Original Investigation

The Burden of Hypertension and Associated Risk for Cardiovascular Mortality in China

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IMPORTANCE Hypertension is a leading cause of premature death in China, but limited evidence is available on the prevalence and management of hypertension and its effect on mortality from cardiovascular disease (CVD).

OBJECTIVES To examine the prevalence, diagnosis, treatment, and control of hypertension and to assess the CVD mortality attributable to hypertension in China.

DESIGN, SETTING AND PARTICIPANTS This prospective cohort study (China Kadoorie Biobank Study) recruited 500 223 adults, aged 35 to 74 years, from the general population in China. Blood pressure (BP) measurements were recorded as part of the baseline survey from June 25, 2004, to August 5, 2009, and 7028 deaths due to CVD were recorded before January 1, 2014 (mean duration of follow-up: 7.2 years). Data were analyzed from June 9, 2014, to July 17, 2015.

EXPOSURES Prevalence and diagnosis of hypertension (systolic BP ≥140 mm Hg, diastolic BP ≥90 mm Hg, or receiving treatment for hypertension) and treatment and control rates overall and in various population subgroups.

MAIN OUTCOMES AND MEASURES Cox regression analysis yielded age- and sex-specific rate ratios for deaths due to CVD comparing participants with and without uncontrolled hypertension, which were used to estimate the number of CVD deaths attributable to hypertension.

RESULTS The cohort included 205 167 men (41.0%) and 295 056 women (59.0%) with a mean (SD) age of 52 (10) years for both sexes. Overall, 32.5% of participants had hypertension; the prevalence increased with age (from 12.6% at 35-39 years of age to 58.4% at 70-74 years of age) and varied substantially by region (range, 22.7%-40.7%). Of those with hypertension, 30.5% had received a diagnosis from a physician; of those with a diagnosis of hypertension, 46.4% were being treated; and of those treated, 29.6% had their hypertension controlled (ie, systolic BP <140 mm Hg; diastolic BP <90 mm Hg), resulting in an overall control rate of 4.2%. Even among patients with hypertension and prior CVD, only 13.0% had their hypertension controlled. Uncontrolled hypertension was associated with relative risks for CVD mortality of 4.1 (95% CI, 3.7-4.6), 2.6 (95% CI, 2.4-2.9) and 1.9 (95% CI, 1.8-2.0) at ages 35 to 59, 60 to 69, and 70 to 79 years, respectively, and accounted for about one-third of deaths due to CVD (approximately 750 000) at 35 to 79 years of age in 2010.

CONCLUSIONS AND RELEVANCE About one-third of Chinese adults in this national cohort population had hypertension. The levels of diagnosis, treatment, and control were much lower than in Western populations, and were associated with significant excess mortality.

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In 2010, cardiovascular disease (CVD) accounted for more than one-third of all adult deaths in China, including 1.7 million deaths due to stroke and 0.9 million deaths due to ischemic heart disease (IHD).[1] Hypertension is one of the most important causes of CVD mortality in China, because of its high prevalence and concomitant vascular risks.[2,3]

Large prospective studies of mainly Western populations have shown a continuous positive association for stroke and IHD-related mortality with systolic blood pressure (SBP) down to at least 115 mm Hg, with each 20-mm Hg lower usual SBP associated with an approximate halving in risk for stroke and IHD mortality.[3] Furthermore, randomized clinical trials of BP-lowering medication (antihypertensives)[4] have demonstrated that lowering SBP by 10 mm Hg lowers the risk for stroke and IHD by about one-fourth, indicating almost complete reversibility of the excess risks for CVD associated with hypertension within a few years of treatment.

Successive population surveys of hypertension in China during the last 30 years have reported an increasing prevalence of hypertension, with the most recent surveys indicating that about one-third of all adults have hypertension.[5-7] Considerable uncertainty remains about the prevalence of hypertension by age, sex, region, and socioeconomic status; the current levels of BP management in the population; and the likely effect of this high burden of uncontrolled hypertension on CVD mortality rates in China.

We herein report findings from the recent large-scale prospective China Kadoorie Biobank Study of 500 223 adults aged 35 to 74 years (when first surveyed during 2004-2008) in 10 diverse regions of China.[8,9] The aims of the present report were to (1) examine the prevalence, diagnosis, treatment, and control of hypertension at baseline, overall and by age, sex, region, and socioeconomic and other characteristics; (2) assess prospectively the age- and sex-specific effects of hypertension on CVD mortality; and (3) estimate the number of CVD deaths attributed to hypertension in 2010 in China.

Methods

Baseline Survey

Details of the study design, survey methods, and participant characteristics have been reported previously.[8,9] Briefly, the baseline survey was conducted from June 25, 2004, to August 5, 2009, in 10 geographically defined regions (5 urban and 5 rural) of China. The regions were chosen to ensure a wide range of risk exposures and disease patterns while taking account of the quality of established disease registries for follow-up and the local capacity to conduct the study. The regions were not selected to be representative of China as a whole. In each region, temporary assessment centers were set up at local residential centers (village or street committees), and permanent residents with no major disability were invited to participate; about one-third of residents responded.[9] Local, national, and international ethics approvals were obtained (see eMethods in the Supplement for details). All participants provided written informed consent.

