## Title

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# Superiority of Out-of-Office Blood Pressure for Predicting Hypertensive Heart Disease in non-Hispanic Black Adults 

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#### Abstract

Black Americans suffer disproportionately from hypertension and hypertensive heart disease. Out-of-office blood pressure is more predictive for cardiovascular complications than clinic BP; however, the relative abilities of clinic and out-of-office BP to predict left ventricular hypertrophy in black and white adults has not been established. Thus, we aimed to compare associations of out-of-office and clinic blood pressure measurement with left ventricular hypertrophy by cardiac magnetic resonance imaging among non-Hispanic black and white adults. In this cross-sectional study, 1,262 black and 927 white participants of the Dallas Heart Study ages 30-64 years underwent assessment of standardized clinic and out-of-office (research staff-obtained) blood pressure and left ventricular mass index. In multivariable-adjusted analyses of treated and untreated participants, out-of-office blood pressure was a stronger determinant of left ventricular hypertrophy than clinic blood pressure (odds ratio [OR] per $10 \mathrm{mmHg}, 1.48,95 \%$ CI 1.34-1.64 for out-of-office systolic BP and 1.15 [1.04-1.28] for clinic systolic BP; 1.71 [1.43-2.05] for out-ofoffice diastolic BP and 1.03 [0.86-1.24] for clinic diastolic BP). Non-Hispanic black race/ethnicity, treatment status and lower left ventricular ejection fraction were also independent determinants of hypertrophy. Among treated Blacks, the differential association between out-of-office and clinic BP with hypertrophy was more pronounced than in treated white or untreated participants. In


[^0]conclusion, protocol-driven supervised out-of-office BP monitoring provides important information that cannot be gleaned from clinic blood pressure assessment alone. Our results underscore the importance of hypertension management programs outside the medical office to prevent hypertensive heart disease, especially in high-risk black adults.

## Graphical Abstract



## Keywords

Blood pressure monitoring; left ventricular hypertrophy; racial disparities; masked hypertension; hypertension control; hypertensive heart disease

## INTRODUCTION

Non-Hispanic (NH) black Americans suffer disproportionately from hypertension (HTN). ${ }^{1}$ Compared with all other US demographic groups, HTN is more prevalent, more severe, and causes more left ventricular hypertrophy (LVH) in NH blacks, ${ }^{2,3}$ which is a powerful predictor of hypertensive complications including heart failure, stroke, kidney failure, and premature death. ${ }^{2,4-8}$.In black individuals, high blood pressure (BP) starts as early as age ten, ${ }^{9}$ and is associated with a more rapid transition from prehypertension to HTN. ${ }^{10}$ The greater aggregate hemodynamic burden from earlier and more severe HTN and greater risk of hypertensive complications has engendered a debate as to whether black patients should have lower-than-usual BP treatment goals. ${ }^{11}$

The debate is over conventional clinic BP measurements, which can lead to both, overtreatment of white-coat aggravated HTN and under-treatment of masked HTN. ${ }^{12,13}$ Ideally, BP is assessed with ambulatory BP monitoring to detect white coat HTN—high/ uncontrolled BP only in the medical clinic— and masked (uncontrolled) HTN—high/ uncontrolled BP only outside the medical clinic-and nocturnal HTN, the latter of which is known to be common in black persons. ${ }^{14-17}$ However, ambulatory BP monitoring is not widely utilized in everyday clinical practice due to its high cost and low reimbursement. 13,18,19

Unlike nocturnal BP assessment, daytime out-of-office BP measurement (usually performed by the patient or a home nurse) is inexpensive, if standardized and protocol-driven, easy to obtain and reasonably reliable. ${ }^{20}$ Yet, previous studies have not determined the importance and differences between out-of-office vs. clinic BP as determinant of LVH in black and white adults.

To obtain unbiased estimates of out-of-office vs. clinic BP values at the population level, we analyzed data of 1,262 black and 927 white adults who participated in the Dallas Heart Study, a multiethnic probability sample of the residential population of Dallas County, Texas, and who underwent standardized out-of-office and clinic BP assessment. ${ }^{21}$

We hypothesized that (1) due to greater life-long hemodynamic burden, LVH is more common among black vs. white participants, (2) due to greater hemodynamic burden and incomplete correction of HTN, LVH is more common in treated vs. untreated participants; (3) because out-of-office BP is a better indicator of an individual's "true BP," it is also a stronger determinant of LVH than clinic BP. If true, this finding would provide further justification to promote HTN diagnosis and treatment programs that occur outside the medical office. ${ }^{22,23}$

## METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request and approval by the institutional review boards and the publication committee of the Dallas Heart Study. The study was approved by the institutional review board (IRB) at both the University of Texas Southwestern Medical Center and the Research Triangle Institute. Secondary analysis of the original data was approved by the Cedars-Sinai IRB. All study participants provided written informed consent.

