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# Association of Isolated Diastolic Hypertension as Defined by the 2017 ACC/AHA Blood Pressure Guideline With Incident Cardiovascular Outcomes

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**IMPORTANCE** In the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guideline, the definition of hypertension was lowered from a blood pressure (BP) of greater than or equal to 140/90 to greater than or equal to 130/80 mm Hg. The new diastolic BP threshold of 80 mm Hg was recommended based on expert opinion and changes the definition of isolated diastolic hypertension (IDH).

**OBJECTIVE** To compare the prevalence of IDH in the United States, by 2017 ACC/AHA and 2003 Joint National Committee (JNC7) definitions, and to characterize cross-sectional and longitudinal associations of IDH with outcomes.

**DESIGN, SETTING, AND PARTICIPANTS** Cross-sectional analyses of the National Health and Nutrition Examination Survey (NHANES 2013-2016) and longitudinal analyses of the Atherosclerosis Risk in Communities (ARIC) Study (baseline 1990-1992, with follow-up through December 31, 2017). Longitudinal results were validated in 2 external cohorts: (1) the NHANES III (1988-1994) and NHANES 1999-2014 and (2) the Give Us a Clue to Cancer and Heart Disease (CLUE) II cohort (baseline 1989).

**EXPOSURES** IDH, by 2017 ACC/AHA (systolic BP <130 mm Hg, diastolic BP ≥80 mm Hg) and by JNC7 (systolic BP <140 mm Hg, diastolic BP ≥90 mm Hg) definitions.

**MAIN OUTCOMES AND MEASURES** Weighted estimates for prevalence of IDH in US adults and prevalence of US adults recommended BP pharmacotherapy by the 2017 ACC/AHA guideline based solely on the presence of IDH. Risk of incident atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), and chronic kidney disease (CKD) in the ARIC Study.

**RESULTS** The study population included 9590 adults from the NHANES (mean [SD] baseline age, 49.6 [17.6] years; 5016 women [52.3%]) and 8703 adults from the ARIC Study (mean [SD] baseline age, 56.0 [5.6] years; 4977 women [57.2%]). The estimated prevalence of IDH in the NHANES was 6.5% by the 2017 ACC/AHA definition and 1.3% by the JNC7 definition (absolute difference, 5.2% [95% CI, 4.7%-5.7%]). Among those newly classified as having IDH, an estimated 0.6% (95% CI, 0.5%-0.6%) also met the guideline threshold for antihypertensive therapy. Compared with normotensive ARIC participants, IDH by the 2017 ACC/AHA definition was not significantly associated with incident ASCVD (n = 1386 events; median follow-up, 25.2 years; hazard ratio [HR], 1.06 [95% CI, 0.89-1.26]), HF (n = 1396 events; HR, 0.91 [95% CI, 0.76-1.09]), or CKD (n = 2433 events; HR, 0.98 [95% CI, 0.65-1.11]). Results were also null for cardiovascular mortality in the 2 external cohorts (eg, HRs of IDH by the 2017 ACC/AHA definition were 1.17 [95% CI, 0.87-1.56] in the NHANES [n = 1012 events] and 1.02 [95% CI, 0.92-1.14] in CLUE II [n = 1497 events]).

**CONCLUSIONS AND RELEVANCE** In this analysis of US adults, the estimated prevalence of IDH was more common when defined by the 2017 ACC/AHA BP guideline compared with the JNC7 guideline. However, IDH was not significantly associated with increased risk for cardiovascular outcomes.

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Supplemental content

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Hypertension can be diagnosed on the basis of elevated systolic blood pressure (BP), elevated diastolic BP, or both.[1,2] The 2017 BP guideline published by the American College of Cardiology (ACC)/American Heart Association (AHA) altered the definition of hypertension from a cutoff of greater than or equal to 140/90 mm Hg (ie, the previous 2003 threshold from the Joint National Committee [JNC] 7 guideline[3]) to a lower threshold of greater than or equal to 130/80 mm Hg.[1] The recommendation to lower the diastolic threshold for hypertension from 90 mm Hg to 80 mm Hg was based on expert opinion,[1] not on trial data. This change has major implications for an entity known as isolated diastolic hypertension (IDH), defined as a systolic BP less than 130 mm Hg with a diastolic BP greater than or equal to 80 mm Hg by new criteria (ACC/AHA 2017),[1] but a systolic BP less than 140 mm Hg with a diastolic BP greater than or equal to 90 mm Hg by the JNC7 criteria.[3] Prior studies suggest that IDH (based on JNC7 diagnostic criteria) is more common in younger individuals, is associated with future systolic hypertension, but is generally not associated with atherosclerotic cardiovascular disease (ASCVD) outcomes independently of baseline systolic BP.[4-14]

This study had 2 objectives: (1) to estimate the prevalence of IDH by JNC7 and by 2017 ACC/AHA definitions in the US adult population and (2) to assess the associations of both IDH definitions with incident ASCVD, heart failure (HF), and chronic kidney disease (CKD).

### Key Points

**Question** What is the prevalence of isolated diastolic hypertension (IDH) in the United States when defined by the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) blood pressure guideline vs the 2003 Joint National Committee (JNC7) guideline and what is the prognosis of individuals with IDH by the 2017 ACC/AHA definition?

**Findings** In a nationally representative US cross-sectional study that included 9590 adults, the estimated prevalence of IDH based on the 2017 ACC/AHA guideline vs the JNC7 guideline was 6.5% vs 1.3%, respectively. In a longitudinal analysis that included 8703 adults, there was no significant association between IDH as defined by the 2017 ACC/AHA guideline and incident atherosclerotic cardiovascular disease, heart failure, or chronic kidney disease.