At the baseline survey, trained health care workers collected detailed information on sociodemographic characteristics, lifestyle, and medical history using a laptop computer-based questionnaire. Each participant also had measurements taken, including height, weight, lung function, and BP. Blood pressure was measured twice by trained staff using a digital sphygmomanometer (Omron UA-779; Live Source) after participants had remained at rest in the seated position for at least 5 minutes. If the difference between the 2 measurements was greater than 10 mm Hg for the SBP, a third measurement was obtained and the last 2 measurements were recorded. The mean of the 2 recorded values of SBP and diastolic BP (DBP) were used in all analyses. All devices were regularly maintained and calibrated to ensure consistency of the measurements. Participants were considered to be hypertensive if they had a measured SBP of at least 140 mm Hg or a measured DBP of at least 90 mm Hg or were receiving treatment for hypertension. The latter was defined as those who reported a diagnosis of hypertension by a physician and use of antihypertensives at baseline.

Mortality Follow-up

Vital status of each participant was obtained through the Disease Surveillance Points system of the Chinese Centre for Disease Control and Prevention, annual checks against local residential records and health insurance records, and active confirmation through street committee or village administrators. Residential records were also used to identify those who had moved out of the area and were therefore lost to follow-up. Fatal CVD events were assigned codes from the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (I00-I25, I27-I88, or I95-I99) by trained Disease Surveillance Points staff who were blinded to baseline information. By January 1, 2014, 25 448 deaths occurred, including 7028 due to CVD, and 2411 participants (0.5%) were lost to follow-up.

Statistical Analysis

Data were analyzed from June 9, 2014, to July 17, 2015. We excluded participants with a baseline age outside the age range of interest for this study (9410 persons <35 years; 3258 persons ≥75 years). We found no missing values for BP or any other key variables in the remaining 500 223 participants. Mean SBP, mean DBP, and prevalence of hypertension were calculated within each age group (35-39, 40-49, 50-59, 60-69, and 70-74 years) separately for men and women. To assess the management of hypertension (as previously defined), we calculated the proportion of those with hypertension who had received a diagnosis from a physician, the proportion of those diagnosed who were treated with antihypertensives, and the proportion of those treated who achieved BP control (ie, SBP <140 mm Hg and DBP <90 mm Hg). These proportions were stratified by age, sex, area, prior CVD (IHD or stroke or transient ischemic attack reported at baseline), the season at the time of the survey, household income, and highest level of education; all subgroups were prespecified. Analyses were adjusted, where appropriate, for age, sex, and region.

Table 1. Selected Characteristics of Study Participants[a]

Characteristic	Men (n = 205 167)	Women (n = 295 056)	All (N = 500 223)
Age at entry, y, No. (%)			
35-39	26 172 (12.8)	42 222 (14.3)	68 394 (13.7)
40-49	59 240 (28.9)	93 508 (31.7)	152 748 (30.5)
50-59	63 725 (31.1)	93 831 (31.8)	157 556 (31.5)
60-69	41 339 (20.2)	50 434 (17.1)	91 773 (18.3)
70-74	14 691 (7.1)	15 061 (5.1)	29 752 (5.9)
Age, mean (SD)	52 (11)	51 (10)	52 (10)
BP, mean (SD)			
Systolic	133 (20)	130 (22)	131 (21)
Diastolic	79 (11)	77 (11)	78 (11)
Area, No. (%)			
Rural	116 158 (56.6)	163 389 (55.4)	279 547 (55.9)
Urban	89 009 (43.4)	131 667 (44.6)	220 676 (44.1)
Annual household income, ¥, No. (%)			
<5000	18 881 (9.2)	29 670 (10.1)	48 551 (9.7)
5000-19 999	92 251 (45.0)	144 431 (49.0)	236 682 (47.3)
≥20 000	94 035 (45.8)	120 955 (41.0)	214 990 (43.0)
Educational level, No. (%)			
No formal school	18 022 (8.8)	74 635 (25.3)	92 657 (18.5)
Primary school	68 974 (33.6)	93 167 (31.6)	162 141 (32.4)
Middle or high school	102 428 (49.9)	114 613 (38.8)	217 041 (43.4)
Technical school or university	15 743 (7.7)	12 641 (4.3)	28 384 (5.7)
Prior CVD, No. (%)			
No	195 373 (95.2)	282 221 (95.6)	477 594 (95.5)
Yes	9794 (4.8)	12 835 (4.4)	22 629 (4.5)
Season of baseline survey, No. (%)[b]			
Winter	44 649 (21.8)	56 015 (19.0)	100 664 (20.1)
Spring or autumn	110 911 (54.1)	165 995 (56.3)	276 906 (55.4)
Summer	49 607 (24.2)	73 046 (24.8)	122 653 (24.5)

Abbreviations: BP, blood pressure; CVD, cardiovascular disease.

[a] Percentages have been rounded and may not total 100.

[b] Winter indicates December to February; spring, March to May; autumn, September to November; and summer, June to August.

