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Long-Term Cardiovascular Risk Associated With Stage 1 Hypertension Defined by the 2017 ACC/AHA Hypertension Guideline

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ABSTRACT

BACKGROUND Systolic/diastolic blood pressure (BP) of 130 to 139/80 to 89 mm Hg has been recently defined as stage 1 hypertension by the 2017 American College of Cardiology/American Heart Association hypertension guideline. To what extent this BP stratum affects cardiovascular risk needs to be quantified in considering its adoption in China.

OBJECTIVES The purpose of this study was to assess the relative risk and population-attributable risk of cardiovascular disease (CVD) associated with stage 1 hypertension and age-specific differences.

METHODS In total, 21,441 participants age ≥35 years and free of CVD at baseline were followed for up to 20 years in the Chinese Multi-provincial Cohort Study. The adjusted hazard ratio (HR) and population-attributable risk for CVD associated with stage 1 hypertension were calculated.

RESULTS Participants with stage 1 hypertension accounted for 25.8% of the cohort. Among participants age 35 to 59 years, the HR comparing stage 1 hypertension to BP <120/<80 mm Hg for CVD incidence was 1.78 (95% confidence interval [CI]: 1.50 to 2.11), coronary heart disease incidence was HR: 1.77 (95% CI: 1.33 to 2.36), stroke incidence was HR: 1.79 (95% CI: 1.45 to 2.22), and CVD mortality was HR: 2.50 (95% CI: 1.66 to 3.77). The proportions of cardiovascular deaths and events attributable to stage 1 hypertension were 26.5% and 13.4% among participants age 35 to 59 years, respectively. Among participants age ≥60 years, however, stage 1 hypertension was not related to increased risk compared with BP <120/<80 mm Hg, and population-attributable risk associated with this stratum was not found. Over a 15-year period, 65.0% of participants age 35 to 59 years with stage 1 hypertension experienced an increase in BP to 140/90 mm Hg or higher, and they had a 3.01-fold increased cardiovascular risk compared with those who maintained BP <130/<80 mm Hg.

CONCLUSIONS The effect of 2017 American College of Cardiology/American Heart Association stage 1 hypertension on cardiovascular risk is evidenced in young and middle-aged Chinese adults, but not in those age ≥60 years. (J Am Coll Cardiol 2018;72:1201–10) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BP = blood pressure
CHD = coronary heart disease
CI = confidence interval
CVD = cardiovascular disease
DBP = diastolic blood pressure
HR = hazard ratio
SBP = systolic blood pressure

The American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Clinical Practice Guidelines recently released the 2017 hypertension guideline (1). One new feature of this guideline is defining a systolic blood pressure (SBP) of 130 to 139 mm Hg or diastolic blood pressure (DBP) of 80 to 89 mm Hg as stage 1 hypertension.

The definition of hypertension has been evolving over time, from an SBP/DBP of 160/100 mm Hg or higher proposed in 1977 (2) to 140/90 mm Hg or higher in 1997 (3), and a further decrease to 130/80 mm Hg in 2017. These changes were largely driven by the importance of hypertension control in preventing cardiovascular disease (CVD), as documented by accumulated evidence from observational studies, clinical trials, and health economics evaluations.

SEE PAGE 1211

Although the impact of new stage 1 hypertension in the U.S. population has been summarized in the 2017 ACC/AHA guideline (1), it is unknown whether this recommendation can be applied to other populations. This is especially true for the Chinese population, in which there is a high risk of stroke mortality (4,5) and high prevalence of hypertension (6–10), as well as a large aging population (11). The rationale for the application of stage 1 hypertension hinges on the impact of this blood pressure (BP) stratum in a population, including the risk of BP progression, the risk of CVD, and the benefit of treatment and its cost effectiveness. In our previous report, 73.2% of participants with SBP of 130 to 139 mm Hg and 68.9% of participants with DBP of 85 to 89 mm Hg developed hypertension, defined as SBP/DBP 140/90 mm Hg or higher over 15 years (12). Moreover, follow-up data from the China National Hypertension Survey showed an elevated cardiovascular risk with prehypertension, broadly defined as an SBP/DBP of 120 to 139/80 to 89 mm Hg, but the risk attenuated among participants age ≥65 years (13). However, to what extent 2017 ACC/AHA stage 1 hypertension defined as SBP/DBP of 130 to 139/80 to 89 mm Hg affects CVD and whether its impact is consistent between young and old individuals warrant careful investigations in the Chinese population.

Therefore, using a 20-year cohort of Chinese participants, we aimed to assess the relative risk and population-attributable risk of CVD associated with 2017 ACC/AHA stage 1 hypertension, and to test whether the risk is age specific.

