Original Article

Natural Variances in Blood Pressure Category among Chinese Adults

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Little is known about the natural progression and regression of blood pressure status, even though such knowledge would help determine the best intervention strategies. Our study aimed to explore natural changes in blood pressure status in a middle-aged Chinese population. A total of 6,129 Chinese men and women, aged 35 to 59 years at baseline, from the China Multi-center Collaborative Study of Cardiovascular Epidemiology, were reexamined 6 years later to determine the probability of progression (from non-hypertension to hypertension) and regression (from hypertension to non-hypertension). The majority (80%) of non-hypertensives among the respondents in this study remained normal or pre-hypertensive; about two-thirds of stage 1 hypertensives either stayed at the same stage or regressed to non-hypertension. However, only 9% of stage 2 hypertensives regressed to non-hypertension. Multi-variable logistic regression analysis showed that the stage 1 hypertension group had a 5-fold chance of regressing to non-hypertension in comparison with the stage 2 hypertension group (odds ratio [OR]=0.2, 95% confidence interval [CI]: 0.1–0.3), whereas the pre-hypertension group had a 4-fold likelihood of progressing to hypertension compared with normotensive subjects (OR=4.4, 95% CI: 3.7–5.3). After excluding participants ever on drug treatment in either examinations, the OR of regression for stage 2 hypertension was over twice that for stage 1 hypertension (OR=0.5, 95% CI: 0.3–0.7), and the possibility of progression decreased, though very slightly (OR=4.3, 95% CI: 3.6–5.1). Weight change significantly influenced progression and regression. Alcohol drinking affected progression significantly. In conclusion, the present findings support the strategy of intensively treating stage 2 hypertension and moderately treating stage 1 hypertension. Persons with pre-hypertension should be monitored for progression and advice on lifestyle modifications should be used. (*Hypertens Res* 2008; 31: 905–911)

***Key Words*: blood pressure, natural changes, hypertension, intervention, Chinese**

Introduction

High blood pressure is one of the leading causes of the global burden of disease, most of which occurs in developing countries (*1*). Control of hypertension should be an important strategy for reducing the incidence of premature death (*2*). However, recently issued guidelines, such as the VIIth Report of the Joint National Committee (JNC) (*3*) and the European Society of Cardiology and European Society of Hypertension Guidelines (*4*), have generated widespread and continuing controversy about the classification of blood pressure levels and corresponding strategies for intervention. An understanding of the natural variance of blood pressure over time in individuals, its progression into clinical hypertension, and its regression to normal levels would aid in formulating strate-

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gies for identification, evaluation, intervention (treatment and prevention), and follow-up. But there is little evidence that is directly toward such an understanding, and all studies reported thus far have studied only blood pressure progression (*5–11*). In the present paper, we analyzed the natural changes in blood pressure status, either progression from normal and pre-hypertension to hypertension or regression from stage 1 or 2 hypertension to non-hypertension, in a middle-aged Chinese population, in order to provide evidence from a different angle for the formulation of intervention strategies.

Methods

Participants and Methods

The China Multi-center Collaborative Study of Cardiovascular Epidemiology (China MUCA) was initiated in 1982 and included 3 major components: population disease surveillance of cardiovascular disease morbidity and mortality, population sampling surveys of cardiovascular disease risk factors, and cohort reexamination of cardiovascular outcomes to identify the major risk factors among Chinese. The design and survey methods of this study have been described in detail previously (*12*, *13*). In 1998, the fourth survey of cardiovascular risk factors was conducted in 14 populations selected on the basis of geographical location and urbanization. One-thousand participants (500 men and 500 women, 35–59 years of age) were drawn from each population using cluster random sampling. A total of 15,395 participants took part in the survey. The response rate was 85%. In 2004, the same method was applied to conduct the fifth survey of cardiovascular risk factors. Participants in 10 of the 14 study populations were invited to come back for a reexamination. The other 4 populations could not be included in the reexamination, due to funding constraints and the retirement of local investigators, thus reducing the total number of participants who could be invited for reexamination to 10,439. A total of 6,129 participants took part in the reexamination; the revisit rate was 58.7%. In the present study, we analyzed data from only those participants who took part in both surveys.

