

ORIGINAL RESEARCH

Association of Hypertension According to New American College of Cardiology/American Heart Association Blood Pressure Guidelines With Incident Dementia in the ARIC Study Cohort

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BACKGROUND: The impact of the new 2017 American College of Cardiology/American Heart Association (ACC/AHA) hypertension guideline on dementia risk at the population level has not been evaluated.

METHODS AND RESULTS: We studied dementia-free participants in the ARIC (Atherosclerosis Risk in Communities) Study cohort in 1987 to 1989. Hypertension was defined by 2003 Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and 2017 ACC/AHA guidelines using blood pressure measured at baseline. Dementia was defined using adjudicated consensus diagnoses, informant telephone interviews, and discharge codes from hospitalizations and death certificates. Cox regression estimated hazard ratios (HRs) for dementia and 95% CIs by hypertension categories, adjusting for confounders. Population attributable fraction of dementia was calculated by hypertension categories. Among 13 971 participants followed up for a median of 23 years, 1381 dementia cases were identified. Prevalence of hypertension was 34% and 48%, according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and ACC/AHA criteria, respectively. HRs (95% CIs) compared with normal blood pressure, according to ACC/AHA categories, were 1.35 (1.12–1.61) for elevated blood pressure, 1.28 (1.07–1.52) for hypertension stage 1, and 1.36 (1.18–1.57) for hypertension stage 2. Population attributable fractions (95% CIs) of dementia from blood pressure categories were 3% (1%–5%), 3% (1%–5%), and 9% (4%–14%), respectively. Population attributable fractions (95% CIs) using the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure categories were 6% (3%–9%) for prehypertension, 0% (–2% to 2%) for hypertension stage 1, and 9% (5%–13%) for hypertension stage 2.

CONCLUSIONS: Risk of dementia increased across hypertension categories defined by ACC/AHA guidelines. The population impact on dementia incidence using ACC/AHA categories was similar to the impact of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

Key Words: dementia ■ epidemiology ■ hypertension ■ population attributable fraction ■ practice guideline

Since the 1960s, studies have linked hypertension to impaired cognitive function and various dementias, especially when hypertension was assessed in midlife and cognition in late life.^{1–7} Numerous analyses from

the ARIC-NCS (Atherosclerosis Risk in Communities Neurocognitive Study) have established associations between cardiovascular risk factors, including midlife hypertension and diabetes mellitus, and the development

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CLINICAL PERSPECTIVE

What Is New?

- Although high blood pressure is an established risk factor for dementia, no prior studies have evaluated the risk and population attributable burden of hypertension in relation with dementia using the new hypertension diagnostic guidelines.
- In a large community-based cohort, risk of dementia increased across hypertension categories defined by new guidelines. The population impact on dementia incidence using current categorization was similar to the impact of older categories.

What Are the Clinical Implications?

- These results reinforce the importance of prevention and treatment of high blood pressure as a population and clinical strategy to reduce the burden of dementia.

Nonstandard Abbreviations and Acronyms

ACC	American College of Cardiology
AHA	American Heart Association
ARIC	Atherosclerosis Risk in Communities
ARIC-NCS	Atherosclerosis Risk in Communities Neurocognitive Study
DBP	diastolic blood pressure
JNC7	Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
PAF	population attributable fraction
SBP	systolic blood pressure
SPRINT-MIND	Systolic Blood Pressure Intervention Trial Memory and Cognition in Decreased Hypertension

of incident dementia and cognitive decline.^{2,8,9} However, in 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) changed the definition of high blood pressure (BP), lowering the cutoff to define hypertension. This announcement marks the first comprehensive change to the categorization of hypertension since 2003 and is estimated to classify ~46% of the US adult population as having hypertension.^{10,11}

The most significant change to the categorization of BP is the removal of the prehypertension classification, instead classifying people as having normal BP

(systolic BP [SBP] <120 mm Hg and diastolic BP [DBP] <80 mm Hg), elevated BP (SBP 120–129 mm Hg and DBP <80 mm Hg), stage 1 hypertension (SBP 130–139 mm Hg or DBP 80–89 mm Hg), or stage 2 hypertension (SBP ≥140 mm Hg or DBP ≥90 mm Hg). The rationale behind changing the categorization of hypertension was a result of recent controlled studies and expert consensus, which concluded that more intensive control of cardiovascular risk factors is needed to reduce the risk of various cardiovascular diseases and all-cause mortality.^{12,13} Earlier analyses in the ARIC-NCS examining the association of hypertension with dementia risk were based on the previously used Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) guidelines, leaving unanswered questions as to how the new categorization of hypertension relates to the development of incident dementia.

The first objective of this analysis was to assess the association of hypertension and of BP categories defined according to the new ACC/AHA guidelines with the risk of incident dementia, and to compare these associations with those using the previous JNC7 categorization. We hypothesized that midlife hypertension (SBP ≥130 mm Hg or DBP ≥80 mm Hg), as defined by the new guidelines, is related to an increased risk of incident dementia. In addition, we hypothesized that the association of stage 2 hypertension with dementia would be stronger than the association for stage 1 hypertension, compared with normal BP. Because Black people have higher prevalence of hypertension and experience higher rates of dementia,^{9,14,15} we examined whether these associations varied by race. The second objective was to calculate the population attributable fraction (PAF) of hypertension and of BP categories, defined according to both the ACC/AHA guidelines and the JNC7 definition, with the risk of incident dementia. We hypothesized that hypertension would be responsible for a large proportion of dementia cases in the ARIC (Atherosclerosis Risk in Communities) Study cohort, although the PAF with the new definition would be only modestly larger than with the old hypertension definition.

