ORIGINAL ARTICLE

Hypertension Control in Community Health Centers Across China: Analysis of Antihypertensive Drug Treatment Patterns

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BACKGROUND
Blood pressure (BP) control in China is generally poor. It is assumed that an important cause of this unsatisfactory situation is the present standard of care provided by primary care physicians.

METHODS
One thousand community health centers (CHCs) were selected across China based on geographical location, previous cooperative experience, and acceptance of an invitation to implement a standardized protocol of community-based BP management. Baseline information for each hypertensive patient under the care of these CHCs was collected, and the present pattern of hypertensive drug treatment was analyzed.

RESULTS
Of all identified hypertensive patients (n = 249,830), 37% were treated with drugs. Characteristics linked with hypertension treatment included systolic BP, age, sex, region, smoking and alcohol consumption status, body mass index, comorbidities, and family history. The most frequently prescribed classes of antihypertensive drugs were diuretics (56.0%), followed by centrally active drugs (CADs) (38.3%), calcium channel blockers (CCBs) (36.8%), vasodilators (26.5%), and angiotensin-converting enzyme inhibitors (ACEIs) (23.3%). In regards to drug combination patterns, diuretics plus CADs was the most frequently used 2-drug combination (61.4%) and vasodilators plus CADs plus diuretics was the most frequently used 3-drug therapy (69.2%). Seventy-seven percent of patients on combination therapy were prescribed single pill combinations, 87.2% of which were composed of CADs and vasodilators and 12.8% of which were composed of ACEIs and diuretics. The control rates of patients on monotherapy and combination therapy were 27.7% and 24.1% ($P < 0.05$), respectively.

CONCLUSIONS
Our study identified major shortcomings in the present status of antihypertensive pharmacotherapy in routine medical practice in China. It is essential to implement a program of professional education regarding the appropriate use of antihypertensive drugs.

Keywords: antihypertensive medication; blood pressure; China; community; hypertension.

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Hypertension (HTN) represents a major therapeutic challenge to healthcare systems worldwide; it affects almost 1 billion people and is estimated to be the cause of approximately 7.5 million deaths per year.[1–3] The prevalence of HTN is expected to increase from 26.4% in 2000 to 29.2% in 2025.[4] In most countries, many hypertensive individuals are not aware of their condition, and among those who are aware, many are either not treated or are treated but not controlled.[5,6] Although various pharmacological and nonpharmacological treatment options exist, blood pressure (BP) control is suboptimal, particularly in low- and middle-income countries.

In China, high BP is the leading risk factor for cardiovascular disease (CVD).[7] Data from 4 large-scale surveys on HTN in China showed that the prevalence of HTN is rising continuously.[8] Currently, it is estimated that there are 153 million patients with HTN in China, and the rates of awareness, treatment, and control are 25%, 20%, and 4%, respectively.[9] The direct medical cost due to HTN is 5.7 billion US dollars per year, and the yearly medical cost of CVD that is closely related to HTN is as high as 20.6 billion US dollars.[7]

The reason for poor control of HTN is complex and relates to healthcare system characteristics, healthcare providers skills, and patients adherence to therapy.[10] Primary care physicians' attitudes and practice patterns (recognition, treatment, and management) have received increased attention as determinants of BP control.[11,12] There has been a marked increase in the number of prescriptions for antihypertensive

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drugs and the use of multiple antihypertensive medications.[13,14] Similar increases in the use of antihypertensive drugs have been noted in longitudinal national surveys.[15,16]

To the best of our knowledge, no data have been published on drug use and associated BP control in community-based routine practice in China.

In this study, we assessed the present pattern of antihypertensive drug therapy and level of HTN control by analyzing relevant information provided to us by cooperating community health centers (CHCs) across China.[17]

METHODS

Project design

The Project of Hypertension Control in CHCs was a government-funded program aimed to improve the control rate of HTN in CHCs across China. For this project, a Coordinating Center was established at Fuwai Hospital, Beijing. A community-based standardized BP management protocol was developed in 2007 based on the 2005 Chinese Hypertension League guidelines,[7] which were similar to the 2003 World Health Organization/ International Society of Hypertension guidelines[18] with respect to classification of BP, stratification of global risk, and the principles of treatment. One thousand CHCs were recruited to test the feasibility of this protocol in a primary care setting and its effect on HTN control. CHCs were selected based on the following: (i) geographical location, to ensure that various areas of China would be covered; (ii) previous cooperation with our group at the Fuwai Hospital; and (iii) acceptance of the invitation to participate in the present project. Primary care physicians from these CHCs were trained by the Coordinating Center.

