Journal of the American Heart Association

ORIGINAL RESEARCH

# Intensive Blood Pressure Strategy on Cardiovascular Diseases in Patients With Metabolic Syndrome: Post Hoc Analysis of a Clinical Trial

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**BACKGROUND:** Blood pressure (BP) management in patients with metabolic syndrome is complex, and optimal targets remain debated. The CRHCP (China Rural Hypertension Control Project) trial demonstrated that intensive BP control reduces cardiovascular events. This secondary analysis assessed its efficacy in patients with hypertension and metabolic syndrome.

**METHODS AND RESULTS:** This a post hoc analysis of a cluster randomized trial (NCT03527719) across 3 Chinese provinces; 18 076 hypertensive patients with metabolic syndrome were followed up for 3 years. Intervention groups received multifaceted BP management by nonphysician health care professionals aiming for <130/80 mm Hg BP under physician supervision. The primary outcome of major adverse cardiovascular events included stroke, myocardial infarction, heart failure, and death from cardiovascular causes, during a 3-year follow-up. A total of 18 076 participants (median [range] age, 63 [54–72] years; 13 056 [72.2%] women) were enrolled in 2 clusters and were adjudicated for the primary outcome (control, 9337; intervention, 8739). At the end of the 3-year follow-up, the mean systolic/diastolic BP was 126.3/73.0 mm Hg in the intervention group versus 147.3/82.0 mm Hg in the usual care group. Compared with the usual care group, the intervention group had a lower rate of major adverse cardiovascular events (1.58% versus 2.42% per year; hazard ratio [HR], 0.65 [95% CI, 0.57–0.74]; $P<0.001$), as well as stroke (HR, 0.68 [95% CI, 0.55–0.83]; $P=0.015$), myocardial infarction (HR, 0.70 [95% CI, 0.51–0.97]; $P=0.034$), death from cardiovascular causes (HR, 0.67 [95% CI, 0.47–0.96]; $P=0.029$), and death from all causes (HR, 0.82 [95% CI, 0.71–0.94]; $P=0.005$).

**CONCLUSIONS:** Intensive BP control (<130/80 mm Hg) by trained nonphysician community health care professionals effectively reduces cardiovascular events in patients with hypertension and metabolic syndrome.

**REGISTRATION:** URL: https://www.clinicaltrials.gov; Unique identifier: NCT03527719.

**Key Words:** cardiovascular diseases ■ intensive blood pressure strategy ■ metabolic syndrome

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that include central obesity, dyslipidemia, insulin resistance, and hypertension.[1,2] MetS is associated with increased risk of developing diabetes, cardiovascular diseases (CVDs), and mortality.[2–4]

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This manuscript was sent to Tazeen H. Jafar, MD, MPH, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.124.036820

For Sources of Funding and Disclosures, see page xxx.



*JAHA* is available at: www.ahajournals.org/journal/jaha

## CLINICAL PERSPECTIVE

### What Is New?

- These are the first data on the effects and safety of an intensive blood pressure control strategy (target, <130/80 mm Hg) led by nonphysician community health care professionals in patients with hypertension and metabolic syndrome.
- The intensive blood pressure control strategy (<130/80 mm Hg) reduced incident cardiovascular diseases in patients with hypertension and metabolic syndrome versus usual care.

### What Are the Clinical Implications?

- The intensive blood pressure control strategy (target, <130/80 mm Hg) led by nonphysician community health care professionals is applicable to patients with hypertension and metabolic syndrome and should be scaled up within this population.

### Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **ACCORD** | Action to Control Cardiovascular Risk in Diabetes |
| **CRHCP** | China Rural Hypertension Control Project |
| **MACE** | major adverse cardiovascular event |
| **MetS** | metabolic syndrome |
| **SBP** | systolic blood pressure |
| **SPRINT** | Systolic Blood Pressure Intervention Trial |

As a critical component of MetS, hypertension expedites the progression of MetS.[5] Importantly, blood pressure (BP) control rate is lower in patients with hypertension and MetS. Specifically, BP control rate (to a level of <140/90 mm Hg) in individuals without MetS is 43% higher than in those with MetS.[6] In a cohort study from rural China,[7] the rate of BP control was 68.17% versus 54.65% after 1-year treatment with antihypertensive medications.[7] Furthermore, results from the Global Cardiometabolic Risk Profile in Patients With Hypertension Disease survey showed that components of MetS (visceral obesity and dyslipidemia) were associated with the poor response to an antihypertensive regimen in patients with MetS.[8] Therefore, patients with hypertension and MetS urgently require more effective BP management strategies.

