

16. The researcher will ask the participant to demonstrate to them how to properly remove and replace the device before moving forward.

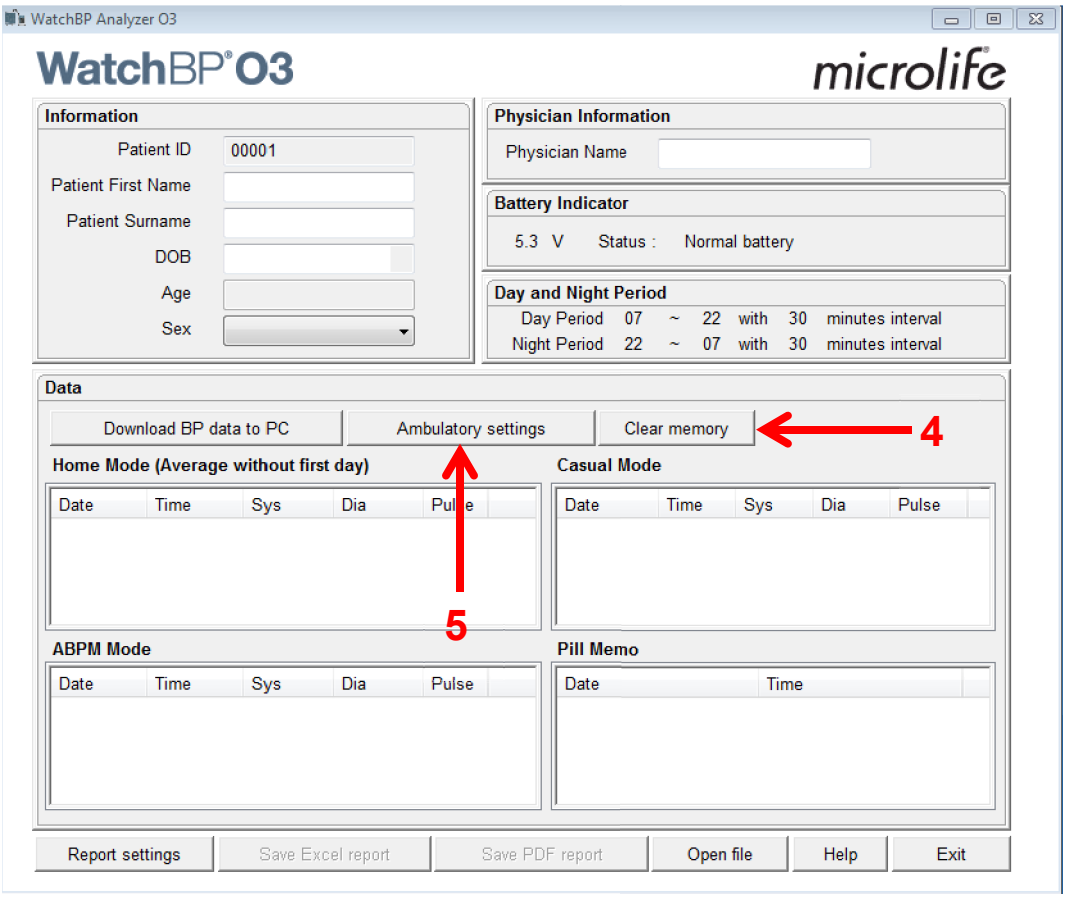
17. Next, the research coordinator will show the participant how to remove and replace the Actiwatch device (see **Participant Instructions**).

O3 Ambulatory Device Initializing Procedures

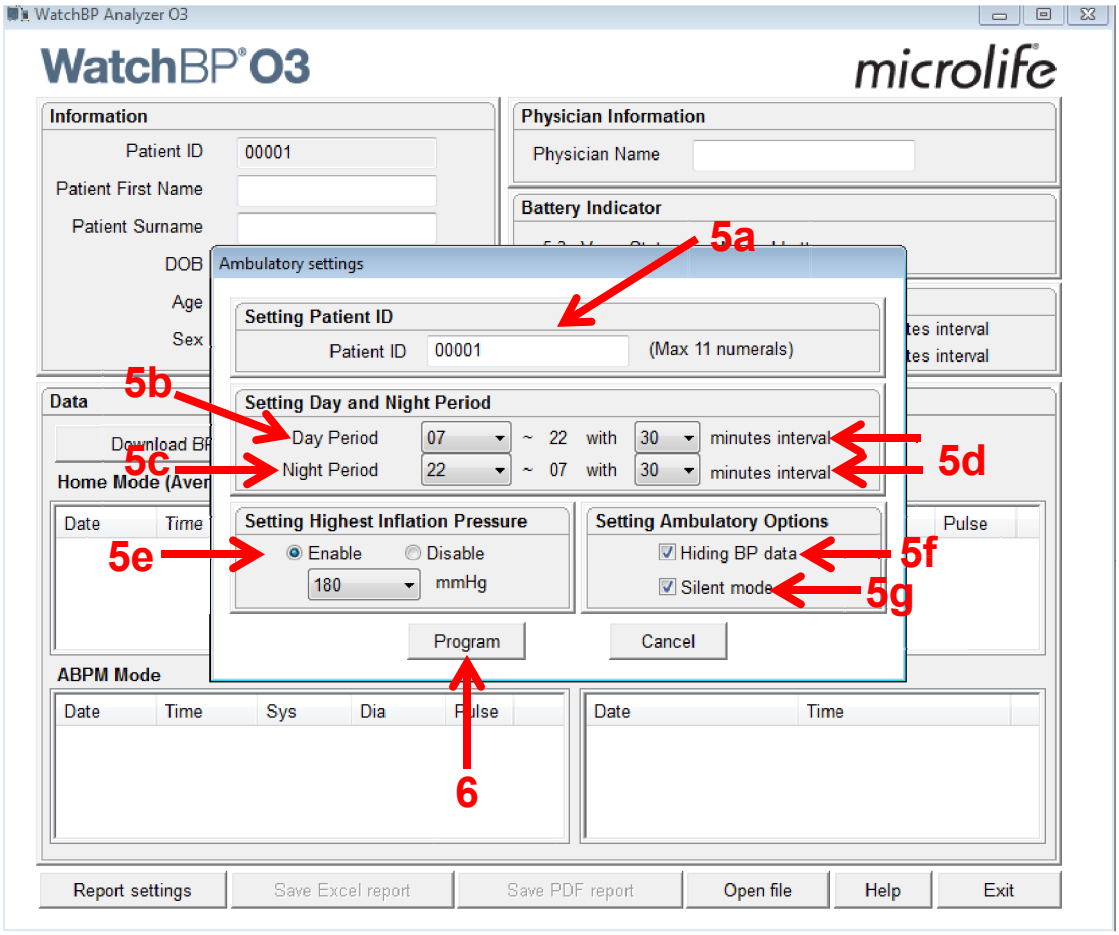
1. On the front of the ABPM device (**lower right**) is the **on/off** (circular) button. Turn the ABPM device on by pressing the **on/off** button.



2. Connect the ABPM device to the computer using the USB to micro-USB computer cable.
3. Launch WatchBP Analyzer O3 software.
4. To ensure that the data from a previous participant has been cleared, select ‘Clear Memory’.



5. Select ‘Ambulatory settings’ to set the participant id number, day period, night period, intervals between readings, highest inflation pressure, alert noise, and hiding BP data.
    a. *Participant id number – corresponds to record id number in REDCap*
    b. *Day period – participant reported awake time to sleep time*
    c. *Night period – participant reported sleep time to awake time*
    d. *Intervals – 30 minutes during day period and night period*
    e. *Highest inflation pressure – enabled at 180 mmHg*
    f. *Select ‘Hide BP data’*
    g. *Silent Mode – Make sure that this is checked for each participant*
6. Once everything is entered, select ‘Program’.

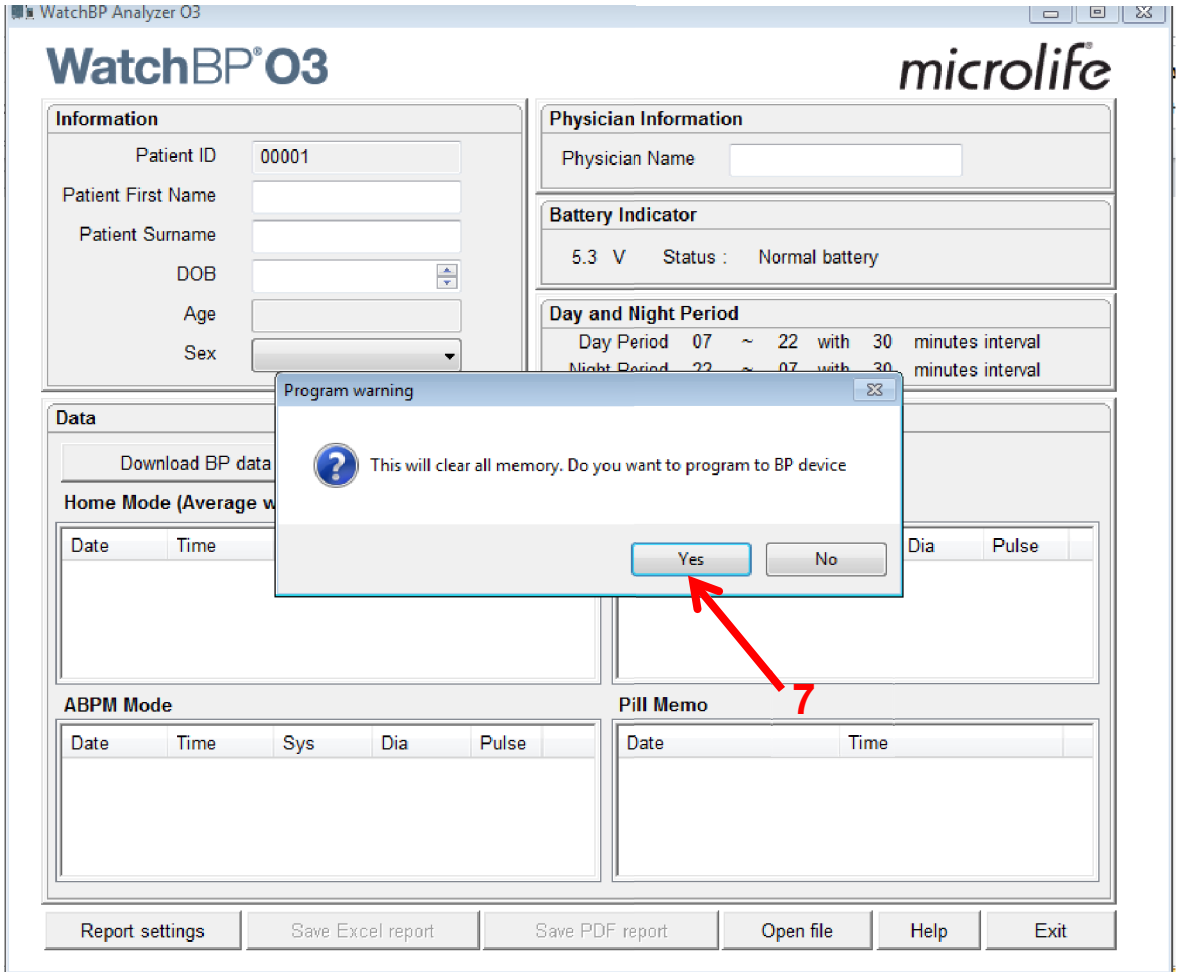

WatchBP Analyzer O3
WatchBP O3
microlife
Information
Patient ID
00001
Patient First Name
Patient Surname
DOB
Age
Sex
Physician Information
Physician Name
Battery Indicator
Ambulatory settings
Setting Patient ID
Patient ID
00001
(Max 11 numerals)
Setting Day and Night Period
Day Period
07
~ 22 with
30
minutes interval
Night Period
22
~ 07 with
30
minutes interval
Setting Highest Inflation Pressure
Enable
Disable
180
mmHg
Setting Ambulatory Options
Hiding BP data
Silent mode
Program
Cancel
Data
Home Mode (Aver
Date
Time
Pulse
ABPM Mode
Date
Time
Sys
Dia
Pulse
Report settings
Save Excel report
Save PDF report
Open file
Help
Exit
5a
5b
5c
5d
5e
5f
5g
6

Buffer:

We will buffer both the sleep and awakening times by at least 30 minutes so that the tone will not awaken participants. Remember the sleep/awake time settings on the O3 ABPM device can only be set to the hour. Take the participant's anticipated wake-up time, add 30 minutes, and round up to the next hour; take the participant's anticipated sleep time, subtract 30 minutes, and round down to the next hour. Here are three examples of how sleep and awake times will be set during the initialization process:

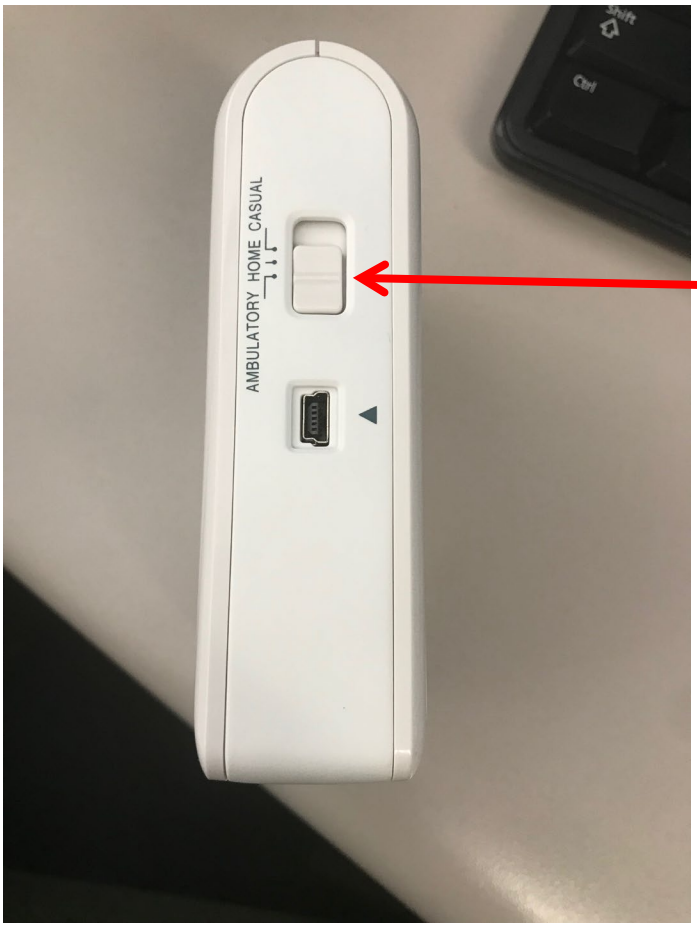
- A participant who reports going to bed at 11pm and waking up at 6am will have their sleep time set to 10pm to 7am.
- A participant who reports going to bed at 11:30pm and waking up at 6:30am will have their sleep time set to 11pm to 7am.
- A participant who reports going to bed at 11:15pm and waking up at 6:15am will have their sleep time set to 10pm to 7am.

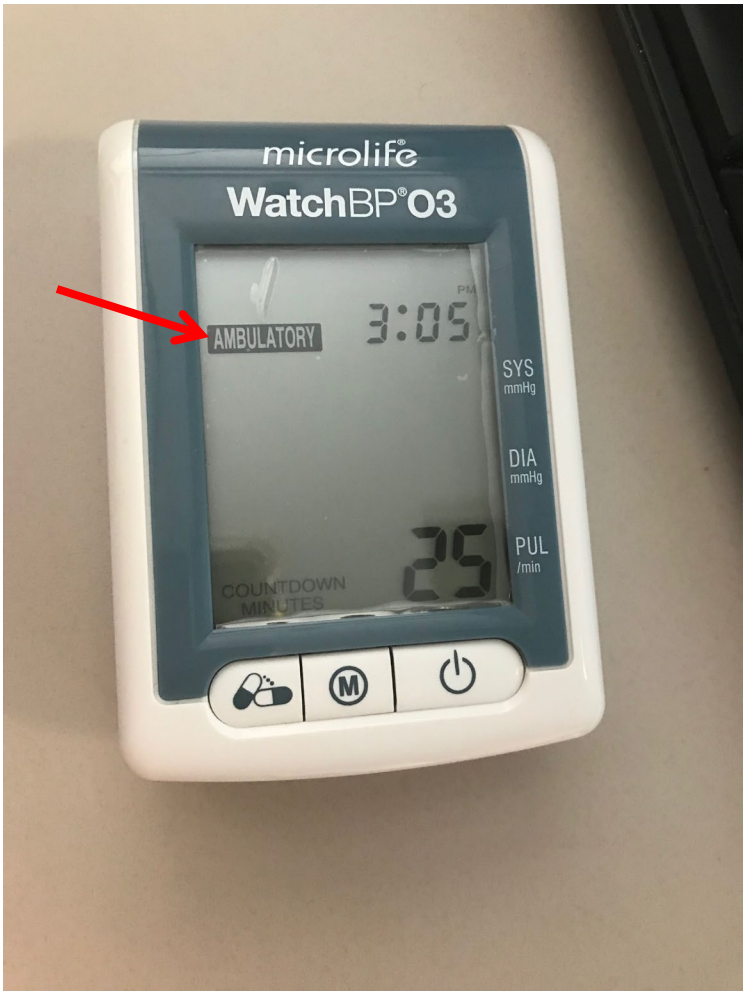
7. A program warning will pop-up (**screen grab below**), select ‘Yes’.



8. A message will appear that programming was successful, press ‘Okay’.

9. Disconnect the device from the computer and make sure the slider on the right side of the device is on ‘Ambulatory’ mode.
10. Once you see ‘Ambulatory’ appear on the screen and a countdown at the bottom right of the device appears, the ABPM device is ready to be used by the participant.




microlife
WatchBP®O3
AMBULATORY
3:05
PM
SYS
mmHg
DIA
mmHg
PUL
/min
25
COUNTDOWN
MINUTES
M

HBPM Procedures

Use the Better BP Study Visit 2 and Study Visit 3 Data Collection Forms to record information from the second and third study visit.

Testing the HBPM Device and Fitting Participant with Equipment

1. The appropriate cuff size should be ready (see arm circumference measurement on Study Visit Form 1 to verify correct size).
2. Demonstrate to the participant how to place the cuff on their non-dominant arm. **If the non-dominant arm cannot be used, use the participant's dominant arm (**this will require using a bladder positioned for the other arm)**.** The cuff must be placed against the skin (not over any clothing). Locate the brachial artery by palpation and mark the skin with a small dot, using a black pen. (The brachial artery is usually found just medial and superior to the cubital fossa, posterior to the biceps muscle and slightly toward the body.) For brachial artery palpation, fingertips or thumb may be used.
3. The research coordinator will explain to the participant that the cuff will feel tight during the first measurement. The participant will be instructed that the HBPM will inflate the cuff to a pressure between 170 and 180 mmHg, but this will only occur on the first reading. Each subsequent reading will go only 20 mmHg higher than the previous systolic reading.
4. The research coordinator will inform the participant that to begin their recordings they should press and hold the **On/Off** button for 3 seconds to begin the initial reading.
5. Next, a reading should be taken to confirm the device is working properly. The research coordinator will press the **On/Off** button and place the device in 'Casual' mode. The first reading will be based on the device's internal algorithm. The purpose is to make sure the cuff inflates and deflates as expected. Once <u>one</u> successful reading is acquired, proceed to the next step. If the cuff does not inflate and then deflate, then check that batteries are properly inserted and if

so, initialize a new HBPM device for use. Also, if three readings are attempted and all result in errors, then a new HBPM device will be initialized for use. If either of the above occurs, the research coordinator will email Paul Muntner (pmuntner@uab.edu) to inform him of a non-functional device.

6. The research coordinator will explain how the HBPM device works to the participant. Note that the HBPM device will automatically take a blood pressure reading at 2, 3, and 4 hours after the initial reading.

7. At this time, the research coordinator tells the participant that the HBPM device will continue to obtain recordings during sleep.

8. The research coordinator will show the participant the phone number for the research team is located inside the **Participant Instructions** that will be provided to them. Therefore, the participant can call with any questions or concerns about any of the equipment. Also, the research coordinator will show the participant the number to call for the research coordinator during regular business hours. For after hours' calls, participants will be provided with a cell phone number for one of the study staff members familiar with the study.

9. The research coordinator will ask the participant to keep the equipment dry at all times. The participant should log the time they went to bed and the time they wake up in the morning. If the participant removes equipment during the night, he/she should log the time the equipment was removed as well as the time it was put back on **(see HBPM Device Log; Appendix 2).**

10. The research coordinator will show the participant how to put the HBPM device on, the participant is instructed to place the cuff on his/her non-dominant arm, lead the white tubing behind his/her neck and let it rest by his/her opposite side. The arrow on the bottom of the cuff should be pointing down and situated over the brachial artery, about 1 inch above the bend in the elbow. If the participant does not know where the brachial artery is located, the research coordinator will offer to mark it with a pen (if this has not already been done) so that the

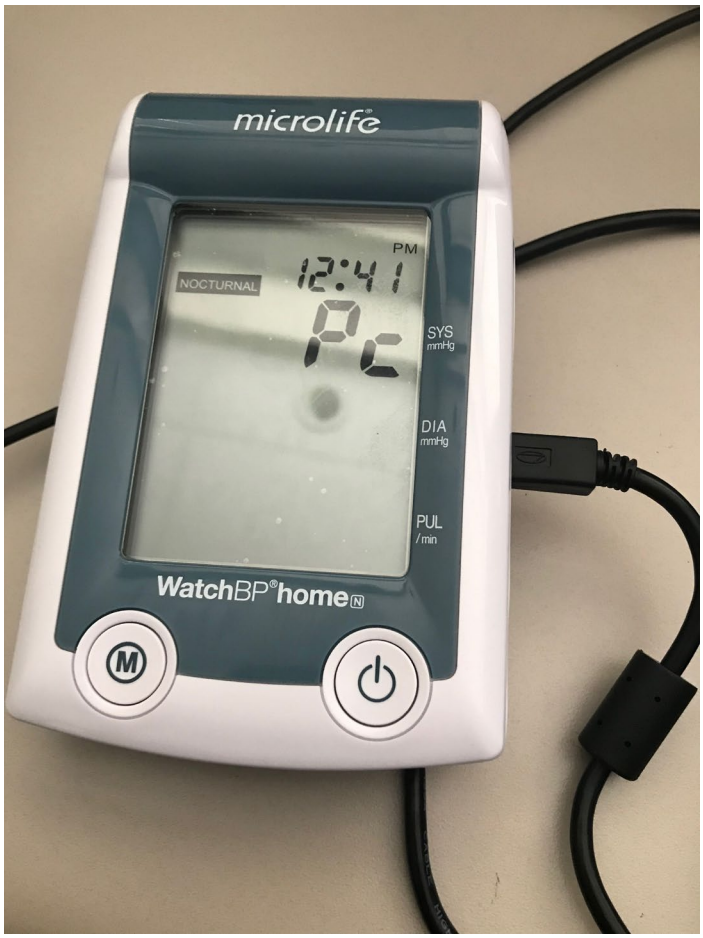
participant can be assured the cuff is situated properly. The research coordinator will inform the participant that they should place the device on their nightstand by the bed or under their pillow.

11. The researcher will ask the participant to demonstrate to them how to properly place the device before moving forward.

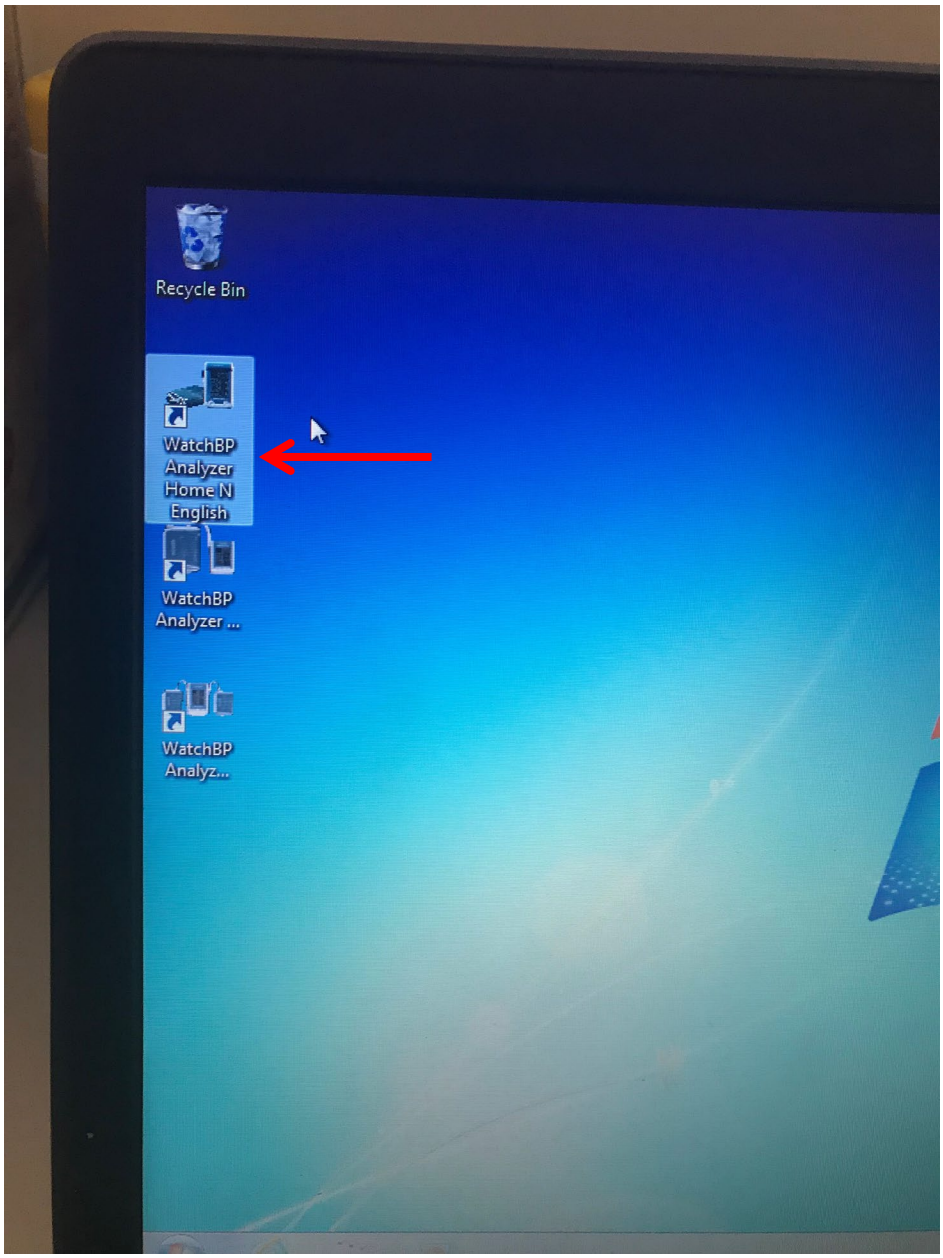
12. Next, the research coordinator will show the participant how to remove and replace the Actiwatch device.

WatchBP Home N Initializing Procedures

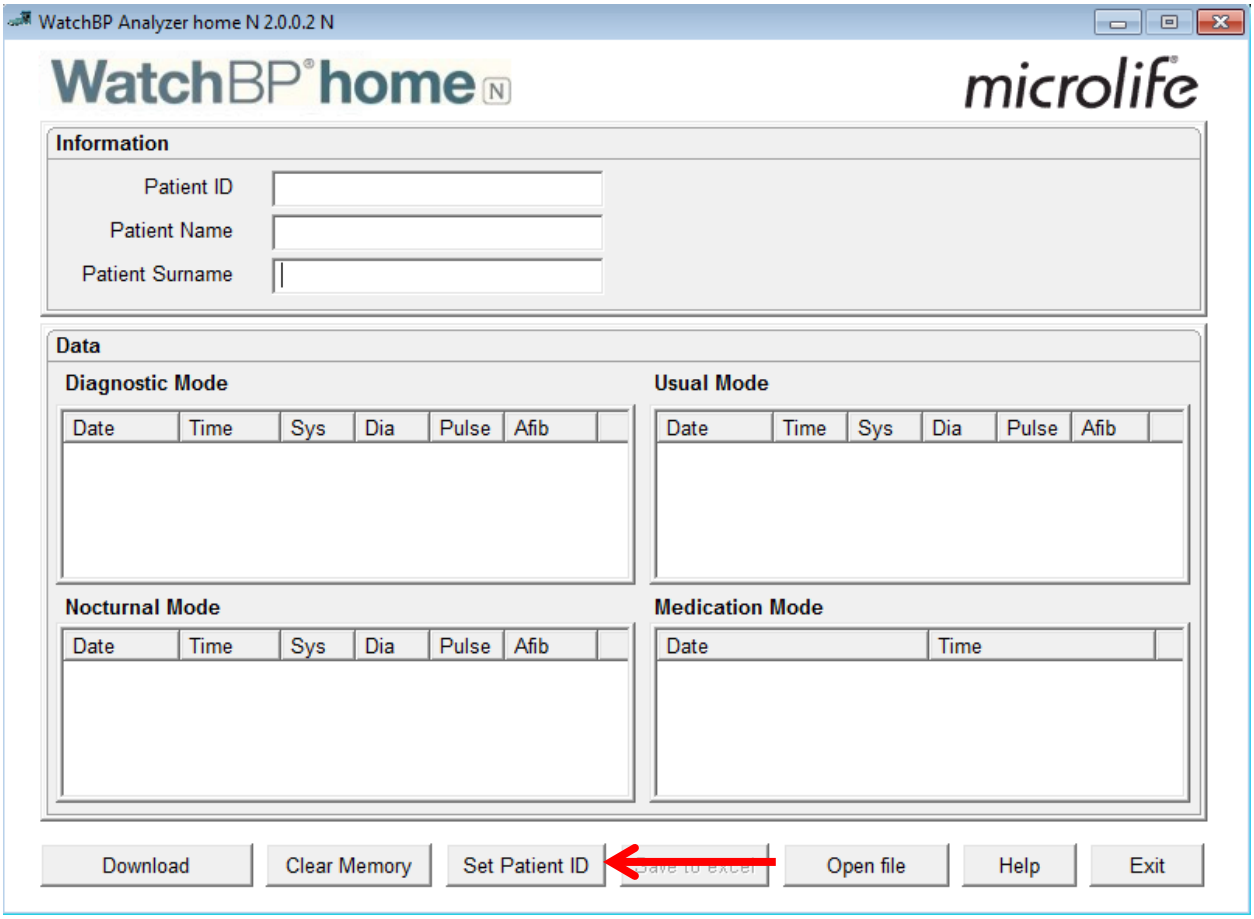
1. Connect the clinic device to the computer using the USB to micro-USB computer cable.



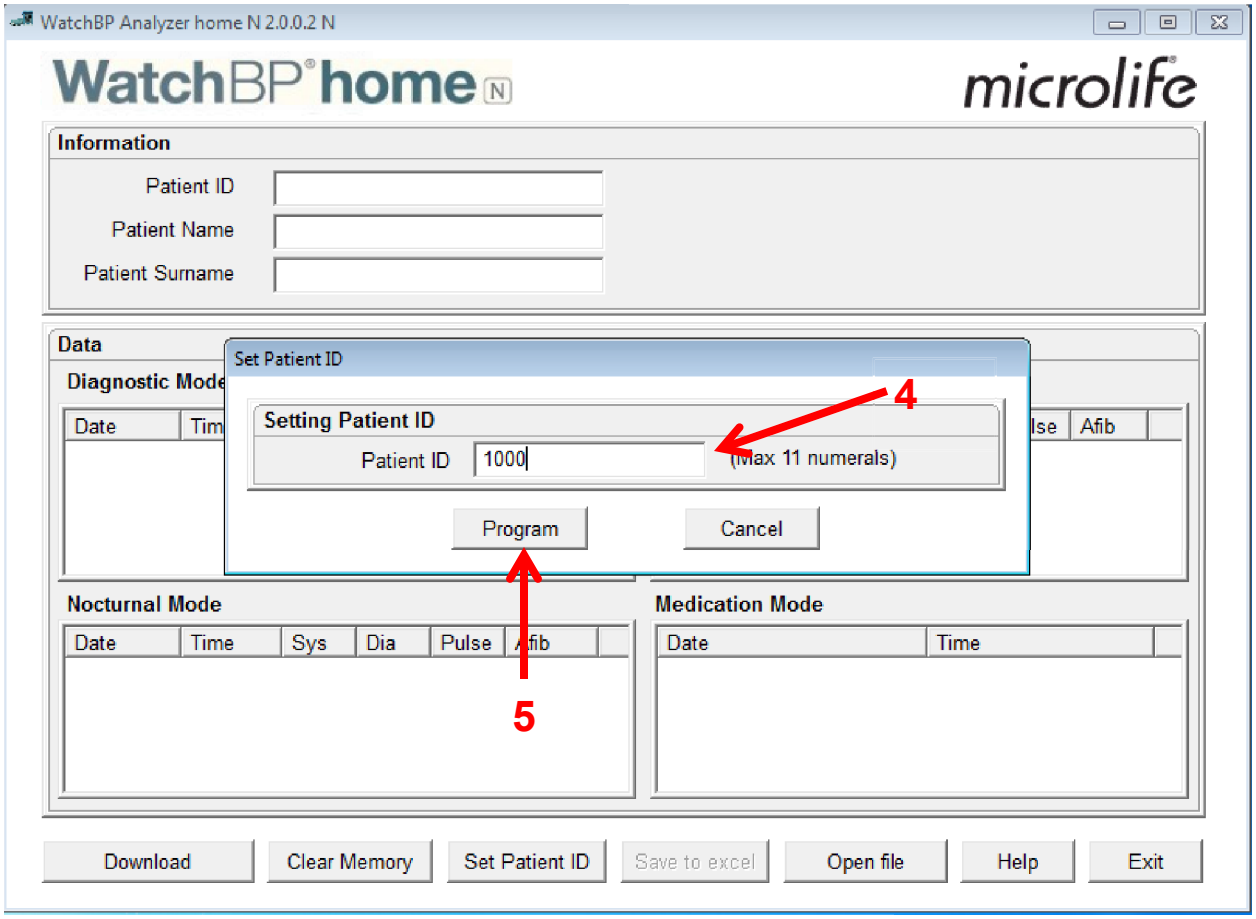
2. Launch WatchBP Analyzer Home N software.



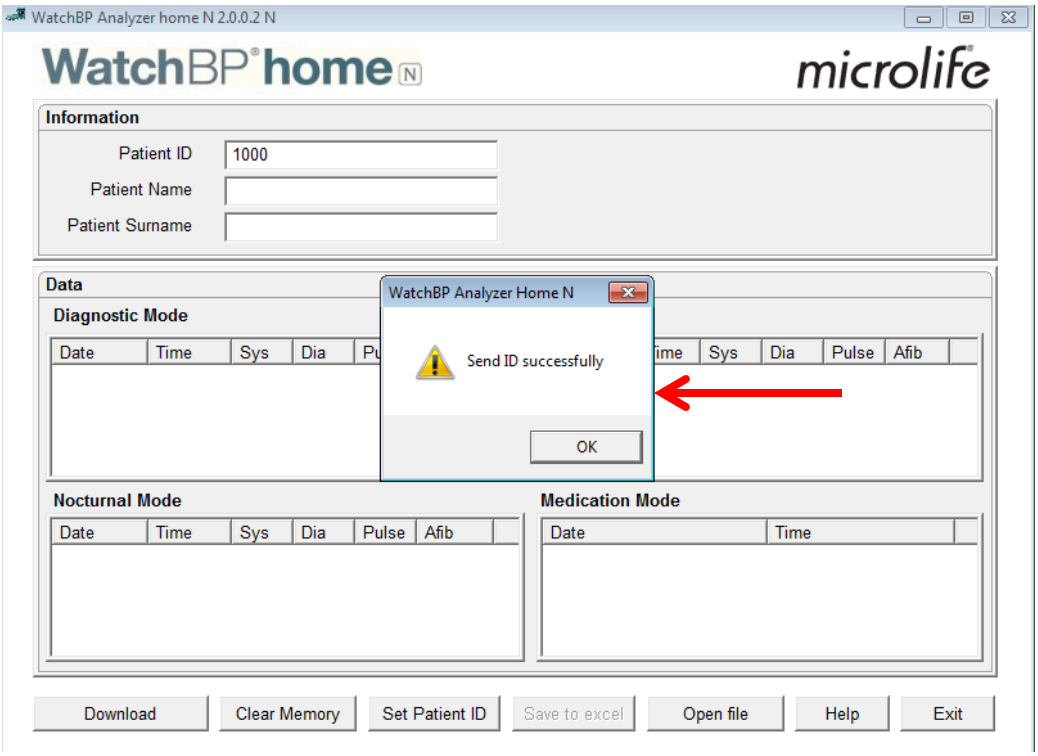
3. Select the “Set Patient ID” button on the main screen.

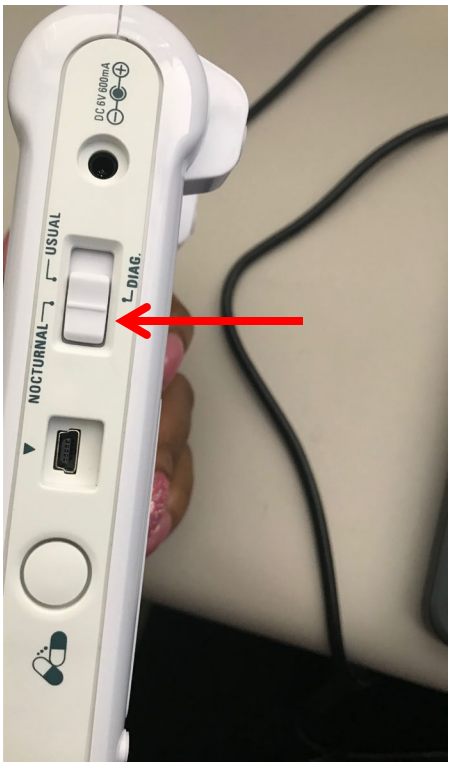


4. Enter the participant record id number.
5. Select ‘Program’.



6. A message will appear that says ‘Send ID successful’, press ‘Okay’.
7. Disconnect the device from the computer.
8. Make sure the device is in ‘Nocturnal’ mode by sliding the slider on the right side of the device to ‘Nocturnal’.


WatchBP Analyzer home N 2.0.0.2 N
WatchBP home N
microlife
Information
Patient ID
1000
Patient Name
Patient Surname
Data
Diagnostic Mode
Date
Time
Sys
Dia
Pulse
Afib
WatchBP Analyzer Home N
Send ID successfully
OK
Nocturnal Mode
Medication Mode
Download
Clear Memory
Set Patient ID
Save to excel
Open file
Help
Exit


USUAL
DIAG.
NOCTURNAL

Fitting the Actiwatch

1. Next, the research coordinator will explain to the participant how the Actiwatch works. The participant will be told the Actiwatch should be worn on the wrist of the non-dominant arm, the same arm as the BP cuff, and that it will provide a measure of his/her overall sleep.
2. The research coordinator will place the Actiwatch on the wrist of the participant's non-dominant arm, and then ask the participant to avoid getting the Actiwatch wet. We would prefer that the light sensor on the device be on the outside of the wrist.
3. After reviewing this information, the research coordinator will ask the participant if they have any questions regarding the Actiwatch.

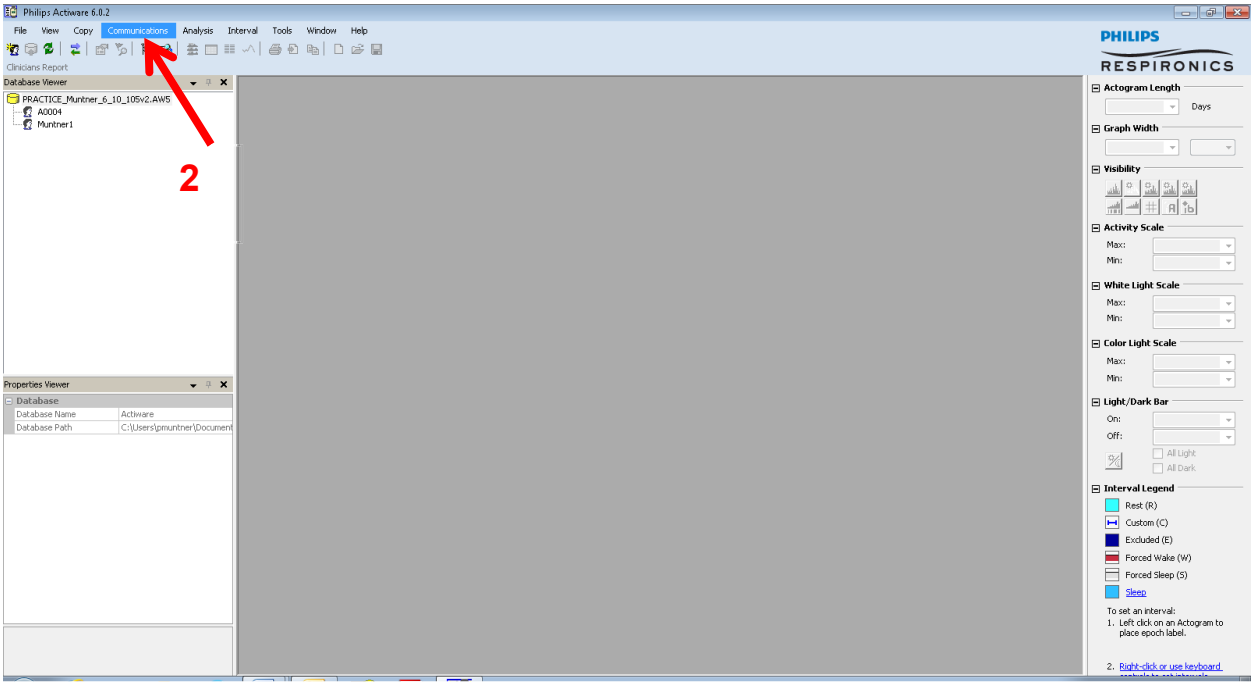
4. Next, the research coordinator will review the **Participant Instructions (see Appendix 3)** with the participant and remind him/her that if anything should happen with the equipment in the next 24 hours, he/she should contact the research team immediately using one of the phone numbers provided.

