

# Association between cumulative blood pressure and long-term risk of cardiovascular disease: findings from the 26-year Chinese Multi-provincial Cohort Study-Beijing Project

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## Abstract

**Background:** Cumulative blood pressure (BP), a measure incorporating the level and duration of BP exposure, is associated with the risk of cardiovascular disease (CVD). However, the level at which cumulative BP could significantly increase the risk remains unclear. This study aimed to investigate the association of 15-year cumulative BP levels with the long-term risk of CVD, and to examine whether the association is independent of BP levels at one examination.

**Methods:** Data from a 26-year follow-up of the Chinese Multi-provincial Cohort Study-Beijing Project were analyzed. Cumulative BP levels between 1992 and 2007 were calculated among 2429 participants free of CVD in 2007. Cardiovascular events (including coronary heart disease and stroke) occurring from 2007 to 2018 were registered. Adjusted hazard ratios (HRs) for CVD incidence associated with quartiles of cumulative systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated.

**Results:** Of the 2429 participants, 42.9% (1042) were men, and the mean age in 2007 was  $62.1 \pm 7.9$  years. Totally, 207 CVD events occurred during the follow-up from 2007 to 2018. Participants with higher levels of cumulative SBP or DBP exhibited a higher incidence rate of CVD ( $P < 0.001$ ). Compared with the lowest quartile of cumulative SBP, the HR for CVD was 1.03 (95% confidence interval [CI]: 0.59–1.81), 1.69 (95% CI: 0.99–2.87), and 2.20 (95% CI: 1.21–3.98) for the second to the fourth quartile of cumulative SBP, and 1.46 (95% CI: 0.86–2.48), 1.99 (95% CI: 1.18–3.35), and 2.08 (95% CI: 1.17–3.71) for the second to the fourth quartile of cumulative DBP, respectively. In further cross-combined group analyses with BP measurements in 2007, 15-year cumulative BP levels higher than the median, that is, 1970.8/1239.9 mmHg·year for cumulative SBP/DBP, which were equivalent to maintaining SBP/DBP levels of 131/83 mmHg or above on average in 15 years, were associated with higher risk of CVD in subsequent years independent of BP measurements at one-time point.

**Conclusion:** Cumulative exposure to moderate elevation of BP is independently associated with increased future cardiovascular risk.

**Keywords:** Blood pressure; Cardiovascular disease; Cohort study

## Introduction

Hypertension is the most important risk factor of cardiovascular disease (CVD).<sup>[1]</sup> In China, high systolic blood pressure (SBP) accounted for 2.54 million deaths in 2017, of which 95.7% were due to CVD.<sup>[2]</sup> Data from prior studies suggest that the risk of CVD increases with baseline blood pressure (BP) even at a level below the clinical threshold which defines hypertension.<sup>[3]</sup> Meanwhile, it has been reported that longer duration of hypertension was associated with CVD risk.<sup>[4]</sup> In recent years, cumulative BP is increasingly gaining attention as it

contains information on both the levels of BP and the duration of exposure to elevated BP.<sup>[5-7]</sup> In the Kailuan study, a cohort of occupational Chinese adults, every 10 mmHg·year increase in cumulative SBP over 6 years was associated with a 1.8% increase in cardiovascular and cerebrovascular events and a 1.3% increase in all-cause mortality.<sup>[5]</sup> In the Coronary Artery Risk Development in Young Adults Study, an increase of 1 standard deviation (SD) in cumulative SBP was associated with a 73% increase in cardiovascular risk.<sup>[7]</sup> However, the level at which cumulative BP could significantly increase cardiovascular risk is unknown. The answer to this question is of

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great value for the early identification and prevention of hypertension-related risk. Therefore, we used data from the Chinese Multi-provincial Cohort Study-Beijing Project to investigate the association of 15-year cumulative BP levels with the long-term risk of CVD, and to examine whether the association is independent of BP levels at one examination.

**Methods**

**Ethical approval**

The study was approved by the ethics committee of Beijing An Zhen Hospital, Capital Medical University. All participants signed to indicate their informed consent.