We used Cox regression analysis[10] to calculate the age- and sex-specific death rate ratios and 95% CIs (adjusted for region) for CVD mortality comparing participants with uncontrolled hypertension (SBP ≥140 mm Hg or DBP ≥90 mm Hg) and those without uncontrolled hypertension. These analyses excluded individuals with a history of CVD to limit the effects of reverse causality. Participants contributed person-years until death, the date lost to follow-up, or the censoring date (December 31, 2013). We calculated the age- and sex-specific population-attributable fractions using the formula P_d (RR − 1)/RR, where P_d is the proportion of participants who died of vascular causes with uncontrolled hypertension and RR is the adjusted death rate ratio for vascular mortality in participants with vs without uncontrolled hypertension.[11] Population-attributable fractions were applied to the estimated age- and sex-specific number of CVD deaths in China for 2010,[12,13] to give the number of deaths attributable to hypertension for that year. The proportionality assumption of the Cox regression was checked by comparing death rate ratios in the first and second half of the follow-up period and confirmed the validity of the analyses. Analyses used SAS software (version 9.3; SAS Institute Inc), and figures were plotted using R software (version 3.0; https://www.r-project.org).

Results

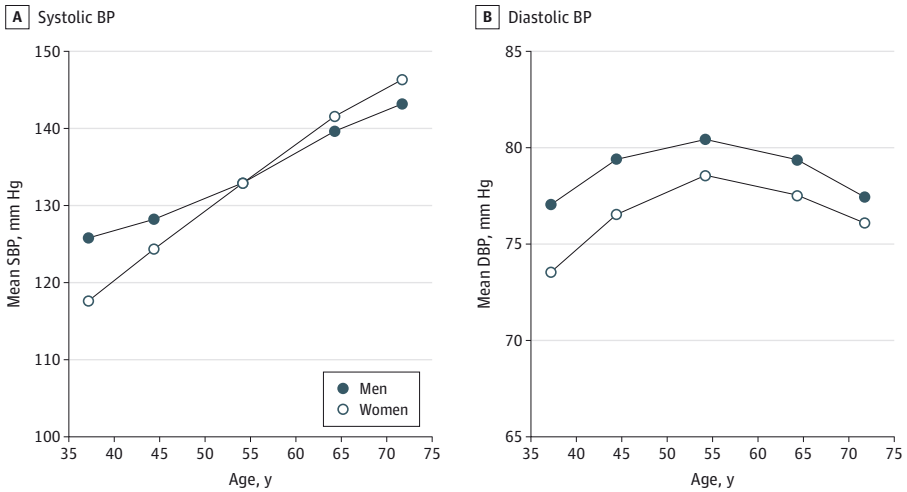
Population Characteristics

Among the 500 223 participants included in the analysis, 59.0% were women and 41.0% were men; the mean (SD) age was 52 (10) years for both sexes (**Table 1**). Overall, 55.9% were from rural areas, 57.0% had an annual household income of less than ¥20 000, and 18.5% had no formal schooling (men, 8.8%; women, 25.3%); 4.5% reported a history of CVD at baseline. More than half of the participants were surveyed during spring or autumn (55.4%); 20.1% were surveyed during winter; and 24.5% were surveyed during summer.

Distribution of BP

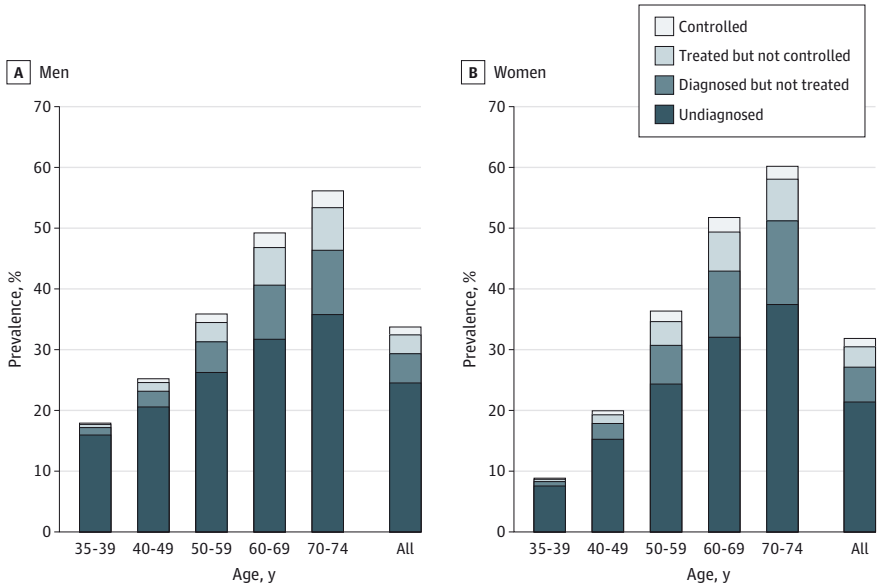
Mean SBP showed an approximately linear increase with age in both sexes, but the association was about twice as extreme in women compared with men (**Figure 1**). Mean levels of SBP were similar in both sexes at about 55 years of age, however, such that men had higher SBP than women at younger than 55 years and women had higher SBP at older than 55 years. The association between DBP and age was nonlinear, with a positive association in those younger than 55 years and an inverse

Figure 1. Mean Systolic (SBP) and Diastolic (DBP) Blood Pressure



Mean values are standardized for region.