**Meaning** IDH as defined by the 2017 ACC/AHA blood pressure guideline may not be associated with increased risk for cardiovascular outcomes.

## Methods

The relevant institutional review boards approved the National Health and Nutrition Examination Survey (NHANES), the Atherosclerosis Risk in Communities (ARIC) Study, and the Give Us a Clue to Cancer and Heart Disease (CLUE) II Study and all participants provided written informed consent.

### Study Populations

The NHANES is a large, serial, cross-sectional survey designed to be nationally representative of the civilian adult population in the United States. For the present study, we combined data from the 2013-2016 survey cycles to evaluate the prevalence of IDH in US adults aged 20 years or older.[15] Additional details of the NHANES design and methods are available elsewhere.[15,16]

The ARIC Study is a prospective observational cohort of 15 792 adults sampled from 4 US communities: Forsyth Country, North Carolina (white and black participants); Jackson, Mississippi (black participants); suburban Minneapolis, Minnesota (white participants); and Washington County, Maryland (white participants). Further details of the ARIC Study protocol and procedures have been published.[17] For the cross-sectional and longitudinal analyses of the ARIC Study, we used baseline data from the second examination, which took place from 1990 to 1992 and is the first visit for which cardiac biomarker data (high-sensitivity cardiac troponin T [hs-cTnT] and N-terminal pro-brain natriuretic peptide [NT-proBNP]) were available. We excluded participants with a history of cardiovascular disease and those who were missing important variables of interest (eFigure 1 in the Supplement). It is standard ARIC procedure to exclude the few participants who were black in the Minnesota and Washington County locations and those who were neither white nor black at any site (this small subgroup is not representative of the sample overall and its limited number precludes meaningful subgroup analysis).

We validated our results from the ARIC Study in 2 external cohorts by examining the association of IDH with all-cause and cardiovascular mortality in (1) the NHANES III (1988-1994) and NHANES 1999-2014 and (2) the CLUE II cohort study (see eMethods in the Supplement for additional information on the methods and analyses of both cohorts). CLUE II is a cohort study of cancer and heart disease that was initiated in 1989 in Washington County, Maryland. Mobile trailers were stationed in a wide variety of locations and open at all times of day (except between 1 AM and 6 AM) in an effort to give all segments of the community an opportunity to participate. A total of 32 898 persons participated, of whom 25 081 gave Washington County addresses. Comparisons with published figures from the 1990 Census indicated that approximately 30% of adult residents had participated.[18]

### Measurement of Baseline Demographic Variables

In both the NHANES 2013-2016 and ARIC studies, demographic and cardiovascular risk factor information was collected by trained examiners using standardized protocols. In the NHANES, BP readings were obtained after 5 minutes of seated rest. Three BP measurements were obtained at 30-second intervals and the mean of the 3 was used to define systolic BP and diastolic BP.[16]

In the ARIC Study, BP was measured after 5 minutes of rest in the sitting position. We recorded BP as the mean of the last 2 of 3 measurements collected over 5-minute intervals. Antihypertensive drug use was assessed with a medication inventory. Diagnosed diabetes was defined as a self-reported physician diagnosis of diabetes or current use of diabetic medications. Low-density lipoprotein cholesterol was calculated

using the Friedewald equation. The estimated glomerular filtration rate (eGFR) was calculated using serum creatinine and the 2009 Chronic Kidney Disease (CKD) Epidemiology Collaboration equation.[19] Information on alcohol use and smoking status was self-reported. Information on race was self-reported (selected from several fixed categories that were defined by the investigators) and was collected in the ARIC Study because race is an important determinant of prognosis relating to cardiovascular risk factors such as BP. Body mass index was calculated from measured weight and height.

In CLUE II, a short questionnaire on demographics and medical history was administered to all participants. Clinical variables, including resting BP and plasma total cholesterol level, were measured for each participant. BP was taken while sitting 3 times; the third reading was used for analyses.[20] Further details on data collection and study methods for CLUE II and for NHANES III/NHANES 1999-2014 are in the eMethods in the Supplement.

In all 3 cohorts, we defined IDH as a systolic BP less than 130 mm Hg with a diastolic BP greater than or equal to 80 mm Hg by 2017 ACC/AHA criteria[1] and a systolic BP less than 140 mm Hg with a diastolic BP greater than or equal to 90 mm Hg by JNC7 criteria.[3]

### Follow-up for Incident Clinical Outcomes in the ARIC Study

Clinical outcomes analyzed in the ARIC Study were prespecified on the basis of being known sequelae of hypertension; these included incident ASCVD, incident HF, and incident CKD. Incident ASCVD events were ascertained during active surveillance of ARIC participants for all hospitalizations and deaths. All cardiovascular events were adjudicated by an end points committee. We defined ASCVD as a composite of nonfatal myocardial infarction, nonfatal ischemic stroke, or cardiovascular death. Details on the ascertainment of deaths and classification of myocardial infarction and stroke in the ARIC Study have been published elsewhere.[21,22]

Hospitalizations for HF were identified from diagnosis codes and deaths caused by HF from hospital discharge records for inpatient deaths and death certificates for deaths occurring outside the hospital. Beginning in 2005, the ARIC Study conducted retrospective adjudication of hospitalized HF events. Hospitalized medical records indicating signs or symptoms of HF were abstracted and reviewed.[23] We defined CKD as either (1) individuals developing a creatinine-based eGFR less than 60 mL/min/1.73 $m^2$ and a creatinine-based eGFR decline from visit 2 of at least 25%; (2) identification in the US Renal Data System national registry or death with a kidney disease code in the first position on the death certificate; or (3) hospitalizations or deaths with relevant *International Classification of Diseases, Ninth Revision, Clinical Modification* or *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes in any position.[24]

### Measurement of Cardiac Biomarkers in the ARIC Study

Hs-cTnT level and NT-proBNP were measured in stored serum samples from ARIC Study visit 2 at the University of Minnesota in 2012-2013 on the Elecsys 2010 Analyzer (Roche Diagnostics).