METHODS

The data, analysis, and study materials are not available to other researchers for purposes of reproducing the results or replicating the analysis because of human subject restrictions. Interested investigators may contact the ARIC Study Center at the University of North Carolina to request access to ARIC Study data.

Participants

The ARIC Study was a prospective cohort that recruited 15 792 participants, aged 45 to 64 years in 1987 to 1989, from field centers in 4 US communities: Washington County, Maryland; Forsyth County, North Carolina; Jackson, Mississippi; and Minneapolis suburbs, Minnesota.^{9,16} The goals of the ARIC Study were to investigate the cause of atherosclerosis and the variation in cardiovascular risk factors by race, sex, location, and time.^{9,16} After the initial baseline visit, participants were followed up by telephone (annually before 2012; twice yearly after) and took part in several additional clinic visits, including visit 5 (2011–2013), which was the baseline examination for the ARIC-NCS, where dementia was ascertained through neurocognitive measures.¹⁶

A total of 13 971 of the initial 15 792 participants who were recruited to the ARIC Study cohort were included in the analysis. These participants were dementia free (participants with a diagnosis of dementia before enrollment were excluded from the analysis) and had information on BP and other covariates at visit 1 (the baseline visit). For the purposes of this analysis, those who were not identified as Black or White people were excluded from all field centers. In addition, the small number of Black participants from the Maryland and Minnesota field centers were excluded to preempt issues of adjusting for race and center that would arise because the 2 samples in question are small. The ARIC Study was approved by each field center's institutional review board (Johns Hopkins University, Wake Forest University, University of Mississippi, and University of Minnesota), and all participants provided written informed consent (along with proxies, when required).^{2,9}

Blood Pressure

At baseline, sitting BP was measured 3 times with a random-zero sphygmomanometer after 5 minutes of rest, and the average of the last 2 measurements was used to define BP categories. Hypertension was defined by the 2003 JNC7 and 2017 ACC/AHA guidelines using baseline BP. For both sets of guidelines, participants using antihypertensive medication were classified as having stage 2 hypertension.

Hypertension, defined according to the old JNC7 guidelines, is SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg, and SBP ≥ 130 mm Hg or DBP ≥ 80 mm Hg according to the new ACC/AHA guidelines. The classification of normal BP remained the same between the 2 sets of guidelines (<120/80 mm Hg), whereas the prehypertensive category (SBP 120–139 mm Hg or DBP 80–89 mm Hg) from the JNC7 guidelines was changed to elevated BP (SBP 120–129 mm Hg and DBP <80 mm Hg) in the ACC/AHA guidelines (Tables 1 and 2).^{11,17}

Covariates

Covariates measured at visit 1 (the baseline visit) that were considered as potential confounders include age, sex, race, field center, and education level (grade school or 0 years; high school, no degree; high school graduate; vocational school; college; or graduate or professional school), of which sex, race, and education level were self-reported. Apolipoprotein E $\epsilon 4$ carriers were identified by genotyping and were defined by the number of $\epsilon 4$ alleles (0, 1, or 2) they carried. History of smoking (current, former, or never) and alcohol use (g/wk) were self-reported. Physical activity (a calculated score based on the intensity, hours a week, and months a year spent in sport or exercise during leisure time) was assessed using the ARIC Study/Baecke questionnaire, which recorded information on physical activity in sports, during leisure time, and at work.¹⁸ Total cholesterol (mmol/L), high-density lipoprotein cholesterol (mmol/L), and body mass index (kg/m²) were measured and included as potential confounders. Presence of diabetes mellitus was defined as fasting blood glucose level of at least 126 mg/dL, nonfasting blood glucose level of at least 200 mg/dL, use of diabetes mellitus medications or insulin, or self-report of a physician's diagnosis. Prevalent coronary heart disease, prevalent heart failure, and prevalent stroke (all measured yes or no) were defined on the basis of self-reported information.^{2,9}

Dementia

Dementia was defined using adjudicated dementia diagnoses at visit 5 (2011–2013), which included data from longitudinal cognitive evaluations, a complete neuropsychological battery at visit 5, and informant telephone interview.¹⁹ For participants who did not attend visit 5, dementia was also identified by telephone interviews using standardized questionnaires and *International Classification of Diseases, Ninth Revision (ICD-9)*, codes from hospitalizations and death certificates through 2013.¹⁹ The *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes used to define dementia referred to Alzheimer's disease (331.0), vascular dementia (290.4), or dementia of other cause, including senile, presenile, and frontotemporal dementias and dementias secondary to general medical conditions (290.0, 290.1, 290.2, 290.3, 290.9, 294.1, 294.2, 294.8, 294.9, 331.1, 331.2, 331.8, and 331.9).²⁰ Date of dementia onset was defined as the earliest of the date of the visit 5 assessment, hospitalization discharge or death certificate with dementia diagnosis, or date of the telephone interview.

Table 1. Baseline Characteristics of ARIC Study Participants by JNC7 Hypertension Guidelines, 1987 to 1989