Figure 2. Prevalence of Hypertension by Age and Sex



Hypertension is defined as a measured systolic blood pressure (BP) of at least 140 mm Hg, a measured diastolic BP of at least 90 mm Hg, or treatment for hypertension. Hypertension is categorized as undiagnosed, diagnosed but not treated, treated but not controlled, or controlled. Prevalences are standardized for region and additionally for age within the group 35 to 74 years (All).

association thereafter. The shape of this association was similar in both sexes, but mean DBP was higher at all ages in men.

Prevalence of Hypertension

Overall, 32.5% of participants (33.7% of men and 31.9% of women) had hypertension (**Figure 2**); 17.3% of the total population had isolated systolic hypertension, 2.0% had isolated diastolic hypertension, 11.8% had both, and 1.4% had controlled hypertension (eTable 1 in the Supplement). Overall, 20.1% of participants had stage 1 hypertension (SBP 140-159 mm Hg or DBP 90-99 mm Hg), 11.0% had stage 2 hypertension (SBP ≥160 mm Hg or DBP ≥100 mm Hg) (eTable 2 in the Supplement), and 39.5% had prehypertension (SBP 120-139 mm Hg or DBP 80-89 mm Hg). The prevalence of hypertension increased with age (from 12.6% at 35-39 years of age to 58.4% at 70-74 years of age), but the age-specific prevalence of hypertension was higher in men than women when younger (age 35-39 years, 17.9% for men and 8.8% for women) and slightly higher in women than men when older (age 70-74 years, 60.2% for women and 56.2% for men) (Figure 2 and eTables 3 and 4 in the Supplement).

Diagnosis, Treatment, and Control of Hypertension

Overall, only 30.5% of participants with hypertension had received a diagnosis by a physician (eTable 3 in the Supplement). This proportion increased with age and ranged from 15.2% at ages 35 to 39 years to 37.9% at ages 70 to 74 years in women and 10.8% at ages 35 to 39 years to 36.1% at ages 70 to 74 years in men. Among participants with a diagnosis of hypertension, less than half were being treated, and this proportion did not vary substantially by age or sex (48.3% for men

Table 2. Prevalence, Diagnosis, Treatment, and Control of Hypertension by Selected Characteristics[a]

Characteristic	No. of Participants	Prevalence of Hypertension, %	Diagnosis Among Participants With Hypertension, %	Treated Hypertension Among Participants With a Diagnosis, %	Controlled Hypertension, %	
					Among Treated for Hypertension	Among All With Hypertension
Region (type)						
Haikou (U)	28 394	22.7	36.4	51.5	37.2	6.8
Sichuan (R)	54 268	25.0	21.0	36.6	26.1	2.0
Liuzhou (U)	49 379	27.3	43.8	64.1	39.0	11.0
Harbin (U)	55 118	29.3	35.7	48.7	31.8	5.6
Hunan (R)	59 651	32.6	35.1	60.3	22.0	4.7
Suzhou (U)	52 591	34.8	30.5	36.7	34.7	4.0
Gansu (R)	46 845	35.2	20.9	50.0	13.8	1.4
Qingdao (U)	35 194	35.7	34.2	36.2	25.5	3.2
Henan (R)	61 655	37.6	23.6	53.2	31.3	4.1
Zhejiang (R)	57 128	40.7	28.1	18.5	25.2	1.3
Annual household income, ¥						
<5000	48 551	32.7	28.3	40.4	22.7	2.7
5000-19 999	236 682	32.4	29.7	45.4	28.3	3.8
≥20 000	214 990	32.1	34.7	49.3	33.2	5.7
Educational level						
No formal school	92 657	34.8	28.2	36.6	23.8	2.6
Primary school	162 141	32.9	29.7	46.5	26.1	3.5
Middle or high school	217 041	31.7	35.4	55.0	32.7	6.4
Technical school or university	28 384	30.7	42.6	63.2	43.3	12.6
Prior CVD						
No	477 594	31.8	27.2	44.1	28.8	3.4
Yes	22 629	49.4	72.4	58.4	32.0	13.0
Season of baseline survey[b]						
Winter	100 664	39.6	27.6	44.3	20.9	2.6
Spring or autumn	276 906	33.3	30.6	45.8	29.2	4.1
Summer	122 653	24.9	34.4	49.7	38.0	6.6
Overall	500 223	32.5	30.5	46.4	29.6	4.2

Abbreviations: CVD, cardiovascular disease; R, rural; U, urban.

[a] Hypertension is defined as measured systolic blood pressure of at least 140 mm Hg, measured diastolic blood pressure of at least 90 mm Hg, or treatment for hypertension. Each percentage is calculated as a percentage of the specified subgroup of the participants in each row (eg, in the first row of the table, there were 51.5% of participants with diagnosed hypertension in Haikou who were treated for hypertension). All analyses are standardized for age and sex, and, where appropriate, for region.