Patients

Patients with diagnosed HTN who were aged 18–79 years were recruited by the physicians in the cooperating CHCs to participate in this project. The following exclusion criteria were applied: (i) diagnosis of secondary HTN; (ii) diagnosis of acute coronary syndrome and/or stroke (<3 months after onset); (iii) mental disease, hearing difficulty, physical incapacitation, or uncooperative behavior; and (iv) life expectancy of <1 year.

Written informed consent for the baseline survey was required from each participant. Institutional ethics review board approval was obtained at the Coordinating Center, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the International Conference on Harmonization of Good Clinical Practice.

Data collection

Data on demographics, cardiovascular risk profile, comorbidities, BP, and antihypertensive drug usage were collected using a case report form designed by the Coordinating Center (see Supplementary Appendix 1).

In this study, the prescription information on antihypertensive drugs was analyzed for each patient. Medications were classified as diuretic (DIU), beta-blocker (BB), alpha-blocker, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), AT1 receptor blocker (ARB), centrally acting drugs (CADs, such as reserpine, clonidine), vasodilators (VASOs, such as dihydralazine, dibazole, pargyline), and Chinese traditional medicine (CTM). Single-pill combinations (SPCs), which normally contain ≥2 active ingredients (see Supplementary Appendix 2), were separated into their generic components. Each medication was classified into only 1 category. Respondents who used only 1 drug were defined as receiving monotherapy; those using ≥2 drugs were defined as combination therapy.

BP was measured on the right arm in a seated position and after 5 minutes of rest in all participants during the clinic visit using a mercury sphygmomanometer. The mean of 2 measurements was used for analysis. HTN was defined as systolic BP ≥140 mm Hg, and/or diastolic BP ≥90 mm Hg, and/or use of antihypertensive drug. Respondents smoking at least 1 cigarette per day were classified as smokers. Drinking was defined as having alcoholic beverages at least once a week. Self-reported diabetes, coronary heart disease, stroke, and renal disease were recorded as associated clinical conditions (ACCs). Family history of CVD, such as HTN, diabetes, coronary heart disease, and stroke among first-degree relatives, was also noted.

Statistical analysis

Data from each local center were recorded in uniform record forms and submitted to the Coordinating Center by trained staff using an online data entry system. The data were analyzed centrally at the Fuwai Hospital in Beijing. All statistical analyses were performed with SPSS software version 15.0 (SPSS, Chicago, IL). Continuous variables were expressed as means (SD), and categorical variables were expressed as counts (percentages). Z tests were used for continuous data, and χ^2 tests were used to compare the categorical variables. All statistical tests were 2-tailed, and $P < 0.05$ was considered statistically significant.

RESULTS

From March 2007 to December 2010, a total of 255,168 hypertensive patients were enrolled from 8 provinces in China: Hebei, Guangdong, Zhejiang, Gansu, Jiangsu, Beijing, Qinghai, and Shandong. From this sample, 249,830 patients were eligible for analysis, of which 48.3% of respondents were men and their mean age was 61.0 ± 10.5 years. With respect to treatment, 92,325 (37%) respondents from the study sample were treated with antihypertensive drugs (Table 1). Age, systolic BP, and urban residence, as well as proportions of smoking, drinking, obesity, ACC, and family history, were higher among treated patients with HTN ($P < 0.05$).

Overall, 27% of patients with HTN had their BP controlled (Table 2). The control rate of BP was higher among patients who were elderly, female, or living in urban area ($P < 0.05$). On the other hand, smoking, drinking, and higher body mass index were associated with lower BP control rate, whereas patients with positive family history and ACCs had a higher BP control rate.

Table 1. Characteristics of untreated and treated patients with hypertension in community health centers in China

