Antihypertensive Medications in Primary Health Care in China: Availability, Cost, and Prescription Patterns

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Summary

Background. Rates of hypertension treatment and control are low in China. Available and affordable medications are important for successfully controlling hypertension, but little is known about current patterns of access to and use of antihypertensive medications in Chinese primary health care.

Methods. By using medication inventory data and prescriptions from a nationwide cross-sectional survey, we studied the availability, cost, and prescription patterns of 62 antihypertensive medications at 3362 primary health care sites across 31 Chinese provinces. Site variation by geography and types were also evaluated. We also assessed the current use of high-value medications, defined as guideline-recommended and low-cost. Finally, we evaluate the association of medication cost with availability and prescription patterns.

Findings. Of 3362 sites, 8% stocked no antihypertensive medications; 34% stocked all four classes. Village clinics and sites in the western region had the lowest availability. Only 33% of all sites stocked high-value medications. Few high-value medications were prescribed (11% of all sites). Higher-cost medications were more likely to be prescribed than lower-cost alternatives.

Interpretation. China has marked deficiencies in the availability, cost, and prescription of antihypertensive medications. High-value medications are not preferentially used. Future efforts to reduce the burden of hypertension, particularly through the work of primary health care providers, will need to improve access and use of antihypertensive medications, with particular attention to those with high value.

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Research in context

Evidence before this study

We searched PubMed for literature in English and the China National Knowledge Infrastructure (CNKI) for literature in Chinese, published before May 2016, using the terms “primary health care”, “pharmaceutical policy”, “essential medication”, “essential medicine”, “hypertensive medication”, OR “hypertension”. We also reviewed the references from the identified articles and the highly relevant articles and reports. The awareness, treatment, and control of hypertension was found to be low. The National Essential Medicine Program, a “zero-profit” policy for essential medications, was implemented by all primary health care sites in 2009 to meet residents’ medication needs and reduce their out-of-pocket costs. However, conflicting results on availability and cost were found, and few studies reported prescription patterns of antihypertensive medications. Previous studies were limited to specific regions, populations, and data sources.

Added value of this study

We used a national primary health care study and a screening study of high risk for cardiovascular disease in China to depict the current status of availability, cost, and prescription patterns of antihypertensive medications in primary health care settings in China. We collected the data directly from primary health care sites, rather than analyzing secondary data from other reports. We found marked deficiencies in availability, cost, and prescription of hypertensive medications. Overall, 8% of primary health care pharmacies did not stock any antihypertensive medications. Village clinics and sites in the western region had the lowest availability. High-cost medications were more likely to be prescribed than low-cost medications. High-value medications, those that are guideline-recommended and low-cost, were not preferentially prescribed.

Implications of all the available evidence

Our findings suggest that interventions to improve hypertension treatment and control in China will need to ensure that antihypertensive medications area adequately available in primary health care settings. Implementation of the essential medicine policy at the local level is currently inadequate. Use of high-value medications may help to reduce the cost burden of hypertension treatment.

Introduction

An estimated 200 million adults have hypertension in China, and fewer than 15% are treated.[1-4] Moreover, among those who are treated, about two thirds do not achieve adequate blood pressure control.[5-7] Inadequate management of hypertensive patients may have significant health and economic consequences: the sequelae of hypertension, including stroke and heart disease, are the leading causes of morbidity and mortality in China,[8,9] and are associated with significant expense to patients and the health system.

The successful mitigation of hypertension in China requires, in addition to lifestyle and behavioral modifications, that antihypertensive medications be made available and affordable, and that they be prescribed appropriately in primary health care (PHC) settings, a primary point of contact with the health system in China. Recent studies have suggested availability and high medication costs as major barrier to optimal utilization rates and adherence to essential antihypertensive medications, especially among low-income rural areas in China.[10]

The Chinese health reform in 2009 strengthens role of PHC that serve as gatekeepers to the health care system.[11] It also introduced the National Essential Medicine Program that was designed to "provide affordable and equitable basic health care for all by 2020." The pharmaceutical policy has also evolved quickly in recent years, such as allowance for primary health care sites to procure non-essential medicines in

2014 and abolishment on the government price ceiling in 2015 (Appendix 1). While availability of medications may have increased after the National Essential Medicine Policy was launched,[12-14] little is known about current patterns of access to antihypertensive medications across Chinese PHC settings, where higher financial burdens and limited medication choices may result in lower treatment and control rates. This information is essential for developing targets for interventions that are designed to improve national hypertension treatment and control.