Dallas Heart Study Sample—Participants in the Dallas Heart Study constitute a probability-based residential population sample for examining cardiovascular health problems disproportionately affecting NH black individuals, who therefore were oversampled; the methods, participation rates, and sample validation have been described previously. ${ }^{21}$ The analyses in this report are based on 1262 NH black and 927 NH white participants who had a complete set of BP measurements in the home ("out-of-office BP") and in the research clinic, completed the health survey, and underwent cardiac MRI (patient flow chart, Figure 1). Hispanic white and black participants as well as other groups were excluded due to low sample size.

## Outcome variables

Measurement of BP—Both out-of-office and clinic BP were measured using a validated oscillometric monitor (Welch Allyn, series 52000, Arden, North Carolina) ${ }^{24}$ by research staff who were trained in proper technique. ${ }^{21}$ For each participant, the appropriately sized arm cuff was determined, recorded, and used for all subsequent BP measurements. After at least 10 minutes of rest with the subject seated, back supported, legs uncrossed and the cuff at heart level, five consecutive measurements at each of two home visits (separated by a mean of $\sim 14$ days) followed by a research clinic visit (a mean of $\sim 30$ days after the second home visit). Measurements on the first home monitoring day are known to be higher and unstable and therefore were excluded, as recommended ${ }^{25}$ and substantiated by preparatory field work. ${ }^{21}$ To further reduce the influence of an alerting reaction on BP measurements, ${ }^{26}$ the average of the last three of five readings at the second home visit and the average of the last three of five readings at the clinic visit were used to calculate mean values for out-ofoffice and clinic BP, respectively.

Definition of BP categories-We list BP categories based on clinic and out-of-office BP as normotension, white-coat HTN, masked HTN and sustained HTN in the untreated; and controlled HTN, office-only uncontrolled HTN (which may include unnecessarily treated participants with white-coat HTN or appropriately treated participants with a residual whitecoat tendency), masked uncontrolled HTN and uncontrolled HTN both per previous (out-ofoffice $<135 / 85 \mathrm{mmHg}$; clinic $<140 / 90 \mathrm{mmHg}$ define normality) and current guidelines ( $<130 / 80 \mathrm{mmHg}$ for both out-of-office and clinic BP define normality) due to the ongoing and unresolved debate about normal cut-off values and nomenclature for these categories. 25,27-29

Cardiac MRI—Electrocardiographic-gated stacks of short axis images were obtained during breath-hold with a 1.5 T MRI system (Phillips Medical Systems, Best, The Netherlands). Left ventricular muscle mass was obtained by manual tracing of the endocardial and epicardial border of each slice and summation using the method of disks. As previously reported, interobserver variability was $9.2 \pm 5 \mathrm{~g}(5.8 \pm 3.5 \%$; $\mathrm{n}=15)$, intraobserver variability was $10.5 \pm 8.6 \mathrm{~g}(7.1 \pm 6.0 \% ; \mathrm{n}=8)$ and interscan variability was $4.9 \pm 10.9 \mathrm{~g}$ $(2.9 \pm 7.5 \% ; n=8) .{ }^{30}$ Furthermore, left ventricular ejection fraction was derived from: (left ventricular enddiastolic volume-left ventricular endsystolic volume)/left ventricular enddiastolic volume; and expressed as \% (standard error). Cardiac MRIs were performed on the same day when research clinic BP was assessed.

Definition of LVH by cardiac MRI—In a healthy subpopulation of Dallas Heart Study participants with normal body weight, gender-specific values of LV mass indexed to body surface (left ventricular mass index, LVMI) were obtained to define normal values as previously described. ${ }^{30}$ LVH was defined as LVMI values greater than $97.5^{\text {th }}$ percentile: 89 $\mathrm{g} / \mathrm{m}^{2}$ for women and $112 \mathrm{~g} / \mathrm{m}^{2}$ for men. ${ }^{30}$

Statistical methods-Descriptive statistics of participant characteristics of antihypertensive medication untreated and treated NH black vs. NH white participants were summarized as means and standard deviation (SD) for continuous variables and as percentages for categorical variables (Table 1). Differences in baseline characteristics between black and white subjects were compared with student $t$-test and Chi-square statistics, as appropriate. In logistic regression models for LVH in the overall population, and the subgroups of antihypertensive untreated and treated participants, we considered the following explanatory variables for the models: age, gender, race/ethnicity, body mass index (BMI), marital status, history of diabetes, current smoking, poverty factor (calculated as annual income divided by 2007 U.S. poverty threshold: $\$ 10,210$ for a single person and $\$ 20,650$ for a 4-person household), health insurance status and established primary physician care. In the LVH prediction model we also added clinic and out-of-office systolic BP. Non-linear relationships were evaluated with restricted cubic splines in the model, as were interaction terms (no non-linear terms or interaction-terms were statistically significant). Backward variable elimination of non-significant variables at an $\alpha$-level>0.05 except for age and diabetes (previously described risk factors for LVH) derived a parsimonious model for masked HTN and LVH. Adjusted odds ratios (aOR) and 95\% confidence intervals (CI) are reported. To address collinearity between clinic and out-ofoffice systolic BP (correlation coefficient $=0.72$, variance inflation factor 2.1 to 2.2 ) in the regression models, we centered each BP variable (to a normal systolic BP value of 120) and included their interaction as a predictor (not significant thus not included in the model). We compared model fit using the Akaike and Bayesian Information Criteria. We used changes in the deviance statistic, Delta(-2LogLikelihood), to determine that the model with both BP variables had significantly better statistical fit than models with only one BP predictor. To further demonstrate the greater independent association between out-of-office than clinic systolic BP with LVH, we created separate models for LVH, with only clinic or out-of-office systolic BP included and compared the strength of association ( $\beta$-estimates) of out-of-office vs. clinic BP with LVH by cardiac MRI using the Wald's test. Uniformly, out-of-office
systolic BP was the stronger determinant of LVH compared to clinic systolic BP (Wald's test $\mathrm{p}<0.01$ ), in the overall population, as well as in the untreated and treated subgroups. Model fit/performance also was better with out-of-office systolic BP and best with inclusion of both in the model. In addition, we repeated multivariable analyses with clinic and out-of-office diastolic BP in the model. SAS version 9.4 (SAS Institute Inc., Cary, NC) and Frank Harrell's rms library in R version 2.15.3 (The R Foundation for Statistical Computing) were used for statistical analyses.