### Statistical Analyses

For analyses of IDH by the 2017 ACC/AHA definition, the reference group was BP less than 130/80 mm Hg. For analyses of IDH by the JNC7 definition, the reference group was defined as BP less than 140/90 mm Hg. We calculated the percentage of US adults (NHANES 2013-2016) with IDH and recommended for antihypertensive medication according to the 2017 ACC/AHA guideline, the JNC7 guideline, and the difference between the 2 (ie, the 2017 ACC/AHA guideline but not the JNC7 guideline). These calculations were performed in the sample overall and within subgroups defined by age. All analyses of NHANES data accounted for the complex survey design and were weighted to generate nationally representative estimates for adults aged 20 years or older in the US population.

In the ARIC Study, we compared demographics and cardiovascular risk factors between participants who did and did not meet criteria for IDH using both definitions. Because black participants were recruited at only 2 of the 4 centers, we evaluated characteristics by race-center. Adjustment for race-center is standard in ARIC analyses due to the race-center aliasing inherent in the original design and recruitment of participants in this study. The race-center variable had 5 categories: Minnesota white participants, Maryland white participants, Mississippi black participants, North Carolina white participants, and North Carolina black participants. We used the *t* test to compare normally distributed continuous variables and the $\chi^2$ test for proportions.

For ARIC participants, we evaluated the cumulative incidence of ASCVD, HF, or CKD, according to baseline IDH status with follow-up through December 31, 2017. We used Cox regression models to characterize the longitudinal associations of IDH with incident ASCVD, HF, and CKD outcomes. We verified the proportionality of the hazards visually and with Schoenfeld residuals.

Model 1 included age, sex, race-center, and educational attainment. Model 2 included all variables in model 1 plus smoking status, alcohol consumption, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, eGFR, body mass index, antihypertensive medication use, and diabetes status. Model 3 included all variables in model 2 plus baseline systolic BP.

We evaluated the cross-sectional associations of both IDH definitions with hs-cTnT and NT-proBNP (both log-transformed), using multiple linear regression. We also used multiple logistic regression to evaluate the independent associations of IDH with elevated hs-cTnT (≥14 ng/L) and elevated NT-proBNP (≥100 pg/mL).

We conducted a number of sensitivity analyses in the ARIC Study. First, we examined the association of IDH with incident ASCVD after stratification by baseline age (above vs below the median) or antihypertensive treatment status. We tested for interaction by age and antihypertension treatment status using the likelihood ratio test. Second, we adjusted for antihypertensive medication use and systolic BP as time-varying variables by updating information over the course of follow-up. Third, we conducted analyses of the associations between IDH (both definitions) and ASCVD using a uniform

Table 1. US Adults Meeting the Definition for IDH and Recommended Antihypertensive Medication Based on the Presence of IDH, According to the 2017 ACC/AHA Guideline and the JNC7 Guideline (From the 2013-2016 NHANES)[a]

| | % (95% CI) | | | | | |
|---|---|---|---|---|---|---|
| | 2017 ACC/AHA Guideline | | 2003 JNC7 Guideline | | Difference (ACC/AHA Minus JNC7) | |
| | IDH | IDH-Recommended Antihypertensive Medication | IDH | IDH-Recommended Antihypertensive Medication | Difference in IDH | Difference in Antihypertensive Medication Eligibility |
| Overall | 6.5 (5.8-7.3) | 2.2 (1.8-2.6) | 1.3 (1.1-1.6) | 1.6 (1.3-2.0)[b] | 5.2 (4.7-5.7) | 0.6 (0.5-0.6) |
| By age group, y[c] | | | | | | |
| 20-44 | 6.7 (5.7-7.8) | 1.8 (1.4-2.5) | 1.4 (1.0-2.1) | 1.7 (1.3-2.3) | 5.3 (4.7-5.7) | 0.1 (0.1-0.2) |
| 45-54 | 11.9 (9.7-14.5) | 3.5 (2.5-4.8) | 2.6 (1.6-4.0) | 3.0 (2.1-4.3) | 9.3 (8.1-10.5) | 0.5 (0.4-0.5) |
| 55-64 | 5.3 (3.9-7.2) | 2.6 (1.6-4.2) | 0.7 (0.3-1.5) | 1.0 (0.5-1.9) | 4.6 (3.6-5.7) | 1.6 (1.1-2.3) |
| 65-74 | 3.2 (2.0-5.0) | 1.9 (1.1-3.3) | 0.8 (0.3-2.2) | 1.4 (0.7-2.9) | 2.4 (1.7-2.9) | 0.5 (0.4-0.5) |
| ≥75 | 0.3 (0.1-0.9) | 0.3 (0.1-0.9) | 0 | 0.1 (0.03-0.6) | 0.3 (0.1-0.9) | 0.2 (0.1-0.4) |

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; BP, blood pressure; IDH, isolated diastolic hypertension; JNC7, 2003 Joint National Committee; NHANES, National Health and Nutrition Survey.

[a] Definition of IDH by the 2017 ACC/AHA guideline is systolic BP less than 130 mm Hg and diastolic BP greater than or equal to 80 mm Hg. Definition of IDH by the 2003 JNC7 guideline is a systolic BP less than 140 mm Hg and diastolic BP greater than or equal to 90 mm Hg.

[b] The reason more US adults can be recommended for treatment than are diagnosed as having hypertension in the old JNC7 guideline is because that guideline recommended treating those with diabetes or chronic kidney disease to a target BP of 130/80 mm Hg.