BP control to <140/90 mm Hg was associated with reduced incidence of adverse cardiovascular events in older Japanese patients with MetS.[9] A recent subgroup analysis of the SPRINT (Systolic Blood Pressure Intervention Trial) also indicated that intensive BP control (systolic blood pressure [SBP], <120 mm Hg) is equally effective in patients with MetS versus those without MetS.[10] However, SPRINT excluded patients with diabetes, a common and crucial subset within the population affected by MetS. More importantly, MetS in SPRINT was defined by body mass index and not waist circumference and thus did not faithfully capture the component of central obesity in the currently recognized diagnostic criteria for MetS.[1,11,12] Major guidelines, including the 2017 American Heart Association, 2020 International Society of Hypertension, and 2023 European Society of Hypertension guidelines, emphasized the elevated CVD risk in individuals with MetS and a need for revision in BP management but did not provide a specific BP target for patients with MetS.[13–15] In summary, the effect of intensive BP control on CVD and death has not been established in the general population with hypertension and MetS.

The CRHCP (China Rural Hypertension Control Project) trial is a cluster randomized trial that examined whether implementation of BP control to <130/80 mm Hg by training community health care professionals could reduce incident CVDs in adult patients with hypertension.[16,17] We conducted a secondary analysis to examine the efficacy of intensive BP control in the subgroup of patients with hypertension and MetS.

## METHODS

### Design and Participants

The data used in the current analysis are available from the corresponding author upon reasonable request.

The current study is a post hoc subgroup analysis of the patients with hypertension and MetS in the CRHCP trial, a cluster randomized trial that compared intensive BP control strategy (<130/80 mm Hg) versus usual care in a community setting in rural areas in China.[16,17] For inclusion in the CRHCP trial, participants must be aged ≥40 years and have a mean untreated SBP of ≥140 mm Hg or a mean untreated diastolic blood pressure of ≥90 mm Hg, based on 6 measures taken on 2 different days. Alternatively, they could have a mean treated SBP of at least 130 mm Hg or a mean treated diastolic blood pressure of at least 80 mm Hg. For patients with a history of coronary heart disease, heart failure, stroke, diabetes, or chronic kidney disease, the requirement was ≥130 mm Hg for SBP and ≥80 mm Hg for diastolic blood pressure. The study was approved by the Ethics Committee of the First Hospital of China Medical University and all participating research institutes. Informed consent was obtained from

all participants on trial enrollment. Details of the trial design, conduct, and outcomes have been described previously.[15,17]

MetS was defined on the basis of the criteria by the National Cholesterol Education Program's Adult Treatment Panel III report[18,19] as ≥3 of the following: (1) waist circumference ≥90 cm in men and ≥80 cm in women; (2) triglyceride ≥150 mg/dL; (3) high-density lipoprotein cholesterol <40 mg/dL in men and <50 mg/ dL in women; (4) BP ≥130/85 mm Hg or the use of antihypertensive medications; and (5) fasting plasma glucose ≥110 mg/dL or the use of antidiabetic medications.

Among 33 995 participants, a total of 18 076 with MetS (13 056 [72.2%] women) were included in the analysis. They were enrolled during the CRHCP trial between July 18 and November 27, 2018.

## Intervention

The study implemented a stepwise management plan for hypertension. The intervention group received multifaceted treatment from well-trained nonphysician community health care professionals with a BP target of <130/80 mm Hg, and the control group received usual care. These health care professionals received a series of training sessions covering antihypertensive treatment, including drug selection, contraindications, dosage adjustments, and patient education on home BP monitoring, medication adherence, and lifestyle modifications, with the guidance of primary care physicians. They were also responsible for medication management, health coaching, home BP monitoring instruction, and organizing social support groups, with compensation of a base salary plus performance incentives from research grants. To improve adherence, the intervention group was offered monthly antihypertensive medications for free or at a reduced cost and home BP monitoring devices, along with regular health coaching, providing a strong support system.

## Follow-Up Data Collection

Participants were followed up every 6 months after their enrollment, with the 36-month follow-up for each participant concluding on October 29, 2021. At each follow-up visit, BP was measured and information was gathered on lifestyle factors, antihypertensive medication use and adherence, trial outcomes, health-related cost, and adverse events. During each follow-up visit, BP was also monitored for 2 days, 3 times daily, and the average of all 6 measurements from these 2 days was used in analyses, using an Omron HBP-1100U automatic BP monitor (Omron Corporation, Tokyo, Japan). At the last follow-up, an overnight fasting blood sample was collected from participants in the morning to measure glucose, lipid, and electrolyte levels, as well as liver and kidney function and other routine blood biochemical indexes.

## Study Outcome

The primary outcome of major adverse cardiovascular events (MACEs) included stroke, myocardial infarction, heart failure requiring hospitalization, and deaths within the 3-year follow-up, as evaluated by an end point adjudication committee unaware of group allocation.