5. The research coordinator will thank the participant and confirm how the participant will bring back the ABPM/HBPM and Actiwatch devices along with the Device Log (**Appendix 2**) (see procedures for returning the equipment and Device Log below). **Be sure to instruct the participant where he/she should record their sleep and wake times on the Device Log (Appendix 1), and any times the equipment was removed.**

6. Finally, the participant should be given the **Participant Instructions (see Appendix 3)**. The participant should be informed of how to contact the research coordinators if he/she has a question/concern. The location of this information in the Participant Instructions should be shown to the participants.

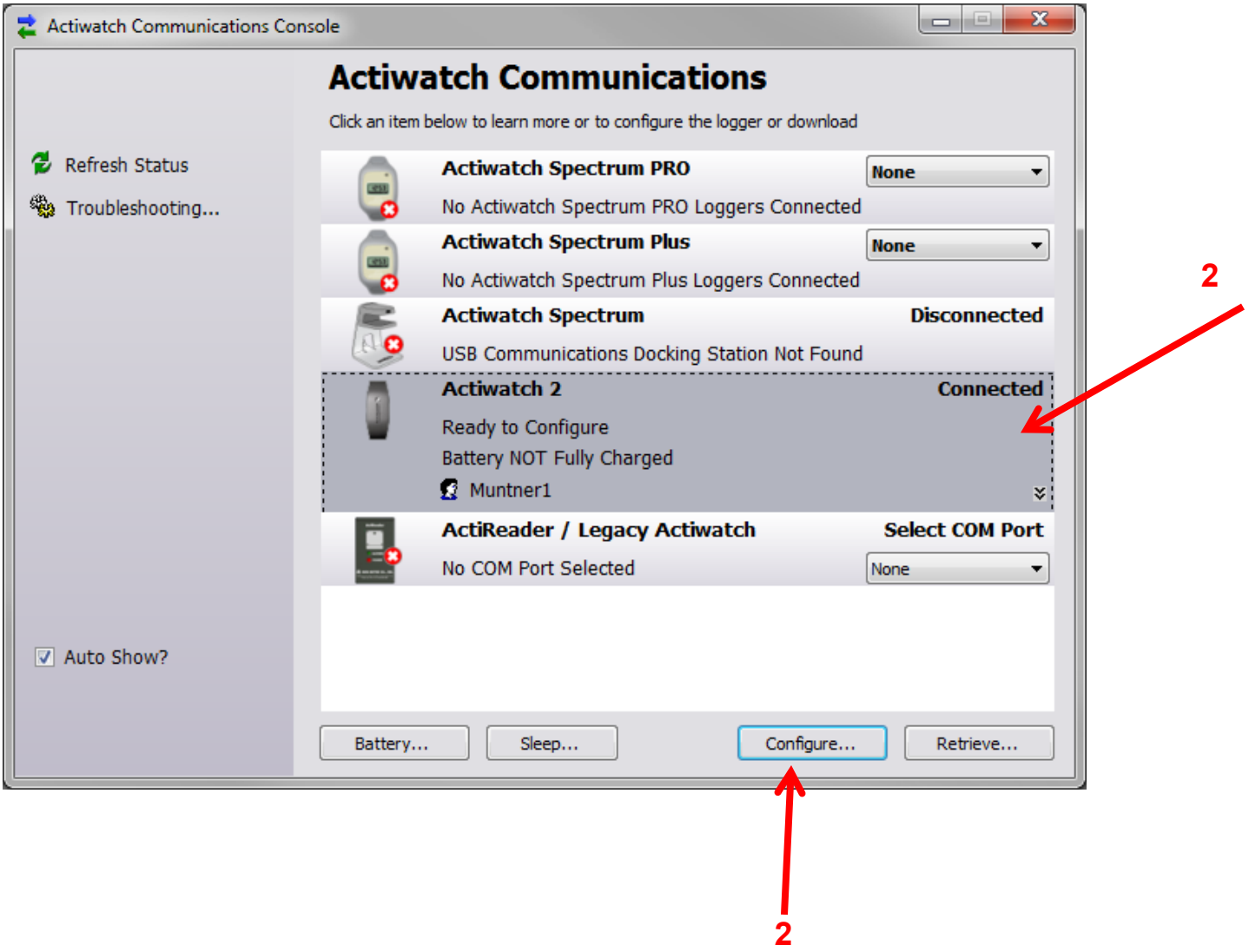
Configure/Initialize the Actiwatch

1. Make sure before using an Actiwatch device that it is fully charged. When the watch is on the charger, a solid green light indicates the watch is fully charged. A blinking light indicates that the watch is not fully charged. Before starting the process below, place the Actiwatch to be used in the charging station. Open the Philips Actiware 6.02 software (NOTE: the same computer must be used to initialize the ABPM and Actiwatch; ideally the data would also be downloaded to the same computer). Then select “Communications” on the menu bar at the top of the window, and select “Actiwatch Console”, which will bring up the “Actiwatch Communications Console”.

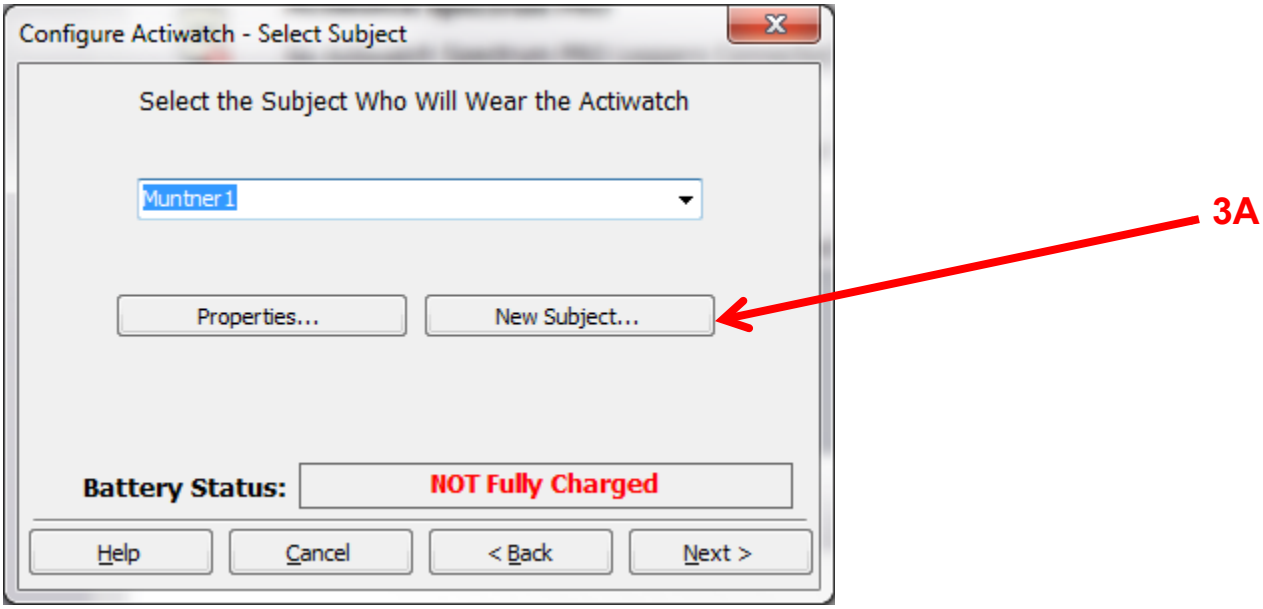


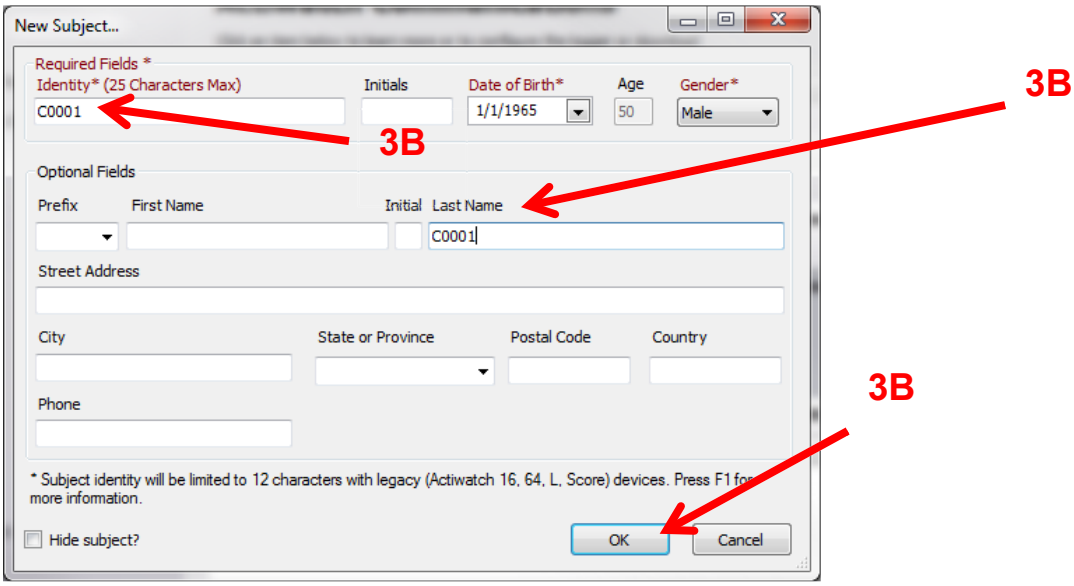
2. Select the “Actiwatch 2 device” and then select the “Configure” button at the bottom of

the screen.

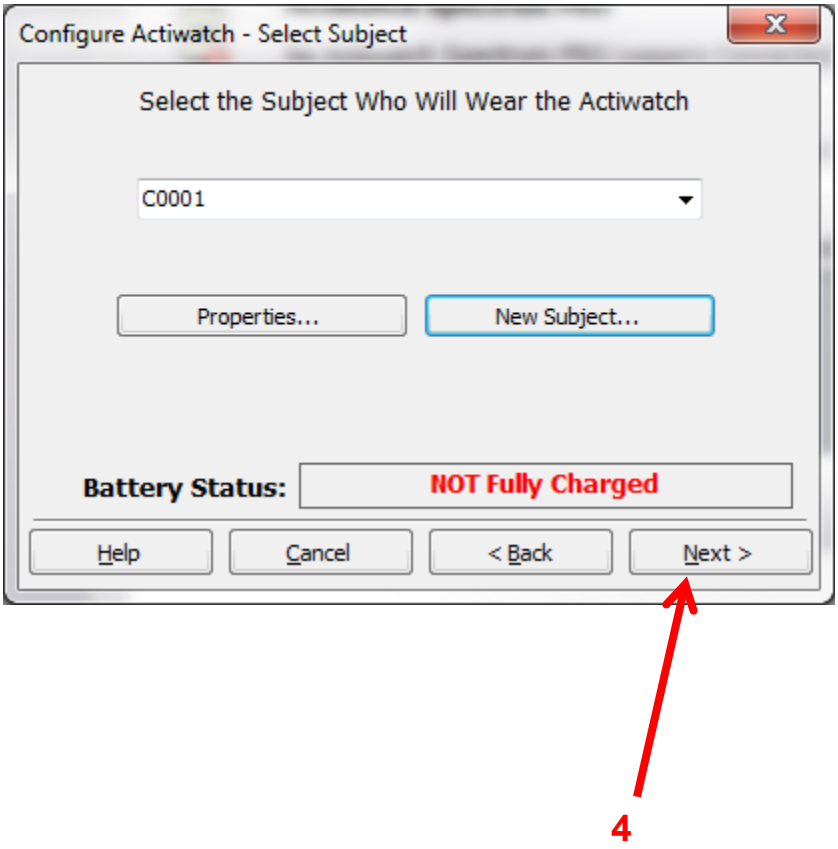

Actiwatch Communications Console
Actiwatch Communications
Click an item below to learn more or to configure the logger or download
Refresh Status
Troubleshooting...
Actiwatch Spectrum PRO
None
No Actiwatch Spectrum PRO Loggers Connected
Actiwatch Spectrum Plus
None
No Actiwatch Spectrum Plus Loggers Connected
Actiwatch Spectrum
Disconnected
USB Communications Docking Station Not Found
Actiwatch 2
Connected
Ready to Configure
Battery NOT Fully Charged
Muntner1
ActiReader / Legacy Actiwatch
Select COM Port
No COM Port Selected
None
Auto Show?
Battery...
Sleep...
Configure...
Retrieve...
2
2

3. Select “New Subject” button (see screen grab 3A below). Under the “Identity” field, type the participant ID (see screen grab 3B below). Do not enter the date of birth or gender. Leave as the default settings. Then under the “Last Name” field, enter the participant ID again (see screen grab 3B below). Then select the “OK” button.

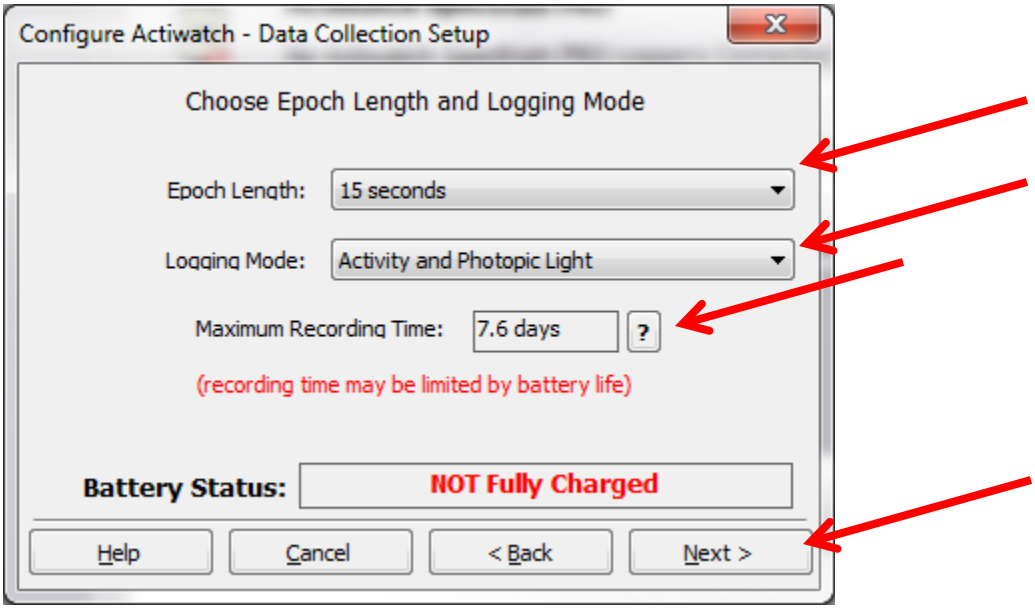




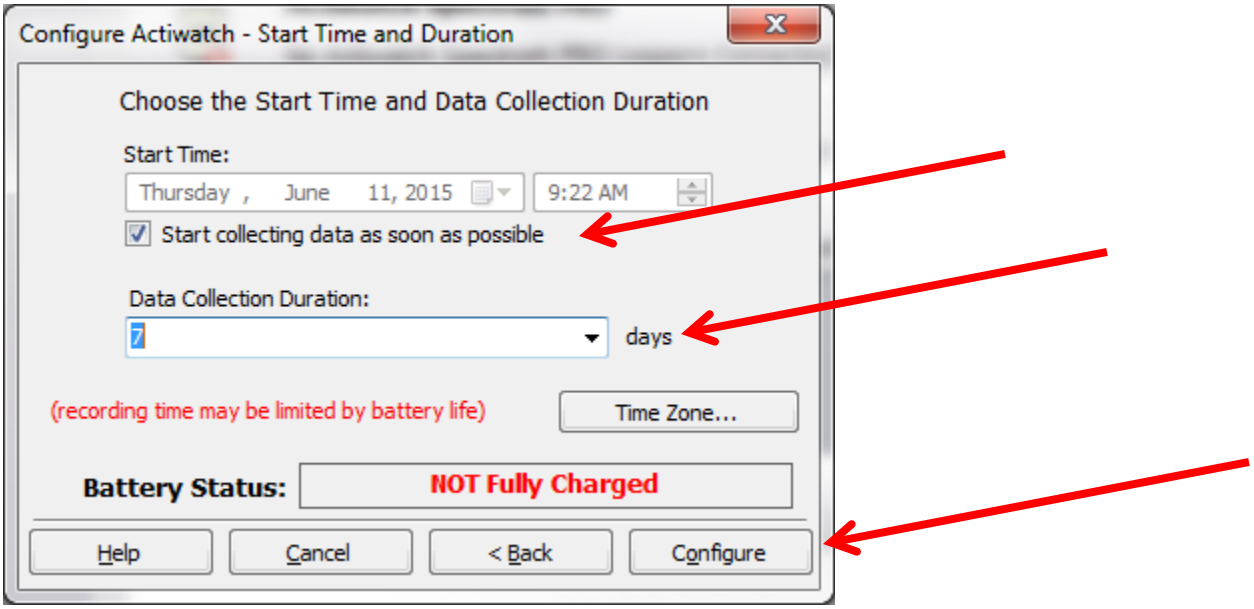
4. Then the “Configure Actiwatch” window will be shown on the screen. Select the “Next” button.



5. Make sure that the “Epoch Length” is 15 seconds and the “Logging Mode” is “Activity and Photopic Light”. Make sure that the “Maximum Recording Time” is at least 3 days. Select the “Next” button.



6. Select the check box for “Start collecting data as soon as possible”. The “Data Collection Duration” should be set at 7 days. Select “Configure” button. Then select “Continue” button. When done, hit “OK”.



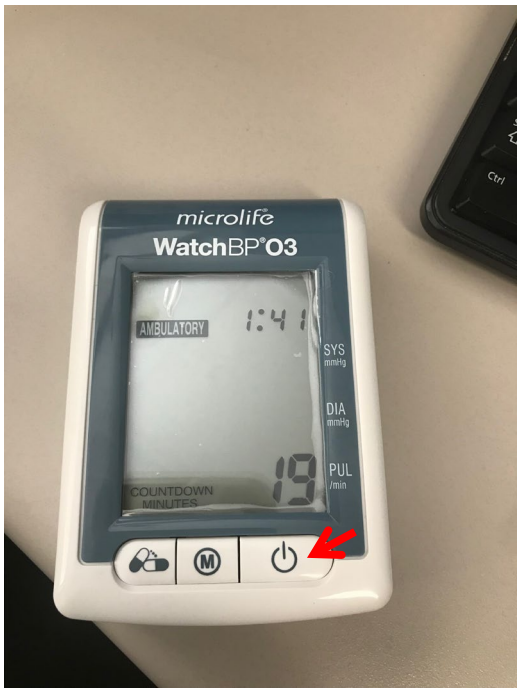
Instruction for Returning the ABPM/HBPM Device and Actiwatch

To return the ABPM/HBPM and actigraphy (Actiwatch) devices and the participant device log, participants must return to the clinic the day after performing the ABPM or HBPM (**REQUIRED**).

ABPM, HBPM, and Actiwatch Data Download Procedures

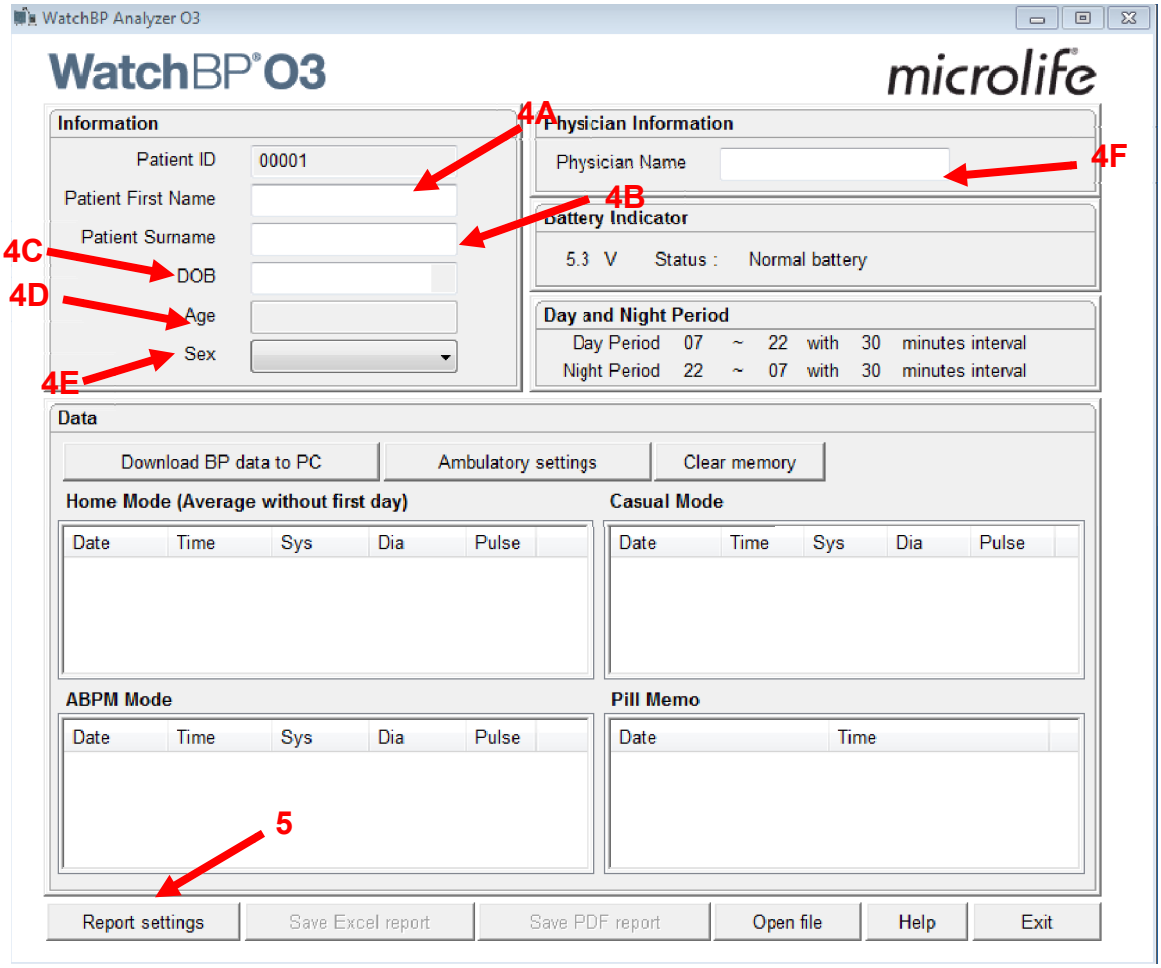
ABPM

1. On the front of the ABPM device (lower right) is the on/off (round) button. Make sure the monitor is on (if needed - press the on/off button).

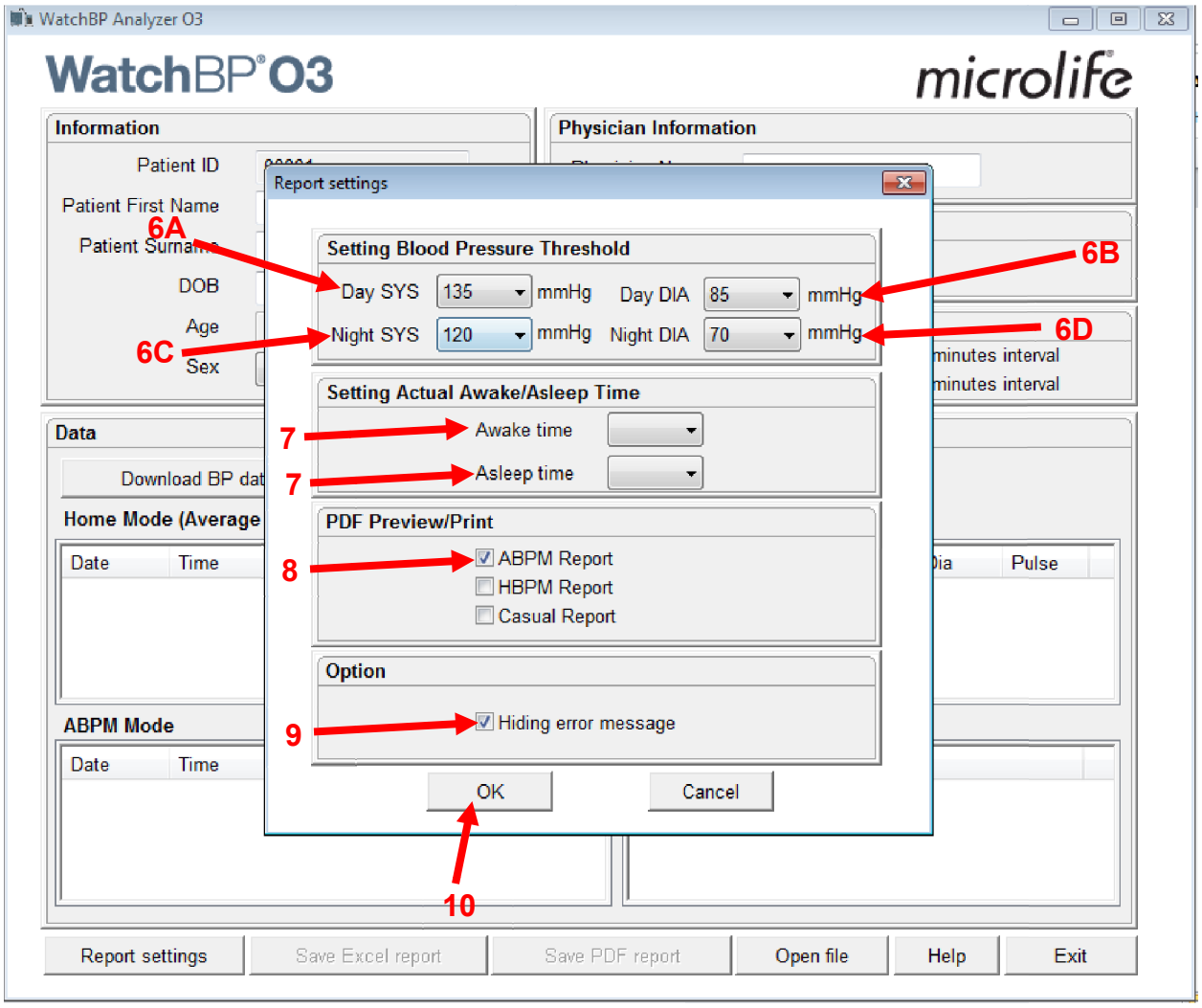


2. Connect the ABPM device to the computer using the USB to micro-USB computer cable.
3. Launch Microlife O3 Analyzer software.

4. Enter the participant's ID number. The patient id number should match the id number you entered prior to their ABPM period, but it should not match their record id number in REDCap. **Do not enter the participant's first and last name, date of birth, age, or sex [do not included any protected health information (PHI)]**:
    a. *Participant's first name; use participant's id number*
    b. *Participant's last name; use participant's id number*
    c. *Participant's date of birth; select 1/1/1950*
    d. *Participant's age; this field should auto-populate an age based on DOB*
    e. *Participant's sex; select 'M' for male for all participants*
    f. *Physician Name; enter 'NA'*



5. Select ‘Report Settings’.
6. Make sure the blood pressure thresholds for day and night systolic and diastolic blood pressure are correct.
    a. Day SYS – 130 mmHg
    b. Day DIA – 80 mmHg
    c. Night SYS – 110 mmHg
    d. Night DIA – 65 mmHg
7. Set the participant’s reported ‘Awake time’ and ‘Asleep time’ based on their device log.
8. Select ‘ABPM Report’.
9. De-select ‘Hiding error message’.



10. Select ‘OK’.

11. Select ‘Download BP data’.

12. Select ‘Save Excel report’.

13. Open the Excel report to verify that the data is present and accurate.

14. Go back to the WatchBP Analyzer O3.

15. Enter the participant’s information.

    a. *Participant’s first name;*

    b. *Participant’s last name;*

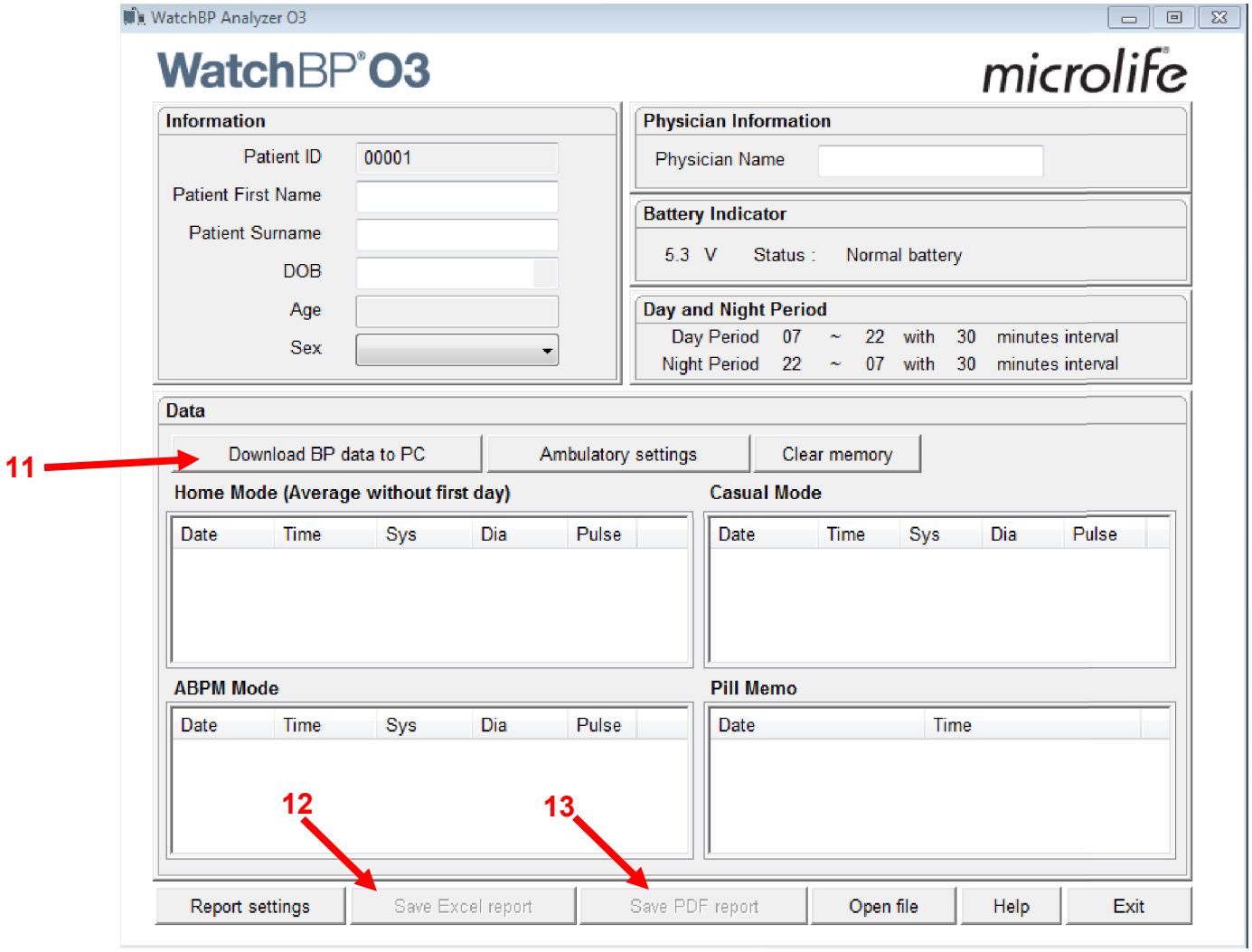
    c. *Participant’s date of birth;*

d. *Participant's age; this field should auto-populate an age based on DOB*

e. *Participant's sex;*

f. *Physician Name – if it is not provided or the participant did not consent to sharing their results with their provider; enter 'NA"*

16. Select 'Report settings' again. Select 'Hiding error message' then 'Okay'. Select 'Save PDF report'.



17. The PDF report will automatically open once it is downloaded and a comment box will appear. Make sure that you remove the following from the comment box before selecting 'OK'.

a. *White coat hypertension; remove from the comment box if it appears*

b. *Masked hypertension; remove from the comment box if it appears*

18. Once finished, remove the ABPM device from the computer by disconnecting it from the USB to micro-USB computer cable connector. **Turn off** the ABPM device and remove the batteries.

If at least 35 readings are obtained, ask the participant to complete the "POST ABPM QUESTIONNAIRE".

Ask the participant to complete questions regarding the quality of sleep over the 24-hour monitoring period and the comfort of the ABPM device.

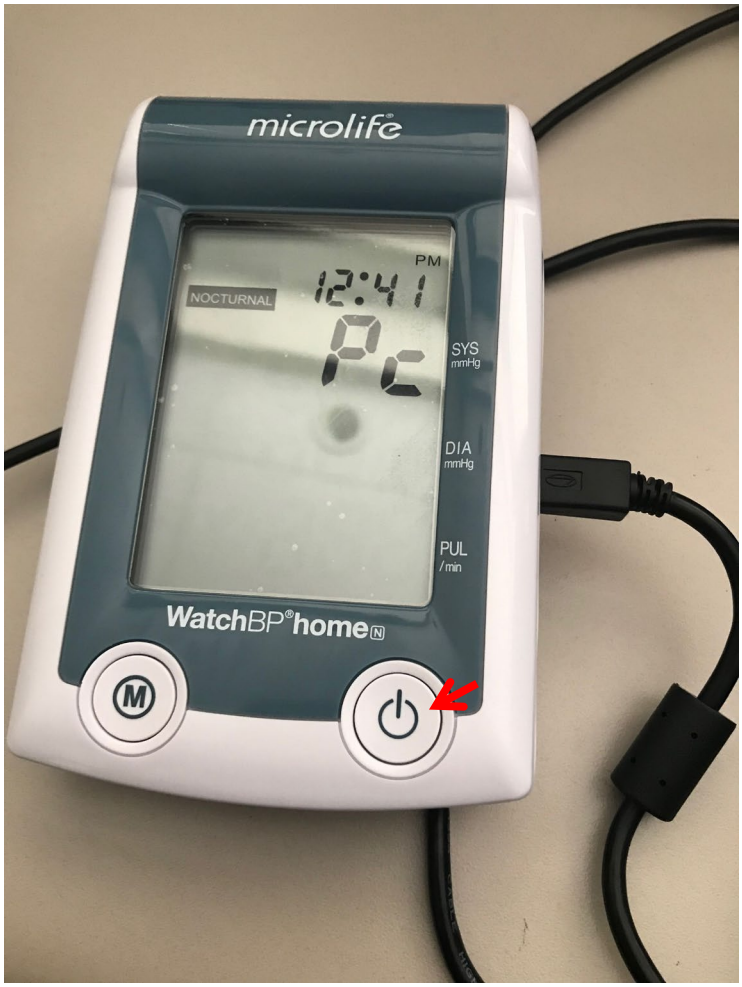
If at least 35 readings are NOT obtained, ask the participant to repeat the ABPM monitoring period for one night.

If they say yes, clear the memory and re-initialize the device with the participant's id number and adding the text ('-2') at the end (i.e. - 1101-2). Replace the device on the participant and review the instructions again. Give the participant a new ABPM device log to complete.

If they say no, ask the participant to complete questions regarding the quality of sleep over the 24-hour monitoring period and the comfort of the ABPM device using the "POST ABPM QUESTIONNAIRE".

HBPM

1. On the front of the HBPM device (lower right) is the on/off (round) button. Make sure the monitor is on (if needed - press the on/off button).

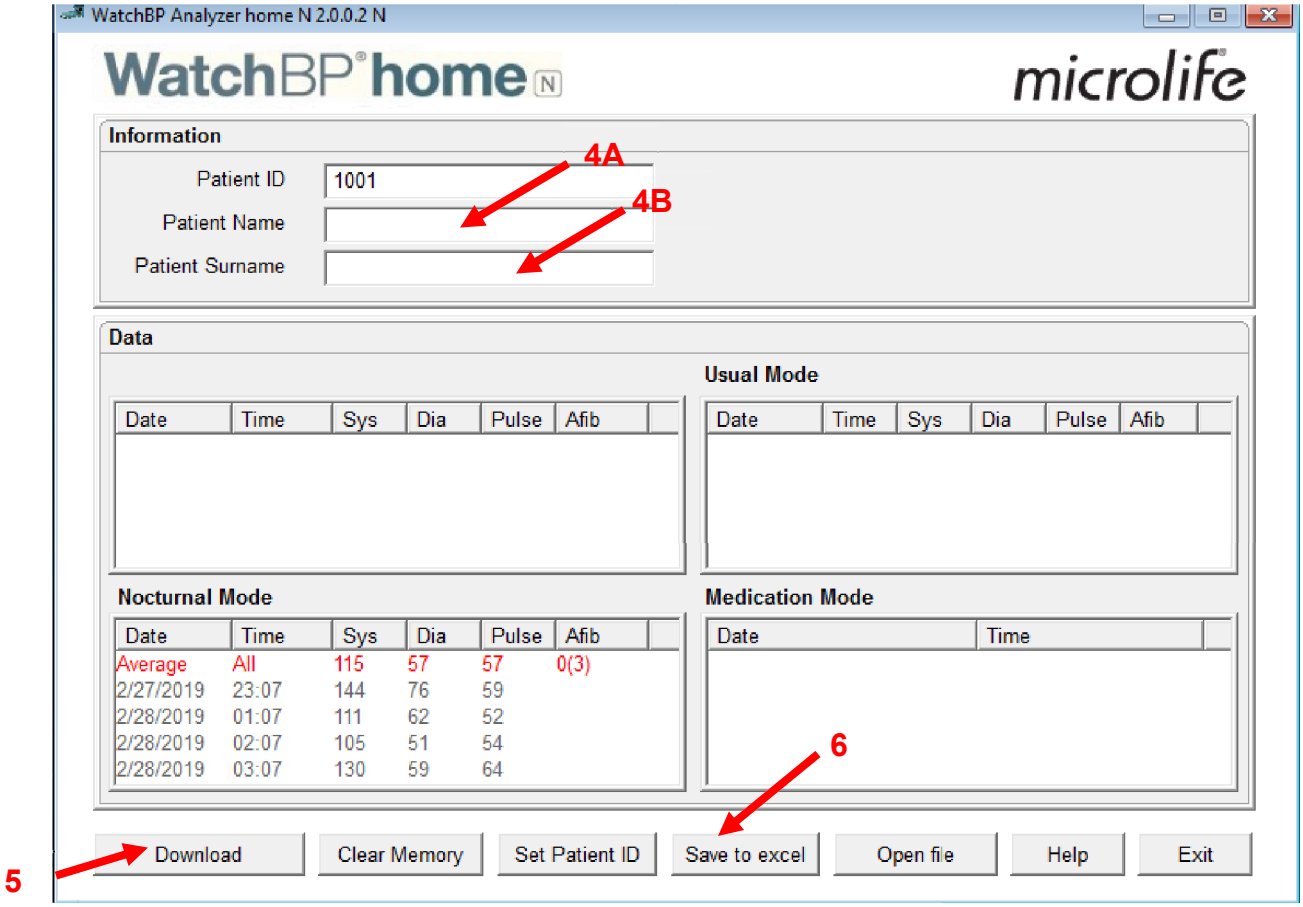


2. Connect the HBPM device to the computer using the USB to micro-USB computer cable.
3. Launch Microlife Home N Analyzer software.

4. Make sure the Patient ID matches the participant's record id number in REDCap. Enter the following:

    a. *Participant's first name; enter participant id number*

    b. *Participant's last name; ; enter participant id number*



5. Select ‘Download’.
6. Select ‘Save to excel’.

   Once you have confirmed the Excel document has the data in it by opening the file, remove the HBPM device from the computer by disconnecting it from the USB to micro-USB computer cable connector. **Turn off** the HBPM device and remove the batteries.

If at least 2 readings are obtained, have the participant complete the “POST HBPM QUESTIONNAIRE”

Have the participant complete questions regarding the quality of sleep over the overnight monitoring period and the comfort of the HBPM device.

If at least 2 readings are NOT obtained, ask the participant to repeat the HBPM period overnight.

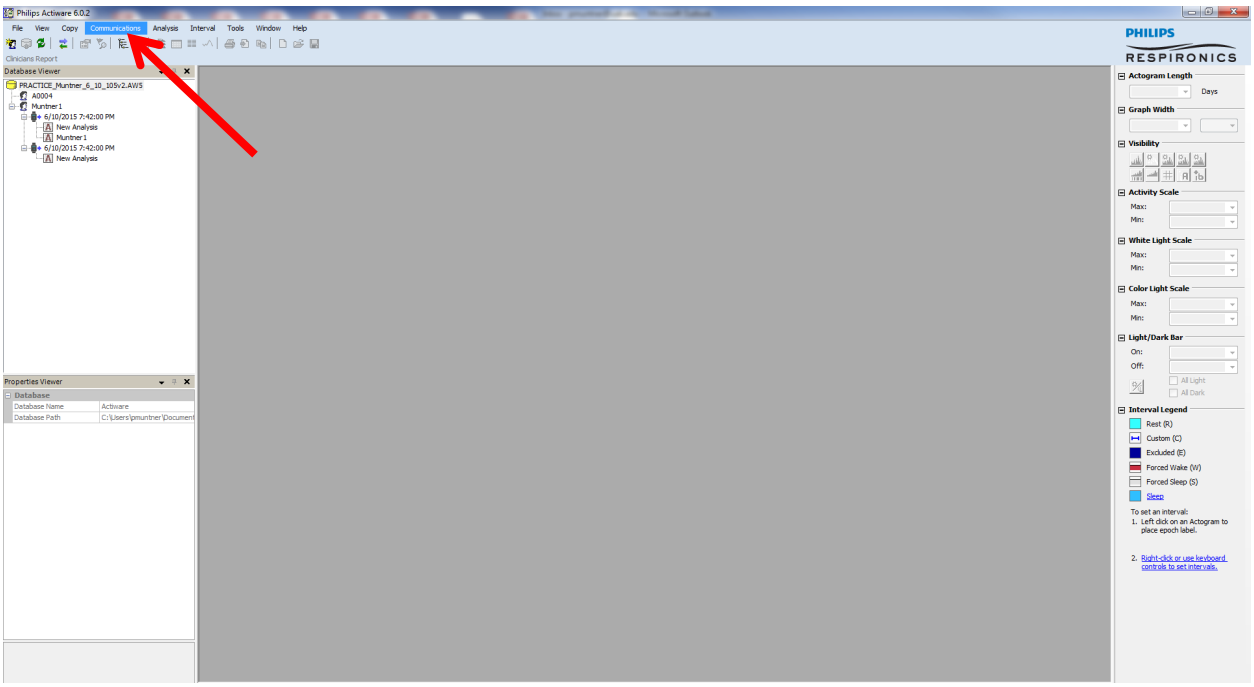
If they say yes, give the device back to the participant and provide them with instructions again on how to place the device and begin the readings. Also, provide them with a new HBPM device log.

