Phenotypes of Hypertensive Ambulatory Blood Pressure Patterns: Design and Rationale of the ECHORN Hypertension Study

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Objective: To describe the rationale and design of a prospective study of ambulatory blood pressure measurement (ABPM) combined with measurement of contextual factors to identify hypertensive phenotypes in a Caribbean population with high rates of HTN and cardiovascular disease.

Design: Prospective, multi-center sub-study.

Setting: Eastern Caribbean Health Outcomes Research Network Cohort (ECHORN) Study, with study sites in Puerto Rico, the US Virgin Islands, Trinidad and Tobago, and Barbados.

Participants: Community-residing adults without a diagnosis of HTN and not taking antihypertensive medication.

Intervention: Ambulatory BP patterns are assessed using 24-hour ABPM. Contextual factors are assessed with: ecological momentary assessment (7-item survey of experiences, exposures and responses associated with daytime BP measurements); actigraphy (capturing physical activity and sleep quality); and self-report surveys (assessing physical and social health, environmental and social stressors and supports).

Main Outcome Measures: Phenotypes of contextual factors associated with hypertensive BP patterns (sustained HTN, masked HTN, and nocturnal non-dipping)

Methods and Results: This study will enroll 500 participants; assessments of blood pressure and contextual factors will be conducted during Waves 2 and 3 of the ECHORN parent study, occurring 2 years apart. In Wave 2, we will assess the association between contextual factors and ABPM patterns. Using advanced analytic clustering

Introduction

The Caribbean region is characterized by a high burden of hypertension (HTN), stroke and heart disease,[1-4] with rates similar to that of Black or African American populations residing in the United States.[5-7]

methods, we will identify phenotypes of contextual factors associated with hypertensive ABPM patterns. We will then test the stability of these phenotypes and their ability to predict change in ABPM patterns between Waves 2 and 3.

Conclusions: Assessment of ABPM, and the contextual factors influencing ABPM, can identify unique phenotypes of HTN, which can then be used to develop more precision-based approaches to the prevention, detection and treatment of HTN in high-risk populations. *Ethn Dis.* 2019;29(4):535-544; doi:10.18865/ed.29.4.535

Compared with US White adults, HTN onset occurs at an earlier age and target organ damage (eg, ventricular hypertrophy; retinopathy; renal impairment) is more frequent and severe, with an associated higher incidence of acute myocardial infarction, heart failure, stroke, cognitive

and functional limitations, and end stage renal disease.[4, 8-12] One explanation for these disparities is that high-risk blood pressure patterns that lead to future disease may go undetected by the standard resting clinic blood pressure. Specifically, masked HTN, in which the clinic blood pressure (BP) is normal but the ambulatory BP is elevated, and nocturnal non-dipping, in which the normal BP

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fall (or dip) during sleep is less than 10% of the daytime BP - both of which are associated with target organ damage and future cardiovascular outcomes - are more common in Black and Hispanic populations.[13,14] Moreover, contextual factors such as stress, unhealthy lifestyle behaviors, poor sleep quality, less social support, and aspects of the physical and social environment may negatively impact ambulatory BP and may be associated with masked hypertension and nocturnal non-dipping HTN.[15-22]

To detect these ambulatory phenotypes and their association with activity, stress and emotional response, 24-hour ambulatory blood pressure measurement (ABPM) alongside assessment of contextual factors is required. Yet ABPM is not routinely assessed in clinical practice, and connections between ABPM and individuals' lived experiences and social context often go undetected or are disregarded, limiting opportunities to detect HTN in ambulatory settings and mitigate its burden, especially in vulnerable populations. Given the known associations between masked HTN and nocturnal non-dipping with cardiovascular events and mortality, and the higher prevalence of these sub-types of HTN among African American and Hispanic populations, it is no longer sufficient to rely solely on resting BP to diagnose and manage BP; moreover, doing so may perpetuate health disparities.[23-25]

Accordingly, we designed a prospective study (herein referred to as the ECHORN HTN study) to identify the contextual factors influencing ABPM in a cohort of Caribbean residents participating in the Eastern Caribbean Health Outcomes Research Network (ECHORN) study. The primary aim of our prospective study is to identify phenotypes of hypertensive ambulatory BP patterns and the specific contextual factors associated with these patterns. Findings from this study will be incorporated into tools that capture the most relevant contextual factors influencing high-risk BP patterns, which can then be used to screen high-risk populations who may most benefit from ABPM,

and which can guide a more precision-based approach to the prevention, detection, and control of hypertension.