METHODS

STUDY DESIGN AND POPULATION. This study was an extension of the previously published CMCS (Chinese Multi-provincial Cohort Study) (14). In total, 21,953 Chinese participants from 8 of the 11 provinces in the original CMCS were included, of whom 16,811 participants age 35 to 64 years were recruited in 1992 and 1993. Additionally, 3,129 participants age 35 to 64 years were recruited from 1996 to 1999, and 2,013 participants age ≥35 years were recruited in 2004. The sampling methods are detailed in Online Figure 1. The study was approved by the ethics committee of Beijing An Zhen Hospital, Capital Medical University. Informed consent was obtained from all participants in the surveys.

Follow-up for the occurrence of new CVD events was conducted every 1 to 2 years from baseline to December 31, 2013, by active interview, supplemented with linkage to local disease surveillance systems. The 20-year follow-up rate was 81.0%. In the current study, 21,441 participants (11,047 men, 10,394 women) with complete data were eligible for the analysis of the association between baseline BP levels and cardiovascular risk, and 5,752 participants with complete data from baseline examination in 1992 and 1993 and re-examination in 2007 were eligible for the analysis of the association between change in BP and cardiovascular risk.

RISK FACTOR MEASUREMENT. In all surveys, demographic information, smoking status, and personal medical history were collected using standardized questionnaires. Anthropometric measurements and BP levels were recorded during physical examinations. BP was measured in the right arm in a sitting position using a mercury sphygmomanometer after at least 5 min of rest. DBP was defined as the beginning of Korotkoff phase 5. The mean value of 2 consecutive BP measurements was used. Current smoking was defined as ≥1 cigarette/day. Diabetes was defined as fasting blood glucose ≥126 mg/dl or previously diagnosed diabetes.

Venous blood samples were collected after at least 8 h of fasting. Total cholesterol, high-density lipoprotein cholesterol, triglycerides, and fasting blood glucose were measured on the day of collection according to previous reports (14,15).

CASE ASCERTAINMENT. All fatal and nonfatal acute coronary and stroke events were registered and reported. Acute coronary heart disease (CHD) events included acute myocardial infarction, sudden death, and other coronary deaths. Acute stroke events included subarachnoid hemorrhage, intracerebral

TABLE 1 Baseline Characteristics of Study Participants

	Total (N = 21,441)	Age Groups (yrs)		
		35–44 (n = 8,551)	45–59 (n = 10,734)	≥60 (n = 2,156)
Age, yrs	48.0 ± 8.8	39.3 ± 2.9	51.7 ± 4.2	64.0 ± 4.6
Men	11,047 (51.5)	3,992 (46.7)	5,865 (54.6)	1,190 (55.2)
Current smoking status	6,165 (28.8)	2,538 (29.7)	3,111 (29.0)	516 (23.9)
Body mass index, kg/m^2	24.2 ± 3.3	23.7 ± 3.2	24.4 ± 3.2	24.8 ± 3.6
Waist circumference, cm	80.5 ± 9.7	78.0 ± 9.2	81.6 ± 9.5	85.4 ± 10.4
Fasting blood glucose, mg/dl	93.9 ± 25.4	91.3 ± 21.5	95.0 ± 26.6	98.6 ± 31.9
Diabetes	1,597 (7.4)	406 (4.7)	881 (8.2)	310 (14.4)
Total cholesterol, mg/dl	184.5 ± 38.1	176.4 ± 35.0	188.3 ± 37.9	198.0 ± 43.4
HDL cholesterol, mg/dl	53.9 ± 14.3	54.7 ± 14.3	53.7 ± 14.2	51.5 ± 14.0
Triglycerides, mg/dl	106.0 (75.0–145.0)	98.0 (69.0–134.0)	110.0 (79.0–153.0)	115.0 (84.0–155.3)
Lipid-lowering medications	248 (1.2)	23 (0.3)	189 (1.8)	36 (1.7)
Antihypertensive medications	1,790 (8.3)	230 (2.7)	1,059 (9.9)	501 (23.2)
SBP, mm Hg	123.7 ± 20.3	116.6 ± 16.2	126.5 ± 20.7	137.6 ± 22.3
DBP, mm Hg	80.2 ± 12.0	77.7 ± 11.3	81.7 ± 12.1	82.1 ± 12.0
SBP/DBP categories, mm Hg				
<120/<80	8,158 (38.0)	4,349 (50.9)	3,454 (32.2)	355 (16.5)
120–129/<80	1,659 (7.7)	595 (7.0)	840 (7.8)	224 (10.4)
130–139/80–89	5,529 (25.8)	2,072 (24.2)	2,890 (26.9)	567 (26.3)
140–159/90–99	3,952 (18.4)	1,085 (12.7)	2,266 (21.1)	601 (27.9)
≥160/≥100	2,143 (10.1)	450 (5.2)	1,284 (12.0)	409 (18.9)

