## **Original Article**

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## Comparison of the association of masked hypertension defined by the 2017 ACC/AHA BP guideline versus the JNC7 guideline with left ventricular hypertrophy

Bharat Poudel<sup>a</sup>, Anthony J. Viera<sup>b</sup>, Daichi Shimbo<sup>c</sup>, Joseph E. Schwartz<sup>c,d</sup>, James M. Shikany<sup>a</sup>, Swati Sakhuja<sup>a</sup>, Donald M. Lloyd-Jones<sup>e</sup>, Paul Muntner<sup>a</sup>, and Yuichiro Yano<sup>b,f</sup>

**Background:** Compared with the Seventh Report of the Joint National Committee (JNC7), the 2017 American College of Cardiology/American Heart Association (ACC/ AHA) blood pressure (BP) guideline uses lower BP thresholds to define hypertension and BP control.

**Methods:** We pooled data from five US-based studies to compare the association of masked hypertension (MHT) and masked uncontrolled hypertension, defined using the 2017 ACC/AHA guideline (n = 1653 without high office BP; <130/80 mmHg) versus the JNC7 guideline (n = 2451 without high office BP; <140/90 mmHg), with left ventricular hypertrophy (LVH). MHT and masked uncontrolled hypertension were defined using office BP and awake BP alone and awake, asleep, or 24-h BP. LVH was assessed by echocardiography.

Results: Among participants without high office BP not taking antihypertensive medication, the prevalence of MHT defined by the JNC7 guideline and the 2017 ACC/AHA BP guideline was 25.0 and 33.5% using awake BP only and 37.1 and 52.0% when using awake, asleep, or 24-h BP. The adjusted prevalence ratios for LVH associated with MHT versus sustained normotension defined by the JNC7 and 2017 ACC/AHA BP guidelines were 1.72 [95% confidence interval (CI): 1.12-2.64] and 1.56 (95% CI: 0.97–2.51), respectively, when using awake BP only and 2.16 (95% CI: 1.36-3.44) and 1.03 (95% CI: 0.58-1.82), respectively, when using awake, asleep or 24-h BP. There was no evidence that masked uncontrolled hypertension was associated with LVH when defined using the BP thresholds in either the JNC7 or the 2017 ACC/AHA BP guideline.

**Conclusion:** The association of MHT with LVH may depend on the BP thresholds used.

**Keywords:** ambulatory blood pressure, masked hypertension, left ventricular hypertrophy, guideline

**Abbreviations:** ABPM, ambulatory blood pressure monitoring; ACC, American College of Cardiology; AHA, American Heart Association; BP, blood pressure; CARDIA, Coronary Artery Risk Development in Young Adults; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; IDH, Improving Detection of Hypertension; JHS, Jackson Heart Study; JNC7, Seventh Report of the Joint National Committee; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index; MHT, Masked Hypertension Study; NCMH, North Carolina Masked Hypertension

dults not taking antihypertensive medication are considered to have masked hypertension (MHT) if their mean blood pressure (BP) when measured in a healthcare setting (i.e. office BP) is below the threshold for defining hypertension and their mean BP is above the threshold for defining hypertension when measured outside of a healthcare setting (i.e. out-of-office BP) [1]. The analogous term for adults taking antihypertensive medication is masked uncontrolled hypertension. In previous studies, individuals with MHT and masked uncontrolled hypertension had a higher prevalence of subclinical cardiovascular disease (CVD) when compared with those whose BP both in and outside the office were below the threshold used to define hypertension, phenotypes called sustained normotension for those not taking antihypertensive medication and sustained controlled BP for those taking antihypertensive medication [2,3]. The 2017 American

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<sup>&</sup>lt;sup>a</sup>University of Alabama at Birmingham, Birmingham, Alabama, <sup>b</sup>Duke University, Durham, North Carolina, <sup>c</sup>Columbia University, New York, <sup>d</sup>Stony Brook University, Stony Brook, New York, <sup>e</sup>Northwestern University, Chicago, Illinois, USA and <sup>f</sup>Yokohama City University, Kanagawa, Japan

Correspondence to Yuichiro Yano, MD, PhD, Vice Director and Associate Professor, Center for Novel and Exploratory Clinical Trials, Yokohama City University, 1–1–1, Fukuura, Kanazawa-ku, Yokohama 236-0004, Kanagawa, Japan; Adjunct Associate Professor, Department of Family Medicine and Community Health, Duke University, 2200 W. Main Street, Erwin Square Building, Suite 600, Durham, NC 27705, USA. Tel: +1 919 613 1466; e-mail: yano.yuichiro@jichi.ac.jp/yyano@jichi.jp

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College of Cardiology (ACC)/American Heart Association (AHA) BP guideline recommends consideration of antihypertensive medication initiation for adults with MHT depending on their out-of-office BP levels and the presence of other risk factors, while adults who have masked uncontrolled hypertension should be considered for intensification of their antihypertensive medication regimen [4].