If they say no, have the participant complete questions regarding the quality of sleep over the overnight monitoring period and the comfort of the HBPM device using the “POST HBPM QUESTIONNAIRE”.

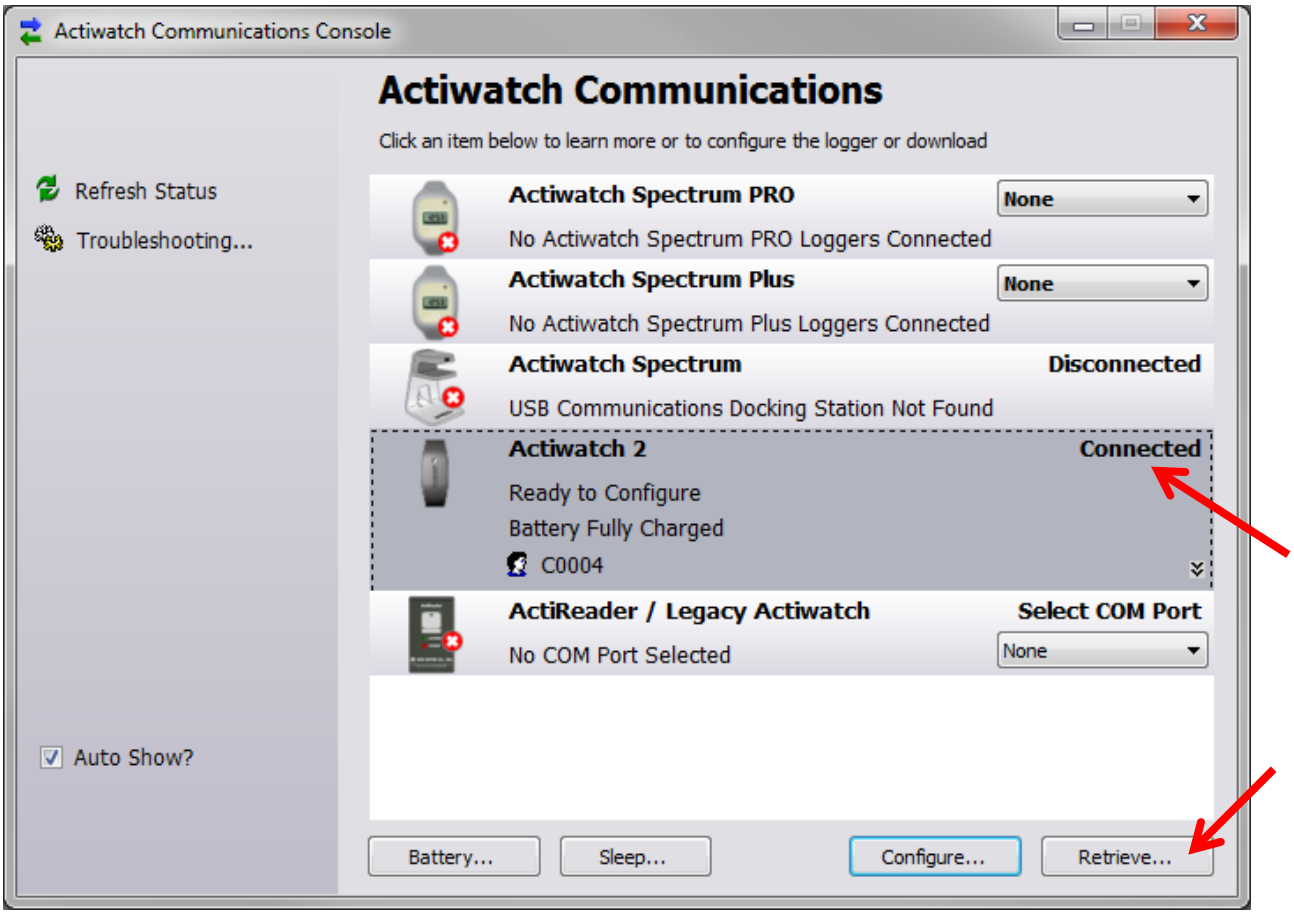
Actiwatch*

The Actiwatch database is updated with each new participant's downloaded data. Before starting the study (before the first participant), the database should be saved onto a network drive that is backed up daily. This is done by selecting File → Database → New. Then the Database should be saved into the appropriate location.

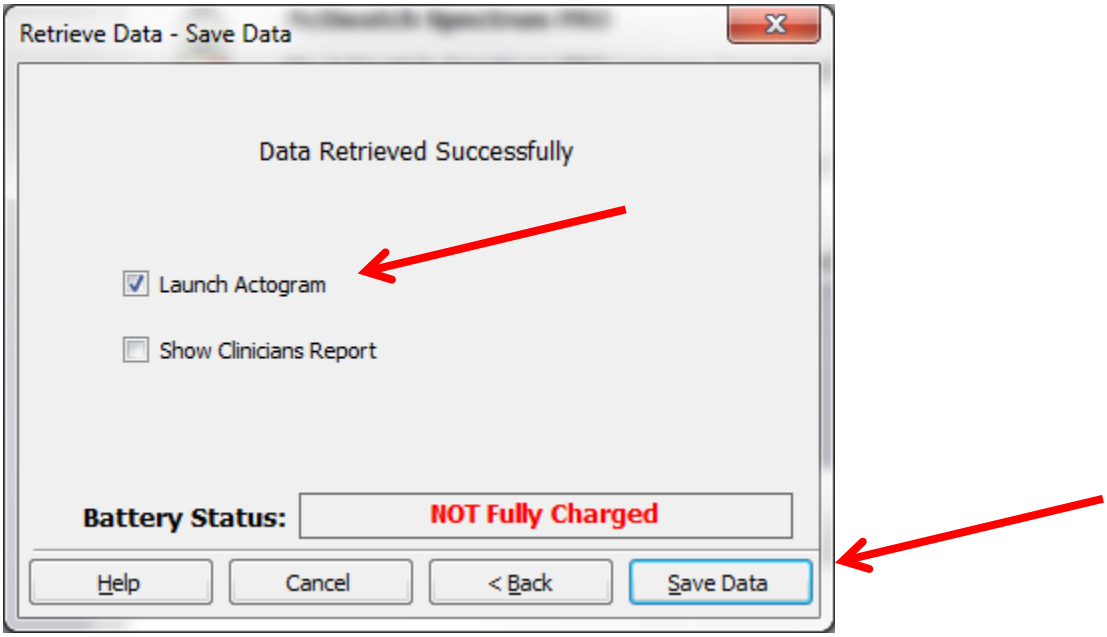
1. Place Actiwatch device onto the charger.
2. Launch Philips Actiware 6 software.
3. In the Actiwatch software window, click "Communications" on the Menu Bar at the top of the window and then select "Actiwatch Communications Console".



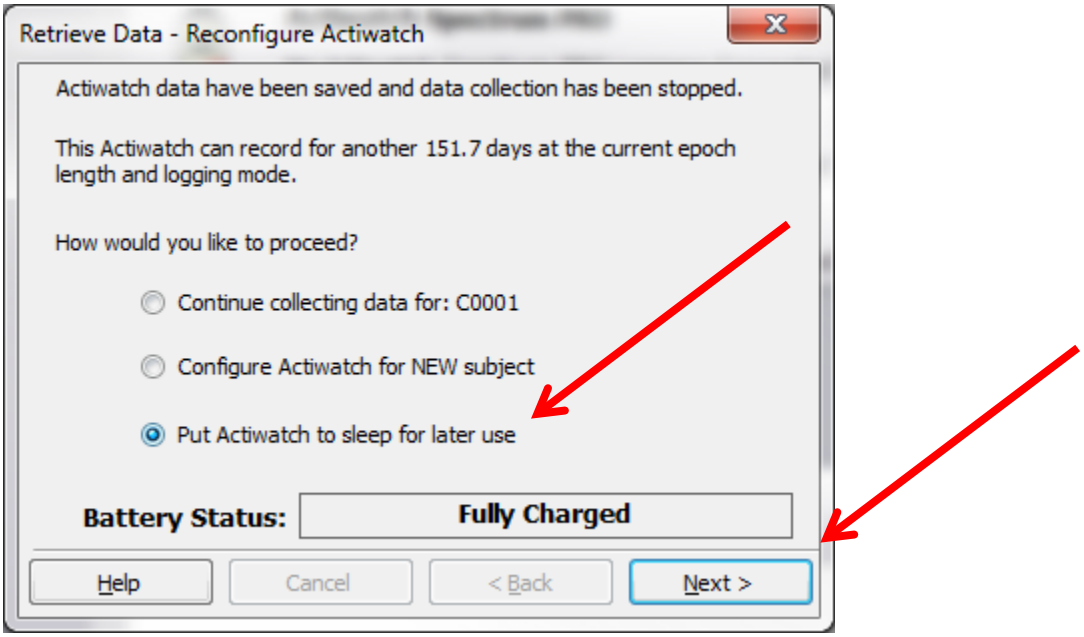
4. Select the “Actiwatch 2” device (the participant’s ID number should be located under the “Actiwatch 2”). Click the “Retrieve” button at the bottom of the window.



5. Make sure that the “Launch Actogram” check box is selected. Then select the “Save Data” button.



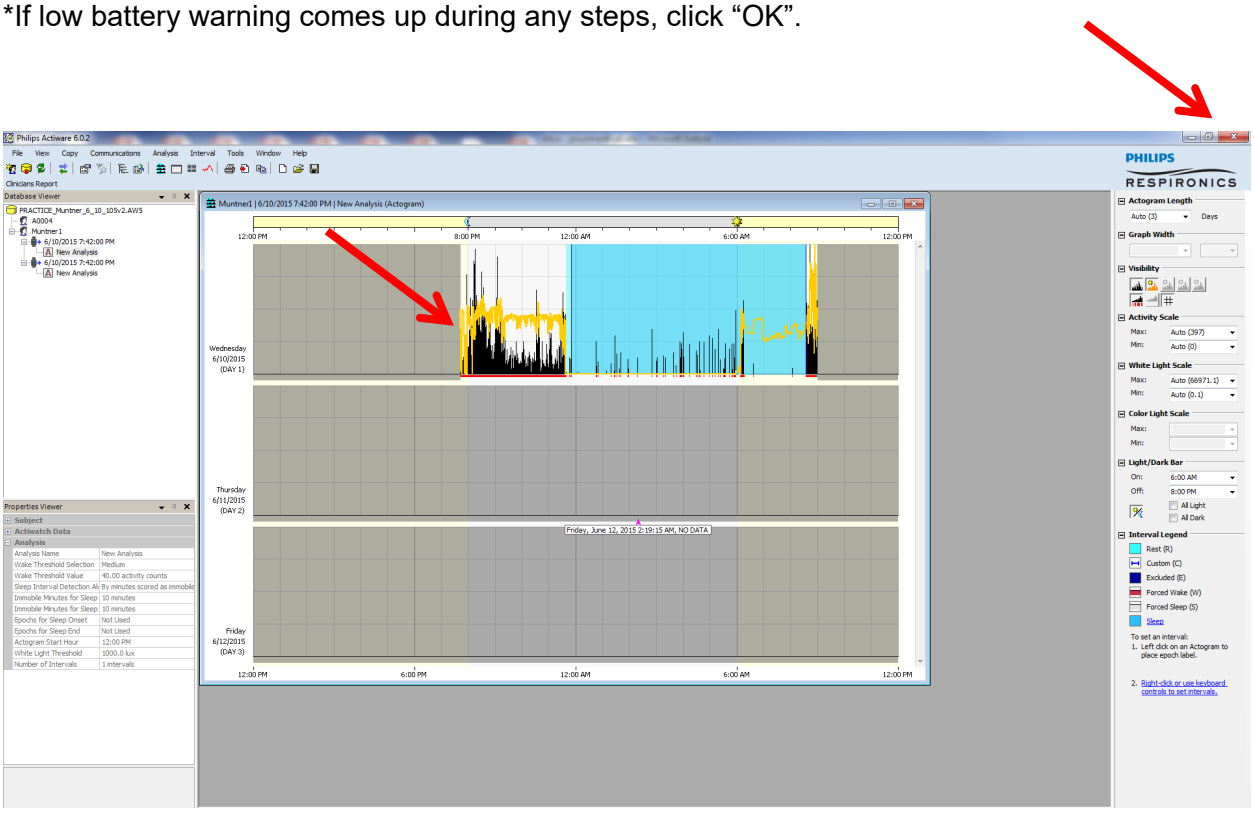
6. Make sure the radio button for “Put Actiwatch to sleep for later use” is selected and then click “Next”. Then select “Put Actiwatch to Sleep” (if this message comes up).



7. Next, click the “OK” button on the “Actogram window” (if this appears).

8. Review the Actogram window to make sure that data has been collected. Then close “Actogram” window (see screen grab below).

*If low battery warning comes up during any steps, click “OK”.



Troubleshooting Devices

If the **Office AFIB device** is not working properly, please check the following:

- If the opening screen does not read ‘Connected’ in the bottom left corner, please turn the device off and back on until it is connected.
- If still not connected, check to make sure the proper USB connection cable is being used (labeled ‘Office AFIB’).
- If the cuff does not inflate, please make sure that the blood pressure cuff is connected to the correct side of the device (i.e., if ‘Left’ is selected, then the device cuff should be connected to the left side of the device).

If the **O3 ABPM device** is not working properly, please check the following:

- If the opening screen does not provide information on the battery life then the device is not properly connected. Check to make sure the proper USB connection cable is being used (labeled ‘WatchBP O3’).
- If the data is not downloading, disconnect the device from the laptop and reconnect. If there is still trouble connecting, use another USB connection cable.
- If the cuff is not inflating, please check the connector on the tube (**see picture below**). If still not inflating correctly, use another blood pressure cuff.

If the **Home N device** is not working properly, please check the following:

- If the opening screen does not provide information on the battery life then the device is not properly connected. Check to make sure the proper USB connection cable is being used (labeled ‘WatchBP Home N’).
- If the data is not downloading, disconnect the device from the laptop and reconnect. If there is still trouble connecting, use another USB connection cable.
- If the cuff is not inflating, please check the connector on the tube (**see picture below**). If still not inflating correctly, use another blood pressure cuff.

If none of these troubleshooting methods work, please call Dr. Muntner at **(205)-975-8077**.

Storing and Sending Results

Once you have downloaded the participant's data from the ABPM and HBPM devices, verify that the reports contain the data and is named using the participant's study id number.

ABPM Excel reports should be stored in the following folder on the shared CVD drive:

'O:\BetterBP\ABPM Excel Reports'

ABPM PDF reports should be stored in the following folder on the shared CVD drive:

'O:\BetterBP\ABPM PDF Reports'

HBPM Excel reports should be stored in the following folder on the shared CVD drive:

'O:\BetterBP\ HBPM Excel Reports'

For ABPM PDF reports that will be sent to participants and their providers, you must use Adobe Pro to redact the participant's ID number (i.e., place a black box over the id number). All PDF reports that are redacted and ready to be sent must be stored in the following folder:

'O:\BetterBP\ABPM PDF Reports\To be sent to participants (redacted)'

We will mail all results to the participant following the conclusion of their study visits. For participants who indicated they would like their results sent to their provider, please refer to the list of physician fax numbers in the **Appendix**.

Device Storage and Cleaning Cuffs

Clinic

On the top of the clinic device, there is a battery indicator light. If the indicator light blinks '**Orange**', the battery is at half power. '**Red**' indicates that the battery is low. Please plug in the device and charge until the indicator light turns '**Green**'.

Once the device is fully charged, please unplug the device and store in the storage room (CHB19 Rm 116).

After each participant, please wipe the blood pressure cuff and tubing with a mild antiseptic wipe. Allow it to dry and then store in the storage room (CHB19 Rm 116).

Once the participant has returned their device and their data has been downloaded, please do the following:

ABPM

Remove the batteries from the device, wipe the cuff and tubing with a mild antiseptic wipe, and store in the proper place. Place the used batteries in the box labeled 'Used Batteries'. Store the device in the storage room (CHB19 Rm 116).

HBPM

Remove the batteries from the device, wipe the cuff and tubing with a mild antiseptic wipe, and store in the proper place. Place the used batteries in the box labeled 'Used Batteries'. Store the device in the storage room (CHB19 Rm 116).

Actiwatch

Wipe the device with an alcohol wipe and place it on the docking station to charge. Once the indicator light on the front of the docking station remains firmly '**Green**', remove the device and store the device in the storage room (CHB19 Rm 116).

Blood and Urine Specimen Collection

The following table includes the volume and processing procedures of specimen to be collected and sent to Columbia. **Note: The volume for collection includes enough for both processing and storage for future use. Please only send the volume for processing to Columbia's CALM Lab.**

Supplies Needed

1. (Velcro) Tourniquets
2. Vacutainer Safety-Lok Blood Collection 21 G
3. Vacutainer Safety-Lok Blood Collection 23 G
4. Vacutainer Needle Holder
5. Gauze pads 2x2
6. Band-Aids
7. Non-latex Gloves (Small and medium)
8. Hypoallergenic Tape
9. Alcohol swabs

Blood samples summary

Blood draw order	Tube type	Test type
1	5 mL Gold top tube	Creatinine Complete Lipid Panel Glucose
2	2 mL EDTA lavender top tube	HbA1c
3*	4 mL EDTA lavender top tube	Genetic Testing
4*	5 mL Gold top tube	TBD testing
5*	5 mL EDTA lavender top tube	TBD testing
6*	Citrate blue top tube	TBD testing

*Only if the participant consented to future testing**.**

Overview of specimen processing and aliquots

Order	Specimen type	Volume	Collection	Test	Procedures after collection
NA	Urine	3 mL	Urine collection container w/o preservatives	Urine albumin and urine creatinine	Transfer 3ml of urine to a 5ml cryovial for storage in freezer (-20 to -80 C) until shipment Store remaining sample for future use
1	Blood	5 mL	Gold top tube	Creatinine Complete Lipid Panel Glucose	1. Centrifuge sample at least 30 minutes after collection but no more than 2 hours 2. Aliquot serum into (1) 1ml cryovial 3. Store cryovial in freezer (-20 to -80 C) until shipment
2	Blood	2 mL	EDTA lavender top tube	HbA1c	No processing needed by UAB staff, store tube in freezer (-15 to -25C) until shipment
3*	Blood	4 mL	EDTA lavender top tube	Genetic testing	No processing needed by UAB staff, store tube in freezer (-15 to -25C) for future use
4*	Blood	5 mL	Gold top tube	TBD testing	1 mL aliquots x 2 for storage
5*	Blood	5 mL	EDTA lavender top tube	TBD testing	1 mL aliquots x 3 for storage
6*	Blood	4.5 mL	Citrate blue top tube	TBD testing	1 mL aliquots x 2 for storage

*Only if the participant consented to future testing.

Processing Procedures and Timing

One 5 mL Gold Top Tube (for Creatinine Complete Lipid Panel Glucose, immediate)

- Allow the sample to sit for at least 30 minutes prior to centrifuging.
- Centrifuge using 2300 g for 10 minutes at room temperature.
- 1 mL of serum needed for processing at CALM Lab

One 2 mL EDTA lavender top tube (for Hemoglobin A1c, immediate)

- Do not centrifuge this sample. Store in tube.
- 2 mL of whole blood needed for processing at CALM Lab.

One 4 mL EDTA lavender top tube (for Genetic testing)

- Do not centrifuge this sample. Store in tube.
- 4 mL of whole blood needed for processing at CALM Lab.

One 5 mL Gold top tube (for TBD testing)

- Allow the sample to sit for at least 30 minutes prior to centrifuging.
- Centrifuge using 2300 g for 10 minutes at room temperature.
- Store two (2) 1 mL aliquots for future use.

One 5 mL EDTA lavender top tube (for TBD testing)

- Allow the sample to sit for at least 30 minutes prior to centrifuging.
- Centrifuge using 2300 g for 10 minutes at room temperature.
- Store three (3) 1 mL aliquots for future use.

One 4.5 mL Citrate blue top tube (for TBD testing)

- Allow the sample to sit for at least 30 minutes prior to centrifuging.
- Centrifuge using 2300 g for 10 minutes at room temperature.
- Store two (2) 1 mL aliquots for future use.

Storage of specimen

Once processed and aliquoted, please label each sample using the pre-printed labels with the participant id number, study name, and sample type.

Place the samples in the -20C freezer in CHB19 Rm 101-G.

Shipping Specimen to CALM Lab

SPECIMEN TO SHIP TO CALM LAB	ASSAYS PERFORMED ON SINGLE SPECIMEN	SHIPPING PROCEDURES
At least 3ml of urine housed in 5ml cryovial	Urine albumin Urine creatinine	**1.** Place cryovial or tube in specimen tube mailer and wrap mailer with a rubber band **2.** Place mailer in a biohazard bag **3.** Place bag inside a FedEx shipping cooler that is filled with dry ice **4.** Adhere dry ice and biohazard labels to outside of FedEx package
At least 1ml of serum in a 2ml cryovial	Serum creatinine Complete lipid panel Glucose	
2ml of whole blood in a 2ml EDTA lavender top tube	HbA1C	

shipping procedures are the same for all specimens: **overnight shipping <u>every 1st Monday of the month (if holiday, please ship next business day)</u>

**make sure all vials, tubes and boxes are labeled properly with IDs, study name (Better BP Study), and test to be done

**keep tracking numbers with UAB staff to ensure delivery at CALM lab

**send all requisition forms to CALM lab for detailed processing instructions

**confirm someone from Dr. Shimbo's group will be able to receive the specimen

Samples should be shipped to: Daichi Shimbo, MD
Columbia University Medical Center
622 West 168th Street
PH 9-310
NEW YORK, NY 100323720

Echocardiograms

Cardiac measurements will be obtained according to the 2015 recommendations* of the American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging (EACVI). Left ventricular (LV) measurements for LV end-diastolic dimension (LVEDd), septal wall thickness (SWTd), and posterior wall thickness (PWTd) will be obtained.

LVM (grams) will be determined using the ASE formula. LVMI will be calculated as LVM divided by body surface area (g/m^2) and secondarily by dividing by $height^{2.7}$ ($g/m^{2.7}$).

The following are additional measures to be conducted:

- Shortening (FS, %)
- LV systolic function defined by LV ejection fraction (LVEF, %) = 100 x (LVEDV-LVESV) / LVEDV using modified Simpson's rule.

The following are measures that may be obtained at a future date. Imaging will be conducted now to capture these items, but measurements will not be performed.

- LV diastolic function: E/A ratio, E' (cm/s), A' (cm/s), E/E' ratio, isovolumetric relaxation time (ms), deceleration time (ms)
- Other parameters: Left atrial volume (mL), right ventricular fractional area change, tricuspid annular plane systolic excursion (TAPSE) and tricuspid annulus s', and global longitudinal strain (GLS)
- Hemodynamics: stroke volume (SV, mL) = VTI x cross-sectional $area_{LVOT}$; heart rate (HR); cardiac output (L/min) = SV x HR

*_J Am Soc Echocardiogr_ 2015;28:1-39.

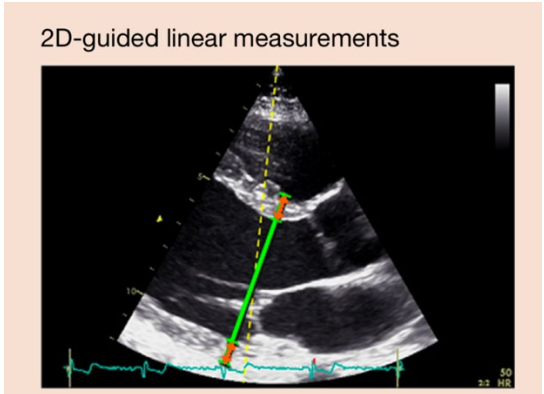
Adult Transthoracic Echocardiogram Protocol

Note: Heart Rate should be <u>continuously</u> documented on screen during image acquisition. Heart rate is needed to calculate different formulae. All spectral Doppler should be displayed at a sweep speed of 100 mm/sec.

Also, the disk (CD or DVD) should be labeled with a participant ID#.

A. Parasternal Long Axis:

1. Show at increased depth to show extra-cardiac structures.
2. Decrease depth and then show at least 3 beats in parasternal long axis view for LV wall motion. LV chamber and wall thickness measurements will be performed using 2D-guided linear measurements (see **Figure 1**).
3. Zoom on aortic valve. Show aortic valve and LVOT (for diameter measurements).
4. Perform Color Doppler of aortic valve.



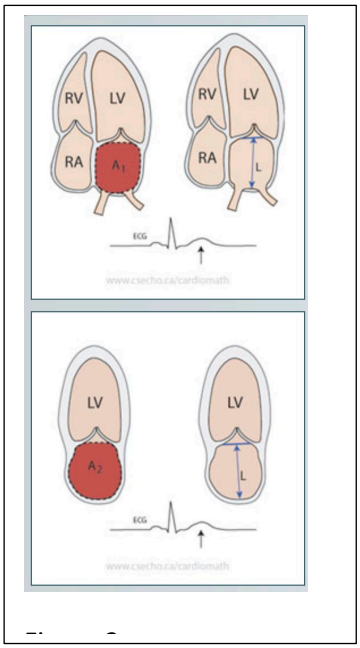
B. Parasternal Short Axis:

1. Will not obtain images.

C. Apical Views:

1. Start 2D with the apical four-chamber view at increased depth to show extra-cardiac structures.

2. Decrease depth and show the LV in **apical four-chamber view** for at least 3 beats. This view will be used for LVEF assessment (using modified Simpson's rule).



Then optimally show the left atrium for assessment of left atrial volume (see **Figure 2**). Put Color Doppler on the mitral valve to show a complete jet of regurgitation if any is present.

Interrogate the mitral valve with PW Doppler with the sample volume at the tips of the mitral leaflets (show E and A waves). Show for at least 3 beats. If mitral stenosis is present, switch to CW Doppler, and show enough of E and A waves for assessment of mean gradient and pressure half-time.

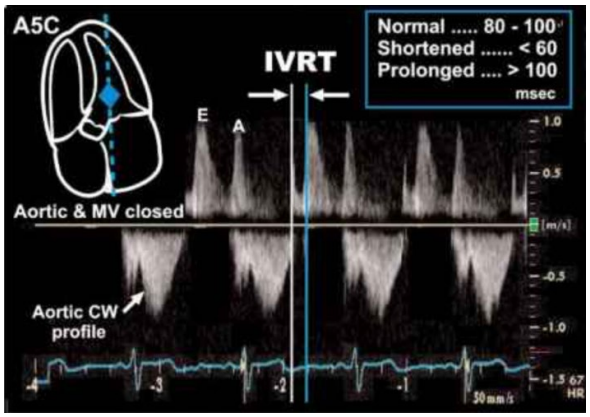
Perform DTI of mitral annulus (lateral and medial) and show e' and a'. Show for at least 3 beats for each annulus.

Show RV for size and function in apical four-chamber view for at least 3 beats. Switch to M-mode for assessment of tricuspid annular plane systolic excursion (TAPSE). Show for at least 3 beats. Finally, switch to DTI of tricuspid annulus. Show for at least 3 beats

Angle and show the **apical five-chamber view** for at least 3 beats. Then interrogate across AV and LVOT with CW Doppler. If increased gradient is present, slide the sample volume using PW from the LV apex, down the LVOT, and to the AV to pinpoint the area of increased gradient. Once area of increased gradient is identified, switch to CW Doppler and show the peak resting gradient for at least 3 beats.

Perform PW Doppler of the LVOT for the assessment of LVOT VTI for at least 3 beats.

3. Also, in the **apical five-chamber view**, using CW Doppler, place the sample volume at the junction of the LVOT and the anterior mitral leaflet to capture both LVOT mitral valve inflow profiles (see **Figure 3**).



4. Rotate to **apical two-chamber view:** show the LV at least 3 beats for LVEF assessment. Then optimally show the left atrium for assessment of left atrial volume (see **Figure 2**). Put Color Doppler on the mitral valve to show a complete jet of regurgitation if any is present.

5. Rotate to **apical three-chamber view:** show the LV at least 3 beats. Put Color Doppler on the mitral valve to show a complete jet of regurgitation if any is present.

Echocardiogram Checklist

Record all images at least 3 beats. For more details, refer to the protocol.

Parasternal long axial view	
Show at increased depth for extra cardiac structure	☐
Show at decreased depth for 2D measurements	☐
Zoom on AV and LVOT	☐
Color Doppler of AV	☐
Apical 4-ch view	
Show at Increased depth for extra cardiac structure	☐
Show at decreased depth for LVEF assessment	☐
Show LA optimally for LA volume assessment	☐
Color Doppler of MV	☐
PW Doppler for E and A wave assessment	☐
CW Doppler if mitral stenosis is present	☐ Absent ☐ CW
DTI of mitral annulus (both lateral and medial)	☐ Lateral annulus
	☐ Medial annulus
Show RV optimally for RV volume assessment	☐
M-mode for TAPSE	☐
DTI of tricuspid annulus	☐
Apical 5-ch view	
Show plain 5-ch image	☐

CW Doppler across AV and LVOT	☐
PW and CW Doppler if increased gradient is present	☐ Not increased ☐ PW ☐ CW
PW Doppler for LVOT VTI	☐
CW Doppler for IVRT	☐
Apical 2-ch view	
Show plain 2-ch image for LVEF assessment	☐
Show LA optimally for LA volume assessment	☐
Color Doppler of MV (for MR)	☐
Apical 3-ch view	
Show plain 3-ch image	☐
Color Doppler of MV (for MR)	☐

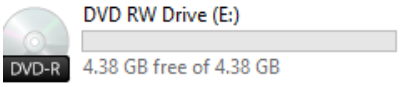
AV, aortic valve; CW continuous wave; DTI, Doppler tissue imaging; IVRT, isovolumetric relaxation time; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract; MV, mitral valve; PW, pulse wave; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; VTI, velocity time integral.

Protocol for Handling Echocardiograms

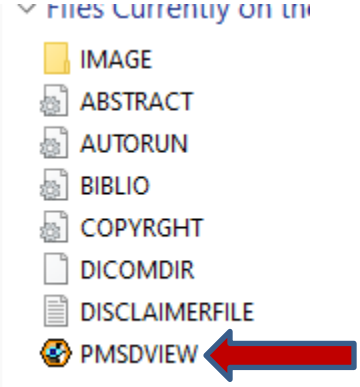
1. Participants will return to the Hypertension Clinic on the day of their echocardiogram appointment.
2. The study coordinator will provide the participant with a sealed envelope which contains the following:
    a. Two pre-made labels for the DVDs with the participant ID number and date
    b. A hand-written reminder card with the participant name and ID number
    c. An instruction sheet for the sonographer on how to enter the participant information into the PACS system before downloading the scan onto the DVD
3. The participant will take the envelope with them to the Echo Lab and give it to the sonographer. If the study coordinator is not with a participant, he/she should offer to escort the participant to the echo lab.
4. The study coordinator will go pick up the DVDs from the Echo Lab receptionist desk before the end of the day. If he/she is not available, he/she will contact the alternate(s) to pick up the DVD.
5. The person who picks up the DVD will enter into the REDCap database that the echocardiograms have been retrieved from the Echo Lab.
6. The study coordinator will check the echo scans every Monday to confirm there is no PHI and that the participant information (i.e. –participant ID number) is accurate
    a. Each reviewed DVD will be labeled with a colored sticky dot and initialed by the reviewer so that we can confirm that they have been reviewed and by whom.
    b. The reviewer will also enter that the DVD has been reviewed into REDCap on the ‘Echocardiogram’ form.
7. All DVDs that have been reviewed will be shipped to CUMC every Monday with the exception of holidays. If Monday is a holiday, the DVDs will be shipped on Tuesdays.

How to View Echocardiograms on a Desktop

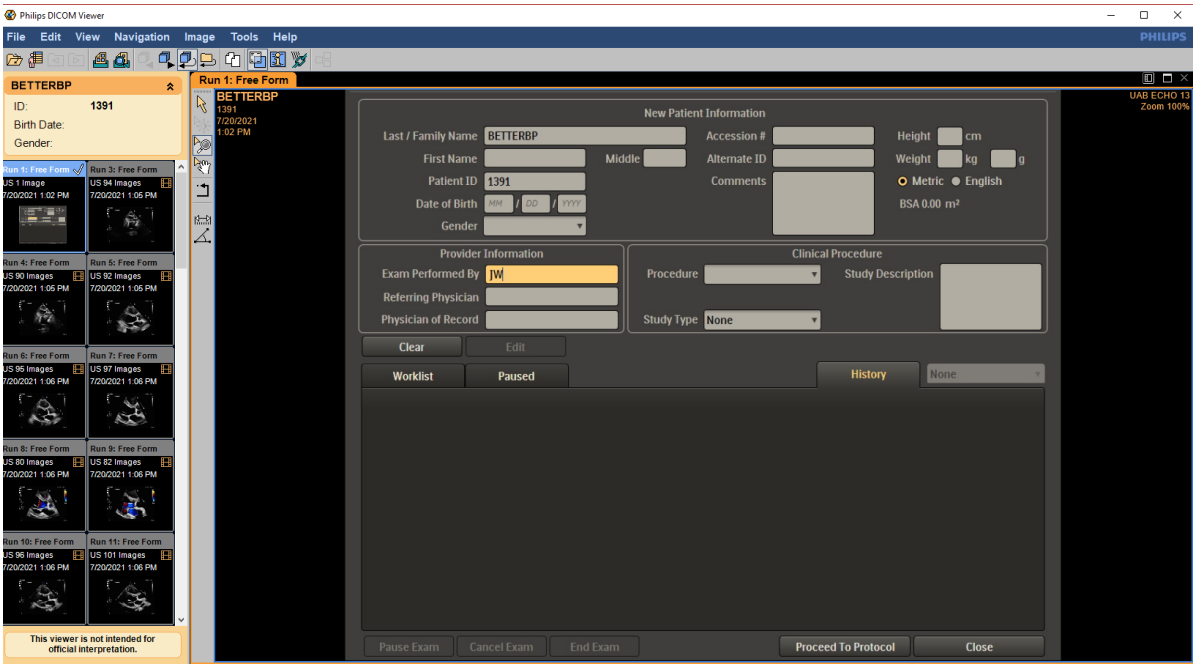
1. Once the DVD has been placed in the CD drive, Click on the DVD drive in File Explorer.



2. Once the drive is open there will be several options, click on the PMSDVIEW option



3. This will allow the viewer to be opened and you can see all images that are on that disk.



- If these options are not available, please contact **Christian Carter (christiancarter@uabmc.edu)**

Shipping Echocardiograms

All echocardiogram CDs should be shipped by study staff to the following address using FedEx overnight shipping **every Monday of the month (if holiday, please ship on the following business day)**:

Daichi Shimbo, MD
Columbia University Medical Center
622 West 168th Street
PH 9-310
NEW YORK, NY 100323720

During the COVID-19 epidemic, please mail all echocardiogram CDs to the following address:

Daichi Shimbo
310 West 114th Street
Apt. 6
New York, NY 10026
Phone: 646-462-1083

Please do not delete the participant echocardiograms from the echo machine until they have been received and analyzed at Columbia University.

Payment Structure (Reimbursing Participants)

There will be two potential approaches for reimbursement:

1. Please see the following compensation schedule:

   Study visit 1 - $15

   Study visit 2 - $15

   Study visit 3 - $45

   Study visit 4 - $75

If you are having difficulty scheduling a participant for their next study visit within two weeks, call the participant to encourage them to continue the study.

If they say 'yes', please schedule the participant for their next visit within a week.

If they say 'no', ask them if they would like you to call back in two weeks to confirm that they would no longer like to be in the study.

> **If they say 'yes'**, schedule a day and time that would be best for you to call back.
>
> **If they say 'no'**, let them know that they will receive compensation on a ClinCard in the next 7-10 business days for the study visits they completed.

2. Upon completion of each study visit, inform the participant that they will receive compensation for their visit on a ClinCard. They will receive a ClinCard from the study coordinator at Visit 1. All participants will need to have completed all payment forms prior to the conclusion of their study visits.

Paying Participants

Please use the Clincard Site Coordinator reference guide to access the Clincard system:

Link to reference guide:

https://www.uab.edu/medicine/ctao/images/ClinCard_Reference_Guide_for_Site_Coordinators_with_Graphics.pdf

Our study number: 379600000-2020672-300001727

To order additional Clincards, please contact Deonna Rasberry-Elmore (eternal2@uab.edu).

Parking and Transportation Reimbursement

A parking decal will be provided to participants for the UAB Hypertension Clinic prior to their first visit in their participant packet. Inform participants that an additional $5 for parking at the 4th or 6th Avenue parking deck will be included in their compensation for those who would prefer to drive to UAB West Pavilion to complete their echocardiograms.

OnCore Management

Prior to entering information into OnCore, you will need the following information:

1. **Participant Medical Record Number (MRN**)
    - You may request the MRN number using the EMMI Request Form that is completed by the study coordinator during study visit 1.
    - **To download EMMI Request Forms**, go to the link listed and scroll down and select 'Additional Forms' and it will navigate to a SharePoint page. Select the "EMMI Form" and download and print.
    - **https://www.uab.edu/ccts/research-commons/oncore/resources**

2. **Participant Race/Ethnicity**
    - This may be found in REDCap.

3. **Participant Schedule of Visits**
    - This may be found in REDCap.

Once you have the above mentioned information, you may follow the instructions for **'Subject Administration' pages 4 – 19**. You may find the instructions at the bottom of the page at this web address:

https://www.uab.edu/ccts/research-commons/oncore/training

Once you register the participant, click on 'Calendar' and click each visit and enter their visit date and select 'Occurred'.

For **Visit 4**, make sure to scroll down and enter the date of the echocardiogram next to 'Echocardiogram'. If the echocardiogram did not occur, select the checkbox for 'Missed'.