[c] Percentages are within each age group.

reference group consisting of participants with systolic BP less than 120 mm Hg and diastolic BP less than 80 mm Hg. Fourth, we additionally adjusted for pulse pressure at baseline. Fifth, to evaluate persistent IDH, we conducted an analysis of ASCVD after ARIC visit 2 among participants who had IDH by the 2017 ACC/AHA definition at both visit 1 and visit 2 (6 years apart) compared with participants who had IDH at just 1 of these visits or were normotensive at both. Sixth, we repeated all Cox model analyses of incident ASCVD using Fine-Gray models instead, which can account for noncardiovascular death as a competing risk. Seventh, to maximize power, we examined a composite outcome of time to first occurrence of either ASCVD, HF, or CKD.

We validated our results for the association of IDH with outcomes by analyzing all-cause and cardiovascular mortality in the NHANES III and NHANES 1999-2014 and the CLUE II cohorts, in both study samples overall as well as after stratification by age and by antihypertensive medication status at baseline (additional details are provided in the eMethods in the Supplement). Using the *admetan* command in STATA, we also performed a DerSimonian-Laird random-effects model meta-analysis of cardiovascular mortality data from the 3 cohorts (ARIC, NHANES, and CLUE II) to estimate a pooled hazard ratio (HR) for IDH relative to normotension.

All analyses were conducted with Stata version 15 (StataCorp). $P < .05$ (2-sided) was considered statistically significant.

## Results

Of the 20 146 participants in the NHANES 2013-2016 survey cycles, those aged younger than 20 years (n = 8658) and missing relevant data (n = 1898) were excluded, leaving 9590 for analysis. Based on weighted analyses of NHANES 2013-2016, the estimated prevalence of IDH in the US adult population was 1.3% by the JNC7 definition and 6.5% by the 2017 ACC/AHA definition, which represents a difference in prevalence of 5.2% (95% CI, 4.7%-5.7%) (**Table 1**). This difference in prevalence was most pronounced in younger age categories. Few US adults were recommended for BP drug therapy on the basis of IDH alone, using either the JNC7 or the 2017 ACC/AHA definitions (1.6% and 2.2%, respectively). Comparing JNC7 vs 2017 ACC/AHA definitions, a cross tabulation of the estimated prevalences for each of the categories of normotension, IDH, and systolic hypertension is presented in **Table 2**.

In total, 14 348 ARIC participants attended visit 2 (the baseline for our analysis). We excluded ARIC participants who were neither white nor black (n = 42), the small number of black persons at the Minnesota and Washington County sites (n = 49), and those with prevalent ASCVD, HF, or missing variables of interest (n = 1477). For analyses of IDH by the JNC7 definition, we also excluded participants with systolic BP greater than or equal to 140 mm Hg (n = 2240); for analyses of IDH using the 2017 ACC/AHA definition, we excluded those with systolic BP greater than or equal to 130 mm Hg (n = 4077) (eFigure 1 in the Supplement). The percentage of ARIC participants at visit 2 (age range, 46-69 years; median age, 55 years) who met the definition of IDH was higher when using the 2017 ACC/AHA definition (11%) compared with the JNC7 definition (2%). ARIC participants with IDH by both the definitions were less likely to smoke but more likely than normotensive participants without IDH to be younger, male, black, overweight, or have less favorable lipid profiles (**Table 3**).

During a median of 25.2 years of follow-up in the ARIC Study (range, 0.03-27.9; interquartile range, 16.6-26.4), 1386 ASCVD events occurred in the 8703 participants included in the analysis of the 2017 ACC/AHA IDH definition. There were 1810 ASCVD events among the 10 540 participants included

Table 2. US Adults Meeting the Definitions for Normotension, IDH, and Systolic Hypertension, According to the 2017 ACC/AHA Guideline and the JNC7 Guideline (From the 2013-2016 NHANES)

| | % (95% CI) | | |
|---|---|---|---|
| | SBP <140 and DBP <90 mm Hg (JNC7 normal) | SBP <140 and DBP ≥90 mm Hg (JNC7 IDH) | SBP ≥140 mm Hg (JNC7 systolic hypertension) |
| SBP <130 and DBP <80 mm Hg (2017 ACC/AHA normal) | 66.0 (64.7-67.3) | NA | NA |
| SBP <130 and DBP ≥80 mm Hg (2017 ACC/AHA IDH) | 6.1 (5.4-6.9) | 0.3 (0.2-0.5) | NA |
| SBP ≥130 mm Hg (2017 ACC/AHA systolic hypertension) | 12.8 (11.7-13.9) | 1.0 (0.8-1.3) | 13.8 (12.6-15.0) |

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; DBP, diastolic blood pressure; IDH, isolated diastolic hypertension; JNC7, 2003 Joint National Committee; NA, not applicable; NHANES, National Health and Nutrition Survey; SBP, systolic blood pressure.

in the analysis of the JNC7 IDH definition. Compared with normal BP, there were no statistically significant associations of IDH by either definition with incident ASCVD (eg, HR, 0.86 [95% CI, 0.61-1.22] for JNC7 and HR, 1.06 [95% CI, 0.89-1.26] for the 2017 ACC/AHA definition in model 2) (**Figure 1** and **Figure 2**). Compared with normotensive participants without IDH, those with IDH by the 2017 ACC/AHA definition did not have significantly increased risk of HF (1396 events) or CKD (2433 events) (eTable 1 and eFigure 2 in the Supplement). IDH by the 2017 ACC/AHA definition was also not significantly associated with the composite outcome of ASCVD, HF, or CKD (3729 events; HR, 1.03 [95% CI, 0.93-1.15]; model 2) (eTable 2 in the Supplement). In cross-sectional analyses of the ARIC Study, there were no significant associations of IDH by either definition with elevations in hs-cTnT or NT-proBNP (eTable 3 in the Supplement).