[b] Winter indicates December to February; spring, March to May; autumn, September to November; and summer, June to August.

and 45.1% for women) (eTable 3 in the Supplement; eTable 5 in the Supplement provides information on the type of antihypertensive used). Among those treated for hypertension, only 29.6% achieved control of hypertension and this proportion was similar in men and women. This proportion declined with increasing age and to a slightly greater extent in women than men. Overall, the control of hypertension as a proportion of all participants with hypertension increased with age, but never exceeded 5.0% in both sexes and at all ages (eTable 3 in the Supplement).

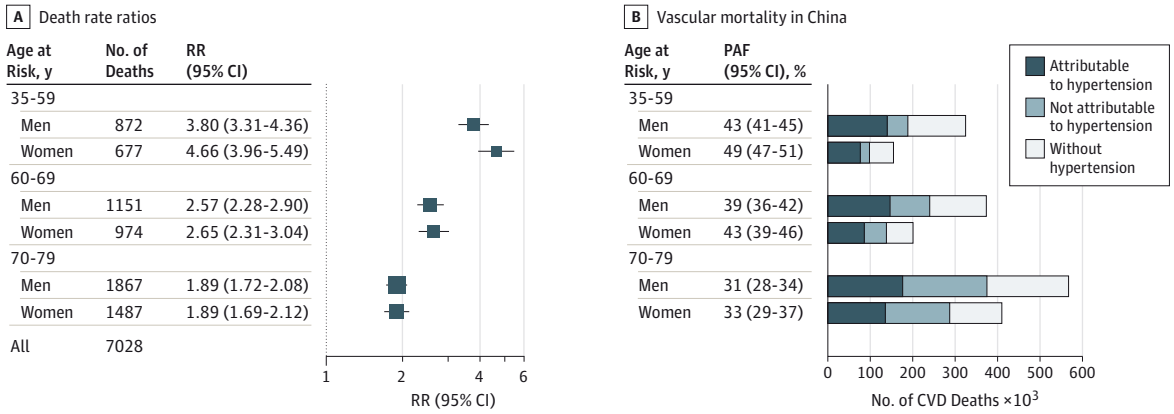
Regional Differences in Prevalence and Control of Hypertension

The prevalence of hypertension varied markedly by region, ranging from 22.7% in Haikou to 40.7% in Zhejiang (**Table 2** and eTable 6 in the Supplement). The prevalence was slightly higher in rural than urban areas, but no clear difference by geography (north vs south or east vs west) was found. We detected a 2-fold variation by region in the proportions of participants with hypertension who were diagnosed (range, 21.0% in Sichuan to 43.8% in Liuzhou) and a 3-fold variation in the proportions of participants with diagnosed hypertension who received treatment (range, 18.5% in Zheijiang to 64.1% in Liuzhou) and those in whom treated hypertension was controlled (range, 13.8% in Gansuto to 39.0% in Luizhou). Overall, however, the proportion of hypertensive participants with controlled BP was low in all regions (range, 1.3% in Zhejiang to 11.0% in Liuzhou).

Prevalence and Control of Hypertension by Socioeconomic and Other Factors

Hypertension was slightly more common at lower levels of education (no formal school, 34.8%; technical school or univer-

Figure 3. Age- and Sex-Specific Association of Hypertension With Mortality Due to Cardiovascular Disease (CVD)



A, Death rate ratios (RR) are calculated for participants with vs without uncontrolled hypertension. Rate ratios are adjusted for region and age (in 5-year bands) within each age group and exclude participants with a history of CVD disease at baseline. For each RR, the area of the data point is inversely proportional to the variance of the log risk. The overall RR (adjusted for age, sex, and region) at ages 35 to 79 years (mean age at death, 67.6 years) was 2.49 (95% CI, 2.37-2.62). B, CVD mortality due to uncontrolled hypertension in 2010 is calculated by applying population-attributable fractions (PAF) to the estimated age- and sex-specific number of CVD deaths in China for 2010 to give the number of deaths attributable to uncontrolled hypertension for that year. Hypertension is defined as a measured systolic blood pressure of at least 140 mm Hg, a measured diastolic blood pressure of at least 90 mm Hg, or treatment for hypertension. Deaths due to CVD are categorized as attributable to hypertension in persons with hypertension, not attributable to hypertension in persons with hypertension, and in persons without hypertension.

sity, 30.7%), but did not vary materially by income (Table 2 and eTable 6 in the Supplement). Diagnosis, treatment, and control of hypertension, however, were substantially less common at lower levels of education and income. Those with prior CVD at baseline had a higher prevalence of hypertension than those without prior CVD (49.4% vs 31.8), but they also had higher rates of diagnosis, treatment, and control. Control of BP in participants with hypertension and prior CVD, however, was still low (13.0%). The estimated prevalence of hypertension was substantially higher in winter (39.6%) than summer (24.9%) and intermediate in spring or autumn (33.3%).