Accordingly, to address the need for information about the availability, cost, and prescription of antihypertensive medications in PHC settings across China, we analyzed data from a national, government-funded study of the PHC system and a large national cardiovascular screening project.[15] Specifically, our study focused on examining the availability, cost, and prescription of antihypertensive medications at all four types of PHC sites in China. We then evaluated the availability of antihypertensive medications across PHC sites. Finally, we determined how the costs of antihypertensive medications were associated with the availability and prescription of antihypertensive medications, with a particular focus on lower-cost, guideline-recommended treatments.

Methods

Data Source and Study Sample

Data on the availability, cost, and prescription of antihypertensive medications were

151 derived from the China Patient-Centered Evaluative Assessment of Cardiac Events
152 (PEACE) Million Persons Project (MPP) PHC Survey. The design of this nationwide
153 survey, conducted from November 2016 through May 2017, has been described
154 previously.[16] Briefly, we established a nationwide epidemiologic collaborative
155 network of the China PEACE MPP, which consists of 141 county/district-level
156 regions from all 31 provinces in mainland China.[15] The MPP enrolled the eligible
157 study sites according to the number of residents of the catchment area, population
158 stability, local economic conditions, and geographic location. The collaborative
159 network therefore captures great diversity in geographic location, ethnicity of
160 residents, economic development, and level of urbanization. The PHC services are
161 provided by community health centres and community health stations (one level
162 below) in urban areas, and township health centres and village clinics (one level
163 below) in rural areas (Appendix 2). We surveyed 203 community health centres, 401
164 community health stations, 284 township health centres, and 2474 village clinics to
165 quantify the care-delivery capacity and the quality of PHC. The distribution of
166 primary health care study sites sampled across rural and urban areas (township health
167 centres/village clinics and community health centres/stations) reflects the national
168 ratio.[17]
169
170 Data on hypertension treatment and control rates were derived from the
171 cardiovascular risk screening program of the China PEACE MPP, which to date has
172 enrolled 1·7 million permanent residents, aged 35 to 75 years, who lived in 141

selected county-/district-level regions for at least 6 months in the past year. The interview data of China PEACE MPP included information about the history of hypertension diagnosis and treatment, collected by face-to-face administration of a questionnaire. In total, 1·09 million people with information in the MPP lived in the 435 townships/communities that are the focus of this study. We linked the characteristics of PHC sites with local population epidemiologic data at the township/community level (i.e., one level below county/district), China's 2015 National Census data, and geographic location information (longitude and latitude) from a Chinese web mapping service (AMAP).[18]

Data Collection and Definitions

Pharmacy inventory. Lists of medications in stock at the time of the survey (November to December 2016) were obtained from each participating PHC site, copied, and reviewed. For each medication on the list, generic name, brand name, dosage form, specification, manufacturer, and retail price per sale unit were collected. We cleaned and checked the reported generic names against China Pharmacopoeia 2015,[19] achieving 95% in accuracy.