THE ECHORN COHORT STUDY

The ECHORN Cohort Study (ECS, parent study) is a community-based prospective cohort of adults aged ≥40 years residing on the islands of Trinidad and Tobago, Barbados, the US Virgin Islands, and Puerto Rico. The primary aim of the cohort study is to assess the prevalence and incidence of cardiovascular disease, cancer, and diabetes and their known and potential risk factors. Sampling methodology for the ECS are described elsewhere.[26] Briefly, stratified multi-stage probability sampling was used on the islands of Puerto Rico, Barbados, and Trinidad. Adults in Puerto Rico and Trinidad were recruited from households within randomly selected enumeration districts. In Barbados, a random sample was obtained from the entire island. Simple random sampling was used on the US Virgin Islands of St. Thomas and St. Croix where researchers used random digit dialing by phone to invite adults to participate in the study.

Baseline or Wave 1 assessments (N=2,959) were completed between 2013 and 2016. The baseline assessment included anthropometric measurements: resting clinic blood pressure, weight, height, waist, hip, and neck circumference, ankle brachial index, and grip strength; biological measurements: hemoglobin A1c, hemoglobin, comprehensive metabolic panel, lipid panel; and an extensive self-reported survey of participants' physical and mental health status, and social and behavioral risk factors.

The ECHORN Hypertension (HTN) Study

The ECHORN HTN study is designed to identify the contextual factors influencing ABPM in a sub-sample of adults participating in the ECS. The primary objective is to identify phenotypes of HTN based on the contextual factors associated with high-risk BP patterns. The purpose of this article is to describe the study design, research protocol, and analytic approach to phenotyping blood pressure patterns among 500 participants.

Methods

Sample

The sample for the ECHORN HTN study will be obtained during the ECS Wave 2 assessment. Participants who successfully complete the ECS Wave 2 survey and meet study inclusion criteria (described below) will be asked to participate. In addition to existing ECS participants, their first-degree relatives aged <40 years, without a prior diagnosis of HTN will also be recruited to participate in this study. Study visits occur at 1 of 5 Community Assessment Centers, which were established during year 1 of the ECS and maintained to facilitate research recruitment and enrollment efforts.

Inclusion criteria for the ECHORN HTN study are: 1) completed the ECS Wave 2 follow-up survey; 2) are not taking an anti-hypertensive medication for any reason; 3) have a resting clinic systolic blood pressure (SBP) <180 mm Hg or a dia-stolic blood pressure (DBP) <110 mm Hg. Participants with SBP ≥ 180 or DBP ≥ 110 are excluded and referred for immediate medical attention.

Qualifying individuals who agree to participate in the study have the informed consent procedures described to them, have the opportunity to ask and have answered any questions, and then sign an informed consent document in their native language (either English or Spanish). The Human Subjects Investigations Committees of Yale University, the University of Puerto Rico Medical Sciences Campus, the University of the Virgin Islands, the University of the West Indies Cave Hill Campus, and the Ministries of Health of the countries of Barbados and Trinidad & Tobago approved this study.

Outcome Measures

Phenotypes of hypertensive patterns based on 24 hour ABPM (sustained HTN, masked HTN, and nocturnal non-dipping) and their associated contextual factors will be identified (Table 1). We will assess their prevalence and their ability to predict BP patterns in Wave 3 of the ECS.

Procedures

Ambulatory BP and contextual factors are assessed at baseline (ECS Wave 2) and at follow-up (ECS Wave 3). Participants wear an ABPM for 24 hours, complete an ecological momentary assessment (EMA) following each wake-time blood pressure measurement, and wear an actigraphy watch. The ActiGraph watch, which monitors activity and sleep, is worn for 3 days/2 nights, with the first 24 hours overlapping with the ABPM. Clinic BP and survey data are completed at the time of the ECS Wave 2 and 3 study visits. Participants at 4 of the 5 sites are compensated $25 upon return of study equipment (1 site does not permit participant compensation). Each of these elements is described in more detail below.