Safety outcomes included hypotension, symptomatic hypotension, syncope, injurious falls, and renal function deterioration (≥30% reduction in estimated glomerular filtration rate to <60 mL/min per 1.73 $m^2$ in patients without chronic kidney disease at baseline or ≥50% reduction in estimated glomerular filtration rate in patients with chronic kidney disease at baseline). Electrolyte abnormalities were also analyzed.

## Statistical Analysis

Data analyses were conducted in a modified intent-to-treat population that included all enrolled patients with MetS. Patients with missing baseline data that did not allow for accurate assessment of MetS status were excluded. Continuous variables are presented as mean±SD; categorical variables are reported as number (percentage). BP was compared between the 2 groups using a generalized estimating equation linear model with an exchangeable correlation structure. To compare the long-term trends in BP between the 2 groups, we used a generalized estimating equation model to account for both intraparticipant and interparticipant correlations. The intervention group and follow-up time points were treated as fixed effects, whereas participant-level clustering was addressed through the repeated measures design. An interaction term between the intervention and time points was included to evaluate differences in BP changes over time between the 2 groups. The *P* value for the interaction term was <0.05, indicating a statistically significant difference in the long-term BP trends between the groups throughout the follow-up period. The clustered marginal Cox proportional-hazards regression models were used to estimate the risk of CVDs; the results are presents as hazard ratio (HR) and 95% CI. The unit for trial randomization (village) was treated as a random unit, whereas province, county, and township were considered fixed effects in the analyses. A robust sandwich covariance matrix was applied to address village clustering. We examined the duration until follow-up loss or occurrence of the last event without conducting hypothesis testing because of lack of adjustment for multiple comparisons in the reported CIs. Additionally, event

rates per 100 person-years were calculated. Analyses were adjusted for baseline covariates, including age, sex, smoking, history of CVD, estimated glomerular filtration, physical activity status, and education level. This analysis is a post hoc evaluation, which may lead to baseline imbalances. Adjustments were made to improve accuracy, focusing on CVD risk factors, as specified in the CRHCP trial protocol. Besides, important predefined covariates were adjusted to enhance statistical precision and limit potential confounding effects. We also conducted a sensitivity analysis that included only intervention group patients with a last SBP <120 mm Hg before any composite CVD event (or their last recorded BP if no event occurred), with the entire usual care group as a comparison. $P<0.05$ (2 sided) was considered statistically significant. Statistical analysis was conducted with SAS 9.4 (SAS Institute, Cary, NC) and R, version 4.2.0 (R Project for Statistical Computing, Vienna, Austria).

# RESULTS

## Study Participants

The CRHCP trial enrolled a total of 33 995 patients. In addition to those without MetS at the baseline, 224 were excluded because of missing data (n=198 and n=26 for waist circumference and blood sample data, respectively) at the baseline that resulted in unknown MetS status. The final analysis included 18 076 patients with hypertension and MetS: 9337 in the intervention group and 8739 in the usual care group (Figure S1). Among 18 076 patients, 17 980 (99.5%) were successfully followed up, providing sufficient data to evaluate the relationship between the intervention and CVD outcomes. Demographic and baseline characteristics of the 2 groups are shown in Table 1. When compared with the usual care group, the intervention group had a lower mean age, more use of baseline antihypertensive medication, and higher BP.

## BP During Follow-Up

The mean baseline BP was 157.4/88.0 mm Hg in the intervention group versus 155.8/87.4 mm Hg in the usual care group (Figure 1). BP started to diverge between the 2 groups at 6 months. At the end of the 3-year follow-up, the mean BP was 126.3/73.0 mm Hg in the intervention group versus 147.3/82.0 mm Hg in the usual care group ($P<0.001$). The percentage of the patients with BP <130/80 mm Hg at the end of the 3-year follow-up was 71.7% and 11.9% in the intervention and usual care groups, respectively (Figure S2); the percentage of the patients with BP <140/90 mm Hg was 87.9% and 34.3%, respectively. The use of antihypertensive medications at 12, 24, and 36 months is shown in Table S1.