Better BP Supplement

Questionnaire Administration

1. **State Anxiety Index** (Prior to unattended and attended blood pressure measurements at visits 1 and 2 [based on randomization order]; during night of ABPM and HBPM)
2. **Trait Anxiety Index** (At visit 4 – optional to administer electronically)
3. **Expectations of Outcomes** (At visit 4 - optional to administer electronically)

Examples of Questionnaire Administration

If participant is randomized to Unattended→Attended and ABPM → HBPM, please administer the questionnaires in the following order:

Visit 1	**Visit 2**	**Visit 3**	**Visit 4**
After office BP randomization, the **state anxiety inventory** will be administered **unattended** in concordance with the first clinic BP measurement.	After office BP randomization, the **state anxiety inventory** will be administered **attended** in concordance with the first clinic BP measurement.		**After participants complete the device satisfaction questionnaire**, the **trait anxiety questionnaire** and **expectations of outcomes survey** will be completed.
	After ABPM or home randomization, **the state anxiety inventory** will be **completed at bedtime on the night of ABPM**	After ABPM or home randomization, **the state anxiety inventory** will be **completed at bedtime on the night of HBPM**	

Unattended = give the participant the questionnaire and leave the room for 5 minutes
Attended = give the participant the questionnaire and remain in the room while they complete it

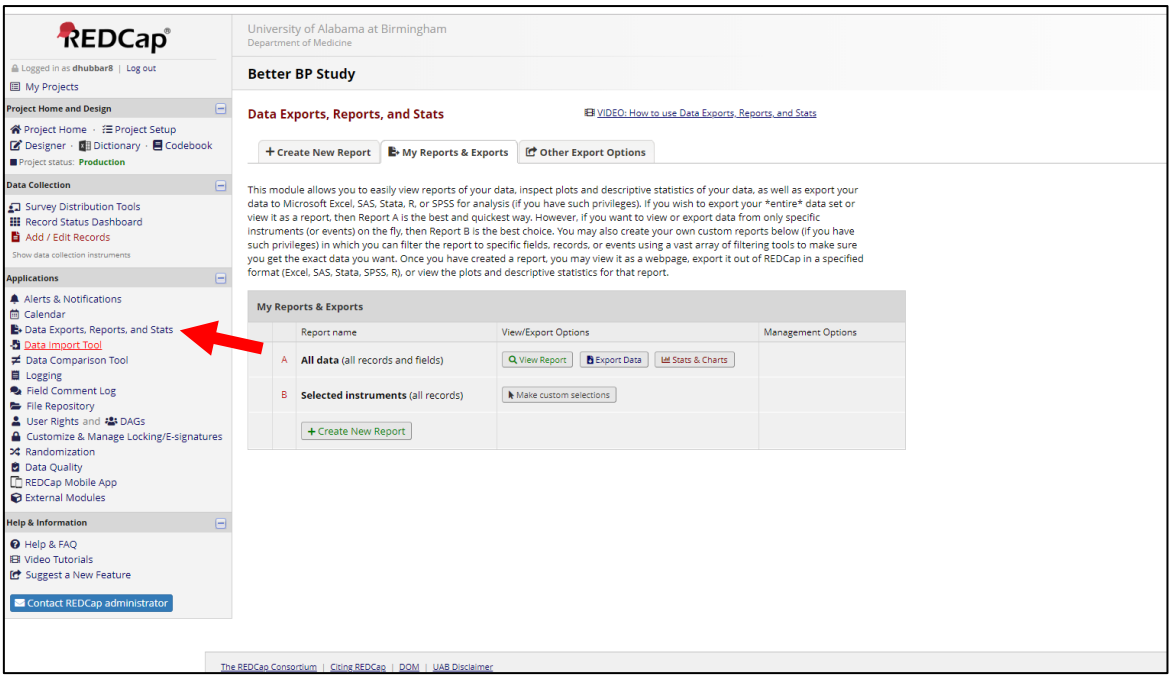
If participant is randomized to Attended→Unattended and HBPM → ABPM, please administer the questionnaires in the following order:

Visit 1	**Visit 2**	**Visit 3**	**Visit 4**
After office BP randomization, the **state anxiety inventory** will be administered **attended** in concordance with the first clinic BP measurement.	After office BP randomization, the **state anxiety inventory** will be administered **unattended** in concordance with the first clinic BP measurement.		**After participants complete the device satisfaction questionnaire**, the **trait anxiety questionnaire** and **expectations of outcomes survey** will be completed.
	After ABPM or home randomization, **the state anxiety inventory** will be **completed at bedtime on the night of HBPM**	After ABPM or home randomization, **the state anxiety inventory** will be **completed at bedtime on the night of ABPM**	

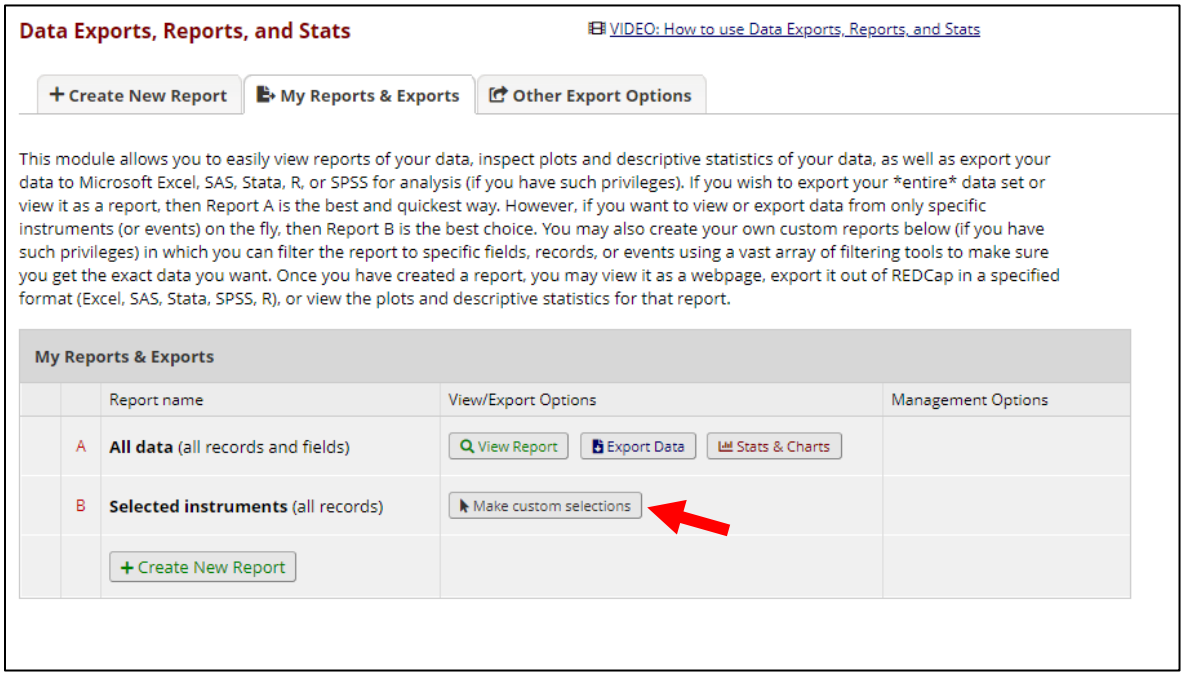
Unattended = give the participant the questionnaire and leave the room for 5 minutes
Attended = give the participant the questionnaire and remain in the room while they complete it

Checking Statistics in REDCap

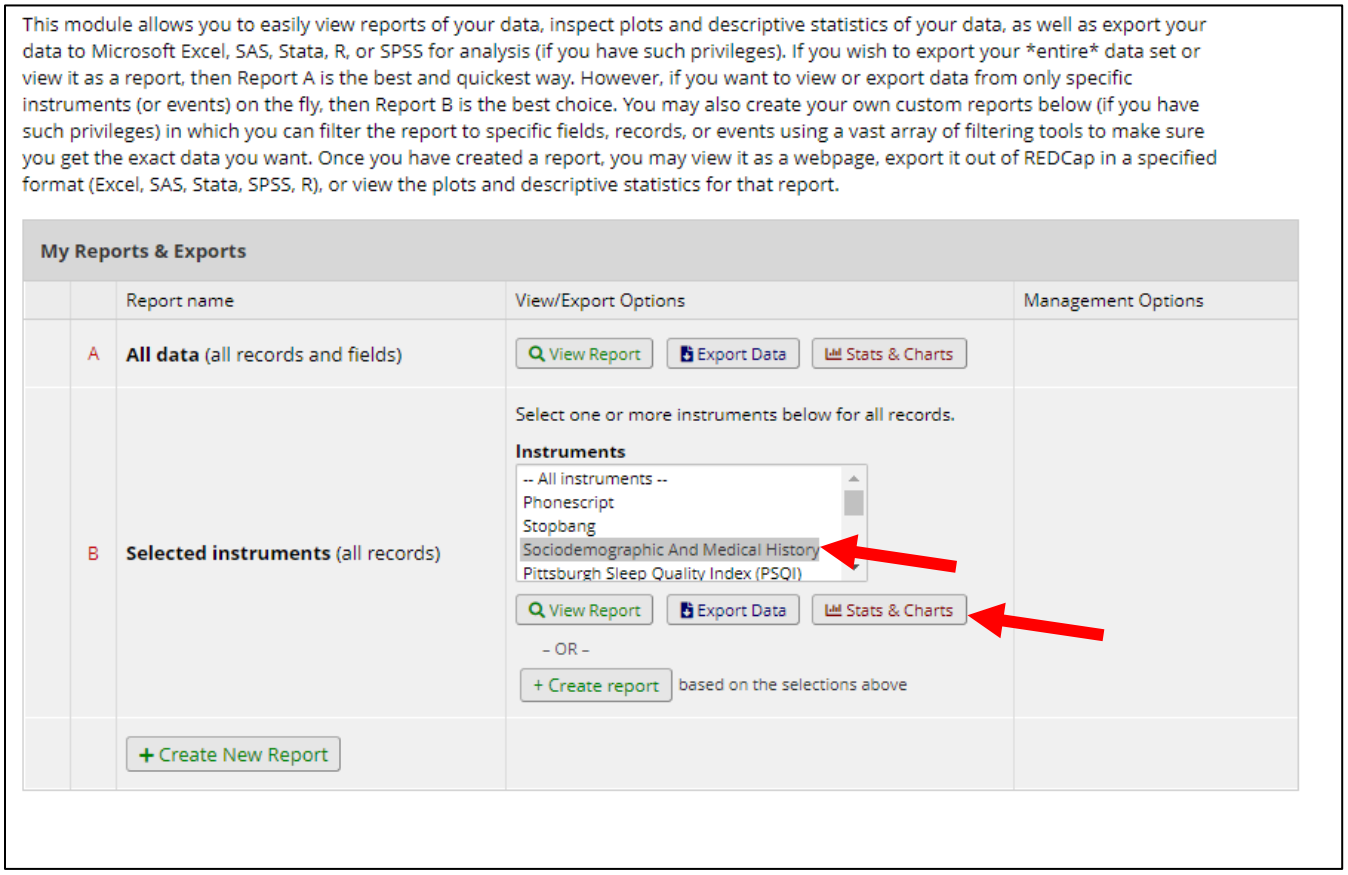
1. **On the REDCap database home screen, in the applications panel to the left-hand side, select 'Data Exports, Reports, and Stats'.**



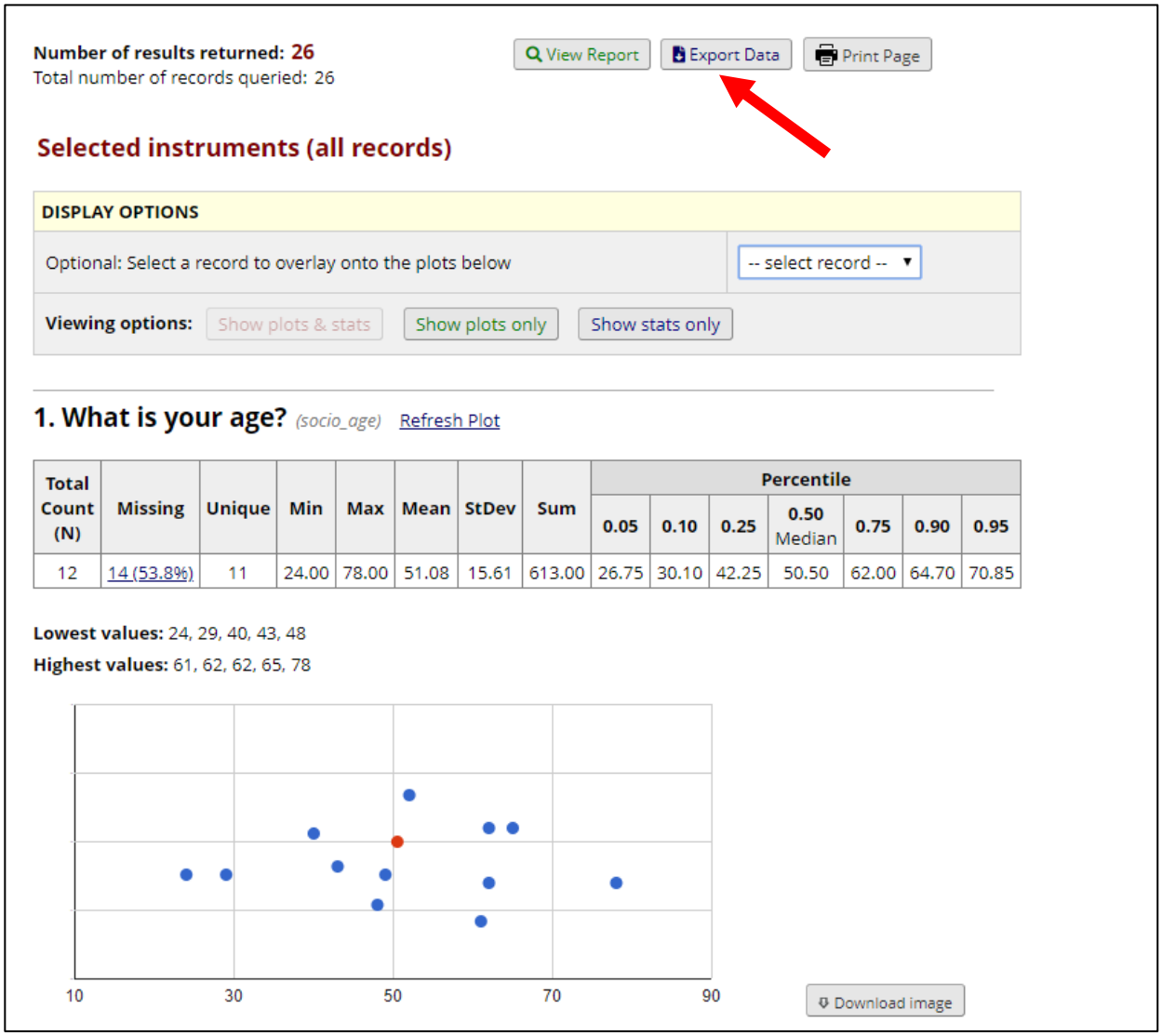
2. **Click on 'Selected Instruments – Make custom selections'.**



3. Select ‘Sociodemographic and Medical History’ and click ‘Stats & Charts’.



4. **You should now see statistics and plots for every question in this survey. If you would like to export the data, please select 'Export Data' in the top right hand corner.**



Total Count (N)	Missing	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
12	14 (53.8%)	11	24.00	78.00	51.08	15.61	613.00	26.75	30.10	42.25	50.50	62.00	64.70	70.85

Calculating Better BP Results

Codebook Location (For REDCap data):

O:\BetterBP\Data Dictionary

File Locations:

```
libname data 'O:\BetterBP\Database Back-Up\November 2019';
libname echo 'O:\BetterBP\Echo Data';
libname labs 'O:\BetterBP\Lab Data';
```

Items to be calculated:

1. Left ventricular mass index
2. Left ventricular ejection fraction
3. Average attended systolic blood pressure
4. Average attended diastolic blood pressure
5. Average attended heart rate
6. Average unattended systolic blood pressure
7. Average unattended diastolic blood pressure
8. Average unattended heart rate
9. Estimated glomerular filtration rate
10. Microalbumin-to-creatinine ratio

NOTES:

- For the lab data, please use the ‘month_year_clean’ SAS datasets for analyses.
- I have noted the correct variables to use for the echo equations on the next page.
- Provided sample code for EGFR

Echo Equations

Left ventricular mass index (g/m^2) = Left ventricular mass (g)/ Body surface area (m^2)

Left ventricular mass (g) = $0.8 \times 1.04 \times [(A+B+C)^3-C^3] + 0.6$

A = Average of SWTd#1, SWTd#2, and SWTd#3 **[Variable: ivsd1…ivsd3]**

B = Average of PWTd#1, PWTd#2, and PWTd#3 **[Variable: pwtd1…pwtd3]**

C = Average of LVEDd#1, LVEDd#2, and LVEDd#3 **[Variable: lvidd1…lvidd3]**

Body surface are (m^2) = $0.007184 \times [\text{height (cm)}]^{0.725} \times [\text{weight (kg)}]^{0.425}$

Left ventricular ejection fraction (%) ＝100 x (D-E)/D

D= Average of LVEDV#1, LVEDV#2, and LVEDV#3 **[Variable: lvedv1…lvedv3]**

E= Average of LVESV#1, LVESV#2, and LVESV#3 **[Variable: lvesv1…lvesv3]**

Paul's Example Code for Calculating EGFR (CKD-Epi Equation)

```
**** Calculate estimated glomerular filtration rate;

if black=1 and male=0 and lbxscr<=0.7 then eGFR =166*((lbxscr/0.7)**(-
0.329))*(0.993**(ridageyr));

if black=1 and male=0 and lbxscr>0.7 then eGFR =166*((lbxscr/0.7)**(-
1.209))*(0.993**(ridageyr));

if black=1 and male=1 and lbxscr<=0.9 then eGFR =163*((lbxscr/0.9)**(-
0.411))*(0.993**(ridageyr));

if black=1 and male=1 and lbxscr>0.9 then eGFR =163*((lbxscr/0.9)**(-
1.209))*(0.993**(ridageyr));

if black=0 and male=0 and lbxscr<=0.7 then eGFR =144*((lbxscr/0.7)**(-
0.329))*(0.993**(ridageyr));

if black=0 and male=0 and lbxscr>0.7 then eGFR =144*((lbxscr/0.7)**(-
1.209))*(0.993**(ridageyr));

if black=0 and male=1 and lbxscr<=0.9 then eGFR =141*((lbxscr/0.9)**(-
0.411))*(0.993**(ridageyr));

if black=0 and male=1 and lbxscr>0.9 then eGFR=141*((lbxscr/0.9)**(-
1.209))*(0.993**(ridageyr));
```

Appendices

HIPAA Authorization Form

University of Alabama at Birmingham

Authorization to Use and Disclose Information for Research Purposes

Participant Name: _____
Research Protocol: Evaluating Novel Approaches for Estimating Awake and Sleep Blood Pressure - Better BP Study

UAB IRB Protocol Number: IRB-300001727
Principal Investigator: Paul Muntner, PhD
Sponsor: NIH/NHLBI

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?

All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Who may use and give out information about you?

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?

All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. “Sponsor” includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children’s of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children’s of Alabama and its billing agents

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?

By signing this authorization form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others, including others outside of UAB, without your permission.

Signature of participant: _____ Date: _____

or participant's legally authorized representative: _____ Date: _____

Printed Name of participant's representative: _____

Relationship to the participant: _____

Telephone Screening Form

Confirm that you are speaking with the potential participant that has contacted us or who has filled out a contact card.

Introduction: We're enrolling 660 adults to take part in a research study about how to measure blood pressure. If you enroll, you will be asked to visit the UAB Hypertension Research Clinic four times for this study. We will try to schedule these visits on consecutive days but there may be a need to schedule these visits a few days apart. During the course of the study, you will have your blood pressure measured twelve times over your first two visits in the Hypertension Clinic, you will wear an automated blood pressure monitor that measures your blood pressure every 30 minutes for 24 hours, and you will wear a new blood pressure monitor that you put on before going to bed and it measures your blood pressure three times at night while you are asleep. Afterwards, you will answer some questions about your experience while wearing each of the monitors. At your last visit, we will ask you to provide a blood and urine sample and complete an echocardiogram. Does this sound like something you might be interested in doing? *If no—thank them for their time. If yes, see text for screen.*

Screen: Now I'd like to ask you a few questions to make sure you're eligible to participate. Go to question 1.

1. Are you willing to complete four or more study visits over the course of 2 weeks at UAB?

If yes, go to question 2. If no, see text for not eligible.

2. Do you have reliable transportation to and from UAB Hypertension Research Clinic located on 19th Street?

If yes, go to question 3. If no, see text for not eligible.

3. How old are you?

If ≥ 19 years, go to question 4. If < 19 years, see text for not eligible.

4. What is your sex?*

   If female and age < 60 years, go to question 3. Otherwise, go to question 5.

**The protocol specifies recruitment of 330 women and 330 men. Once the recruitment cap in each group is met, we will no longer accept participants in that group.*

5. Are you currently pregnant?

   If no, go to question 6. If yes, see text for not eligible.

6. Which of the following race/ethnicities would you consider yourself?

Non-Hispanic white

Non-Hispanic black

Non-Hispanic Asian

Hispanic

Other

7. Are you currently taking medication for high blood pressure or hypertension?

   If no, go to question 8. If yes, see text for not eligible.

8. Have you ever been told by a physician that you have sleep apnea?

   If yes, see text for not eligible. If no, administer STOP-BANG questionnaire.

STOP		
*Do you **S**NORE loudly (louder than talking or loud enough to be heard through closed doors)?*	*Yes*	*No*
*Do you often feel **T**IRED, fatigued, or sleepy during daytime?*	*Yes*	*No*
*Has anyone **O**BSERVED you stop breathing during your sleep?*	*Yes*	*No*
*Do you have or are you being treated for high blood **P**RESSURE?*	*Yes*	*No*
BANG		
***B**MI more than 35kg/m2?*	*Yes*	*No*
***A**GE over 50 years old?*	*Yes*	*No*
***N**ECK circumference > 16 inches (40cm)?*	*Yes*	*No*
***G**ENDER: Male?*	*Yes*	*No*
Total Score		

High risk of OSA: Yes 5 - 8

Intermediate risk of OSA: Yes 3 - 4

Low risk of OSA: Yes 0 - 2

**If STOP-BANG score (minus neck circumference and BMI) is greater than 3, then see text for ineligible.*

**If STOP-BANG score (minus neck circumference and BMI) 3 or less, then see text for eligible.*

9. Have you ever been told by a physician that you have heart disease?

   If no, go to question 9. If yes, see text for not eligible.

10. Have you ever been told by a physician that you have had a heart attack?

    If no, go to question 10. If yes, see text for not eligible.

11. Have you ever been told by a physician that you have had a stroke?

    If no, go to question 11. If yes, see text for not eligible.

12. Have you ever been told by a physician that you have congestive heart failure?

    If no, go to question 12. If yes, see text for not eligible.

13. Have you ever been told by a physician that you have an arrhythmia (e.g. atrial fibrillation and/or ventricular tachycardia)?

    If no, go to question 13. If yes, see text for not eligible.

14. Have you ever had heart surgery?

    If no, go to question 14.

If yes, please ask them for the reason for the surgery.

If for revascularization or coronary artery bypass surgery, see text for ineligible.

If for other reasons (e.g. congenital heart defect), please go to question 14.

15. Have you completed ABPM over 24 hours in the past year?

    If no, go to question 15. If yes, see text for not eligible.

16. Do you work overnight shift (e.g. – 11pm to 7am)?

    If no, go to question 17. If yes, see text for not eligible.

17. Do you have a permanent address?
If yes, see text for not eligible.

Not eligible: *Sorry, it looks like you are not eligible to participate at this time. Thank you for taking the time to learn more about our study. I hope you have a nice day.*

Eligible: *Great! It looks like you are eligible to participate in the study. If I can collect your name and contact information, I will send you a consent form with more details.*

Full Name _____

Email Address _____

Mailing Address _____

Phone Number _____

Thank you. Due to the current ongoing pandemic, we now have the option for you to complete your study documents electronically. Would you prefer to complete your study documents in-person or electronically?

Electronically

In-Person

If participant would like to complete forms **electronically**: *We would like to give you time to read over the consent form and answer any questions you may have over a conference call. Can we schedule you for a conference call this week?*

If participant would like to complete forms **in-person**: *We would like to give you time to read over the consent form but we can find a convenient time for you to start the study. Can we schedule your first visit now?*

Just to make you aware, prior to each of your in-person visits, we will ask you to complete COVID-19 screening questions and a temperature check. We also ask that you wear a mask to each of your visits. We will call and email you the day before your first visit as a reminder. Thank you for taking the time to learn about our study. I hope you have a nice day.

Blood Pressure Screening Form

ID: _____ Date: ___/___/___

Participant First Name: _____

Participant Last Name: _____

First blood pressure reading: _____/_____/_____
SBP DBP HR

Second blood pressure reading: _____/_____/_____
SBP DBP HR

Average blood pressure reading: _____/_____/_____
SBP DBP HR

COVID-19 Screening Form

VISIT ____ ID _____

Symptom Tracker:

I need to ask about any symptoms you may have related to COVID-19.

Do you have any of the following?

 A current diagnosis of COVID-19? [ ] Yes [ ] No

If yes, have you had a negative test result since? [ ] Yes [ ] No

 A new cough [ ] Yes [ ] No

 Shortness of breath or difficulty breathing [ ] Yes [ ] No

 Chills [ ] Yes [ ] No

 Muscle pain [ ] Yes [ ] No

 Sore throat [ ] Yes [ ] No

 New loss of taste or smell [ ] Yes [ ] No

Temperature: _____

Draft Telephone Screening Email

Hello (insert potential participant name),

Thank you for your interest in the Better BP study. We are currently enrolling 660 adults to take part in this research study about how to measure blood pressure. To confirm your eligibility for this study, please respond to this email with a day and time that would work best for us to schedule your telephone screening. The screening call should take approximately 10 minutes.

Thank you again for your interest in the Better BP study.

Sincerely,

(Insert your name)

Consent Form (Study Participant)

Title of Research: Evaluating Novel Approaches for Estimating Awake and Sleep Blood Pressure –Better BP study.
UAB IRB Protocol #: IRB-300001727
Principal Investigator: Paul Muntner, PhD
Sponsor: National Heart, Lung, and Blood Institute (NHLBI)

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described in the consent form.
Purpose	The purpose of the study is to test whether blood pressure measured in a clinic setting without medical staff present is comparable to blood pressure levels measured during the daytime outside of the clinic. Also, we will test whether blood pressure can be accurately measured while you're asleep using a new home blood pressure monitoring device.
Duration & Visits	You will be in this study for approximately 1 to 2 weeks. You will come to the UAB Hypertension Research Clinic for four study visits.
Overview of Procedures	Prior to the start of this study, you will have your blood pressure measured two times in the clinic to confirm your eligibility. During this study, you will have your blood pressure measured in the clinic a total of twelve times during the first two study visits. You will wear a device called an ambulatory blood pressure monitor that measures your blood pressure every 30 minutes for 24 hours and wear a home blood pressure monitor for one night while you sleep. Also, you will complete questionnaires regarding your demographics, medical history, your sleeping habits and your experience wearing both the ambulatory blood pressure monitor and home blood pressure monitor. You will conclude the study with a brief physical exam, which includes blood and urine collection and an echocardiogram (a procedure that involves getting a picture of your heart image with a wand that is rubbed on your skin).
Risks	The most common risk is minimal discomfort and/or skin irritation from the inflation of the blood pressure cuff every 30 minutes for 24 hours. You may also experience difficulty sleeping while having your blood pressure measured.
Benefits	We will provide you with your blood pressure measurements and the results from the echocardiogram. Also, the principal investigator hopes that the information from this study will be able to provide knowledge that will improve the measurement of blood pressure for patients in the future.

Purpose of the Research Study

For many people, blood pressure levels differ when measured in a doctor's office versus during normal daily activities. Ambulatory blood pressure monitoring, also called ABPM, involves wearing a blood pressure cuff attached to a device that is programmed to measure your blood pressure every 30 minutes for a 24-hour period. ABPM can help better estimate a person's true average blood pressure. Although ABPM is recommended for diagnosing high blood pressure and it also measures blood pressure while people sleep, it is not available in many clinics and some people find the procedure to be uncomfortable. The purpose of this research study is to test whether blood pressure measured in a clinic setting without medical staff present is comparable to blood pressure levels measured during the daytime measured using an ABPM device. Also, we will test whether asleep blood pressure can be accurately measured using a home blood pressure monitoring device. These findings may help identify new approaches for diagnosing high blood pressure without the need for ABPM. We will enroll a total of 660 participants at the University of Alabama at Birmingham (UAB) and Columbia University in New York. UAB will enroll 330 adults who recently had a doctor's visit and are not currently taking a blood pressure lowering medication to take part in this study. Each participant will complete four study visits.

Study Participation & Procedures

We are asking you to take part in a research study. If you enroll, you will be asked to visit the UAB Hypertension Research Clinic, located at 933 19th Street South, four times for this study. Ideally, the study visits will occur on four consecutive days. However, the timing of the visits will be determined by your availability and that of the study staff. During the course of the study, you will:

- During the screening process, you will have your blood pressure measured two times in the clinic by study staff to confirm your eligibility.
- Have your blood pressure measured in the clinic, six times at each of the first two study visits for a total of twelve blood pressure measurements).
- Sign a medical release form for us to review your medical records from the past three months and record your blood pressure levels as measured when you visit your doctor's office.
- Complete questionnaires about your demographics, medical history, and your sleeping habits.
- Have 4 tablespoons of blood drawn and provide a sample of your urine.
- Wear a Food and Drug Administration-approved ABPM device (Microlife WatchBP O3) for 24 hours.
- Wear a Food and Drug Administration-approved home blood pressure monitor (Microlife WatchBP Home N) while you sleep for one night.
- Wear an activity monitor (Actiwatch) for two 24-hour periods. The Actiwatch activity monitor is like a watch worn on your wrist and it measures your activity levels and can be used to identify when you are asleep.
- Answer some questions about your experience while wearing the ABPM and home blood pressure monitoring
- Have an echocardiogram performed. An echocardiogram is a procedure where a wand is rubbed along your ribcage, under your shirt, to obtain an image of your heart.

First UAB Hypertension Center visit
At the beginning of this visit, we will ask you to sign this form agreeing to participate in the study. Prior to beginning any study procedures, a staff member will measure your blood pressure two times separated by a I-minute interval following a 5-minute rest period using an automated blood pressured device. These measurements will be used to confirm that you are eligible to participate in this study. To be eligible, your systolic blood pressure will need to be greater than or equal to 110 mm Hg and your diastolic blood pressure will need to be greater than or equal to 70 mm Hg. Your systolic blood pressure will need to be less than 160 mm Hg and your diastolic blood pressure will need to be less than 100 mm Hg. Additionally, we will ask you questions about your sleep and measure your neck circumference. If you are eligible to participate, we will continue your first visit by measuring your arm circumference and medical staff will take your blood pressure three times using a machine, similar to how it is done in your doctor ' s office. We will also measure your blood pressure three times using the same machine after it is programmed to measure your blood pressure without staff being present. You will be randomly picked (like the flip of a coin) by a computer to have your blood pressure measured by staff first, followed by the automated measurements or to have your blood pressure measured by the automated device first and then by a staff member. Next, you will complete a brief physical exam, which includes height, weight and waist circumference measurements. Finally, you will be asked to complete questionnaires at the conclusion of this visit. These questionnaires will ask you questions about your medical history, stress you may experience, and your sleeping habits. This visit will last about 45 minutes to one hour.

Second visit at the UAB Hypertension Center
Your second visit will ideally occur the day after the first visit. At this visit, we will measure your blood pressure three times using a machine, similar to how it is done in your doctor’s office and three times using the same machine without another person in the room. The ordering of these blood pressure measurements will be the opposite of your first visit. For example, if your blood pressure is measured at the first visit without a staff member present three times and then with the staff member present then at the second visit your blood pressure will first be measured three times with the staff member present and then three times without the staff member present. Next, you will be asked to wear one of two different types of blood pressure monitors (a Microlife WatchBP O3 ABPM device or a Microlife WatchBP Home N blood pressure device). Which device you will be asked to wear after the second visit will be randomly picked by a computer. You will wear either the Microlife WatchBP O3 ABPM device for 24 hours and then the Microlife WatchBP Home N sleep blood pressure device for one night or the Microlife WatchBP Home N sleep blood pressure device for one night and then the Microlife WatchBP O3 ABPM device for 24 hours. You will also be asked to wear an Actiwatch activity monitor for the same duration as the device you are assigned. This visit will last about 45 minutes to one hour.

24-hour blood pressure recording
Your blood pressure over 24 hours will be measured by a Microlife WatchBP O3 ABPM device. This device has an arm cuff, similar to the one your doctor uses to measure your blood pressure during an examination. The cuff is attached to a small monitor about two or three times larger than a cell phone. You will wear this part of the ABPM device on your waist. A study staff member who is trained to measure blood pressure will instruct you on how to use the ABPM device, and how to remove it if necessary. The ABPM device will take your blood pressure automatically every 30 minutes while you are awake and while you are asleep.

Asleep home blood pressure recording
For the asleep home blood pressure recording, you will be given a Microlife WatchBP Home N home blood pressure monitoring device and cuff and instructed on how to put on the cuff and use the monitor properly. This device has an arm cuff similar to what your doctor uses to measure your blood pressure during an examination. This will be attached to a device, which is two or three times larger than a cell phone. You will be asked to put on the cuff and start the device before going to bed and keep it on until you wake up in the morning. The device will measure your blood pressure when you put it on and then three times while you sleep (at 2, 3, and 4 hours after you have gone to sleep).

Third visit at the UAB Hypertension Center
Your third visit will ideally occur the day after the second visit and involves returning the electronic device you were given during the second visit (either the Microlife WatchBP O3 ABPM device or the Microlife WatchBP Home N sleep blood pressure device) and answering a questionnaire about your experiences with the device. You will then be provided with the blood pressure device you haven't worn yet (either the Microlife WatchBP O3 ABPM device or the Microlife WatchBP Home N sleep blood pressure device) for the next stage of the protocol. You will again wear an Actiwatch on your wrist for another 24 hours. A staff member from the clinic will instruct you how to use this device. This visit will last about 30 minutes.

Fourth visit at the UAB Hypertension Center
Your fourth visit will ideally occur the day after the third visit and involves returning the devices you were given during the third visit and answering a written questionnaire about your experiences with the device you wore (either the Microlife WatchBP O3 ABPM device or the Microlife WatchBP Home N sleep blood pressure device). Next, a staff member will collect a sample of your blood and urine. You will then have an echocardiogram done (or scheduled within the next two weeks). Upon completion of the echocardiogram, you will have successfully completed the study. An echocardiogram is a procedure where a wand is rubbed along your ribcage, under your shirt, to obtain an image of your heart. The wand has some gel on it that may be cold. This visit should last 45 minutes to one and a half hours depending on whether the echocardiogram is done at this visit or scheduled to occur at a later visit.

Your de-identified private information and de-identified biospecimens (private information and biospecimens with all identifiers removed) may be used for future research studies or distributed to another researcher for future research studies without additional informed consent. **This is only when there are no identifiers associated with the data or biospecimens.**

<u>Risks and Discomforts</u>

The following risks/discomforts may occur as a result of your participation in this study: There may be minimal pain or discomfort during the inflation of the blood pressure device arm cuffs (as might occur when your doctor takes your blood pressure). This discomfort is temporary and minor. Both the Microlife WatchBP O3 and the Microlife WatchBP Home N blood pressure monitoring devices take measurements while you sleep. This may produce some disturbance of your sleep. You may also experience bruising or skin irritation from wearing the blood pressure devices.

Questionnaires will include potentially sensitive information concerning possible sources of stress. It is possible that you could feel temporarily upset, tired, or anxious when reporting this

information. If you need to talk with someone, we can consult the principal investigator, a counselor, social worker, or chaplain.

There may be some slight discomfort when taking a blood sample and you may experience bruising, soreness, and pain at the site of the needle stick. A trained technician will draw your blood and every effort will be made to minimize any discomfort. The risk of infection is minimal, and only sterile materials will be used.

There may also be risks that are unknown at this time. You will be given more information if other risks are found.

Benefits

Every research participant has the opportunity to receive a report with their 24-hour blood pressure recording, lab results, and an echocardiogram. Blood pressure measured on ABPM has been shown to provide information above and beyond the usual measurements taken in the doctor's office. An echocardiogram provides information on how well your heart pumps your blood to the rest of your body. This can be used to detect if your heart is not pumping blood as well as it should. These results will be shared with you and your doctor if you would like. Please initial your choice below to indicate whether you would like us to send you a report describing your study results:

_____ No, do not mail my blood pressure readings, lab results or echocardiogram results to me.
_____ Yes, I would like a copy of my blood pressure readings, lab results or echocardiogram results mailed to me.

_____ No, do not mail my blood pressure readings, lab results or echocardiogram results to my doctor.
_____ Yes, I would like a copy of my blood pressure readings, lab results or echocardiogram results mailed to my doctor.

In addition to providing you and your doctor with these results, we hope that this study will provide knowledge to improve cardiovascular outcomes for patients in the future.

Alternatives

Your alternative is to not participate in this study.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The investigator must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Who may use and give out information about you?
Information about your health may be used and given to others by the study investigator and research staff at UAB and Columbia University. They might see the research information during and after the study.

Who might get this information?
All individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:
- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents
- Columbia University – physicians and staff working on the research study

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to participate in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the principal investigator. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Taking part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research at any time. Your choice to leave the study will not affect your relationship with UAB. You may be removed from the study without your consent if the sponsor ends the study, if the principal investigator decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. All devices and exams related to this study will be provided to you at no cost during the study period.

Payment for Participation

There will be no compensation for screening to determine if you are eligible to participate in the study. If you are eligible and participate in the study, you will be paid the following amount for each study visit you complete: $15 for study visit 1, $15 for study visit 2, $45 for study visit 3, and $75 for study visit 4. You will also receive an additional $5 for parking at the 6th Avenue parking deck to receive their echocardiograms at Kirklin Clinic. You may be paid a total of $155 for completing all four study visits, including successfully completing the questionnaires, blood and urine collection, blood pressure recordings and echocardiogram. All three measurements must be successfully taken by the Microlife WatchBP Home N sleep blood pressure device and at least 80% (39 or more) of the measurements must be successfully taken by the Microlife WatchBP O3 ABPM device, with at least 10 measurements taken during the day and 5 measurements taken at night. If fewer than 3 of the Microlife WatchBP Home N sleep blood pressure device measurements or fewer than 80% (38 or fewer) of the Microlife WatchBP O3 ABPM device measurements are successful and you have completed the study visits, you may choose to wear the device(s) for which you had incomplete measurements again to complete the study and receive the full $150 compensation. You will be compensated 2-3 weeks following the last visit you complete. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash, gift card, direct deposit).

Payment for Research-Related Injuries

UAB and the NHLBI will not provide for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

New Findings

You will be told by the study investigator or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional Research

This section of the consent form is about optional research that may be done with people who are taking part in this study. You may take part in this optional research if you want to. You can be a part of this study even if you decline to take part in any of the optional research.

Future Research Use of Private Information and/or Biospecimens

We would like your permission to keep your private information (data containing personal information) and biospecimens (blood and urine specimen) collected in this study for future research. The future research may be similar to this study or may be completely different. Your private information and biospecimens will be stored indefinitely or until used.

Your private information and biospecimens will be labeled with a code that only the study investigators can link back to you. Results of any future research will not be given to you or your doctor.

You can take part in this study even if you decide not to let us keep your private information and biospecimens for future research.

If you give us permission now to keep your private information and biospecimens, you can change your mind later and ask us to destroy it. However, once we have analyzed your private information and biospecimens, we may not be able to take it out of our future research.

We may share your private information and biospecimens, so that others can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your private information and biospecimens with other researchers, we will not be able to get it back.

Future research use of your private information and biospecimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your private information and biospecimens. Allowing us to do future research on your private information and biospecimens will not benefit you directly.

The private information and biospecimens used for future research may be used for commercial profit. There are no plans to provide financial compensation to you should this occur.

Initial your choices below:

Research related to cardiovascular disease and/or hypertension

___ I agree to allow my private information and biospecimens to be kept and used for future research related to cardiovascular disease and/or hypertension.

___ I do not agree to allow my private information and biospecimens to be kept and used for future research related to cardiovascular disease and/or hypertension.

Research not related to cardiovascular disease and/or hypertension

___ I agree to allow my private information and biospecimens to be kept and used for future research not related to cardiovascular disease and/or hypertension.

___ I do not agree to allow my private information and biospecimens to be kept and used for future research not related to cardiovascular disease and/or hypertension.

Research related to genetic testing

In the future, the DNA from your blood sample may be used to measure inherited factors that might relate to cardiovascular disease or hypertension. Results of these tests will not be reported to you without your permission and unless they have a clinical meaning. If we happen to find a gene problem that is linked to a medically treatable genetic disease, we will contact you if have given us permission to do so. Results from these tests will not be released, placed in your medical record, or shared in any way with your relatives, personal physicians, insurance companies, or any other third party unless you authorize the Better BP study staff, in writing, to do so.

___ I agree to allow my private information and biospecimens to be kept and used for future research related to genetic testing.

___ I do not agree to allow my private information and biospecimens to be kept and used for future research related to genetic testing.

Results related to genetic testing

___ Yes, I would like to be notified if a potentially treatable genetic condition is identified during future research related to genetic testing.

___ No, I would not like to be notified if a potentially treatable genetic condition is identified during future research related to genetic testing

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study principal investigator. You may contact Dr. Paul Muntner at (205) 975-8077.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

Signature of Participant Date

Signature of Investigator or Person Obtaining Consent Date

Consent Form (Mock Participant)

Title of Research: Evaluating Novel Approaches for Estimating Awake and Sleep Blood Pressure –Better BP study.

UAB IRB Protocol #: IRB-300001727

Principal Investigator: Paul Muntner, PhD

Sponsor: National Heart, Lung, and Blood Institute (NHLBI)

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described in the consent form.
Purpose	The purpose of the study is to test whether blood pressure measured in a clinic setting without medical staff present is comparable to blood pressure levels measured during the daytime outside of the clinic. Also, we will test whether blood pressure can be accurately measured while you're asleep using a new home blood pressure monitoring device. The purpose of the mock participants is to test protocol procedures before we recruit and enroll study participants.
Duration & Visits	You will be in this study for approximately 1 to 2 weeks. You will come to the UAB Hypertension Research Clinic for four study visits.
Overview of Procedures	During this study, you will have your blood pressure measured in the clinic a total of twelve times during the first two study visits. You will wear a device called an ambulatory blood pressure monitor that measures your blood pressure every 30 minutes for 24 hours and wear a home blood pressure monitor for one night while you sleep. Also, you will complete questionnaires regarding your demographics, medical history, your sleeping habits and your experience wearing both the ambulatory blood pressure monitor and home blood pressure monitor. You will conclude the study with a brief physical exam, which includes blood and urine collection and an echocardiogram (a procedure that involves getting a picture of your heart image with a wand that is rubbed on your skin). Your data will not be used in the study data analysis.
Risks	The most common risk is minimal discomfort and/or skin irritation from the inflation of the blood pressure cuff every 30 minutes for 24 hours. You may also experience difficulty sleeping while having your blood pressure measured.
Benefits	We will provide you with your blood pressure measurements and the results from the echocardiogram. Also, the principal investigator hopes that the information from this study will be able to provide

	knowledge that will improve the measurement of blood pressure for patients in the future.

Purpose of the Research Study

For many people, blood pressure levels differ when measured in a doctor's office versus during normal daily activities. Ambulatory blood pressure monitoring, also called ABPM, involves wearing a blood pressure cuff attached to a device that is programmed to measure your blood pressure every 30 minutes for a 24-hour period. ABPM can help better estimate a person's true average blood pressure. Although ABPM is recommended for diagnosing high blood pressure and it also measures blood pressure while people sleep, it is not available in many clinics and some people find the procedure to be uncomfortable. The purpose of this research study is to test whether blood pressure measured in a clinic setting without medical staff present is comparable to blood pressure levels measured during the daytime measured using an ABPM device. Also, we will test whether asleep blood pressure can be accurately measured using a home blood pressure monitoring device. These findings may help identify new approaches for diagnosing high blood pressure without the need for ABPM. We will enroll a total of 10 mock study participants at the University of Alabama at Birmingham (UAB) and Columbia University in New York. UAB will enroll 5 adults who are not currently taking a blood pressure lowering medication to take part in this study. Each participant will complete four study visits. The purpose of the mock participants is to test protocol procedures.

Study Participation & Procedures

We are asking you to take part in a research pilot study. If you enroll, you will be asked to visit the UAB Hypertension Research Clinic, located at 933 19th Street South, four times for this study. Ideally, the study visits will occur on four consecutive days. However, the timing of the visits will be determined by your availability and that of the study staff. During the course of the study, you will:

- Have your blood pressure measured in the clinic, six times at each of the first two study visits for a total of twelve blood pressure measurements).
- Complete questionnaires about your demographics, medical history, and your sleeping habits.
- Have 4 tablespoons of blood drawn and provide a sample of your urine.
- Wear a Food and Drug Administration-approved ABPM device (Microlife WatchBP O3) for 24 hours.
- Wear a Food and Drug Administration-approved home blood pressure monitor (Microlife WatchBP Home N) while you sleep for one night.
- Wear an activity monitor (Actiwatch) for two 24-hour periods. The Actiwatch activity monitor is like a watch worn on your wrist and it measures your activity levels and can be used to identify when you are asleep.
- Answer some questions about your experience while wearing the ABPM and home blood pressure monitoring
- Have an echocardiogram performed. An echocardiogram is a procedure where a wand is rubbed along your ribcage, under your shirt, to obtain an image of your heart.