The 2017 ACC/AHA BP guideline uses lower office and out-of-office BP thresholds to define hypertension and BP control compared with the Seventh Report of the Joint National Committee (JNC7) guideline [4,5] (Table 1). Prior studies evaluating the association of MHT and masked uncontrolled hypertension with subclinical CVD have used the higher BP thresholds in the JNC7 guideline [4,6]. Estimating the prevalence of MHT and masked uncontrolled hypertension, and their association with subclinical CVD when defined by the lower BP thresholds in the 2017 ACC/AHA BP guideline may inform the value of screening for these phenotypes when using this guideline in clinical practice. We compared the prevalence of MHT and masked uncontrolled hypertension, defined using the 2017 ACC/AHA versus the JNC7 guideline. In addition, we compared the strength of the associations of MHT and masked uncontrolled hypertension when defined by the 2017 ACC/AHA guideline versus the JNC7 guideline with left ventricular mass index (LVMI) and left ventricular hypertrophy (LVH). To make these comparisons, we analyzed individual-level data pooled from five population-based, community-based, and practice-based studies conducted in the United States.

### **METHODS**

#### **Study participants**

We analyzed data from the Coronary Artery Risk Development in Young Adults (CARDIA) study, Jackson Heart Study (JHS), MHT study, Improving Detection of Hypertension (IDH) study, and North Carolina Masked Hypertension (NCMH) study. Details of the design and methods of each study have been described previously [7-11]. In brief, the CARDIA study enrolled 5115 Black and White adults, 18-30 vears of age, at four field centers in 1985–1986 [7]. Ambulatory blood pressure monitoring (ABPM) was conducted in 831 participants at the Birmingham and Chicago field centers as an ancillary study at the Year 30 examination in 2015-2016 and 740 participants had a complete ABPM recording as defined below [7]. The JHS is a communitybased prospective cohort study that enrolled 5306 Black adults aged at least 21 years between 2000 and 2004 [8]. Overall, 1148 JHS participants volunteered to undergo ABPM as part of their baseline study visit and 928 had a complete ABPM recording. The MHT study enrolled 1011 employees of Stony Brook University and Columbia University and affiliated hospitals, and a private hedge fund [9]. Between 2005 and 2012, 892 participants underwent ABPM of whom 731 had a complete ABPM recording. The IDH study is a community-based study that enrolled 408 participants between 2011 and 2013 of whom 376 had a complete ABPM recording [10]. The NCMH study enrolled 420 adults from primary care clinics in North Carolina between 2012 and 2014, and 272 participants had a complete ABPM recording [11]. No participants in the MHT, IDH and NCMH studies were taking antihypertensive medication, while CARDIA and JHS included participants not taking and taking antihypertensive medication. Each study's protocol was approved by the relevant institutional review board, and all participants provided written informed consent. The study protocol for the analysis of data from the five studies was approved by the institutional review board at the University of Alabama at Birmingham.

#### Data collection

Data were collected following standardized protocols in accordance with the quality control procedures of each study (Supplemental Table 1, http://links.lww.com/HJH/ B965).

 TABLE 1. Definitions of masked hypertension using office blood pressure and awake blood pressure only and office blood pressure and awake, asleep, or 24-h blood pressure according to the Seventh Report of the Joint National Committee guideline and the 2017 American College of Cardiology/American Heart Association blood pressure guideline

	JNC7 blood pre	ssure guideline	2017 ACC/AHA blood pressure guideline				
	Masked hypertension defined using awake BP only	Masked hypertension defined using awake, asleep, or 24-h BP	Masked hypertension defined using awake BP only	Masked hypertension defined using awake, asleep, or 24-h BP			
Office-measured BP	SBP < 140 mmHg and DBP < 90 mmHg	SBP < 140 mmHg and DBP < 90 mmHg	SBP < 130 mmHg and DBP < 80 mmHg	SBP < 130 mmHg and DBP < 80 mmHg			
	AND	AND	AND	AND			
Awake BP	SBP $\geq$ 135 mmHg or DBP $\geq$ 85 mmHg	SBP $\geq$ 135 mmHg or DBP $\geq$ 85 mmHg	SBP $\geq$ 130 mmHg or DBP $\geq$ 80 mmHg	SBP $\geq$ 130 mmHg or DBP $\geq$ 80 mmHg			
		OR		OR			
Asleep BP	-	SBP $\geq 120 \text{ mmHg or}$ DBP $\geq 70 \text{ mmHg}^{a}$	-	SBP $\geq$ 110 mmHg or DBP $\geq$ 65 mmHg			
		OR		OR			
24-h BP	-	SBP $\geq$ 130 mmHg or DBP $\geq$ 80 mmHg	-	SBP $\geq$ 125 mmHg or DBP $\geq$ 75 mmHg			

ACC/AHA, American College of Cardiology/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; BP, blood pressure; JNC7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. <sup>3</sup>The SBP and DBP thresholds for asleep blood pressure according to the JNC7 guideline are 120/75 mmHg. However, guidelines and scientific statements have adopted asleep SBP/DBP thresholds of 120/70 mmHg to correspond with office-measured SBP/DBP of 140/90 mmHg.

## Office and ambulatory blood pressure monitoring blood pressure measurements

The assessment of office BP and ABPM in each study followed standardized protocols as summarized in Supplemental Table 2, http://links.lww.com/HJH/B965. Office BP was measured at least two times in participants' nondominant arm at at least 1-min intervals after they had been seated in a quiet room for 5 min during multiple study visits for the MHT, IDH, and NCMH studies and during a single study visit at baseline in the JHS and at Year 30 in the CARDIA study. For consistency across studies, we used office BP from the first visit for the MHT, IDH, and NCMH studies. We averaged three office BP measurements for CARDIA, MHT, IDH, and NCMH participants and two office BP measurements for JHS participants.