Values are mean ± SD, n (%), or median (interquartile range).
DBP = diastolic blood pressure; HDL = high-density lipoprotein; IQR = interquartile range; SBP = systolic blood pressure.

hemorrhage, or cerebral infarction. Diagnostic criteria were according to the World Health Organization-Monitoring of Trends and Determinants in Cardiovascular Disease protocol in the early stage of the study, but were modified beginning in 2003 following advances in diagnostic technology for myocardial infarction (14,16–18). All reported events and CVD deaths were adjudicated by a panel of physicians. During up to 20 years of follow-up (mean 13.7 years; median 14.7 years; 294,886 person-years), 1,622 first CVD events (550 CHD events, 1,142 strokes) and 395 CVD deaths occurred in the entire cohort, and 523 first CVD events occurred among 5,752 participants with complete data from 2 examinations.

STATISTICAL ANALYSIS. Continuous variables were expressed either as mean ± SD or median (interquartile range). Categorical variables were expressed as numbers and/or percentages.

To evaluate cardiovascular risk associated with BP level, participants were stratified by BP category (SBP/DBP: <120/<80, 120 to 129/<80, 130 to 139/80 to 89, 140 to 159/90 to 99, and ≥160/≥100 mm Hg). The hazard ratio (HR) of CVD incidence, CHD incidence, stroke incidence, and CVD mortality associated with different BP categories were calculated using the Cox proportional hazards model, adjusting for age, sex, body mass index, current smoking status, diabetes, total cholesterol, high-density lipoprotein cholesterol, and antihypertensive medications at baseline, after testing for the assumptions underlying the use (19). Participants with SBP/DBP <120/<80 mm Hg were considered as reference. To explore whether heterogeneity existed in the cardiovascular risk associated with stage 1 hypertension between the age groups of 35 to 59 years and ≥60 years, an age group × stage 1 hypertension interaction was determined using a Cox proportional hazards model with terms for stage 1 hypertension comparing to BP <120/<80 mm Hg, age group, stage 1 hypertension × age group, and age × other covariates. The population-attributable risk was used to estimate the proportion of CVD attributable to stage 1 hypertension, using the prevalence and adjusted HR of this category.

Changes in BP strata over 15 years and their associated cardiovascular risk were evaluated. Participants were stratified by baseline BP and reexamination BP (SBP/DBP: <130/<80, 130 to 139/80 to 89, and ≥140/≥90 mm Hg or taking antihypertensive medications), and cross-combined into 9 subgroups. The HR of CVD incidence by changes in BP strata was calculated after adjustment for classical CVD risk factors at baseline using the Cox proportional hazard regression model, with SBP/DBP maintaining <130/<80 mm Hg as reference.

