

# Patterns and predictors of antihypertensive medication used 1 year after ischemic stroke or TIA in urban China

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**Background:** Antihypertensive treatment is recommended for secondary prevention in patients with ischemic stroke or transient ischemic attack. Prescription of and persistence with antihypertensives for secondary prevention is high in developed countries; whether this is true in China is unclear. The aim of this study was to describe the patterns of antihypertensive medication use, and factors associated with its use, 1 year after stroke in China.

**Methods:** A total of 7880 hypertensive patients diagnosed with ischemic stroke or transient ischemic attack in the China National Stroke Registry were analyzed. Multivariate logistic regression was used to identify factors associated with antihypertensive medication use at discharge and 12 months.

**Results:** Antihypertensive medication was used by 4458 (56.6%) participants at discharge and 2927 (37.1%) at 12 months. Calcium channel blockers were the most common among five classes of antihypertensive medication prescribed at discharge, and participants prescribed this class had the highest 1-year persistence. In-hospital health education was the strongest predictor of antihypertensive medication use at discharge; age and stroke severity were the strongest negative predictors of use at 12 months.

**Conclusion:** Use of antihypertensive medication 1 year after stroke is extremely low in China. Intervention is needed to improve adherence to antihypertensive medication, especially for the elderly and severe stroke patients.

**Keywords:** antihypertensive agents, secondary stroke prevention, stroke

## Introduction

Hypertension is the strongest modifiable risk factor for recurrent stroke, and the efficacy of antihypertensive medication to prevent stroke recurrence has been established in several clinical trials.<sup>1</sup> Current American Heart Association/American Stroke Association guidelines advocate blood pressure reduction as a class 1A recommendation in patients who have had an ischemic stroke (IS) or transient ischemic attack (TIA).<sup>2</sup> Previous studies conducted in Germany,<sup>3</sup> Canada,<sup>4</sup> the USA,<sup>5</sup> and Sweden<sup>6</sup> have suggested that persistence with antihypertensive medication 1 year after initial stroke is high (>85% of patients). In China, however, few data are available on the prescription of and persistence with antihypertensive medication in patients with hypertension who have had an IS or TIA. Using the China National Stroke Registry (CNSR), the patterns of antihypertensive medication use at discharge from hospital and up to 1 year after stroke were investigated. In addition, the factors associated with antihypertensive medication use at discharge and at 1 year were determined.

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## Methods

### The CNSR

The CNSR is a nationwide, hospital-based registry, as described in detail elsewhere.<sup>7</sup> Briefly, the CNSR prospectively collected data on consecutive patients aged 18 years or older with stroke who were admitted to one of 132 participating hospitals in urban China within 14 days after the onset of symptoms. A total of 22,216 participants were recruited between September 2007 and August 2008. The ethics committees at all participating hospitals approved the protocol, and all patients or their designated relatives provided informed consent.

### Clinical data

IS and TIA were diagnosed according to World Health Organization criteria.<sup>8</sup> Participants were classified as having hypertension when any of the following criteria were met: a self-reported physician diagnosis of hypertension, use of antihypertensive drug(s) before the onset of stroke, or a final diagnosis of hypertension at discharge. Patient baseline information included gender, age, and level of education. Medical history included history of stroke, coronary heart disease, atrial fibrillation (confirmed by at least one electrocardiogram), diabetes mellitus, dyslipidemia, previous antihypertensive medication use, current or previous smoking, and moderate or heavy alcohol use (more than two standard alcoholic beverages consumed per day). Stroke severity was measured using the National Institutes of Health Stroke Scale on admission. In-hospital health education included information about physical exercise, quitting smoking, refraining from drinking alcohol, and medication advice.

### Collection of antihypertensive medication information

Information about the use of antihypertensive medication at discharge was extracted from medical records, whereas information about the use of antihypertensive medication at 3, 6, and 12 months was obtained by telephone interview with patients or their designated relatives. Classes of antihypertensive medication included angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers (CCBs), diuretics,  $\beta$ -blockers, and "other" antihypertensives (including centrally acting adrenergics, peripherally acting antiadrenergics, and vasodilators), as recommended by Liu.<sup>9</sup>

### Statistical analysis

Multivariate logistic regression models were used to identify factors associated with antihypertensive medication use at

discharge or at 1 year among participants with IS or TIA and hypertension. Effect sizes are expressed as odds ratios and 95% confidence intervals. Statistical significance was defined as a two-tailed  $P < 0.05$ . All statistical analyses were performed using SAS 9.1.3 (SAS Institute Inc, Cary, NC, USA).