**Study population**

This cohort study initially enrolled 4151 participants in Beijing from the Chinese Multi-provincial Cohort Study (CMCS), a nationwide, multicenter, prospective cohort study on CVD which has been reported previously.<sup>[8,9]</sup> Participants were in the age group of 35 to 64 years and free of CVD in 1992 (year 0). They were invited to re-examinations in 2002 (year 10) and 2007 (year 15). This study included all participants who attended two examinations in 1992 and 2007, and who were free of CVD in 2007. Participants were prospectively followed up from 2007 to 2018 for the development of CVD [Figure 1].

**Risk factor measurement**

Demographic information, smoking status, and personal medical history were collected from each participant using standardized questionnaires in all surveys. Height, weight, waist circumference, and BP levels were measured during physical examinations. The mean value of two consecutive BP readings was used. Body mass index (BMI) was calculated as weight in kilograms divided by square of the height in meters. Waist circumference was measured at a level midway between the lower rib margin and the iliac crest while participants were semi-clothed. Smoking was

defined as at least one cigarette per day. Diabetes was defined as fasting blood glucose (FBG) at least 7.0 mmol/L or a condition of previously diagnosed diabetes. Fasting blood samples were collected for laboratory measurements. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and FBG were measured on the day of survey.

**Cumulative BP**

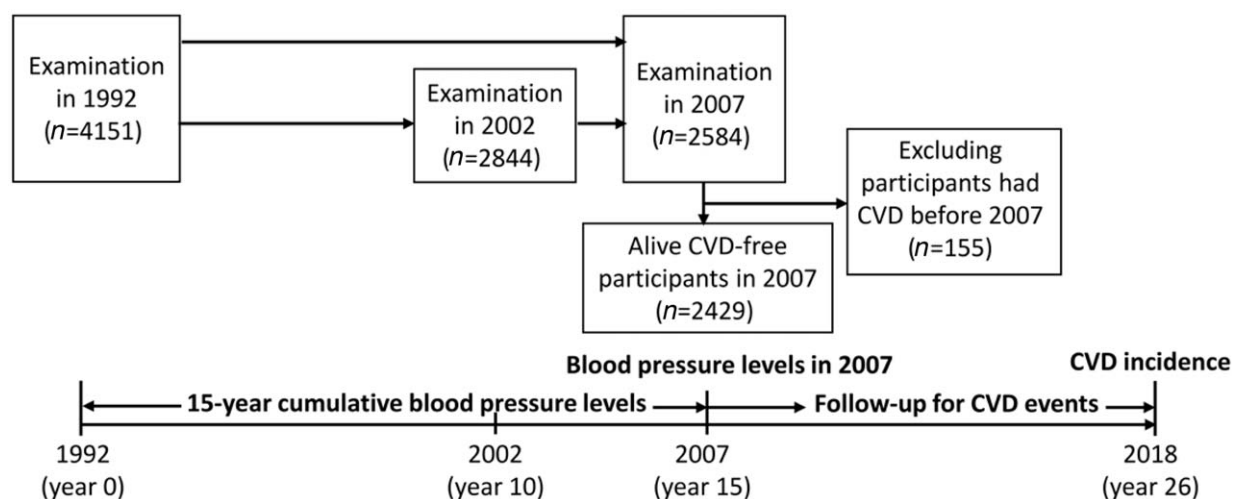
Cumulative BP was calculated by summing the product of the mean BP for each pair of consecutive examinations and the time interval between these two consecutive examinations in years; the formula can be expressed as: Cumulative BP =  $[(BP_1+BP_2)/2 \times time_{1-2} + (BP_2+BP_3)/2 \times time_{2-3}]$ , where BP<sub>1</sub>, BP<sub>2</sub>, and BP<sub>3</sub> were BP measurements at years 0, 10, and 15; time<sub>1-2</sub> and time<sub>2-3</sub> were the time intervals from year 0 to 10, and from year 10 to 15, respectively. For participants who did not return for year 10, cumulative BP was calculated as  $(BP_1+BP_3)/2 \times time_{1-3}$ .