Clinic Blood Pressure (CBP) and 24-hour Ambulatory Blood Pressure Measurement (ABPM)

During the ECS study visit, blood pressure is measured in a seated position, after at least 5 minutes of rest, with back supported and both feet flat. Three measurements are automatically taken 1 minute apart and averaged to obtain the resting CBP. During the 3 cuff inflations, the research coordinator is instructed to leave the room or perform other tasks. The mean blood pressure measurement serves as the "clinic blood pressure," necessary for establishing the diagnosis of white coat hypertension and masked hypertension.

Table 1. Definitions of hypertensive ABP patterns

	Clinic HTN (mm Hg)	Mean Daytime ABPM (mm Hg)
Sustained HTN	>120/80	>130/80
Masked HTN	<120/80	>130/80
Nocturnal non-dipping	Any	Mean sleep BP <10% lower than mean wake BP

ABP, ambulatory blood pressure; ABPM, ambulatory blood pressure monitoring; HTN, hypertension; BP, blood pressure

Following the completion of the ECS Wave 2 visit, participants are fitted with the ABP ONTRAK MONITOR (Spacelabs Healthcare). Cuff size is determined by measuring the widest part of the upper arm with a paper tape measure. The ABPM is programmed to take a measurement every 30 minutes during waking hours and every 60 minutes while the participant is asleep. The participant's self-reported wake and sleep times are entered as part of the initialization process to facilitate interpretation of wake and sleep time BP readings. ABPM readings with at least 8 and 4 wake and sleep readings, respectively, will be included.[27]

Ecological Momentary Assessment (EMA)

The EMA questions were adapted from an ongoing trial,[28] with input from ECHORN project managers at each of the enrolling sites in order to ensure language and cultural appropriateness. The resulting 7-item survey assesses self-reported: posture, lo-

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Table 2. ECHORN Hypertension Study Ecological Momentary Assessment

Question	Response Options
During this blood pressure measurement:	
1. Your posture was (select one):	Reclining
	Sitting
	Standing
	Walking
	Running
2. Your location was (select one):	Home
	Work
	Vehicle
	Outside
	Other: _____
Just before this blood pressure measurement:	
3. What were you doing? (check all that apply):	Working
	Chores/errands
	Exercising
	Meal-time
	Traveling to/from home
	Socializing
	Relaxing
	None of the above
4. What was your level of physical activity:	None
	Light (eg, light walk or chores)
	Moderate (eg, brisk walk or heavy lifting)
	Heavy (eg, activity causing heavy breathing)
5. How stressed/anxious were you feeling?	Not at all
	Very little
	Somewhat
	Very much
6. How irritated/vexed/angry were you feeling?	Not at all
	Very little
	Somewhat
	Very much
Since the last blood pressure measurement:	
7. Have you (check all that apply):	Eaten a meal
	Had a caffeine drink
	Had any alcohol
	Smoked a cigarette/cigar
	None of the above

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cation, current task, physical activity, levels of stress and irritation/anger,[21] and lifestyle behaviors (Table 2). Participants are prompted to repeatedly answer these 7 questions immediately following each wake-time blood pressure measurement. EMAs have been used in several prior studies,[29,30] and have demonstrated to be easy to use and acceptable to patients.[31]

The electronic diary 'app' from LifePak is used, which can be downloaded for free onto participants' smartphone through the Wi-Fi connection at each Community Assessment Center. Importantly, participants do not need to be connected to WiFi to respond to survey items, and thus do not need a data plan to use the app. Instead, data are stored in the app and downloaded at the time of return of the equipment to the study site. Participants without a smartphone, and those who are not comfortable using a mobile device, are given a notebook with printed surveys for each data entry. Notebooks are returned to the Community Assessment Center and EMA data are entered directly into REDCap project management software by research staff. Notebooks are saved for later shipment to Yale for double data entry of all EMA data.