Variables	Untreated (n = 157,505)	Treated (n = 92,325)	Total (n = 249,830)
Sex, male[a]	77,809 (49.4)	42,899 (46.5)	120,708 (48.3)
Age, y, mean (±SD)*	60.7 (10.6)	61.5 (10.3)	61.0 (10.5)
Age group, y*			
18–44	5,562 (3.5)	2,423 (2.6)	7,985 (3.2)
45–64	64,992 (41.3)	36,903 (40.0)	101,895 (40.8)
>64	86,951 (55.2)	52,999 (57.4)	139,950 (56.0)
SBP, mm Hg, mean (±SD)*	143 (16)	145 (17)	144 (17)
DBP, mm Hg, mean (±SD)	88 (10)	88 (11)	88 (10)
BP level, mm Hg*			
<140/90	43,987 (28.0)	23,470 (25.5)	67,457 (27.0)
141–159/91–99	73,587 (46.8)	41,714 (45.3)	115,301 (46.2)
160–179/100–109	30,711 (19.5)	19,932 (21.6)	50,643 (20.3)
≥180/110	9,023 (5.7)	7,066 (7.7)	16,089 (6.4)
Region*			
Rural area	109,931 (69.8)	54,556 (59.1)	164,487 (65.8)
Urban area	47,574 (30.2)	37,769 (40.9)	85,343 (34.2)
Smoking*	26,807 (17.0)	17,096 (18.5)	43,903 (17.6)
Drinking*	22,354 (14.2)	15,039 (16.3)	37,393 (15.0)
Obesity*	21,399 (13.6)	14,580 (15.8)	35,979 (14.4)
ACC*	20,258 (12.9)	17,460 (18.9)	37,718 (15.1)
Family history*	30,935 (19.6)	25,182 (27.3)	56,117 (22.5)

Data are presented as No. (%) unless otherwise indicated. Variations in numbers are because of missing data. Obesity was defined as a body mass index ≥28 kg/m^2, and family history was positive if cardiovascular disease history, such as hypertension, diabetes, coronary heart disease, and stroke among first-degree relatives, was reported.

Abbreviations: ACC, associated clinical condition, including self-reported diabetes, coronary heart disease, stroke, and renal disease; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

*Difference between untreated and treated groups significant at $P < 0.05$.

Overall, DIUs were the most frequently prescribed drugs, followed by CADs, CCBs, and VASOs. The proportions of prescriptions were 24.5% for ACEIs, 4.1% for ARBs, 10.4% for BBs, and 0.1% for alpha-blockers (Figure 1).

For patients on monotherapy, CCBs had the highest prescription rate, followed by ACEIs, DIUs, and BBs; no alpha blockers, CADs, or VASOs were prescribed (Figure 1). With respect to combination therapy, the most commonly prescribed 2-drug combination was DIUs+CADs; 2.6% of patients used ACEIs+BBs combination. VASOs+CADs+DIUs was the most frequent 3-drug combination. About 77% of patients on combination therapy were prescribed SPCs. As to the content of SPCs, 87.2% were composed of CADs, VASOs, and DIUs; 12.8% were composed of ACEIs and DIUs; and <1% were composed of others (Figure 2).

Overall, 36.5% of patients were on monotherapy, and 63.5% were on combination therapy, with corresponding HTN control rates of 27.7% and 24.1%, respectively ($P < 0.05$) (Table 3). Patients with controlled HTN were more often on monotherapy than on combination therapy ($P < 0.05$). The control rate was higher in women, the elderly, those living in urban areas, and those with self-reported ACCs ($P < 0.05$), whereas it was lower among those who smoked, consumed alcohol, had a body mass index ≥28 kg/m^2, and reported a positive family history.

DISCUSSION

Knowledge about the characteristics associated with hypertensive treatment and the present prescription pattern of antihypertensive drugs by primary care physicians helps to identify shortcomings in the treatment of hypertensive patients and facilitate the development of plans for improvement.

In this study, almost all patients recruited from CHCs were aware of their condition and had higher rates of treatment (37.3%) and control (27%) than those identified in a cross-sectional survey of the general population in 2002 (20% and 4%, respectively).[9] However, the control rate was lower than that from the survey on outpatients in tertiary hospitals in 2009 (30.6%).[19] This is expected because doctors in tertiary hospitals have more knowledge and experience in antihypertensive treatment and patients treated in these hospitals can usually afford the cost of diagnosis and treatment.

Table 2. Control rate for untreated and treated patients with hypertension by characteristics