We used international standard methods (*12*, *14*) and followed a common protocol at both baseline and reexamination. Key investigators from each local center, including trainers, quality control persons, and data input technicians, were trained and certified centrally according to a uniform protocol and operation manual. All staff were trained by the trainers and certified within 2 weeks before data collection.

The surveys were approved by the Ethics Committee of the Cardiovascular Institute and Fu Wai Hospital, Beijing. All participants were provided a written description of the study, and in turn provided their informed consent at both baseline and reexamination.

Measurement and Classification of Blood Pressure

Blood pressure was measured between 8:00 and 11:00 AM by trained investigators using standard mercury sphygmomanometers at each local center at baseline and reexamination, both of which were conducted in the autumn. Three cuffs were used according to the participant's upper arm circumference, at least 80% which the bladder must cover but without any overlap. The cuff sizes were the standard, 12×26 cm; large, 14×40 cm; and small, 12×18 cm. The sphygmomanometer was kept at heart level during measurement. Three blood pressure measurements were obtained with the participant in the seated position after 5 min of rest. All participants were asked to take off heavy coats and were advised to avoid cigarettes, alcohol, caffeinated beverages, and physical exercise for at least 30 min before measurement. The average of these three readings was used for placement of participants into blood pressure categories: normal (systolic blood pressure [SBP] <120 mmHg and diastolic blood pressure [DBP] <80 mmHg), pre-hypertension (SBP 120–139 mmHg and/or DBP 80–89 mmHg), stage 1 hypertension (SBP 140–159 mmHg and/or DBP 90–99 mmHg), and stage 2 hypertension (SBP ≥160 mmHg and/or DBP ≥100 mmHg), according to JNC 7 (*3*). If SBP and DBP readings belonged to different categories, the participant was placed in the higher category. Further, if the participants were taking medication at baseline or reexamination, the BP category was upgraded by one, as follows: stage 2 hypertension stayed in the same rank, stage 1 hypertension moved to stage 2, and the rest moved to stage 1. The same method was applied to baseline and reexamination. If the participants were not taking medication during either survey, the BP category was unchanged, *i.e.*, they remained the JNC 7 categories.

Other Measurements

Height and weight were measured without heavy clothing and shoes. Height was measured to an accuracy of 0.5 cm by a fixed vertical ruler with the participant standing straight up, and weight was measured to an accuracy of 0.1 kg with the use of a spring balance calibrated daily with standard weights. Body mass index (BMI) was calculated as weight in kg divided by height square m (kg/m^2). Weight change was defined by the difference between baseline weight and weight at reexamination 6 years later. Weight change was classified into 3 categories: loss (<-2 kg), maintenance (-2 to 2 kg) and gain (≥2 kg). Alcohol drinking was defined as drinking at least once per week, and this information was collected on a questionnaire during the interviews. Smoking was defined as smoking at least one cigarette a day for at least 1 year continuously. Exercise was defined as exercising at least three times per week.