TABLE 2 Hazard Ratios of CVD Endpoints Associated With Blood Pressure Categories

SBP/DBP Categories (mm Hg)	n	CVD Incidence		CHD Incidence		Stroke Incidence		CVD Mortality	
		No. of Events	Adjusted HR (95% CI)	No. of Events	Adjusted HR (95% CI)	No. of Events	Adjusted HR (95% CI)	No. of Events	Adjusted HR (95% CI)
Total									
<120/<80	8,158	265	Reference	97	Reference	173	Reference	45	Reference
120–129/<80	1,659	106	1.51 (1.20–1.89)	43	1.56 (1.09–2.25)	67	1.48 (1.12–1.97)	17	1.32 (0.75–2.31)
130–139/80–89	5,529	387	1.70 (1.45–1.99)	153	1.69 (1.31–2.20)	251	1.73 (1.42–2.11)	84	2.13 (1.48–3.08)
140–159/90–99	3,952	434	2.24 (1.91–2.63)	135	1.65 (1.25–2.17)	318	2.62 (2.16–3.18)	102	3.03 (2.10–4.35)
≥160/≥100	2,143	430	3.79 (3.20–4.49)	122	2.27 (1.69–3.04)	333	4.77 (3.90–5.83)	147	7.18 (5.01–10.29)
Age 35–44 yrs									
<120/<80	4,349	83	Reference	26	Reference	60	Reference	10	Reference
120–129/<80	595	24	1.75 (1.11–2.76)	9	1.99 (0.93–4.29)	15	1.51 (0.86–2.67)	1	0.64 (0.08–5.00)
130–139/80–89	2,072	93	1.87 (1.38–2.54)	34	1.97 (1.16–3.35)	61	1.74 (1.21–2.51)	22	4.07 (1.90–8.73)
140–159/90–99	1,085	82	2.65 (1.92–3.66)	31	2.65 (1.52–4.63)	55	2.56 (1.74–3.77)	15	4.87 (2.11–11.24)
≥160/≥100	450	57	3.81 (2.61–5.55)	16	2.40 (1.20–4.80)	44	4.50 (2.91–6.96)	12	7.98 (3.17–20.08)
Age 45–59 yrs									
<120/<80	3,454	145	Reference	56	Reference	90	Reference	25	Reference
120–129/<80	840	58	1.49 (1.09–2.02)	24	1.52 (0.94–2.46)	38	1.57 (1.07–2.29)	9	1.29 (0.60–2.77)
130–139/80–89	2,890	233	1.72 (1.39–2.12)	92	1.63 (1.16–2.28)	152	1.83 (1.41–2.38)	49	2.08 (1.28–3.38)
140–159/90–99	2,266	262	2.20 (1.78–2.71)	75	1.40 (0.98–2.01)	198	2.77 (2.14–3.58)	54	2.54 (1.56–4.14)
≥160/≥100	1,284	274	3.97 (3.18–4.94)	77	2.21 (1.50–3.24)	213	5.20 (3.99–6.80)	86	6.48 (4.00–10.49)
Age ≥60 yrs									
<120/<80	355	37	Reference	15	Reference	23	Reference	10	Reference
120–129/<80	224	24	0.93 (0.55–1.55)	10	0.93 (0.42–2.08)	14	0.87 (0.45–1.70)	7	1.05 (0.40–2.76)
130–139/80–89	567	61	1.04 (0.69–1.57)	27	1.13 (0.60–2.12)	38	1.04 (0.62–1.75)	13	0.89 (0.39–2.05)
140–159/90–99	601	90	1.43 (0.97–2.12)	29	1.13 (0.60–2.13)	65	1.66 (1.02–2.69)	33	2.23 (1.08–4.57)
≥160/≥100	409	99	2.16 (1.45–3.21)	29	1.47 (0.77–2.83)	76	2.64 (1.62–4.31)	49	4.60 (2.27–9.31)

CHD = coronary heart disease; CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; other abbreviations as in Table 1.

Sensitivity analyses were performed after excluding participants who were taking antihypertensive medications, considering competing events using the Fine and Gray competing-risk regression methodology (20), and for subgroup analysis of the cardiovascular risk associated with stage 1 hypertension compared with SBP/DBP of <130/<80 mm Hg between the age groups.

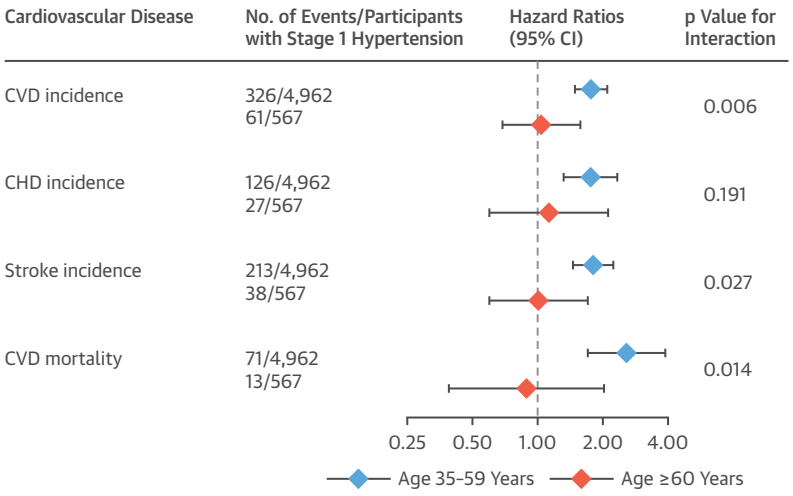
Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, North Carolina). A 2-sided value of $p < 0.05$ was considered statistically significant.

RESULTS

BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS. The means for SBP and DBP were 123.7 ± 20.3 mm Hg and 80.2 ± 12.0 mm Hg, respectively. Of the participants, 25.8% had SBP/DBP 130 to 139/80 to 89 mm Hg, the stage 1 hypertension definition according to the 2017 ACC/AHA hypertension guideline. The proportions of participants with this BP stratum were similar among the 3 age groups, whereas the proportions decreased with age for those with SBP <120 mm Hg and DBP <80 mm Hg (normal BP) but increased for those with SBP ≥140 mm Hg or DBP ≥90 mm Hg (Table 1).