## RESULTS

## Characteristics of Treated and Untreated NH Black and NH White Participants

The patient flow diagram is shown in Figure 1. Characteristics of the included untreated and treated black and white participants are shown in Table 1. Untreated participants were younger, less likely to be obese and NH Blacks had lower adjusted household annual income and were less likely to be married than NH Whites, had higher clinic and out-of-office BPs and greater LV mass index by cardiac MRI than Whites regardless of treatment status.

## Clinic and out-of-office BP measurements

BP measurements obtained both in the clinic and at the participants home showed a downward trend with repeated measurements (i.e., alerting reaction during initial cuff inflation, Figure 2). This alerting reaction was previously shown in the Dallas Heart Study to be independently associated with target organ complications. ${ }^{31}$ On average, while BP readings obtained from NH Blacks were higher than those of Whites, at all readings and sittings, in untreated participants-both black and white-out-of-office systolic BP was lower than clinic systolic BP, suggesting a white-coat effect. However, in treated participants this difference was smaller in white participants and reverse in NH Blacks suggesting a masked HTN effect (Table 1, Figure 2).

## Effect of the 2017 revision of the JNC-7 guidelines

As shown in supplemental table S1, the adoption of the 2017 revision of the JNC-7 guidelines ${ }^{25,27-29}$ immediately caused the prevalence of participants in the BP categories that definitively infer elevated risk-sustained HTN and masked HTN in the untreated and uncontrolled and masked uncontrolled HTN in the treated subgroups-to rise from $23 \%$ to $37 \%$ in black untreated and from $11 \%$ to $17 \%$ in white untreated participants. Furthermore, the proportion of treated participants that fall into these elevated risk BP categories increased from $62 \%$ to $70 \%$ in NH Blacks and from $45 \%$ to $53 \%$ in NH Whites.

## Factors Associated with LVH

Both systolic and diastolic out-of-office and clinic BPs were higher in white and black participants with LVH. After multi-variable adjustment among all participants, while LVH was strongly associated with clinic systolic BP (per 10 mmHg , aOR $1.15,95 \%$ CI 1.04-1.28) it was more strongly associated with out-of-office systolic BP (per 10 mmHg , aOR 1.48 , $95 \%$ CI 1.34-1.64). NH Black race/ethnicity was a strong independent determinate of LVH (aOR 1.82, $95 \%$ CI 1.28-2.61) , as was lower left ventricular ejection fraction (aOR 0.78, $95 \%$ CI 0.73-0.84), current smoking and antihypertensive medication treatment, while
higher adjusted household income was protective from presence of LVH (table 2, supplemental table S2; no other characteristics listed in Table 1 were independently associated with LVH).

Results were similar in the subgroups of untreated and treated black participants. However, we found a greater odds ratio for LVH associated with clinic systolic BP among untreated black participants-indicating that in this group, clinic BP evaluation appears to be a reasonable screening tool which should be confirmed with home or ambulatory BP assessment. Out-of-office systolic BP was strongly associated with LVH in treated but not in untreated white participants (supplemental Table S3). Statistical power in the latter group however was low with an LVH prevalence of only $4 \%$.

In the treated subgroup of participants, clinic systolic BP was not a significant determinant of LVH after adjustment for out-of-office systolic BP, underscoring the differential importance of evaluating out-of-office BP to guide HTN treatment. The fact that all other variables—including NH black race/ethnicity—did not associate at an alpha level of 0.05, may be at least partially explained by the significantly lower statistical power in this subgroup.

Additional multivariable-adjusted analyses of determinants of LVH with inclusion of diastolic BP values showed also a stronger association of out-of-office than clinic diastolic BP with LVH among other predictors (supplemental table S2). Overall model fit for LVH was worse with diastolic BP values than with systolic BP values.

Figure 3 shows that the gradient of increased LVH probability with increased systolic BP was much steeper for out-of-office BP than for clinic BP among treated black participants ( $\mathrm{p}<0.01$ ). Similar trends were found for treated white participants and for untreated black and white participants, but these trends did not achieve statistical significance.