Participants were fitted with a validated ABPM device on their nondominant arm and asked to wear it for 24 h. The awake and asleep periods during the ABPM procedure were documented using actigraphy supplemented by sleep diaries for CARDIA, MHT, and IDH participants. Selfreported awake and asleep times were used in the JHS and NCMH studies. The mean awake and asleep SBP and DBP were calculated using all readings while participants were awake and asleep, respectively. The mean 24-h SBP and DBP were calculated as a weighted average of the mean awake and mean asleep BP readings, with weights proportional to the amount of the 24-h period spent awake and asleep, for CARDIA, MHT, and IDH studies, and using the average of all readings during the ABPM recording period for the JHS and NCMH studies. A complete ABPM recording was defined as having at least 70% of the total number of planned readings over 24 h, and at least 20 awake and at least seven asleep SBP and DBP measurements [12].

For simplicity, we use the terms sustained normotension, MHT, white coat hypertension and sustained hypertension in the current article for participants not taking and taking antihypertensive medication. These BP phenotypes were defined using office BP and awake BP only and office BP and awake, asleep, or 24-h BP and the thresholds in the JNC7 and the 2017 ACC/AHA BP guidelines, separately (Table 1 and Supplemental Table 3, http://links.lww. com/HJH/B965).

### Echocardiography

Sonographers were trained and certified to conduct 2Dguided M-mode echocardiography following a standardized protocol [13-15]. Among participants who had a complete ABPM recording, 681 (92.0%) in CARDIA, 905 (97.5%) in JHS, 696 (95.2%) in MHT, 369 (98.1%) in IDH, and 261 (96.0%) participants in NCMH had an interpretable echocardiogram recording. Interventricular septal thickness at end-diastole (IVSd), left ventricular internal diameter at end-diastole (LVIDd), and posterior wall thickness at end-diastole (PWTd) were measured in accordance with the 2015 American Society of Echocardiography and European Society of Cardiovascular Imaging recommendations [16]. LVMI was quantified as LVM defined as  $0.8 \times \{1.04 \times ([IVSd + LVIDd + PWTd]^3 - LVIDd)^3)\}$ + 0.6, which was indexed to height<sup>2.7</sup>. LVH in males and females was defined as LVMI at least 49 g/m<sup>2.7</sup> and LVMI at least  $45 \text{ g/m}^{2.7}$ , respectively.

### Statistical analyses

We used data from five studies with 3047 participants who had a complete information on ABPM. We excluded 10 participants who did not have information on antihypertensive medication use and 135 participants missing information on LVMI, resulting in an overall sample of 2902 participants. Unless stated below, the analysis was restricted to participants who had office SBP less than 140 mmHg and office DBP less than 90 mmHg (n = 2451).

All analyses were conducted for participants not taking and taking antihypertensive medication, separately. Participant characteristics were calculated for those with office SBP/DBP less than 140/90 mmHg and less than 130/ 80 mmHg, separately. We calculated the prevalence of MHT defined using office BP and awake BP alone and office BP and awake, asleep, or 24-h BP with BP thresholds from the JNC7 and the 2017 ACC/AHA BP guidelines, separately. For the JNC7 guideline, the prevalence of MHT was calculated among participants with office SBP less than 140 mmHg and DBP less than 90 mmHg (n = 2451)and in the overall study population (n = 2902). For the 2017 ACC/AHA BP guideline, the prevalence of MHT was calculated among participants with office SBP less than 130 mmHg and DBP less than 80 mmHg (n = 1653) and in the overall study population (n = 2902). The mean LVMI and prevalence of LVH were calculated among participants with sustained normotension and MHT defined using BP thresholds in the JNC7 guideline and the 2017 ACC/AHA BP guideline. The mean difference in LVMI and prevalence ratio for LVH associated with MHT versus sustained normotension were calculated after multivariable adjustment using linear regression and modified Poisson regression with robust standard errors, respectively. The first model included adjustment for age, sex, race, education, study cohort, smoking, alcohol consumption, family history of hypertension, total and HDL cholesterol, BMI, diabetes, statin use, glucose-lowering medication use, and estimated glomerular filtration rate (eGFR) less than 60 ml/min per  $1.73 \,\mathrm{m}^2$ . The second model was conducted after further controlling for office SBP and DBP. eGFR, family history of hypertension, lipid-lowering, and glucose-lowering medication use were not collected in NCMH study, so these variables were not included in the models described above. The statistical significance of the difference in the prevalence of MHT and LVH, mean differences in LVMI, and prevalence ratios for LVH among participants with MHT versus sustained normotension when defined by the 2017 ACC/AHA versus the JNC7 guideline were estimated by a bias-corrected bootstrap procedure with 1000 iterations [17]

For a secondary analysis, participants were grouped as having sustained normotension, MHT, white coat hypertension, and sustained hypertension defined by BP thresholds in the 2017 ACC/AHA BP guideline cross-classified by having sustained normotension or MHT using BP thresholds in the JNC7 guideline (Supplemental Table 3, http:// links.lww.com/HJH/B965). As participants with office SBP at least 140 mmHg or DBP at least 90 mmHg were excluded from these analyses, no one had white coat hypertension or sustained hypertension according to the JNC7

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guideline. The mean LVMI and prevalence of LVH for participants in each of these groups were calculated using awake BP alone and awake, asleep, or 24-h BP. The mean difference in LVMI and prevalence ratios for LVH for participants in each of these groupings were calculated using those with sustained normotension according to both guidelines as the referent. These were considered secondary analyses due to the small sample size in some of the groupings. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). Statistical significance was defined by a two-sided *P* value less than 0.05.