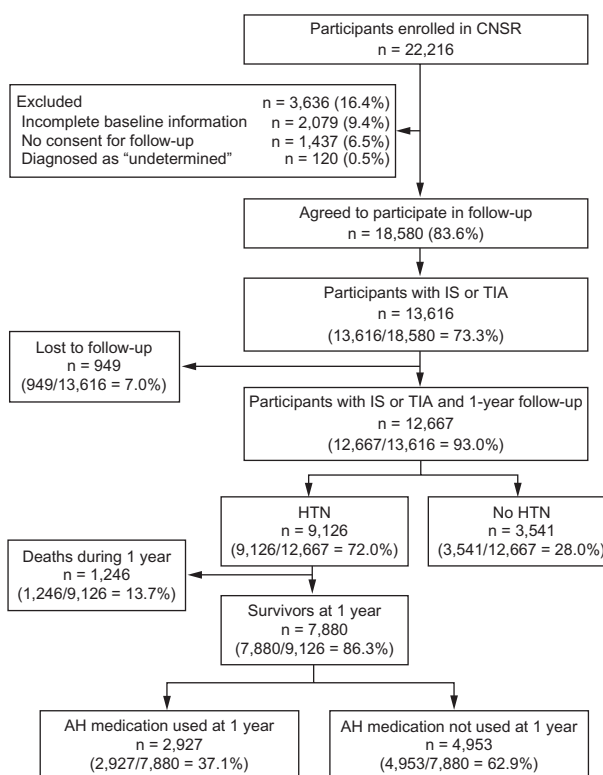
## Results

### Participant information

A total of 7880 participants (4817 men, 3063 women; mean age  $64.9 \pm 11.4$  years) with hypertension who have had an IS or TIA were analyzed in this study (Figure 1). Baseline characteristics of patients who did or did not have 1-year follow-up data are shown as supplementary data (Table S1). Baseline characteristics of the study population are shown in Table 1.

### Patterns of antihypertensive medication use during 1 year

Among the 7880 participants, 4458 (56.6%) were discharged with antihypertensive medication, 4607 (58.5%) used antihypertensive medication at 3 months, 4660 (59.1%) at 6 months, and 2927 (37.1%) at 12 months (Figure 2A). Of the 4458 participants who were discharged with antihypertensive



**Figure 1** Participant flow diagram.

**Abbreviations:** AH, antihypertensive; CNSR, China National Stroke Registry; HTN, hypertension; IS, ischemic stroke; TIA, transient ischemic attack.