CARDIOVASCULAR RISK ASSOCIATED WITH BP CATEGORIES. Compared with normal BP, stage 1 hypertension was significantly related to an increased risk of CVD in the age groups of 35 to 44 and 45 to 59 years, but not in the group of ≥60 years (Table 2, Figure 1). Overall, the HR associated with this BP stratum for CVD incidence was 1.78 (95% confidence interval [CI]: 1.50 to 2.11), CHD incidence was HR: 1.77 (95% CI: 1.33 to 2.36), stroke incidence was HR: 1.79 (95% CI: 1.45 to 2.22), and CVD mortality was HR: 2.50 (95% CI: 1.66 to 3.77) among participants age 35 to 59 years. Compared with normal BP, the HR of CVD mortality related to stage 1 hypertension was significantly higher than that related to SBP of 120 to 129 and DBP <80 mm Hg, and it was close to the HR associated with SBP of 140 to 159 mm Hg or DBP of 90 to 99 mm Hg. In contrast, among participants age ≥60 years, stage 1 hypertension was not associated with increased risk of any CVD endpoint, while only participants with SBP/DBP ≥140/≥90 mm Hg had a significantly higher risk of stroke incidence and CVD

FIGURE 1 Hazard Ratios of CVDs Associated With 2017 ACC/AHA Stage 1 Hypertension by Age Groups



ACC = American College of Cardiology; AHA = American Heart Association; CHD = coronary heart disease; CI = confidence interval; CVD = cardiovascular disease.

mortality. Results were similar after excluding participants who were receiving antihypertensive treatments at baseline (n = 1,790) (Online Table 1), considering competing risk (Online Table 2), and in a subgroup analysis with SBP/DBP of <130/<80 mm Hg as a reference (Online Figure 2).

The population-attributable risk for the incidence of CVD, CHD, and stroke associated with stage 1 hypertension ranged from 10.6% to 14.7% in the age groups of 35 to 44 and 45 to 59 years, whereas the corresponding proportions ranged from 1.8% to 4.0% in the age group of ≥60 years. The population-attributable risks related to stage 1 hypertension were higher for CVD mortality than those for incidence in the 2 younger age groups (**Central Illustration**). Overall, 26.5% of CVD mortality and 13.4% of CVD incidence were attributable to stage 1 hypertension among participants age 35 to 59 years.

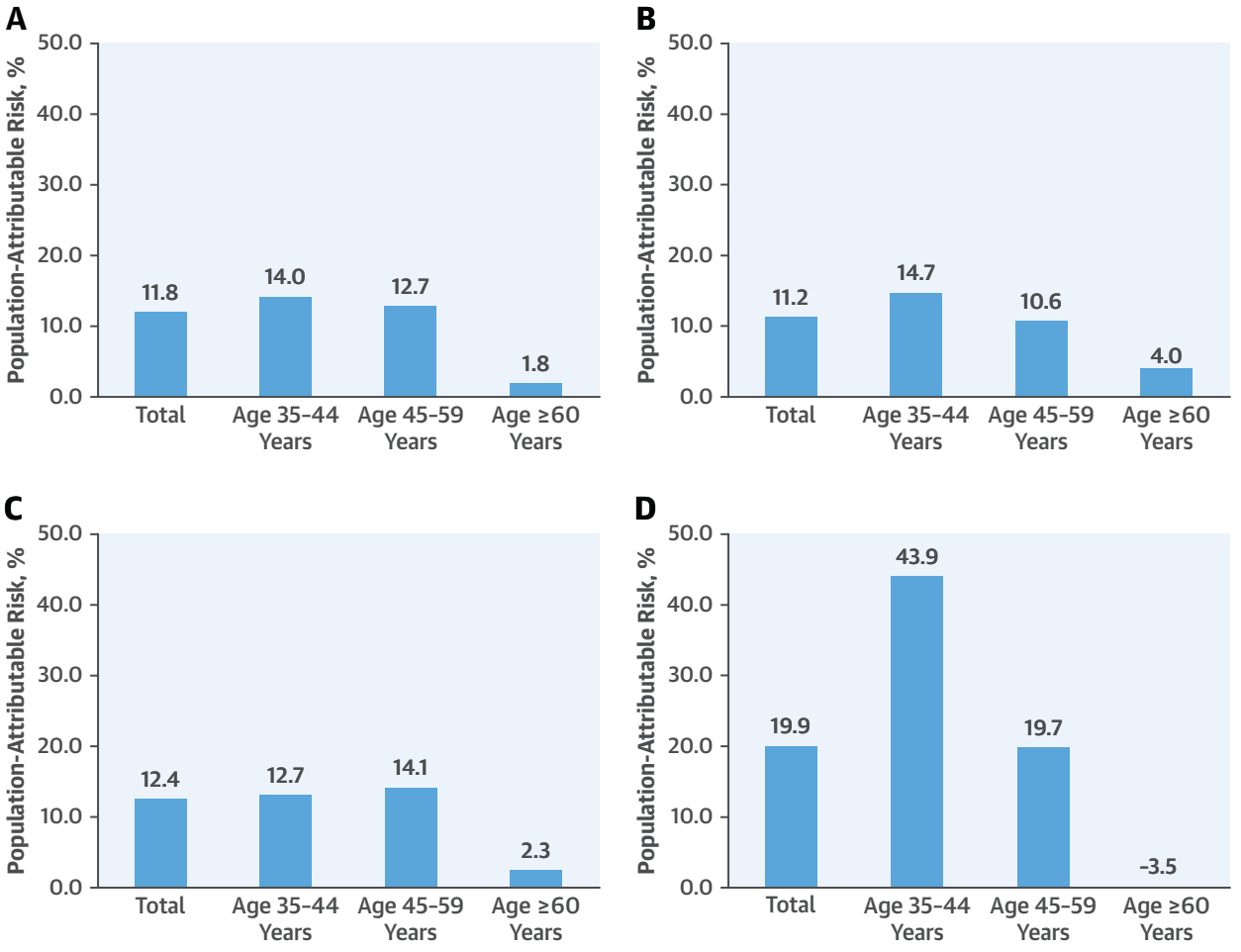
CARDIOVASCULAR RISK ASSOCIATED WITH BP CHANGES. Changes in BP over a 15-year period and their association with the risk of CVD incidence were further investigated among participants age 35 to 59 years (n = 5,502). Among participants with stage 1 hypertension in 1992, 65.0% experienced an increase in BP to 140/90 mm Hg or higher over a 15-year period, and they had a 3.01-fold higher risk for CVD incidence (95% CI: 1.94 to 4.69), compared with those who maintained their SBP <130 mm Hg and DBP <80 mm Hg. Another 21.5% of participants maintained stage 1 hypertension over the period, and they had a 2.28-fold higher risk of developing CVD (95% CI: 1.28 to 4.06), which was comparable to the HR for participants whose BP decreased from ≥140/≥90 mm Hg to stage 1 hypertension (HR: 2.37; 95% CI: 1.16 to 4.81). In contrast, participants whose BP decreased from stage 1 hypertension to <130/<80 mm Hg had similarly low risk for CVD incidence as those who maintained their BP <130/<80 mm Hg (**Figure 2**). Similar results were found after excluding participants on antihypertensive treatments in 2 examinations (n = 1,739) (Online Figure 3), and considering competing risk (Online Figure 4).