Table 1. Characteristics of Subjects

Variables	Reexamination				All in reexamination	Lost to reexamination
	Use of med. at baseline	Use of med. at reexamination	Use of med. at both examination	Without med. at either examination		
n	51	593	220	5,265	6,129	4,310
Female (%)	64.7	59.0	59.1	54.0	54.8	48.6*
Baseline						
Age (years)	51.0±5.8	49.6±6.7	51.1±6.3	46.5±7.0$	47.0±7.0	46.59±7.45*
SBP (mmHg)	140.9±18.5	144.6±22.2	152.8±21.2	119.0±15.7$	122.9±19.3	122.3±19.5
DBP (mmHg)	87.8±9.3	89.6±12.4	93.6±11.3	75.6±10.2$	77.7±11.7	77.8±12.0
Weight (kg)	66.8±12.5	63.6±11.0	67.9±10.5	58.5±10.3$	59.4±10.7	59.8±10.4
BMI (kg/m^2)	26.1±3.7	24.7±3.5	26.2±3.6	22.8±3.2$	23.1±3.4	22.9±3.3*
Alcohol drinking %	17.6	21.9	12.3	25.5$	24.6	24.3
Smoking %	25.0	30.4	32.3	33.9	33.4	39.7
Exercise %	56.9	39.8	56.8	28.4	30.7	37.5
BP category (%)						
Normal	—	10.1	—	49.8	43.7	43.8
Pre-HT	—	24.6	—	36.2	33.4	34.6
Stage 1 HT	41.2	33.7	20.9	11.1	13.9	13.7
Stage 2 HT	58.8	31.5	79.1	2.9$	8.9	8.0
Reexamination						
SBP (mmHg)	144.5±25.2	145.9±20.0	149.4±23.4#	123.6±17.7#	126.9±20.0#	—
DBP (mmHg)	85.8±13.0	87.8±11.6#	88.0±11.1#	78.5±10.6#	79.8±11.3#	—
Weight (kg)	65.0±13.7	65.4±11.2#	67.7±11.0	59.6±10.9#	60.5±11.1#	—
BMI (kg/m^2)	25.5±4.3	25.5±3.6#	26.2±3.5	23.2±3.4#	23.6±3.5#	—
Alcohol drinking %	17.6	24.6#	18.6#	28.0#	27.3#	—
Smoking %	25.5	29.5	30.5	34.4	33.7	—
Exercise %	55.8	39.6	57.2	29.5	31.8	—
BP category (%)						—
Normal	17.6	—	—	38.2	33.0	—
Pre-HT	21.6	—	—	39.8	34.3	—
Stage 1 HT	35.3	33.4	32.3	16.3	18.7	—
Stage 2 HT	25.5	66.6#	67.7#	5.7#	14.0#	—

med, medication; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; BP, blood pressure; Normal, normal BP; Pre-HT, pre-hypertension; Stage 1 HT, stage 1 hypertension; Stage 2 HT, stage 2 hypertension. *$p<0.05$, comparison with all participants in reexamination. $$p<0.05$, comparison with participants with medication use. #$p<0.05$, comparison with baseline data.

Statistical Methods

All data were entered twice into a computer by two persons at local centers using centrally provided software. The diskettes were then shipped to a coordinating center for further data management and statistical analysis. We constructed transition matrices in which each participant's blood pressure category at the reexamination was cross-tabulated by his or her blood pressure category at baseline to evaluate the possibility of progression to a higher category or regression to a lower one for men and women separately, after adjustment for age. To further estimate the odds of progression and regression, we combined men and women and adjusted for age in corresponding models.

In this paper, we defined progression as a change in blood pressure status from normal or pre-hypertension to hypertension, and regression as a change from stage 1 or 2 hypertension to non-hypertension. We used logistic regression analysis to model the risk of progression in pre-hypertension in comparison with normal blood pressure, as well as the probability of regression in stage 2 hypertension in comparison with stage 1 hypertension, adjusting for sex, age, and baseline BMI and alcohol drinking. The effects of changes in weight and alcohol drinking on progression and regression were analyzed using the same model. The Mantel-Haenszel test for linear trends was used to observe the trends among weight loss, maintenance, and gain groups.

To understand the possible effects of medication use on our findings, we did the same analyses separately in all study participants and in those without medication use at both surveys, as a test of sensitivity.