	Untreated[a]		Treated		Total	
Subgroup	No.	%	No.	%	No.	%
Total	43,987	27.9*	23,470	25.4	67,457	27.0
Sex						
Male	20,010	25.7*	9,920	23.1	29,930	24.8
Female	23,977	30.1*	13,543	27.4	37,520	29.1
Age group, y						
18–44	990	17.8*	374	15.4	1,364	17.1
45–64	16,461	25.3*	8,538	23.1	24,999	24.5
>64	26,536	30.5*	14,558	27.5	41,094	29.4
Region						
Rural area	27,720	25.2*	11,430	21.0	39,150	23.8
Urban area	16,267	34.2	12,040	31.9	28,307	33.2
Smoking						
Nonsmoker	37,401	28.6	20,063	26.7	57,464	27.9
Smoker	6,586	24.6	3,404	19.9	9,990	22.8
Drinking						
Nondrinker	38,675	28.6*	20,521	26.6	59,196	27.9
Drinker	5,312	23.8*	2,946	19.6	8,258	22.1
BMI, kg/m^2						
< 28	39,254	28.8*	20,676	26.6	59,930	28.0
≥ 28	4,733	22.1*	2,794	19.2	7,527	20.9
ACC						
No	37,895	27.6*	18,803	25.1	56,698	26.7
Yes	6,092	30.1*	4,667	26.7	10,759	28.5
Family history						
No	34,119	27.0*	17,442	26.0	51,561	26.6
Yes	9,868	31.9*	6,028	23.9	15,896	28.3

Data are presented as number and percentage of hypertensive patients with controlled blood pressure.

Abbreviations: ACC, associated clinical condition, including self-reported diabetes, coronary heart disease, stroke, and renal disease; BMI, body mass index.

[a]During our survey, a large number of patients previously diagnosed with hypertension had a normal blood pressure (BP); however, they were not using antihypertensive medication at the time of the survey. The possible explanations for this are as follows: (i) patients could have been incorrectly labelled as hypertensive based on 1 or 2 casual measurements of elevated BP, however, their BP reading at the time of the survey was in the normal range; (ii) similarly, some individuals could have had elevated BP initially but spontaneously reversed to normal BP values (i.e., regression towards the mean); (iii) an unknown number of patients could have been on antihypertensive medication but discontinued use before inclusion in the survey, which resulted in them falling in the untreated subgroup with non-elevated BP; and (iv) finally, patients could have been treated with nonpharmacological methods.

*$P < 0.05$ for the difference between untreated and treated groups.

Patients' characteristics associated with untreated HTN included male sex, young age, low systolic BP, living in a rural area, being a nonsmoker and nondrinker, having a lower body mass index, absence of comorbidities, and negative family history. These characteristics were consistent with other studies.[20,21]

Interestingly, the BP control rate among treated patients with HTN was found to be lower than that of untreated hypertensive patients. Further analysis showed that treated patients were more likely to be current smokers and drinkers, had a higher body mass index, indicated the presence of ACCs, and reported a positive family history. Among these types of patients, it is usually difficult to reach the BP control goal. Another possible explanation for this observation may be that the problem lies with poor adherence to prescribed therapy. With respect to untreated hypertensive patients with controlled BP, it is possible that they may have taken drugs or undertaken lifestyle changes in the past but were not taking any antihypertensive medication at the time of the survey. It would also be important to note that it is now a common phenomenon in China for hypertensive patients to discontinue taking their antihypertensive drugs when

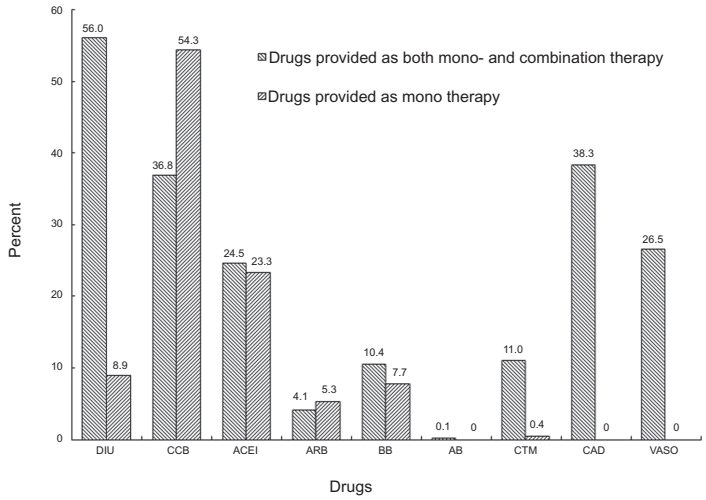

Figure 1. Proportion of antihypertensive drugs provided as both monotherapy and combination therapy or as monotherapy in community health centers in China. In the drugs provided as both mono- and combination therapy group, ingredients of the single-pill combinations were separated and pooled with the classes of drugs that were used as monotherapy. Abbreviations: AB, alpha-blocker; ACEI, angiotensin-converting enzyme inhibitor; ARB, AT1 receptor blocker; BB, beta-blocker; CAD, centrally acting drug; CCB, calcium channel blocker; CTM, Chinese traditional medicine; DIU, diuretic; VASO, direct vasodilator.