## DISCUSSION

In the largest and, to our knowledge, the first population-based study comparing out-ofoffice vs. clinic BP with cardiac MRI-derived LVH among NH white and NH black adults, yielded several important insights: First, in treated NH blacks out-of-office BP values were not lower, but numerically higher than clinic BP values suggesting a masked HTN effect in this high-risk group. Second, out-of-office systolic BP was a more potent determinant of LVH in all participants irrespective of race/ethnicity or treatment status. Third, among treated NH black participants, the gradient of increased LVH probability with increased systolic BP was much steeper for out-of-office BP than for clinic BP, suggesting that assessment of systolic BP outside the doctor's office is crucially important and that ignoring these values constitutes a potentially missed opportunity for preventing or treating hypertensive heart disease.

Two distinctive features of the Dallas Heart Study—rigorous protocol-driven measurement of both out-of-office BP and clinic BP, and a high prevalence of untreated HTN—allowed us to uncover the importance of out-of-office BP assessment. The effect was especially strong

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in high-risk NH black hypertensives, who have in general a much higher rate of HTN-related complications including hypertensive heart disease, compared to other groups. ${ }^{2,3}$

In our multi-ethnic population-based study, antihypertensive drug therapy uncovered a "masked HTN" effect in treated hypertensive NH blacks. Previously, in strictly non-black clinic cohorts, antihypertensive therapy has been shown to lower conventional clinic/office BP more than it lowers 24-hour ambulatory BP, thus in many patients converting sustained HTN to masked (or partially-treated) HTN. ${ }^{26,32-35}$ Our data show that out-of-office BP monitoring is sufficient-except for the detection of uncontrolled nocturnal HTN which can only be derived from ambulatory BP monitoring-to detect cases of such partially-treated HTN that merit intensification of therapy. These results agree with echocardiogram-derived LVH of a smaller study, which indicated that home BP and ambulatory BP have a similar ability to detect HTN-related target organ damage. ${ }^{36}$ In addition, in a large study from Belgium research-staff obtained out-off-office BP readings-similarly to our studypredicted cardiovascular events underscoring the validity and importance of our findings. ${ }^{37}$

While many prior studies have emphasized nocturnal HTN as one cause for the excessive LVH in blacks, ${ }^{9,14,15,38,39}$ our data implicate daytime uncontrolled out-of-office systolic BP as another potential cause. Among treated black adults the dramatically steeper gradient of LVH with out-of-office than clinic systolic BP suggests that evidence-based out-of-office BP treatment goals will need to be established to optimize the medical management of HTN and the prevention of hypertensive heart disease. The comparatively flat slope of the clinic systolic BP- LVH relationship suggests that the debate over lower-than-usual BP goals for black patients is less important than whether out-of-office BP monitoring should become the gold standard for managing HTN. Although previous studies have established optimal thresholds for out-of-office BP among different ethnic groups, the thresholds were established based on cardiovascular outcomes rather than left ventricular structure or function. ${ }^{25,40}$

We also demonstrate a close association of lower LVEF with LVH, which has been previously described in the population-based Cardiovascular Health Study. ${ }^{41}$ Increased LV mass indexed to body surface area was a strong predictor of depressed left ventricular function after an average of 4.9 years of follow up independently of age, baseline blood pressure, diabetes, and coronary artery disease.

Several limitations of our study should be noted. Our data do not provide information on causality or a mechanistic explanation for the higher out-of-office than clinic BP in treated black hypertensives; greater psychosocial life stress is one documented cause. ${ }^{42}$ Out-ofoffice BP measurement was assessed in a standardized fashion by research staff not participants, which may have resulted in a small residual white-coat effect associated with out-of-office BP readings. Our out-of-office BP measurements are therefore not completely interchangeable with usual self-home BP monitoring. However, because of this small residual white-coat effect the magnitude of the difference between clinic and out-of-office BP as well as the association of out-of-office BP with LVH is-if at all-underestimated in our study. Furthermore, ambulatory monitoring data, which provides more measurements during daily activities including sleep and thus is superior to out-of-office BP assessment
alone, was not assessed. Nonetheless, these out-of-office BP readings were sufficient to show an independent association with LVH. Although out-of-office BP assessment has inferior sensitivity to detect masked HTN or uncontrolled (daytime and nighttime) HTN, 43,44 it plays an important role in the management of HTN. ${ }^{37}$ Lastly, we cannot completely exclude that antihypertensive treatment was started or intensified between home and clinic visits, which may have lowered clinic BP and overestimate the prevalence of masked HTN. However, other community-based BP screening studies show that only a very small percentage of patients receive a new diagnosis of HTN or get started on antihypertensive treatment in such programs. ${ }^{45-47}$ Furthermore, the prevalence of masked HTN in our study is consistent with ${ }^{48}$ or even below that of previous studies, ${ }^{49}$ which in part may be due to the fact that masked HTN is linked to older age and that the mean age in our study was comparably lower.