All analysis was performed with the SPSS 11.5 statistical

Table 2. Changes in Blood Pressure Category on Follow-Up According to Baseline Blood Pressure Category after Adjustment for Age and Its Transition by Sex (%)

Blood pressure categories at baseline	Blood pressure categories at follow-up									
	Participants with no medication use (n=5,265)					All participants (n=6,129)				
	n	Normal	Pre-HT	Stage 1 HT	Stage 2 HT	n	Normal	Pre-HT	Stage 1 HT	Stage 2 HT
Male										
Normal	1,095	51.6	40.1	7.5	0.8	1,114	50.7	39.4	8.5	1.3
				8.3					9.8	
Pre-HT	902	21.4	49.8	23.1	5.7	954	20.2	47.1	24.1	8.6
				28.8					32.7	
Stage 1 HT	331	5.4	36.6	33.8	24.2	436	4.6	28.0	34.2	33.3
		42.0					32.6			
Stage 2 HT	92	2.2	18.5	34.8	44.6	267	1.5	7.1	27.7	63.7
		20.7					8.6			
Female										
Normal	1,526	60.7	33.4	5.4	0.5	1,567	59.1	32.5	6.6	1.8
				5.9					8.4	
Pre-HT	1,002	28.7	46.3	20.9	4.1	1,096	26.3	42.3	21.9	9.5
				25.0					31.4	
Stage 1 HT	256	7.4	30.9	42.2	19.5	418	4.8	20.3	40.2	34.7
		38.3					25.1			
Stage 2 HT	61	3.3	26.2	37.7	32.8	277	2.2	6.5	30.7	60.6
		29.5					8.7			
Total										
Normal	2,621	56.9	36.2	6.3	0.6	2,681	55.6	35.4	7.4	1.6
				6.9					9.0	
Pre-HT	1,904	25.2	48.0	22.0	4.8	2,050	23.5	44.5	22.9	9.1
				26.8					32.0	
Stage 1 HT	587	6.3	34.1	37.5	22.1	854	4.7	24.2	37.1	34.0
		40.4					28.9			
Stage 2 HT	153	2.6	21.6	35.9	39.9	544	1.8	6.8	29.2	62.1
		24.1					8.6			

Normal, normal blood pressure; Pre-HT, pre-hypertension; Stage 1 HT, stage 1 hypertension; Stage 2 HT, stage 2 hypertension.

software package (SPSS, Chicago, USA).

Results

Characteristics of Participants

A total of 864 participants took antihypertensive drugs in the 2 weeks prior to the baseline examination and/or the reexamination, including 51 only at baseline, 593 only at reexamination, and 220 at both. The characteristics of the participants at baseline and reexamination are shown in Table 1, by status of antihypertension medication use and whether or not reexamination occurred. There were no differences between participants who underwent reexamination and those who did not, with regard to SBP, DBP, body weight, and prevalence of hypertension, alcohol drinking, cigarette smoking, and exercise. However, participants in the reexamination had a higher mean age and BMI, and a higher proportion were women. In comparison with those having used medication, participants without medication use were significantly younger and had lower SBP, DBP, body weight, BMI, prevalence of hypertension, and prevalence of alcohol drinking and exercise. In comparison with data at baseline, data at reexamination showed an increase in SBP in all groups except those taking medication at both examinations, among whom mean SBP decreased significantly during the 6 years. DBP decreased in all groups except for those not taking medication at both examinations. Among those taking medication only at baseline, 39.2% had blood pressure below 140/90 mmHg; among those taking medication at both examinations, the proportion of stage 2 hypertension decreased significantly, from about 80% to 67%; however, the prevalence of hypertension increased significantly for those not taking medication at either examination. BMI and alcohol drinking varied little between the examinations.

Progression from Normal and Pre-Hypertension to Hypertension in All Participants

Among all participants, including those taking medication at either examination, the probability of progression to hypertension 6 years later was only 9% for those with normal blood pressure at baseline and 32% for those with pre-hypertension; the majority remained normal or pre-hypertensive (Table 2). There was no significant difference between men and women ($p>0.05$).