First UAB Hypertension Center visit

At this visit, we will ask you to sign this form agreeing to participate in the study and a form that will allow us to retrieve your medical records from the past three months. Additionally, we will ask you questions about your sleep and measure your neck circumference. Next, we will measure

your arm circumference and medical staff will take your blood pressure three times using a machine, similar to how it is done in your doctor's office. We will also measure your blood pressure three times using the same machine after it is programmed to measure your blood pressure without staff being present. You will be randomly picked (like the flip of a coin) by a computer to have your blood pressure measured by staff first, followed by the automated measurements or to have your blood pressure measured by the automated device first and then by a staff member. Next, you will complete a brief physical exam, which includes height, weight and waist circumference measurements. Finally, you will be asked to complete questionnaires at the conclusion of this visit. These questionnaires will ask you questions about your medical history, stress you may experience, and your sleeping habits. This visit will last about 45 minutes to one hour.

Second visit at the UAB Hypertension Center
Your second visit will ideally occur the day after the first visit. At this visit, we will measure your blood pressure three times using a machine, similar to how it is done in your doctor's office and three times using the same machine without another person in the room. The ordering of these blood pressure measurements will be the opposite of your first visit. For example, if your blood pressure is measured at the first visit without a staff member present three times and then with the staff member present then at the second visit your blood pressure will first be measured three times with the staff member present and then three times without the staff member present. Next, you will be asked to wear one of two different types of blood pressure monitors (a Microlife WatchBP O3 ABPM device or a Microlife WatchBP Home N blood pressure device). Which device you will be asked to wear after the second visit will be randomly picked by a computer. You will wear either the Microlife WatchBP O3 ABPM device for 24 hours and then the Microlife WatchBP Home N sleep blood pressure device for one night or the Microlife WatchBP Home N sleep blood pressure device for one night and then the Microlife WatchBP O3 ABPM device for 24 hours. You will also be asked to wear an Actiwatch activity monitor for the same duration as the device you are assigned. This visit will last about 45 minutes to one hour.

24-hour blood pressure recording
Your blood pressure over 24 hours will be measured by a Microlife WatchBP O3 ABPM device. This device has an arm cuff, similar to the one your doctor uses to measure your blood pressure during an examination. The cuff is attached to a small monitor about two or three times larger than a cell phone. You will wear this part of the ABPM device on your waist. A study staff member who is trained to measure blood pressure will instruct you on how to use the ABPM device, and how to remove it if necessary. The ABPM device will take your blood pressure automatically every 30 minutes while you are awake and while you are asleep.

Asleep home blood pressure recording
For the asleep home blood pressure recording, you will be given a Microlife WatchBP Home N home blood pressure monitoring device and cuff and instructed on how to put on the cuff and use the monitor properly. This device has an arm cuff similar to what your doctor uses to measure your blood pressure during an examination. This will be attached to a device, which is two or three times larger than a cell phone. You will be asked to put on the cuff and start the device before going to bed and keep it on until you wake up in the morning. The device will measure your blood pressure when you put it on and then three times while you sleep (at 2, 3, and 4 hours after you have gone to sleep).

Third visit at the UAB Hypertension Center

Your third visit will ideally occur the day after the second visit and involves returning the electronic device you were given during the second visit (either the Microlife WatchBP O3 ABPM device or the Microlife WatchBP Home N sleep blood pressure device) and answering a questionnaire about your experiences with the device. You will then be provided with the blood pressure device you haven't worn yet (either the Microlife WatchBP O3 ABPM device or the Microlife WatchBP Home N sleep blood pressure device) for the next stage of the protocol. You will again wear an Actiwatch on your wrist for another 24 hours. A staff member from the clinic will instruct you how to use this device. This visit will last about 30 minutes.

Fourth visit at the UAB Hypertension Center
Your fourth visit will ideally occur the day after the third visit and involves returning the devices you were given during the third visit and answering a written questionnaire about your experiences with the device you wore (either the Microlife WatchBP O3 ABPM device or the Microlife WatchBP Home N sleep blood pressure device). Next, a staff member will collect a sample of your blood and urine. You will then have an echocardiogram done (or scheduled within the next two weeks). Upon completion of the echocardiogram, you will have successfully completed the study. An echocardiogram is a procedure where a wand is rubbed along your ribcage, under your shirt, to obtain an image of your heart. The wand has some gel on it that may be cold. This visit should last 45 minutes to one and a half hours depending on whether the echocardiogram is done at this visit or scheduled to occur at a later visit.

Risks and Discomforts

The following risks/discomforts may occur as a result of your participation in this study: There may be minimal pain or discomfort during the inflation of the blood pressure device arm cuffs (as might occur when your doctor takes your blood pressure). This discomfort is temporary and minor. Both the Microlife WatchBP O3 and the Microlife WatchBP Home N blood pressure monitoring devices take measurements while you sleep. This may produce some disturbance of your sleep. You may also experience bruising or skin irritation from wearing the blood pressure devices.

Questionnaires will include potentially sensitive information concerning possible sources of stress. It is possible that you could feel temporarily upset, tired, or anxious when reporting this information. If you need to talk with someone, we can consult the principal investigator, a counselor, social worker, or chaplain.

There may be some slight discomfort when taking a blood sample and you may experience bruising, soreness, and pain at the site of the needle stick. A trained technician will draw your blood and every effort will be made to minimize any discomfort. The risk of infection is minimal, and only sterile materials will be used.

There may also be risks that are unknown at this time. You will be given more information if other risks are found.

Benefits

Every research participant has the opportunity to receive a report with their 24-hour blood pressure recording, lab results, and an echocardiogram. Blood pressure measured on ABPM has

been shown to provide information above and beyond the usual measurements taken in the doctor's office. An echocardiogram provides information on how well your heart pumps your blood to the rest of your body. This can be used to detect if your heart is not pumping blood as well as it should. These results will be shared with you and your doctor if you would like. Please initial your choice below to indicate whether you would like us to send you a report describing your study results:

_____ No, do not mail my blood pressure readings, lab results or echocardiogram results to me.
_____ Yes, I would like a copy of my blood pressure readings, lab results or echocardiogram results mailed to me.

_____ No, do not mail my blood pressure readings, lab results or echocardiogram results to my doctor.
_____ Yes, I would like a copy of my blood pressure readings, lab results or echocardiogram results mailed to my doctor.

In addition to providing you and your doctor with these results, we hope that this study will provide knowledge to improve cardiovascular outcomes for patients in the future.

Alternatives

Your alternative is to not participate in this study.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The investigator must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Who may use and give out information about you?
Information about your health may be used and given to others by the study investigator and research staff at UAB and Columbia University. They might see the research information during and after the study.

Who might get this information?
All individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents
- Columbia University – physicians and staff working on the research study

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to participate in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the principal investigator. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Taking part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research at any time. Your choice to leave the study will not affect your relationship with UAB. You may be removed from the study without your consent if the sponsor ends the study, if the principal investigator decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. All devices and exams related to this study will be provided to you at no cost during the study period.

Payment for Participation

You will not be compensated for your participation in this study.

Payment for Research-Related Injuries

UAB and the NHLBI will not provide for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

New Findings

You will be told by the study investigator or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional Research

Your data will not be stored for future use in optional research.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study principal investigator. You may contact Dr. Paul Muntner at (205) 975-8077.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

Signature of Participant	Date
Signature of Investigator or Person Obtaining Consent	Date

Better BP Screening Visit Checklist

[ ] COVID-19 Screening [ ] Yes [ ] No

[ ] Symptom Tracker

[ ] Temperature Check

Consent sign and dated [ ] Yes [ ] No

BP cuff verified [ ] Yes [ ] No

Left arm ___

Right arm ___

Two Blood Pressure Measurements [ ] Yes [ ] No

Continue to visit 1 [ ] Yes [ ] No

Screen fail [ ] Yes

To be re-screen in one month [ ] Yes [ ] No

Date _____

Inform participants that qualify for the study that the morning of the clinic visit, participant should avoid coffee (and other caffeine containing food of beverages) smoking, exercise or eating for at least 30 minutes prior to office BP measurements.

Completed by_____ Date _____

Better BP Study Visit 1 Checklist

[ ] COVID-19 Screening [ ] Yes [ ] No
- [ ] Symptom Tracker
- [ ] Temperature Check

[ ] Consent sign and dated [ ] Yes [ ] No

[ ] BP cuff verified [ ] Yes [ ] No

[ ] Vital signs done [ ] Yes [ ] No
- [ ] Height and Weight
- [ ] Waist and Neck circumference

[ ] Questionnaires done [ ] Yes [ ] No
- [ ] Social demographic (**circle one**: email or in-person)
- [ ] Pittsburg Sleep Quality Index (**circle one**: email or in-person)
- [ ] State Anxiety Index (Based on randomization order)
  - [ ] Unattended [ ] Attended

[ ] Randomization 1
- [ ] Unattended then attended
- [ ] Attended then unattended

Inform participant that the morning of the clinic visit, participant should avoid coffee (and other caffeine containing food or beverages) smoking, exercise or eating for at least 30 minutes prior to office BP measurements.

Completed by _____ Date_____

Better BP Study
Study Visit 1 Data Collection Form

ID: _____ Date of Visit: _____

Name of tech performing visit: _____ Time of Visit: _____

BEFORE PARTICIPANT ARRIVES

1. Complete symptom tracker and temperature check
2. Print consent form and all questionnaires (if not completed electronically) ☐
3. Verify cuffs of various sizes are available:

AFTER PARTICIPANT ARRIVES

4. Ask the participant if he/she needs to use the restroom prior to beginning
5. Consent participant, if not previously completed electronically ☐
6. Measure height, weight, waist and neck circumference
    a. Height (cm) _____
    b. Weight (lbs) _____
    c. Waist circumference (cm) _____
    d. Neck circumference (cm) _____

7. Allow participants to complete the following questionnaires: Sociodemographic, Perceived Stress, and Pittsburgh Sleep Quality Index (PSQI) [if not completed electronically]

8. Measure arm circumference
    a. Is participant right or left handed (i.e., dominant arm; circle one): Left Right
    b. Arm circumference of dominant arm: _____.__ cm
    c. Arm circumference of non-dominant arm: _____.__ cm
    d. Is the clinic device being worn on the (**non-dominant**)? Yes No
        i. Reason if not worn on non-dominant _____
    e. Put "×" next to cuff sizes that will be used

	Clinic (Microlife Office AFIB)		
Cuff Size	Arm circumference	Dominant arm	Non-dominant arm
Small adult	17-21.9 cm		
Med adult	22-32 cm		
Large adult	32.1-42 cm		
Extra-large	42.1-52 cm		

9. Identify randomization assignment.

Record randomization order:

Unattended then attended

Attended then unattended

10. If the participant is randomized to unattended BP,
    a. Explain to participant the steps involved in obtaining unattended BP measurements:
        i. You will position them and they should not move or talk
        ii. You will start the blood pressure measurement device
        iii. You will leave the room for 10 minutes
        iv. After 5 minutes, they will have their blood pressure measured
        v. They will have their blood pressure measured two more times at one minute intervals
        vi. They should relax but not move until you return to the room
    b. Connect the BP device to the cuff
    c. Position patient for their BP measurement
    d. Start the device for a 5 minute waiting period
    e. Leave the room for 10 minutes

8. If the participant is randomized to attended BP measurements
    h. Explain to participant the steps involved in obtaining unattended BP measurements:
        i. You will position them and they should not move or talk
        ii. You will start the blood pressure measurement device

iii. After 5 minutes, they will have their blood pressure measured

iv. They will have their blood pressure measured two more times at one minute intervals

v. They should relax but not move and there should be no talking until the three blood pressure measurements are taken

i. Connect the BP device to the cuff

j. Position patient for their BP measurement

k. Start the device for a 5 minute waiting period

11. Record measurements of clinic blood pressure assessments in the order determined by randomization using the WatchBP Office AFIB device.

Attended

A) _____/_____/_____ B) _____/_____/_____ C) _____/_____/_____
SBP DBP HR SBP DBP HR SBP DBP HR

Unattended

A) _____/_____/_____ B) _____/_____/_____ C) _____/_____/_____
SBP DBP HR SBP DBP HR SBP DBP HR

RESULTS WILL NOT BE PROVIDED TO PARTICIPANTS UNTIL THEY COMPLETE THE STUDY

12. Schedule the participant for their next visit (visit 2). The participant should be strongly encouraged to schedule their visit for the same time the following day.

13. Answer any questions that the participant may have.

NOTES: _____

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Better BP Study Visit 2 Checklist

[ ] COVID-19 Screening [ ] Yes [ ] No

[ ] Symptom Tracker

[ ] Temperature Check

[ ] Confirm that participant has avoid caffeinated products, food, smoking, and exercise for at least 30 minutes prior to this visit.

[ ] State Anxiety Index (Opposite of Visit 1)

[ ] Unattended [ ] Attended

[ ] Clinic BP measurements: (order will be opposite of Visit 1)

[ ] Attended then Unattended

[ ] Unattended then Attended

[ ] Randomization 2

[ ] ABPM device

[ ] HBPM device

[ ] Actiwatch activity monitor device

(Actiwatch device will be remove at visit 4)

[ ] Provide participant with the assigned Device Log form

[ ] Provide participant with State Anxiety Index for home
(To be completed during night of monitoring)

Completed By_____ Date_____

Better BP Study
Study Visit 2 Data Collection Form

ID: _____ Date of Visit: _____

Name of tech performing visit: _____ Time of Visit: _____

BEFORE PARTICIPANT ARRIVES

1. Verify cuff size worn at Visit 1: ☐

AFTER PARTICIPANT ARRIVES

2. Greet the participant and explain what will be done during their visit:
    a. They will have their blood pressure measured six more times.
    b. They will begin their 24-hour blood pressure monitoring period or asleep blood pressure monitoring
    c. They will begin wearing an activity monitor on their wrist.

3. Ask the participant if he/she needs to use the restroom prior to beginning their measurements.

4. Identify the order for blood pressure measurement for the second visit (opposite order of visit 1).

    If BP is being measured unattended:
    a. Explain to participant the steps involved in obtaining unattended BP measurements:
        i. You will position them and they should not move or talk
        ii. You will start the blood pressure measurement device
        iii. You will leave the room for 10 minutes
        iv. After 5 minutes, they will have their blood pressure measured
        v. They will have their blood pressure measured two more times at one minute intervals
        vi. They should relax but not move until you return to the room
    b. Connect the BP device to the cuff

c. Position patient for their BP measurement
d. Start the device for a 5 minute waiting period
e. Leave the room for 10 minutes

If BP is being measured attended:

l. Explain to participant the steps involved in obtaining unattended BP measurements:
   i. You will position them and they should not move or talk
   ii. You will start the blood pressure measurement device
   iii. After 5 minutes, they will have their blood pressure measured
   iv. They will have their blood pressure measured two more times at one minute intervals
   v. They should relax but not move and there should be no talking until the three blood pressure measurements are taken
m. Connect the BP device to the cuff
n. Position patient for their BP measurement
o. Start the device for a 5 minute waiting period

5. Record measurements of clinic blood pressure assessments in the using the WatchBP Office AFIB device.

Attended

A) _____/_____/_____ B) _____/_____/_____ C) _____/_____/_____
SBP DBP HR SBP DBP HR SBP DBP HR

Unattended

A) _____/_____/_____ B) _____/_____/_____ C) _____/_____/_____
SBP DBP HR SBP DBP HR SBP DBP HR

6. Identify randomization assignment – ambulatory blood pressure monitoring or home sleep blood pressure monitoring.

Ambulatory Blood Pressure Monitoring

Home Blood Pressure Monitoring

IF PARTICIPANT IS ASSIGNED THE ABPM DEVICE FIRST

7. Ask participant what time he/she anticipates going to sleep tonight and waking up tomorrow
    a. Anticipated time going to sleep: _____
    b. Anticipated time waking up: _____
8. Initialize ABPM device. Serial number: _____
9. Use the participant's non-dominant arm for the WatchBP O3 ABPM.
    a. Arm where ABPM device will be worn (**non-dominant**)? Left Right
        i. Reason if not worn on non-dominant _____
    b. Put "✕" next to cuff sizes that will be used

	ABPM (Microlife WatchBP O3)	
Cuff Size	Arm circumference	Non-dominant arm
Small adult	17-21.9 cm	
Med adult	22-32 cm	
Large adult	32.1-42 cm	
Extra-large	42.1-52 cm	

10. Place cuff on arm
    a. Find brachial artery (perhaps make small mark)
    b. Arrow on cuff over brachial artery, non-latex tubing coming out of cuff top
    c. Bottom of cuff 1" above bend/crease in elbow (if possible)
    d. Equal tension top and bottom of cuff (1 finger easily, 2 fingers snug, top and bottom)
    e. Wrap grey non-latex tubing around back of neck
11. Connect tubing to ABPM device (make sure it will not pull out)
12. Place the O3 device in 'Ambulatory' mode.
13. Explain to participant about importance of remaining still during readings and keeping arm a) relaxed at side or in a "sling-like" position if standing, b) resting on table, arm rest, bed, etc. if sitting/reclining
14. Take one test reading; repeat until obtain a valid reading (max 5 tries)
    a. If cannot get a valid reading, check for cuff too loose, kink in tubing, tubing not securely connected to ABPM device; if need be, change cuff and/or ABPM device (be sure to record new serial #)
    b. After getting a good reading, wait 30 secs, then start another reading & immediately cancel it
15. Decide if participant will use shoulder strap (preferred), Microlife belt, own belt, or jacket pocket. Instrument ABPM cover appropriately, insert ABPM in cover, and make sure participant is comfortable with this method of wearing device.
16. Review ABPM device log with participant (and remind them to bring it tomorrow or their next study visit)

17. If the participant intends to remove the device to shower/changes clothes, require the participant to practice placing the device correctly with you present.
18. Review with participant:
    a. Importance of remaining still when BP readings are being taken
    b. Importance of keeping arm relaxed/supported
    c. If there is a failed reading, device will attempt three (3) retries ~1 minute apart.
    d. If participant is consistently getting 2 failed readings, should call the study cellphone
    e. ABPM cannot get wet
    f. If they intend to remove the device at any point, please do so between readings
    g. Payment depends on getting 80% successful readings

IF PARTICIPANT IS ASSIGNED THE HBPM DEVICE FIRST

19. Ask participant what time he/she anticipates going to sleep tonight and waking up tomorrow
    a. Anticipated time going to sleep: _____
    b. Anticipated time waking up tomorrow: _____
20. Initialize HBPM device. Serial number: _____
21. Use the participant's non-dominant arm for the WatchBP Home N.
    a. Arm where HBPM device will be worn (**non-dominant**)? Left Right
        i. Reason if not worn on non-dominant _____
    b. Put "✕" next to cuff sizes that will be used

	HBPM (Microlife WatchBP Home N)	
Cuff Size	Arm circumference	Non-dominant arm
Small adult	17-21.9 cm	
Med adult	22-32 cm	
Large adult	32.1-42 cm	
Extra-large	42.1-52 cm	

22. Demonstrate to the participant how to place the cuff on their arm
    a. Find brachial artery (perhaps make small mark)
    b. Arrow on cuff over brachial artery, non-latex tubing coming out of cuff top
    c. Bottom of cuff 1" above bend/crease in elbow (if possible)
    d. Equal tension top and bottom of cuff (1 finger easily, 2 fingers snug, top and bottom)
    e. Wrap grey non-latex tubing around back of neck
    f. Connect tubing to HBPM device (make sure it will not pull out)
23. Require the participant practice placing the cuff on their arm with you present.
24. Explain to participant the importance of placing the device correctly and initializing the device when they get in bed by holding the on/off button for 3 seconds to start the initial reading and the following readings will occur 2, 3, and 4 hours after they have gone to bed.
25. Take one test reading in 'Usual' mode; repeat until obtain a valid reading (max 3 tries)

a. If cannot get a valid reading, check for cuff too loose, kink in tubing, tubing not securely connected to HBPM device; if need be, change cuff and/or HBPM device (be sure to record new serial #)

26. Place the device in ‘Nocturnal’ mode.

27. Place the device in a carrier bag for the participant.

28. Review with participant:
    a. Importance of initializing the device before going to bed by holding the on/off button for 3 seconds
    b. If there is a failed reading, device will attempt three (3) ~1 minute apart.
    c. If participant is consistently getting 2 failed readings while initializing the device, they should call the study cellphone
    d. Payment depends on getting three successful readings while asleep

29. Schedule participant for their return visit (24 hours later).

30. Answer any questions that the participant may have.

NOTES: _____

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Better BP Study Visit 3 Checklist

[ ] COVID-19 Screening [ ] Yes [ ] No
[ ] Symptom Tracker
[ ] Temperature Check

[ ] Device return

[ ] Check the device for complete readings

[ ] HBPM three sleep BP readings [ ] Yes [ ] No

[ ] ABPM ~35 measurements [ ] Yes [ ] No

If No, ask participant to wear the device again to collect all necessary readings or measurements.

If yes, complete the Post Questionnaire (**circle one**: email or in-person)

[ ] Post ABPM Questionnaire

[ ] Post HBPM Questionnaire

[ ] Participant will wear the opposite monitor of Visit 2

[ ] ABPM device

[ ] HBPM device

(Actiwatch device will be remove at visit 4)

[ ] Provide participant with the assigned Device Log Form

[ ] Provide participant with State Anxiety Index for home
(To be completed during night of monitoring)

Completed by _____ Date _____

Better BP Study

Study Visit 3 Data Collection Form

ID: _____ Date of Visit: _____

Name of tech performing visit: _____ Time of Visit: _____

BEFORE PARTICIPANT ARRIVES

4. Verify cuffs of various sizes are available for the WatchBP O3 and WatchBP Home N: ☐

AFTER PARTICIPANT ARRIVES

IF PARTICIPANT COMPLETED THE HBPM DEVICE FIRST

1. Check a complete recording (i.e. – two sleep BP readings) was obtained.
    a. Yes No
2. If yes, complete the post-HBPM questionnaire.
3. If no, ask the participant to repeat the HBPM. Discuss with participant the challenges they encountered with obtaining a complete HBPM.
4. Ask participant what time he/she anticipates going to sleep tonight and waking up tomorrow
    a. Anticipated time going to sleep: _____
    b. Anticipated time waking up tomorrow: _____
5. Initialize ABPM device. Serial number: _____
6. Is the participant's non-dominant arm being used for the WatchBP O3 ABPM? Yes No
7. Reason for not using the non-dominant arm: _____
    a. Put "✕" next to cuff sizes that will be used

		ABPM (Microlife WatchBP O3)	
Cuff Size	Arm circumference	Dominant arm	Non-dominant arm
Small adult	17-21.9 cm		
Med adult	22-32 cm		
Large adult	32.1-42 cm		
Extra-large	42.1-52 cm		

8. Place cuff on arm
    a. Find brachial artery (perhaps make small mark)
    b. Arrow on cuff over brachial artery, non-latex tubing coming out of cuff top
    c. Bottom of cuff 1" above bend/crease in elbow (if possible)
    d. Equal tension top and bottom of cuff (1 finger easily, 2 fingers snug, top and bottom)
    e. Wrap grey non-latex tubing around back of neck

9. Connect tubing to ABPM device (make sure it will not pull out)
10. Place the O3 device in ‘Ambulatory’ mode.
11. Explain to participant about importance of remaining still during readings and keeping arm a) relaxed at side or in a “sling-like” position if standing, b) resting on table, arm rest, bed, etc. if sitting/reclining
12. Take one test reading; repeat until obtain a valid reading (max 5 tries)
    a. If cannot get a valid reading, check for cuff too loose, kink in tubing, tubing not securely connected to ABPM device; if need be, change cuff and/or ABPM device (be sure to record new serial #)
    b. After getting a good reading, wait 30 secs, then start another reading & immediately cancel it
13. Decide if participant will use shoulder strap (preferred), Microlife belt, own belt, or jacket pocket. Instrument ABPM cover appropriately, insert ABPM in cover, and make sure participant is comfortable with this method of wearing device.
14. Review ABPM device log with participant (and remind them to bring it tomorrow or their next study visit)
15. If the participant intends to remove the device to shower/changes clothes, require the participant to practice placing the device correctly with you present.
16. Review with participant:
    a. Importance of remaining still when BP readings are being taken
    b. Importance of keeping arm relaxed/supported
    c. If there is a failed reading, device will attempt three (3) retries ~1 minute apart
    d. If participant is consistently getting 2 failed readings, should call study cellphone
    e. ABPM cannot get wet
    f. If they intend to remove the device at any point, please do so between readings
    g. Payment depends on getting 80% successful readings

IF PARTICIPANT COMPLETED THE ABPM DEVICE FIRST

17. Check a complete recording (i.e. ~35 BP measurements) was obtained.
    a. Yes No
18. If yes, complete the post-ABPM questionnaire.
19. If no, ask the participant to repeat the ABPM. Discuss with participant the challenges they encountered with obtaining a complete ABPM.
20. Ask participant what time he/she anticipates going to sleep tonight and waking up tomorrow
    a. Anticipated time going to sleep: _____
    b. Anticipated time waking up tomorrow: _____
21. Initialize HBPM device. Serial number: _____
22. Is the participant's non-dominant arm being used for the WatchBP Home N? Yes No
23. Reason for not using the non-dominant arm: _____
    a. Put "✕" next to cuff sizes that will be used

		HBPM (Microlife WatchBP Home N)	
Cuff Size	Arm circumference	Dominant arm	Non-dominant arm
Small adult	17-21.9 cm		
Med adult	22-32 cm		
Large adult	32.1-42 cm		
Extra-large	42.1-52 cm		

24. Demonstrate to the participant how to place the cuff on their arm
    a. Find brachial artery (perhaps make small mark)
    b. Arrow on cuff over brachial artery, non-latex tubing coming out of cuff top
    c. Bottom of cuff 1" above bend/crease in elbow (if possible)
    d. Equal tension top and bottom of cuff (1 finger easily, 2 fingers snug, top and bottom)
    e. Wrap grey non-latex tubing around back of neck
    f. Connect tubing to HBPM device (make sure it will not pull out)
25. Allow the participant to practice placing the cuff on their arm with you present.
26. Explain to participant the importance of placing the device correctly and initializing the device when they get in bed by holding the on/off button for 3 seconds to start the initial reading and the following readings will occur 2, 3, and 4 hours after they have gone to bed.
27. Take one test reading in 'Usual' mode; repeat until obtain a valid reading (max 3 tries)
    a. If cannot get a valid reading, check for cuff too loose, kink in tubing, tubing not securely connected to HBPM device; if need be, change cuff and/or HBPM device (be sure to record new serial #)
28. Place the device in 'Nocturnal' mode.
29. Place the device in a carrier bag for the participant.
30. Review with participant:
    a. Importance of initializing the device before going to bed by holding the on/off button for 3 seconds
    b. If there is a failed reading, device will attempt three (3) retries ~1 minute apart

c. If participant is consistently getting 2 failed readings while initializing the device, they should call the study cellphone
d. Payment depends on getting three successful readings while asleep

31. Answer any questions that the participant may have.

NOTES: _____

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Better BP Study Visit 4 Checklist

[ ] COVID-19 Screening [ ] Yes [ ] No
- [ ] Symptom Tracker
- [ ] Temperature Check

[ ] Device return

[ ] Check the device for complete readings

- [ ] HBPM two sleep BP readings [ ] Yes [ ] No
- [ ] ABPM ~35 measurements [ ] Yes [ ] No
- [ ] Actiwatch to be remove at this visit

If No, ask participant to wear the device again to collect all necessary readings or measurements.

If yes, complete the following questionnaires
(**circle one**: email or in-person)

- [ ] Post ABPM Questionnaire
- [ ] Post HBPM Questionnaire
- [ ] Comparability Questionnaire
- [ ] Trait Anxiety Index
- [ ] Expectations of Outcomes

[ ] Collect non-fasting blood work

- [ ] Biospecimens
- [ ] Urine sample
- [ ] Genetic sample

[ ] Echocardiogram

Completed by _____ Date_____

Better BP Study

Study Visit 4 Data Collection Form

ID: _____ Date of Visit: _____

Name of tech performing visit: _____ Time of Visit: _____

AFTER PARTICIPANT ARRIVES

32. Participant will return the device and device log for you to check for completion.
33. Check a complete recording (i.e. – two sleep BP readings or ~35 ABPM readings) was obtained.
    a. Yes No
34. If yes, complete the post-HBPM or post-ABPM questionnaire.
35. If no, ask the participant to repeat the HBPM or ABPM. Discuss with participant the challenges they encountered with obtaining a complete HBPM or ABPM.
36. Participant will complete the post-HBPM questionnaire or post-ABPM questionnaire.
37. Complete a non-fasting blood draw
38. Collect a spot urine collection.
39. Take the participant to complete their echocardiogram or schedule them for an echocardiogram within the next 2 weeks.
40. Please confirm the participant's mailing address.
41. Remind the participant that they will:
    a. Be compensated for all 4 study visits within 2-3 weeks following their echocardiogram
    b. Receive their 24-hour ABPM report, labs and echocardiogram results in the mail
    c. We may contact them in the future for additional studies if they have consented to be contacted
42. Answer any questions that the participant may have.

NOTES: _____

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Sociodemographic and Medical History Questionnaire

1. What is your age? ____

2. What is your date of birth? _______________

3. Are you Hispanic?

    a. Yes
    b. No
    c. Decline to respond

4. What is your race?
    a. White
    b. Black
    c. American Indian/Alaska Native
    d. Asian
    e. Native Hawaiian or Other Pacific Islander
    f. More than one race
    g. Decline to respond

5. What is your sex?
    a. Male
    b. Female

6. What is your highest level of education completed?
    a. Less than high school
    b. High school diploma or equivalency
    c. Some college
    d. Bachelor's degree
    e. Graduate degree

7. What is your combined annual household income?
    a. < $25,000
    b. $25,000 to $49,999
    c. $50,000 to $74,999
    d. $75,000 or greater

8. What is your marital status?
    a. Single
    b. Married
    c. Separated
    d. Divorced
    e. Widowed

9. Are you living alone?
    a. Yes
    b. No

10. Have you ever been told by a doctor or a health professional that you have any of the following? Check those to which the answer is yes (leave other blank).

☐ High blood pressure or hypertension (excluding during pregnancy)
☐ High cholesterol
☐ Diabetes
☐ Asthma or hay fever

11. Have you smoked 100 cigarettes in your lifetime?
    a. Yes
    b. No

12. If you answered 'Yes' to Q11, do you smoke cigarettes now, even occasionally?
    a. Yes
    b. No

13. How many times per week do you engage in intense physical activity, enough to work up a sweat? _____

14. Do you presently drink alcoholic beverages, including beer, wine, and other drinks made with hard liquor, even occasionally?
    a. Yes
    b. No

If yes, how many alcoholic beverages do you drink during an average week?

Pittsburg Sleep Quality Index

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. **Please answer all questions.**

1. During the past month, what time have you usually gone to bed at night? _____

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night? _____

3. During the past month, what time have you usually gotten up in the morning? _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.) _____

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe:				
6. During the past month, how often have you taken medicine to help you sleep (prescribed or “over the counter”)?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
8. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?				
	Very good	Fairly good	Fairly bad	Very bad

9. During the past month, how would you rate your sleep quality overall?				
	No bed partner or roommate	Partner/roommate in other room	Partner in same room but not same bed	Partner in same bed
10. Do you have a bed partner or roommate?				
	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
If you have a roommate or bed partner, ask him/her how often in the past month you have had:				
a. Loud snoring				
b. Long pauses between breaths while asleep				
c. Legs twitching or jerking while you sleep				
d. Episodes of disorientation or confusion during sleep				
e. Other restlessness while you sleep, please describe:				

Scoring the PSQI

The order of the PSQI items has been modified from the original order in order to fit the first 9 items (which are the only items that contribute to the total score) on a single page. Item 10, which is the second page of the scale, does not contribute to the PSQI score.

In scoring the PSQI, seven component scores are derived, each scored 0 (no difficulty) to 3 (severe difficulty). The component scores are summed to produce a global score (range 0 to 21). Higher scores indicate worse sleep quality.

Component 1: Subjective sleep quality—question 9

Response to Q9	Component 1 score
Very good	0
Fairly good	1
Fairly bad	2
Very bad	3

Component 1 score:_____

Component 2: Sleep latency—questions 2 and 5a

Response to Q2	Component 2/Q2 subscore
< 15 minutes	0
16-30 minutes	1
31-60 minutes	2
> 60 minutes	3

Response to Q5a	Component 2/Q5a subscore
Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Sum of Q2 and Q5a subscores	Component 2 score
0	0
1-2	1
3-4	2
5-6	3

Component 2 score:_____

Component 3: Sleep duration—question 4

Response to Q4	Component 3 score
> 7 hours	0
6-7 hours	1
5-6 hours	2
< 5 hours	3

Component 3 score:_____

Component 4: Sleep efficiency—questions 1, 3, and 4

Sleep efficiency = (# hours slept/# hours in bed) X 100%

hours slept—question 4

hours in bed—calculated from responses to questions 1 and 3

Sleep efficiency	Component 4 score
> 85%	0
75-84%	1
65-74%	2
< 65%	3

Component 4 score:_____

Component 5: Sleep disturbance—questions 5b-5j

Questions 5b to 5j should be scored as follows:

Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Sum of 5b to 5j scores	Component 5 score
0	0
1-9	1
10-18	2
19-27	3

Component 5 score:_____

Component 6: Use of sleep medication—question 6

Response to Q6	Component 6 score
Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Component 6 score:_____

Component 7: Daytime dysfunction—questions 7 and 8

Response to Q7	Component 7/Q7 subscore
Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Response to Q8	Component 7/Q8 subscore
No problem at all	0
Only a very slight problem	1
Somewhat of a problem	2
A very big problem	3

Component 7 score:_____

Global PSQI Score: Sum of seven component scores:_____

Citation: Buysse, DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index (PSQI): A new instrument for psychiatric research and practice. Psychiatry Research 28:193-213, 1989

Post-ambulatory Blood Pressure Monitoring Questionnaire

For the following questions, please circle the answer that corresponds to your response on a scale from 'Not at all' to "A lot":

1. Did you find the monitor heavy?

Not at all A little A moderate amount A lot

2. Did you find the monitor uncomfortable to wear?

Not at all A little A moderate amount A lot

3. Did you find the monitor straightforward to use?

Not at all A little A moderate amount A lot

4a. Did you find the monitor cumbersome or awkward to wear?

Not at all A little A moderate amount A lot

4b. If you did not answer 'Not at all' in question 4a, did you find the monitor cumbersome or awkward to wear… (Check all that apply):

At home ☐

At work ☐

While driving ☐

At other times ☐

5a. Did the noise of the monitor disturb you?

Not at all A little A moderate amount A lot

5b. If you did not answer ‘Not at all’ in question 5a, did the noise of the monitor bother you… (Check all that apply):

At home ☐

At work ☐

While driving ☐

At other times ☐

6. Did the noise of the monitor disturb others?

Not at all A little A moderate amount A lot

7. Did you find the monitor embarrassing to wear?

Not at all A little A moderate amount A lot

8. Did you find the monitor interfered with your normal sleeping pattern?

No Yes

9a. If you answered ‘Yes’ to Q8, how much was your sleep disturbed?

A little A moderate amount A lot

9b. If your sleep was disturbed, did the monitor wake you up after you had fallen asleep?

No Yes

10. Did the monitor disturb you so much that you removed it during the day while awake?

No Yes

11. Did the monitor disturb you so much during the night while asleep that you removed it?

No Yes

12. How much pain did you experience while wearing the monitor?

None A little A moderate amount A lot

13. How much irritation did you experience while wearing the monitor?

None A little A moderate amount A lot

14. How much bruising did you experience while wearing the monitor?

None A little A moderate amount A lot

Post-sleep Blood Pressure Monitoring Questionnaire

For the following questions, please circle the answer that corresponds to your response on a scale from "Not at all" to "A lot":

1. Did you find the monitor heavy?

Not at all A little A moderate amount A lot

2. Did you find the monitor comfortable to wear?

Not at all A little A moderate amount A lot

3. Did you find the monitor straightforward to use?

Not at all A little A moderate amount A lot

4. Did you find the monitor cumbersome or awkward to wear?

Not at all A little A moderate amount A lot

5. Did the noise of the monitor disturb you?

Not at all A little A moderate amount A lot

6. Did the noise of the monitor disturb others?

Not at all A little A moderate amount A lot

7. Did you find the monitor embarrassing to wear?

Not at all A little A moderate amount A lot

8. Did you find the monitor interfered with your normal sleeping pattern?

No Yes

9a. If you answered ‘Yes’ to Q8, how much was your sleep disturbed?

A little A moderate amount A lot

9b. If your sleep was disturbed, did the monitor wake you up after you had fallen asleep?

No Yes

10. Did the monitor disturb you so much during the night that you removed it?

No Yes

11. How much pain did you experience while wearing the monitor?

None A little A moderate amount A lot

12. How much irritation did you experience while wearing the monitor?

None A little A moderate amount A lot

13. How much bruising did you experience while wearing the monitor?

None A little A moderate amount A lot

Comparability questionnaire

Ambulatory blood pressure monitoring involves wearing a device that measures blood pressure every 30 minutes during a 24-hour period. Home blood pressure monitoring involves you taking your own two blood pressure measurements in the morning and two blood pressure measurements in the evening, each day for one week (a total of 28 blood pressure measurements).

1. If your doctor thought it would be helpful to have information about what your blood pressure was during sleep,

    a. How willing would you be to perform a 24-hour ambulatory blood pressure recording?

0	1	2	3	4
Not at all willing	A little willing	Moderately willing	Very willing	Completely willing

    b. How willing would you be to wear the home blood pressure monitor for one night?

0	1	2	3	4
Not at all willing	A little willing	Moderately willing	Very willing	Completely willing

2. If your doctor thought it would be helpful to have information about what your blood pressure was outside the clinic,

    a. How willing would you be to perform a 24-hour ambulatory blood pressure recording?

0	1	2	3	4
Not at all willing	A little willing	Moderately willing	Very willing	Completely willing

    b. How willing would you be to perform home blood pressure monitoring for a week?

0	1	2	3	4
Not at all willing	A little willing	Moderately willing	Very willing	Completely willing

3. Which device would you prefer to wear if you had to repeat this study?
    a. Ambulatory blood pressure monitor
    b. Home blood pressure monitor
    c. Neither

State Anxiety Questionnaire

Better BP

Spielberger's State Anxiety Inventory

Study ID

Directions: Read each statement below and then mark the appropriate circle to the right of the statement to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	Not at all	Somewhat	Moderately so	Very Much So
1. I feel calm	O	O	O	O
2. I feel secure	O	O	O	O
3. I feel tense	O	O	O	O
4. I feel strained	O	O	O	O
5. I feel at ease	O	O	O	O
6. I feel upset	O	O	O	O
7. I am presently worrying over possible misfortunes	O	O	O	O
8. I feel satisfied	O	O	O	O
9. I feel frightened	O	O	O	O
10. I feel comfortable	O	O	O	O
11. I feel self-confident	O	O	O	O
12. I feel nervous	O	O	O	O
13. I am jittery	O	O	O	O
14. I feel indecisive	O	O	O	O
15. I feel relaxed	O	O	O	O
16. I feel content	O	O	O	O
17. I feel worried	O	O	O	O
18. I feel confused	O	O	O	O
19. I feel steady	O	O	O	O
20. I feel pleasant	O	O	O	O

Trait Anxiety Questionnaire

Better BP

Spielberger's Trait Anxiety Inventory

Study ID

Directions: Read each statement below and then mark the appropriate circle to the right of the statement to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	Never	Sometimes	Often	Always
1. I feel pleasant	○	○	○	○
2. I feel nervous and restless	○	○	○	○
3. I feel satisfied with myself	○	○	○	○
4. I wish I could be as happy as others seem to be	○	○	○	○
5. I feel like a failure	○	○	○	○
6. I feel rested	○	○	○	○
7. I am "calm, cool, and collected"	○	○	○	○
8. I feel that difficulties are piling up so that I cannot overcome them	○	○	○	○
9. I worry too much over something that really doesn't matter	○	○	○	○
10. I am happy	○	○	○	○
11. I have disturbing thoughts	○	○	○	○
12. I lack self-confidence	○	○	○	○
13. I feel secure	○	○	○	○
14. I make decisions easily	○	○	○	○
15. I feel inadequate	○	○	○	○
16. I am content	○	○	○	○
17. Some unimportant thought runs through my mind and bothers me.	○	○	○	○
18. I take disappointments so keenly that I can't put them out of my mind	○	○	○	○
19. I am a steady person	○	○	○	○
20. I get in a state of tension or turmoil as I think over my recent concerns and interests	○	○	○	○

Expectations of Outcomes Questionnaire

Better BP

Expectations of Outcomes

Study ID

Instructions: Please read each question carefully and mark the number on the -5 to +5 scale which represents your best estimate of what you believe will occur.

1. When your physician enters the room and does a blood pressure check, do you expect your blood pressure to be:

O	O	O	O	O	O	O	O	O	O	O
-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5

Much lower than usual — Exactly the same as usual — Much higher than usual

2. When your physician enters the room and does a blood pressure check, do you expect your heart rate to be:

O	O	O	O	O	O	O	O	O	O	O
-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5

Much lower than usual — Exactly the same as usual — Much higher than usual

3. When your physician enters the room and does a blood pressure check, do you expect your anxiety level to be:

O	O	O	O	O	O	O	O	O	O	O
-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5

Much lower than usual — Exactly the same as usual — Much higher than usual

4. When your physician enters the room and does a blood pressure check, do you expect your stress level to be:

O	O	O	O	O	O	O	O	O	O	O
-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5

Much lower than usual — Exactly the same as usual — Much higher than usual

5. When a nurse or physician takes your blood pressure, how uncomfortable or painful is it?:

O	O	O	O	O
0	+1	+2	+3	+4

Not at all Uncomfortable — Very Painful

ABPM Device Log

ID: _____ Date: ___/___/___

It is important for us to know approximately what time you went to sleep and what time you woke up in the morning

Time went to sleep _____:_____ AM PM (circle one)

Time woke up in the morning _____:_____ AM PM (circle one)

If you took a nap during the monitoring period, please write down the time you went to sleep for your nap and the time you woke up from your nap

First Nap

Nap time went to sleep _____:_____ AM PM (circle one)

Nap time woke up _____:_____ AM PM (circle one)

Second Nap

Nap time went to sleep _____:_____ AM PM (circle one)

Nap time woke up _____:_____ AM PM (circle one)

It is also important that we know what times, if any, you removed ABPM device. Please record these times in the following table.