**Table 1** Baseline characteristics of participants with ischemic stroke or transient ischemic attack and hypertension

Variable	All participants (n = 7880)	Discharged with AH medication			Using AH medication at 1 year		
		Yes (n = 4458)	No (n = 3422)	P-value	Yes (n = 2927)	No (n = 4953)	P-value
Female	3063 (38.9%)	1730 (38.8%)	1333 (39.0%)	0.89	1155 (39.5%)	1908 (38.5%)	0.41
Age							
18–45 years	443 (5.6%)	275 (6.2%)	168 (4.9%)	0.06	180 (6.1%)	263 (5.3%)	<0.001
46–65 years	3400 (43.1%)	1894 (42.5%)	1506 (44.0%)		1360 (46.5%)	2040 (41.2%)	
66–75 years	2559 (32.5%)	1466 (32.9%)	1093 (31.9%)		929 (31.7%)	1630 (32.9%)	
≥76 years	1478 (18.8%)	823 (18.5%)	655 (19.1%)		458 (15.6%)	1020 (20.6%)	
Monthly household income (yuan)							
≤500	836 (10.6%)	488 (10.9%)	348 (10.2%)	<0.001	315 (10.8%)	521 (10.5%)	0.06
500–1000	1824 (23.1%)	1079 (24.2%)	745 (21.8%)		692 (23.6%)	1132 (22.9%)	
1001–3000	2781 (35.3%)	1677 (37.6%)	1104 (32.3%)		1063 (36.3%)	1718 (34.7%)	
≥3000	567 (7.2%)	378 (8.5%)	189 (5.5%)		219 (7.5%)	348 (7.0%)	
Unknown	1872 (23.8%)	836 (18.8%)	1036 (30.3%)		638 (21.8%)	1234 (24.9%)	
Level of education							
Elementary or below	3396 (43.1%)	1848 (41.5%)	1521 (44.4%)	0.022	1131 (38.6%)	2238 (45.2%)	<0.001
Middle school	2106 (26.7%)	1206 (27.1%)	900 (26.3%)		806 (27.5%)	1300 (26.2%)	
High school or above	2405 (30.5%)	1404 (31.5%)	1001 (29.3%)		990 (33.8%)	1415 (28.6%)	
Type of health insurance							
Urban employee	5038 (63.9%)	2904 (65.1%)	2134 (62.4%)	0.011	1898 (64.8%)	3140 (63.4%)	0.46
Rural cooperative	1196 (15.2%)	664 (14.9%)	532 (15.5%)		433 (14.8%)	763 (15.4%)	
Commercial	245 (3.1%)	147 (3.3%)	98 (2.9%)		82 (2.8%)	163 (3.3%)	
Own expense	1401 (17.8%)	743 (16.7%)	658 (19.2%)		514 (17.6%)	887 (17.9%)	
Married	7226 (91.7%)	4081 (91.5%)	3145 (91.9%)	0.56	2686 (91.8%)	4540 (91.7%)	0.87
Living alone	251 (3.2%)	145 (3.3%)	106 (3.1%)	0.70	82 (2.8%)	169 (3.4%)	0.14
Medical history							
Stroke	2816 (35.7%)	1568 (35.2%)	1248 (36.5%)	0.23	1029 (35.2%)	1787 (36.1%)	0.41
Coronary heart disease	1219 (15.5%)	681 (15.3%)	538 (15.7%)	0.59	481 (16.4%)	738 (14.9%)	0.07
Atrial fibrillation	586 (7.4%)	343 (7.7%)	243 (7.1%)	0.32	183 (6.3%)	403 (8.1%)	0.002
Diabetes mellitus	2358 (29.9%)	1390 (31.2%)	968 (28.3%)	0.006	869 (29.7%)	1489 (30.1%)	0.73
Dyslipidemia	4833 (61.3%)	2921 (65.5%)	1912 (55.9%)	<0.001	1862 (63.6%)	2971 (60.0%)	0.001
Smoking	3124 (39.6%)	1777 (39.9%)	1347 (39.4%)	0.65	1168 (39.9%)	1956 (39.5%)	0.72
Alcohol use	759 (9.6%)	419 (9.4%)	340 (9.9%)	0.42	260 (8.9%)	499 (10.1%)	0.08
Previous use of AH medication	5129 (65.1%)	2912 (65.3%)	2217 (64.8%)	0.62	2059 (70.3%)	3070 (62.0%)	<0.001
NIHSS scores at admission							
0–4	4582 (58.1%)	2671 (59.9%)	1911 (55.8%)	<0.001	1742 (59.5%)	2840 (57.3%)	<0.001
5–14	2808 (35.6%)	1570 (35.2%)	1238 (36.2%)		1045 (35.7%)	1763 (35.6%)	
≥15	490 (6.2%)	217 (4.9%)	273 (8.0%)		140 (4.8%)	350 (7.1%)	
SBP, mmHg (mean ± SD)	158.0 ± 23.1	157.6 ± 23.4	158.2 ± 22.9	0.38	–	–	–
Event type							
TIA	681 (8.6%)	385 (8.6%)	296 (8.6%)	0.98	250 (8.5%)	431 (8.7%)	0.81
Ischemic stroke	7,199 (91.4%)	4,073 (91.4%)	3,126 (91.4%)		2,677 (91.5%)	4,522 (91.3%)	
In-hospital health education	7047 (89.4%)	4369 (98.0%)	2678 (78.3%)	<0.001	2631 (89.9%)	4416 (89.2%)	<0.001