**Case ascertainment**

CVD events comprised of fatal and nonfatal acute coronary and stroke events. Acute coronary heart disease events included acute myocardial infarction, sudden death, and other coronary deaths. Acute stroke events included subarachnoid hemorrhage, intracerebral hemorrhage, and cerebral infarction. Diagnostic criteria were ascertained according to the World Health Organization’s Monitoring of Trends and Determinants in Cardiovascular Disease protocol. A total of 207 incidents of CVD events occurred during the follow-up period from 2007 to 2018, with a mean follow-up of 10.2 years (SD 1.9 years).

**Statistical analysis**

Characteristics for participants were demonstrated as means ± SD if normally distributed or expressed as median (interquartile ranges) if skewed distributed. Categorical variables were expressed as frequencies and percentages



**Figure 1:** Flowchart of participant selection from the Chinese Multi-provincial Cohort Study (CMCS), a nationwide, multicenter, prospective cohort study on CVD. CVD: Cardiovascular disease.

(%). Levels and proportions of BP in 1992, 2002, and 2007 were compared by quartiles of cumulative BP. Cutoff points were 1818.2, 1970.8 and 2152.8 mmHg-year for the quartiles of cumulative SBP, and 1156.8, 1239.9 and 1334.9 mmHg-year for the quartiles of cumulative diastolic blood pressure (DBP). The cumulative incidence of CVD by quartiles of cumulative BP was calculated using the Kaplan–Meier method and compared with a log-rank test. The multivariate Cox proportional hazards regression was used to obtain hazard ratios (HRs) of CVD incidence associated with quartiles of 15-year cumulative SBP and cumulative DBP. In a first step, we adjusted for the classical risk factors, including age, sex, smoking status, diabetes, levels of HDL-C and LDL-C, and the use of antihypertensive and lipid-lowering drugs in 2007. Subsequently, the models were further adjusted for SBP or DBP levels in 2007. The restricted cubic spline was used to further display the relationship between risk (HRs) for CVD incidence and cumulative BP. Meanwhile, the risk of CVD associated with BP in 2007 and 15-year cumulative BP levels were evaluated separately after adjusting for the classical risk factors mentioned above. The discrimination values of cumulative BP and BP in 2007 were assessed using C-statistic. To explore the effect of cumulative BP independent of BP measurements in 2007, we performed 2 × 2 combined group analyses. First, 15-year cumulative BP levels from 1992 to 2007 and BP levels in 2007 were categorized by median levels, with 1970.8 mmHg-year for cumulative SBP, 1239.9 mmHg-year for cumulative DBP, 134.7 mmHg for 2007 SBP, and 81.7 mmHg for 2007 DBP. Subsequently, four combined groups were generated between cumulative BP levels and 2007 BP levels (*ie*, low cumulative SBP and low SBP, low cumulative SBP and high SBP, high cumulative SBP and low SBP, and high cumulative SBP and high SBP). Combinations of cumulative DBP levels with 2007 DBP levels were generated similarly. HRs for the long-term risk of CVD and 95% confidence intervals (CIs) were calculated for combina-

tions of cumulative SBP with 2007 SBP in SBP model and for cumulative DBP with 2007 DBP in DBP model. The groups with low levels of both cumulative BP and baseline BP were used as the reference. Age, sex, smoking status, diabetes, levels of HDL-C and LDL-C, antihypertensive medications, and lipid-lowering drug use were adjusted in both the SBP model and DBP model.

Analyses were performed using STATA version 14.2 (Stata Corp LP, College Station, TX, USA). A two-sided *P* value of <0.05 was considered as statistical significance. For variables with missing data, we imputed the missing values using the sequential regression multiple imputation method implemented by IVEware software version 0.2 (Survey Research Center, University of Michigan, Ann Arbor, MI, USA). The rate of missing variables ranged from 0.05% to 3.56%. Sensitivity analyses were conducted after excluding data with missing values.

## Results

### Characteristics of study participants

The mean age was 46.4 ± 8.0 years in 1992 and 62.1 ± 7.9 years in 2007 among the 2429 participants included in the analyses, of whom 42.9% were men. The levels of TC, LDL-C, TG, SBP and DBP, the prevalence of diabetes, and the use of antihypertensive and lipid-lowering drugs increased, and the level of HDL-C maintained stability during the 15 years from 1992 to 2007. The levels of BMI and waist circumference increased, but the proportion of smoking decreased from 1992 to 2002 and maintained stability through 2002 to 2007 [Table 1]. Participants with higher levels of cumulative SBP were older and more likely to be male [Supplementary Table 1, <http://links.lww.com/CM9/A463>]. The levels of BMI, waist circumference, FBG, and BP showed an increase with cumulative SBP and cumulative DBP [Supplementary Table 1, <http://links.lww.com/CM9/A463>].