Characteristic	Normal	Prehypertension	Stage 1	Stage 2*	Overall
No. (%)	5793 (41.5)	3369 (24.1)	1000 (7.2)	3809 (27.3)	13 971 (100)
BP (SBP and/or DBP), mm Hg	<120 and <80	120–139 or 80–89	140–159 or 90–99	≥160 or ≥100	Not applicable
Women, n (%)	3362 (58.0)	1665 (49.4)	493 (49.3)	2191 (57.5)	7711 (55.2)
White, n (%)	4978 (85.9)	2521 (74.8)	625 (62.5)	2114 (55.5)	10 238 (73.3)
Age, mean (SD), y	52.3 (5.5)	54.5 (5.8)	55.3 (5.7)	55.6 (5.6)	54.1 (5.8)
Education level, n (%)					
Grade school or 0 y	327 (5.6)	293 (8.7)	147 (14.7)	537 (14.1)	1304 (9.3)
High school, no degree	628 (10.8)	460 (13.7)	144 (14.4)	707 (18.6)	1939 (13.9)
High school graduate	1898 (32.8)	1112 (33.0)	310 (31.0)	1185 (31.1)	4505 (32.3)
Vocational school	529 (9.1)	308 (9.1)	83 (8.3)	278 (7.3)	1198 (8.6)
College	1724 (29.8)	874 (25.9)	235 (23.5)	794 (20.9)	3627 (26.0)
Graduate or professional school	687 (11.9)	322 (9.6)	81 (8.1)	308 (8.1)	1398 (10.0)
Smoking status, n (%)					
Current	1678 (29.0)	809 (24.0)	241 (24.1)	927 (24.3)	3655 (26.2)
Former	1809 (31.2)	1173 (34.8)	317 (31.7)	1228 (32.2)	4527 (32.4)
Never	2306 (39.8)	1387 (41.2)	442 (44.2)	1654 (43.4)	5789 (41.4)
Alcohol consumption, mean (SD), g/wk	37.2 (79.5)	48.1 (100.5)	58.1 (130.6)	39.8 (98.9)	42.0 (94.8)
Physical activity score, mean (SD)	2.5 (0.8)	2.5 (0.8)	2.4 (0.8)	2.3 (0.8)	2.4 (0.8)
BMI, mean (SD), kg/m ²	26.0 (4.3)	27.8 (5.2)	28.5 (5.8)	29.8 (5.9)	27.7 (5.4)
SBP, mean (SD), mm Hg	106.3 (8.4)	126.2 (6.5)	144.1 (8.2)	133.4 (22.2)	121.2 (18.8)
DBP, mean (SD), mm Hg	66.4 (7.1)	76.2 (7.6)	84.3 (9.2)	79.7 (12.7)	73.7 (11.3)
Total cholesterol, mean (SD), mmol/L	5.4 (1.0)	5.6 (1.1)	5.6 (1.1)	5.7 (1.2)	5.5 (1.1)
HDL cholesterol, mean (SD), mmol/L	1.4 (0.4)	1.3 (0.5)	1.4 (0.5)	1.3 (0.4)	1.3 (0.4)
Diabetes mellitus, n (%)	339 (5.9)	317 (9.4)	120 (12.0)	869 (22.8)	1645 (11.8)
Prevalent coronary heart disease, n (%)	203 (3.5)	112 (3.3)	23 (2.3)	329 (8.6)	667 (4.8)
Prevalent heart failure, n (%)	90 (1.6)	58 (1.7)	13 (1.3)	488 (12.8)	649 (4.7)
Prevalent stroke, n (%)	82 (1.4)	42 (1.3)	20 (2.0)	109 (2.9)	253 (1.8)
APOE ε4 genotype, n (%)					
0 Alleles	4072 (70.3)	2361 (70.1)	681 (68.1)	2541 (66.7)	9655 (69.1)
1 Allele	1604 (27.7)	904 (26.8)	291 (29.1)	1149 (30.2)	3948 (28.3)
2 Alleles	117 (2.0)	104 (3.1)	28 (2.8)	119 (3.1)	368 (2.6)
Antihypertensive use, n (%)	0	0	0	3505 (92.0)	3505 (25.1)

APOE indicates apolipoprotein E; ARIC, Atherosclerosis Risk in Communities; BMI, body mass index; BP, blood pressure; DBP, diastolic BP; HDL, high-density lipoprotein; JNC7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; and SBP, systolic BP.

*Participants using antihypertensive medication were included in the hypertension stage 2 category.

Statistical Analysis

Statistical software SAS Version 9.4 was used for this analysis. Primary analyses used Cox proportional hazards regression models to estimate hazard ratios (HRs) and 95% CIs of incident dementia by hypertension categories, adjusting for potential confounders. The primary end point was time between visit 1 and diagnosis of dementia, loss to follow-up, or administrative censoring (at the latest date for visit 5 assessment or the date of last participant contact up to September 1, 2013), whichever occurred first.⁹ Several models were run, the first of which included all variables that were considered potential confounders: age, sex, race/field

center, education level, apolipoprotein E ε4 genotype, smoking status, alcohol use, physical activity, total cholesterol, high-density lipoprotein cholesterol, body mass index, presence of diabetes mellitus, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke. Subsequent models were stratified by sex, race, and age (<55 or ≥55 years) separately. We also tested for an interaction between BP categories and the stratifying variable. These models were run for both the new ACC/AHA and the old JNC7 guidelines, and each model was run using the full BP categories (all 4 categories) in addition to binary categories (normal and prehypertension/elevated were

Table 2. Baseline Characteristics of ARIC Study Participants by ACC/AHA Hypertension Guidelines, 1987 to 1989