CVD Mortality Attributable to Hypertension

Uncontrolled hypertension was associated with relative risks for CVD mortality for both men and women combined of 4.13 (95% CI, 3.72-4.59), 2.61 (95% CI, 2.38-2.85), and 1.89 (95% CI, 1.76-2.03) at ages 35 to 59, 60 to 69, and 70 to 79 years, respectively (**Figure 3**). We found no evidence that further adjustment for a broad range of socioeconomic and lifestyle risk factors (listed in eTable 7 in the Supplement) materially changed the strength of these associations. Overall, uncontrolled hypertension accounted for about one-third of all CVD deaths at ages 35 to 79 years (almost half of all CVD deaths at ages 35-59 years). In 2010, approximately 750 000 CVD deaths could be attributed to uncontrolled hypertension in China.

Discussion

This large study provides important new evidence about the current burden of hypertension in China, particularly the extent of its undertreatment and the consequences of uncontrolled hypertension for premature vascular death. Overall, about one-third of the adult population had hypertension. The prevalence increased steeply with age, varied substantially by region, and was higher in those with prior CVD. About one-third of those with hypertension were diagnosed; of those diagnosed, about half were treated; and, of those treated, about one-third had their hypertension controlled, resulting in less than 5% of participants with hypertension who achieved properly controlled BP. Undertreatment was observed in all regions and subgroups assessed, including those with prior CVD. Although the prevalence of hypertension was not strongly related to socioeconomic status, the control of BP was lower among participants with lower levels of education and income. Uncontrolled hypertension was estimated to cause 750 000 CVD deaths annually in China.

Although the China Kadoorie Biobank Study was not designed as a nationally representative study, the prevalence of hypertension observed in this study is consistent with previous reports of recent nationally representative hypertension surveys in China.[5,6,14] Only a few studies (all substantially smaller than the present study) have reported the age-specific proportions of persons with hypertension who have received a diagnosis and in whom the hypertension is treated and controlled. The 2007 to 2008 China National Diabetes and Metabolic Disorders Survey[6] and the 2000 to 2001 Chinese InterAsia Survey[5] reported higher levels of diagnosed hypertension than the present study, with about half of participants with hypertension receiving a diagnosis at 45 to 64 years of age (vs one-third in the present study). As in the present study, the participants in those studies were not randomly selected. Unlike the present study, however, the levels of diagnosed hypertension were based on diagnosis by any health care professional rather than specifically by a fully qualified physician. The InterAsia Survey[5] also reported that at 45 to 64 years of

age, two-thirds of participants with diagnosed hypertension were treated (vs half in the present study), but less than one-third of those treated achieved control of hypertension, consistent with the present study.

A systematic review in 2005 of the prevalence of hypertension in different regions of the world reported that the prevalence in China was higher than in other parts of Asia, but lower than in established market economies.[2] The levels of diagnosis, treatment, and control of hypertension in China, however, are substantially lower than those achieved in many high-income countries, where recent surveys indicate that more than two-thirds of the population with hypertension receive a diagnosis, more than two-thirds of those with a diagnosis are treated, and about two-thirds of those treated achieve BP control.[15] Although previous reports indicated that the prevalence of hypertension was slightly lower on average in China than in the West, the present study indicates that the prevalence of hypertension in China is now comparable to that of Western populations, but the prevalence of uncontrolled hypertension is much higher in China than in Western populations. Occlusive CVD mortality has fallen significantly during the last few decades in the West, due at least in part to better management of hypertension; by contrast, occlusive CVD mortality has increased in China during the same period.[16-18]

A large prospective cohort study[19] reported that about 60% of CVD deaths in China at ages 55 to 64 years in 2005 were attributable to hypertension, compared with about 40% in this age group in the present study. In this study, the risk for CVD mortality in persons with hypertension was compared with that in persons with normal BP (defined as SBP <120 mm Hg and DBP <80 mm Hg). In the present study, usual BP in those who did not have hypertension was in the prehypertensive range (SBP 120-139 mm Hg and DBP 80-89 mm Hg), which is the standard target range for those with hypertension; as such, the population-attributable fractions and associated attributable deaths more closely estimate the effect of addressing hypertension than reducing BP to much lower levels. A large trial[20] and a meta-analysis of all available trials[21] recently demonstrated reductions in major cardiovascular events from antihypertensive regimens targeting SBP less than 140 mm Hg even in those older than 60 years, consistent with the evidence from prospective cohort studies. A combination of antihypertensives is generally required to reach this target BP range, but only a small proportion (17.0%) of those treated for hypertension in the present study were taking more than 1 type of antihypertensive (eTable 5 in the Supplement).