**Table 1: Characteristics of study participants in 1992, 2002, and 2007.**

| Parameters                | 1992<br>(n = 2429) | 2002<br>(n = 2043) | 2007<br>(n = 2429) |
|---------------------------|--------------------|--------------------|--------------------|
| Age (year)                | 46.4 ± 8.0         | 57.1 ± 7.9         | 62.1 ± 7.9         |
| Male                      | 1042 (42.9)        | 843 (41.3)         | 1042 (42.9)        |
| BMI (kg/m <sup>2</sup> )  | 23.9 ± 3.2         | 25.4 ± 3.3         | 25.1 ± 3.4         |
| Waist circumference (cm)  | 79.4 ± 9.2         | 84.4 ± 8.9         | 84.8 ± 9.7         |
| FBG (mmol/L)              | 5.3 ± 0.9          | 5.0 ± 1.3          | 5.9 ± 1.4          |
| TC (mmol/L)               | 4.7 ± 0.9          | 5.4 ± 1.0          | 5.4 ± 1.0          |
| LDL-C (mmol/L)*           | 2.7 ± 0.8          | 3.3 ± 0.9          | 3.4 ± 0.9          |
| HDL-C (mmol/L)            | 1.4 ± 0.4          | 1.4 ± 0.3          | 1.3 ± 0.3          |
| TG (mmol/L)               | 1.0 (0.7–1.4)      | 1.3 (0.9–1.9)      | 1.5 (1.1–2.1)      |
| SBP (mmHg)                | 120.6 ± 17.3       | 130.8 ± 19.0       | 136.1 ± 18.0       |
| DBP (mmHg)                | 77.4 ± 10.8        | 81.9 ± 10.3        | 82.4 ± 9.9         |
| Smoking                   | 404 (16.6)         | 241 (11.8)         | 283 (11.7)         |
| Diabetes                  | 101 (4.2)          | 218 (10.7)         | 424 (17.5)         |
| Antihypertensive drug use | 127 (5.2)          | 457 (22.4)         | 829 (34.1)         |
| Lipid-lowering drug use   | 46 (1.9)           | 138 (6.8)          | 216 (8.9)          |

Data are presented as n (%) or mean ± standard deviation or median (interquartile range). \* LDL-C in 1992 was calculated using the Friedewald formula calculation method from 2394 participants with TG < 4.5 mmol/L. Values are presented as the mean ± SD, median (interquartile range), or n (%). DBP: Diastolic blood pressure; FBG: Fasting blood glucose; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Triglycerides.

com/CM9/A463 and Supplementary Table 2, <http://links.lww.com/CM9/A463>.

### Cumulative BP and changes in BP levels

Individuals with higher levels of cumulative BP also had higher levels of SBP and DBP in each examination during the 15 years from 1992 to 2007. Mean levels of SBP increased steadily with time in the first to third quartiles of cumulative SBP, whereas mean SBP level peaked at a 5-year early in the fourth quartile. Changes in DBP levels exhibited a pattern similar to SBP over time, except that the increase in DBP levels in the first to third quartiles was flatter compared with the slope of SBP [Figure 2]. Consistent with changes in mean BP level, the proportion of SBP  $\geq 140$  mmHg or DBP  $\geq 90$  mmHg also increased over the 15 years from 1992 to 2007 in the first to third quartiles of cumulative BP, while the proportion peaked in 2002 and then decreased in 2007 in the fourth quartile [Supplementary Figure 1, <http://links.lww.com/CM9/A463>].