### RESULTS

#### **Participant characteristics**

We included 2451 participants who had office SBP less than 140 mmHg and DBP less than 90 mmHg in the analysis using BP thresholds in the JNC7 guideline, of whom 1811 participants were not taking and 640 participants were

taking antihypertensive medication. There were 1653 participants with office SBP less than 130 mmHg and DBP less than 80 mmHg, including 1235 and 418 participants not taking and taking antihypertensive medication, respectively, in the analysis using BP thresholds in the 2017 ACC/AHA BP Guideline. Among participants with office SBP less than 140 mmHg and DBP less than 90 mmHg and office SBP less than 130 mmHg and DBP less than 80 mmHg, those taking antihypertensive medication were older, less likely to be male and more likely to not drink alcohol, have diabetes and a family history of hypertension, to be taking lipidlowering and glucose-lowering medication, have a history of CVD, and to have eGFR less than 60 ml/min per  $1.73 \text{ m}^2$ and albumin-to-creatinine ratio more than 30 mg/g compared with their counterparts not taking antihypertensive medication (Table 2). Moreover, mean BMI, total cholesterol, LVMI and office, awake, asleep, 24-h SBP, and asleep DBP were higher while mean HDL cholesterol was lower among participants taking versus not taking antihypertensive medication.

TABLE 2. Characteristics of participants with office SBP/DBP less than 140/less than 90 mmHg and less than 130/less than 80 mmHg for participants not taking and taking antihypertensive medication, separately

Characteristics	Office SBP/DBP < 140/<90 mmHg		Office SBP/DBP < 130/<80 mmHg			
	Not taking antihyperten- sive medication, $n = 1811$	Taking antihypertensive medication, <i>n</i> = 640	Not taking antihyperten- sive medication, <i>n</i> = 1235	Taking antihypertensive medication, <i>n</i> =418		
Age, years	47.7±11.6	$58.8 \pm 8.6$	47.1±11.6	59.0±8.5		
Age category (%)						
<40	25.3	1.6	26.6	1.2		
40-59	62.1	56.9	62.4	55.5		
≥60	12.6	41.6	11.0	43.3		
Male (%)	39.9	29.4	36.0	28.5		
Less than high school (%)	5.1	11.8	4.0	13.5		
Current smoking (%)	9.2	10.4	9.6	10.1		
Alcohol intake (%)						
No alcohol	24.4	64.9	25.2	68.2		
Light or moderate	50.0	31.6	48.9	28.0		
Heavy	25.6	3.5	25.8	3.7		
BMI (kg/m <sup>2</sup> )	$28.1\pm5.8$	$32.7 \pm 6.7$	$27.4 \pm 5.6$	32.8±6.9		
Total cholesterol (mg/dl)	$193.5 \pm 36.8$	$195.3 \pm 41.0$	191.1±37.2	$192.7 \pm 42.1$		
HDL cholesterol (mg/dl)	$57.4 \pm 16.4$	$55.5\pm16.9$	$58.7 \pm 16.7$	$55.7 \pm 17.2$		
Diabetes (%)	6.2	34.0	6.3	36.1		
Family history of hypertension (%)	61.5	92.5	64.2	92.8		
Glucose-lowering medication use (%)	) 3.0	27.4	3.0	29.7		
Lipid-lowering medication use (%)	5.9	30.9	5.3	31.3		
History of CVD (%)	0.9	12.5	0.9	12.2		
eGFR < 60 (ml/min per 1.73 m <sup>2</sup> )	0.7	9.2	0.7	9.3		
ACR > 30 (mg/g)	2.8	12.1	2.4	10.1		
Heart rate (bpm)	$69.0 \pm 10.6$	$65.0 \pm 10.7$	$68.6 \pm 10.7$	$65.5 \pm 10.8$		
SBP (mmHg)						
Office	$116.1 \pm 11.3$	$121.5 \pm 10.9$	$111.4 \pm 9.4$	$115.9 \pm 8.7$		
Awake	$124.8 \pm 12.0$	$128.3\pm12.6$	$121.7 \pm 10.6$	$125.8 \pm 12.2$		
Asleep	$109.3 \pm 12.6$	$117.7 \pm 14.9$	$106.6 \pm 11.6$	$115.4 \pm 14.9$		
24-h	$120.3 \pm 11.7$	$124.3\pm12.4$	$117.2 \pm 10.4$	$122.0 \pm 12.2$		
DBP (mmHg)						
Office	74.0±8.0	72.6±8.1	$70.4 \pm 6.4$	$69.3 \pm 6.4$		
Awake	78.0±7.7	77.6±9.2	$76.0 \pm 7.1$	$75.9 \pm 8.6$		
Asleep	64.0±8.2	$67.3\pm9.5$	$62.3 \pm 7.6$	$65.9\pm9.0$		
24-h	73.8±7.4	73.8±8.7	$71.9 \pm 6.7$	72.2±8.1		
Left ventricular mass index (g/m <sup>2.7</sup> )	32.9±8.7	$40.6\pm12.6$	32.0±8.8	$40.0 \pm 12.4$		
Left ventricular hypertrophy (%)	6.1	25.2	5.8	23.7		

Data are expressed as means (standard deviation) or percentages. Left ventricular mass index calculated as left ventricular mass indexed to height<sup>2.7</sup>. Left ventricular hypertrophy defined as increased left ventricular mass index at least 49 g/m<sup>2.7</sup> in females and at least 45 g/m<sup>2.7</sup> in males. ACC, American College of Cardiology; ACR, urinary albumin-to-creatinine ratio; AHA, American Heart Association; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate.