In sensitivity analyses of the ARIC Study, our results for incident ASCVD were similar according to baseline hypertension treatment status (all *P* for interaction >.05; eTable 4 in the Supplement) and median age (all *P* for interaction >.10; eTable 5 in the Supplement). Results were also similar when using a uniform reference group (participants with systolic BP <120 mm Hg and diastolic BP <80 mm Hg) (eTable 6 in the Supplement). Adjustment for temporal changes in antihypertensive medication use and time-varying systolic BP levels (eTable 7 in the Supplement) or baseline pulse pressure (eTable 8 in the Supplement) had no appreciable effect on our findings. The null associations seen in Cox models for incident ASCVD were replicated in Fine-Gray models that accounted for noncardiovascular death as a possible competing risk (eTable 9 in the Supplement). In addition, analyses evaluating those who met 2017 ACC/AHA criteria for IDH at both ARIC visits 1 and 2 (compared with participants with normotension at both visits) demonstrated no significantly increased risk for ASCVD events occurring after visit 2 (eTable 10 in the Supplement).

In validation analyses of all-cause and cardiovascular mortality combining NHANES III and NHANES 1999-2014, there were 4562 deaths (including 1012 cardiovascular deaths) during a median of 9.8 years of follow-up (range, 0.1-27.2; interquartile range, 5.2-16.3) among the 36 280 participants included (median age, 40 years). IDH by the 2017 ACC/AHA definition was not significantly associated with all-cause death (HR, 0.92 [95% CI, 0.80-1.07]; n = 4562 events) or cardiovascular death (HR, 1.17 [95% CI, 0.87-1.56]; n = 1012 events) in this nationally representative sample of US adults (eTable 11 in the Supplement). Among 13 263 participants from the CLUE II cohort (median age, 42 years) with a median of 28.7 years of follow-up (range, 27.5-28.9), IDH by the 2017 ACC/AHA definition was not significantly associated with all-cause death (HR, 1.02 [95% CI, 0.94-1.10]; n = 2992 events) or cardiovascular death (HR, 1.02 [95% CI, 0.92-1.14]; n = 1497 events; eTable 12 in the Supplement). Results in both cohorts were similar when stratified by median age (all *P* for interaction >.05; eTables 13 and 14 in the Supplement) or by baseline hypertension treatment status (all *P* for interaction >.05; eTables 15 and 16 in the Supplement).

The pooled HRs for cardiovascular mortality among those with IDH by both the 2017 ACC/AHA and JNC7 definitions (combining ARIC, NHANES, and CLUE II) were also not statistically significant (eg, HR of 0.94 [95% CI, 0.85-1.05] for IDH by the 2017 ACC/AHA definition; eFigure 3 in the Supplement). In addition, there was no significant association with cardiovascular mortality among pooled participants aged younger than 40 years at baseline (eg, HR of 1.04 [95% CI, 0.66-1.63] for IDH by the 2017 ACC/AHA definition; eTable 17 in the Supplement).

## Discussion

The prevalence of IDH in the NHANES 2013-2016, defined using the 2017 ACC/AHA hypertension guideline, was higher than when defined according to the 2003 JNC7 guideline. There were no significant associations between baseline IDH (by either definition) and either subclinical cardiac disease or incident ASCVD, HF, or CKD in the ARIC Study. Similarly, there were no significant associations between IDH and all-cause and cardiovascular mortality in 2 large cohorts used for external validation.

The lack of statistically significant association of IDH with any of the clinical outcomes examined calls into question the pathogenicity of IDH. The lack of statistically significant association between IDH and elevated cardiovascular biomarkers in the ARIC Study is also important because these sensitive biomarkers indicate subclinical structural damage to the heart.[25,26] Based on the results of this analysis evaluating both JNC7 and 2017 ACC/AHA definitions (and based on the prior work of others examining the JNC7 definition[4-9,27]), IDH appears to be a distinct phenotype of BP that has no consistently significant association with either subclinical or clinical ASCVD.

Table 3. Characteristics of Participants According to IDH Status by JNC7 and 2017 ACC/AHA Definitions in the ARIC Study (Visit 2, 1990-1992)