### Cumulative BP and future CVD risk

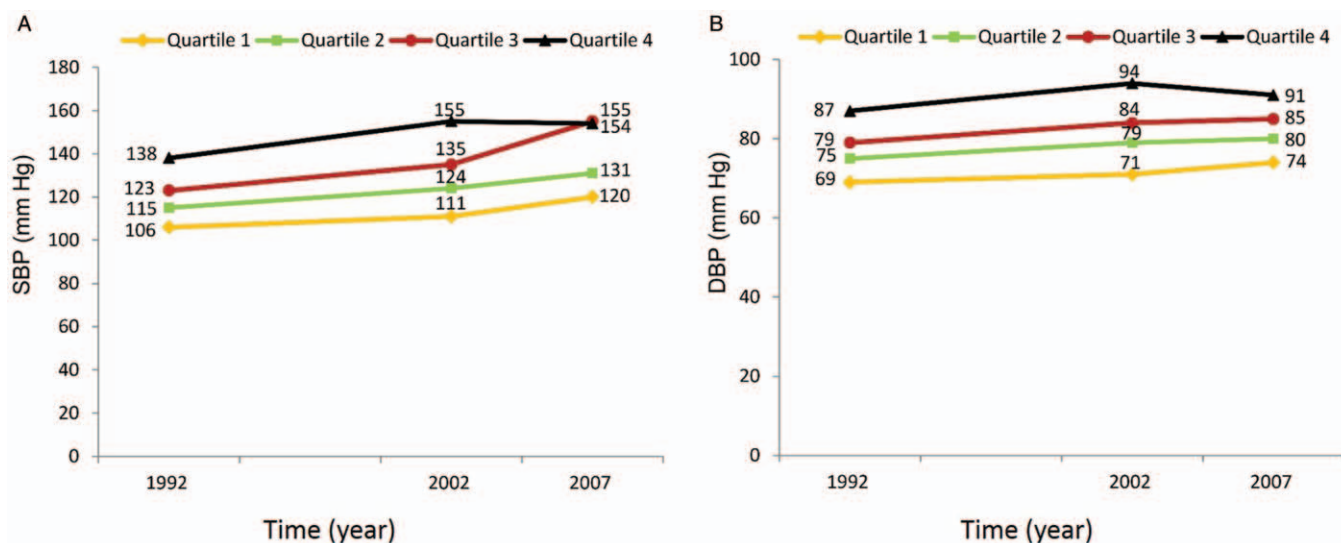
During the follow-up period, CVD incidence rates were 357.4, 505.0, 1054.4, and 1819.6 per 100,000 person-years for participants with the first to fourth quartiles of cumulative SBP, respectively, and the counterpart rates were 354.7, 693.4, 1102.3 and 1556.7 per 100,000 person-years for the first to fourth quartiles of cumulative DBP, respectively. The Kaplan-Meier curves showed that the participants with higher levels of cumulative SBP or cumulative DBP exhibited significantly higher incidence risk of CVD during follow-up (log-rank  $P < 0.001$ ) [Figure 3].

After adjusting for classical risk factors with the Cox proportional hazards regression models, the HRs (95% CI) of the second to fourth quartiles of cumulative BP for

predicting CVD were 1.17 (0.67–2.04), 2.10 (1.27–3.48), and 3.27 (1.97–5.43) for cumulative SBP, and 1.61 (0.96–2.71), 2.36 (1.43–3.87), and 2.78 (1.69–4.60) for cumulative DBP, compared with the first quartile [Table 2]. After further adjusting for SBP or DBP levels in 2007, the associations were attenuated but were still of statistical significance or borderline statistical significance in the third and fourth quartiles of cumulative SBP and cumulative DBP. The results were similar in sensitivity analysis in participants with complete data ( $n = 2326$ ) [Supplementary Table 3, <http://links.lww.com/CM9/A463>]. In the restricted cubic spline analysis, a significantly increased risk for CVD was also observed when cumulative BP was higher than the median, that is, 1970.8/1239.9 mmHg-year for cumulative SBP/DBP [Supplementary Figure 2, <http://links.lww.com/CM9/A463>].