**Table 1. Baseline Characteristics of the Patients With MetS**

| Characteristics | Intervention (N=9337) | Usual care (N=8739) | *P* value |
|---|---|---|---|
| Age, mean±SD, y | 61.9±8.9 | 62.3±8.9 | 0.002 |
| Female sex, n (%) | 6689 (71.6) | 6367 (72.9) | 0.068 |
| Education, n (%) | | | |
| Primary school or less | 6124 (66.1) | 5851 (67.7) | 0.113 |
| Junior high school | 2550 (27.5) | 2282 (26.4) | |
| High school | 524 (5.7) | 446 (5.2) | |
| College or higher | 70 (0.8) | 61 (0.7) | |
| Smoking, n (%) | | | |
| Never smoked | 7137 (76.9) | 6613 (76.5) | 0.475 |
| Former smokers | 632 (6.8) | 629 (7.3) | |
| Current smokers | 1506 (16.2) | 1397 (16.2) | |
| Weekly alcohol drinking, n (%) | 1142 (12.3) | 1049 (12.1) | 0.733 |
| Physical activity ≥5 times/wk, n (%)* | 4423 (47.7) | 4270 (49.5) | 0.017 |
| Duration of hypertension, median (IQR), y | 8 (5–11) | 7 (4–11) | 0.005 |
| Use of antihypertensive medications, n (%) | 6088 (65.2) | 5183 (59.3) | <0.001 |
| History of major cardiovascular disease, n (%)† | 2020 (21.6) | 1785 (20.4) | 0.046 |
| History of previously diagnosed diabetes, n (%) | 1426 (15.3) | 1265 (14.5) | 0.132 |
| History of chronic kidney disease, n (%)‡ | 68 (0.7) | 59 (0.7) | 0.669 |
| Body mass index, mean±SD, kg/m$^2$ | 27.4±3.6 | 27.2±3.5 | 0.011 |
| Waist circumference, mean±SD, cm | 93.0±8.5 | 92.5±8.4 | <0.001 |
| Systolic blood pressure, mean±SD, mm Hg | 157.4±18.1 | 155.8±17.5 | <0.001 |
| Diastolic blood pressure, mean±SD, mm Hg | 88.0±10.6 | 87.4±10.5 | <0.001 |
| Total cholesterol, mean±SD, mg/dL | 201.1±41.0 | 200.5±41.3 | 0.371 |
| Low-density lipoprotein cholesterol, mean±SD, mg/dL | 107.3±33.5 | 107.0±33.0 | 0.506 |
| High-density lipoprotein cholesterol, mean±SD, mg/dL | 51.1±12.2 | 50.7±12.0 | 0.012 |
| Triglycerides, mean±SD, mg/dL | 231.0±169.7 | 230.2±166.3 | 0.755 |
| Fasting plasma glucose, mean±SD, mg/dL | 122.0±43.9 | 121.5±43.1 | 0.468 |
| Uric acid, mean±SD, mg/dL | 5.2±1.4 | 5.2±1.5 | 0.009 |
| Estimated glomerular filtration rate, mean±SD, mL/min per 1.73 m$^2$§ | 95.4±13.4 | 95.0±13.1 | 0.048 |
| 10-y Risk for atherosclerotic cardiovascular disease, mean±SD, %‖ | 14.1±11.9 | 14.0±11.7 | 0.725 |

(*Continued*)

**Table 1. Continued**

| Characteristics | Intervention (N=9337) | Usual care (N=8739) | *P* value |
|---|---|---|---|
| No. of risk factor categories associated with MetS, n (%) | | | |
| 3 | 4878 (52.2) | 4531 (51.8) | 0.721 |
| 4 | 3305 (35.4) | 3143 (36.0) | |
| 5 | 1154 (12.4) | 1065 (12.2) | |

IQR indicates interquartile range; and MetS, metabolic syndrome.
*Moderate or heavy physical activity ≥30 minutes/time.
†Major cardiovascular disease includes myocardial infarction, stroke, and heart failure requiring hospitalization.
‡Self-reported chronic kidney disease is history of estimated glomerular filtration rate <60 mL/min per 1.73 $m^2$ at baseline.
§Estimated glomerular filtration rate was calculated on the basis of the 2021 Chronic Kidney Disease Epidemiology Collaboration creatinine equations.
‖Atherosclerotic cardiovascular disease risk was calculated on the basis of the American College of Cardiology/American Heart Association pooled cohort equations.

## Clinical Outcomes

Within the median 3.02-year follow-up, MACE was reported in 424 patients (1.58% per year) in the intervention group and 599 participants (2.42% per year) in the usual care group (HR, 0.65 [95% CI, 0.57–0.74]; *P*<0.001) (Table 2). Cumulative incidence of MACE over time in the 2 groups is shown in Figure 2. The intervention group also had a lower rate of myocardial infarction (HR, 0.70 [95% CI, 0.51–0.97]; *P*=0.034), stroke (HR, 0.64 [95% CI, 0.56–0.74]; *P*<0.001), death from cardiovascular causes (HR, 0.61 [95% CI, 0.47–0.78]; *P*<0.001), and death from all causes (HR, 0.82 [95% CI, 0.71–0.94]; *P*=0.005). After adjusting relevant covariates (age, sex, different provinces, smoking, history of CVD, estimated glomerular filtration, physical activity status, and educational level), protective effects were observed in all components of MACEs, including heart failure (HR, 0.61 [95% CI, 0.38–0.99]; *P*=0.043) (Table 2).