■JNC7 BP guideline ■ 2017 ACC/AHA BP guideline

FIGURE 1 Prevalence of masked hypertension as defined using the Seventh Report of the Joint National Committee and the 2017 American College of Cardiology/ American Heart Association blood pressure guideline thresholds and awake blood pressure alone and awake, asleep or 24-h blood pressure among participants not taking and taking antihypertensive medication.

High office blood pressure was defined by the: 2017 American College of Cardiology/American Heart Association guideline as: SBP at least 130 mmHg or DBP at least 80 mmHg, and Seventh Report of the Joint National Committee guideline: SBP at least 140 mmHg or DBP at least 90 mmHg. Using awake blood pressure: Masked hypertension and masked uncontrolled hypertension was defined by having high awake blood pressure (see Table 1). Using awake, asleep or 24-h blood pressure: masked hypertension was defined by having high awake, osleep or 24-h blood pressure (see Table 1). Using awake, asleep or 24-h blood pressure: masked hypertension was defined by having high awake, asleep or 24-h blood pressure (see Table 1). Out of 2087 total participants not taking antihypertensive medication, 1811 and 640, respectively, did not have high office blood pressure defined using the Seventh Report of the Joint National Committee Blood Pressure guideline, and 1235 and 418, respectively, did not have high office blood pressure defined using the 2017 American College of Cardiology/American Heart Association Blood Pressure guideline. The *P* value for the difference in the prevalence of masked hypertension among the overall population and those without high office blood pressure, and awake blood pressure alone and awake, asleep or 24-h blood pressure for participants not taking and taking antihypertensive medication when defined by the 2017 American College of Cardiology/American Heart Association and the Seventh Report of the Joint National Committee guideline were estimated using a bias-corrected bootstrap procedure with 1000 iterations. ACC/AHA, American College of Cardiology/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; BP, blood pressure; JNC7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

#### Prevalence of masked hypertension

Among participants without high office BP not taking and taking antihypertensive medication, the prevalence of MHT was higher when defined using BP thresholds in the 2017 ACC/AHA BP versus the JNC7 guideline (Fig. 1). When estimated in the overall population, the prevalence of MHT was not higher when defined by the 2017 ACC/AHA BP guideline versus the JNC7 guideline. Among participants with office SBP less than 140 mmHg and DBP less than 90 mmHg, the prevalence of sustained normotension, MHT, white coat hypertension and sustained hypertension defined by BP thresholds in the 2017 ACC/AHA BP guideline cross-classified by sustained normotension and MHT in the JNC7 guideline are presented in Supplemental Table 4, http://links.lww.com/HJH/B965.

## Masked hypertension and left ventricular mass index

Among participants not taking and taking antihypertensive medication, mean LVMI was higher among those with MHT compared with those with sustained normotension when defined using office BP and awake BP only and office BP and awake, asleep, or 24-h BP and BP thresholds from the JNC7 guideline and the 2017 ACC/AHA BP guideline (Fig. 2). After adjustment for the variables in Model 1, LVMI was higher among those with MHT versus sustained normotension when defined using office BP and awake BP only and BP thresholds in the JNC7 and the 2017 ACC/AHA BP guidelines and there was no evidence of a difference in the association between guidelines (*P* value = 0.326, Table 3). After adjustment for the variables in Model 1 and among participants not taking antihypertensive medication and using office BP and awake, asleep, or 24-h BP to define

MHT, the mean difference in LVMI for participants with MHT versus sustained normotension was larger when based on the JNC7 guideline  $[2.31 \text{ g/m}^{2.7}, 95\%$  confidence interval (CI): 1.50, 3.12] than using the 2017 ACC/AHA BP guideline (0.70 g/m<sup>2.7</sup>, 95% CI: -0.19, 1.59; P value for difference between guidelines = 0.001). Among participants taking antihypertensive medication, there was no evidence that the association with LVMI for those with MHT versus sustained normotension differed between the two guidelines (P value for difference = 0.504 when using office BP and awake BP only and P value = 0.895when using office BP and awake, asleep, or 24-h BP to define MHT). The mean and mean difference in LVMI for participants with sustained normotension, MHT, white coat hypertension and sustained hypertension defined by BP thresholds in the 2017 ACC/AHA BP guideline cross-classified by sustained normotension and MHT defined by the JNC7 guideline are presented in Supplemental Table 5, http://links.lww.com/HJH/B965.

## Masked hypertension and left ventricular hypertrophy

Among participants not taking antihypertensive medication, the prevalence of LVH was higher for those with MHT versus sustained normotension when defined by office BP and awake BP only and office BP and awake, asleep, or 24h BP using the BP thresholds in the JNC7 guideline and the 2017 ACC/AHA guideline (Fig. 3). Among participants not taking antihypertensive medication and after adjustment for the variables in Model 1, the prevalence ratios for LVH associated with MHT versus sustained normotension using BP thresholds in the JNC7 guideline and the 2017 ACC/AHA BP guideline were 1.91 (95% CI: 1.29, 2.84) and 1.97 (95%