Characteristic	Normal	Elevated	Stage 1	Stage 2*	Overall
No. (%)	5793 (41.5)	1433 (10.3)	1936 (13.9)	4809 (34.4)	13 971 (100)
BP (SBP and/or DBP), mm Hg	<120 and <80	120–129 and <80	130–139 or 80–89	≥140 or ≥90	Not applicable
Women, n (%)	3362 (58.0)	755 (52.7)	910 (47.0)	2684 (55.8)	7711 (55.2)
White, n (%)	4978 (85.9)	1168 (81.5)	1353 (69.9)	2739 (57.0)	10 238 (73.3)
Age, mean (SD), y	52.8 (5.5)	55.4 (5.7)	53.9 (5.8)	55.5 (5.6)	54.1 (5.8)
Education level, n (%)					
Grade school or 0 y	327 (5.6)	117 (8.2)	176 (9.1)	684 (14.2)	1304 (9.3)
High school, no degree	628 (10.8)	195 (13.6)	265 (13.7)	851 (17.7)	1939 (13.9)
High school graduate	1898 (32.8)	497 (34.7)	615 (31.8)	1495 (31.1)	4505 (32.3)
Vocational school	529 (9.1)	128 (8.9)	180 (9.3)	361 (7.5)	1198 (8.6)
College	1724 (29.8)	362 (25.3)	512 (26.5)	1029 (21.4)	3627 (26.0)
Graduate or professional school	687 (11.9)	134 (9.4)	188 (9.7)	389 (8.1)	1398 (10.0)
Smoking status, n (%)					
Current	1678 (29.0)	375 (26.2)	434 (22.4)	1168 (24.3)	3655 (26.2)
Former	1809 (31.2)	485 (33.9)	688 (35.5)	1545 (32.1)	4527 (32.4)
Never	2306 (39.8)	573 (40.0)	814 (42.1)	2096 (43.6)	5789 (41.4)
Alcohol consumption, mean (SD), g/wk	37.2 (79.5)	45.9 (91.3)	49.7 (106.8)	43.6 (106.5)	42.0 (94.8)
Physical activity score, mean (SD)	2.5 (0.8)	2.5 (0.8)	2.4 (0.8)	2.3 (0.8)	2.4 (0.8)
BMI, mean (SD), kg/m ²	26.0 (4.3)	27.5 (5.0)	28.1 (5.4)	29.5 (5.9)	27.7 (5.4)
SBP, mean (SD), mm Hg	106.3 (8.4)	123.9 (2.8)	128.0 (7.7)	135.6 (20.5)	121.2 (18.8)
DBP, mean (SD), mm Hg	66.4 (7.1)	71.4 (6.2)	79.7 (6.6)	80.7 (12.2)	73.7 (11.3)
Total cholesterol, mean (SD), mmol/L	5.4 (1.0)	5.6 (1.0)	5.6 (1.1)	5.7 (1.1)	5.5 (1.1)
HDL cholesterol, mean (SD), mmol/L	1.4 (0.4)	1.3 (0.4)	1.3 (0.5)	1.3 (0.4)	1.3 (0.4)
Diabetes mellitus, n (%)	339 (5.9)	135 (9.4)	182 (9.4)	989 (20.6)	1645 (11.8)
Prevalent coronary heart disease, n (%)	203 (3.5)	52 (3.6)	60 (3.1)	352 (7.3)	667 (4.8)
Prevalent heart failure, n (%)	90 (1.6)	26 (1.8)	32 (1.7)	501 (10.4)	649 (4.7)
Prevalent stroke, n (%)	82 (1.4)	19 (1.3)	23 (1.2)	129 (2.7)	253 (1.8)
APOE ε4 genotype, n (%)					
0 Alleles	4072 (70.3)	1020 (71.2)	1341 (69.3)	3222 (67.0)	9655 (69.1)
1 Allele	1604 (27.7)	366 (25.5)	538 (27.8)	1440 (29.9)	3948 (28.3)
2 Alleles	117 (2.0)	47 (3.3)	57 (2.9)	147 (3.1)	368 (2.6)
Antihypertensive use, n (%)	0	0	0	3505 (72.9)	3505 (25.1)

ACC indicates American College of Cardiology; AHA, American Heart Association; APOE, apolipoprotein E; ARIC, Atherosclerosis Risk in Communities; BMI, body mass index; BP, blood pressure; DBP, diastolic BP; HDL, high-density lipoprotein; and SBP, systolic BP.

*Participants using antihypertensive medication were included in the hypertension stage 2 category.

grouped as not having hypertension, and stage 1 and stage 2 hypertension were grouped as having hypertension). In sensitivity analyses, we ignored use of antihypertensive medication in assigning participants to categories of hypertension. We estimated the cumulative survival by hypertension (binary categories) using JNC7 and ACC/AHA definitions, overall and by age, considering death as a competing risk.

PAF of dementia by categories of hypertension was calculated using standard approaches to determine the possible impact, if any, of preventing hypertension on the incidence of dementia. Rate ratios (RRs) were calculated using Poisson regression, and the prevalence of hypertension in the population was calculated

for each BP category. The equation $pd \left[\frac{RR-1}{RR} \right]$, where pd is equal to the proportion of cases exposed to hypertension, was used to calculate the PAF.^{21,22} The PAF was calculated for the 2 sets of hypertension guidelines and for the full BP categories and binary categories, as described above for the Cox proportional hazards models.

RESULTS

Cohort Characteristics

A total of 13 971 participants contributed to the analysis. The mean age of this sample at baseline was 54.1

years (SD, 5.8 years), 55.2% (n=7711) were identified as women, and 73.3% (n=10 238) were identified as White individuals. In total, 1381 cases of dementia were identified during a mean (median) follow-up of 20.3 (23.0) years among the 13 971 participants, which represents 9.9% of the sample. The overall incidence rate of dementia among the cohort was 4.9 per 1000 person-years.

According to the previous JNC7 guidelines, 41.5% of participants were categorized as having normal BP, 24.1% as prehypertensive, 7.2% as stage 1 hypertension, and 27.3% as stage 2 hypertension. Overall, those with hypertension were more likely to be Black individuals, were more likely to be older, had higher body mass index, and had higher prevalence of diabetes mellitus and cardiovascular disease (Table 1).

According to the new ACC/AHA guidelines, 41.5% of participants were categorized as having normal BP, 10.3% as elevated, 13.9% as stage 1 hypertension, and 34.4% as stage 2 hypertension. Those with hypertension were more likely to be Black individuals, were more likely to be older, and had higher prevalence of cardiovascular disease and cardiovascular risk factors (Table 2).