Prescriptions. For outpatient prescriptions (April 2015 to March 2016), we collected each patient's age, gender, and diagnosis, which are routinely on the prescriptions, as well as medication name, dosage, and administration. In PHC sites with an electronic prescription system, relevant information was directly imported into a digital

195 database. For sites without electronic prescription system, we included the first 100
196 outpatient prescriptions in each 10-day period for the 12 months in our analysis (3600
197 total prescriptions during the study period). We scanned copies, and trained staff
198 manually abstracted relevant information, with double-entry methods as a quality
199 check to ensure an accuracy standard of at least 98%.
200
201 *Blood pressure measurement, hypertension treatment, and control.* In MPP, blood
202 pressure was measured twice during the interview, using a unified electronic blood
203 pressure monitor (Omron HEM-7430; Omron Corporation, Kyoto, Japan) and
204 standardized procedures.[20] Treatment rate was defined as the proportion of the
205 hypertensive population who self-reported use of antihypertensive medications at the
206 baseline interview in the China PEACE MPP population; control rate was defined as
207 the proportion of the hypertensive population with a blood pressure <140/90 mm Hg
208 at the baseline interview. Treatment and control rate of hypertension were measured
209 by aggregating participant data at the township/community level.
210
211 *Site characteristics.* We obtained information on characteristics of each PHC site,
212 including workforce and use of information technology, through a survey of site
213 leaders and health care professionals.
214
215 *Antihypertensive medications.* We focused on 62 oral medications by generic names
216 listed in the database of the China Clinical Guideline for Hypertension Management

2010 regardless of whether they were recommended,[2,21] and the essential medicine lists.[22,23] We placed each of these medications in one of eight mutually exclusive pharmacologic classes, including: (1) angiotensin-converting-enzyme inhibitors (ACEIs), (2) angiotensin-receptor blockers (ARBs), (3) beta-blockers, (4) calcium-channel blockers (CCBs), (5) diuretics, (6) fixed-dose combination medications, (7) compound medications with ingredients from traditional Chinese medicine (TCM), and (8) centrally active drugs. Alpha-blockers and alpha-beta blockers were not included because of their scarcity in the primary care sector.

We ascertained the availability of each antihypertensive medication in any dose in the site pharmacy, which was calculated as the proportion of all participating sites with a specific antihypertensive medication or medication class in stock. We calculated the annual median cost for each medication, using its median price across different PHC sites and the guideline-recommended dosage.

We defined high-value medications as those that satisfied these two criteria: (1) the medication is recommended by the Chinese Guideline for Hypertension Management in Primary Health Care 2014,[24, 25] and (2) annual medication cost of no more than 200 RMB, a threshold corresponding to 1% of the average annual disposable income per capita in China in 2015. The guideline recommends medicines based on clinical effectiveness. We used the 2014 guideline as a framework to guide our investigation of a wider range of antihypertensive medications expected for routine use.

239

240 *Statistical Analysis*

241 First, to examine availability, cost, and prescription of antihypertensive medications at
242 different types of PHC sites, we calculated percentages for categorical variables, and
243 mean and standard deviations or median and interquartile ranges (IQRs) for
244 continuous variables, as appropriate. To determine site-specific characteristics
245 associated with the availability of antihypertensive medications, we used a mixed
246 model with township/community as random effects and a logit-link function. The
247 model included a spherical covariate structure to account for spatial autocorrelation
248 and differences among townships/communities. The final model included 6
249 characteristics beside type of sites and regions, i.e. density of healthcare professionals,
250 licensed physicians, physicians with a medical bachelor degree (5-year medical
251 education), physicians who took continuing education course in the last year, social
252 insurances for contracted healthcare professional, healthcare professionals who
253 routinely use of IT system (Appendix 3a).

254

255 Secondary, we modeled the prescribed medication as a function of its cost, both
256 overall and rural/urban subgroups. To address potential sampling variation and
257 imbalances in number between electronic and scanned-copy–abstracted prescriptions,
258 we adapted a resampling approach to conducting a simulation analysis with a
259 nonparametric bootstrap method.[26,27] Specifically, for scanned-copy–abstracted
260 prescription data, we randomly selected records with a sample size equal to the total

number of records; for electronic prescription data, we randomly selected a sample size equal to the sample size of the scanned-copy–abstracted prescription data. We then appended the two resampled datasets together and fitted the mixed model to estimate the association between the medication's prescription and its cost. We repeated this process 10,000 times to obtain the distributions of the estimated associations and their 95% confidential intervals (CIs).