**FIGURE 2** Mean left ventricular mass index (g/m<sup>2.7</sup>) among participants with sustained normotension and masked hypertension as defined using awake blood pressure alone and awake, asleep or 24-h blood pressure thresholds from the Seventh Report of the Joint National Committee blood pressure guideline and the 2017 American College of Cardiology/American Heart Association blood pressure guideline among participants not taking and taking antihypertensive medication. Left ventricular mass index calculated as left ventricular mass indexed to height<sup>2.7</sup>. Using awake blood pressure: Masked hypertension and masked uncontrolled hypertension was defined by having high awake blood pressure (see Table 1). Using awake, asleep, or 24-h blood pressure: Masked hypertension was defined by having high awake blood pressure (see Table 1). Using awake, asleep, or 24-h blood pressure: Masked hypertension was defined by having high awake blood pressure alone and awake, asleep or 24-h blood pressure: Masked hypertension, and awake blood pressure alone and awake, asleep or 24-h blood pressure: Masked hypertension, and awake blood pressure alone and awake, asleep or 24-h blood pressure: Masked hypertension, and taking antihypertensive medication when defined by the 2017 American College of Cardiology/American Heart Association and the Seventh Report of the Joint National Committee guideline were estimated by a bias-corrected bootstrap procedure with 1000 iterations. ACC/AHA, American College of Cardiology/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; LVMI, left ventricular mass index.

TABLE 3. Multivariate-adjusted mean	difference in lef	ft ventr	icular mass	index (g/m <sup>2</sup>	<sup>7</sup> ) associa	ated with mas	ced hy	pertensi	on as	defined
using the Seventh Report	of the Joint Na	tional	Committee	blood press	sure guid	eline and the	2017	America	an Col	lege of
Cardiology/American Hear	t Association	blood	pressure	guideline	among	participants	not	taking	and	taking
antihypertensive medication	า									

	Not taking antihypertensive medication		Taking antihype tio	rtensive medica- on	
Masked hypertension defined using office BP and awake BP					
	Mean difference (95% CI) in LVMI		Mean difference (95% CI) in LVMI		
JNC7 guideline definition	Model 1	Model 2	Model 1	Model 2	
Sustained normotension	0 (ref)	0 (ref)	0 (ref)	0 (ref)	
Masked hypertension	2.46 (1.55, 3.38)	1.89 (0.93, 2.86)	3.27 (1.02, 5.20)	2.43 (0.10, 4.75)	
2017 ACC/AHA BP guideline definition					
Sustained normotension	0 (ref)	0 (ref)	0 (ref)	0 (ref)	
Masked hypertension	1.91 (0.97, 2.85)	1.49 (0.51, 2.48)	1.96 (-0.72, 4.64)	1.63 (-1.11, 4.37)	
P value for 2017 versus JNC7 difference	0.326	0.495	0.257	0.504	
Masked hypertension defined using office BP and awake, asleep, or 24-h BP					
JNC7 guideline definition	Model 1	Model 2	Model 1	Model 2	
Sustained normotension	0 (ref)	0 (ref)	0 (ref)	0 (ref)	
Masked hypertension	2.31 (1.50, 3.12)	1.79 (0.93, 2.65)	3.06 (0.92, 5.19)	2.49 (0.28, 4.69)	
2017 ACC/AHA BP guideline definition					
Sustained normotension	0 (ref)	0 (ref)	0 (ref)	0 (ref)	
Masked hypertension	0.70 (-0.19, 1.59)	0.17 (-0.77, 1.10)	2.59 (-0.44, 5.63)	2.23 (-0.88, 5.34)	
P value for 2017 versus JNC7 difference	0.001	0.001	0.775	0.895	

Model 1: Adjusted for age, sex, less than high school, study, smoking status, alcohol consumption, family history of hypertension, total and HDL cholesterol, BMI, prevalent diabetes, statin use, antihyperglycemic medication use, and estimated glomerular filtration rate less than 60 ml/min per 1.73 m<sup>2</sup>. Model 2: Adjusted for variables in Model 1 and office SBP and DBP. *P*-value comparing mean difference in left ventricular mass index for participants with masked hypertension defined using office and awake blood pressure (bottom panel) when using the INC7 and the 2017 ACC/AHA blood pressure guidelines among participants not taking and taking antihypertensive medication. ACC/AHA, American College of Cardiology/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure; LVMI, left ventricular mass index.

CI: 1.20, 3.23), respectively, when using office BP and awake BP only (*P* value for difference = 0.909), and 2.28 (95% CI: 1.49, 3.49) and 1.38 (95% CI: 0.78, 2.44), respectively, when using office BP and awake, asleep, or 24-h BP (*P* value for difference = 0.069) (Table 4). After further adjustment for office SBP and DBP (Model 2), there was no evidence of a difference in the association of MHT with LVH in the 2017 ACC/AHA BP guideline versus the JNC7

guideline when defined using office BP and awake BP only, but there was evidence of a difference when MHT was defined using office BP and awake, asleep, or 24-h BP (prevalence ratio 2.16; 95% CI: 1.36, 3.44 when defined using the JNC7 guideline definition and 1.03; 95% CI: 0.58, 1.82 when defined using the 2017 ACC/AHA BP guideline definition; *P* value for difference = 0.010). Among participants taking antihypertensive medication, there was no