Association of Hypertension Categories With Incidence of Dementia

Compared with individuals in the normal BP category, the HRs and 95% CIs of dementia using the JNC7 categories were 1.31 (95% CI, 1.13–1.51) for prehypertension, 1.12 (95% CI, 0.89–1.41) for stage 1 hypertension, and 1.44 (95% CI, 1.24–1.66) for stage 2 hypertension (Table 3).

Similarly, using the ACC/AHA guidelines, HRs and 95% CIs of dementia were 1.35 (95% CI, 1.12–1.61) for elevated BP, 1.28 (95% CI, 1.07–1.52) for stage 1 hypertension, and 1.36 (95% CI, 1.18–1.57) for stage 2 hypertension, compared with those with normal BP (Table 3).

In an analysis ignoring use of antihypertensive medication when creating hypertension categories, results were essentially unchanged for categories based on the ACC/AHA guideline, but a stronger association between stage 2 hypertension and dementia was observed (HR, 1.81; 95% CI, 1.44–2.28) (Table S1).

Association of Hypertension (Binary Variable) With Incidence of Dementia

Incidence of dementia was increased among hypertensive participants compared with nonhypertensive participants using both the JNC7 and ACC/AHA definitions. The HR (95% CI) of dementia in hypertensive individuals, according to the JNC7 guideline definition, was 1.19 (95% CI, 1.06–1.34), whereas it was 1.22 (95%

CI, 1.08–1.37) using the ACC/AHA guideline definition (Table 4). Cumulative incidence risk of dementia by hypertension category, considering death as a competing risk, is presented in the Figure.

Analyses stratified by sex and race showed nominally stronger associations between hypertension and dementia in women compared with men, and White individuals compared with Black individuals. However, none of these differences was statistically significant (all *P* values for interaction >0.10) (Tables S2 and S3). In contrast, the association of hypertension with dementia tended to be stronger among younger participants, particularly those with hypertension stage 2 (*P* value for interaction <0.10; Table S2) and when categorizing hypertension as a dichotomous variable (*P* value for interaction <0.05; Table S3). Figure S1 shows the cumulative risk of dementia by hypertension categories and age group.

PAF of Dementia From Hypertension Categories

According to the JNC7 guidelines, the PAF values of dementia from hypertension categories were 6.3% (95% CI, 2.9%–9.1%), 0.1% (95% CI, –1.6% to 1.5%), and 9.4% (95% CI, 5.1%–13.2%) for prehypertension, stage 1 hypertension, and stage 2 hypertension, respectively. According to the ACC/AHA guidelines, the PAF values were 3.1% (95% CI, 1.3%–4.7%), 3.1% (95% CI, 0.9%–4.9%), and 9.1% (95% CI, 4.0%–13.7%) for elevated, stage 1 hypertension, and stage 2 hypertension, respectively (Table 5).

PAF of Dementia From Hypertension (Binary Variable)

According to the JNC7 guidelines, the RR of dementia was 1.11 (95% CI, 0.98–1.24) and the PAF of dementia was 4.4% (95% CI, –0.9% to 8.5%). According to the ACC/AHA guidelines, the RR was 1.16 (95% CI, 1.03–1.30) and the PAF was 8.1% (95% CI, 1.7%–13.5%) (Table 6).

DISCUSSION

This study showed that hypertension, defined with the new ACC/AHA guidelines, was associated with an increased risk of dementia, with a similar magnitude to the association using hypertension defined by JNC7 guidelines. Overall, the HRs using BP categories according to the ACC/AHA guidelines were comparable to those obtained using the JNC7 guideline categories, with associations in general being stronger among younger individuals. However, the PAF of dementia from hypertension according to the ACC/AHA guidelines was higher than the PAF of dementia according

Table 3. Association of JNC7 and ACC/AHA Hypertension Guideline Categories With Incident Dementia, ARIC Study, 1987 to 2013

JNC7 (Old) Guidelines	Normal	Prehypertension	Hypertension Stage 1	Hypertension Stage 2*
No. (%)	5793 (41.5)	3369 (24.1)	1000 (7.2)	3809 (27.3)
BP (SBP and/or DBP), mm Hg	<120 and <80	120–139 or 80–89	140–159 or 90–99	≥160 or ≥100
No. of incident dementia cases	396	376	96	513
Person-years	123 571	68 882	19 501	71 369
Incidence rate (per 1000 person-years)	3.2	5.5	4.9	7.2
Hazard ratio (95% CI) [†]	1 (Reference)	1.31 (1.13–1.51)	1.12 (0.89–1.41)	1.44 (1.24–1.66)
ACC/AHA (New) Guidelines	Normal	Elevated	Hypertension Stage 1	Hypertension Stage 2*
No. (%)	5793 (41.5)	1433 (10.3)	1936 (13.9)	4809 (34.4)
BP (SBP and/or DBP), mm Hg	<120 and <80	120–129 and <80	130–139 or 80–89	≥140 or ≥90
No. of incident dementia cases	396	176	200	609
Person-years	123 571	29 053	39 830	90 871
Incidence rate (per 1000 person-years)	3.2	6.1	5.0	6.7
Hazard ratio (95% CI) [†]	1 (Reference)	1.35 (1.12–1.61)	1.28 (1.07–1.52)	1.36 (1.18–1.57)

ACC indicates American College of Cardiology; AHA, American Heart Association; ARIC, Atherosclerosis Risk in Communities; BP, blood pressure; DBP, diastolic BP; JNC7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; and SBP, systolic BP.

*Participants using antihypertensive medication were included in the hypertension stage 2 category.

[†]Cox proportional hazards model adjusted for age, sex, race/field center, education level, apolipoprotein E ε4 genotype, smoking status, alcohol consumption, physical activity, total cholesterol, high-density lipoprotein cholesterol, body mass index, diabetes mellitus, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke.

to the JNC7 guidelines (8% versus 4%), consistent with the higher prevalence of hypertension using the new definition.