In comparison with those with normal blood pressure at baseline, those with pre-hypertension had 4.9-fold the risk of

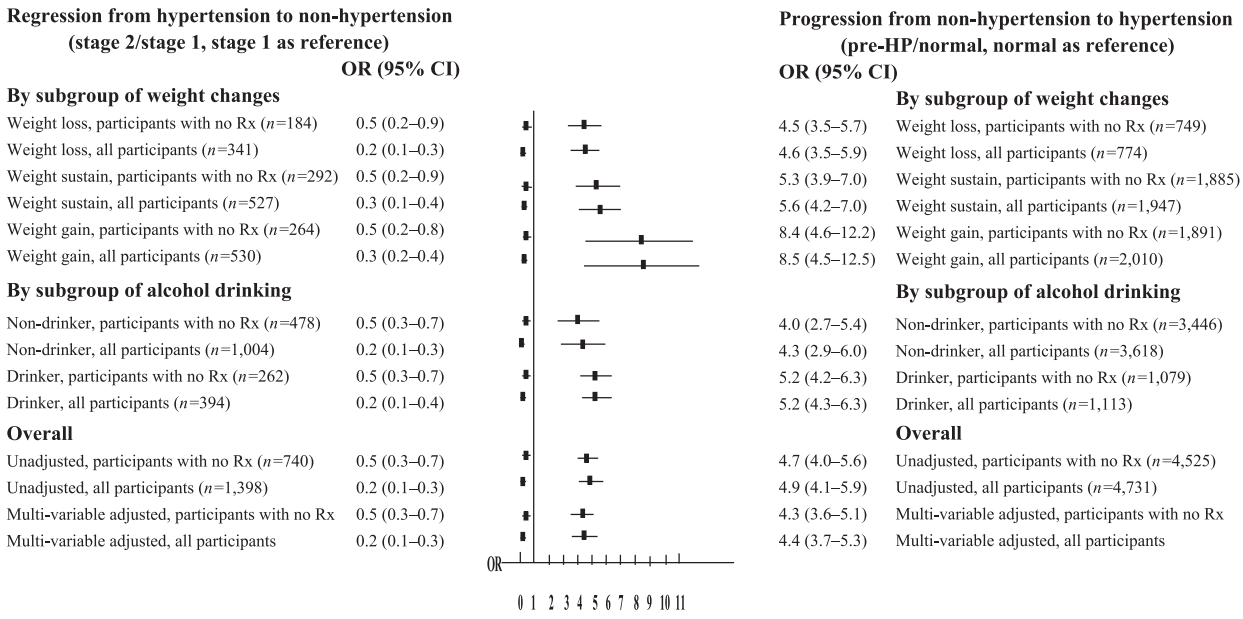

Fig. 1. *ORs and 95% confidence intervals for the probability of regression from hypertension to non-hypertension and of progression from non-hypertension to hypertension in the studied Chinese population.*

becoming hypertensive in the subsequent 6 years (odds ratio [OR]=4.9; 95% confidence interval [CI]: 4.1–5.9). Multiple logistic regression analysis adjusting for baseline age, sex, BMI, alcohol drinking, and changes in BMI and alcohol drinking showed a slightly lower OR (OR=4.4; 95% CI: 3.7–5.3).

Regression from Stage 1 and Stage 2 Hypertension to Non-Hypertension in All Participants

For the stage 1 hypertension group, the majority either remained at stage 1 (37%) or regressed to a lower category (29%), and about one-third progressed to stage 2 hypertension 6 years later. For the stage 2 hypertension group, the majority (about 91%) stayed as hypertensive (either stage 2 or stage 1), and less than 10% regressed to non-hypertension. However, the possibility of regression to non-hypertension was higher for women than men ($p<0.05$) (Table 2).

Compared with stage 1 hypertension, the OR of regression to non-hypertension from stage 2 hypertension was only 0.2 (95% CI: 0.1–0.3). Multiple logistic regression analysis adjusting for age, sex, BMI, alcohol drinking, and changes in BMI and alcohol drinking did not change the OR at all (Fig. 1).