**FIGURE 3** Prevalence of left ventricular hypertrophy among participants with sustained normotension and masked hypertension as defined using awake blood pressure alone and awake, asleep or 24-h blood pressure thresholds from the Seventh Report of the Joint National Committee blood pressure guideline and the 2017 American College of Cardiology/American Heart Association blood pressure guideline among participants not taking and taking antihypertensive medication. Left ventricular hypertrophy defined as increased left ventricular mass index at least 49 g/m<sup>2.7</sup> in females and at least 45 g/m<sup>2.7</sup> in males. Using awake blood pressure: Masked hypertension was defined by having high awake blood pressure (see Table 1). Using awake, asleep or 24-h blood pressure: Masked hypertension versus sustained normotension, and awake blood pressure alone and awake, asleep or 24-h blood pressure for participants with masked hypertension versus sustained normotension, and awake blood pressure alone and awake, asleep or 24-h blood pressure for participants not taking and taking antihypertensive medication when defined by the 2017 American College of Cardiology/American Heart Association and the Seventh Report of the Joint National Committee guideline were estimated by a bias-corrected bootstrap procedure with 1000 iterations. ACC/AHA, American College of Cardiology/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; LVH, left ventricular hypertrophy.

# TABLE 4. Prevalence ratio for left ventricular hypertrophy associated with masked hypertension as defined using the Seventh Report of the Joint National Committee blood pressure guideline and the 2017 American College of Cardiology/American Heart Association blood pressure guideline

	Not taking antihypertensive medication		Taking antihype cation	ertensive medi-
Masked hypertension defined using office BP and awake BP				
	Prevalence ratio (95% CI) of LVH		Prevalence ratio	(95% CI) of LVH
JNC7 guideline definition	Model 1	Model 2	Model 1	Model 2
Sustained normotension	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Masked hypertension	1.91 (1.29, 2.84)	1.72 (1.12, 2.64)	1.45 (1.07, 1.96)	1.30 (0.95, 1.79)
2017 ACC/AHA BP guideline definition				
Sustained normotension	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Masked hypertension	1.97 (1.20, 3.23)	1.56 (0.97, 2.51)	1.10 (0.74, 1.65)	0.99 (0.65, 1.49)
P value for 2017 versus JNC7 difference	0.909	0.717	0.130	0.125
Masked hypertension defined using office BP and awake, asleep, or 24-h BP				
JNC7 guideline definition	Model 1	Model 2	Model 1	Model 2
Sustained normotension	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Masked hypertension	2.28 (1.49, 3.49)	2.16 (1.36, 3.44)	1.16 (0.86, 1.58)	1.09 (0.80, 1.50)
2017 ACC/AHA BP guideline definition				
Sustained normotension	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Masked hypertension	1.38 (0.78, 2.44)	1.03 (0.58, 1.82)	1.06 (0.69, 1.63)	1.00 (0.64, 1.55)
P value for 2017 versus JNC7 difference	0.069	0.010	0.682	0.696

Model 1: Adjusted for age, sex, less than high school, study, smoking status, alcohol consumption, family history of hypertension, total and HDL cholesterol, BMI, prevalent diabetes, statin use, antihyperglycemic medication use, and estimated glomerular filtration rate less than 60 ml/min per 1.73 m<sup>2</sup>. Model 2: Adjusted for variables in Model 1 and office SBP and DBP. *P*-value comparing the prevalence ratio for left ventricular hypertrophy for participants with masked hypertension defined using office and awake blood pressure (top panel), and office and awake, asleep, or 24-h blood pressure (bottom panel) when using the JNC7 and the 2017 ACC/AHA blood pressure guidelines among participants not taking antihypertensive medication. ACC/AHA, American College of Cardiology/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; BP, blood pressure; CI, confidence interval; JNC7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; LVH: left ventricular hypertrophy.

evidence of an association of MHT with LVH defined using BP thresholds in either guideline after adjustment for the variables in Model 2. The prevalence and prevalence ratio for LVH associated with sustained normotension, MHT, white coat hypertension, and sustained hypertension defined by BP thresholds in 2017 ACC/AHA guideline cross-classified by sustained normotension and MHT defined by the JNC7 guideline are presented in Supplemental Table 6, http://links.lww.com/HJH/B965.

#### DISCUSSION

In the current pooled analysis of individual-level data for participants without high office BP from five studies, the prevalence of MHT was higher when defined according to the 2017 ACC/AHA BP guideline versus the JNC7 guideline. When using office BP and awake BP only, there was no evidence of a difference in the association of MHT with LVMI or LVH, when defined by the 2017 ACC/AHA guideline versus the JNC7 guideline among those not taking antihypertensive medication. When using office BP and awake, asleep, or 24-h BP to define MHT, the associations of MHT with LVMI and LVH were stronger using BP thresholds in the JNC7 guideline versus the 2017 ACC/AHA BP guideline. There was an association of masked uncontrolled hypertension with LVMI when defined using the JNC7 guideline but not the 2017 ACC/AHA BP guideline. These data suggest that the prognostic importance of masked and masked uncontrolled hypertension may differ when using the BP thresholds in the 2017 ACC/AHA guideline versus the JNC7 guideline.

Prior studies have estimated that 15–30% of adults with office BP not in the hypertensive range have MHT when defined using awake BP and BP thresholds in the JNC7 guideline [18,19]. Moreover, 16 million US adults have been estimated to have MHT [20]. Results from the current study suggest that adults without high office BP, the prevalence of MHT defined by office BP and awake BP only is higher when defined using the 2017 ACC/AHA BP guideline versus the JNC7 guideline, with over 30% of participants without high office BP having MHT and masked uncontrolled hypertension according to the 2017 ACC/AHA BP guideline. The prevalence of MHT was above 50% when out-of-office BP was defined using awake, asleep, or 24-h measurements and BP thresholds in the 2017 ACC/AHA BP guideline.