Table 4. Association of Hypertension (Binary Variable), According to JNC7 and ACC/AHA Guidelines, With Incident Dementia, ARIC Study, 1987 to 2013

Variable	No Hypertension	Hypertension
JNC7 (old) guidelines		
No. of incident dementia cases	772	609
Person-years	192 454	90 871
Incidence rate (per 1000 person-years)	4.0	6.7
Hazard ratio (95% CI) [*]	1 (Reference)	1.19 (1.06–1.34)
ACC/AHA (new) guidelines		
No. of incident dementia cases	572	809
Person-years	152 624	130 701
Incidence rate (per 1000 person-years)	3.7	6.2
Hazard ratio (95% CI) [*]	1 (Reference)	1.22 (1.08–1.37)

ACC indicates American College of Cardiology; AHA, American Heart Association; ARIC, Atherosclerosis Risk in Communities; and JNC7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

^{*}Cox proportional hazards model adjusted for age, sex, race/field center, education level, apolipoprotein E ε4 genotype, smoking status, alcohol consumption, physical activity, total cholesterol, high-density lipoprotein cholesterol, body mass index, diabetes mellitus, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke.

This analysis supports previous findings that, in general, high midlife BP is associated with a higher risk of incident dementia.^{2–9} For example, among men participating in the HAAS (Honolulu-Asia Aging Study), midlife elevated SBP was associated with increased dementia risk (HR, 2.29; 95% CI, 1.23–4.25, comparing SBP ≥140 with <120 mm Hg).³ Similarly, elevated SBP (≥160 mm Hg) in midlife was associated with increased risk of Alzheimer disease among participants in the North Karelia project and FINMONICA (Finnish portion of the Multinational Monitoring of Trends in Determinants in Cardiovascular Disease) study (odds ratio, 2.3; 95% CI, 1.0–5.5, compared with normal SBP).⁶

More recently, the SPRINT-MIND (Systolic Blood Pressure Intervention Trial Memory and Cognition in Decreased Hypertension) randomized clinical trial provided additional evidence that interventions to control hypertension can be successful in the prevention of adverse cognitive outcomes. In this trial, 9361 participants were randomized to an intensive treatment group (SBP goal of <120 mm Hg) or a standard treatment group (SBP goal of <140 mm Hg) to determine if these interventions reduced the occurrence of adjudicated probable dementia, adjudicated mild cognitive impairment, and a composite outcome of either cognitive outcome.¹³ Compared with standard treatment group, the intensive treatment group had a decreased rate of adjudicated probable dementia by 17%, mild cognitive impairment alone by

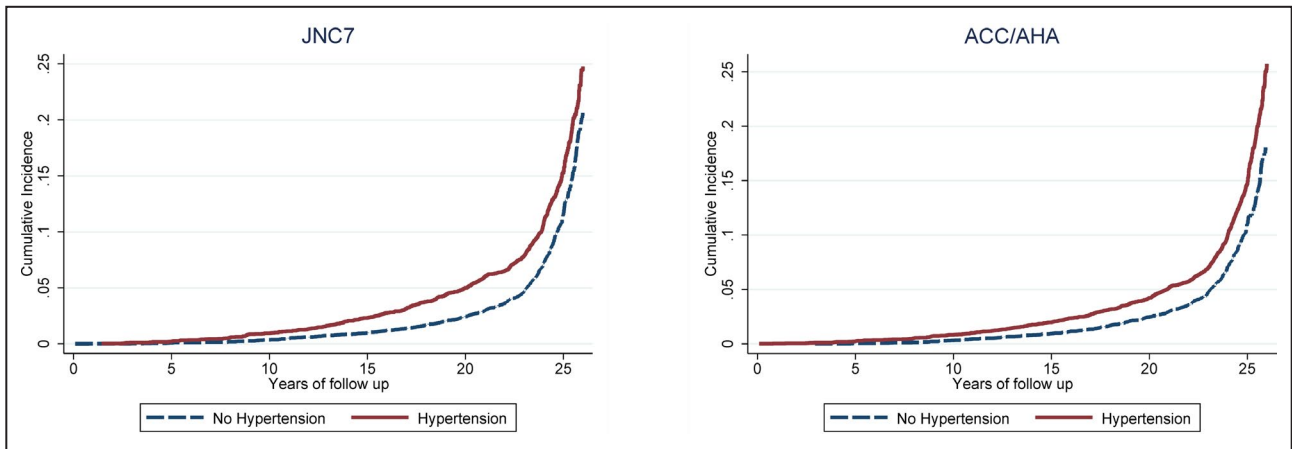


Figure 1. Cumulative incidence of dementia by hypertension, according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) and American College of Cardiology/American Heart Association (ACC/AHA) guidelines, ARIC (Atherosclerosis Risk in Communities) Study, 1987 to 2013.

19%, and the combined outcomes of mild cognitive impairment or probable dementia by 15%.¹³ This clinical trial adds support to the hypothesis that treating hypertension can reduce the risk of cognitive decline and probable dementia.

Although the new ACC/AHA guidelines recategorized more participants from prehypertension/elevated BP categories into stage 1 and stage 2 hypertension categories, the associations of hypertension with incident dementia were similar between the JNC7 and ACC/AHA guidelines. In analyses using multiple categories of BP, risk of dementia was highest for stage 2 hypertension. Using both JNC7 and ACC/AHA definitions, participants with stage 1 hypertension had slightly lower risk than those with prehypertension, whereas the risk was similar to

those with elevated BP, which could be attributable to chance or misclassification related to the choice of categorization for participants using antihypertensive medication.