| Characteristic | By JNC7 Definition | | | | By ACC/AHA Definition | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Normotension | IDH | Difference (95% CI)[a] | *P* Value[a] | Normotension | IDH | Difference (95% CI)[b] | *P* Value[b] | IDH Definition Difference (95% CI)[c] | *P* Value[c] |
| Participants, No. (%) | 10 325 (98.0) | 215 (2.0) | | | 7769 (89.3) | 934 (10.7) | | | | |
| Age, y | 56.4 (5.6) | 54.5 (5.3) | 1.9 (1.1 to 2.7) | <.001 | 56.2 (5.6) | 54.3 (5.2) | 1.9 (1.6 to 2.3) | <.001 | 0.2 (−0.6 to 0.9) | .66 |
| Sex, No. (%) | | | | | | | | | | |
| Male | 4424 (42.8) | 133 (61.9) | −19.0 (−25.7 to −12.3) | <.001 | 3178 (40.9) | 548 (58.7) | −17.8 (−21.1 to −14.4) | <.001 | 3.2 (−4.1 to 10.5) | .39 |
| Female | 5901 (57.2) | 82 (38.1) | 19.0 (12.3 to 25.7) | | 4591 (59.1) | 386 (41.3) | 17.8 (14.4 to 21.1) | | −3.2 (−10.5 to 4.1) | |
| Center populations by race, No. (%) | | | | | | | | | | |
| White population | | | | | | | | | | |
| Forsyth County, NC | 2584 (25.0) | 25 (11.6) | 13.4 (7.6 to 19.2) | <.001 | 2088 (26.9) | 153 (16.4) | 10.5 (7.5 to 13.5) | <.001 | −4.8 (−10.1 to 6.1) | .01 |
| Minneapolis, MN | 2864 (27.7) | 70 (32.6) | −4.8 (−1.9 to 1.2) | | 2123 (27.3) | 310 (33.2) | −5.9 (−8.9 to −2.8) | | −0.6 (−7.6 to 6.4) | |
| Washington County, MD | 2651 (25.7) | 34 (15.8) | 9.9 (4.0 to 15.7) | | 2051 (26.4) | 193 (20.7) | 5.7 (2.8 to 8.7) | | −4.8 (−10.8 to 1.1) | |
| Black population | | | | | | | | | | |
| Forsyth County, NC | 239 (2.3) | 3 (1.4) | .9 (−1.1 to 2.9) | | 162 (2.1) | 22 (2.4) | −0.3 (−1.2 to 0.7) | | −1.0 (−3.1 to 1.2) | |
| Jackson, MS | 1987 (19.2) | 83 (38.6) | −19.4 (−24.7 to −14.0) | | 1345 (17.3) | 256 (27.4) | −10.1 (−12.7 to −7.5) | | 11.2 (4.5 to 17.9) | |
| Education, No. (%) | | | | | | | | | | |
| <High school | 1948 (18.9) | 47 (22.0) | −3.1 (−8.4 to 2.2) | .23 | 1401 (18.1) | 147 (15.8) | 2.3 (−0.3 to 4.9) | <.001 | 6.2 (0.6 to 11.8) | .06 |
| High school or equivalent | 4332 (42.0) | 78 (36.4) | 5.6 (−1.1 to 12.2) | | 3327 (42.9) | 338 (36.2) | 6.7 (3.3 to 10.0) | | 0.2 (−6.9 to 7.4) | |
| >High school | 4030 (39.1) | 89 (41.6) | −2.5 (−9.1 to 4.1) | | 3031 (39.1) | 448 (48.0) | −9.0 (−12.3 to −5.6) | | −6.4 (−13.8 to 1.0) | |
| SBP, mean (SD), mm Hg | 114.5 (11.9) | 129.3 (6.7) | −14.8 (−16.4 to −13.2) | <.001 | 110.2 (9.8) | 120.1 (6.2) | −9.9 (−10.6 to −9.3) | <.001 | 9.2 (8.3 to 10.1) | <.001 |
| Pulse pressure, mean (SD), mm Hg | 44.9 (9.6) | 39.5 (6.6) | 5.5 (4.2 to 6.8) | <.001 | 43.2 (8.4) | 38.5 (6.0) | 4.7 (4.2 to 5.3) | <.001 | 1.0 (0.1 to 1.9) | .03 |
| Antihypertensive medication use, No. (%) | 2477 (24.0) | 90 (41.9) | −17.9 (−23.7 to −12.1) | <.001 | 1593 (20.5) | 320 (34.3) | −13.8 (−16.6 to −11.0) | <.001 | 7.6 (0.5 to 14.7) | .04 |
| Smoking status, No. (%) | | | | | | | | | | |
| Current | 2333 (22.6) | 22 (10.3) | 12.3 (6.7 to 18.0) | <.001 | 1851 (23.8) | 155 (16.6) | 7.2 (4.4 to 10.1) | <.001 | −6.4 (−11.7 to −1.0) | .07 |
| Former | 3791 (36.8) | 91 (42.5) | −5.8 (−12.3 to 0.8) | | 2813 (36.2) | 370 (39.7) | −3.5 (−6.7 to −0.2) | | 2.8 (−4.5 to 10.1) | |
| Never | 4191 (40.6) | 101 (47.2) | −6.6 (−13.2 to 0.1) | | 3099 (39.9) | 407 (43.7) | −3.7 (−7.1 to −0.4) | | 3.5 (−3.9 to 10.9) | |
| Alcohol status, No. (%) | | | | | | | | | | |
| Current | 6032 (58.5) | 128 (59.8) | −1.3 (−8.0 to 5.3) | .88 | 4570 (58.9) | 603 (64.8) | −5.9 (−9.2 to −2.6) | <.001 | −5.0 (−12.1 to 2.2) | .21 |
| Former | 2018 (19.6) | 39 (18.2) | 1.3 (−4.0 to 6.7) | | 1484 (19.1) | 170 (18.3) | 0.9 (−1.8 to 3.5) | | −0.04 (−5.8 to 5.7) | |
| Never | 2264 (22.0) | 47 (22.0) | 0.0 (−5.6 to 5.6) | | 1708 (22.0) | 158 (17.0) | 5.0 (2.2 to 7.8) | | 5.0 (−0.7 to 10.7) | |
| Diagnosed diabetes | 1206 (11.7) | 31 (14.7) | −3.0 (−7.4 to 1.4) | .19 | 789 (10.2) | 101 (10.9) | −0.7 (−2.8 to 1.4) | .50 | 3.8 (−1.0 to 8.6) | .12 |

(continued)