DISCUSSION

This 20-year prospective cohort study found that stage 1 hypertension defined by the 2017 ACC/AHA hypertension guideline was associated with a significantly increased risk of CVD compared with normal BP, and accounted for 26.5% of cardiovascular deaths and 13.4% of cardiovascular events in Chinese adults age 35 to 59 years. However, among participants age ≥60 years, stage 1 hypertension was not related to increased cardiovascular risk compared with normal BP, and no population-attributable risk associated with this stratum was found (**Central Illustration**).

The definition of stage 1 hypertension in the 2017 ACC/AHA guideline has been the subject of significant interest globally. In addition to the concern regarding the increased number of patients with hypertension under this new definition (8,21–23), to what extent this BP stratum affects cardiovascular risk in the

CENTRAL ILLUSTRATION **Population-Attributable Risks Associated With 2017 ACC/AHA Stage 1 Hypertension**



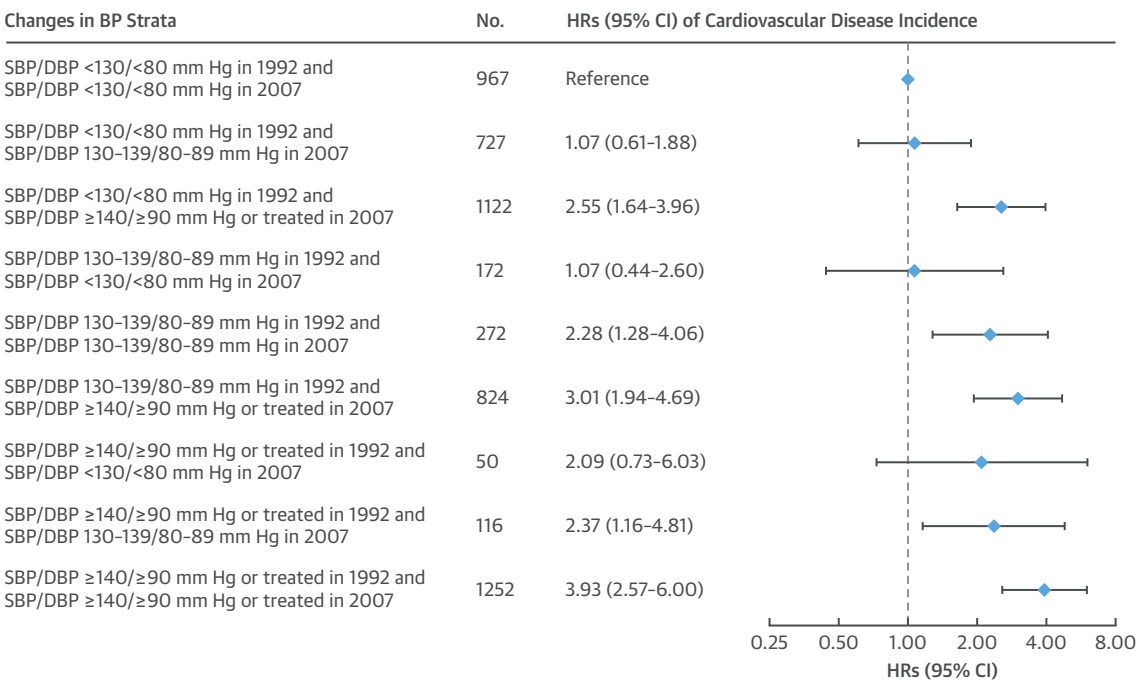
Qi, Y. et al. J Am Coll Cardiol. 2018;72(11):1201-10.