In our analysis, associations between hypertension and dementia risk were nominally stronger in women compared with men, and in White individuals compared with Black individuals, using both sets of guidelines. However, interaction tests between BP categories and sex or race were not statistically significant. In contrast, associations were stronger among younger than older individuals. This observation is consistent with prior studies demonstrating that cardiovascular risk factors measured in midlife are strong predictors of dementia compared with risk factors measured later in life.⁸

Table 5. RRs of Incident Dementia and PAF of Dementia for Hypertension Based on JNC7 and ACC/AHA Hypertension Guidelines Categories, ARIC Study, 1987 to 2013

JNC7 (Old) Guidelines	Normal	Prehypertension	Hypertension Stage 1	Hypertension Stage 2
BP (SBP and/or DBP), mm Hg	<120 and <80	120–139 or 80–89	140–159 or 90–99	≥160 or ≥100*
RR (95% CI)†	1 (Reference)	1.30 (1.12–1.50)	1.02 (0.81 to 1.28)	1.34 (1.16–1.55)
PAF % (95% CI)	...	6.3 (2.9–9.1)	0.1 (–1.6 to 1.5)	9.4 (5.1–13.2)
ACC/AHA (New) Guidelines	Normal	Elevated	Hypertension Stage 1	Hypertension Stage 2
BP (SBP and/or DBP), mm Hg	<120 and <80	120–129 and <80	130–139 or 80–89	≥140 or ≥90
RR (95% CI)†	1 (Reference)	1.32 (1.11–1.59)	1.27 (1.07 to 1.51)	1.26 (1.10–1.45)
PAF % (95% CI)	...	3.1 (1.3–4.7)	3.1 (0.9 to 4.9)	9.1 (4.0–13.7)

ACC indicates American College of Cardiology; AHA, American Heart Association; ARIC, Atherosclerosis Risk in Communities; BP, blood pressure; DBP, diastolic BP; JNC7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; PAF, population attributable fraction; RR, rate ratio; and SBP, systolic BP.

*Participants using antihypertensive medication were included in the hypertension stage 2 category.

†Poisson regression model adjusted for age, sex, race/field center, education level, apolipoprotein E ε4 genotype, smoking status, alcohol consumption, physical activity, total cholesterol, high-density lipoprotein cholesterol, body mass index, diabetes mellitus, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke.

Table 6. RRs of Incident Dementia and PAF of Dementia for Hypertension Based on JNC7 and ACC/AHA Hypertension Guideline Categories (Binary Categories), ARIC Study, 1987 to 2013

Variable	No Hypertension	Hypertension
JNC7 (old) guidelines		
RR (95% CI)*	1 (Reference)	1.11 (0.98 to 1.24)
PAF % (95% CI)	...	4.4 (−0.9 to 8.5)
ACC/AHA (new) guidelines		
RR (95% CI)*	1 (Reference)	1.16 (1.03 to 1.30)
PAF % (95% CI)	...	8.1 (1.7 to 13.5)

ACC indicates American College of Cardiology; AHA, American Heart Association; ARIC, Atherosclerosis Risk in Communities; JNC7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; PAF, population attributable fraction; and RR, rate ratio.

*Poisson regression model adjusted for age, sex, race/field center, education level, apolipoprotein E ε4 genotype, smoking status, alcohol consumption, physical activity, total cholesterol, high-density lipoprotein cholesterol, body mass index, diabetes mellitus, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke.

Strengths and Limitations

Our analysis has some important strengths, such as a large and racially diverse sample that was followed up for several decades. Additional information through hospitalization codes, death certificates, and informant interviews allowed for the inclusion of deceased participants and those who did not attend the clinic examination. This helped mitigate the problem of greater loss to follow-up among cognitively impaired participants.

Our study, however, has some limitations. Using hospitalizations to identify dementia may lead to missed cases, although it has reasonable positive predictive value.²³ Also, cases of dementia that were identified through this approach may be incorrect because of misclassification of episodes of delirium as dementia and the higher likelihood that participants with vascular comorbidities attributable to hypertension may be more likely to be hospitalized. If many cases of dementia were misclassified, the association between hypertension and other vascular risk factors on incident dementia may be underestimated or overestimated.⁹ Estimates of the onset of dementia may also be imprecise as dementia often has an onset of years before a diagnosis is made. Black participants have higher mortality rates than White participants in the ARIC Study cohort, leading to fewer Black participants surviving to visit 5. This selective survival of Black participants could underestimate the effect of hypertension on dementia in this analysis because of less chance of observing incident dementia among this population. Issues with generalizability may arise as the ARIC Study was initiated

in the late 1980s and focused on only 4 communities and 2 races, with most Black participants recruited from 1 site. Last, residual confounding is possible despite careful consideration of well-known potential confounders, many of which were based on self-reported data.

CONCLUSIONS

The associations of incident dementia with midlife hypertension and BP categories, defined according to the new ACC/AHA guidelines, were generally similar to those using the old JNC7 guidelines. However, the PAFs of hypertension and of BP categories, according to the new guidelines, were slightly larger than those with the old BP guidelines, indicating the potential benefit on reducing dementia burden by preventing and treating hypertension using the new guidelines.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Tables S1–S3
Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Association of JNC7 and ACC/AHA Hypertension Guideline Categories with Incident Dementia, ARIC, 1987-2013.