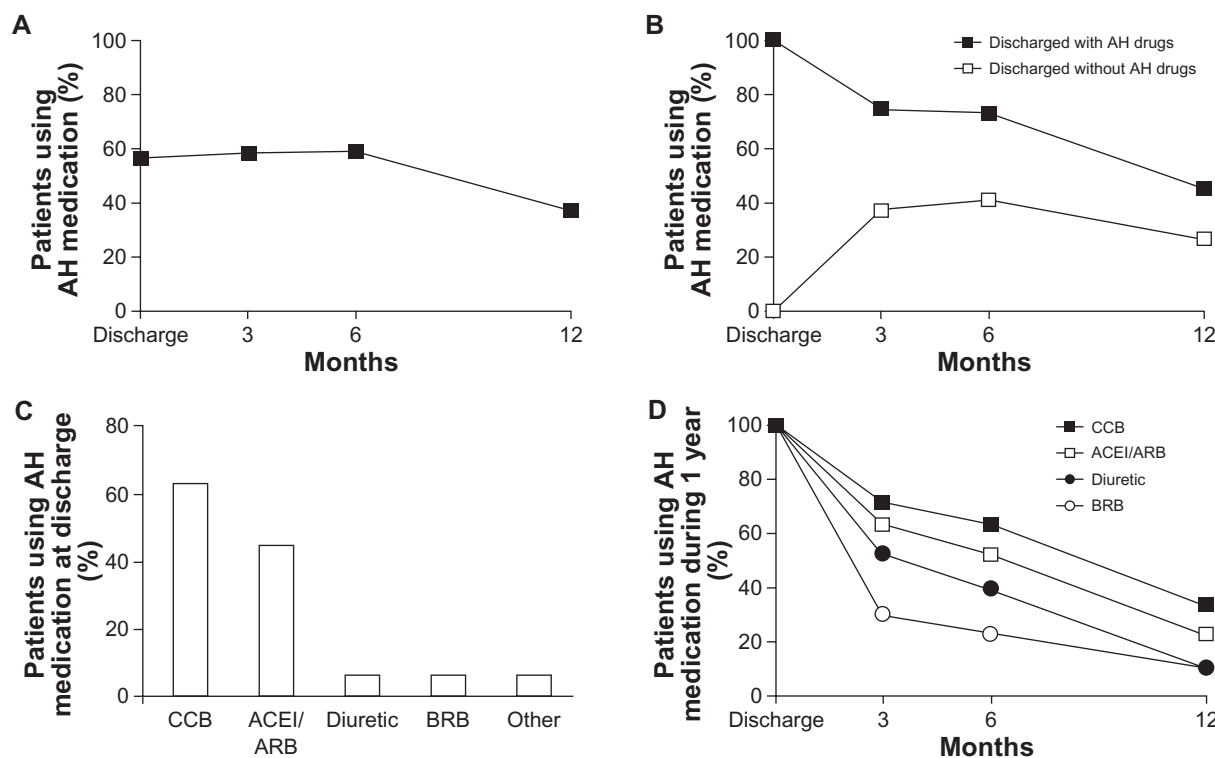
**Note:** Data are shown as n (%).

**Abbreviations:** AH, antihypertensive; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; SD, standard deviation; TIA, transient ischemic attack.

medication, 2012 (45.1%) used antihypertensive medication at 12 months (Figure 2B), and only 1619 (36.3%) remained on antihypertensive medication at all three follow-up time points (3, 6, and 12 months). Of the 3422 participants who were discharged without antihypertensive medication, 1652 (48.3%) never started treatment with antihypertensive

medication by the end of the 1-year follow-up period. Discontinuation of antihypertensive drugs at 3, 6, and 12 months among patients who received the medication at discharge is shown as supplementary data (Figure S1).

Moreover, CCBs were the most common antihypertensive drugs prescribed at discharge, followed by the combination



**Figure 2** Patterns of AH medication use. **(A)** Proportion of all participants with hypertension who used AH medication (n = 7880) during the 1-year follow-up. **(B)** Proportion of participants who used AH medication during the 1-year follow-up among participants discharged with (n = 4458) or without (n = 3422) AH medication. **(C)** Proportion of participants who were discharged with AH medication, stratified by medication class. Percentages do not total 100% because some patients received more than one AH medication. **(D)** Persistence with each specific class of AH medication during the 1-year follow-up among participants who were discharged with AH medication.

**Abbreviations:** ACEI, angiotensin-converting enzyme inhibitors; AH, antihypertensive; ARB, angiotensin receptor blockers; BRB,  $\beta$ -blockers; CCB, calcium channel blockers.

of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (Figure 2C). There were differences in persistence among the classes of antihypertensive medications during 1 year, with the lowest persistence observed with diuretics and  $\beta$ -blockers and the highest with CCBs (Figure 2D).