All analyses were conducted using SAS 9·4 (SAS Institute Inc., Cary, North Carolina). All statistical testing was 2-sided, at a significance level of 0·05. The Fuwai Hospital Institutional Review Board approved the study; the site survey was deemed exempt; informed consent was obtained from all MPP study participants.

Role of funding source

The funders of the study had no role in its design, data collection, data analysis, data interpretation, or writing of the report. The corresponding and lead authors had full access to all the data in the study, and all authors had final responsibility for the decision to submit for publication.

Results

Study Sample

The study sample included 3362 PHC sites (18% urban, 82% rural) across China (Appendix 4). Site characteristics are shown in Table 1. Township health centres

283 constituted 8% of sites, village clinics 74%, community health centres 6%, and
284 stations 12%.
285
286 The 435 townships/communities, which collectively enrolled 1·09 million people in
287 the China PEACE MPP, served as the study sample for determining hypertension
288 treatment and control rates. The median sample size of participants at the
289 township/community level was 2128 (IQR: 1165-3103). Participant characteristics are
290 shown in Table 1.
291
292 *Availability, Cost, and Prescription Patterns of Antihypertensive Medications*
293 Among the 3362 centres, the availability of agents by class was 76% for CCBs, 63%
294 for ACEIs, 60% for diuretics, 47% for beta-blockers, 34% for ARBs, and 10% for
295 fixed-dose combinations (Table 2). The most commonly stocked medications in each
296 class were nifedipine extended release (41%), captopril (44%), hydrochlorothiazide
297 (35%), metoprolol (41%), valsartan (21%), and the fixed-dose combination of
298 irbesartan and hydrochlorothiazide (6%) (Table 2). Compounds containing TCM were
299 available in 56% of the PHC pharmacies.
300
301 The pattern of medication availability varied by site. Overall, 8% of PHC pharmacies
302 did not have any antihypertensive medications; 89% stocked either ACEIs/ARBs,
303 beta-blockers, CCBs, or diuretics; and 34% had all four classes of medications (Figure
304 1).

Availability, defined as having any class of medication, was associated with type of site and economic region (Appendix 5), and adjusted for other PHC–specific characteristics. Township health centres were more likely and sites in the western region were less likely to stock any kind of antihypertensive medication; village clinics and sites in the western region were also less likely to have all four classes (Figure 1). Urban sites prescribed ARBs more frequently than rural sites. Within rural and urban sites, however, there was substantial variation in the availability of medications, and no characteristic besides types of PHC sites and region was strongly associated with their availability (Appendix 3b).

Individual medication median annual cost per patient varied substantially (Table 2). The median annual cost of the most-stocked medications in each of the most commonly used classes were nifedipine extended release (412 RMB), captopril (16 RMB), hydrochlorothiazide (3 RMB), metoprolol (251 RMB), valsartan (663 RMB), and irbesartan and hydrochlorothiazide (1152 RMB). Figure 2 shows the medications in value quadrants, according to their guideline-recommended status and their cost. Only 33% of all sites stocked medications in the high-value care category.

Across 396 townships/communities, we sampled 26,159 of 518,915 hypertension prescriptions. The most commonly prescribed individual medication was amlodipine; the most frequently prescribed medicine classes were CCBs (45%), ARBs (22%),

beta-blockers (10%), ACEIs (9%), and diuretics (5%) (Table 2). Overall, 86% of prescriptions were for one medication, whereas less than 1% were for three or more medications. When at least two medications were used, fixed-dose combinations (39%), ACEI plus CCB (18%), and ARB plus CCB (17%) were most commonly prescribed together (Appendix 6). In all, 2234 prescription records (8%) were for non–guideline-recommended medications, 3276 (11%) for high-value medications, and 23,603 (81%) for higher-cost, guideline-recommended medications (Figure 2).