Population-attributable risks related to 2017 ACC/AHA stage 1 hypertension were estimated for cardiovascular disease incidence **(A)**, coronary heart disease incidence **(B)**, stroke incidence **(C)**, and cardiovascular disease mortality **(D)**. ACC = American College of Cardiology; AHA = American Heart Association.

population is a critical question to answer. To the best of our knowledge, this is the first prospective study to quantitatively determine the cardiovascular risk associated with the new stage 1 hypertension in the Chinese population. In addition, the repeated measurement of BP over 15 years provides a valuable opportunity to investigate the impact of sustained elevated BP of 130 to 139/80 to 89 mm Hg on CVD incidence and mortality.

In Chinese adults age 35 to 59 years, we observed an approximately 80% higher risk of CVD incidence associated with baseline stage 1 hypertension compared with normal BP, which was more pronounced than the associated risk found for broadly defined pre-hypertension (relative risk: 1.40; 95% CI: 1.30 to 1.51) in participants age <65 years from the follow-up of the China National Hypertension Survey (13). In particular, compared with normal BP, the HR of CVD mortality related to stage 1 hypertension was significantly higher than that related to SBP/DBP of 120 to 129/<80 mm Hg in our study. Similarly, a study among Chinese women showed that the risk of stroke mortality increased significantly in participants with high-range pre-hypertension (SBP/DBP of 130 to 139/85 to 89 mm Hg), but not in those with low-range pre-hypertension (SBP/DBP of 120 to 129/80 to

FIGURE 2 Hazard Ratios of Cardiovascular Incidence Associated With BP Changes Among Participants Age 35 to 59 Years



BP = blood pressure; CI = confidence interval; DBP = diastolic blood pressure; HR = hazard ratio; SBP = systolic blood pressure.

84 mm Hg) (24). The adverse effects associated with stage 1 hypertension were further supported by our data on changes in BP over time among participants age 35 to 59 years. During a 15-year follow-up period, 65.0% of participants in this BP stratum showed an increase in BP to ≥140/≥90 mm Hg and had a 3-fold higher risk of CVD incidence compared with those who maintained BP <130/<80 mm Hg. The long-term impact of BP changes on cardiovascular risk were also observed in pooling data from 7 diverse cohort studies in the United States, which showed that individuals who experience increases from normal BP to pre-hypertension in middle age had a higher remaining lifetime risk for CVD (25).

The significantly elevated risk and large population-attributable risk associated with stage 1 hypertension observed among young and middle-aged participants in our study may be of great importance for CVD prevention in China. First, the excessive population-attributable risk of CVD related to stage 1 hypertension indicates the considerable potential for the threat of premature events and death to be reduced if BP is adequately controlled below this stratum. It is reported that stroke and ischemic heart disease are the 2 leading causes of years of life lost in China (26). Our analysis estimated that more than one-quarter of CVD deaths and 13% of CVD events among working-age Chinese adults could be eliminated if stage 1 hypertension could be prevented. Second, the large likelihood of progression to a higher BP category and the CVD risk associated with sustained exposure of stage 1 hypertension highlight the importance of early BP control to maintain BP <130/<80 mm Hg in younger Chinese adults. It has been reported that the prevalence of hypertension has increased much more rapidly between 1991 and 2000 to 2001 among the younger Chinese compared with the older populations, with a 4-fold greater increase in percentage in individuals age 35 to 44 years compared with those age 65 to 74 years (27). It is anticipated that early detection of stage 1 hypertension and subsequent intervention should retard BP progression, maintain vascular health, protect against organ damage, and ultimately lower CVD risk. Last, our results call for strict lifestyle intervention for high BP. The 2017 ACC/AHA guideline advocates non-pharmacological therapy for patients with stage 1 hypertension unless they have a 10-year CVD risk