JNC7 (Old) Guidelines	Normal	Prehypertension	Hypertension Stage 1	Hypertension Stage 2
N (%)	6703 (48.0)	4852 (34.7)	1776 (12.7)	640 (4.6)
BP (SBP and/or DBP, mm Hg)	<120 and <80	120-139 or 80-89	140-159 or 90-99	≥160 or ≥100
No. of incident dementia cases	505	579	202	95
Person-years	141,493	97,449	33,738	10,645
Incidence rate (per 1000 person-years)	3.6	5.9	6.0	8.9
Hazard Ratio (95% CI)[†]	1 [Reference]	1.28 (1.13, 1.46)	1.19 (1.00, 1.41)	1.81 (1.44, 2.28)
ACC/AHA (New) Guidelines	Normal	Elevated	Hypertension Stage 1	Hypertension Stage 2
N (%)	6703 (48.0)	1908 (13.7)	2944 (21.1)	2416 (17.3)
BP (SBP and/or DBP, mm Hg)	<120 and <80	120-129 and <80	130-139 or 80-89	≥140 or ≥90
No. of incident dementia cases	505	246	333	297
Person-years	141,493	38,023	59,426	44,383
Incidence rate (per 1000 person-years)	3.6	6.5	5.6	6.7
Hazard Ratio (95% CI)[†]	1 [Reference]	1.32 (1.13, 1.54)	1.25 (1.08, 1.44)	1.33 (1.14, 1.55)

Blood pressure categories based on study measurements, ignoring use of antihypertensive medications.

[†] Cox proportional hazards model adjusted for age, sex, race/field center, education level, APOE ε4 genotype, smoking status, alcohol consumption, physical activity, total cholesterol, HDL cholesterol, BMI, diabetes, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke.

JNC7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; ACC/AHA, American College of Cardiology/American Heart Association

Table S2. Association of JNC7 and ACC/AHA Hypertension Guideline Categories with Incident Dementia by Sex, Race, and Age, ARIC, 1987-2013.

JNC7 (Old) Guidelines	Normal	Prehypertension	Hypertension Stage 1	Hypertension Stage 2	p-value for Interaction
Female	1 [Reference]	1.37 (1.13, 1.68)	1.22 (0.90, 1.66)	1.47 (1.21, 1.79)	0.72
Male	1 [Reference]	1.23 (0.99, 1.52)	1.00 (0.71, 1.42)	1.36 (1.08, 1.71)	
White	1 [Reference]	1.35 (1.14, 1.60)	1.16 (0.87, 1.54)	1.48 (1.24, 1.77)	0.33
Black	1 [Reference]	1.10 (0.81, 1.49)	0.97 (0.66, 1.44)	1.25 (0.95, 1.64)	
Age <55	1 [Reference]	1.23 (0.94, 1.62)	1.32 (0.84, 2.06)	1.54 (1.16, 2.03)	0.09
Age ≥55	1 [Reference]	1.28 (1.08, 1.52)	1.06 (0.81, 1.38)	1.35 (1.13, 1.61)	
ACC/AHA (New) Guidelines	Normal	Elevated	Hypertension Stage 1	Hypertension Stage 2	p-value for Interaction
Female	1 [Reference]	1.36 (1.07, 1.74)	1.38 (1.08, 1.76)	1.42 (1.18, 1.71)	0.73
Male	1 [Reference]	1.33 (1.02, 1.75)	1.16 (0.90, 1.49)	1.26 (1.02, 1.57)	
White	1 [Reference]	1.38 (1.13, 1.68)	1.32 (1.07, 1.63)	1.40 (1.18, 1.66)	0.37
Black	1 [Reference]	1.13 (0.74, 1.73)	1.08 (0.78, 1.50)	1.20 (0.91, 1.56)	
Age <55	1 [Reference]	1.22 (0.82, 1.81)	1.24 (0.91, 1.69)	1.49 (1.14, 1.95)	0.06
Age ≥55	1 [Reference]	1.35 (1.10, 1.65)	1.20 (0.97, 1.49)	1.28 (1.08, 1.51)	

* Cox proportional hazards model adjusted for age, sex, race/field center, education level, APOE ε4 genotype, smoking status, alcohol consumption, physical activity, total cholesterol, HDL cholesterol, BMI, diabetes, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke.

JNC7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; ACC/AHA, American College of Cardiology/American Heart Association

Table S3. Association of Hypertension (Binary Variable) according to JNC7 and ACC/AHA Guidelines with Incident Dementia by Sex, Race, and Age, ARIC, 1987-2013.

JNC7 (Old) Guidelines	No Hypertension	Hypertension
Female	1 [Reference]	1.21 (1.04, 1.41)
Male	1 [Reference]	1.14 (0.95, 1.37)
p-value for Interaction	-	0.58
White	1 [Reference]	1.21 (1.05, 1.41)
Black	1 [Reference]	1.13 (0.93, 1.38)
p-value for Interaction	-	0.27
Age <55	1 [Reference]	1.35 (1.07, 1.69)
Age ≥55	1 [Reference]	1.13 (0.98, 1.29)
p-value for Interaction	-	0.01
ACC/AHA (New) Guidelines	No Hypertension	Hypertension
Female	1 [Reference]	1.28 (1.09, 1.50)
Male	1 [Reference]	1.13 (0.94, 1.35)
p-value for Interaction	-	0.29
White	1 [Reference]	1.24 (1.08, 1.43)
Black	1 [Reference]	1.13 (0.90, 1.41)
p-value for Interaction	-	0.21
Age <55	1 [Reference]	1.34 (1.07, 1.69)
Age ≥55	1 [Reference]	1.14 (0.99, 1.30)
p-value for Interaction	-	0.003

* Cox proportional hazards model adjusted for age, sex, race/field center, education level, APOE ε4 genotype, smoking status, alcohol consumption, physical activity, total cholesterol, HDL cholesterol, BMI, diabetes, prevalent coronary heart disease, prevalent heart failure, and prevalent stroke.

JNC7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; ACC/AHA, American College of Cardiology/American Heart Association

Figure S1. Cumulative incidence of dementia by hypertension according to JNC7 and ACC/AHA guidelines, by age group, ARIC 1987-2013,