	Time	**AM / PM (circle one)**	**Comment (why did you remove it?)**
Time removed	:	AM PM	
Time put back on	:	AM PM	
Time removed	:	AM PM	
Time put back on	:	AM PM	
Time removed	:	AM PM	
Time put back on	:	AM PM	
Time removed	:	AM PM	
Time put back on	:	AM PM	

Please be sure to return this piece of paper when you return the equipment.

HBPM Device Log

ID: _____ Date: ___/___/___

It is important for us to know approximately what time you went to sleep and what time you woke up in the morning

Time went to sleep _____:_____ AM PM (circle one)

Time woke up in the morning _____:_____ AM PM (circle one)

It is also important that we know what times, if any, you removed the HBPM device during the night. Please record these times in the following table.

	Time	**PM/AM (circle one)**	**Comment (why did you remove it?)**
Time removed	:	PM AM	
Time put back on	:	PM AM	
Time removed	:	PM AM	
Time put back on	:	PM AM	
Time removed	:	PM AM	
Time put back on	:	PM AM	

<u>Please be sure to return this piece of paper when you return the equipment</u>

APPENDIX 6. REMINDER CARDS

ABPM Reminder Card

- **Stand or sit still** and **do not talk** when blood pressure readings are being taken.
- **Keep your arm relaxed or supported** during the blood pressure readings.
- The blood pressure cuff should be **1 inch above your elbow,** and should be snug**.**
- The arrow on the cuff should be pointed towards the **inner part of your elbow.**
- **Keep the blood pressure monitor and watch dry.**

If you have trouble getting successful readings, please contact Julia Medina at: (205) 975-4455

Return to the clinic tomorrow on: _____ at _____ AM PM

APPENDIX 6. REMINDER CARDS

HBPM Reminder Card

- **Remember to press and hold the on/off button for 3 seconds** to begin initial reading.

- The blood pressure cuff should be **1 inch above your elbow,** and should be snug**.**

- The arrow on the cuff should be pointed towards the **inner part of your elbow.**

- **Keep the blood pressure monitor and watch dry.**

If you have trouble getting an initial reading, please contact Julia Medina at: (205) 975-4455

Return to the clinic tomorrow on: _____ at _____ AM PM

APPENDIX 7. PHYSICAN FAX NUMBERS

Physician Fax Numbers

Hoover Clinic

- Fax line (205) 989-4202

Leeds Clinic

- Front desk-205.699.0662
- Nurses Station #1-205.699.4189
- Nurses Station #2-205.699.4191

Gardendale Clinic

- Front desk – 608-7001
- Fax- 631-3173
- Fax- 443-1752

Internal Medicine I/ 3 West	**113050**	**705714**
Michael Skellie, RN Manager	**801-8359**	**pager: 9514**
Provider Teams	**Extension**	**Fax**
Stephen Bell, MD	1-8368	801-5775
James Williams, MD	1-7810	801-8118
Brittany Payne, MD	1-7073	801-8118
Paige Harkness, CRNP	*1-7397*	801-8118
Stuart Cohen, MD	1-7398	801-5776
Patricia Garver, MD	1-8311	502-9936
Mark Stafford, MD	1-8321	801-5776
Hayley Entrekin, CRNP	1-8350	502-9936
Michael Geer, MD	1-8543	801-5777
Jennifer Vigil, MD	1-9037	801-5778
Linda Kirkman, DNP	1-5503	801-5778

APPENDIX 7. PHYSICAN FAX NUMBERS

Front Desk	**Extension**	Fax
PES	1-8303	801-5779
Ebony Allen	1-8115	801-5779

Internal Medicine II/ 2 West	**113075**	**705715**
RN Manager (Jillian Stone)	**801-8392**	**pager: 1472**
Doctors	**Extension**	**Fax**
Alan Gruman, MD	1-8278	801-7945
David Gettinger, MD	1-8320	801-7945
Carla Stefanescu, MD	1-8006	801-7553
Allison G. Wilkin, MD	1-9934	801-7553
James V. Davis, MD	1-8310	801-8897
Larry Steven Hunt, MD	1-8497	801-7833
Hernando D. Carter, MD	1-8955	801-7833
Murkta Tripathi, MD	1-8340	
Nurse Practitioner		
Heather Hardy Williams, CRNP	1-8308	
Joanne Shaughnessy, CRNP	1-8254	801-7945

Internal Medicine III/ 2 East	**113080**	**705716**
Jillian Stone, RN Manager	**801-8560**	**pager: 3331**
Doctors	**Extension**	**Fax**
Mary Balkovetz, MD	1-8748	583-8058

APPENDIX 7. PHYSICAN FAX NUMBERS

Laurie Hall, MD	1-8314	583-8058
Rachel Labovitz, MD	1-8325	583-8058
Stephen Stair, MD	1-7776	801-8806
Sarah French, MD	1-5326	801-8522

Residents Clinic- Internal Medicine 4	**801-7440**	**113375**	
Jillian Stone, RN Manager	**801-8560**	**pager: 3331**	
Tamara Underwood, LPN	1-7756	fax: 801-7441	
ShirDonna Banks, CMA	1-8186		
Dorothea Rutledge RN	1-7442		
General Internal Medicine	**934-9638**	**113010**	705713
			Fax: 801-8067
Jillian Stone, RN Manager	**801-8560**	**pager: 3331**	Fax: 975-7797

ID __ __ __ __ __

Ambulatory Blood Pressure Monitor - Participant Instructions

Picture 1

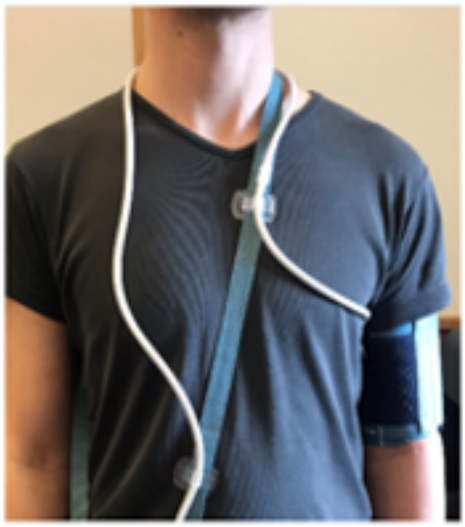
How to care for the Ambulatory Blood Pressure Monitor

Remember to keep the Ambulatory Blood Pressure Monitor in the dark blue plastic case **(Picture 1)**. It is important that the monitor does not get wet. We prefer that you do not remove the monitor. However, if you will be showering, swimming or exercising, you must remove the monitor.

How to take the Ambulatory Blood Pressure Monitor off

When removing the monitor, pull the velcro flap on the cuff away from your body and slide the cuff off your arm. Gently take the white tube and pull it over your head and away from your body. Be careful not to disconnect the white tube from the monitor. Lastly, when taking off the monitoring, remember to put the monitor on "Casual mode" by switching it from "Ambulatory mode" to "Casual mode". The switch button is on the side of the device **(Picture 2)**.

Picture 2



Picture 3

How to put the Ambulatory Blood Pressure Monitor back on

When putting the equipment back on, place the cuff on the same arm you removed the equipment from. The cuff should be worn with the white tube facing up toward your shoulder **(Picture 3).** Place the tube around the back of your neck and down the front of the opposite shoulder. Check to make sure that the arterial mark (the red arrow is pointing to it in **Picture 4**) on the cuff is lying directly on and situated over the brachial artery. The research assistant marked where your brachial artery is located with their finger by the crease of your elbow

Picture 4

(Picture 4). Be sure that the bottom of the cuff is situated about one to two inches above the crease in your elbow, and that the cuff is snug and is equally tight at the top and bottom. Check that you are able to place 1 finger easily and 2 fingers snugly under the cuff at the top and bottom of the cuff **(Picture 5)**. Lastly, please remember to switch the monitor to "Ambulatory mode". The switch button is on the side of the device (see **Picture 2**).

Picture 5

Frequently Asked Questions about the Ambulatory Blood Pressure Monitor

1. What do I do when the monitor is taking a reading? The monitor is going to take a reading every 30 minutes, both during the day and at night, for example: 5PM, 5:30PM, 6PM, etc. When you feel the cuff inflate, please remain motionless, with your arm relaxed either gently by your side or bent (as if in a sling), or gently resting on a table/desk so that your arm is elevated at heart level. We also ask that you do not talk while the monitor is taking a blood pressure reading.

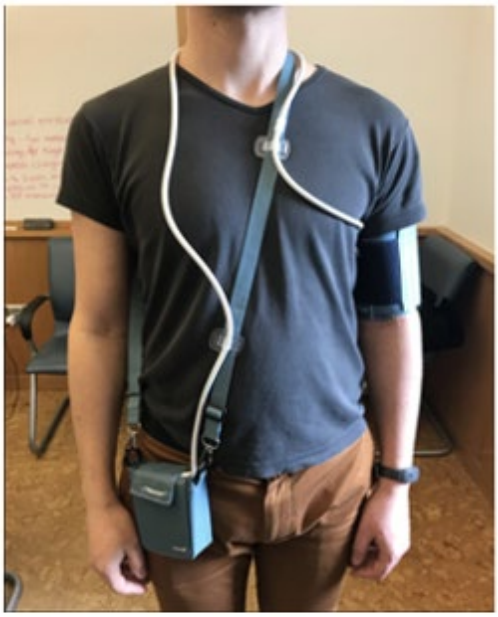
2. How often will the monitor take a reading? The monitor is going to take a reading every 30 minutes, both during the day and at night, for example: 5PM, 5:30PM, 6PM, etc. There will be a half inflation to notify you that the device will take a reading in one minute so that you can prepare yourself for the reading.

3. What should I do if a reading fails? If a reading fails (usually because of motion, including during driving/riding, or because the arm is not relaxed), the monitor will

attempt to repeat the reading 2 minutes later (shown on the device as 120 seconds). If the 2nd attempt fails, the monitor will attempt to repeat the reading 4 minutes later (shown on the device as 240 seconds). The monitor will attempt to take a total of 3 readings. If the 2nd attempt fails, no further attempts will be made until the next scheduled reading (30 minutes later). If the readings continue to fail when you are motionless and your arm is relaxed, check that the cuff is positioned properly two inches above your elbow, with the “artery mark” lying directly on and situated over the brachial artery. If the readings continue to fail, even after you have remained still and have positioned the cuff properly, please call us at **(205) 586-0383.**

4. What should I do if the cuff does not deflate after a reading? In the very unlikely event that the cuff inflates and does not deflate properly, you can abort the reading by changing the device to “Casual mode” from “Ambulatory mode” using the switch on the device’s right side (see **Picture 2**) and disconnecting the white tubing connected to the device’s left side. Reconnect the tubing back to the device and take a test-reading in “Casual mode.” If the cuff re-inflates and the device is working properly, switch the device settings back to “Ambulatory mode” (see **Picture 2**). If this does not work, please call us at **(205) 586-0383**.

5. What should I do if the cuff or monitor gets wet? There is no personal danger to you if the monitor or cuff gets wet. The cuff will be uncomfortable if it gets wet, but there will be no permanent damage. If the monitor gets wet, please wipe it down with a towel. If it does not turn on or if it does not take a reading 30 minutes after the monitor got wet, please call us at **(205) 586-0383.**



Picture 6

In **Picture 6**, the monitor is worn in a plastic case. A strap is attached to both corners of the dark blue plastic case and acts as a harness for the bag. **Picture 6** demonstrates the final placement of the monitor if worn in a harness bag.

Please note that you can place the blood pressure cuff, strap holding the monitor, and tubing underneath your shirt

Picture 7

In **Picture 7**, the monitor inside the dark blue plastic case is worn on a belt. In the back of the dark blue plastic case there is a belt loop in which the belt can be inserted in to hold the monitor. **Picture 7** demonstrates this final placement of the monitor worn as a belt.

Please note that you can place the blood pressure cuff, plastic case holding the monitor, and tubing underneath your shirt

ID __ __ __ __ __

Home Blood Pressure Device - Participant Instructions

Picture 1

How to care for the Home Blood Pressure Device

Remember to keep the Home Blood Pressure Device **(Picture 1)** in a safe area, where it does not get damaged due to a fall (e.g., not near the corner of the bed). It is important that the monitor does not get wet. We prefer that you do not remove the cuff during the night. However, if the cuff is causing you pain, you may remove it.

Picture 2

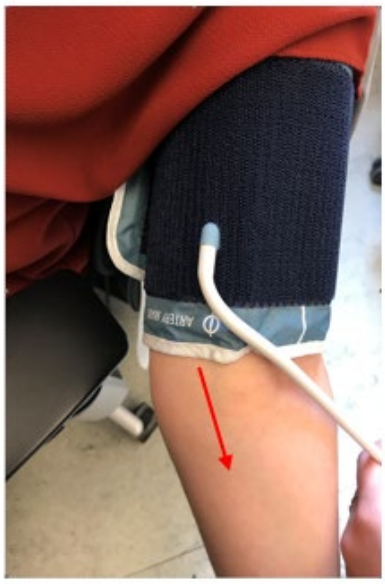
How to take the Home Blood Pressure Cuff off

When removing the cuff, pull the velcro flap on the cuff away from your body and slide the cuff off your arm. Gently take the white tube and pull it away from your body. Be careful not to disconnect the white tube from the monitor. Lastly, remember to put the monitor on "Usual mode" by switching it from "Nocturnal mode" to "Usual mode". The switch button is on the side of the device **(Picture 2)**.

How to put the Home Blood Pressure Cuff on

When going to bed put the blood pressure cuff on. You should place it on the same arm you removed the equipment from during your Visit. The cuff should be worn with the white tube facing down toward your elbow/hand **(Picture 3)**. Check to make sure that the arterial mark on the cuff is lying directly on and situated over the brachial artery. The research assistant marked where your brachial artery is located with a red arrow **(Picture 4)**. Be sure that the bottom of the cuff is situated about one to two inches above the crease in your elbow, and that the cuff is snug

Picture 3



Picture 4

and is equally tight at the top and bottom. Check that you are able to place 1 finger easily and 2 fingers snugly under the cuff (both at the top and bottom) **(Picture 5)**.

Take your first test reading on Nocturnal mode by pressing the on/off button for three seconds **when you are going to lie in bed and about to go to sleep**. It will take your first blood pressure reading immediately. If you cannot get a valid reading, check if the cuff is too loose, if there is a kink in the tubing, or the tubing is not securely connected to the home blood pressure device, then retry the reading. Once you get a valid reading, place the device under your pillow or on somewhere on your bed in a safe area where it will not fall or cause the device damage. The monitor will take 3 readings at 2 hours, 3 hours, and 4 hours after your first test reading.

Picture 5

Frequently Asked Questions about the Home Blood Pressure Device

1. What do I do when the device is taking a reading? The device will be taking three readings while you are sleeping. Make sure before you go to sleep that the tubing is not compressed or obstructed and that you do not sleep on the arm where the cuff is placed. If you feel the cuff inflate and wake up, please remain motionless and do not talk while the monitor is taking a blood pressure reading.

2. How often will the device take a reading? After your first test reading, the monitor is going to take a total of three readings, two hours, three hours, and four hours later. For example, if you take your test reading at 10:30PM, the monitor will take one reading at 12:30AM, 1:30AM and 2:30AM.

3. What should I do if a reading fails? If a reading fails (usually because of motion, the tube being obstructed, or the cuff not being properly placed), the monitor will NOT attempt to repeat the reading. If you happen to wake up and realize there is an error reading, please adjust the cuff and check that the

cuff is positioned properly two inches above your elbow with the arrow pointing to your brachial artery. If the readings continue to fail, and you are aware of such even after you have remained still and have positioned the cuff properly, please call us at **(205) 586-0383** in the morning.

5. What should I do if the device or cuff gets wet? Please try to keep the monitor dry. There is no personal danger to you if the monitor or cuff gets wet. The cuff will be uncomfortable if it gets wet, but there will be no permanent damage. If the monitor gets wet, please wipe it down with a towel. If it does not turn on or if it does not take a test reading after the monitor gets wet, please call us at **(205) 586-0383**.

ID __ __ __ __ __

Wrist Activity Monitor - Participant Instructions

ACTIWATCH (Wrist Activity Monitor)

Instructions for the Actiwatch

Remember to keep the Actiwatch on your non-dominant arm wrist. It is important that the device does not get wet. We prefer that you not remove the device. Remember to press the side button of the Actiwatch when you go to sleep and when you wake up to measure the time you woke up and when you went to bed.

How to care for the Actiwatch

It is important that the monitor does not get wet. We prefer that you do not remove the monitor. However, if you will be showering, swimming or exercising, you should remove the monitor. Please write down the times on the Device Log that you took the monitor off and put it back on.

Frequently Asked Questions about the Actiwatch

1. What does the Actiwatch measure? The primary purpose of this monitor is to provide information about movement during sleep. This is why it is desirable that you wear the monitor to bed. During waking hours, it also provides a measure of physical activity.

2. Should I wear the Actiwatch to bed? Yes, we would like you to wear the wrist activity monitor to bed. It will not disturb your sleeping.

ID __ __ __ __ __

Instructions for Sonographers

1. In the server, please store the participant information as follows:
    a. Last Name – 'BetterBP'
    b. Patient ID – Participant ID Number (located on the participant appointment card)
    c. Exam Performed by – Please enter your initials
    d. Leave all other fields blank
2. Following the procedure, please download the scan to the two CDs enclosed within the envelope.
    a. **NOTE:** Please make sure the worklist is not pulled up before downloading the scan.
3. Once downloaded, please return the two CDs to the envelope and give to the study coordinator.

Results Packet

UAB Hypertension Research Clinic
933 19th Street S, CHB19-115
University of Alabama at Birmingham
Birmingham, AL 35294

Paul Muntner, PhD
Principal Investigator
Tel: 205-975-8077
Fax: 205-975-7058

Letter to Participants (Physician)

Dear [Participant Name],

Thank you for participating in the Better BP study. Enclosed you will find your results from the study including your blood pressure values, lab results, and the results of your echocardiogram.

If any of your lab values are above or below normal ranges, please contact your health care provider. If you do not have a health care provider, please contact the study physician, Dr. Suzanne Oparil, at **(205)-934-5951**.

You indicated that you would like a copy of your results sent to your healthcare provider. We will fax them to the physician that you have noted on file with us within the next 3-5 business days.

If you have not received payment for completing the study or you have received a bill from UAB hospital regarding your echocardiogram, please contact the Better BP study staff at **(205)-975-7653** or **(205)-975-4455**.

If you have any additional questions or concerns, please feel free to reach out to us at the numbers listed above or email us at **bpstudy@uab.edu**.

Thank you again for your participation in the Better BP study. We hope that you will consider participating in future studies.

Sincerely,

Paul Muntner, PhD
Professor
Department of Epidemiology
School of Public Health
University of Alabama at Birmingham

Suzanne Oparil, MD
Professor
Department of Medicine
School of Medicine
University of Alabama at Birmingham

UAB Hypertension Research Clinic
933 19th Street S, CHB19-115
University of Alabama at Birmingham
Birmingham, AL 35294

Paul Muntner, PhD
Principal Investigator
Tel: 205-975-8077
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Letter to Participants (No Physician)

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Sincerely,

Paul Muntner, PhD
Professor
Department of Epidemiology
School of Public Health
University of Alabama at Birmingham

Suzanne Oparil, MD
Professor
Department of Medicine
School of Medicine
University of Alabama at Birmingham

UAB Hypertension Research Clinic
933 19th Street S, CHB19-115
University of Alabama at Birmingham
Birmingham, AL 35294

Paul Muntner, PhD
Principal Investigator
Tel: 205-975-8077
Fax: 205-975-7058

Blood Pressure Measurement Results

Date of Visits: _____

Participant's Last Name: _____

Participants' First Name: _____

Your blood pressure measurements:

Attended Blood Pressure*	Unattended Blood Pressure*
Systolic Blood Pressure: _____ mmHg Diastolic Blood Pressure: _____ mmHg Heart Rate: _____ beats per minute	Systolic Blood Pressure: _____ mmHg Diastolic Blood Pressure: _____ mmHg Heart Rate: _____ beats per minute

*Average of six blood pressure measurements.

Based on 2017 guidelines from the American College of Cardiology and American Heart Association, categories of clinic blood pressure are defined as follows:

Blood Pressure Category	Systolic Blood Pressure		Diastolic Blood Pressure
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130-139 mm Hg	or	80-89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

This is based on average of the blood pressure readings taken during your first two clinic visits.

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Principal Investigator
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Fax: 205-975-7058

Echocardiogram and Lab Test Results

Participant's Last Name: _____

Participants' First Name: _____

Date of Collection: _____ Date of Echocardiogram: _____

TEST NAME	IN RANGE	OUT OF RANGE	REFERENCE RANGE
---ECHOCARDIOGRAM---			
LEFT VENTRICULAR MASS INDEX			Women: <96 m^2 Men: <116 m^2
LEFT VENTRICULAR EJECTION FRACTION			> 50%
---BLOOD TESTS---			
METABOLIC PANEL			
CREATININE			0.7-1.3 mg/dL
eGFR			>=60 ml/min/1.73m^2
LIPID PANEL			
CHOLESTEROL, TOTAL			<200 mg/dL
HDL CHOLESTEROL			40-60 mg/dL
GLYCOSYLATED HEMOGLOBIN HbA1C			<6.5%
---URINE TESTS----			
CREATININE			
MICROALBUMIN MICROALB/CREAT RATIO			<30 mg/g

ABPM Results Guide

We appreciate you taking time to participate in the Better BP study. In this study, we recorded your blood pressure every 30 minutes for as long as you wore the ambulatory blood pressure monitor (ABPM). Attached is a report that details your results.

Here is a guide to your ABPM report:

Top Left Panel

- We provide your personal information, the day and night time period as set by the ABPM device software, and the awake and asleep times you reported on your ABPM device log.
- The last box in the top left panel is the level (threshold) for defining high daytime and nighttime blood pressure by national hypertension guidelines.

Graph of Blood Pressure Values

- The top red line is your systolic blood pressure (i.e., top number of the blood pressure), the bottom red line is your diastolic blood pressure (i.e., bottom number of your blood pressure), and the gray line at the bottom of the graph is your heart rate (HR). These are the values taken over the course of the day from when you put on to when you took off the blood pressure cuff. The blue box represents the nighttime period as set by the ABPM device software.

Middle Box

- This box contains your average blood pressure values and heart rate for 24-hours, awake readings, and asleep readings.
- Everyone's blood pressure varies between measurements. SD stands for standard deviation and this number represents how much your blood pressure varied throughout the period when it was being measured.

Here is how to interpret your readings:
Based on 2017 guidelines from the American College of Cardiology and American Heart Association, high average blood pressure on ambulatory blood pressure monitoring is defined by:

High 24-hour blood pressure	Systolic (sys) blood pressure greater than or equal to 125 mm Hg or diastolic (dia) blood pressure greater than or equal to 75 mm Hg

This is based on blood pressure readings taken over the entire period that you wore the device.

High awake blood pressure	Systolic (sys) blood pressure greater than or equal to 130 mm Hg or diastolic (dia) blood pressure greater than or equal to 80 mm Hg

This is based on blood pressure readings taken during the period that you were awake.

High asleep blood pressure	Systolic (sys) blood pressure greater than or equal to 110 mm Hg or diastolic (dia) blood pressure greater than or equal to 65 mm Hg

This is based on blood pressure readings taken during the period that you were asleep.

Bottom of the page, we provide all of the individual blood pressure readings that were obtained for you, the time they were taken and your heart rate. The readings in red represent blood pressure values that were greater than the pre-defined blood pressure level (threshold) shown in the last box in the top left panel. You shouldn't worry if a few readings were high as blood pressure varies from beat to beat.

Analysis Plan: Evaluating novel approaches for estimating awake and sleep blood pressure (The Better BP Study)

Aims and hypotheses

Primary Aim 1: To examine whether measuring unattended clinic BP with an automated device will provide a more accurate estimate of awake BP on ABPM than measuring attended clinic BP with an automated device.

Hypothesis 1a: The absolute difference with awake BP will be smaller for unattended vs. attended clinic BP.

Hypothesis 1b: The agreement between hypertension status using BP measured in the clinic and on ABPM while awake will be higher when clinic BP is measured unattended vs. attended. Also, the prevalence of both white coat and masked hypertension will be lower when measuring unattended clinic BP.

Primary Aim 2: To examine whether a new HBPM device provides an accurate approach for measuring sleep BP.

Hypothesis 2a: Sleep BP on HBPM will provide an accurate estimate of sleep BP on ABPM.

Hypothesis 2b: HBPM will be better tolerated (e.g., less awakening during sleep, pain, bruising) than ABPM.

Primary Aim 3: To compare the associations of unattended versus attending clinic BP, unattended clinic BP versus awake BP on ABPM, and sleep BP on HBPM versus ABPM with two markers of end-organ damage, left ventricular mass index (LVMI) and urinary albumin-to-creatinine ratio (ACR).

Hypothesis 3a: The association with end-organ damage will be stronger for unattended vs. attended clinic BP.

Hypothesis 3b: The association with end-organ damage will be similar for unattended clinic BP and awake BP.

Hypothesis 3c: The association with end-organ damage will be similar for sleep BP by HBPM and ABPM.

Objectives:

1. Determine the absolute mean difference in awake systolic and diastolic BP, separately, between attended and unattended BP; awake BP from ABPM and attended BP; and awake BP from ABPM and unattended BP.
2. Determine the prevalence of hypertension, white coat hypertension, and masked hypertension on attended, unattended, and ABPM BP measurements.
3. Determine the agreement between hypertension phenotypes on ABPM and clinic BP (i.e., attended and unattended).
4. Determine the absolute mean difference in asleep systolic and diastolic BP, separately, between asleep BP measurements from ABPM and HBPM.
5. Determine the tolerability of ABPM and HBPM.

6. Determine the associations of unattended versus attending clinic BP, unattended clinic BP versus awake BP on ABPM, and sleep BP on HBPM versus ABPM with left ventricular mass index (LVMI) and urinary albumin-to-creatinine ratio (ACR).

The following will be conducted using data from the Better BP study.

Data management:
Create the following variables to define hypertension:

1. Create the variable ABPM_HYPER by assigning 1 to those with mean awake ABPM ≥135 mm Hg (systolic BP) or 85 mm Hg (diastolic BP) and 0 if otherwise.
2. Create the variable ATTENDED_HYPER by assigning 1 to those with mean attended BP ≥140 mm Hg (systolic BP) or 90 mm Hg (diastolic BP) and 0 if otherwise.
3. Create the variable UNATTENDED_HYPER by assigning 1 to those with mean unattended BP ≥135 mm Hg (systolic BP) or 85 mm Hg (diastolic BP) and 0 if otherwise.
4. Identify the following individuals:
    1. HYP_AB_ATTEND should equal 1 if ABPM_HYPER = 1 and ATTENDED_HYPER = 1, and 0 if otherwise.
    2. HYP_AB_UNATTEND should equal 1 if ABPM_HYPER = 1 and UNATTENDED_HYPER = 1, and 0 if otherwise.
    3. WHIT_AB_ATTEND should equal 1 if ABPM_HYPER = 0 and ATTENDED_HYPER = 1, and 0 if otherwise.
    4. WHIT_AB_UNATTEND should equal 1 if ABPM_HYPER = 0 and UNATTENDED_HYPER = 1, and 0 if otherwise.
    5. MASK_AB_ATTEND should equal 1 if ABPM_HYPER = 1 and ATTENDED_HYPER = 0, and 0 if otherwise.
    6. MASK_AB_UNATTEND should equal 1 if ABPM_HYPER = 1 and UNATTENDED_HYPER = 0, and 0 if otherwise.

Statistical analysis:

1. Calculate the distribution of the variables in **Table 1**, overall, and separately for participants who were attended then unattended, unattended then attended, as well as participants who underwent ABPM before HBPM, and HBPM before ABPM.

2. Do the following analysis for **Table 2** for those with complete BP data on ABPM, attended, and unattended:
    a. For awake systolic BP, calculate the mean (with standard deviation) BP on ABPM, attended, and unattended
    b. Calculate the absolute mean difference with 95% confidence intervals for ABPM vs. attended, ABPM vs. unattended, and attended vs. unattended, using mixed model to determine the difference between the differences.
    c. Repeat items **2a** and **2b** for awake diastolic BP on ABPM, attended and unattended.

3. Do the following analysis for **Table 3** for those with complete BP data on ABPM, attended, and unattended:
    a. Calculate the percentage (with 95% confidence interval) of participants with hypertension on awake ABPM (i.e., ABPM_HYPER = 1)
    b. Calculate the percentage (with 95% confidence interval) of participants with hypertension on attended BP measurements (i.e., ATTENDED_HYPER = 1).
    c. Calculate the percentage (with 95% confidence interval) of participants with hypertension on unattended BP measurements (i.e., UNATTENDED_HYPER = 1).
    d. Calculate the percentage (with 95% confidence intervals) of participants with hypertension on attended and awake ABPM (i.e., HYP_AB_ATTEND = 1).
    e. Calculate the percentage (with 95% confidence intervals) of participants with hypertension on unattended and awake ABPM (i.e., HYP_AB_UNATTEND = 1).
    f. Calculate the percentage (with 95% confidence intervals) of participants with white coat hypertension on ABPM and attended BP (i.e., WHIT_AB_ATTEND = 1).
    g. Calculate the percentage (with 95% confidence intervals) of participants with white coat hypertension on ABPM and unattended BP (i.e., WHIT_AB_UNATTEND = 1)
    h. Calculate the percentage (with 95% confidence intervals) of participants with masked hypertension on ABPM and attended BP (i.e., MASK_AB_ATTEND = 1).
    i. Calculate the percentage (with 95% confidence intervals) of participants with masked hypertension on ABPM and unattended BP (i.e., MASK_AB_UNATTEND = 1)

4. Do the following analysis for those with complete BP data on ABPM, attended, and unattended:
    a. **Table 4**, use a 2 x 2 table to determine the agreement hypertension on ABPM and clinic BP (i.e., HYP_AB_ATTEND versus HYP_AB_UNATTEND); provide the p-value from kappa statistics.
    b. **Table 5**, use a 2 x 2 table to determine the agreement white coat hypertension on ABPM and clinic BP (i.e., WHIT_AB_ATTEND versus WHIT_AB_UNATTEND); provide the p-value from kappa statistics.
    c. **Table 6**, use a 2 x 2 table to determine the agreement masked hypertension on ABPM and clinic BP (i.e., WHIT_AB_ATTEND versus WHIT_AB_UNATTEND); provide the p-value from kappa statistics.

5. Do the following analysis for **Table 7** for those with complete sleep BP data on ABPM and HBPM:
    a. For sleep systolic BP, calculate the mean BP (with standard deviation) on ABPM and HBPM.
    b. Calculate the absolute mean difference with 95% confidence intervals for ABPM vs. HBPM, using a paired T-test.
    c. Repeat items 5a and 5b for sleep diastolic BP on ABPM and HBPM.

6. **Table 8**. Calculate the number and percentage of side effects and tolerability (**listed in Table 8**) that occurred in ABPM only, HBPM only, both ABPM and HBPM, and occurred for neither ABPM nor HBPM.

7. **Table 9**. Restrict the analysis to those with complete data on attended and unattended BP and complete data on left ventricular mass index .
    a. Use linear regression to determine the relationship between attended SBP with left ventricular mass index.
    b. Repeat the analysis for attended DBP, unattended SBP, unattended DBP with left ventricular mass index, separately.

8. **Table 10**. Restrict the analysis to those with complete BP data on unattended and awake ABPM and complete data on left ventricular mass index.
    a. Use linear regression to determine the relationship between unattended SBP with left ventricular mass index.
    b. Repeat the analysis for unattended DBP, awake SBP on ABPM, awake DBP on ABPM with left ventricular mass index, separately.

9. **Table 11**. Restrict the analysis to those with complete sleep BP data on ABPM and HBPM and complete data on left ventricular mass index.
    c. Use linear regression to determine the relationship between sleep SBP on ABPM with left ventricular mass index.
    d. Repeat the analysis for sleep DBP on ABPM, sleep SBP on HBPM, and sleep DBP on HBPM with left ventricular mass index, separately.

10. **Table 12**. Restrict the analysis to those with complete data on attended and unattended BP and complete data on urinary albumin-to-creatinine ratio.
    c. Use linear regression to determine the relationship between attended SBP with urinary albumin-to-creatinine ratio.
    d. Repeat the analysis for attended DBP, unattended SBP, unattended DBP with urinary albumin-to-creatinine ratio, separately.

11. **Table 13**. Restrict the analysis to those with complete BP data on unattended and awake ABPM and complete data on urinary albumin-to-creatinine ratio.
    e. Use linear regression to determine the relationship between unattended SBP with urinary albumin-to-creatinine ratio.
    f. Repeat the analysis for unattended DBP, awake SBP on ABPM, awake DBP on ABPM with urinary albumin-to-creatinine ratio, separately.

12. **Table 14**. Restrict the analysis to those with complete sleep BP data on ABPM and HBPM and complete data on urinary albumin-to-creatinine ratio.
    g. Use linear regression to determine the relationship between sleep SBP on ABPM with urinary albumin-to-creatinine ratio.
    h. Repeat the analysis for sleep DBP on ABPM, sleep SBP on HBPM, and sleep DBP on HBPM with urinary albumin-to-creatinine ratio, separately.

Table 1. Characteristics of Better BP participants by randomization.

	Overall N = 603	Attended then unattended, N = 301	Unattended then attended, N = 302	ABPM then HBPM, N =302	HBPM then ABPM, N = 301
Age, yrs,					
Mean (SD)	38.6 (15.1)	39.4 (16.0)	37.9 (14.1)	39.2 (15.7)	38.1 (14.5)
Median (min – max)	34.0 (18.0 - 83.0)	35.0 (19.0 - 83.0)	34.0 (18.0 - 83.0)	35.5 (18.0 - 79.0)	33.0 (19.0 - 83.0)
Women, %	382 (63.3)	190 (63.1)	192 (63.6)	191 (63.2)	191 (63.5)
Race, %					
Hispanic	39 (6.5)	24 (8.0)	15 (5.0)	22 (7.3)	17 (5.6)
Non-Hispanic, Asian	90 (14.9)	39 (13.0)	51 (16.9)	47 (15.6)	43 (14.3)
Non-Hispanic, Black	132 (21.9)	64 (21.3)	68 (22.5)	61 (20.2)	71 (23.6)
Non-Hispanic, White	291 (48.3)	150 (49.8)	141 (46.7)	148 (49.0)	143 (47.5)
Other non-Hispanic race/ethnicity	51 (8.5)	24 (8.0)	27 (8.9)	24 (7.9)	27 (9.0)
Body Mass Index					
Mean (SD)	27.2 (5.9)	26.8 (5.9)	27.5 (5.8)	27.2 (5.6)	27.2 (6.1)
Median (min – max)	25.9 (13.0 - 55.5)	25.6 (13.0 - 55.5)	26.5 (17.2 - 53.0)	26.0 (13.0 - 53.0)	25.9 (17.3 - 55.5)
Attended office blood pressure					
Systolic BP					
Mean (SD)	119.4 (12.0)	118.9 (12.1)	120.0 (12.0)	119.7 (11.9)	119.2 (12.2)
Median (min – max)	118.2 (92.2 - 179.5)	117.5 (92.2 - 179.5)	118.7 (95.2 - 170.7)	118.3 (94.2 - 161.2)	117.8 (92.2 - 179.5)
Diastolic BP					
Mean (SD)	72.7 (7.8)	72.5 (7.9)	72.9 (7.8)	72.7 (7.5)	72.7 (8.1)
Median (min – max)	71.5 (53.5 - 97.7)	71.0 (53.5 - 97.7)	71.7 (54.8 - 96.3)	71.6 (53.5 - 95.5)	71.3 (59.2 - 97.7)
Unattended office blood pressure					
Systolic BP					
Mean (SD)	118.7 (11.8)	118.2 (11.8)	119.2 (11.8)	119.0 (11.6)	118.3 (12.1)
Median (min – max)	117.3 (90.5 - 179.8)	116.8 (90.5 - 179.8)	117.8 (95.2 - 179.0)	117.7 (91.7 - 158.5)	116.8 (90.5 - 179.8)
Diastolic BP					
Mean (SD)	72.2 (7.7)	71.8 (7.8)	72.5 (7.6)	72.1 (7.5)	72.2 (7.9)
Median (min – max)	71.0 (47.2 - 98.5)	70.8 (47.2 - 98.5)	71.4 (55.7 - 96.8)	71.3 (47.2 - 94.5)	70.8 (57.8 - 98.5)

Table 1 continued.

Ambulatory blood pressure monitoring					
Awake systolic BP Mean (SD) Median (min – max)	 118.7 (10.2) 117.8 (87.6 - 172.8)	 118.4 (10.4) 117.3 (87.6 - 172.8)	 119.1 (9.9) 118.3 (97.5 - 154.5)	 119.2 (10.0) 118.3 (96.7 - 154.5)	 118.3 (10.4) 117.5 (87.6 - 172.8)
Awake diastolic BP Mean (SD) Median (min – max)	 74.2 (7.0) 73.3 (52.9 - 98.9)	 73.8 (7.0) 73.1 (52.9 - 94.0)	 74.6 (7.0) 73.7 (60.3 - 98.9)	 74.4 (6.8) 73.5 (60.3 - 91.3)	 74.0 (7.2) 73.1 (52.9 - 98.9)
Asleep systolic BP Mean (SD) Median (min – max)	 104.1 (10.5) 103.2 (72.3 - 145.0)	 104.0 (10.5) 103.0 (77.1 - 145.0)	 104.1 (10.5) 103.3 (72.3 - 139.4)	 104.7 (10.6) 103.6 (78.6 - 145.0)	 103.4 (10.3) 102.8 (72.3 - 136.1)
Asleep diastolic BP Mean (SD) Median (min – max)	 60.3 (7.5) 59.7 (42.1 - 95.4)	 60.3 (7.7) 59.6 (43.2 - 95.4)	 60.3 (7.4) 60.2 (42.1 - 89.3)	 60.4 (7.4) 59.7 (45.1 - 95.4)	 60.1 (7.6) 59.9 (42.1 - 89.3)
Home blood pressure monitoring					
Asleep systolic BP Mean (SD) Median (min – max)	 106.3 (11.6) 106.0 (74.0 - 159.0)	 106.5 (11.3) 107.0 (74.0 - 155.0)	 106.2 (12.0) 105.0 (81.0 - 159.0)	 105.7 (11.7) 106.0 (80.0 - 159.0)	 106.9 (11.6) 107.0 (74.0 - 155.0)
Asleep diastolic BP Mean (SD) Median (min – max)	 62.3 (8.3) 62.0 (38.0 - 88.0)	 62.5 (8.1) 62.0 (42.0 - 85.0)	 62.1 (8.5) 62.0 (38.0 - 88.0)	 61.8 (8.3) 61.0 (38.0 - 88.0)	 62.9 (8.3) 62.0 (44.0 - 86.0)
Hypertension, %	40 (6.6)	25 (8.3)	15 (5.0)	17 (5.6)	23 (7.6)
High cholesterol, %	56 (9.3)	28 (9.3)	28 (9.3)	29 (9.6)	27 (9.0)
Diabetes, %	10 (1.7)	2 (0.7)	8 (2.6)	5 (1.7)	5 (1.7)
Asthma or hey fever, %	68 (11.3)	32 (10.6)	36 (11.9)	32 (10.6)	36 (12.0)
Married, %	213 (35.3)	105 (34.9)	108 (35.8)	102 (33.8)	111 (36.9)
Not living alone, %	152 (25.2)	77 (25.6)	75 (24.8)	78 (25.8)	74 (24.6)
Smoking status, % Never Former Current	 509 (84.6) 79 (13.1) 14 (2.3)	 250 (83.1) 44 (14.6) 7 (2.3)	 259 (86.0) 35 (11.6) 7 (2.3)	 260 (86.1) 35 (11.6) 7 (2.3)	 249 (83.0) 44 (14.7) 7 (2.3)

Table 1 continued.