Among the 4458 participants discharged with antihypertensive medication, 14 (0.3%) were discharged on at least four antihypertensive agents, 266 (6.0%) on three agents, 949 (21.3%) on two agents, and 3229 (72.4%) on one agent.

### Predictors of discharge with antihypertensive medication

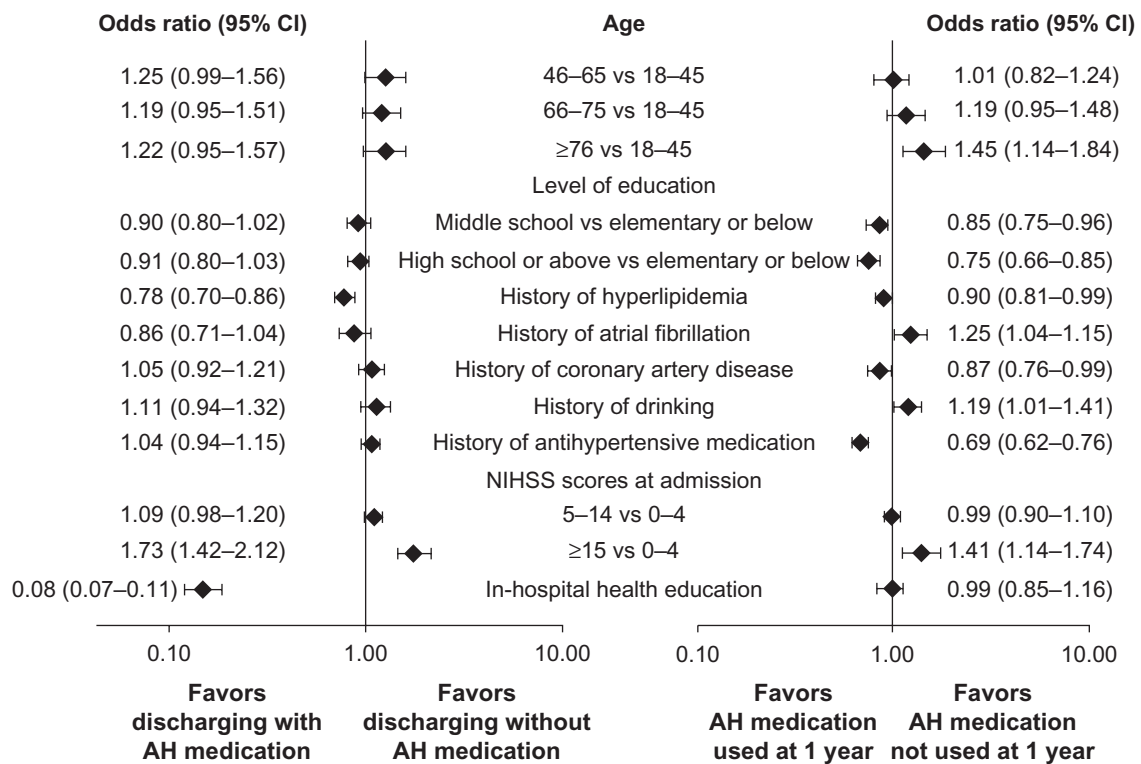
Multivariate analyses showed that among participants who had an IS or TIA and hypertension, those who received health education in hospital, and those who had a history of hyperlipidemia were more likely to be discharged with antihypertensive medication (Figure 3). In contrast, participants admitted with a severe stroke (National Institutes of Health Stroke Scale score  $\geq 15$ ) were less likely to be discharged with antihypertensive medication (Figure 3).

### Predictors of antihypertensive medication use at 1 year

Among the total study population, age and stroke severity were the strongest negative predictors of antihypertensive medication use at 1 year (Figure 3). Among patients who received the medication at discharge, age, level of education, history of dyslipidemia, history of antihypertensive medication, and stroke severity were determinants of new onset discontinuation at 12 months.

### Discussion

In this study of data from the CNSR, it was found that the use of antihypertensive medication for secondary prevention at 1 year after stroke is extremely low in China. Previous studies conducted in other, developed countries have reported rates of antihypertensive medication use at 1 year after stroke of 86%–90%.<sup>3–6</sup> The Swedish registry study found that of the 15,809 stroke patients discharged with antihypertensive medication, 86% used antihypertensive medication at 1 year after stroke and 74% at 2 years.<sup>6</sup> In the AVAIL (Adherence Evaluation After Ischemic Stroke Longitudinal) study, 88% of the 1884 stroke patients discharged with antihypertensive



**Figure 3** Multiple regression analysis model identifying factors associated with discharge from hospital with AH medication (left panel) and use of AH medication at 1 year (right panel).