Table 3. Characteristics of Participants According to IDH Status by JNC7 and 2017 ACC/AHA Definitions in the ARIC Study (Visit 2, 1990-1992) (continued)

| Characteristic | By JNC7 Definition | | | | By ACC/AHA Definition | | | | IDH Definition |
|---|---|---|---|---|---|---|---|---|---|
| | Normotension | IDH | Difference (95% CI)[a] | *P* Value[a] | Normotension | IDH | Difference (95% CI)[b] | *P* Value[b] | Difference (95% CI)[c] | *P* Value[c] |
| BMI, mean (SD) | 27.4 (5.1) | 29.5 (6.0) | −2.0 (−2.7 to −1.4) | <.001 | 27.0 (4.8) | 28.6 (5.3) | −1.6 (−1.9 to −1.2) | <.001 | 0.9 (0.1 to 1.7) | .03 |
| LDL-C level, median (IQR), mg/dL | 130 (108.6 to 154.4) | 139.8 (112 to 163.4) | −9.8 (−15.7 to −3.9) | .001 | 129.4 (108.4 to 153.8) | 132 (111 to 156.2) | −2.6 (−5.5 to 0.3) | .08 | 7.8 (1.5 to 14.1) | .02 |
| HDL-C level, mean (SD), mg/dL | 50.2 (16.7) | 48.2 (14.5) | 2.0 (−0.3 to 4.3) | .08 | 50.5 (16.6) | 49.1 (17.3) | 1.4 (0.2 to 2.5) | .02 | −0.9 (−3.4 to 1.6) | .48 |
| Triglyceride level, median (IQR), mg/dL | 111 (80 to 156) | 119 (85 to 171) | −8.0 (−17.1 to 1.1) | .09 | 108 (79 to 151) | 114 (82 to 170) | −6.0 (−10.7 to −1.3) | .01 | 5.0 (−6.5 to 16.5) | .39 |
| Lipid medication, No. (%) | 557 (5.4) | 2 (0.9) | 4.5 (1.4 to 7.5) | .004 | 418 (5.4) | 38 (4.1) | 1.3 (−0.2 to 2.8) | .09 | −3.1 (−5.9 to −0.4) | .02 |
| eGFR, mean (SD), mL/min/1.73 m$^2$ | 97.1 (14.6) | 95.2 (17.1) | 1.9 (−0.1 to 3.9) | .06 | 97.1 (14.3) | 97.8 (15.6) | −0.7 (−1.7 to 0.3) | .16 | −2.7 (−5.0 to −0.3) | .03 |

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; ARIC, Atherosclerosis Risk in Communities; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; IDH, isolated diastolic hypertension; IQR, interquartile range; JNC7, 2003 Joint National Committee; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

SI conversion factors: To convert HDL-C and LDL-C to mmol/L, multiply by 0.0259; and triglycerides to mmol/L, multiply by 0.0113.

[a] Difference and *P* value comparing those with normotension (systolic BP <140 mm Hg and diastolic BP <90 mm Hg) vs those with IDH (systolic BP <140 mm Hg and diastolic BP ≥90 mm Hg), using the JNC7 definition.

[b] Difference and *P* value comparing those with normotension (systolic BP <130 mm Hg and diastolic BP <80 mm Hg) vs those with IDH (systolic BP <130 mm Hg and diastolic BP ≥80 mm Hg), using the 2017 ACC/AHA definition.

[c] Difference and *P* value comparing those with IDH by the JNC7 definition vs those with IDH by the 2017 ACC/AHA definition.

The estimated prevalence of IDH in the NHANES can be applied to 2016 US Census data to approximate the corresponding numbers of adults with this diagnosis. Because hypertension is defined on the basis of either a systolic BP greater than or equal to 130 mm Hg or a diastolic BP greater than or equal to 80 mm Hg,[1] the 5.2% higher prevalence of IDH in the US population translated into an estimated 12.1 million more US adults being newly labeled as "hypertensive" (despite having a systolic BP <130 mm Hg). Classifying a person as hypertensive has psychosocial and financial implications (eg, insurance premiums may change).[28] While most new hypertension diagnoses based on the presence of IDH applied to younger adults who are unlikely to be candidates for drug therapy because of predicted 10-year ASCVD risk less than 10%,[1] the analyses in this study nonetheless estimated that 0.6% of US adults (1.4 million) were newly considered candidates for pharmacologic treatment on the basis of IDH alone. Thus, IDH may represent the sole indication for treatment among about one-quarter of the 4.2 million US adults overall who have been newly recommended for BP therapy since the 2017 ACC/AHA BP guideline.[15]

Given prior epidemiologic studies have consistently reported increased ASCVD risk above a diastolic BP of 75 mm Hg[11,29-32] (these data significantly informed the decision to reduce the diastolic BP threshold for hypertension from 90 to 80 mm Hg in the 2017 guideline), the finding that IDH is neither associated with increases in subclinical nor clinical ASCVD in this analysis might appear contradictory at first. However, this study was not an examination of whether elevated diastolic BP is harmful per se, rather it evaluated the prognostic implications of a specific BP phenotype (IDH). In addition, the above results, demonstrating that diastolic BPs between 80 and 90 mm Hg have no adverse prognostic significance when systolic BP is well controlled, appear to be supported indirectly by other observational data[10] and also by the Hypertension Optimal Treatment (HOT) Trial.[33] For example, the HOT Trial reported that a strategy to treat diastolic BP to 80 mm Hg was not associated with significant benefit on the primary end point compared with treatment to 90 mm Hg.