Lower MACE in the intervention group was observed in all subgroup analyses, including different sex (HR, 0.65 [95% CI, 0.54–0.79] for men and HR, 0.65 [95% CI, 0.55–0.76] for women), different age (HR, 0.62 [95% CI, 0.48–0.80] for age<60 years and HR, 0.67 [95% CI, 0.58–0.77] for age≥60 years), patients with history of CVD (HR, 0.72 [95% CI, 0.60–0.86]), patients without history of CVD (HR, 0.59 [95% CI, 0.50–0.69]), use of antihypertensive medication (HR, 0.63 [95% CI, 0.54–0.74] for treated and HR, 0.70 [95% CI, 0.56–0.87] for untreated), and number of risk factor categories associated with MetS (HR, 0.62 [95% CI, 0.52–0.75] for 3 risk factors, HR, 0.73 [95% CI, 0.59–0.86] for 4 risk factors, and HR, 0.61 [95% CI, 0.45–0.82] for 5 risk factors) (*P*<0.05 for all) (Figure S3). Detailed subgroup analysis on different combination of risk factor categories associated with MetS is also conducted (Table S2). In the sensitivity analysis with a treatment SBP <120 mm Hg, intensive treatment demonstrated a greater protective effect against both the primary (HR, 0.27 [95% CI, 0.20–0.38]; *P*<0.001) and other and secondary outcomes (Table S3).

## Safety and Renal Outcomes

The rate of hypotension was higher in the intervention group (1.6% versus 0.9%; risk ratio [RR], 1.69 [95%

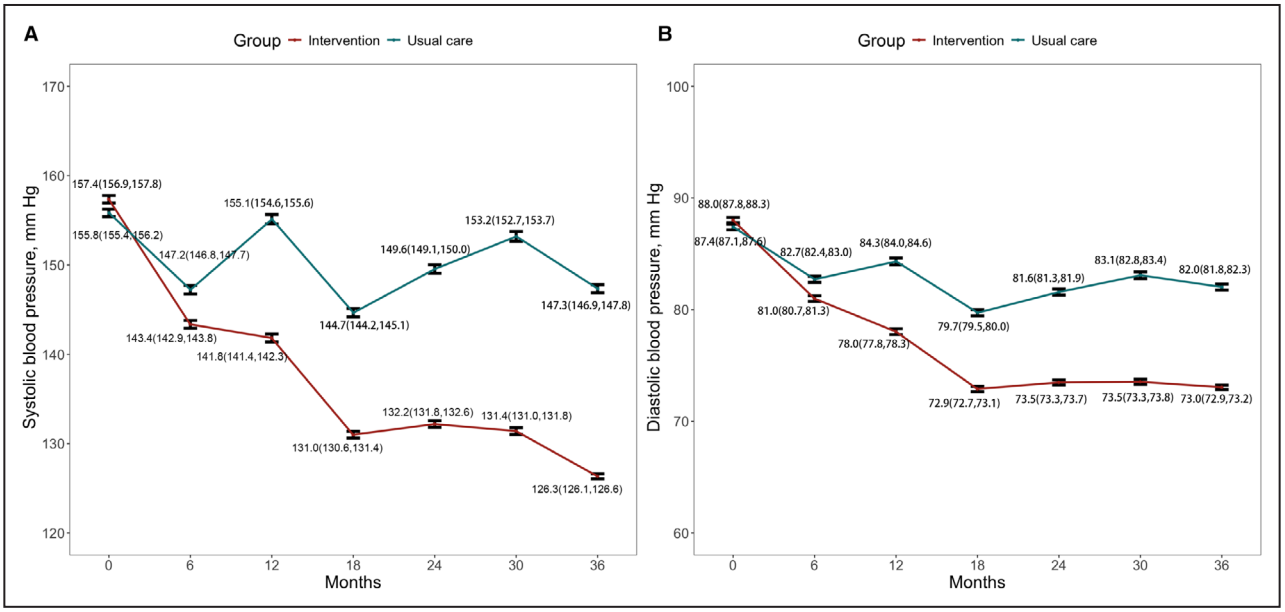


**Figure 1. Blood pressure during follow-up in participants with MetS.**
**A**, Systolic blood pressure (mm Hg) trends over 36 months in both groups. **B**, Diastolic blood pressure (mm Hg) trends over 36 months in both groups. Systolic blood pressure (**A**) and diastolic blood pressure change (**B**) of patients with MetS in intervention and usual care group. Error bars indicate 95% CIs. All *P* values for interactions between the intervention and follow-up time are <0.001. MetS indicates metabolic syndrome.