Treatment Rates and Hypertension Control Rates

The sites varied by treatment and control rates (Appendix 7). The median risk-standardized treatment and control rates were 35·6% and 8·3%, respectively. The worst 10% of sites had risk-standardized median treatment and control rates of 4·2% and 1·2%, respectively, whereas the best 10% had rates of 72·7% and 30·0%.

Cost and Availability

The cost of a medication was directly associated with being prescribed (Figure 3 and Appendix 8), but not with its availability (Figure 3). On average, higher-cost medications were more likely than lower-cost medications to be prescribed in PHC clinics. Lower-cost medications accounted for 40·5% of the medications in the pharmacies. Of all the prescriptions, 12·6% were for lower-cost medications and 4·8% were for diuretics, the lowest-cost medication.

Discussion

This national study of antihypertensive medications in China reveals marked deficiencies in the availability, cost, and prescription of antihypertensive medications. First, hypertension medications are inconsistently available in PHC pharmacies across China, and 1 in 12 pharmacies did not stock any antihypertensive medications. Second, despite the availability of low-cost antihypertensive medications, higher-cost medications were more often prescribed. In fact, the higher the cost of the medication, the more likely that it was prescribed. The higher-cost medications did not represent medications with higher efficacy.

This study adds to the literature in important ways. It is the first national study of the availability, cost, and prescription of antihypertensive medications in China, involving all provinces. National policies with regard to essential medications and reimbursement may aim to improve access;[28] this study provides a contemporary assessment of the availability and use of antihypertensive therapies in PHC sites around the country and shows that deficiencies exist at the point of care. This study has the distinct strength of being based on actual investigations of the pharmacies and inspection of the prescriptions. Conducting this evaluation required government support, partnership with PHC providers and administrators, and site access to inspect pharmacies and examine prescriptions. The study did not depend on reports from the sites but, rather, involved direct data collection. Previous studies were limited to

specific regions, populations, and data sources.[14,29-32]

The reasons for gaps in the availability and prescription of antihypertensive medications are not clear. Chinese national policies dictate that essential medications should be available and affordable. However, we uncovered problems in the inventory of antihypertensive medication that can be supplied to patients at PHC sites. Despite the national focus on blood pressure control — and the responsibility of many of the sites for hypertension management[33] — a significant proportion of these pharmacies either lacked any antihypertensive medication or had limited stocks, especially for lower-cost medications.[13] One possible contributor to our finding that low-cost, high-value medications are not frequently prescribed is the zero mark-up policy. Initiated in 2009, this policy prohibits health care providers from selling essential medicines at prices higher than their wholesale cost. This policy reportedly exerted a large net effect on the revenue of village clinics, despite increased government subsidies increased to compensate for revenue loss.[34,35] Some have suggested that these reforms may have led to a less reliable drug supply system in China; for instance, village clinics, for instance, may no longer provide essential medicines at zero mark-up due to the lack of profit.[36] With respect to drug prescribing patterns, there has been an increase in the use of expensive medications that are not covered by the policy since its implementation.[10] Refinements to this policy may provide stronger incentives for the use of lower cost medications. Mandating the availability of medicines may not be sufficient to improve hypertension rates, but it is arguably a necessary component of

disease management programs. Additional studies are needed to carefully examine the impact from zero mark-up policies on access to antihypertensive medicines throughout Chinese primary healthcare centres.[11,37] Also, some patients and doctors may prefer antihypertensive TCM, though its use was generally low in our study.

The implications of this study for hypertension management in China are substantial. The reality of care delivery in the clinics is not consistent with the health needs of the nation, and the deficiencies in primary care pharmacies have implications for patient health, as evidenced by suboptimal treatment and control rates. As such, interventions to improve hypertension treatment and control will need to focus not only on bolstering education, screening, and protocols, but also on ensuring that antihypertensive medications are adequately stocked by PHC pharmacies.[38] The adequacy of the medication inventory is not sufficient for progress in hypertension treatment and control, but it is certainly a fundamental component. Policymakers will need to grapple with why the aspiration of national policies is being stymied at the local level and, likely, thwarting efforts by practitioners to address hypertension in their patients.