Current drinker, %	405 (67.2)	202 (67.1)	203 (67.2)	202 (66.9)	203 (67.4)
Good self-reported sleep quality, %	179 (30.1)	87 (29.4)	92 (30.8)	89 (30.0)	90 (30.2)
Self-reported physical activity per week, % Mean (SD) Median (min – max)	 2.8 (2.0) 3.0 (0.0 - 20.0)	 2.9 (2.1) 3.0 (0.0 - 20.0)	 2.8 (2.0) 3.0 (0.0 - 10.0)	 2.8 (2.1) 3.0 (0.0 - 20.0)	 2.9 (1.9) 3.0 (0.0 - 10.0)

Table 2. Mean difference in awake systolic and diastolic BP, separately, with ABPM vs. attended BP, ABPM vs. unattended BP, and Attended vs. Unattended BP, N=569

	ABPM Mean (SD) Median (min – max)	**Attended** Mean (SD) Median (min – max)	**Unattended** Mean (SD) Median (min – max)	Mean difference for ABPM vs. Attended BP (95% CI)	Mean difference for ABPM vs. Unattended BP (95% CI)	Mean difference for Attended vs. Unattended BP (95% CI)	P (difference in differences = 0)
Awake systolic BP	118.7 (10.2) 117.8 (87.6 - 172.8)	119.4 (12.1) 117.8 (92.2 - 179.5)	118.7 (11.9) 117.2 (90.5 - 179.8)	-0.69 (-1.36, -0.03)	-0.004 (-0.64, 0.64)	0.69 (0.39, 0.99)	<.0001
Awake diastolic BP	74.2 (7.0) 73.3 (52.9 - 98.9)	72.7 (7.8) 71.3 (53.5 - 97.7)	72.2 (7.7) 71.0 (47.2 - 98.5)	1.55 (1.08, 2.03)	2.03 (1.55, 2.51)	0.47 (0.25, 0.69)	<.0001

Table 3. The prevalence of hypertension by awake ABPM, attended, and unattended BP reading, N=569

Hypertension	Prevalence (95% CI)
ABPM hypertensive range	10.0 (7.7,12.8)
Attended clinic BP in hypertensive range	7.2 (5.2,9.7)
Unattended clinic BP in hypertensive range	14.1(11.3,17.2)
ABPM and attended clinic BP in hypertensive range	4.6 (3.0,6.6)
ABPM and unattended clinic BP in hypertensive range	6.9 (4.9,9.3)
White coat hypertension	
Hypertensive attended clinic BP with normal ABPM	2.6(1.5,4.3)
Hypertensive unattended clinic BP with normal ABPM	7.2 (5.2,9.7)
Masked hypertension	
Hypertensive ABPM with normal attended clinic BP	5.5 (3.7,7.6)
Hypertensive ABPM with normal unattended clinic BP	3.2 (1.9,5.0)
Hypertension will be defined as: Awake ABPM readings ≥135 or 85 mm Hg Attended: SBP/DBP readings ≥140 or 90 mm Hg Unattended: SBP/DBP readings ≥135 or 85 mm Hg	

Table 4. Agreement between hypertension on ABPM and clinic BP, N=569

		ABPM and unattended clinic BP in hypertensive range		
		Yes, %	No, %	N (%)
ABPM and attended clinic BP in hypertensive range	Yes, %	25 (4.4)	1 (0.2)	26 (4.6)
	No, %	14 (2.5)	529 (93.0)	543 (95.4)
	N (%)	39 (6.9)	530 (93.2)	569 (100)
Kappa: 0.76				

Table 5. Agreement between white coat hypertension on ABPM and clinic BP, N

		Hypertensive unattended clinic BP with normal ABPM		
		Yes, %	No, %	N (%)
Hypertensive attended clinic BP with normal ABPM	Yes, %	15 (2.6)	0 (0.0)	15 (2.6)
	No, %	26 (4.6)	528 (92.8)	554 (97.4)
	N (%)	41(7.2)	528 (92.8)	569 (100)
Kappa: 0.52				

Table 6. Agreement between masked hypertension on ABPM and clinic BP, N

		Hypertensive ABPM with normal unattended clinic BP		
		Yes, %	No, %	N (%)
Hypertensive ABPM with normal attended clinic BP	Yes, %	17 (3.0)	14 (2.5)	31 (5.5)
	No, %	1 (0.2)	537 (94.4)	538 (94.6)
	N (%)	18 (3.2)	551 (96.8)	569 (100)
Kappa: 0.68				

Table 7. The difference between sleep BP on HBPM versus sleep BP on ABPM, N = 547

	ABPM Mean (SD) Median, (min – max)	HBPM Mean (SD) Median (min – max)	Mean difference, (95% CI)	P (difference = 0)
Sleep systolic BP	104.1 (10.5) 103.3 (72.3 - 145.0)	106.4 (11.5) 106.0 (74.0 - 159.0)	-2.3 (-3.0, -1.5)	<.0001
Sleep diastolic BP	60.4 (7.5) 59.8 (42.1 - 95.4)	62.3 (8.3) 62.0 (38.0 - 88.0)	-1.9 (-2.5,-1.4)	<.0001

Table 8. Side effects and tolerability of HBPM versus ABPM, N = 603.

	Occurred with ABPM only, N (%)	Occurred with HBPM only, N (%)	Occurred with both ABPM and HBPM, N (%)	Didn't occur for ABPM or HBPM, N (%)
Side effects				
Pain while wearing the monitor	160 (26.5)	37 (6.1)	128 (21.2)	278 (46.1)
Irritation while wearing the monitor	178 (29.5)	26 (4.3)	232 (38.5)	167 (27.7)
Bruising while wearing the monitor	84 (13.9)	19 (3.2)	54 (9.0)	446 (74.0)
Tolerability				
Monitor was heavy to wear	133 (22.1)	57 (9.5)	139 (23.1)	274 (45.4)
Monitor was uncomfortable to wear	109 (18.1)	68 (11.3)	399 (66.2)	27 (4.5)
Monitor was straightforward to use	12 (2.0)	6 (1.0)	578 (95.9)	7 (1.2)
Monitor was cumbersome or awkward to wear	130 (21.6)	27 (4.5)	377 (62.5)	69 (11.4)
Noise of the monitor was disturbing to me	91 (15.1)	71 (11.8)	102 (16.9)	339 (56.2)
Noise of the monitor disturb others	67 (11.1)	24 (4.0)	43 (7.1)	469 (77.8)
Monitor was embarrassing to wear	212 (35.2)	10 (1.7)	93 (15.4)	288 (47.8)
Monitor interfered with normal sleeping pattern	124 (20.6)	56 (9.3)	219 (36.3)	204 (33.8)
Removed monitor due to disturbance while sleeping	23 (3.8)	23 (3.8)	16 (2.7)	541 (89.7)

Table 9. The relationship between attended and unattended clinic BP with left ventricular mass index (g/m^2), N=587.

Model	Unstandardized beta	Lower limit of 95% confidence intervals for beta	Upper limit of 95% confidence intervals for beta	Standard Error	t-statistic	P-value	Standardized beta
Attended clinic systolic BP	0.43	0.32	0.55	0.06	7.55	<.001	0.30
Attended clinic diastolic BP	0.42	0.24	0.60	0.09	4.66	<.001	0.19
Unattended clinic systolic BP	0.44	0.33	0.56	0.06	7.50	<.001	0.30
Unattended clinic diastolic BP	0.37	0.19	0.55	0.09	4.04	<.001	0.16
Dependent variable: left ventricular mass index (g/m^2) as continuous variable							

Table 10. The relationship between unattended clinic BP versus awake BP on ABPM with left ventricular mass index (g/m^2), N=554

Model	Unstandardized beta	Lower limit of 95% confidence intervals for beta	Upper limit of 95% confidence intervals for beta	Standard Error	t-statistic	P-value	Standardized beta
Unattended systolic BP	0.44	0.32	0.56	0.06	7.38	<0.001	0.30
Unattended diastolic BP	0.38	0.19	0.56	0.09	3.99	<0.001	0.17
Awake systolic BP on ABPM	0.61	0.47	0.74	0.07	8.69	<0.001	0.35
Awake diastolic BP on ABPM	0.45	0.25	0.66	0.10	4.36	<0.001	0.18
Dependent variable: left ventricular mass index (g/m^2) as continuous variable							

Table 11. The relationship between sleep BP on HBPM versus ABPM with left ventricular mass index (g/m^2), N=533

Model	Unstandardized beta	Lower limit of 95% confidence intervals for beta	Upper limit of 95% confidence intervals for beta	Standard Error	t-statistic	P-value	Standardized beta
Sleep systolic BP on HBPM	0.31	0.19	0.44	0.06	4.98	<0.001	0.21
Sleep diastolic BP on HBPM	0.23	0.05	0.40	0.09	2.54	0.01	0.11
Sleep systolic BP on ABPM	0.45	0.32	0.59	0.07	6.63	<0.001	0.28
Sleep diastolic BP on ABPM	0.36	0.16	0.55	0.10	3.64	<0.001	0.16
Dependent variable: left ventricular mass index (g/m^2) as continuous variable							

Table 12. The relationship between attended and unattended clinic BP with urinary albumin-to-creatinine ratio (mg/g), N=555.

Model	Unstandardized beta	Lower limit of 95% confidence intervals for beta	Upper limit of 95% confidence intervals for beta	Standard Error	t-statistic	P-value	Standardized beta
Attended clinic systolic BP	-0.2	-0.47	0.08	0.14	-1.39	0.17	-0.06
Attended clinic diastolic BP	-0.28	-0.7	0.15	0.22	-1.27	0.20	-0.05
Unattended clinic systolic BP	-0.26	-0.55	0.02	0.14	-1.84	0.07	-0.08
Unattended clinic diastolic BP	-0.37	-0.8	0.06	0.22	-1.68	0.09	-0.07
Dependent variable: : urinary albumin-to-creatinine ratio (mg/g) as continuous variable							

Table 13. The relationship between unattended clinic BP versus awake BP on ABPM with urinary albumin-to-creatinine ratio (mg/g), N=523.

Model	Unstandardized beta	Lower limit of 95% confidence intervals for beta	Upper limit of 95% confidence intervals for beta	Standard Error	t-statistic	P-value	Standardized beta
Unattended systolic BP	-0.18	-0.44	0.07	0.13	-1.39	0.16	-0.06
Unattended diastolic BP	-0.09	-0.49	0.31	0.20	-0.45	0.65	-0.02
Awake systolic BP on ABPM	0.01	-0.29	0.31	0.15	0.07	0.94	0.00
Awake diastolic BP on ABPM	0.22	-0.21	0.66	0.22	1.01	0.31	0.04
Dependent variable: urinary albumin-to-creatinine ratio (mg/g) as continuous variable							

Table 14. The relationship between sleep BP on HBPM versus ABPM with urinary albumin-to-creatinine ratio (mg/g), N=505.

Model	Unstandardized beta	Lower limit of 95% confidence intervals for beta	Upper limit of 95% confidence intervals for beta	Standard Error	t-statistic	P-value	Standardized beta
Sleep systolic BP on HBPM	-0.01	-0.28	0.26	0.14	-0.08	0.94	-0.00
Sleep diastolic BP on HBPM	-0.02	-0.40	0.36	0.20	-0.09	0.93	-0.00
Sleep systolic BP on ABPM	0.09	-0.21	0.40	0.15	0.61	0.54	0.03
Sleep diastolic BP on ABPM	0.26	-0.16	0.68	0.21	1.20	0.23	0.05
Dependent variable: urinary albumin-to-creatinine ratio (mg/g) as continuous variable							

The standard approach to measuring blood pressure (BP), in the clinic with an observer present (attended BP measurement), results in the misdiagnosis of hypertension for many adults.[1] Among adults with high BP in the clinic (systolic BP [SBP]/diastolic BP [DBP] ≥ 140/90 mm Hg), ~20% to 30% do not have high BP (SBP/DBP <135/85 mm Hg) while awake outside of the clinic, a phenotype called white coat hypertension.[2] White coat hypertension is not associated with increased cardiovascular disease (CVD) risk.[3, 4] Also, 15% to 30% of people without high BP (SBP/DBP <140/90 mm Hg) when measured by an observer in the clinic have high BP (SBP/DBP ≥135/85 mm Hg) while awake outside of the clinic.[5, 6] This phenotype, called masked hypertension, is associated with high CVD risk.[5, 7] Due to the high degree of misclassification of hypertension when using clinic BP, the US Preventive Services Task Force recommends out-of-clinic BP measurement be performed to exclude the presence of white coat hypertension before initiating antihypertensive treatment.[2]

Data from non-randomized studies from Canada suggest that using an automated oscillometric BP (AOBP) device without an observer present (unattended BP) results in lower clinic BP compared to attended measurements taken using the auscultatory method.[8, 9] *The 2017 Canadian hypertension guideline recommended measuring unattended BP in clinical practice for reducing the risk of white coat hypertension but acknowledged the low level of evidence supporting this recommendation (i.e., Grade D, "very low quality" and "expert opinion").[10] Currently, obtaining unattended BP has not been adopted in US guidelines. Few studies have compared unattended clinic BP to attended clinic BP measured with an oscilometric device, which is increasingly being used for measuring BP in the US. In an analysis of the Systolic Blood Pressure Intervention Trial (SPRINT) data, there was no difference in BP when measured unattended and attended (personal communication, S. Oparil). Thus, there is equipoise as to whether unattended BP reduces the risk of white coat hypertension. Further, the effect of unattended BP measurement on masked hypertension risk is also unclear.*

Nocturnal hypertension, typically defined by mean sleep SBP/DBP ≥ 120/70 mm Hg, affects ~1 in 3 adults and is associated with increased CVD risk, independent of clinic and awake BP.[11-13] Therefore, a comprehensive approach to diagnosing hypertension requires measuring sleep BP in addition to awake BP. Ambulatory BP monitoring (ABPM) is a procedure wherein people have their BP measured automatically every 15 to 30 minutes, typically for 24 hours, outside of the clinic setting. ABPM is widely considered to be the reference standard for diagnosing hypertension. However, ABPM is not available in most clinics in the US and is poorly tolerated by patients.[14-16] Recently, home BP monitoring (HBPM) devices have been developed that measure BP during sleep. These devices may be better tolerated than ABPM as they are only worn at night and fewer BP measurements are obtained. ***We propose to compare novel non-ABPM approaches for measuring BP and diagnosing hypertension with ABPM, the reference standard.[2]*** The study aims are:

Aim 1. Test whether measuring unattended clinic BP with an automated device will provide a more accurate estimate of awake BP on ABPM than measuring attended clinic BP with an automated device.
Hypothesis 1a: The absolute difference with awake BP will be smaller for unattended vs. attended clinic BP.
Hypothesis 1b: The agreement between hypertension status using BP measured in the clinic and on ABPM while awake will be higher when clinic BP is measured unattended versus attended. Also, the prevalence of both white coat and masked hypertension will be lower when measuring unattended versus attended clinic BP.
Aim 2. Test whether a new HBPM device provides an accurate approach for measuring sleep BP.
Hypothesis 2a: Sleep BP on HBPM will provide an accurate estimate of sleep BP on ABPM.
Hypothesis 2b: HBPM will be better tolerated (e.g., less awakening during sleep, pain, bruising) than ABPM.

Aim 3. Compare the associations of unattended versus attended clinic BP, unattended clinic BP versus awake BP on ABPM, and sleep BP on HBPM versus ABPM with two markers of end-organ damage, left ventricular mass index (LVMI) and urinary albumin-to-creatinine ratio (ACR).
Hypothesis 3a: The association with end-organ damage will be stronger for unattended vs. attended clinic BP.
Hypothesis 3b: The association with end-organ damage will be similar for unattended clinic BP and awake BP.
Hypothesis 3c: The association with end-organ damage will be similar for sleep BP by HBPM and ABPM.

We will enroll *630 adults*, not taking antihypertensive medication, with screening clinic SBP of 110 to 159 mm Hg and DBP of 70 to 99 mm Hg in New York, NY and Birmingham, AL. Participants will undergo unattended and attended clinic BP measurements, in a random order, and 24-hour ABPM and sleep HBPM, in a random order. Health behaviors, psychosocial factors, anthropometrics, LVMI, and ACR will also be assessed.

Public Health Significance: This study will help determine whether the conduct of unattended BP measurement in the clinic can reduce the need for measuring awake BP on ABPM, and also test whether a HBPM device can replace ABPM for measuring sleep BP. *These data will inform whether these novel non-ABPM approaches for measuring BP and diagnosing hypertension should be used in clinic practice.*

B. SIGNIFICANCE. *The significance of the proposed study is summarized in* ***Table 1****.*

B.1. Clinic BP as a CVD risk factor. Compared with other risk factors, elevated BP is associated with more CVD events and disability-adjusted life years lost in the US and worldwide.[17, 18] To identify patients with hypertension and monitor their BP while taking antihypertensive medication, most US guidelines and scientific statements recommend BP be measured in the clinic setting by a trained healthcare professional.[19-21] This recommendation is supported by extensive data, demonstrating that elevated BP, measured using this approach, is associated with increased risk for CVD and renal disease events.[22, 23] In clinical practice and research studies conducted in the US, BP is almost universally measured in the clinic with an observer present (attended clinic BP).

Table 1. Significance of the proposed study.

BP, measured by an observer in the clinic, does not provide an accurate estimate of a person's true BP and hypertension status.

- *Out-of-clinic BP assessment by ABPM is widely recommended to:*
  - *Identify white coat hypetension and masked hypertesion.*
  - *Identify hypertension during sleep.*
- *Many clinics in the US do not have access to ABPM.*
- *Many patients do not tolerate ABPM.*
- *It has been suggested that ABPM can be replaced by BP measured in the clinic using an automated device without an observer present.*

Prior studies of BP measurement with automated devices without an observer present have major limitations.

- *The order of BP measurement (observed or unobserved occurring first) was not randomized.*
- *Observer measured BP was most commonly performed using a mercury sphygmometer, which is no longer the recommended approach for measuring BP in clinic practice.*
- *Select patients with high BP or treated hypertension were enrolled.*

Studies of sleep BP using HBPM vs. ABPM have major limitations.

- *Sleep BP is associated with sub-clinical and clinical CVD events.*
- *The ordering of HBPM and ABPM was not randomized.*
- *Studies have focused on patients on antihypertensive medication.*
- *No data are available in the US including among African Americans, who have a high prevalence of nocturnal hypertension.*

Potential solutions to be tested in the proposed study:

- *Measuring clinic BP without an observer to assess awake BP.*
  - *Will this reduce the need to screen for white coat hypertension?*
  - *What is the effect of this approach on masked hypertension?*
- *Using a novel HBPM device to measure asleep BP.*
  - *Does this accurately assess sleep BP / nocturnal hypertension?*
  - *Is HBPM better tolerated than ABPM in assessing sleep BP?*

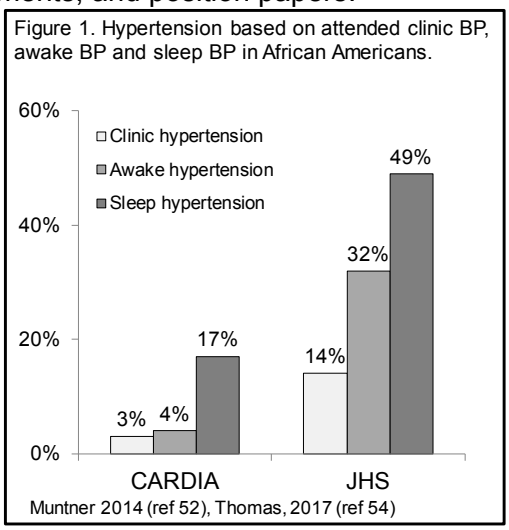
B.2. Measuring BP outside of the clinic. Several studies have found that compared with attended clinic BP, BP measured outside of the clinic is a better predictor of a person's CVD risk.[4, 24] The US Preventive Services Task Force (USPSTF) and the UK National Institute for Health and Care Excellence recommend that elevated BP measured in the clinic be confirmed by out-of-clinic BP measurements prior to diagnosing hypertension.[2, 25] *ABPM is the reference standard for out-of-clinic BP assessment and making the diagnosis of hypertension.[4, 26, 27] ABPM monitors are compact, worn on a belt or in a pouch, and connected to a BP cuff on the upper arm by a tube. The monitors are programmed to obtain readings using the oscillometric method, every 15 to 30 minutes, typically for 24 hours, throughout the day and night.*

B.3. Mismatch between clinic and out-of-clinic BP. In some people, there is a transient BP increase that occurs in the clinic setting (i.e., white coat effect).[28, 29] For others, BP is lower in the clinic when compared to measurements obtained outside of the clinic environment (i.e., masked effect).[7, 30] White coat hypertension is defined as hypertension based on clinic-measured BP (≥ 140/90 mm Hg) but not when measured outside of the clinic setting (awake BP < 135/85 mm Hg). In most ABPM studies, white coat hypertension has not been associated with increased CVD risk.[3, 31] In contrast, masked hypertension, defined as not having hypertension based on BP measured in the clinic setting (< 140/90 mm Hg) but hypertension based on out-of-clinic measurements (awake BP ≥ 135/85 mm Hg) is associated with a markedly increased CVD risk.[5, 7] Among adults with SBP/DBP ≥ 140/90 mm Hg, defined using attended BP measured in the clinic, 20% to 30% have white coat hypertension.[4, 32] Additionally, between 15% and 30% of adults with SBP/DBP < 140/90 mm Hg, defined using attended BP measured in the clinic, have masked hypertension.[6, 33]

B.4. Sleep BP. There is a diurnal pattern of BP, which normally falls to its lowest level during sleep.[34-36] Nocturnal hypertension, defined by having high mean sleep BP (SBP/DBP ≥ 120/70 mm Hg), is associated with an increased risk for CVD events, independent of BP measured in the clinic and awake BP on ABPM.[37-39] Assessing sleep BP may be particularly important for African Americans, a population with high CVD risk and approximately two times higher prevalence of nocturnal hypertension compared with whites.[40-42] In the Jackson Heart Study (JHS), a cohort comprised exclusively of African Americans, 60% of participants had nocturnal hypertension and the multivariable-adjusted hazard ratio for CVD events was 1.84 (95% CI: 1.00, 3.38) comparing participants with and without nocturnal hypertension. Also, a high percentage of African Americans with nocturnal hypertension do not have hypertension based on clinic BP or awake BP on ABPM (**Figure 1**).[41,

[43] **Until recently, ABPM has been the only method that could assess sleep BP (Section B.6.2.1.).**

B.5. Challenges with ABPM. The misdiagnosis of hypertension when BP is measured by an observer in the clinic versus by ABPM is well recognized by guidelines, scientific statements, and position papers.[1, 24] However, there are several challenges that have prevented the wide-spread use of ABPM in clinical practice.



B.5.1. Health care provider perspective. Recently, we conducted a nominal groups study, a qualitative research approach, with 40 physicians in Alabama and New York to identify barriers to performing ABPM.[44] Reported barriers included need for staff training, time constraints in patient preparation, and lack of infrastructure and inaccessibility of equipment and specialists to whom providers could refer their patients for the ABPM procedure.[15] Also, ABPM devices cost over $2,000 each, insurance companies do not commonly reimburse for indications other than white coat hypertension, and when reimbursed, the compensation is low.[14, 45]

B.5.2. Patient perspective. Low patient tolerability for ABPM has been reported in previous studies.[16, 46, 47] For example, in one study, side effects associated with ABPM ranged from 7% for bruising to 70% for the device awakening the participant during sleep.[16]

B.6. New approaches for diagnosing hypertension. Given the real world limitations of ABPM, novel approaches are needed for measuring awake and sleep BP.

B.6.1. New approach for assessing awake BP. An emerging method that has been proposed for estimating awake BP is to measure BP in the clinic using a fully automated oscillometric device (AOBP) without an observer being present (unattended clinic BP measurement).

B.6.1.1. AOBP. There are currently two validated oscillometric devices available in the US (Omron HEM-907XL and Microlife's Watch BP office) that can be programmed to measure BP automatically without an observer being present.[48-50] Using these devices, the technician or healthcare provider leaves the room after a person has a BP cuff placed on their arm and they are positioned for measurements. After a minute rest, the device inflates the cuff and BP is measured. AOBP devices can obtain several BP measurements at preset (e.g., one minute) intervals. The maker of BPTru, a third device, went out of business in 2017.

B.6.1.2. Can unattended clinic BP measurements replace the need for assessing awake BP on ABPM? *Canadian studies suggest that patients with hypertension have lower unattended BP compared with attended BP.[8, 9, 51-53] Therefore, the use of unattended clinic BP may result in a lower prevalence of white coat hypertension. In a pooled analysis of 8558 adults, the mean clinic BP was 10/7 mm Hg lower with unattended AOBP versus BP recorded by a provider in clinical practice by auscultation and a mercury sphygmometer.[54] In the only randomized study of AOBP published to date, the difference between BP when measured observed and unobserved was small (< 5 mm Hg).[8] In 2017, the Hypertension Canada guideline recommended unattended BP (i.e., AOBP) as the preferred method of clinic BP measurement.[10] However, this recommendation was based on a Grade D level of evidence (i.e. quality of evidence is very low, based on expert opinion, no direct research evidence, and studies had very severe limitations). US guidelines do not currently recommend AOBP for use in clinic practice. Recently, in a post-hoc analysis of SPRINT data, there was no difference in clinic BP between sites that measured it unattended versus attended (manuscript under review at Hypertension, personal communication, S. Oparil). At each visit, SPRINT participants did not have both unattended and attended BP measurements; there was no randomization; information about the conduct of unattended or attended BP measurements was obtained retrospectively after study end; and no comparison to ABPM was made.* ***Table 2*** *summarizes the major limitations of published studies on AOBP. There is currently equipoise as to whether unattended clinic BP provides an accurate estimate of awake BP on ABPM.*

B.6.1.3. Can unattended BP be successfully implemented in clinical practice? *Two issues have been raised as barriers to implementing AOBP in clinical practice: the time it takes to perform this procedure and the need for dedicated space. Although AOBP takes longer than <u>unstandardized</u> clinic BP measurement (clinic BP taken without following guideline-recommended approaches), AOBP takes a shorter amount of time than clinic BP measurements taken following American Heart Association (AHA) recommendations.[52] Further, unstandardized clinic BP measurements are very common in clinical practice, generate poor estimates of BP, and interventions targeted at observers to obtain standardized clinic BP have been largely unsuccessful.[55] Having a dedicated room to perform unattended BP has been reported as a barrier to AOBP. However, if clinic space is not available, unattended AOBP can be successfully performed while a patient is in a waiting room.[56]*

Table 2. Limitations of published studies comparing attended and unattended BP versus awake BP on ABPM
1. ***The order of clinic BP measurement (attended and unattended clinic BP) was not randomized.*** *In prior studies, unattended clinic BP was performed after attended clinic BP. Thus, order effects cannot be excluded.*
2. ***Attended clinic BP was not measured in a standardized way (guideline recommendations)****. The difference in unattended and attended BP could be explained by poor measurement techniques when obtaining attended BP.*
3. ***Attended clinic BP was measured by auscultation using a mercury sphygmometer****. In the US, this method is no longer performed, and oscillometric devices have become a common method for BP measurement in practice.*
4. ***Enrollment was restricted to patients with high clinic BP.*** *Enrollment of patients with only high clinic BP makes it impossible to separate the effect of unattended clinic BP measurements from regression to the mean. Few data are available comparing unattended and attended clinic BP among adults with normal clinic BP or prehypertension.*
5. ***Patients often were taking antihypertensive medication****. The role of unattended clinic BP measurement for the initial diagnosis of hypertension (which is the focus on the proposed study) remains unclear.*
6. ***Studies have focused on the diagnosis of white coat hypertension.*** *Scarce data are available from studies evaluating the effect of measuring unattended BP on masked hypertension. An unintended consequence of unattended BP is that it may increase the prevalence of masked hypertension as individuals who would have previously been identified as having sustained hypertension (elevated clinic BP and awake BP on ABPM) will now have masked hypertension because clinic BP is no longer elevated.[57] However, if unattended clinic BP measurement provides an accurate estimate of awake BP on ABPM, then the prevalence of masked hypertension should decrease.*

B.6.2. New approach for assessing sleep BP. Recently, home BP monitors (HBPM) have been adapted to measure asleep BP. As described below, there are compelling preliminary data supporting this approach.

B.6.2.1. A novel HBPM device for measuring sleep BP. Until recently, sleep BP could only be assessed by ABPM. HBPM devices have been developed that measure BP automatically during sleep. These devices have been previously validated for accuracy.[49, 58] Before going to sleep, a person attaches a BP cuff to their arm and turns on the HBPM device, which is programmed to take BP measurements while the person is asleep. In a prior study conducted in Japan, an HBPM device (Omron HEM-5001) was programmed to obtain BP measurements at 2am, 3am and 4am.[59] Given that only three readings are obtained during the sleep period and that a prior study demonstrated the feasibility for measuring sleep BP, there is great potential for using these HBPM devices for accurately measuring sleep BP with less burden than ABPM. ***Table 3*** *shows the major limitations of published studies using HBPM to assess sleep BP.* In the current study, we will test whether HBPM is an accurate and better tolerated approach for measuring sleep BP than ABPM.[59]

Table 3. Limitations of prior studies comparing sleep BP on HBPM versus ABPM
1. ***The order of home monitoring and ABPM to assess sleep BP was not randomized.*** *In prior studies, patients chose the order in which they completed home monitoring and ABPM to assess sleep BP.*
2. ***Studies did not include US populations****. Sleep BP and nocturnal hypertension have not been compared between HBPM and ABPM in African Americans, a population with a high prevalence of nocturnal hypertension.*
3. ***Over 80% of patients were taking antihypertensive medication****. Prior studies have primarily included people taking antihypertensive medication, with some people taking medication before bedtime. The role of home monitoring to assess sleep BP has not been evaluated among people not taking antihypertensive medication.*
4. ***The agreement of nocturnal hypertension defined using HBPM versus ABPM was not reported.*** *Prior studies have only reported the correlation and mean difference in sleep BP levels on HBPM and ABPM.*
5. ***The tolerability of assessing sleep BP on HBPM was not assessed.*** *Sleep HBPM may be better tolerated than ABPM.*

C. INNOVATION. The proposed study has several innovative features:

- We will enroll patients with a wide range of clinic BP and who are not taking antihypertensive medication. The study examines unattended clinic BP measurement for the diagnosis of hypertension.
- The study will use a within-subjects randomized design which will control for order effects and regression to the mean. Participants will be randomized to have their BP measured in the clinic attended or unattended in counterbalanced order (i.e. attended followed by unattended or vice versa). Additionally, participants will be randomized to have their sleep BP measured first by ABPM then by HBPM or vice-versa. *The lack of randomized controlled data on BP measured unattended versus attended has resulted in a low grade of evidence (Grade D) in the Canadian hypertension guideline.*
- *The study will compare unattended clinic BP versus attended clinic BP using the same oscillometric device. In prior studies, attended clinic BP was measured by auscultation. The use of oscillometric BP devices is becoming more widespread in clinical practice as mercury sphygmomanometers have environmental concerns and the need for frequent calibration of aneroid devices is recognized as a major problem.*
- We will test whether BP during sleep can be accurately measured using an HBPM device and whether this device is better tolerated than ABPM. To our knowledge this HPBM device has not been tested in the US and there are no data on sleep BP from HBPM for race/ethnicity groups (i.e. African Americans or Hispanics). The study will enroll a multi-ethnic sample of white, African American and Hispanic participants in the Northeast and Southeast US, which will increase the generalizability of the results.
- *We will determine the prevalence of both white coat hypertension and masked hypertension using*

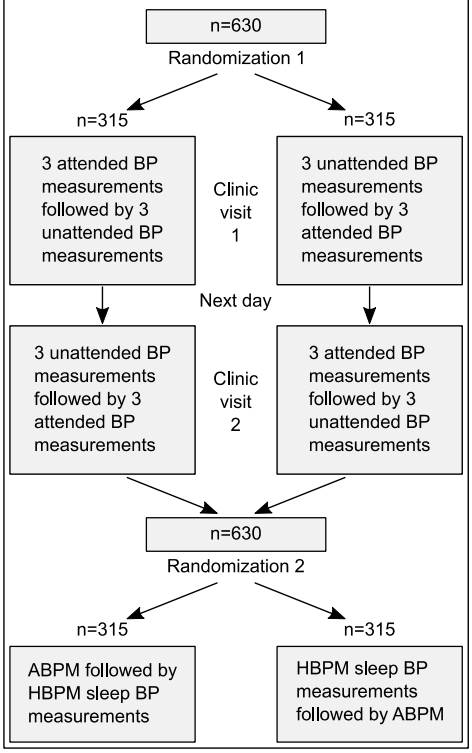
unattended clinic BP versus attended clinic BP measurements.

- We will determine the predictive value of unattended clinic BP by comparing its association with LVMI *and ACR*, two validated measures of hypertension-related end-organ damage, versus the associations of attended clinic BP and awake BP on ABPM with these end-organ damage measures.
- We will also determine the prognostic value of sleep BP assessed on HBPM by comparing its association with LVMI *and ACR*, with sleep BP assessed by ABPM.

D. APPROACH.

D.1. Overall strategy of proposed study. This study consists of two parallel cross-over randomized controlled trials conducted in the same participants. A schematic showing the study design is provided in **Figure 2**. We will recruit *630* community-dwelling participants from centers in Birmingham, AL and New York, NY (n=315 at each site). We will enroll a population with a sufficient number of whites, African Americans, and Hispanics to investigate differences in BP measurement techniques by race/ethnicity. Also, information on tolerability of the ABPM and HBPM devices will be collected, and a brief examination and an echocardiogram, will be conducted. A random spot urine sample will be collected to measure the ACR.

Figure 2. Study diagram.



D.2. Proposed Timeline. Funding for the study is being requested for four years (July 1, 2018 to June 30, 2022). During the first six months, we will finalize the study protocol, develop the randomization assignment and study databases, and conduct staff training. From January 2019 through December 2021, we will enroll *630* participants (*n=105* participants per site annually) and conduct study visits. The preparation of data for analysis, including clinic BP, ABPM and sleep BP on HBPM, will be conducted throughout the study, and the final six months (January through June 2022) will be dedicated to analyses and preparation of manuscripts and presentations.

D.3. Feasibility of conducting the proposed study at two sites. Drs. Muntner and Shimbo (co-PIs) have collaborated for 10 years. Their strong collaboration is demonstrated by co-funded grants and over 80 published papers including many related to BP measurement. Studies with primary data collection have included 888 participants enrolled in the Masked Hypertension (MHT) Study and 408 participants enrolled in the Improving the Detection of Hypertension (IDH) Study, which are both part of a NIH/NHLBI Program Project. Dr. Shimbo was responsible for successfully leading the echocardiography core laboratory for the assessment of LVMI in the MHT Study and IDH Study. In the AHA Strategically Focused Research Network (AHA-SFRN) center on hypertension, they conducted clinic BP measurements and ABPM in 835 participants over a 12-month period. Additional details of the investigators' experience is provided in their biosketches. Overall, the proposed study is highly feasible.

D.4. Recruitment. We will enroll a racially/ethnically diverse sample of *630* adults (50% men; 50% women) who are ≥ 19 years of age. We will identify participants from patients visiting their physician for outpatient care at UAB or Columbia University. BP is measured at all outpatient visits at both institutions. We will query the I2B2 data warehouse at UAB and the CUMC data warehouse at Columbia University on a weekly basis and extract BP, medical history regarding the exclusion criteria, and pharmacy/medication data from electronic clinic health records. We will obtain Institutional Review Board (IRB) and HIPAA waiver approvals for the search. With the permission of the physician who conducted the clinic visit, we will be able to contact individual patients directly, briefly describe the study, and determine their interest in participating. People who are interested will be administered a brief telephone questionnaire to confirm their eligibility. Those who continue to be eligible will be invited to attend a screening visit and, if eligible, they will initiate the study.

D.4.1. Eligibility criteria. To increase the generalizability of the study, a limited number of exclusion criteria are being applied. Inclusion criteria are:

- Age ≥ 19 years and ability to speak English or Spanish.
- Mean screening SBP of 110 to < 160 mm Hg and mean screening DBP of 70 to <100 mm Hg based on the two most recent outpatient clinic visits, extracted from clinical records. As people with clinic SBP < 110 mm Hg and DBP < 70 mm Hg are very unlikely to have masked hypertension, we will not include these participants in our study.[60, 61] Also, people with clinic SBP ≥ 160 mm Hg or DBP ≥ 100 mm Hg are typically referred for additional BP management with a high percentage initiated on antihypertensive medication.

Exclusion criteria are:

- Lack of willingness to provide written informed consent.
- Use of antihypertensive or other medications that substantially affect BP (e.g., NSAIDS, steroids).
- History of CVD or major arrhythmias (e.g. atrial fibrillation, ventricular tachycardia).
- *Individuals who work second shift or overnight, as diurnal BP patterns may be different for this group, or with jobs that will not allow the ABPM device to measure BP every 30 minutes (e.g., truck drivers).*
- *History of sleep apnea by self-report, identified in their clinic records, and/or a score ≥ 3 on the STOP-BANG questionnaire. The sensitivity of a STOP-BANG score ≥ 3 for identifying sleep apnea is 90%.*
- *Orthostatic hypotension assessed during the screening visit (**Section D.5**). Mean awake BP on ABPM may be affected by hypotensive episodes during standing or walking.*
- Pregnancy (as no ABPM devices have been validated in pregnant women).

Although there is no estimated glomerular filtration rate (eGFR) exclusion criteria, we anticipate the prevalence of an eGFR < 60 ml/min/1.73 m^2 will be low. Only 3% of US adults not taking antihypertensive medication in NHANES 2011-2014 had an eGFR < 60 ml/min/1.73 m^2. We will adjust for eGFR in multivariable analyses.

D.4.2. Recruitment by race-ethnicity. Nighttime BP differs substantially by race/ethnicity.[41, 42] We will not exclude people on the basis of race/ethnicity. To provide statistical power to detect differences in the validity of study results by race-ethnicity, we will recruit at least *160 white, 160 African American and 160 Hispanic participants*. In a preliminary query of the I2B2 database, there were over 50,000 whites, 40,000 African Americans and 3,000 Hispanics who met the eligibility criteria at UAB in 2016. At Columbia, over 550 African Americans and 900 Hispanics have been enrolled in our recent studies of ABPM and HBPM.

D.4.3. Recruitment by BP levels. To ensure a broad range of clinic BP values for the current study, we will recruit 50% of our sample to have SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg based on the average of the most recent two clinic visits in their medical record.

Table 4. Domains of data collection
1. Unattended clinic BP
2. Attended clinic BP
3. 24-hour ABPM with actigraphy
4. One night of HBPM with actigraphy
5. Questionnaires including HBPM and ABPM tolerability
6. A brief physical examination
7. *Spot urine to assess albuminuria*
8. Transthoracic echocardiogram

D.5. Screening visit. *Participants will have BP measured three times in each arm (as recommended by AHA guidelines) to determine which arm (one with higher mean BP) to use for assessing clinic BP and to confirm participants do not have orthostatic hypotension. The arm with the higher BP will be used for all BP measurements obtained during the study. For assessment of orthostatic hypotension, additional readings will be obtained after the participant has been supine for at least 5 minutes and after both 1 and 3 minutes of standing.[62] Orthostatic hypotension will be defined as a maximum decline in SBP from supine to standing ≥ 20 mmHg. We will use the STOP-BANG Questionnaire to assess the probability of having sleep apnea.[63] Those with a STOP-BANG score ≥ 3 will be considered to have a high probability of sleep apnea and excluded from enrollment.*

D.6. Study visits. After obtaining consent, the protocol involves eight domains of data collection (**Table 4**). Data will be collected over one to two weeks during four study visits (**Figure 3**). The protocol is similar in complexity to ones we have implemented in the IDH and MHT studies and the AHA-SFRN.[64-66]

D.6.1. Study Visit 1. Study staff will log onto the secure HIPAA-compliant study website to enter the participant's eligibility information and receive their randomization assignment for ordering of clinic BP measurement (i.e., randomization 1 in **Figure 2**). **Section D.10.1** has descriptions of the study database and website. Clinic BP will be measured unattended and then attended or attended then unattended with the order determined by the randomization assignment (see **Section D.7**). Next, participants will complete a brief physical examination and questionnaires on health behaviors, psychosocial factors, and sleep. This examination will include anthropometrics and fasting blood and urine specimen collection.

D.6.2. Study Visit 2. The second study visit will occur the day after the first visit. During the second study visit, participants will have their clinic BP measured three times attended then three times unattended or vice-versa depending on their randomization assignment. After completion of the clinic BP measurements, staff will obtain the participant's randomization assignment for measurement of ABPM or HBPM (i.e., ABPM followed by HBPM or HBPM followed by ABPM; randomization 2 in **Figure 2**) from the study website. Depending on their randomization assignment, participants will be fitted with the ABPM device and given instructions on the procedure (**Section D.8.4.2.**) or given the HBPM device and instructed in its use (**Section D.8.4.3.**). All participants will be fitted with an Actiwatch (wrist actigraph) and given an ABPM or HBPM Device Log.

D.6.3. Study Visit 3. Study Visit 3 will occur the day after Study Visit 2 and will follow one of two protocols contingent on whether participants were randomized to have ABPM then HBPM or HBPM then ABPM.

D.6.3.1. Participants randomized to undergo ABPM then HBPM. At Study Visit 3, participants will have the

ABPM monitor and actigraph removed. Data will be downloaded onto computers dedicated to the current study. The ABPM recording will be checked for completeness. If a complete recording is not obtained, participants will be asked to repeat the ABPM procedure. Once a complete ABPM is confirmed, participants will fill out the ABPM tolerability questionnaire (**Section D.8.5**). This questionnaire will be self-administered unless participants are unable to read, in which case, it will be interviewer administered. Participants will be given an HBPM device and instructed in its use as described in **Section D.8.4.3**.

D.6.3.2. Participants randomized to undergo HBPM then ABPM. At Study Visit 3, participants will return the HBPM device and have the actigraph removed. Data will be downloaded onto computers dedicated to the current study and the recording will be checked for completeness. Next, participants will be asked to fill out a questionnaire on the tolerability of HBPM (**Section D.8.5**). This questionnaire will be self-administered unless participants are unable to read, in which case, it will be interviewer administered. Participants will be fitted with an ABPM device and instructed in its use as described in **Section D.8.4.2.**

D.6.4. Study Visit 4. Identical activities will occur at Study Visits 3 and 4 (i.e., the ABPM or HBPM devices will be returned, checked for a complete recording, and a tolerability questionnaire will be filled out). At the conclusion of Study Visit 4, participants will be escorted by study staff to the laboratory for an echocardiogram. Upon completion of the echocardiogram, participants will have successfully completed the study.

Figure 3. Activities conducted at a screening visit and the four study visits.

Screening visit	Visit 1	Visit 2	Visit 3	Visit 4
• Informed consent • BP measurement in both arms • Sleep apnea screener • Orthostatic hypotension assessment • Questionnaires	• Informed consent • Randomization 1 • Clinic BP measurements (attended then unattended or unattended then attended) • Brief physical exam • Questionnaires	• Clinic BP measurements (attended then unattended or unattended then attended)† • Randomization 2 • Initiate ABPM or provide instructions for HBPM sleep assessment † Order will be opposite of Visit 1	• Return equipment for ABPM or HBPM • Check completeness of readings • Tolerability questionnaire • Initiate alternate procedure (ABPM or HBPM)	• Return equipment • Check completeness of readings • Tolerability questionnaire • Echocardiogram

D.7. Randomization. Each participant will be randomized two times in the current study. At Study Visit 1, we will randomize participants to have their clinic BP measured either unattended and then attended or attended and then unattended. After the assessment of clinic BP at Study Visit 2, participants will be randomized to complete ABPM then HBPM or HBPM then ABPM. Each randomization will be separate and independent. Randomization will be performed by site (i.e., UAB and Columbia University) and we will use block sizes of 2, 4, or 8. Randomization assignments will be generated by a statistician at UAB using SAS Version 9.4 and stored in a RedCap database created and maintained by a programmer at UAB (**Section D.10.1**).

D.8. Measures. A brief examination will occur at the end of Study Visit 1. This exam will include anthropometrics, fasting blood and urine collection, and completion of questionnaires.

D.8.1. Anthropometric measures. With participants wearing a gown provided by the study, a calibrated scale will be used to measure weight. Height will be measured with the participants' shoes off using a metal centimeter tape-measure. A flexible tape measure will be used to measure waist circumference midway between the lowest ribs and the iliac crest and neck circumference at the level of the cricothyroid membrane.