**Table 2. Effectiveness of Intervention Strategy on the Primary and Secondary Outcomes in Participants With MetS**

| Study outcomes | Intervention | | Usual care | | Hazard ratio (95% CI)* | *P* value | Multiple-adjusted hazard ratio (95% CI)*† | *P* value |
|---|---|---|---|---|---|---|---|---|
| | No. of events | Rate, % per year | No. of events | Rate, % per year | | | | |
| Primary outcome | | | | | | | | |
| Major adverse cardiovascular events | 424 | 1.58 | 599 | 2.42 | 0.65 (0.57–0.74) | <0.001 | 0.64 (0.56–0.73) | <0.001 |
| Secondary outcomes | | | | | | | | |
| Stroke | 329 | 1.22 | 472 | 1.90 | 0.64 (0.56–0.74) | <0.001 | 0.63 (0.54–0.73) | <0.001 |
| Myocardial infarction | 64 | 0.24 | 83 | 0.33 | 0.70 (0.51–0.97) | 0.034 | 0.71 (0.51–0.99) | 0.041 |
| Heart failure | 27 | 0.10 | 38 | 0.15 | 0.64 (0.40–1.02) | 0.061 | 0.61 (0.38–0.99) | 0.043 |
| Death from cardiovascular causes | 92 | 0.34 | 141 | 0.55 | 0.61 (0.47–0.78) | <0.001 | 0.60 (0.47–0.78) | <0.001 |
| Death from all causes | 315 | 1.16 | 363 | 1.42 | 0.82 (0.71–0.94) | 0.005 | 0.85 (0.74–0.97) | 0.018 |

MetS indicates metabolic syndrome.
*In the marginal Cox models, the village was used as a random effect.
†Additionally adjusted for age, sex, different provinces, smoking, history of cardiovascular disease, baseline estimated glomerular filtration rate, physical activity, and educational level.

CI, 1.28–2.24]; *P*<0.001) (Figure 3). The 2 groups did not differ in all other adverse events, including symptomatic hypotension (0.8% versus 0.8%; RR, 0.95 [95% CI, 0.67–1.34]; *P*=0.758), syncope (0.5% versus 0.4%; RR, 1.10 [95% CI, 0.70–1.74]; *P*=0.652), injurious falls (0.6% versus 0.5%; RR, 1.23 [95% CI, 0.81–1.88]; *P*=0.322), electrolyte disturbance, and renal function deterioration (Figure 3).

## DISCUSSION

The current study confirmed a lower rate of MACEs in the intervention group in patients with MetS. The risk reduction was 35%. The absolute reduction of yearly rate of MACEs was 0.84%. Reduced MACEs was apparent in all subgroups stratified by age, sex, different provinces, history of CVD, antihypertensive medication use, and number of risk factor categories associated with MetS. With the exception of higher hypotension, the 2 groups did not differ in all other adverse events, including symptomatic hypotension, syncope, injurious falls, and renal function deterioration. These results demonstrated that training nonphysician community health care professionals to implement intensive BP control could improve long-term outcomes in patients with hypertension and MetS. These results suggested that BP target of <130/80 mm Hg is appropriate for such a population. Furthermore, the result of the sensitivity analysis indicated that in this population, lowering the BP target to <120 mm Hg might be another optional choice.

The percentage of the patients with hypertension and MetS in the patients with hypertension enrolled in the CRHCP trial was 53.5% (18 076/33 771). With the development of economic society and improvement of living standards, the prevalence of MetS has steadily increased (eg, reaching 24.2% in mainland China as of 2014 and 34.7% in the United States as of 2016), emerging as a significant global public health concern.[11,20,21] Previous studies have shown that BP lowering is more difficult in people with MetS than in those without MetS.[7,8] In additions, MetS increased the risk of cardiovascular morbidity and mortality.[22] Therefore, BP management is essential for individuals with MetS.

The BP target in the CRHCP trial was 130/80 mm Hg as opposed to 120 mm Hg SBP in SPRINT.[23] Despite such a difference, the relative reduction of MACE risk in the intervention group in the current study (35%) was higher than that reported for intensive BP control by post hoc analysis of SPRINT in patients with MetS (25%).[10] However, the participants in SPRINT were without diabetes, and the trial did not measure waist circumference.[23] Our secondary analysis of CRHCP trial data had a larger sample size than SPRINT, which excluded patients with stroke and diabetes. We included these populations, thereby providing a valuable complement to SPRINT.