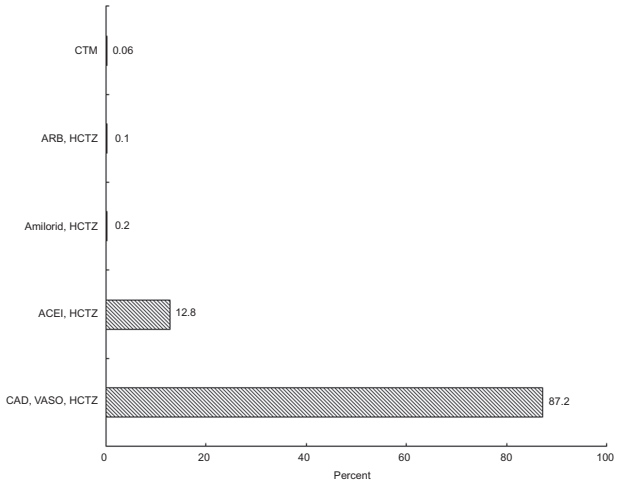

Figure 2. Proportion of active ingredients in single-pill combinations widely used for the treatment of hypertension in community health centers in China. Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, AT1 receptor blocker; CAD, centrally acting drug, such as reserpine and clonidine; CTM, Chinese traditional medicine; HCTZ, hydrochlorothiazide; VASO, direct vasodilator; such as dihydralazine, dibazole, and pargyline.

BP control is achieved, resulting in a false control status for untreated patients. Finally, perhaps untreated hypertensives had transiently elevated BP at an earlier occasion, which may have spontaneously returned to normal at the time of our survey, resulting in the detection of BP levels <140/90 mm Hg in the absence of antihypertensive drug therapy.

The 2005 Chinese Hypertension League guidelines,[7] as well as the 2003 World Health Organization/ International Society of Hypertension guidelines,[18] recommend that all classes of antihypertensive drugs can be used for initiation and maintenance of treatment in all hypertensive patients. Our data showed that DIUs were most frequently used (56.0%), followed by CADs (38.3%), CCBs (36.8%), VASOs (26.5%) and ACEIs (24.5%). For patients on monotherapy, CCBs were the preferred drugs (54.3%), followed by ACEIs (23.3%), DIUs (8.9%), and BBs (7.7%). An alpha-blocker was seldom prescribed. The major cause of this significant difference was that most SPCs, which mostly consist of CADs, VASOs, and DIUs, were prescribed for patients on ≥2 therapies but not on monotherapy.

On the basis of clinical trial results, ARBs/ACEIs are recommended for several compelling indications, such as diabetes, nephropathy, coronary and cerebrovascular disease, heart failure, and left ventricular hypertrophy.[7,18] In this sample, the prescription rate of ARBs was not >5.0%, much lower than that in tertiary hospitals in China (32.0%)[19] and, for example, in Canada (71%).[22] Newer drugs were seldom used, despite the recommendation in the guidelines.[7]

HTN guidelines suggest the use of a single drug initially, which may be followed by adding more medications according to the patients' response to the drug to achieve the goal BP. Based on our observations, about 63.5% of patients were on combination therapy, with DIUs+CADs as the highest prescribed 2-drug combination (61.4%), and VASOs+CADs+DIUs as the highest prescribed combination of 3 drugs (69.2%). SPCs, as a fixed combination tablet, have advantages in terms of compliance and BP-lowering efficacy and are recommended as a substitute for free combination of drugs.[23] In this study, nearly 90% of SPCs were conventional fixed-dose combination drugs, which were mostly produced by domestic companies in China. New fixed-dose combination drugs were rarely prescribed (e.g., 12.8% for ACEIs/hydrochlorothiazide, 0.1% for ARBs/ hydrochlorothiazide). Remarkably, the treatment of HTN showed great adherence to conventional pharmacotherapy, whereas newer drugs were being added at a slow pace. The reasons for frequent use of traditional SPCs could be as follows: (i) deeply entrenched traditional prescription habits of the primary care physicians; (ii) physicians' lack of knowledge or willingness to adhere to the new guidelines for the treatment of HTN; (iii) easy availability; and (iv) affordable pricing for most traditional SPCs compared with new SPCs.