We previously used data from the CARDIA study and compared the prevalence of MHT and masked uncontrolled hypertension defined using the 2017 ACC/AHA BP guideline versus the JNC7 guideline, with out-of-office BP defined using awake BP only [21]. Consistent with the current study, among adults with office-measured BP not in the hypertensive range, the prevalence of MHT and masked uncontrolled hypertension was higher when using the lower BP thresholds in the 2017 ACC/AHA BP guideline compared with the JNC7 guideline. However, in the current study, the prevalence of MHT and masked uncontrolled hypertension in the overall population, including those with office BP in the hypertensive range, was not higher according to the 2017 ACC/AHA versus the JNC7 guideline. These data suggest that the higher proportion of adults meeting the definitions of MHT and masked uncontrolled hypertension according to the 2017 ACC/AHA BP guideline results from the smaller number of people without high office BP according to this guideline compared with the JNC7 guideline. Given the high proportion of adults with MHT and masked uncontrolled hypertension among those without high office BP according to the 2017 ACC/AHA BP guideline, screening for these phenotypes may be efficient.

Prior studies have reported MHT to be associated with a higher prevalence of LVMI and LVH compared with sustained normotension [19,21–23]. Moreover, studies have reported that masked uncontrolled hypertension is associated with increased CVD risk.[18,24] These studies have used awake BP and BP thresholds consistent with the JNC7 guideline to define high out-of-office BP. In the current study, associations were present between MHT with LVMI and LVH when using office and awake BP and BP thresholds in either the JNC7 guideline or the 2017 ACC/AHA BP guideline. While masked uncontrolled hypertension was

associated with higher LVMI and LVH using office BP and awake BP alone and BP thresholds in the JNC7 guideline, no association was present using BP thresholds in the 2017 ACC/AHA BP guideline. Antihypertensive medication prevents the progression of LVMI [25]. Assessing if antihypertensive medication attenuates the association between MHT and LVMI was beyond the scope of the current study.

The 2017 ACC/AHA BP guideline recommends using awake BP to define out-of-office hypertension on ABPM and the 2018 European Society of Cardiology and the European Society of Hypertension guideline for the management of arterial hypertension recommends using awake, asleep, and 24-h BP [4,12]. Using awake, asleep, or 24-h BP, MHT defined by BP thresholds in the JNC7 guideline but not the 2017 ACC/AHA BP guideline was associated with LVMI and LVH. A substantial higher proportion of participants met the definition of MHT by either guideline when out-of-office hypertension was defined using awake, asleep, or 24-h BP compared with awake BP only. These findings suggest a high prevalence of isolated nocturnal hypertension. An association between isolated nocturnal hypertension, high asleep BP but not high awake BP, with LVH and CVD has been present in some but not all studies [10,26]. Results from the current study suggest that individuals without high office or awake BP but with high asleep or 24-h BP according to the 2017 ACC/AHA BP guideline may not have increased CVD risk.

The results from the current study suggest that screening for MHT using awake BP and the 2017 ACC/AHA BP guideline thresholds to define in-office and out-of-office hypertension status could identify adults more likely to have LVH compared with using the JNC7 BP guideline thresholds. However, according to the results of the current study, screening for masked uncontrolled hypertension using BP thresholds from the 2017 ACC/AHA BP guideline may not be useful for identifying individuals with a high probability of LVH. It is unclear whether antihypertensive medication lowers the risk for LVH or CVD among individuals with MHT or masked uncontrolled hypertension [27]. Several randomized trials are underway evaluating the effect of antihypertensive medication on LVH regression among individuals with masked uncontrolled hypertension [28 - 30].

The current study has several strengths. The analyses were conducted pooling the data from selected participants from five population-based, community-based, and practice-based US studies. These studies were conducted in diverse populations and across a broad geographic area. Office and ambulatory BP were measured following standardized protocols. The conduct of high-quality echocardiograms permitted the assessment of the association of BP thresholds from the 2017 ACC/AHA guideline on target organ damage. The results should also be interpreted in the context of potential and known limitations. Office BP was obtained on a single occasion versus multiple occasions as recommended by clinical practice guidelines [4]. Information on CVD events were not available for most study participants. We may have lacked statistical power when assessing the association of LVH with MHT. Future studies should compare the association of MHT defined using the 2017 ACC/AHA BP guideline versus the JNC7

guideline with CVD events. Some characteristics, including eGFR, family history of hypertension, lipid-lowering, and glucose-lowering medication use were not collected in NCMH study.

In conclusion, the prevalence of MHT among participants without high office BP was higher when defined using the 2017 ACC/AHA BP guideline versus the JNC7 guideline. Among participants not taking antihypertensive medication and using awake BP only to define out-of-office hypertension status, MHT was associated with LVMI and LVH using each guideline. However, there was no evidence that MHT was associated with LVH when using awake, asleep, or 24-h BP and BP thresholds in the 2017 ACC/AHA BP guideline while there was an association using BP thresholds in the JNC7 guideline. These data suggest that screening for MHT defined by the 2017 ACC/AHA BP guideline using office BP and awake BP only may identify a population with a high prevalence of LVH while those with MHT defined by awake, asleep, or 24-h BP or masked uncontrolled hypertension may not have a high prevalence of LVH.

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#### **Conflicts of interest**

There are no conflicts of interest.

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