**Abbreviations:** AH, antihypertensive; CI, confidence interval; NIHSS, National Institute of Health Stroke Severity; vs, versus.

medication reported using these medications at 1 year.<sup>5</sup> In contrast, only 45% of the 4458 patients discharged with antihypertensive medication in the current study reported using these medications at 1 year, ie, half the rate of the above studies.

This large discrepancy between China and other, more developed countries in persistence with antihypertensive medication after stroke has not been reported previously. Previous studies of secondary stroke prevention in China have been conducted in urban areas and tertiary care centers,<sup>10,11</sup> which may have overestimated persistence with antihypertensive medication.

The ChinaQUEST (Quality Evaluation of Stroke Care and Treatment) study, a multicenter, prospective, hospital registry study conducted in China, found that the rate of antihypertensive medication use at 1 year after IS in patients with hypertension was 73%,<sup>12</sup> almost twice the rate found in the current study (37%). There are several possible explanations for this discrepancy. First and most importantly, only the five classes of antihypertensive medication recommended by the American Heart Association/American Stroke Association guidelines were included,<sup>2</sup> and not other types of antihypertensives such as traditional Chinese medicines. Second, ChinaQUEST was conducted in 62 hospitals located

in major cities,<sup>12</sup> where patients are likely to receive higher standards of care than patients in other locations in China. In contrast, the CNSR was conducted in 132 hospitals from each of the 27 provinces and four municipalities in mainland China, including the less developed, western region of the country.<sup>7</sup> Thus, the current study is more likely than the ChinaQUEST study to reflect the overall, nationwide use of antihypertensive medication as secondary prevention after stroke in China.

The current study also found that the use of antihypertensive medication was relatively well maintained during the first 6 months after stroke, but rapidly declined between 6 months and 1 year. To maintain blood pressure reduction and minimize the risk of recurrent stroke or death, patients with hypertension should persist with antihypertensive medication. The decline of antihypertensive medication between 6 months and 1 year highlights the importance of repeated intervention to improve long-term antihypertensive medication use.

Previous studies suggest that there may be important differences in persistence among the classes of antihypertensives, with angiotensin receptor blockers and angiotensin-converting enzyme inhibitors having the highest levels of adherence in Western countries.<sup>13</sup> However, in the current study in China,

CCBs were the most common antihypertensive drugs prescribed at discharge and had the highest persistence during 1 year among the five classes of antihypertensive drugs. This may be because CCB-based antihypertensive regimens were the first to be recommended by Chinese guidelines for the management of hypertension,<sup>9</sup> which has influenced the medication choice of doctors and patients.

Identifying predictors of antihypertensive medication use, particularly long-term use, is critical for improving the low persistence rate of patients in China. In this study, it was found that participants with a severe stroke were less likely to be discharged with antihypertensive medication and less likely to use antihypertensive medication at 1 year. Patients who have experienced a severe stroke are at high risk of death, and persistent use of antihypertensive medication could reduce mortality after stroke. For these reasons, it is especially important to prompt patients in China who have had a severe stroke to take antihypertensive medication for secondary prevention. It was also found that participants who were older, less educated, or had a history of alcohol use were less likely to use antihypertensive medication at 1 year. In contrast, participants with comorbidities, including hyperlipidemia and coronary artery disease, were more likely to use antihypertensive medication at 1 year. The finding that participants with atrial fibrillation were less likely to use antihypertensive medication at 1 year was unexpected. This observation may be related to age, as patients with atrial fibrillation are usually older.<sup>14</sup> Notably, it was found that in-hospital health education was a strong predictor for being discharged with antihypertensive medication, but not for antihypertensive medication use at 1 year. This phenomenon emphasizes that ongoing health education is needed for patients after being discharged from hospital.

This study does have several limitations. First, there were no hospitals from rural areas, where patients are less likely to receive standard treatment for secondary prevention. Hence, the true rate of antihypertensive medication use after stroke in China may be even lower than this study suggests. Second, data on the potential contraindications or adverse reactions that might have prevented the use of certain antihypertensive drugs were not collected. Finally, information about medication use at 3, 6, and 12 months was based on self-report via telephone interview, which may be subject to social desirability and recall bias.