Activity and Sleep Monitoring

Participants are given an Acti-Graph watch, a wearable monitor that captures physical activity and sleep. The device uses previously developed and validated algorithms to estimate daily activity (steps, kcal, activity counts); bouts of sustained physical activity; intensity of physical activity (moderate, vigorous, sed-

entary); and sleep time end efficiency based on sleep onset and offset, sleep latency, and micro-awakenings. Participants wear the device for 2 consecutive nights (3 days total), overlapping with the 24-hour ABPM. For the period of ABPM, the ActiGraph sleep data will be merged with the corresponding BP measurements, based on the synchronized time stamps recorded by both devices. Additionally, while sleep disturbance caused by wearing the ABPM is not frequent, we will be able to detect any impact by comparing the first night of sleep (when the ABPM cuff is worn) to the 2nd night of sleep (when the ABPM cuff is not worn).

Survey and Clinical Data

Anthropometric, laboratory, and self-reported survey data captured as part of the larger ECHORN Wave 2 assessment are also used in the HTN study. These include anthropometric measurements: resting clinic blood pressure, weight, height, and waist circumference; survey data: sociodemographics, health status, health behaviors, social experience,and social support; and laboratory measurements: comprehensive metabolic panel, lipid panel, hemoglobin A1c, hemoglobin, and microalbumin/creatinine.

Training, Quality Assurance, and Data Management

Research teams from each island site (including a project manager, research assistant, and clinical research nurse) participated in a 2-hour training session on the use of the equipment, including instructions on how to initialize the equipment for each

participant and download the data on return. Teams were also taught best practices for instructing the patient in using the equipment. Finally, research staff were encouraged to take home the equipment and practice using it according to the study protocol so that they were better able to answer participant questions. Training sessions were conducted live, either by webinar or in-person; video-recordings of the sessions were available for review. During the enrollment period, regular meetings were held to provide opportunities for research personnel to ask questions and troubleshoot challenges with the devices and the study protocol. Booster trainings were provided on an as-needed basis.

To facilitate understanding and maximize adherence with study protocols, participants are fitted with the devices at the time of the study visit or at an agreed upon return date. Participants are given a local number to call for questions or problems related to the equipment or procedures. Finally, the devices are returned in-person or collected by research staff, which in some sites is feasible given the proximity of participants to the Community Assessment Centers. Only in Puerto Rico, where participants may live far from the study site, is the equipment returned by mail. ABPM results are provided to participants upon request.

Upon return of the devices, data are downloaded to a laptop computer, managed by Yale Information Technology. All computers are password protected and equipped with antivirus software. Each computer is backed up daily to secure Yale servers in accordance with university policy for the storage and transfer of protect-

ed health information. On a weekly basis, data are electronically uploaded to the secured server at the ECHORN Coordinating Center (ECC) at Yale. This method of local data collection and storage, prior to data transfer, was selected given the variability in WiFi connectivity at the Community Assessment Centers. Data are reviewed for quality and completion at the ECC on a regular basis.

Analytic Plan

First, using univariate statistics, the prevalence of hypertensive ABPM patterns, based on the US American College of Cardiology and American Heart Association 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults[32] (defined in Table 1) will be described. Second, the following bivariate associations will be examined using traditional methods (t-tests, Chi-square tests, Wilcoxon tests, Spearman correlations, etc.): 1) correlations between EMA and ABP: a) immediate correlation: relationship between momentary EMA and its associated momentary ABP reading; and b) lagged correlation: relationship between momentary EMA with subsequent ABP readings; 2) whether cumulative EMA (eg, average stress rating, average negative emotion rating) is associated with the primary ABP outcomes as well as sleep quality; and 3) how self-reported sociodemographic and health characteristics, health behaviors, social experiences, and community-level variables about the social and physical environment are associated with the primary ABP outcomes.

Contextual factors (EMA and survey data) that are significant at the P<.1 level will be carried into the second phase to identify phenotypes – or groups of individuals who share similar patterns of contextual factors associated with ABP patterns. First, unsupervised multivariable modeling will be used to separate participants into subgroups based on patterns in contextual factors (not the outcome of ABP measurement), ensuring clusters are large enough and meaningful. The clustering methods include machine learning techniques commonly used to analyze patterns of data. The differences between methods will be analyzed to compare the 'distance' of patients in relation to others and the degree of homogeneity found in the subgroups. These methods of clustering are similar to traditional factor analysis, but they enable the utilization of large, heterogeneous, highly dimensional data and the modeling of relationships between variables that are often non-linear. The number of clusters, and the variables used to define each cluster, will be reviewed by clinical experts for theoretical plausibility (ie, the association between the contextual factor and the outcome is theoretically plausible) and for prioritization of factors that are actionable (ie, clusters should include several factors that are modifiable).