## Perspectives

This cross-sectional study shows that protocol-driven out-of-office BP monitoring provides important information that cannot be gleaned from clinic BPs alone. This finding has strong implications for the diagnosis and medical management of HTN in the high-risk black population in whom out-of-office BP is commonly higher than clinic BP (i.e., masked HTN). In this era of evidence-based practice guidelines, a randomized controlled trial is needed to prove that treatment of out-of-office (or ambulatory) BP is superior to the treatment of clinic BP. Yet, our observational data raise a potential concern that strict reliance on conventional clinic/office-based BPs promotes missed opportunities for preventing hypertensive heart disease in blacks. Importantly, our data justify HTN detection and management programs that focus on BP measured outside the medical office. ${ }^{22,23}$ Clinical outcome trials that evaluate out-of-office BP as treatment target are indicated.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## References

1. Guo F, He D, Zhang W, Walton RG. Trends in prevalence, awareness, management, and control of hypertension among United States adults, 1999 to 2010. Journal of the American College of Cardiology. 2012;60(7):599-606. [PubMed: 22796254]
2. Akintoye E, Mahmoud K, Shokr M, et al. Racial/ethnic differences in the prognostic utility of left ventricular mass index for incident cardiovascular disease. Clin Cardiol. 2018;41(4):502-509. [PubMed: 29663526]
3. Abdalla M, Booth JN 3rd, Diaz KM, Sims M, Muntner P, Shimbo D. Hypertension and alterations in left ventricular structure and geometry in African Americans: the Jackson Heart Study. J Am Soc Hypertens. 2016;10(7):550-558 e510. [PubMed: 27339075]
4. Liao Y, Cooper RS, McGee DL, Mensah GA, Ghali JK. The relative effects of left ventricular hypertrophy, coronary artery disease, and ventricular dysfunction on survival among black adults. JAMA : the journal of the American Medical Association. 1995;273(20):1592-1597. [PubMed: 7745772]
5. Peterson GE, de Backer T, Contreras G, et al. Relationship of left ventricular hypertrophy and diastolic function with cardiovascular and renal outcomes in African Americans with hypertensive chronic kidney disease. Hypertension. 2013;62(3):518-525. [PubMed: 23836799]
6. Peterson GE, de Backer T, Gabriel A, et al. Prevalence and correlates of left ventricular hypertrophy in the African American Study of Kidney Disease Cohort Study. Hypertension. 2007;50(6):10331039. [PubMed: 17968003]
7. Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. Journal of the American College of Cardiology. 2008;52(25):2148-2155. [PubMed: 19095132]
8. Pandey A, Keshvani N, Ayers C, et al. Association of Cardiac Injury and Malignant Left Ventricular Hypertrophy With Risk of Heart Failure in African Americans: The Jackson Heart Study. JAMA Cardiol. 2019;4(1):51-58 [PubMed: 30566191]
9. Wang X, Poole JC, Treiber FA, Harshfield GA, Hanevold CD, Snieder H. Ethnic and gender differences in ambulatory blood pressure trajectories: results from a 15-year longitudinal study in youth and young adults. Circulation. 2006;114(25):2780-2787. [PubMed: 17130344]
10. Selassie A, Wagner CS, Laken ML, Ferguson ML, Ferdinand KC, Egan BM. Progression is accelerated from prehypertension to hypertension in blacks. Hypertension. 2011;58(4):579-587. [PubMed: 21911708]
11. Flack JM, Sica DA, Bakris G, et al. Management of high blood pressure in Blacks: an update of the International Society on Hypertension in Blacks consensus statement. Hypertension. 2010;56(5): 780-800. [PubMed: 20921433]
12. Pickering TG, Coats A, Mallion JM, Mancia G, Verdecchia P. Blood Pressure Monitoring. Task force V: White-coat hypertension. Blood pressure monitoring. 1999;4(6):333-341. [PubMed: 10602537]
13. Pickering TG, White WB, American Society of Hypertension Writing G. ASH Position Paper: Home and ambulatory blood pressure monitoring. When and how to use self (home) and ambulatory blood pressure monitoring. Journal of clinical hypertension (Greenwich, Conn). 2008;10(11):850-855.
14. Profant J, Dimsdale JE. Race and diurnal blood pressure patterns. A review and meta-analysis. Hypertension. 1999;33(5):1099-1104. [PubMed: 10334794]
15. Harshfield GA, Barbeau P, Richey PA, Alpert BS. Racial differences in the influence of body size on ambulatory blood pressure in youths. Blood pressure monitoring. 2000;5(2):59-63. [PubMed: 10828891]
16. Redmond N, Booth JN 3rd, Tanner RM, et al. Prevalence of Masked Hypertension and Its Association With Subclinical Cardiovascular Disease in African Americans: Results From the Jackson Heart Study. J Am Heart Assoc. 2016;5(3):e002284. [PubMed: 27025968]
17. Abdalla M, Caughey MC, Tanner RM, et al. Associations of Blood Pressure Dipping Patterns With Left Ventricular Mass and Left Ventricular Hypertrophy in Blacks: The Jackson Heart Study. J Am Heart Assoc. 2017;6(4).
18. Pickering TG, Miller NH, Ogedegbe G, et al. Call to action on use and reimbursement for home blood pressure monitoring: a joint scientific statement from the American Heart Association, American Society Of Hypertension, and Preventive Cardiovascular Nurses Association. Hypertension. 2008;52(1):10-29. [PubMed: 18497370]
19. Krause T, Lovibond K, Caulfield M, McCormack T, Williams B, Guideline Development G. Management of hypertension: summary of NICE guidance. BMJ (Clinical research ed). 2011;343:d4891.
20. Mengden T, Chamontin B, Phong Chau N, Luis Palma Gamiz J, Chanudet X. User procedure for self-measurement of blood pressure. First International Consensus Conference on Self Blood Pressure Measurement. Blood Press Monit. 2000;5(2):111-129. [PubMed: 10828898]
21. Victor RG, Haley RW, Willett DL, et al. The Dallas Heart Study: a population-based probability sample for the multidisciplinary study of ethnic differences in cardiovascular health. The American Journal of Cardiology. 2004;93(12):1473-1480. [PubMed: 15194016]
22. Victor RG, Lynch K, Li N, et al. A Cluster-Randomized Trial of Blood-Pressure Reduction in Black Barbershops. N Engl J Med. 2018;378(14):1291-1301. [PubMed: 29527973]