The strengths of the present study include the very large sample size, the diversity (geographic and socioeconomic) of the areas sampled, the range of population subgroups assessed, and the standardization of techniques to measure BP at baseline, including the training of technicians. In addition, because the baseline survey was conducted throughout the year and for several years, we were able to examine the effect of the season on the estimates of prevalence and control, and health care professionals and policy makers should be aware of such effects when evaluating the burden and control of BP in China.[22] The study was not designed to collect a representative sample of the Chinese population, which limits the generalizability of the findings to China as a whole, despite the consistency of the age-specific prevalence with recently conducted nationally representative surveys. Before the analyses in this study, the real prevalence of hypertension in China was expected, if anything, to be underestimated in this cohort of generally healthy volunteers. Another limitation is that the diagnosis of hypertension was based on serial BP measurements recorded on a single occasion (as is standard in BP surveys), whereas ideally 2 or more readings would be taken on separate occasions. The estimated prevalence of hypertension at baseline will be affected by regression to the mean of subsequent BP measurements. This regression to the mean is unlikely to affect the estimated prevalence of hypertension materially at 60 to 69 years of age (because the mean BP at this age is approximately equal to the threshold BP for hypertension), but the prevalence may be somewhat overestimated at younger ages and underestimated at older ages.

Conclusions

In 2013, the World Health Assembly set voluntary targets for the control of noncommunicable diseases, including a 25% reduction in the prevalence of elevated BP by 2025. We estimate that such a reduction would have prevented about 130 000 vascular deaths in China for those who were from 35 to 79 years of age in 2010 alone. Detection and adequate treatment of hypertension in primary care have a key role to play in meeting this goal, and the present study shows an enormous potential for improvement, given that no regions or subgroups had satisfactory BP control; such an approach ideally would be expanded to lower the BP of all individuals at high absolute risk for a cardiovascular event.[23] Furthermore, public health initiatives are required that focus on the major determinants of BP at a population level, including salt intake (known to be particularly high in China[24]), harmful alcohol consumption, obesity, and poor home heating (shown to have a substantial effect on BP in China[22]). Ongoing research seeks to identify the most effective population-level approaches for BP control in China.[25] These population-based approaches also would have the added benefit of reducing the large proportion of vascular deaths that occur in persons with normal BP. Unless concerted efforts are made to lower BP levels in China, rates of death due to CVD are likely to increase further during the next few decades.

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REFERENCES

1. Yang G, Wang Y, Zeng Y, et al. Rapid health transition in China, 1990-2010: findings from the Global Burden of Disease Study 2010. *Lancet*. 2013;381(9882):1987-2015.

2. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365(9455):217-223.

3. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360(9349):1903-1913.

4. Turnbull F, Neal B, Ninomiya T, et al; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials. *BMJ*. 2008;336(7653):1121-1123.

5. Wu X, Duan X, Gu D, Hao J, Tao S, Fan D. Prevalence of hypertension and its trends in Chinese populations. *Int J Cardiol*. 1995;52(1):39-44.

6. Gao Y, Chen G, Tian H, et al; China National Diabetes and Metabolic Disorders Study Group. Prevalence of hypertension in China: a cross-sectional study. *PLoS One*. 2013;8(6):e65938.

7. Wu Y, Huxley R, Li L, et al; China NNHS Steering Committee; China NNHS Working Group. Prevalence, awareness, treatment, and control of hypertension in China: data from the China National Nutrition and Health Survey 2002. *Circulation*. 2008;118(25):2679-2686.

8. Chen Z, Lee L, Chen J, et al. Cohort profile: the Kadoorie Study of Chronic Disease in China (KSCDC). *Int J Epidemiol*. 2005;34(6):1243-1249.

9. Chen Z, Chen J, Collins R, et al; China Kadoorie Biobank (CKB) collaborative group. China Kadoorie Biobank of 0.5 million people: survey methods, baseline characteristics and long-term follow-up. *Int J Epidemiol*. 2011;40(6):1652-1666.

10. Cox DR. Regression models and life-tables. *J R Stat Soc*. 1972;34(2):187-220.

11. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. *Am J Public Health*. 1998;88(1):15-19.

12. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2095-2128.

13. Institute for Health Metrics and Evaluation. Global Burden of Disease (GBD). Global Health Data Exchange. http://www.healthdata.org/gbd. 2013. Accessed April 23, 2015.

14. Wu YK, Lu CQ, Gao RC, Yu JS, Liu GC. Nation-wide hypertension screening in China during 1979-1980. *Chin Med J (Engl)*. 1982;95(2):101-108.

15. Joffres M, Falaschetti E, Gillespie C, et al. Hypertension prevalence, awareness, treatment and control in national surveys from England, the USA and Canada, and correlation with stroke and ischaemic heart disease mortality: a cross-sectional study. *BMJ Open*. 2013;3(8):e003423.

16. Zhou M, Wang H, Zhu J, et al. Cause-specific mortality for 240 causes in China during 1990-2013: a systematic subnational analysis for the Global Burden of Disease Study 2013 [published online October 23, 2015]. *Lancet*. doi:10.1016/S0140-6736(15)00551-6.

17. Moran AE, Forouzanfar MH, Roth GA, et al. Temporal trends in ischemic heart disease mortality in 21 world regions, 1980 to 2010: the Global Burden of Disease 2010 Study. *Circulation*. 2014;129(14):1483-1492.

18. Bennett DA, Krishnamurthi RV, Barker-Collo S, et al; Global Burden of Diseases, Injuries, and Risk Factors 2010 Study Stroke Expert Group. The global burden of ischemic stroke: findings of the GBD 2010 study. *Glob Heart*. 2014;9(1):107-112.