Supervised predictive modeling (eg, random forest or support vector machines) will then be used to test for associations between the primary outcomes of sustained hypertension, masked HTN or nocturnal non-dipping and each of the previously defined clusters. After clustering, we will design supervised predictive models within each cluster, to evaluate over-

all predictive performance as well as validate the use of different predictive factors for the models trained in each cluster. The goal is to sufficiently train the model to maximally cluster individuals with homogenous contextual profiles that have clinical significance, ie, phenotypes that are associated with sustained HTN, masked HTN or nocturnal non-dipping. The results of these analyses will be used to develop a screening tool that assesses the relevant contextual factors necessary to cluster individuals into phenotypes associated with ambulatory BP precursors of HTN and CVD.

At follow-up, 24-hour ABPM, EMA, and activity and sleep data will be reassessed. Participant clustering by phenotypes at baseline and follow-up will be compared to identify specific contextual factors that changed between the two time-periods. Differences in ABP and resting study-visit blood pressure from Wave 2 to Wave 3 will also be assesed to determine the distribution of the following trajectories: a) no change; b) increase/decrease in mean ABP and resting BP; c) change from normal ABP to HTN, masked HTN, or nocturnal non-dipping; d) change from masked HTN or nocturnal non-dipping to HTN; and e) change from masked HTN or nocturnal non-dipping to normal ABP. Next, we will test whether contextual factors captured at baseline and follow-up are predictive of BP trajectories. Specifically, prediction models will be tested and compared using only baseline contextual data, combining baseline and follow-up contextual data, and differences in contextual data from these two time points. This work will inform wheth-

er single or repeat use of the screening tool is necessary to predict BP trajectory. Data will be analyzed using R version 3.5.1 and associated packages.

RESULTS

A preliminary analysis of baseline (Wave 1) ECS data found that 49.2% of participants self-reported, "no," to having a prior diagnosis of elevated BP or prehypertension or hypertension. Among this group, 8.5% had elevated clinic BP, 15.2% had Stage 1 HTN, and 13.4% had Stage 2 HTN. Individuals with Stage 2 HTN were categorized as having "undiagnosed HTN." Among those who self-reported, "yes," to a prior diagnosis of HTN, 66.8% were treated; of these, 55.9% were controlled (SBP <140/90 mm Hg). Table 3 compares the characteristics of the population by HTN awareness, treatment and control.

DISCUSSION

HTN is the most potent risk factor contributing to health disparities in cardiovascular outcomes, with populations of African and Hispanic descent, including Caribbean popula-tions, shouldering a disproportionate burden of HTN. The parent ECS is characterized by very high rates of hypertension – both diagnosed and undiagnosed. Overall, only 16% of the cohort had a resting clinic BP in the ideal range of <120/80 mm Hg and more than 40% had a resting clinic BP ≥140/90 mm Hg. The HTN sub-study will extend these findings to identify ambulatory BP patterns associated with cardiovascular risk, including masked HTN and nocturnal non-dipping, which we suspect to be common in this population. Additionally, a primary aim of the HTN sub-study is to capture the most rel-

Table 3. Characteristics of ECS participants at baseline by hypertension status[a]