23. Victor RG, Blyler CA, Li N, et al. Sustainability of Blood Pressure Reduction in Black Barbershops. Circulation. 2019;139(1):10-19. [PubMed: 30592662]
24. Jones CR, Taylor K, Poston L, Shennan AH. Validation of the Welch Allyn 'Vital Signs’ oscillometric blood pressure monitor. Journal of human hypertension. 2001;15(3):191-195. [PubMed: 11317204]
25. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/ American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2017. doi: 10.1016/j.jacc.2017.11.006.
26. Mancia G, Parati G. Office compared with ambulatory blood pressure in assessing response to antihypertensive treatment: a meta-analysis. Journal of hypertension. 2004;22(3):435-445. [PubMed: 15076144]
27. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42(6):1206-1252. [PubMed: 14656957]
28. Franklin SS, Thijs L, Hansen TW, O'Brien E, Staessen JA. White-coat hypertension: new insights from recent studies. Hypertension. 2013;62(6):982-987. [PubMed: 24041952]
29. Feitosa ADM, Mota-Gomes MA, Miranda RD, et al. Impact of 2017 ACC/AHA hypertension guidelines on the prevalence of white-coat and masked hypertension: A home blood pressure monitoring study. J Clin Hypertens (Greenwich). 2018;20(12):1745-1747. [PubMed: 30378263]
30. Drazner MH, Dries DL, Peshock RM, et al. Left ventricular hypertrophy is more prevalent in blacks than whites in the general population: the Dallas Heart Study. Hypertension. 2005;46(1): 124-129. [PubMed: 15939807]
31. Velasco A, Ayers C, Das SR, et al. Target organ complications and prognostic significance of alerting reaction: analysis from the Dallas Heart Study. J Hypertens. 2016;34(2):226-234. [PubMed: 26485459]
32. Staessen JA, Den Hond E, Celis H, et al. Antihypertensive treatment based on blood pressure measurement at home or in the physician's office: a randomized controlled trial. JAMA : the journal of the American Medical Association. 2004;291(8):955-964. [PubMed: 14982911]
33. Staessen JA, Byttebier G, Buntinx F, Celis H, O’Brien ET, Fagard R. Antihypertensive treatment based on conventional or ambulatory blood pressure measurement. A randomized controlled trial. Ambulatory Blood Pressure Monitoring and Treatment of Hypertension Investigators. JAMA : the journal of the American Medical Association. 1997;278(13):1065-1072. [PubMed: 9315764]
34. Franklin SS, Thijs L, Li Y, et al. Masked hypertension in diabetes mellitus: treatment implications for clinical practice. Hypertension. 2013;61(5):964-971. [PubMed: 23478096]
35. Franklin SS, Thijs L, Hansen TW, et al. Significance of white-coat hypertension in older persons with isolated systolic hypertension: a meta-analysis using the International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes population. Hypertension. 2012;59(3):564-571. [PubMed: 22252396]
36. Stergiou GS, Argyraki KK, Moyssakis I, et al. Home blood pressure is as reliable as ambulatory blood pressure in predicting target-organ damage in hypertension. Am J Hypertens. 2007;20(6): 616-621. [PubMed: 17531917]
37. Schutte R, Thijs L, Liu YP, et al. Within-subject blood pressure level--not variability--predicts fatal and nonfatal outcomes in a general population. Hypertension. 2012;60(5):1138-1147. [PubMed: 23071126]
38. Ogedegbe G, Spruill TM, Sarpong DF, et al. Correlates of isolated nocturnal hypertension and target organ damage in a population-based cohort of African Americans: the Jackson Heart Study. American journal of hypertension. 2013;26(8):1011-1016. [PubMed: 23676475]
39. Hebert LA, Agarwal G, Ladson-Wofford SE, et al. Nocturnal blood pressure in treated hypertensive African Americans Compared to treated hypertensive European Americans. Journal of the American Society of Nephrology : JASN. 1996;7(10):2130-2134. [PubMed: 8915972]
40. Vongpatanasin W, Ayers C, Lodhi H, et al. Diagnostic Thresholds for Blood Pressure Measured at Home in the Context of the 2017 Hypertension Guideline. Hypertension. 2018;72(6):1312-1319. [PubMed: 30571225]
41. Drazner MH, Rame JE, Marino EK, et al. Increased left ventricular mass is a risk factor for the development of a depressed left ventricular ejection fraction within five years: the Cardiovascular Health Study. Journal of the American College of Cardiology. 2004;43(12):2207-2215. [PubMed: 15193681]
42. Schoenthaler AM, Schwartz J, Cassells A, Tobin JN, Brondolo E. Daily interpersonal conflict predicts masked hypertension in an urban sample. American journal of hypertension. 2010;23(10): 1082-1088. [PubMed: 20616788]
43. Zhang L, Li Y, Wei FF, et al. Strategies for classifying patients based on office, home, and ambulatory blood pressure measurement. Hypertension. 2015;65(6):1258-1265. [PubMed: 25870194]
44. Hanninen MR, Niiranen TJ, Puukka PJ, Jula AM. Comparison of home and ambulatory blood pressure measurement in the diagnosis of masked hypertension. J Hypertens. 2010;28(4):709-714. [PubMed: 20061982]
45. Fleming S, Atherton H, McCartney D, et al. Self-Screening and Non-Physician Screening for Hypertension in Communities: A Systematic Review. Am J Hypertens. 2015;28(11):1316-1324. [PubMed: 25801901]
46. Victor RG, Ravenell JE, Freeman A, et al. Effectiveness of a barber-based intervention for improving hypertension control in black men: the BARBER-1 study: a cluster randomized trial. Archives of Internal Medicine. 2011;171(4):342-350. [PubMed: 20975012]
47. Hamilton W, Round A, Goodchild R, Baker C. Do community based self-reading sphygmomanometers improve detection of hypertension? A feasibility study. J Public Health Med. 2003;25(2):125-130. [PubMed: 12848401]
48. Wang YC, Shimbo D, Muntner P, Moran AE, Krakoff LR, Schwartz JE. Prevalence of Masked Hypertension Among US Adults With Nonelevated Clinic Blood Pressure. Am J Epidemiol. 2017;185(3):194-202. [PubMed: 28100465]
49. Thomas SJ, Booth JN 3rd, Bromfield SG, et al. Clinic and ambulatory blood pressure in a population-based sample of African Americans: the Jackson Heart Study. J Am Soc Hypertens. 2017;11(4):204-212 e205. [PubMed: 28285829]