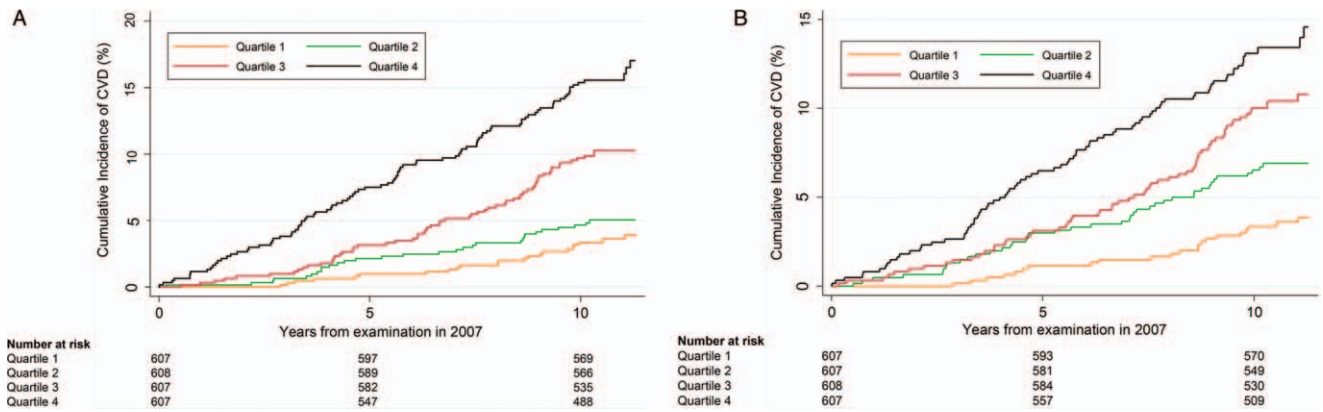
After adjusting for the traditional risk factors, the HRs for CVD incidence associated with per SD increase and the third to fourth quartiles of cumulative SBP and DBP were higher than those associated with 2007 BP levels, respectively, although the 95% CIs were overlapping [Supplementary Table 4, <http://links.lww.com/CM9/A463>]. Moreover, the C-statistic increased from 0.73 (0.69–0.76) in the model with 2007 SBP to 0.74 (0.71–0.77) in the model with cumulative SBP, but the difference was not significant ( $P = 0.129$ ). The results for DBP were similar, with a C-statistic of 0.72 (0.68–0.75) for 2007 DBP vs. 0.73 (0.69–0.76) for cumulative DBP,  $P = 0.312$ .

Moreover, combined group analyses were performed to analyze whether the effect of 15-year cumulative exposure of BP was independent of BP measurements at one examination [Table 3]. Results from both the SBP model and the DBP model showed that after adjustment of other covariates, high cumulative BP levels at the median or above were significantly associated with increased risk of CVD, irrespective of whether the level of BP measurement in 2007 was high or not. If BP levels in 2007 were high but



**Figure 2:** Blood pressure levels in 1992, 2002, and 2007 by quartiles of cumulative blood pressure during 1992–2007. (A) SBP; (B) DBP. DBP: Diastolic blood pressure; SBP: Systolic blood pressure.





**Figure 3:** The Kaplan-Meier curves for CVD incidence in participants with quartiles of cumulative blood pressure during 1992–2007. (A) SBP; (B) DBP. CVD: Cardiovascular disease; DBP: Diastolic blood pressure; SBP: Systolic blood pressure.

**Table 2: Hazard ratios and 95% confidence intervals for incident CVD by quartiles of 15-year cumulative blood pressure.**

| Items      | Cumulative SBP          |        |                               |       | Cumulative DBP          |        |                               |       |
|------------|-------------------------|--------|-------------------------------|-------|-------------------------|--------|-------------------------------|-------|
|            | Classical risk factors* |        | Classical risk factors* + SBP |       | Classical risk factors* |        | Classical risk factors* + DBP |       |
|            | Hazard ratios (95% CI)  | P      | Hazard ratios (95% CI)        | P     | Hazard ratios (95% CI)  | P      | Hazard ratios (95% CI)        | P     |
| Quartile 1 | Reference               |        | Reference                     |       | Reference               |        | Reference                     |       |
| Quartile 2 | 1.17 (0.67–2.04)        | 0.577  | 1.03 (0.59–1.81)              | 0.916 | 1.61 (0.96–2.71)        | 0.073  | 1.46 (0.86–2.48)              | 0.159 |
| Quartile 3 | 2.10 (1.27–3.48)        | 0.004  | 1.69 (0.99–2.87)              | 0.054 | 2.36 (1.43–3.87)        | 0.001  | 1.99 (1.18–3.35)              | 0.010 |
| Quartile 4 | 3.27 (1.97–5.43)        | <0.001 | 2.20 (1.21–3.98)              | 0.009 | 2.78 (1.69–4.60)        | <0.001 | 2.08 (1.17–3.71)              | 0.013 |

\* Classical risk factors include age, sex, smoking status, diabetes, levels of HDL-C and LDL-C, and the use of antihypertensive and lipid-lowering drugs. CVD: Cardiovascular disease; DBP: Diastolic blood pressure; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SBP: Systolic blood pressure.