	No HTN	Undiagnosed HTN	Treated HTN		Untreated HTN	
			Controlled	Uncontrolled	Controlled	Uncontrolled HTN
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Cohort, Total N=2855[b]	1037 (36.3)	368 (12.9)	426 (14.9)	544 (19.1)	185 (6.5)	295 (10.3)
Resting clinic SBP, mean (SD)	122 (9.7)	149 (14.0)	127 (8.3)	158 (18.7)	126 (9.3)	159 (20.3)
Resting clinic DBP, mean (SD)	75 (7.2)	88 (9.1)	76 (7.3)	89 (11.7)	78 (7.1)	94 (11.9)
Age, mean (SD)	53 (9.0)	57 (9.6)	60 (9.7)	63 (9.8)	56 (9.8)	59 (10.2)
Sex (% female)	684 (66.0)	200 (54.3)	316 (74.2)	380 (69.9)	114 (61.6)	176 (59.7)
Race						
African or Caribbean Black	597 (57.6)	218 (59.2)	261 (61.3)	308 (56.6)	114 (61.6)	207 (70.2)
East Indian	89 (8.6)	47 (12.8)	26 (6.1)	55 (10.1)	13 (7.0)	22 (7.5)
Hispanic/Latino	117 (11.3)	30 (8.2)	41 (9.6)	43 (7.9)	18 (9.7)	12 (4.1)
Multi-Racial	117 (11.3)	41 (11.1)	36 (8.5)	78 (14.3)	15 (8.1)	29 (9.8)
White	101 (9.7)	28 (7.6)	59 (13.9)	49 (9.0)	21 (11.3)	18 (6.1)
Other	16 (1.5)	4 (1.1)	3 (0.7)	11 (2.0)	4 (2.2)	7 (2.4)
Health status						
Pre-diabetes	41 (4.0)	6 (1.6)	29 (6.8)	25 (4.6)	10 (5.4)	10 (3.4)
Diabetes	81 (7.8)	36 (9.8)	121 (28.5)	197 (36.4)	30 (16.3)	55 (18.7)
Hyperlipidemia	65 (6.2)	14 (3.8)	146 (34.3)	150 (27.6)	18 (9.7)	17 (5.8)
Overweight or obese	666 (65.1)	268 (72.8)	356 (85.4)	439 (82.2)	144 (79.1)	228 (80.3)
Cardiovascular disease	66 (6.4)	17 (4.6)	82 (19.3)	97 (18.0)	12 (6.5)	30 (10.2)
History of stroke	14 (1.4)	7 (1.9)	26 (6.1)	37 (6.8)	5 (2.7)	11 (3.7)
Depression	143 (14.1)	58 (16.2)	57 (13.7)	87 (16.4)	19 (10.5)	60 (20.8)
Physical activity - low	370 (40.0)	136 (41.2)	203 (53.9)	263 (54.9)	56 (35.4)	117 (44.0)
Physical activity - moderate	184 (19.8)	48 (14.6)	83 (22.0)	87 (18.2)	35 (22.2)	63 (23.7)
Physical activity - high	374 (40.3)	146 (44.2)	91 (24.1)	129 (26.9)	67 (42.4)	86 (32.3)
Current smoking	95 (9.2)	41 (11.4)	25 (6.2)	28 (5.3)	13 (7.5)	18 (6.4)

a. Hypertension status based on: self-reported hypertension diagnosis; self-reported HTN medication use (treated); and resting clinic BP, with controlled defined as SBP <140 mm Hg AND DBP <90 mm Hg.
b. Numbers/percentages may not sum to totals due to missing data.

evant contextual factors associated with distinct ambulatory BP patterns by employing other mobile health devices, including EMA and actigraphy.

The ultimate goal of this study is to identify phenotypes of individuals with shared contextual factors that are associated with the hypertensive ABP patterns detected by ABPM.

Ultimately, phenotyping individuals based on contextual factors can provide an early window into a person's or population's risk, advance more feasible ways to integrate ABPM, and identify areas for personalized, context-specific engagement and intervention.

With these phenotypes, we can then screen individuals and populations to identify who may most benefit from ABPM testing. This is important, as ABPM is not widely available given the resources needed to integrate ABPM into routine clinical care, the low reimbursement, and the inconvenience to patients. Ultimately, phenotyping individuals based on contextual factors can provide an

early window into a person's or population's risk, advance more feasible ways to integrate ABPM, and identify areas for personalized, context-specific engagement and intervention. This precision-based approach to HTN prevention, detection, and control can serve as a viable strategy to reduce health disparities among populations most vulnerable to the contextual factors influencing HTN.

We suspect sustained HTN, masked HTN and nocturnal non-dipping to be common in the ECS population. While we observed some differences by island, nearly 50% self-reported a prior diagnosis of HTN and in the remaining group, two-thirds had a resting clinic BP that was elevated or in the hypertensive range. These rates likely underestimate the total burden of HTN, as prior data suggest that masked HTN (not assessed in ECS Wave 1) is prevalent among 14%-30% of individuals with a normal resting BP. In the Jackson Heart Study, a cohort study of African Americans, masked HTN was observed in 35% of participants, with an associated rate of target organ damage that was similar to the sub-group with diagnosed HTN.[14] In the Coronary Artery Risk Development in Young Adults (CARDIA) study, ambulatory BP was higher in African Americans than Whites, as were several ABP patterns associated with CVD risk, including masked HTN.[13] Given the known associations between masked HTN and nocturnal non-dipping with cardiovascular events and mortality, and the higher prevalence of these sub-types of HTN among African American and Hispanic populations, it is no longer sufficient to

rely solely on resting BP to diagnose and manage BP; moreover, doing so may perpetuate health disparities.[23-25]