## Novelty and Significance

## What is new?

Our unique study correlates protocol-driven clinic and out-of-office BP with left ventricular hypertrophy derived by the gold standard method, cardiac MRI in a large sample of non-Hispanic black and white adults.

What is relevant?
Out-of-office BP correlates much closer with presence of left ventricular hypertrophy than clinic BP.

## Summary:

Relying strictly on clinic BP in the management of hypertension constitutes for potential missed opportunities in the prevention of hypertensive heart disease.


Figure 1. Patient flow chart.
Abbreviations: BP indicates blood pressure; HTN, hypertension; MRI, magnetic resonance imaging; NH, non-Hispanic.

Untreated


Figure 2. Mean values (and standard errors) of subsequent blood pressure readings in untreated (top panels) and treated (bottom panels) in the research clinic and the participants' home.
Due to the alerting reaction initial high blood pressure readings continue to fall in subsequent measurements, leveling out in the last 3 readings. This observation provided rationale to use the average of the last three clinic and out-of-office blood pressure measurements for all analyses.


Figure 3. Adjusted probability of LVH using out-of-office vs. clinic BP measurements in treated and untreated participants.
After multivariate adjustment, the risk of LVH with higher systolic BP increases much more steeply with out-of-office than clinic BP (thicker line), particularly in treated NH black subjects (panel A, left) with less differential slopes in untreated participants (panel B) when other model variables are kept constant. Abbreviations: BP indicates blood pressure; NH, non-Hispanic.

Table 1.
Characteristics of untreated and treated NH black vs NH white participants