19. He J, Gu D, Chen J, et al. Premature deaths attributable to blood pressure in China: a prospective cohort study. *Lancet*. 2009;374(9703):1765-1772.

20. Wright JT Jr, Williamson JD, Whelton PK, et al; SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373(22):2103-2116.

21. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis [published online November 7, 2015]. Lancet.

22. Lewington S, Li L, Sherliker P, et al; China Kadoorie Biobank Study Collaboration. Seasonal variation in blood pressure and its relationship with outdoor temperature in 10 diverse regions of China: the China Kadoorie Biobank. *J Hypertens*. 2012;30(7):1383-1391.

23. Jackson R, Lynch J, Harper S. Preventing coronary heart disease. *BMJ*. 2006;332(7542):617-618.

24. Brown IJ, Tzoulaki I, Candeias V, Elliott P. Salt intakes around the world: implications for public health. *Int J Epidemiol*. 2009;38(3):791-813.

25. Li N, Yan LL, Niu W, et al. A large-scale cluster randomized trial to determine the effects of community-based dietary sodium reduction: the China Rural Health Initiative Sodium Reduction Study. *Am Heart J*. 2013;166(5):815-822.

Invited Commentary

Reducing the Burden of Hypertension
China's Long March Ahead

Nathan D. Wong, PhD; Stanley S. Franklin, MD

Elevated blood pressure (BP) represents the leading cause of death globally, at approximately 7.5 million deaths or 12.8% of all deaths.[1] China bears a significant proportion of the global burden of morbidity and mortality due to hypertension. In this issue of *JAMA Internal Medicine*, Lewington and colleagues[2] describe China's burden of cardiovascular disease (CVD) mortality due to hypertension from the large prospective China Kadoorie Biobank Study conducted from 2004 to 2008 among 500 223 adults aged 30 to 74 years with 7 years of follow-up throughout 10 major provinces. Not surprisingly, the investigators report that only 30.5% of those with hypertension had received a previous diagnosis; of these, only 46.4% were treated, and among those treated, only 29.6% achieved control of hypertension, resulting in an overall control rate of 4.2%. These rates are roughly concordant with those of the recently reported 17-country Prospective Urban Rural Epidemiology (PURE) Study,[3] in which among 45 108 adults in China aged 35 to 70 years, 42% were aware of their hypertension, 34% received treatment, and only 8.2% achieved control. The PURE Study showed treatment and control rates to be worse in western parts of China, and overall among patients receiving documented treatments, more than one-third (37.5%) were only using traditional (non-Western) drugs. A recent pooling of data[4] from 178 studies involving 2 901 464 participants in 30 provinces from 1999 to 2014 shows overall prevalence, treatment, and control rates for hypertension to be 28.9%, 35.3%, and 13.4%, respectively.

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Lewington and colleagues[2] estimate that about 750 000 CVD deaths could be attributed to uncontrolled hypertension alone in China in 2010 and that a 25% reduction in the prevalence of elevated BP as recommended by the World Heart Federation would have averted about 130 000 vascular deaths. They report that overall control of hypertension was less than 5% for 7 of the 10 provinces studied. Although control rates were higher in those participants with higher levels of income or education, they were still low (only 12.6% in those with technical school or university education, and 5.7% in those with household income >¥20 000 [about US $3000]). The authors point to the need for public health initiatives, such as focusing on salt intake, harmful alcohol consumption, obesity, and even poor home heating, which has been found to have a dramatic effect on BP in China.

Clearly, sodium intake has been long recognized as a significant issue, with an effect on the prevalence and adequate control of hypertension; sodium consumption for most adults remains far in excess of World Health Organization recommendations to reduce intake to less than 2300 mg/d. Some initiatives have been successful at reducing the population's salt intake by gradual reformulation on a voluntary basis, such as in the United Kingdom, where such efforts have resulted in significant reductions in the sodium content of processed foods and population urinary sodium levels.[5] Modest reductions of salt intake of 5 to 10 g/d can have a substantial impact in reducing stroke deaths by 14% and coronary deaths by 9%.[6] Nutrition surveys in China indicate that salt intake ranges from 8 to 9 g/d in the south and 12 to 18 g/d in the north,[7] far more than the 5-g/d limit recommended by the World Health Organization.

Although adoption of such a program by a very large country such as China will be challenging, the Chinese government and health organizations have begun to advocate for reduced salt intake along with smoking cessation, restriction of alcohol intake, and moderate exercise. A National Hypertension Day has been promoted. The Cardiovascular Disease Prevention Research Center in the Ministry of Health and the Chinese Hypertension League published a brochure about salt and hypertension for World Hypertension Day of 2009. In 2013, a guide for patients with hypertension that emphasized salt restriction was published. A campaign termed *Limit Salt Spoons* was created calling for the use of a small spoon (1 spoon equals about 2 g of salt) to encourage a "comprehensive healthy lifestyle."[7(p194)]

More needs to be done. Opportunities for improvement include better coordination of efforts among national, provin-