Table 3. Percentage of patients with hypertension by characteristics on monotherapy vs. combination therapy and associated control rates

	Monotherapy		Combination therapy		Total	
Subgroup	%	% Controlled	%	% Controlled	%	% Controlled
Total	36.5	27.7**	63.5	24.1	100.0	25.4
Sex						
Male	47.3*	25.4**	46.0	21.8	46.5	23.1
Female	52.7	29.7**	54.0	26.1	53.5	27.4
Age group, y						
18–44	3.0*	17.1	2.4	14.3	2.6	15.4
45–64	38.6	26.1**	40.8	21.5	40.0	23.1
>64	58.4	29.3**	56.8	26.4	57.4	27.5
BP level, mm Hg						
< 140/90	27.7*	100.0	24.2	100.0	25.5	100.0
141–159/91–99	44.6	—	45.7	—	45.3	—
160–179/100–109	20.9	—	22.0	—	21.6	—
≥ 180/110	6.8	—	8.2	—	7.7	—
Region						
Rural area	47.7*	18.4**	65.6	22.0	59.1	21.0
Urban area	52.3	36.1	34.4	28.2	40.9	31.9
Smoking						
Nonsmoker	82.8*	28.9**	80.7	25.4	81.5	26.7
Smoker	17.2	21.8**	19.3	19.0	18.5	19.9
Drinking						
Nondrinker	84.6*	28.8**	83.2	25.3	83.7	26.6
Drinker	15.4	21.7**	16.8	18.5	16.3	19.6
BMI, kg/m^2						
<28	85.4*	28.6**	83.5	25.4	84.2	26.6
≥28	14.6	21.9**	16.5	17.8	15.8	19.2
ACC						
No	78.9*	27.0**	82.4	24.1	81.1	25.1
Yes	21.1	30.2**	17.6	24.4	18.9	26.7
Family history						
No	74.1*	27.8**	71.9	24.9	72.7	26.0
Yes	25.9	27.2**	28.1	22.2	27.3	23.9

Data are presented as percentage of hypertensive patients on monotherapy or combination therapy and proportion with controlled hypertension.

Abbreviations: ACC, associated clinical condition, including self-reported diabetes, coronary heart disease, stroke, and renal disease; BMI, body mass index; BP, blood pressure.

*P < 0.05 for the difference in proportion of hypertensives between monotherapy and combination therapy groups; **P < 0.05 for the difference in control rate between monotherapy and combination therapy groups.

As to the urban/rural difference, patients in rural areas are usually poorer than those in urban areas, and only a few have medical insurance. Lack of insurance is a factor limiting healthcare use.[24]

The control rate among treated HTN was only 25.4%, somewhat lower than the 29.4% in primary care in Germany[25] and the 30.6% in tertiary hospital clinics in China.[19] The control rate was higher on monotherapy (27.7%) than combination therapy (24.1%), similar to a study in Canada (86% and 80%, respectively),[22] but in contrast with Joshi *et al.*'s study (40.8% and 59.2%, respectively).[26] Because the data are derived from a cross-sectional baseline survey, it is unclear whether the present therapy was the initial one or whether it replaced or amended the original one. A possible reason for the low rate of HTN control on combination therapy may be that, in this sample, there was a larger proportion

of patients with cardiovascular disease risk factors and other clinical conditions requiring intensive treatment. The difficulty of reducing BP level to the recommended target level in these patients is well known.[27–29] One logical option, however, for improving BP control in these patients is to include an additional antihypertensive medication. Unfortunately, as described above, the current combinations of medicines were not only inconsistent with what the guidelines recommend but also included some old agents, thus creating a barrier to better HTN control.

One of the study limitations was that the data were retrieved from a nonrandom sampling program. Second, we did not collect information about physicians' knowledge of antihypertensive drug use. Third, adherence to medication was not assessed, and medication dose and frequency were not recorded. Finally, although lifestyle change is also important for BP control, our analysis focused on drug treatment.

The strength of this project was the large sample size and the cooperation of a large number of CHCs in collecting unique data about the treatment of hypertensive patients by primary care physicians in China.

The finding of low control rates among treated patients in China can be explained by the present pattern of antihypertensive drug therapy in routine practice (i.e., high prescription rates of traditional SPC and suboptimal combinations of contemporary, efficacious drugs).

Our data will be helpful in designing and implementing a program of professional education on the use of appropriate antihypertensive medications alone or in the correct combinations and ensuring that patients receive evidence-based, cost-effective treatments for their health problems.

SUPPLEMENTARY MATERIALS

Supplementary materials are available at *American Journal of Hypertension* (http://ajh.oxfordjournals.org).

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DISCLOSURE

The authors declared no conflict of interest.

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