Effects of Weight Loss on Progression and Regression

The percentage of progression varied by weight change status (data not shown), and the multi-variable adjusted ORs of progression were 8.5, 5.6, and 4.6 ($p<0.05$ for linear trend) whereas those of regression were 0.2, 0.3, and 0.3 ($p<0.05$ for linear trend) in the weight gain, maintenance, and loss groups, respectively (Fig. 1).

Effects of Change in Alcohol Drinking on Progression and Regression

The percentage of progression varies by alcohol drinking status (data not shown). The multi-variable adjusted ORs of progression were 5.2 and 4.3 in drinkers and nondrinkers ($p<0.05$), but those of regression were not significantly different between drinkers (OR=0.2) and nondrinkers (OR=0.2) ($p>0.05$) (Fig. 1).

Test of Sensitivity

Exclusion of participants receiving drug treatment at either examination lowered the progression rate slightly. However, 40.4% regressed to non-hypertension for stage 1 hypertension and about 24% for stage 2 hypertension, instead of 28.9% and 8.6%, respectively, for all participants (Table 2). Similar trends were found when unadjusted and adjusted ORs were computed. In fact, the ORs of regression doubled in all analyses after we excluded participants taking medication (Fig. 1).

Discussion

As in most populations in the world, in this Chinese population blood pressure increased over time as the population aged, where SBP increased 4 mmHg and DBP increased 2 mmHg on average over 6 years. However, the risk of progression to hypertension and the probability of regression to non-

hypertension both differed by baseline blood pressure level. This phenomenon may help elucidate the needs of different strategies in the prevention and control of hypertension according to blood pressure level.

In this study, only 9% of participants with normal blood pressure at baseline progressed to hypertension 6 years later. In comparison, the risk of progression for those with pre-hypertension was more than 4-fold higher, although the majority remained non-hypertensive. On the other hand, only 9% of participants with stage 2 regressed to non-hypertension. In comparison, the probability of regression for those with stage 1 was about 5-fold, although a majority remained at stage 1 or progressed to stage 2. These findings support the strategy of intensively treating stage 2 and moderately treating stage 1. Persons with pre-hypertension should be monitored for progression and advice on lifestyle modification may need to be given to these persons.

It is anticipated that analysis excluding participants with drug treatment may underestimate the risk of progression and overestimate the probability of regression. However, our study showed that excluding those with drug treatment slightly affected the risk of progression and dramatically affected the probability of regression. This was due simply to the very large number of non-hypertensive participants as a denominator for the risk of progression and to the relatively small number of hypertensives as a denominator for the probability of regression, while all drug users were defined as hypertensives. Because the aim of this paper was to define appropriate intervention strategies, which are assumed to be initiated for new cases that should not have been taking any medication, we believe data from those without medication better reflected the true probability of regression. If so, the probability of regression in stage 1 hypertension was actually only twice that for stage 2 hypertension, rather than 5 times. This suggests that intervention at stage 1 should be much more intensive than that for pre-hypertension.

Our findings that most participants with pre-hypertension either remained at the same rank (44.5%) or remitted to normal blood pressure (23.5%) (leaving 32% who developed hypertension) are quite similar to the results of previous reports in Asians (*9*, *10*), but are not compatible with findings on North American and European populations (*6*, *7*, *11*), in which a higher rate of progression to hypertension and a lower rate of remaining at high normal blood pressure were reported. The difference between Asians and North Americans/Europeans may result from higher BMI in the latter than in the former. This hypothesis is supported at least partly by our findings that participants who gained weight during the 6 years between examinations had a much higher probability of progression than those who had lost or maintained weight.