## Conclusion

In summary, this study of the CNSR suggests that persistence with antihypertensive medication as secondary prevention

after stroke in China is low, particularly in comparison with persistence in developed countries. Ongoing intervention is needed to improve long-term antihypertensive medication use and help reduce the risk of stroke recurrence and death in patients, particularly those at high risk of low persistence.

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## Disclosure

The authors report no conflicts of interest in this work.

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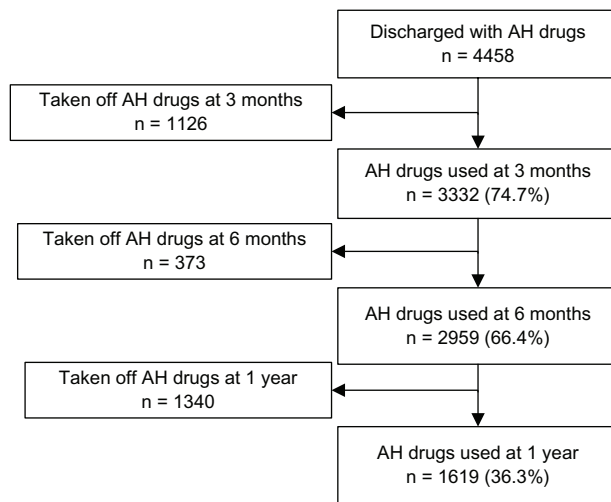
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## Supplementary data

**Table S1** Baseline characteristics of patients who did or did not have 1-year follow-up data

Variable	Study population (n = 7880)	Lost to follow up or death (n = 1902)	P-value
Female	3063 (38.9%)	837 (44.0%)	<0.0001
Age			
18–45 years	443 (5.6%)	53 (2.8%)	<0.0001
46–65 years	3400 (43.2%)	531 (27.9%)	
66–75 years	2559 (32.5%)	593 (31.2%)	
≥76 years	1478 (18.8%)	725 (38.1%)	
Monthly household income (yuan)			
≤500	836 (10.6%)	186 (9.8%)	<0.0001
500–1000	1824 (23.2%)	406 (21.4%)	
1001–3000	2781 (35.3%)	606 (31.9%)	
≥3000	567 (7.2%)	122 (6.4%)	
Unknown	1872 (23.8%)	582 (30.6%)	
Types of health insurance			
Urban employee	5038 (63.9%)	1209 (63.6%)	0.50
Rural cooperative	1196 (15.2%)	291 (15.3%)	
Commercial and other	245 (3.1%)	72 (3.8%)	
Own expense	1401 (17.8%)	330 (17.4%)	
Level of education			
Elementary or below	3396 (42.8%)	1036 (55.4%)	<0.0001
Middle school	2106 (26.7%)	431 (23.0%)	
High school or above	2405 (30.5%)	404 (21.6%)	
Married	7226 (91.7%)	1606 (84.4%)	<0.0001
Living alone	251 (3.2%)	85 (4.5%)	0.006
Medical history			
History of stroke	2816 (35.7%)	820 (43.1%)	<0.0001
History of coronary heart disease	1219 (15.5%)	391 (20.6%)	<0.0001
History of atrial fibrillation	586 (7.4%)	367 (19.3%)	<0.0001
History of diabetes mellitus	2358 (29.9%)	632 (33.2%)	0.005
History of dyslipidemia	4833 (61.3%)	879 (46.2%)	<0.0001
History of smoking	3124 (39.6%)	1238 (34.9%)	0.0001
History of drinking	759 (9.6%)	130 (6.8%)	0.0001
History of AH medication	5129 (65.1%)	1197 (62.9%)	0.08
NIHSS scores at admission			
0–4	4582 (58.2%)	712 (37.4%)	<0.0001
5–14	2808 (35.6%)	616 (32.4%)	
≥15	490 (6.2%)	574 (30.2%)	
In-hospital health education	7047 (89.4%)	1470 (77.3%)	<0.0001

**Abbreviations:** AH, antihypertensive; NIHSS, National Institutes of Health Stroke Scale.



**Figure S1** Discontinuation of AH drugs at 3, 6, and 12 months among patients who received the medication at discharge.

**Abbreviation:** AH, antihypertensive.

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