D.8.2. Blood and urine measurements. A fasting blood draw will be performed by a research coordinator with phlebotomist training, and participants will also be asked to provide an untimed (spot) urine sample. Total and HDL cholesterol, triglycerides, serum creatinine, hemoglobin A1c, and glucose will be assayed. Serum creatinine will be measured using an IDMS-traceable approach. eGFR will be estimated using the CKD-EPI equation.[67] *Urinary albumin and creatinine will be measured using nephelometry.*

D.8.3. Questionnaires. Questionnaires will be self-administered. English and Spanish versions of the questionnaires will be used. For participants who cannot read, questionnaires will be interview administered.

D.8.3.1. Sociodemographic factors and medical history. Age, race/ethnicity, sex, household income, education, medical history (e.g., history of diabetes) and medication use will be determined by questionnaires. We will adapt questionnaires from our prior NIH- and AHA-SFRN funded studies for administration.

D.8.3.2. Psychosocial factors. Depressive symptoms will be assessed using the 20-item Centers for Epidemiologic Studies of Depression (CES-D)[68]; discrimination by a questionnaire used in the Coronary Artery Risk Development in Young Adults (CARDIA) study[69, 70]; perceived stress by the Perceived Stress Scale[71]; and trait anxiety by the State-Trait Anxiety Inventory –Trait Scale (TAI).[72] These scales are written at less than the 8th grade level, should take 20 minutes to complete and have been validated in multi-ethnic populations.[73]

D.8.3.3. Sleep duration and quality. Sleep duration and quality will be assessed using the Pittsburgh Sleep Quality Index (PSQI), a validated instrument that provides a measure of global sleep quality and sleep duration over the previous month.[74]

D.8.3.4. Seasonal temperature. *High and low outdoor temperatures will be recorded using National Oceanic*

and Atmospheric Administration data for the ABPM and home sleep BP monitoring periods. We will use these data to investigate whether temperature affects the association of unattended versus attended clinic BP with ABPM and the correlation of sleep BP on ABPM compared with HBPM. The temperature of the room where clinic BP is measured will be kept at 72 degrees and checked prior to each participant's clinic visits.

D.8.4. Blood pressure.

D.8.4.1. Clinic BP. We will assess clinic BP on two separate occasions, on consecutive days. Every effort will be made to conduct clinic BP measurements at the same time of day with the morning preferred for all participants. At each visit, BP will be measured three times attended and three times unattended using the arm with higher BP during the screening visit. The ordering of approaches will be randomized so that 50% of participants have attended BP measured first and unattended BP measured second at Study Visit 1 and the remaining 50% of participants will have unattended BP measured first followed by attended BP measurements at Study Visit 1. We selected to use the Omron HEM-907XL, rather than the Watch BP Office automated device as it has been used in US studies including a sub-study of NHANES participants and SPRINT.[75-77] We are not using the BPTru automated BP device as its manufacturer went out of business in September 2017.

D.8.4.1.1 Attended clinic BP. For assessment of attended clinic BP, three readings will be obtained from the arm with higher BP during the screening visit, using an appropriate-sized cuff and the Omron HEM-907XL (Omron, Bannockburn, IL, USA), an oscillometric device, by a trained BP technician. The Omron HEM-907XL device has been previously validated against a mercury sphygmomanometer.[49, 50] This device comes with small, regular, large and extra-large cuff sizes and the proper BP cuff size will be determined by measuring the participant's arm circumferences at the mid-point between the acromion and olecranon. Participants will be asked to sit quietly for at least 5 minutes, in a comfortable posture, with feet flat on the floor prior to their BP measurement with the technician in the room. Three BP readings separated by one minute will be obtained with the participant seated with their back supported and their arm positioned at heart level. The BP technician will initiate each reading by pushing the "Start" button on the device. The three BP readings will not be visible to the technician or participant until after the procedure is complete.

D.8.4.1.2. Unattended clinic BP. We will obtain unattended clinic BP measurements using the same Omron device used for attended clinic BP measurements (Omron HEM-907XL). It has a memory chip that stores the individual BP readings. The device will be programmed to take three BP readings automatically, spaced one minute apart from the same arm as the attended readings. After positioning the participant, the technician will program the BP device to wait one minute prior to initiating the three readings. The BP technician will then leave the room (i.e., at the start of the one minute resting period). The BP technician will stay outside of the room for 5 minutes to ensure that all three unattended BP measurements are obtained without interruption. To avoid possible reactive effects in the participant, the three BP readings will not be visible to participants.

D.8.4.2. ABPM and Actigraphy. ABPM will be performed in the same arm used to measure clinic BP. An appropriate BP cuff size will be selected based on the measurement of each participant's arm circumference. The monitor (SpaceLabs 90227) will be initialized, and the participant fitted with it. The SpaceLabs 90227 monitor has been previously validated and we have used this device in a prior project.[78] The ABPM device will be programmed to take readings every 30 minutes over the 24-hour monitoring period. BP readings on the ABPM will not be visible to participants. Each participant will be instructed to keep his/her arm still and in the neutral position from the time that s/he feels the arm cuff begin to inflate until it is fully deflated. Participants will also be fitted with an Actiwatch activity monitor (Philips Respironics, Bend, OR) on their wrist to wear during the 24-hour ABPM period. Actigraphy will provide estimates of sleep and awake times. The actigraphy data will be merged with the corresponding BP measurements, based on the synchronized time stamps recorded by both devices. Participants will be given a phone number to speak with a staff member if a problem with the monitor occurs. Participants will fill out the ABPM Device Log, which will confirm sleep and awake times.

D.8.4.3. Sleep HBPM and Actigraphy. The participant will be given a sleep HBPM device (HEM-7080IC, Omron, Bannockburn, IL, USA) with appropriate-sized cuff and instructed in how to put on the cuff and use the monitor properly. Participants will be instructed to put the HBPM device on the same arm used for all other study procedures, the evening they leave the clinic visit. They will also be fitted with an Actiwatch activity monitor on their wrist to wear during the HBPM period. Participants will be instructed to put on the HBPM device before going to bed and to keep it on until they wake up in the morning (i.e., after 5am). The device will be programmed to take 3 readings, at 2am, 3am, and 4am. Participants will be trained to fill out the HBPM Device Log, which documents sleep and awake times. BP readings on the HBPM will not be visible to participants. One night of sleep HBPM will be conducted.

D.8.5. Tolerability of ABPM and HBPM. Tolerability for undergoing ABPM and HBPM will be assessed using a 15-item questionnaire.[16] This questionnaire has items assessing the comfort with wearing the devices and

disturbances resulting from completing ABPM and HBPM. Additionally, there are questions on pain, skin irritation and bruising resulting from wearing the devices. Eight of the questions are answered with a Likert-type scale (e.g., Did you find the monitor interfered with your normal sleeping pattern? With response options of 0 "Not at all", 5 "Somewhat", 10 "Extremely"). The remaining 7 questions have response options of "yes" or "no" (e.g., "Did you experience pain from wearing the monitor?").

D.8.6. Echocardiogram. Standard high-quality echocardiograms (M-mode, 2D, and Doppler) will be performed by certified research sonographers at UAB and Columbia University using a Phillips iE33 ultrasound machine. All images will be recorded and stored digitally for offline analysis at the Cardiovascular Physiology Research Laboratory at Columbia (Director, Dr. Shimbo). Cardiac measurements will be obtained according to the 2015 recommendations of the American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging (EACVI).[79] Left ventricular (LV) measurements for LV end-diastolic dimension (LVEDd), septal wall thickness (SWTd), and posterior wall thickness (PWTd) will be obtained. LVM (grams) will be determined using the ASE formula. LVMI will be calculated as LVM divided by body surface area (g/m^2) and secondarily by dividing by $height^{2.7}$ ($g/m^{2.7}$). Left ventricular hypertrophy (LVH) will be examined as an outcome in exploratory analyses, defined as LVMI ≥ 96 g/m^2 in females and ≥ 116 g/m^2 in males (or LVMI ≥ 45 $g/m^{2.7}$ in females and ≥ 49 $g/m^{2.7}$ in males, when LVM is indexed to $height^{2.7}$). Per ASE/EACVI guidelines, the method for LV mass estimation and the definition of LVH does not differ by race. **Table 5** shows additional measures.

Table 5. Additional echocardiographic measures.
LV diastolic function: E/A ratio, E' (m/s), A' (m/s), E/E' ratio, isovolumetric relaxation time (ms), deceleration time, ms
LV systolic function defined by LV ejection fraction (LVEF, %) = 100 x (LVEDV-LVESV) / LVEDV.
Other parameters: Shortening (FS, %); left atrial dimension (cm) and volume (cm^2).
Hemodynamics: stroke volume (SV, mL) = VTI x cross-sectional $area_{LVOT}$; heart rate (HR); cardiac output (L/min) = SV x HR.

D.8.7. Albuminuria. *The urine sample collected during the first visit will be used for the measurement of creatinine and albumin. Consistent with prior research, urinary albumin excretion rate will be calculated using the formula: urinary albumin in milligrams per liter / (k * urinary creatinine in grams per liter) (denoted A/kC), where k adjusts for race and sex differences in typical daily creatinine excretion. Urinary creatinine concentration in men will be multiplied by 0.68 and by 0.88 for African Americans.[80] This approach will allow the use of 25 mg/g as the A/kC cut-point for microalbuminuria regardless of a participant's race and sex.*

D.9. Staff training. Prior to initiation of recruitment, Drs. Shimbo, Schwartz, Muntner, and Oparil will conduct centralized training of study staff from each site in the conduct of all study measures including clinic-measured BP, ABPM, HBPM, and echocardiography. Once data collection begins, they will monitor data collection and confirm that the study protocol is being followed. Annual centralized re-training will be conducted.

D.10. Data management. The Pharmacoepidemiology and Economics Research (PEER) Unit (Dr. Muntner – co-director) at UAB will provide coordination and logistical support for all aspects of the proposed study. The PEER Unit has 3 program coordinators, 2 systems analysts/programmers, 15 PhD and Master's level statisticians and 4 research associates with experience designing data collection systems and analyzing data, including ABPM, from epidemiology studies.

D.10.1. Study database. *Data collection for this study will occur electronically through a system and website developed in RedCap by Lei Huang MS, a programmer in the UAB PEER Unit. RedCap provides a secure, password protected, web application that will be accessible to staff at UAB and Columbia University. For the current study, our programmer will develop an online database for randomizing participants and electronic web-based forms for conducting data collection. The RedCap platform is HIPAA compliant and we have used RedCap in prior studies of ABPM.[81] Data collection through RedCap will be converted to SAS Version 9.4.*

D.10.2. Data transfer.

D.10.2.1. ABPM, sleep HBPM, actigraphy, and Device Logs. Upon return of the ABPM, HBPM, actigraph, and Device Logs, data will be downloaded to a computer and then backed up to a secure network server. Data will be transferred daily to the PEER Unit at UAB using DatAnywhere, a HIPAA compliant file transfer protocol that we used in our AHA-SFRN study. Monthly reports that track data quality will be generated. If data issues are identified (e.g., frequent ABPM or HBPM reading errors), staff will be re-trained.

D.10.2.2. Echocardiographic measures. The echocardiographic studies (with unique study identifiers; i.e. de-identified) will be saved to DVD/CD, and backed up to secure research servers at each site. The studies at UAB will be sent to the Cardiovascular Physiology Research Laboratory at Columbia for analysis.

D.10.3. Data management and cleaning. All data cleaning will be managed by a statistician at the UAB PEER Unit supervised by Dr. Muntner. A uniform data editing algorithm, established by Drs. Shimbo and Schwartz and used in prior studies, will be implemented to confirm acceptability of the ABPM data and exclude extreme outliers. Minimal editing is the general rule; less than 0.1% of readings are typically excluded. The awake and sleep periods on ABPM will be defined by the actigraphy recording, complimented by self-report

awake and sleep periods from the Device Log.[64, 82] For sleep BP on HBPM, we will confirm that participants were asleep when the the BP readings were obtained using actigraphy data and the HBPM Device Log.

D.10.4. Minimum number of BP readings required on ABPM and HBPM. No consensus exists on the number of readings required to consider an ABPM recording complete.[36] Consistent with our prior studies, we will require 14+ awake BP readings, and 5+ sleep BP eadings, and ≥ 80% of the planned 48 readings (39+ total valid readings). We will require three SBP and DBP readings for a sleep HBPM recording to be complete. We will continue recruitment until 600 participants have complete ABPM and sleep HBPM readings.

D.10.5. Phenotypic measures on ABPM and HBPM. *Awake and sleep BP values will be computed using the average of all BP readings from the awake and sleep periods, respectively. In addition to studying mean BP levels, we will calculate three BP phenotypes: white coat hypertension, masked hypertension, and nocturnal hypertension (**Table 6**). Unattended clinic BP thresholds are based on the Canadian guidelines.[83]*

Table 6. Phenotypes to be evaluated in the proposed study.

Phenotype	Attended clinic SBP/DBP	Unattended clinic SBP/DBP	Out-of-clinic SBP/DBP
White coat Hypertension	*≥140/90 mm Hg*	*≥135/85 mm Hg*	*Awake <135/85 mm Hg*
Masked Hypertension	*<140/90 mm Hg*	*<135/85 mm Hg*	*Awake ≥135/85 mm Hg*
Nocturnal Hypertension	*Not applicable*	*Not applicable*	*Sleep ≥ 120/70 mm Hg*

D.11. Statistical analysis. All data will be analyzed by a statistician blinded to participants' randomization assignments and a code (e.g., 0 or 1) will be used to represent different randomization assignments. Assignments will be unmasked after completion of the statistical analyses. The distribution of each BP measure, covariate, and echocardiographic measure will be calculated. Variables will be explored for outliers and when identified the staff in the field sites will be asked to investigate them further.

D.11.1 Missing data. Missingness in our prior studies has been uncommon. Our primary approach to missing data is to collect complete data. We will examine missing data and use multiple imputation, as appropriate.[84, 85]

D.11.2 Multivariable adjustment. Several analyses will include multivariable adjustment. Multivariable adjustment will be guided by biologic plausibility and will be contingent on the specific hypothesis being tested. In general, we plan two levels of adjustment. An initial model will include adjustment for age, race/ethnicity, sex and clinic site (UAB or Columbia). A second model will include additional adjustment for education, body mass index, smoking, physical activity, alcohol consumption, stress, anxiety, outdoor temperature, sleep quality, diabetes, eGFR, and 10-year predicted CVD risk. Co-linearity will be assessed using variable inflation factors.

D.11.3. Exploratory statistics comparing unattended and attended BP. We will calculate characteristics of participants by randomization assignment: unattended then attended clinic BP measurement or attended then unattended clinic BP measurement at the first visit. Scatterplots will be assembled to show the relationship between unattended clinic BP versus awake BP and attended clinic BP versus awake BP. For each comparison, 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 attended and unattended clinic BP.[86, 87] We will also assemble Bland-Altman plots showing the differences between unattended and attended BP, separately, versus awake BP on ABPM.

D.11.4. Aim 1. Test whether measuring unattended clinic BP with an automated device will provide a more accurate estimate of awake BP on ABPM than measuring attended clinic BP with an automated device. Our primary analyses for Hypothesis 1 will be tested using the first three clinic BP measurements obtained at Visits 1 and 2. In sensitivity analyses, we will use the fourth through sixth BP measurements from these visits. Separate analyses will be performed for SBP and DBP.

D.11.4.1. Hypothesis 1a: The absolute difference with awake BP will be smaller for unattended vs. attended clinic BP. *The absolute difference between mean unattended clinic BP and awake BP and mean attended clinic BP and awake BP, separately, will be calculated. We will test whether these differences are statistically significantly different from zero using paired t-tests. Next, we will determine whether the absolute difference between unattended clinic BP and awake BP is smaller than the absolute difference between attended clinic BP and awake BP by calculating if the difference in differences (i.e., absolute difference between unattended clinic BP and awake BP minus the absolute difference between attended clinic BP and awake BP) is less than zero using a paired t-test. If the absolute differences between unattended and attended clinic BP and awake BP differs by randomization assignment, we will use a mixed model with randomization assignment as a covariate. This analysis will be performed in the overall population and in sub-groups defined by age (categorized in tertiles), race/ethnicity (white, African American, Hispanic) and sex.*

D.11.4.2. Hypothesis 1b: The agreement between hypertension in the clinic and awake hypertension will be higher for unattended versus attended clinic BP. Also, the prevalence of both white coat and masked hypertension will be lower when BP is measured unattended versus when it is measured

attended in the clinic. *Using the first three clinic BP measurements obtained at each visit and awake BP from ABPM, we will calculate the prevalence of clinic hypertension, based on unattended and attended measurements separately, and awake hypertension. We will calculate overall agreement and agreement above that expected by chance alone (i.e., the Kappa statistic) between (1) clinic hypertension, measured attended, and awake hypertension and (2) clinic hypertension, measured unattended, and awake hypertension. We will calculate the prevalence of white coat hypertension and masked hypertension defined using unattended and attended clinic BP, separately, and awake BP from ABPM. The statistical significance of the differences in these statistics when BP is measured unattended versus attended will be calculated using McNemar tests and bootstrapping techniques as these measures are not independent.*

D.11.5. Aim 2. Test whether a new HBPM device provides an accurate approach for measuring sleep BP. We will calculate the characteristics of participants randomized to have their sleep BP measured by (1) ABPM then HBPM or (2) HBPM then ABPM. The statistical significance of differences across the randomization assignments will be calculated using t-tests and chi-square tests, as appropriate.

D.11.5.1. Hypothesis 2a: Sleep BP on HBPM will provide an accurate estimate of sleep BP on ABPM. We will assemble a scatterplot of mean sleep SBP on HBPM versus ABPM and a intraclass correlation coefficient will be calculated. The statistical significance of the difference in mean sleep SBP on HBPM versus ABPM will be calculated using paired t-tests. The analysis will be repeated using sleep DBP on HBPM versus ABPM. We will create Bland-Altman plots showing the difference between sleep BP on HBPM versus ABPM by ABPM sleep BP level. We will calculate the percentage of participants who have a 10 mm Hg or larger absolute difference in their mean sleep SBP or a 5 mm Hg or larger absolute difference in their mean sleep DBP when measured by HBPM versus ABPM. Differences in mean sleep BP (SBP and DBP, separately) measured on HBPM versus ABPM will be calculated within age, race/ethnicity and sex sub-groupings. *We will calculate the overall agreement and Kappa statistic between nocturnal hypertension on HBPM and ABPM, and test for a difference in prevalence using McNemar's test.* We will compare differences in mean sleep SBP and DBP by randomization assignment using t-tests. If differences are statistically significant, analyses will include adjustment for randomization assignment.

D.11.5.2. Hypothesis 2b: HBPM will be better tolerated than ABPM. An overall score on the HBPM/ABPM tolerability questionnaire will be calculated by summing the scores on the eight Likert-type items after reverse coding positively-framed items (i.e., those with higher scores indicating better tolerability). Consistent with the approach of Viera, poor tolerance will be defined as an overall score ≥75th percentile on the results for ABPM.[16] The cut-point identified for ABPM will be applied to define poor HBPM tolerability. Also, the percent of participants who report "pain", "skin irritation" and "bruising" from the ABPM device, and separately, the HBPM device will be calculated. The statistical significance of differences in responses to these items when wearing the HBPM and ABPM devices will be calculated using McNemar tests.

D.11.6. Aim 3. Compare the associations of unattended versus attended clinic BP, unattended clinic BP versus awake BP on ABPM, and sleep BP on HBPM versus ABPM with two markers of end-organ damage, LVMI *and ACR*.

Hypothesis 3a: The association with end-organ damage will be stronger for unattended vs. attended clinic BP.
Hypothesis 3b: The association with end-organ damage will be similar for unattended clinic and awake BP.
Hypothesis 3c: The association with end-organ damage will be similar for sleep BP by HBPM and ABPM.

Below we describe the analysis plan for testing Hypothesis 3a. The analysis plan will be identical for Hypotheses 3b and 3c. We will calculate the intraclass correlation coefficients between (1) attended clinic BP and (2) unattended clinic BP with LVMI. The statistical significance of the difference in the correlation coefficients will be calculated using the Fisher r-to-z transformation accounting for the within-person correlation between unattended and attended BP measurements.[86, 87] Also, the association between clinic BP, measured unattended and attended, separately, and LVMI will be calculated using linear regression. For these models, clinic BP will be modeled in categories, using restricted quadratic splines, and, if appropriate, as a continuous variable (e.g., per 10 mm Hg higher SBP). Two levels of adjustment will be performed as described in **Section D.11.2**. For secondary testing of Hypothesis 3, we will model the outcome of LVH defined as an LVMI ≥ 96 g/m^2 in women and LVMI ≥ 116 g/m^2 in men using Poisson regression with robust standard errors and two levels of adjustment (**Section D.11.2**). *The analyses will be repeated for the outcome of the ACR. When modeled as a continuous variable, ACR will be log-transformed due to its skewed distribution. As a dichotomous variable, albuminuria will be defined as an sex/race-adjusted ACR > 25 mg/g.[80]*

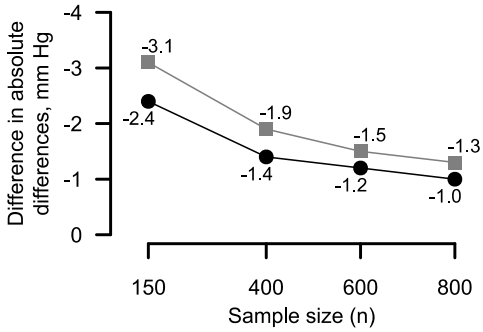
D.12. Sample size/minimum detectable effects.

D.12.1. Aim 1. Sample size and minimal detectable difference calculations were based on 80% statistical power and a two-sided alpha level of 5%. These calculations were performed using simulations and R version

3.3.2. We estimate that a sample size of 600 participants *(630 enrolled participants with 30 participants [5%] not completing the study)* will allow us to detect small but clinically relevant differences for each aim.

D.12.1.1. Sample size considerations for hypothesis 1a. **Figure 4** shows the minimal detectable difference in differences with awake ABPM comparing unattended vs attended clinic BP. With 600 participants we can detect that the absolute difference with awake ABPM is 1.5 and 1.2 mm Hg smaller for unattended vs attended clinc BP assuming a correlation of 0.5 and 0.7, respectively between clinic BP and awake BP on ABPM. In a sub-group of 160 participants (e.g., African Americans), we can detect that the absolute difference with awake ABPM is 3.1 and 2.4 mm Hg smaller for unattended vs. attended clinic BP. Smaller absolute differences can be detected if the correlation between attended and awake BP is higher.

Figure 4. Minimal detectable difference in absolute differences between attended clinic BP vs awake BP and unattended clinic BP vs awake BP.



Symbols ■ and ● identify estimates that assume a correlation coefficient between clinic BP and awake BP on the ABPM of 0.5 and 0.7, respectively with 80% power and 2-tailed α=0.05. Calculations assume a correlation of 0.5 between the differences.

D.12.1.2. Sample size considerations for hypothesis 1b. If 85% of participants have the same concordance/discordance status for both comparisons (i.e., attended clinic hypertension versus awake hypertension and unattended clinic hypertension versus awake hypertension), enrollment of 600 participants will provide 80% statistical power to detect a difference of 5% in the two overall agreements (e.g., 70% vs. 75%). If the expected agreement is 50%, we will have an 80% statistical power to detect a difference between Kappa statistics of 0.4 and 0.5 using a two-sided alpha level of 0.05. With 600 participants and a phenotype prevalence of 15%, we can detect a difference in the prevalence of 4% when clinic BP is measured unattended versus attended. In a sub-group of 160 participants, we can detect a difference of 8%. Based on these estimates, we chose to enroll *630* participants in the proposed study (n=600 with complete data).

D.12.2. Aim 2

D.12.2.1. Minimum detectable effect size - hypothesis 2a. We assumed a standard deviation of sleep SBP of 15 mm Hg and sleep DBP of 10 mm Hg when measured using ABPM and HBPM. Also, the correlation between sleep BP on ABPM and HBPM was assumed to be 0.5 for SBP and DBP. For this analysis, we are testing that mean sleep BP is equivalent when measured by HBPM and ABPM. A sample size of 600 participants will provide 80% statistical power to exclude an absolute mean difference equal to or larger than 2.1 mmHg for SBP or 1.4 mmHg for DBP comparing ABPM versus HBPM exists. In a sub-group of 160 participants, we can exclude an absolute mean difference equal to or larger than 4.0 mmHg for SBP or 2.7 mmHg for DBP. If the correlation of sleep BP on ABPM and HBPM is higher (e.g., 0.7 or 0.9), we can exclude smaller absolute differences. A sample size of 600 participants will provide narrow confidence intervals for the observed agreement and kappa statistic for nocturnal hypertension comparing HBPM and ABPM. For example, the 95% confidence interval for an observed agreement of 80% and 90% would be 77%-83% and 88%-92%, respectively, and for a kappa statistic of 0.6 and 0.8 would be 0.54-0.66 and 0.75-0.85, respectively.

D.12.2.2. Minimum detectable effect size - hypothesis 2b. By definition, 25% of participants will have poor tolerance to ABPM. The minimum detectable difference in the prevalence of poor tolerance comparing HBPM versus ABPM depends on the percentage of participants who have poor tolerance to one method but not to the other. With a sample size of 600 participants, we can detect a difference in poor tolerance of ABPM and HBPM of 3% (25% versus 22%) if 20% of participants report poor tolerance to both methods (e.g., if 5% has poor tolerance to ABPM but not to HBPM, and 2% has poor tolerance to HPBM but not to ABPM). Assuming 5% of participants experience bruising with both ABPM and HBPM, we will have 80% power to detect a difference in the prevalence of bruising of 3% or larger comparing ABPM and HBPM.

Table 7. Minimal detectable correlation coefficients between BP measurements and LVMI.

Correlation between standard and alternative BP measurements†	Correlation coefficient between standard BP measurements and LVMI		
	0.30	0.50	0.60
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; 2-tailed α=0.05. †For example, standard measurement may be attended BP and alternative is unattended BP.

D.12.3. Aim 3. **Table 7** shows minimum detectable differences in correlation coefficients for hypotheses 3a, 3b and 3c with the full population (n=600) or a sub-group (n=160) of participants. For example, if the correlation between attended and unattended clinic BP is 0.5, and the correlation between attended BP and LVMI is 0.3,

we will have 80% power to detect a difference in the correlation between attended and unattended BP and LVMI of 0.11 or larger (e.g., 0.30 versus 0.41). Detectable differences in the correlation coefficients will be modestly larger in sub-groups of 160 participants. The detectable differences will be smaller if the correlation between attended and unattended clinic BP is higher (e.g., 0.7).

D.13. Potential problems and alternative strategies.

D.13.1. Why we are not examining individuals with treated hypertension. The focus of this application is on the diagnosis of hypertension. Many guidelines and scientific statements recommend ABPM for confirming the diagnosis of hypertension.[2, 38] 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.

D.13.2. Why is ABPM and not HBPM the reference standard for 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-clinic BP assessment and confirming hypertension status.[4] 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.*

D.13.3. Why we are not comparing BP dipping and morning surge assessed using HBPM versus ABPM. *We are not studying BP dipping and morning surge because the prognostic value of these phenotypes is unclear. Some studies have reported associations of these phenotypes with outcomes while others have not.[88-90] Additionally, the reproducibility of these phenotypes is poor.[91-93] Finally, these phenotypes are not widely used in clinical practice particularly for the diagnosis of hypertension.*

D.13.4. Hypotheses in Aim 1 but not Aim 2 (or vice versa) are confirmed. If the hypotheses in Aims 1 and 2 are confirmed, there will be a unified approach to accurately diagnose hypertension without ABPM (i.e., conduct unattended BP for detecting awake hypertension and HBPM for detecting sleep hypertension). If the hypotheses for only one aim are confirmed, then our study would inform when unattended BP or sleep HBPM should be used. For example, if Aim 1 but not Aim 2 is confirmed, unattended BP measured in the clinic can be used to assess awake hypertension but an abbreviated form of ABPM (conducted during the sleep period) is needed. If Aim 2 but not Aim 1 is confirmed, ABPM can be used during the awake period to exclude awake hypertension while sleep HBPM, if better tolerated, can be used for assessing sleep hypertension. In both scenarios, the burden of performing ABPM during a 24-hour period is reduced.

D.14. Translation into practice. *Upon completion of the study, we will conduct a stakeholders meeting with clinical leaders in the field of hypertension to develop a statement on the use of unattended BP and sleep HBPM assessment in clinical practice. This meeting will include committee members from the AHA's Scientific Statement on BP measurement, which Dr. Muntner and Dr. Shimbo co-chair. Dr. Muntner is director of the Lister Hill Center for Health Policy at UAB and will use center funds for this meeting.*

D.15. Reproducibility and transparency. We will post the aims, methods, and original analytical plan prior to data collection on the Open Science Framework website, which is hosted by the recently founded Center for Open Science (funded in part by the NIH and the National Science Foundation; https://osf.io), and is open to the public to view. Once the proposed study has been completed and before data analyses are initiated, we will post the code for derivation of study variables and the final sample size (with a flow diagram on how the final sample was derived). For each abstract and manuscript, all coding will be carefully labeled and linked to the final versions of each document. None of the posted documents will contain participant identifiers.

D.16. Consideration of sex and other biological variables. We will make every effort to recruit equal numbers of men and women. As noted above, we will conduct exploratory analyses stratifying by age group, sex, and race/ethnicity (white, African American, and Hispanic; a minimum of 160 each).

D.17. Summary. In clinical practice, BP is typically measured in the clinic by a technician/healthcare provider. This approach often leads to an inaccurate diagnosis of hypertension. Several guidelines and scientific statements recommend the use of ABPM, which measures BP during the awake and sleep periods, for confirming the diagnosis of hypertension.[27, 38, 94] However, ABPM is not being done in clinical practice due to several barriers that limit its widespread use. Therefore, new and innovative approaches for diagnosing hypertension without conducting ABPM are needed. Some data suggest that BP measured unattended versus attended is closer to awake BP on ABPM. However, these data were derived from uncontrolled, non-randomized studies of select patients and were considered sufficiently low quality in the Canadian Guidelines to warrant a Grade D level of evidence. Another approach is to use a new HBPM device that has been developed to assess sleep BP. Using a randomized controlled trial design, the study will rigorously test these two non-ABPM approaches for determining awake and sleep BP. The novel approaches being tested can be adopted in clinical practice and may become the standard-of-care for diagnosing hypertension if our hypotheses are confirmed.

E. HUMAN SUBJECTS
E.1. Protection of Human Subjects
E.1.1. Risks to the Subjects

Human subjects involvement and characteristics: The proposed study will include 630 participants from Birmingham, AL (N=315) and New York, NY (N=315). Study participants will be recruited between 2019 and 2022. Participants will be ≥21 years of age. No participants will have hypertension and no participants will have cardiovascular disease. We plan for the overall sample to include an equal percentage of men (50%) and women (50%) and at least 25% of the population will be white, 25% African Americans and 25% Hispanic.

Sources of materials: Research material for the study includes self-report and physiological data, both of which are collected specifically for the purpose of the study. The physiological measurements consist of the assessment of orthostatic hypotension (from supine and standing blood pressure measurements), noninvasive measurement of blood pressure in the clinic during two study visits and outside of the clinic using ambulatory blood pressure monitoring and home blood pressure monitoring during sleep, a blood and urine sample, actigraphy and an echocardiogram. Height, weight and waist and neck circumference will be measured during a study visit by trained staff. Some participants may experience discomfort during the blood pressure measurements. However, the discomfort that is experienced is no more than that experienced during a routine outpatient doctor's visit. In our experience conducting ambulatory blood pressure monitoring on over 5,000 participants, none have experienced a serious injury. Participants will also complete questionnaires that asks about stress and psychosocial factors.

Potential risks: The physical risks of the studies are minimal, as no invasive procedures are proposed. Some discomfort may occur due to the use of the ambulatory blood pressure arm cuff or home blood pressure cuff, and no/minimal discomfort is expected with using the actigraph device (it is worn on the wrist like a watch). The discomfort, if it occurs, is minimal and temporary. Also, some patients may experience discomfort (i.e., dizziness) from the assessment of orthostatic hypotension. Patients may experience discomfort answering questions about stress and psychosocial risk factors. Study physicians will be available to discuss discomfort with patients and if necessary, participants will be referred to their doctor to discuss psychosocial factors. If the patient does not have a doctor, we will find a doctor for them to see. Data will be stored on encrypted computers at the field centers and at the University of Alabama at Birmingham (the coordinating center for this study). All data will be stored in locked filing cabinets to protect against the risk of a patient being identified. All findings will be presented in aggregate to ensure the confidentiality of all participants. After study completion, the clinic BP, ABPM and HBPM results will be given to the participants and invited to share it with their physician. If the participant does not have a physician, he/she will be referred to a physician for follow-up.

E.1.2. Adequacy of Protection Against Risks

Recruitment and informed consent: Participants for the proposed study will be enrolled following IRB-approved approaches. Potential participants for our study will be attending outpatient clinics affiliated with the University of Alabama at Birmingham or Columbia University. With IRB approval, potential participants will be contacted following a routine clinic by phone and screened for eligibility for the proposed study and, if eligible, will be told about the study, its goals, activities involved, and potential risks. Those who remain interested will be invited to participate. They will be provided with an informed consent for this study. The informed consent that will be used will be written at the sixth grade level and in a language that potential participants can understand. Individuals will be given time to read over the consent thoroughly and will be encouraged to ask questions to help them clarify any issues they might have. The principal investigators, co-investigators and staff at both sites (UAB and Columbia University) have substantial experience conducting research that includes explaining a study's purpose and potential risks and benefits to a broad range of participants.

Protection against risks: The physical risks of the studies are minimal, as no invasive procedures are proposed. Some discomfort may occur due to the use of the arm cuff for measuring blood pressure, and no/minimal discomfort is expected with using the actigraph device. The discomfort from the blood pressure cuffs, if it occurs, is temporary and should disappear when the cuffs are removed. Any discomfort, if it occurs, is minimal and temporary. The risks of having blood drawn include soreness and bruising at the puncture site, and sometimes there may be discomfort during the procedure. Occasionally participants feel lightheaded or faint. This may occur with the assessment of orthostatic hypotension as well. The assessment of orthostatic hypotension and the blood draw will occur in the presence of trained technicians with training handling safety issues for participants. A minimal risk to participants arises from the release of study data. To minimize this risk, staff conducting study visits will be trained in the protection of human subjects. In addition, all study information and the study computer will be kept in a locked room in at the participating field center and University of Alabama at Birmingham. The computer databases will be encrypted and protected by a

password available only to study investigators and other personnel who need access. The link between patient identity and a unique study identification number will be destroyed after the study is completed. Published reports will contain only aggregate and statistical results, and no individual results or patient identifiers will be disclosed. These safeguards make the possibility of a breach of confidentiality or invasion of privacy remote.

Very high or low clinic BP. Individuals with mean screening SBP of 110 to < 160 mm Hg and mean screening DBP of 70 to <100 mm Hg (based on the two most recent outpatient clinic visits, extracted from clinical records) will be included. Therefore, we are not including individuals with severely high or low clinic BP. Among enrolled participants, if clinic BP at any of the study visits ≥160/100 mmHg or <110/70 mmHg they will be referred to their health care provider for evaluation and excluded from the study for safety reasons.

E.1.3. Potential Benefits of the Proposed Research to the Subjects and Others

There is a limited direct benefit to the study participants. Participants will receive a report containing information from their clinic blood pressure measurements, 24-hour ambulatory blood pressure monitoring and sleep blood pressure. This report will contain mean blood pressure from ambulatory monitoring, information on the presence of masked and white coat hypertension as well as information on the level of their blood pressure variability and diurnal blood pressure patterns. Drs. Muntner, Oparil, Shimbo, and Schwartz have over 50 years of cumulative experience preparing reports with results and interpretation for study participants. Although ambulatory blood pressure monitoring is not commonly used in clinical practice, some participants (and their physicians) may find the results of the ambulatory blood pressure monitoring helpful. Reports will be provided to participants within one month of completion of their study visit. As the risks to subjects are minimal, and important prognostic medical information not typically accessible to subjects will be made available, the benefits are considered to outweigh the risks.

E.1.4. Importance of the Knowledge to be Gained

In terms of benefits to others, the proposed research is an attempt to better measure blood pressure. Over 80 million US adults have hypertension. Studies from Canada have reported that blood pressure measured in the clinic by a technician do not represent the true blood pressure a patient experience as they go about their daily activities. However, the gold standard approach to measuring blood pressure, ambulatory blood pressure monitoring, is not readily available and, when available, not well tolerated by patients. We aim to determine whether measuring blood pressure using an automated device without a technician/healthcare provider present can provide a better estimate of blood pressure. Also, we will test whether a novel home blood pressure measurement device can measure blood pressure during sleep. The proposed study may provide data that transforms how blood pressure is measured and hypertension is diagnosed in the United States. We will assess whether using a novel home blood pressure measurement device is better tolerated for assessing sleep blood pressure compared with ambulatory blood pressure monitoring. Therefore, not only will we provide data on how blood pressure should be measured, this approach may be better tolerated by patients.

Data Safety Monitoring Plan

A DSMP is proposed even though it is not required by NIH Policy as the study does not pose a greater than minimal risk to the participant. The proposed study does not meet the NIH definition for a clinical trial (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html) since we are not testing the effects of BP measurement on "health-related biomedical or behavioral outcomes." A Data Safety and Monitoring Board (DSMB) is not needed as the study is not a Phase III trial, does not included a high-risk intervention, and does not enrolled a highly vulnerable patient population (https://www.nhlbi.nih.gov/research/funding/human-subjects/data-safety-monitoring-policy). The MHT Study and IDH Study enrolled participants (with similar eligibility criteria as the proposed study) who underwent a BP measurement protocol (including clinic BP measurement, ABPM, and HPBM) over several study visits and had echocardiogram and laboratory measures). These studies were approved by the IRB, who deemed these two studies as having minimal risk.

The purpose of the DSMP is to monitor study safety, ensure the safety of participants (identify, review, and report adverse events to the IRB and/or NHLBI and ensure appropriate medical follow up), minimize research-associated risk, and protect the confidentiality of participant data. IRB approval will be obtained. The DSMP will contain the following elements: an appropriate monitor (person or group), monitoring procedures, frequency of monitoring, collection and reporting of serious adverse events and adverse events, reporting mechanisms of adverse events/ serious adverse events to the IRB and NHLBI, reporting mechanisms of the IRB actions to NHLBI, reporting mechanisms for changes or amendments to the protocol or consent form, potential risks and benefits to subjects, management of serious adverse events or other study risks, conflicts of interest, data acquisition and transmission, data analysis plans, trial stopping rules, and plans for interim analysis. Dr. Muntner (UAB site) and Dr. Shimbo (CUMC site) will be responsible for ensuring participants' safety on a daily basis. The PIs will be informed of unanticipated problems or unexpected serious adverse events that may be related to the study protocol as soon as they occur, and they will notify the IRB, and/or NHLBI in compliance with their policies. Personnel involved in monitoring activities will include the following: (1) Along with Dr. Muntner, Dr. Oparil, a board-certified cardiologist will be responsible for overseeing medical risks during the study and will review adverse medical events at the UAB site. (2) Dr. Shimbo, a board-certified cardiologist will be responsible for overseeing medical risks and will review adverse medical events at the CUMC site.

Participants who have any problems or suspected adverse events during the course of the study will be instructed to contact the research coordinator or appropriate study personnel immediately. Site-specific research coordinators will contact the respective PIs if any problems or suspected adverse events are reported by participants. If the participant needs immediate medical attention, he/she will be sent to the emergency room for further evaluation. If the participant does not require immediate medical attention, he/she will be scheduled to see their physician. If the participant does not have a physician, he/she will be referred to a physician for follow-up.

On an annual basis, the PIs will submit a progress report that: (1) Confirms adherence to the DSMP. (2) Includes a summary of any data and safety monitoring issues that occurred since the previous reporting period. (3) Describes any changes in the research protocol or the DSMP that may or does affect risk. (4) Provides all new and continuing IRB approvals.

ClinicalTrials.gov requirements. ClinicalTrials.gov registration is not required as this study is not a clinical trial as defined by NIH (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html).

E.1.6 Women and Minority Inclusion in Clinical Research

E.1.6.1. Inclusion of Women

We will not exclude women for any reason from this research besides having a current known pregnancy. Pregnancy is an exclusion because ABPM devices have not been validated for pregnant women. We will not be conducting pregnancy testing because we think that unknown pregnancies will be rare and ABPM devices should be valid in the early stages of pregnancy. We will aim to have a 50%:50% women:men enrollment.

E.1.6.2. Inclusion of Minorities

We will include participants of all race/ethnicities. As we propose conducting analyses for the overall population and for whites, African Americans and Hispanics, separately, we plan to enroll at least 25% (n=160) of our sample to be white, at least 25% (n=160) to be African American and at least 25% (n=160) to be Hispanic. We will track enrollment into our study to ensure that our goal is achieved. The diversity of the populations at Columbia University and UAB is a major strength of this study, and will enhance the generalizability of our results.

Our prior studies at Columbia University (with similar eligibility criteria as the currently proposed study) have enrolled the following percentages of Non-Hispanic Black and Hispanics: 20% to 36% and 29% to 64%, respectively. Our prior studies at UAB (with similar eligibility criteria as the currently proposed study) have recruited equal percentages of men and women and whites and non-Hispanic blacks. Also, Birmingham, Alabama has a rapidly growing Hispanic population facilitating the recruitment of member of this group into the proposed study.

PHS Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

OMB Number:0925-0001 and 0925-0002
Expiration Date: 10/31/2018

***Study Title:** Evaluating novel approaches for estimating awake and sleep blood pressure

***Delayed Onset Study?** ❑ Yes ☑ No

If study is not delayed onset, the following selections are required:

Enrollment Type ☑ Planned ❑ Cumulative (Actual)

Using an Existing Dataset or Resource ❑ Yes ☑ No

Enrollment Location ☑ Domestic ❑ Foreign

Clinical Trial ❑ Yes ☑ No

NIH-Defined Phase III Clinical Trial ❑ Yes ☑ No

Comments:

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0		0	0					0
Asian	0	0		0	0					0
Native Hawaiian or Other Pacific Islander	0	0		0	0					0
Black or African American	105	105		0	0					210
White	105	105		105	105					420
More than One Race	0	0		0	0					0
Unknown or Not Reported										
Total	210	210		105	105					630

Report 1 of 1