**Table 3: Hazard ratios and 95% confidence intervals for the risk of CVD incidence associated with combined groups of cumulative BP levels during 1992–2007 and BP levels in 2007.**

| Variables                        | Hazard Ratios (95%CI) | P      |
|----------------------------------|-----------------------|--------|
| *SBP model                       |                       |        |
| Low cumulative SBP and low SBP   | Reference             |        |
| Low cumulative SBP and high SBP  | 1.21 (0.66–2.22)      | 0.535  |
| High cumulative SBP and low SBP  | 2.01 (1.21–3.36)      | 0.007  |
| High cumulative SBP and high SBP | 2.63 (1.77–3.90)      | <0.001 |
| *DBP model                       |                       |        |
| Low cumulative DBP and low DBP   | Reference             |        |
| Low cumulative DBP and high DBP  | 1.78 (1.06–2.98)      | 0.028  |
| High cumulative DBP and low DBP  | 2.02 (1.27–3.21)      | 0.003  |
| High cumulative DBP and high DBP | 2.38 (1.62–3.48)      | <0.001 |

\* Combined groups of cumulative SBP levels during 1992–2007 and SBP levels in 2007. BP: Blood pressure; CVD: Cardiovascular disease; DBP: Diastolic blood pressure; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SBP: Systolic blood pressure. The 15-year cumulative BP levels and BP levels in 2007 were categorized by median. All the models were adjusted for age, sex, smoking status, diabetes, levels of HDL-C and LDL-C, antihypertensive medications, and lipid-lowering drugs.

cumulative BP levels from 1992 to 2007 were low, the association with CVD risk was only significant for high DBP, but not high SBP.

**Discussion**

In this long-term cohort study, we demonstrated that elevated cumulative BP level was significantly associated

with increased risk of CVD, and that this association was independent of BP measurements at one examination. If the 15-year cumulative BP level was higher than the median, that is, 1970.8/1239.9 mmHg·year for cumulative SBP/DBP, which was equivalent to maintaining a level of SBP/DBP higher than 131/83 mmHg in 15 years, the CVD risk would significantly increase in the future.

The effect of BP load over a long time on CVD risk has been the subject of intensive interest globally. In the original and the offspring Framingham Heart Study, antecedent BP, defined as the average of BP measurements preceding the baseline, was an important determinant of future risk of CVD events above and beyond the baseline BP.<sup>[10-12]</sup> There are also several studies using the trajectory method to represent longitudinal changes in BP and predict the associated CVD risk.<sup>[13-16]</sup> All these studies highlighted the importance of long-term BP exposure from various perspectives. The measurement of cumulative exposure combines information on both the level and the duration of exposure, to provide a more predictive value of CVD. In the current study, we observed that elevated cumulative BP levels were significantly associated with increased risk of CVD in the future; our observation was consistent with findings from previous prospective studies.<sup>[5,7]</sup> Additionally, using combined group analyses, we found that cardiovascular risk associated with cumulative BP levels during the past years was independent of BP measurements at the year of examination. In more detail, CVD risk increased significantly if cumulative BP levels were elevated, irrespective of whether the BP measurements at one examination were high or not. These findings suggest that a single BP measurement at the baseline would misclassify CVD risk. Without taking cumulative BP levels into consideration, individuals with high risk of CVD might miss the chance of early prevention based on their “normal” BP levels at one examination. The results also suggest that participants with a high level of SBP at a single examination but a low level of cumulative SBP exposure over time did not have significantly increased CVD risk; this fact also implies that cumulative BP exposure could provide more insight into CVD risk assessment than BP measurements at a single examination.