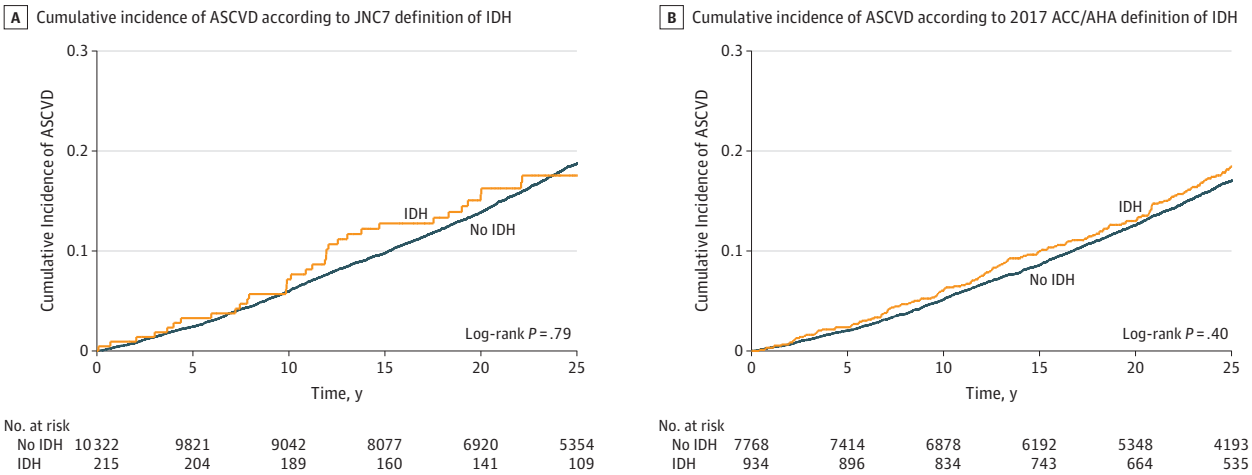
## Limitations

This study has several limitations. First, the possibility of residual confounding cannot be eliminated. For example, while sensitivity analyses adjusted for subsequent antihypertension medication use and follow-up systolic BP levels, it is impossible to rule out confounding by these variables.

Second, because the minimum participant age at baseline in the ARIC Study was 48 years, the results of this analysis may not be generalizable to younger adults.[31] This is important because diastolic BP typically falls with age as large blood vessels become less compliant.[13,34,35] The ARIC Study results were consistent in a nationally representative study using NHANES data (median age, 40 years; age range, ≥20) and in the CLUE II cohort (median age, 42 years), but future studies from even younger cohorts will be informative.

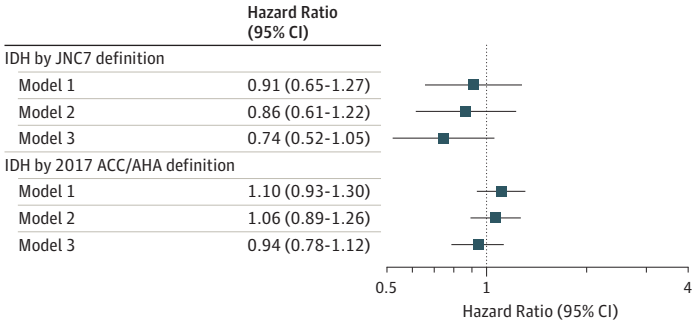
Third, this study included persons using antihypertensive medications in the primary analyses because guideline BP targets apply to both those who are not receiving

**Figure 1. Cumulative Incidence of Cardiovascular Events in the Atherosclerosis Risk in Communities (ARIC) Study, According to Both 2003 Joint National Committee (JNC7) and 2017 American College of Cardiology (ACC)/American Heart Association (AHA) Definitions of Isolated Diastolic Hypertension (IDH)**




A, The median follow-up in the sample testing the JNC7 definition was 25.1 years (interquartile range [IQR], 16.6-26.4) in the no IDH group and 25.1 years (IQR, 14.6-26.4) in the IDH group. B, The median follow-up in the sample testing the 2017 ACC/AHA definition was 25.2 years (IQR, 17.4-26.5) in the no IDH group and 25.4 years (IQR, 17.9-26.6) in the IDH group. ASCVD indicates atherosclerotic cardiovascular disease.

**Figure 2. Associations Between Isolated Diastolic Hypertension (IDH), by 2003 Joint National Committee (JNC7) and 2017 American College of Cardiology (ACC)/American Heart Association (AHA) Definitions, and Incident Atherosclerotic Cardiovascular Disease (ASCVD) Events in the Atherosclerosis Risk in Communities (ARIC) Study**




All comparisons are vs ARIC Study participants with normal blood pressure (BP) (when studying IDH by the JNC7 definition, this group consists of those with systolic BP <140 mm Hg and diastolic BP <90 mm Hg; when studying IDH by the 2017 ACC/AHA definition, this group consists of those with systolic BP <130 mm Hg and diastolic BP <80 mm Hg). Model 1 is adjusted for age, sex, race-center, and educational attainment. Model 2 is adjusted for model 1 plus smoking status, alcohol consumption, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, body mass index, antihypertensive medication, diabetes, and estimated glomerular filtration rate. Model 3 is adjusted for model 2 plus baseline systolic BP.

therapy (ie, whether to initiate treatment) and to those who are (ie, whether to intensify treatment). However, in stratified analyses, the results were similar among participants not taking baseline BP medication.

Fourth, the previously mentioned ARIC Study results may not apply to persons who do not identify as either black or white, though findings were similar in the NHANES (which is designed to be nationally representative after weighting).

Fifth, while these results are consistent with prior research on IDH by the JNC7 definition, this analysis may not have been powered to detect more modest associations between IDH and incident events, a possibility that should motivate further research from other studies. However, there were a large number of ASCVD events (n = 1386) during 25.2 years of follow-up in the ARIC Study and associations for cardiovascular mortality were similar in the approximately 50 000 participants in the 2 younger, external validation cohorts.

## Conclusions

In this analysis of US adults, the estimated prevalence of IDH was more common when defined by the 2017 ACC/AHA BP guideline compared with the JNC7 guideline. However, IDH was not significantly associated with increased risk for cardiovascular outcomes.

## ARTICLE INFORMATION

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