| Participant characteristics | Untreated for HTN |  | Treated for HTN |  |
| :---: | :---: | :---: | :---: | :---: |
|  | NH Black ( $\mathrm{n}=917$ ) | NH White ( $\mathrm{n}=735$ ) | NH Black ( $\mathrm{n}=417$ ) | NH White ( $\mathrm{n}=120$ ) |
| Demographic Characteristics |  |  |  |  |
| Age, mean (SD), years | 42 (9)* | 43 (10) | 51 (8) | 52 (7) |
| Female, \% | 57* | 51 | 64 | 55 |
| Body Mass Index, mean (SD), $\mathrm{kg} / \mathrm{m}^{2}$ | 29 (7) * | 28 (6) | 33 (8) | 32 (7) |
| Married or Living with Partner, \% | $38^{*}$ | 56 | 41* | 57 |
| Poverty Factor, ${ }^{\dagger}$ mean (SD) | 2.6 (1.8)* | 3.9 (2) | 2.6 (1.9)* | 4.0 (2.2) |
| Health Insurance, \% | 71 * | 84 | 81 | 88 |
| Blood Pressure, ${ }^{\not+}$ mean (SD), mmHg |  |  |  |  |
| Systolic, Clinic | 125 (17)* | 121 (13) | 139 (19)* | 133 (15) |
| Diastolic, Clinic | 77 (9)* | 76 (8) | 83 (10) * | 81 (9) |
| Systolic, Out-of-Office | 123 (16)* | 117 (13) | 141 (21)* | 132 (15) |
| Diastolic, Out-of-office | 78 (9)* | 74 (8) | 86 (11)* | 81 (8) |
| Cardiovascular Risk Factors and History |  |  |  |  |
| Family History of Hypertension, \% | 64 * | 54 | 78 | 72 |
| Diabetes, \% | 5 | 4 | 26 | 19 |
| Current Cigarette Smoker, \% | 31 | 28 | 32 * | 19 |
| Obesity, \% | 46* | 32 | 66 * | 56 |
| Prior MI, \% | 2 | 1 | 8 | 8 |
| Prior Stroke, \% | 1 | 1 | 9 | 5 |
| Laboratory data |  |  |  |  |
| Serum Creatinine, mean (SD), mg/dL | 0.9 (0.5)* | 0.9 (0.1) | 1.0 (0.8) | 0.9 (02) |
| Cardiac MRI data |  |  |  |  |
| LVEF, \% (SE) | 71 (0.08 | 71 (0.07) | 71 (0.1) | 72 (0.09) |
| LV Mass Index, mean (SD), $\mathrm{g} / \mathrm{m}^{2}$ | 85 (18)* | 79 (16) | 93 (27) * | 84 (20) |
| LVH, \% | 13* | 4 | $31^{*}$ | 17 |

* $\mathrm{P}<0.05$ for comparison between black and white.
${ }^{\dagger}$ Calculated as income/2007 United States poverty level: $\$ 10210$ for a single person and $\$ 20650$ for a 4-person household.
${ }^{7}$ Average blood pressure from last three of five measurements.
Abbreviations: DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; MI, myocardial infarction; No, number; SBP, systolic blood pressure; SD, standard deviation; SE, standard error.
Table 2.
Multivariable-adjusted determinants of LVH including clinic and out-of-office systolic BP values

|  | All Participants ( $\mathrm{n}=2,189,300$ with LVH) |  |  | Untreated ( $\mathrm{n}=1,652,152$ with LVH) |  |  | Treated ( $\mathrm{n}=537,148$ with LVH) |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Variables included in the model | OR | 95\% CI | $\mathbf{P}$ value | OR | 95\% CI | $P$ value | OR | 95\% CI | $P$ value |
| Clinic systolic BP, per 10 mmHg | 1.15 | 1.04-1.28 | 0.006 | 1.25 | 1.08-1.46 | 0.004 | 1.08 | 0.93-1.25 | 0.3 |
| Out-of-office systolic BP, per 10 mmHg | 1.48 | 1.34-1.64 | $<.0001$ | 1.40 | 1.20-1.63 | $<.0001$ | 1.55 | 1.35-1.79 | $<.0001$ |
| Age, per 10 years | 0.96 | 0.81-1.13 | 0.6 | 0.92 | 0.74-1.14 | 0.5 | 0.99 | 0.76-1.31 | 0.9 |
| NH Black race/ethnicity | 1.82 | 1.28-2.61 | 0.001 | 2.42 | 1.53-3.82 | 0.0002 | 1.21 | 0.67-2.18 | 0.5 |
| Diabetes | 1.35 | 0.88-1.94 | 0.19 | 1.31 | 0.65-2.66 | 0.4 | 1.26 | 0.77-2.05 | 0.4 |
| Smoking | 1.51 | 1.13-2.02 | 0.0003 | 1.69 | 1.16-2.47 | 0.007 | 1.33 | 0.83-2.11 | 0.2 |
| Poverty Factor (lower indicates less income), per 1 unit | 0.91 | 0.85-0.99 | 0.02 | 0.92 | 0.83-1.03 | 0.1 | 0.91 | 0.81-1.02 | 0.1 |
| Left ventricular ejection fraction, per 5\% | 0.78 | 0.73-0.84 | <. 0001 | 0.79 | 0.72-0.88 | <. 0001 | 0.77 | 0.69-0.86 | <. 0001 |
| Treated with antihypertensives | 1.47 | 1.06-2.03 | 0.02 | - | - | - | - | - | - |
| AUC of the regression model |  | 0.83 |  |  | 0.81 |  |  | 0.79 |  |

Abbreviations: HTN, hypertension; LVH, left ventricular hypertrophy; MRI, magnetic resonance imaging; OR, odds ratio; CI, confidence interval; AUC, area under the receiver-operator characteristic curve


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    This manuscript is dedicated to the life and work of our friend and mentor, the late Dr. Ronald Victor.
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    Conflicts of Interest/Disclosures: None