above 10%, a high-risk situation in which pharmacological treatment is recommended additionally. High-risk patients represent only 1.9% of adults in the United States (23) and 2.0% of the general Chinese population (22). Therefore, lifestyle changes should be the cornerstone of the management of stage 1 hypertension. However, lifestyle intervention is far from optimal in China. Nationwide data demonstrated that only 55.5% of patients with a history of hypertension had been instructed by a healthcare provider to use any nonpharmacological therapies, and only 45.4% actually followed the instruction (27). These results emphasize the urgent requirement for national campaigns calling for strict lifestyle intervention as the fundamental approach to the management of hypertension through efforts from both caregivers and patients. Regarding pharmacological treatment, 2 large multicenter randomized controlled trials (28,29) are currently underway in China and will provide essential information on the benefit of BP-lowering medications among Chinese adults with stage 1 hypertension.

In contrast to the remarkable cardiovascular effects related to stage 1 hypertension noted among participants age 35 to 59 years, our analyses showed that this BP stratum was not associated with an increased CVD risk compared with normal BP in participants age ≥60 years. This discrepancy persisted even after adjustment for the competing risk. Similarly, previous meta-analyses of cohort studies showed that pre-hypertension was not associated with CVD risk among older populations (30,31). Our results and other observational evidence have prompted critical discussion on whether individuals age ≥60 years and with SBP/DBP of 130 to 139/80 to 89 mm Hg should be diagnosed with hypertension and should subsequently lower BP to below 130/80 mm Hg. A recently published meta-analysis showed that intensive BP lowering to a target of SBP <140 mm Hg in older hypertensive patients with baseline SBP ranging from 140 to 170 mm Hg could provide CVD benefit (32). In that analysis, the final SBP was around 135 mm Hg in the intensive-treatment group in 3 of the 4 trials, while an SBP <130 mm Hg was only achieved in 1 trial that targeted high-risk patients and used self-operated automated BP measurement devices. Evidence from interventional trials, in line with our observational findings, suggests that the diagnosis of hypertension and subsequent administration of BP-lowering medication should be approached with caution among adults age ≥60 years and with SBP/DBP of 130 to 139/80 to 89 mm Hg.

STUDY LIMITATIONS. First, as typically encountered in long-term cohort studies, cardiovascular risk associated with stage 1 hypertension may be underestimated based on baseline BP levels because of regression dilution bias. Second, although we adjusted for all other classical CVD risk factors in the model, we cannot exclude the impact of some unaccounted-for residual confounding factors. Finally, the sample size was large but only reflected a proportion of the original cohort when analyzing BP changes. In particular, only 250 participants age ≥60 years completed 2 examinations 15 years apart, precluding analysis of cardiovascular risk associated with BP changes among individuals age ≥60 years, although no association between baseline stage 1 hypertension and any cardiovascular endpoint was found in participants of this age group. The sample size of participants age ≥60 years was good for detecting the effects of baseline stage 1 hypertension on all endpoints as comparable to those in the younger participants, except that it was underpowered for the analysis of CHD incidence. Therefore, further validation of our results using a larger sample size of older people is still needed. Last, to determine whether participants lost to follow-up caused potential bias, comparisons were performed between participants with and without data for re-examination. Similar SBP levels (121.4 ± 18.3 mm Hg vs. 121.8 ± 19.9 mm Hg) and DBP levels (79.2 ± 11.6 mm Hg vs. 79.7 ± 12.3 mm Hg) were found between the 2 groups.

CONCLUSIONS

The 2017 ACC/AHA stage 1 hypertension definition significantly increases the risk of cardiovascular incidence and mortality, and a large proportion of CVD events and deaths are attributable to this BP stratum in Chinese people age 35 to 59 years, but not in those age ≥60 years. This study provides important evidence on the cardiovascular risk associated with stage 1 hypertension and foundational data for future health economics studies, which are deemed essential if adoption of this new hypertension definition is to be considered in China.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Newly defined stage 1 hypertension is associated with elevated cardiovascular risk, and a large proportion of cardiovascular events and mortality are attributable to this BP stratum in Chinese people age 35 to 59 years, but not in those age ≥60 years.

TRANSLATIONAL OUTLOOK: Broad strategies are needed to facilitate the detection of stage 1 hypertension in young and middle-aged individuals, whereas more evidence is needed before this threshold is applied to individuals age ≥60 years.

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KEY WORDS cardiovascular disease, cohort study, hypertension, incidence, mortality

APPENDIX For a list of participating study centers and key investigators as well as supplemental figures and tables, please see the online version of this paper.