Given the complexity of MetS, we conducted subgroup analyses. The magnitude of MACE risk reduction was comparable between sexes, but greater in individuals aged <60 versus ≥60 years. This finding is consistent with the results for the overall population in the CRHCP trial.[20] Moreover, in our study, the benefits for individuals with a history of CVD were comparatively smaller than that observed in those without a history of CVD, implying the significance of prioritizing primary prevention for CVD among individuals with MetS. However, in SPRINT and the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial without analysis about patients with MetS, a history of CVD did not impact the outcomes of intensive BP control.[23,24] The benefits were even more pronounced in

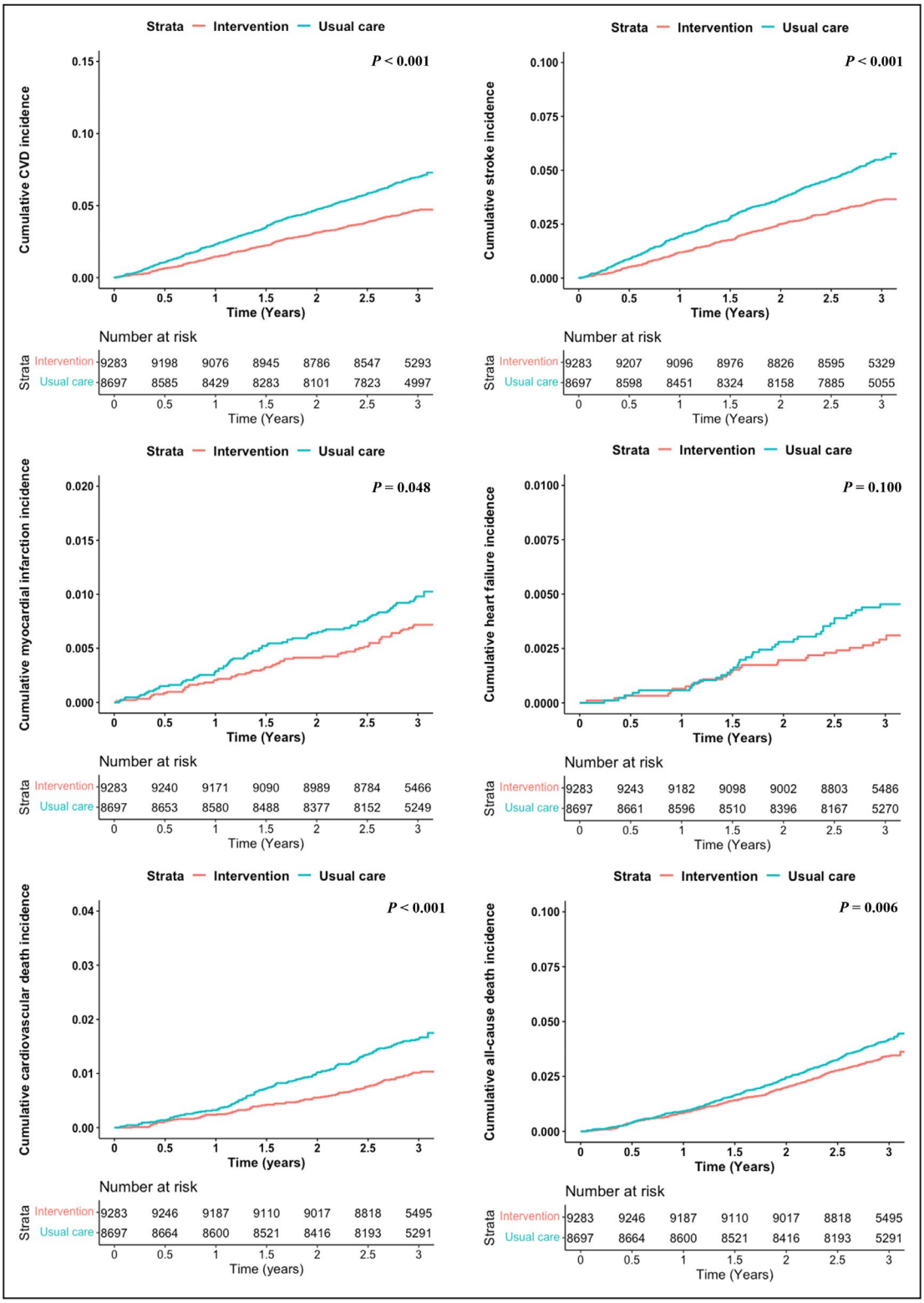


**Figure 2. Cumulative incidence of major adverse cardiovascular events and secondary outcomes in participants with metabolic syndrome.**
CVD indicates cardiovascular disease.

people who had previously taken hypertensive medications, suggesting that long-term treatment for MetS is needed. In addition, the benefits of intensive BP control strategy were most obvious in the population with MetS with 5 risk factors, which emphasizes the necessity of intensive BP control strategy in MetS.[23]