There is also a need to identify the factors contributing to ABP patterns.[33-37] Specifically, the contextual factors that provoke elevations in BP – that, when averaged, result in a diagnosis of masked HTN and that keep the BP elevated during the night - are either overlooked or unlinked to the ABP, with missed opportunities for engagement and intervention. In this study, aspects of the physical and social environment; momentary and chronic stress related to work, relationships, racism, discrimination, and violence; emotional experiences in response to the environment and stressors; and lifestyle choices made in the setting of these exposures, are assessed by combining data from self-reported questionnaires (EMA) with ABPM, and self-reported survey data, captured during each wave of the study. Integration of these data can reveal exposure-experience-response patterns that are critical to addressing health disparities in preventing HTN.

A second innovation is the use of multiple mobile health technologies to capture ABP patterns, physical activity, sleep, and daily life experiences in a high-risk population with documented evidence of chronic and acute stress. The ABPM combined with EMA, along with data from the ActiGraph can reveal the effects of this stress on momentary and lagged ABP, including nocturnal BP dipping, and on sleep, which may relate to nocturnal BP dipping. For example, a person living in an impoverished urban neighborhood,

with few opportunities for work and high crime rates, may experience discrimination in her daily life activities (captured by EMA). In response, she feels angry (EMA) and her BP rises (ABPM). Her BP remains elevated for the next 3 hours (ABPM). That night she sleeps poorly (actigraphy), and her BP does not markedly dip (ABPM). Illuminating such patterns fundamentally changes the patient and clinician's capacity to understand the person-specific factors contributing to HTN risk, while revealing actionable factors related to emotion, coping, and lifestyle. Furthermore, the study will advance the health disparities literature, which has mostly focused on cross-sectional associations, to now include longitudinal data that links individual experience and response to environment/stress with actual change in patterns of blood pressure.

Third, the focus on residents in the Eastern Caribbean may hold important insights for reducing disparities. Prior studies demonstrate an increased risk of cerebrovascular disease among Afro-Caribbean populations compared with other ethnic groups.[4] Additionally, residents of these islands frequently migrate between the United States and home islands, and many permanent residents and citizens of the United States identify genetically and culturally with these islands and other islands in the Eastern Caribbean. In the most recent US Census, the proportion of individuals reporting their country of birth as one of the Caribbean islands grew substantively, with the largest proportion residing in the New York-New Jersey-Pennsylvania metropolitan area.[38]

CONCLUSION

This study will integrate ABPM with other mobile technologies to identify the person-specific contextual factors that influence distinct ABP patterns associated with increased cardiovascular risk. Using advanced computational methods to identify phenotypes of contextually-linked ABP patterns, we aim to inform a more precision-based, culturally sensitive approach for assessing HTN risk among Eastern Caribbean populations, in whom environmental and psychosocial stressors may play a key role in HTN prevalence and outcomes. Data from this study will inform the development of tools to identify persons with contextual factors associated with HTN risk, which can help to facilitate early screening with ABPM and the prevention and management of HTN, with the ultimate goal of engaging people in their health and advancing equity in hypertension outcomes.

CONFLICT OF INTEREST
No conflicts of interest to report.

AUTHOR CONTRIBUTIONS
Research concept and design: Spatz, Burg, Nunez-Smith; Acquisition of data: Tessier-Sherman, Mortazavi; Data analysis and interpretation: Spatz, Martinez-Brockman, Tessier-Sherman, Mortazavi, Roy, Schwartz, Nazario, Maharaj, Nunez, Adams, Burg, Nunez-Smith; Manuscript draft: Spatz; Statistical expertise: Tessier-Sherman, Mortazavi; Acquisition of funding: Nunez-Smith; Administrative: Martinez-Brockman; Supervision: Nunez-Smith, Burg

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