Although several previous studies have reported a better predictive value of cumulative BP compared to a single BP measurement,<sup>[5-7]</sup> it is unclear as to which level of the cumulative BP may significantly increase the risk for CVD. We observed that the long-term risk of CVD significantly increased when the 15-year cumulative SBP was higher than 1970.8 mmHg·year or when cumulative DBP was higher than 1239.9 mmHg·year, which was equivalent to maintaining SBP/DBP levels at 131/83 mmHg or greater during the 15 years. This is consistent with our previous findings that individuals maintaining SBP/DBP in the range of 130–139/80–89 mmHg over the 15 years had a significantly increased CVD risk compared with those who maintained SBP <130 mmHg and DBP <80 mmHg among participants in CMCS.<sup>[9]</sup> Data from six US cohorts also showed that cumulative young adult exposures to SBP >130 mmHg and DBP >80 mmHg were associated with increased CVD risks in later life.<sup>[17]</sup> Recently, a meta-analysis which included 16 cohort studies showed that SBP in the range of 130–139 mmHg or DBP in the range of 80 to 89 mmHg is associated with an elevated risk of CVD morbidity and mortality.<sup>[18]</sup> The current study provides further support for the importance of this BP level.

Our study has several implications for CVD prevention. First, our findings suggest that it is ideal to maintain the

levels of SBP and DBP below 130 mmHg and 80 mmHg, respectively, as long as possible to maintain lifelong cardiovascular health. Although it has been demonstrated by randomized clinical trials that antihypertensive treatment significantly lower risk of CVD,<sup>[19,20]</sup> some studies found that individuals with normal treated BP levels still had twice the risk of incident CVD events than those maintaining normal untreated BP levels.<sup>[21]</sup> The Multi-Ethnic Study of Atherosclerosis confirmed that there was a stepwise increased risk of CVD correlated with increasing SBP levels among individuals without hypertension or other traditional risk factors.<sup>[22]</sup> These evidences are supportive to our study, indicating that it is crucial to maintain a normal BP level in early lifetime and prevent the development of hypertension. On the other hand, active BP management strategies should be implemented once an abnormal BP level is observed. About a quarter of Chinese adults have elevated BP levels at SBP 130–139 mmHg or DBP levels at 80 to 89 mmHg.<sup>[23]</sup> Whether this BP stratum is defined as high, normal, or stage 1 hypertension by different guidelines,<sup>[24,25]</sup> it carries significantly increased cardiovascular risk according to findings from current and previous studies. Lifestyle intervention is the major therapeutic strategy recommended by international and Chinese guidelines on hypertension for individuals at this BP stratum.<sup>[24,25]</sup> However, previous studies found that lifestyle intervention is largely underused in daily life and in clinical settings.<sup>[26,27]</sup> Our findings are from observational study, rather than randomized controlled clinical trials that evaluate the efficacy of any intervention. From a clinical perspective, our study implies that using cumulative BP as a parameter of assessment may help to identify individuals at higher risk of cardiovascular disease. Health care providers should pay attention to the patient’s previous BP exposure, in addition to current BP levels.

The strengths of this study include its long-term follow-up, the standardized procedures used for data collection, and adjudication of suspected CVD using detailed evaluation criteria. Since participants have their BP measured at multiple time points over 15 years, we can analyze the risk of incident CVD associated with both the BP levels and the duration. However, some limitations should also be mentioned. First, for the estimates of cumulative BP, we relied on three measurements over 15 years. The estimation may not have captured more frequent fluctuations in BP levels. Moreover, although we have adjusted for all classical CVD risk factors in the multivariate analysis, we cannot exclude the impact of some unaccounted-for and residual confounding factors.

In conclusion, our study demonstrated that elevated cumulative SBP or DBP was independently associated with increased risk of CVD in the Chinese population. Among participants with 15-year cumulative BP levels higher than the median, that is, 1970.8/1239.9 mmHg·year for cumulative SBP/DBP, which was equivalent to maintaining SBP/DBP level higher than 131/83 mmHg in 15 years, the CVD risk would increase significantly irrespective of whether or not the BP measurements at one examination was high. Our findings emphasize the importance of cumulative BP level in identifying individuals with high risk of CVD in the future.

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## Conflicts of interest

None.

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