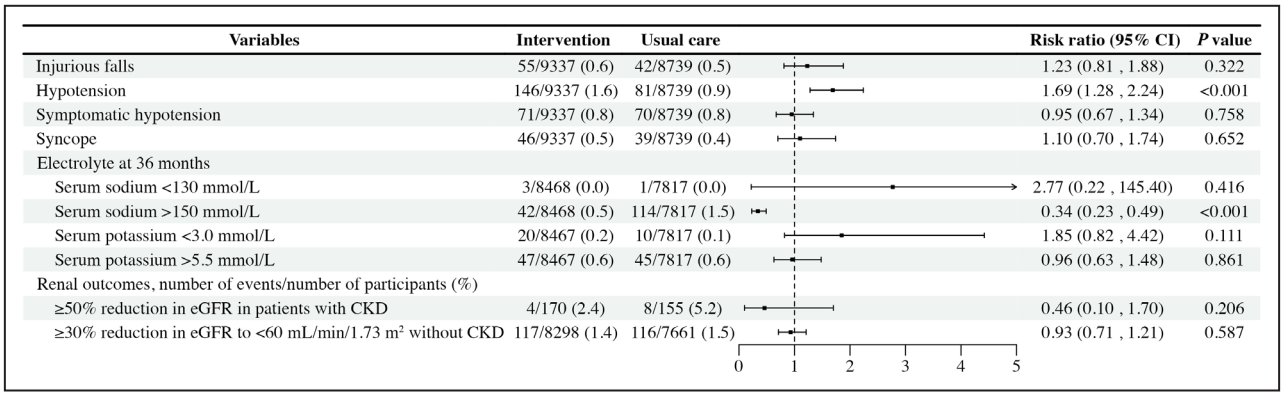


**Figure 3. Safety and renal outcomes by intervention in participants with metabolic syndrome.**
Injurious falls were self-reported and defined as a fall that resulted in seeking medical care. Hypotension was defined as systolic blood pressure <90 mm Hg at a village physician visit or a study data collection visit at months 6, 12, 18, 24, 30, and 36. Symptomatic hypotension was self-reported and confirmed by systolic blood pressure <90 mm Hg at a village physician visit. Syncope was defined as self-reported temporary loss of consciousness that resulted in seeking medical care. CKD indicates chronic kidney disease; and eGFR, estimated glomerular filtration rate.

Our findings demonstrated that the BP control strategy target with <130/80 mm Hg was both safe and effective for patients with MetS. We noted a significantly higher proportion of hypotension in the intervention group, but no significant differences between the 2 groups concerning symptomatic hypotension, injurious falls, or syncope. Furthermore, the rate of hypotension in patients with hypertension and MetS was lower than the results for the overall population in the CRHCP trial (1.6% versus 1.8%).[17] Previous studies have indicated that individuals with MetS were more prone to CVDs and renal damage.[25,26] Our study did not find such a correlation, but in SPRINT, there was a significant increase in the decreasing of kidney function in the intervention group.

This study has several limitations. First, this is a post hoc analysis of the CRHCP trial. Accordingly, the findings need to be verified by future studies. Second, all patients had hypertension at baseline, which, in turn, is a component of MetS. Third, kidney function and fasting plasma glucose and lipidemia were only examined at the end of the 3-year follow-up, and not at any time point during the follow-up period. Finally, at the end of the 3 years, the average blood pressure reported for each group was based on the participants who were still in the study at that time, excluding those who had died or were lost to follow-up, thus introducing bias. However, we believe that the extent of that bias would not change our conclusions.

## CONCLUSIONS

Training nonphysician community health care professionals to implement intensive BP control strategy (<130/80 mm Hg) reduced incident CVDs in patients with hypertension and MetS.

## ARTICLE INFORMATION

Received May 27, 2024; accepted November 22, 2024.

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### Acknowledgments

Conception and design: Yingxian Sun, Guozhe Sun, Xiaofan Guo, Guangxiao Li, Pengyu Zhang, and Yangzhi Yin. Analysis and interpretation of the data: Guozhe Sun, Pengyu Zhang, Chang Wang, Songyue Liu, and Ziyi Xie. Drafting of the article: Guozhe Sun, Xiaofan Guo, Lixia Qiao, Ning Ye, Danxi Geng, Wei Miao, Yao Yu, and Zhi Li. Critical revision of the article for important intellectual content: Yingxian Sun, Guozhe Sun, Xiaofan Guo, Pengyu Zhang, and Yangzhi Yin. Collection and assembly of data: Yangzhi Yin, Pengyu Zhang, Lixia Qiao, Danxi Geng, Wei Miao, Chang Wang, Songyue Liu, Xiaoqiong Jiang, and Xiangyu Tan. Writing and editorial assistance was provided by Kehong Zhang from Ivy Medical Editing in Shanghai, China.

### Sources of Funding

This work received support from the National Key Research and Development Program, Ministry of Science and Technology of China (grant number 2017YFC1307600).

### Disclosures

None.

### Supplemental Material

Tables S1–S3
Figures S1–S3

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