In addition, we found alcohol drinking increased the probability of progression to hypertension. This, plus the findings on the effects of weight loss on progression and regression, suggested that lifestyle modifications should been initiated, although drug treatment could prevent or delay the onset of hypertension in pre-hypertensive participants (*15*). The clinical effects of therapeutic lifestyle changes are definitive in reducing blood pressure (*16–18*), and are the same as medication. Clinically significant long-term reductions in blood pressure and reduced risk for hypertension can be achieved with even modest weight loss (*19*). Combinations of two (or more) lifestyle modifications can achieve even better results (*20*). Failure to prescribe lifestyle modifications may result in inadequate blood pressure control (*3*).

Until now, few studies (*6*, *11*) have explored the regression of hypertension, and none of them have differentiated stage 1 hypertension from stage 2. In the present study, we found that a majority of hypertensive participants (stages 1 and 2) still had hypertension 6 years later. Furthermore, stage 1 participants had about twice the probability of regression to non-hypertension than stage 2 participants, after exclusion of the participants taking medication. This suggested we should treat stage 1 and stage 2 with different strategies. It has been reported that patients with mild hypertension often would withdraw from a regimen not because of immediate, severe side effects, but because of the accumulation of low-grade quality of life effects over time (*21*). Weight loss increased the possibility of regression to non-hypertension in stage 1 participants by about 40% 6 years later in our study. Therefore, patients at low and medium risk (stage 1) should be followed up, and nonpharmacological treatment should be adequately given. Pharmaceutical treatment should only follow after that. Very few individuals with stage 2 hypertension regressed to non-hypertension without any treatment during the 6 years. Thus, active drug treatment should be initiated once it has been identified.

The major limitation of this study is the lower response rate for reexamination. However, this should not induce significant bias on our findings, since there was no significant difference in baseline SBP, DBP, or prevalence of hypertension between responders and non-responders. A second limitation is that occasional blood pressure was used in our analysis. This may induce misclassification to some extent because of hour-to-hour and day-to-day variations in blood pressure. Such misclassification could not be totally eliminated in our study, although we used a standard procedure for blood pressure measurement and the average of 3 readings. A better study with multiple blood pressure measurements on different days—or, better, weeks—should be done to eliminate this kind of misclassification. Lastly, the effect of antihypertensive medication use on blood pressure may induce misclassification too. To minimize the influence, the categories of blood pressure were upgraded by a category in our analysis if the participants were taking medication. Moreover, we repeated all analyses in participants not taking medication in order to test the sensitivity of our findings on medication use. The results suggested that medication use had little effect on progression but a significant effect on regression. However, we believe that data on regression in participants not taking medication are more real. In addition, although the duration

of the current study was relatively short (6 years), the sample size (n=6,129) was large enough to reliably test blood pressure changes.

To summarize, our findings clearly showed that a majority of participants among respondents of this study remained in their original blood pressure category, although progression and regression also took place. Weight loss and avoiding alcohol could help to reduce the risk of progression and increase the probability of regression. These results were similar in all participants and in participants without medication use. The present study provided additional evidence for determining appropriate intervention strategies in hypertension prevention and control.

Appendix

The local principal investigators of the China Multi-center Collaborative Study of Cardiovascular Epidemiology were as follows: Xiao-Qing Liu, Guangdong Provincial Cardiovascular Institute, Guangdong Province; Xiu-Zhen Tian, Shijingshan Institute of Chronic Disease Prevention, Beijing; Li-Min Liu, Zhejiang Medical University, Zhejiang Province; Lian-Sheng Ruan, Putuo Health Bureau, Zhoushan, Zhejiang Province; Hai-Yan Wang, Jiangsu Provincial People's Hospital, Jiangsu Province; Li-Guang Zhu, Guangxi Medical University, Guangxi Province; Dong-Shuang Guo, Yuxian People's Hospital, Shanxi Province; Jun Yang, Hanzhong Cardiovascular Institute, Shaanxi Province; Ying-ru Gou, Huaxi Hospital, Sichuan Province; Jian-min Li, Mudanjiang Institute of Medical Sciences, Heilongjiag Province.

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