The study has some other important implications. The use of high-value medications, those that are guideline-recommended and reasonably priced, should be a priority for all countries but especially for those with limited resources.[39] This study finds that high-value medications are not preferentially used in Chinese PHC settings, even as

414 the evidence for the greater efficacy of higher-priced medications is lacking.[40] A
415 greater emphasis on high-value antihypertensive medications has the potential to
416 mitigate the cost burden of increasing the rates of treatment and providing more value
417 to the country. In this respect, diuretics may be particularly cost-effective. Prior
418 studies have suggested that drugs such as chlorthalidone may even be superior to
419 drugs from other classes.[23] In addition, too few comparative effectiveness studies of
420 antihypertensive agents have been conducted,[41] and it may be beneficial for China to
421 prioritize these studies: by identifying the higher-priced medications with known
422 marginal benefits over lower-cost alternatives, they would provide the basis for high-
423 quality, cost-efficient care.
424
425 The availability of antihypertensive medications varied among types of sites and
426 economic regions, but inadequacies were not confined to certain types of centres. Site
427 characteristics were not strongly associated with the availability of antihypertensive
428 medications. This finding indicates the need for a broad-based strategy that would
429 address problems that almost all types of PHC centres throughout China face.
430
431 The study has several limitations. First, the study sites are not a representative sample
432 despite spanning the entire country geographically and being so large in number. The
433 treatment and control rates, however, are very similar to national estimates.[5] Second,
434 we used a convenience sample and excluded people who were not permanent
435 residents. Those who were excluded would likely have less access to care and would

likely have had even lower control rates. Nevertheless, any inaccuracies in this study would be a bias toward the null, suggesting that our findings might even underestimate the relationship. Of note, the prescription information reflects all prescriptions, including those provided to migrants. Third, this study focused on pharmacies in PHC sites, and people may go elsewhere for their prescriptions. However, half of private pharmacies impose fees that individuals must pay out of pocket.[42] Therefore, we expect that most patients would have a strong preference to obtain their medications from the clinic pharmacy. Future studies should build on these and other emerging primary datasets in China to examine the association between access to antihypertensive medicines and clinical outcomes, including control rates. Fourth, our choice of the 200 RMB threshold for cost may be arbitrary, and it's true that threshold of 1% of annual disposal income may be higher for rural populations. Applying a lower cost threshold however would further restrict the sample of medicines that could be defined as 'high-value', and may therefore lower the percentage of high-value drugs prescribed, further strengthening our findings. Finally, the inventory and prescription data that was collected covered slightly different time periods. If one assumes that any large-scale change in prescription drug inventories and prescribing behaviors are marginal over the span of several months, the impact on this study from similar, albeit non-overlapping time periods for data collection may be negligible.

In conclusion, this study reveals key obstacles to progress in mitigating hypertension

458 in China. Despite advances in healthcare coverage and policy to limit financial risk
459 and improve health outcomes,[43] this study reveals deficiencies in the availability, cost,
460 and prescription of antihypertensive medications. Future policies aimed at alleviating
461 the burden of hypertension in China, particularly through the work of PHC providers,
462 will need to improve access to high-value antihypertensive medications.
463

464 **Declaration of Interests**

465 HMK discloses that he is a recipient of research agreements from Medtronic and from
466 Johnson & Johnson (Janssen), through Yale, to develop methods of clinical trial data
467 sharing; is the recipient of a grant from the Food and Drug Administration and
468 Medtronic, through Yale, to develop methods for post-market surveillance of medical
469 devices; works under contract with the Centers for Medicare & Medicaid Services to
470 develop and maintain performance measures; chairs a cardiac scientific advisory
471 board for UnitedHealth; is a participant/participant representative of the IBM Watson
472 Health Life Sciences Board; is a member of the Advisory Board for Element Science
473 and the Physician Advisory Board for Aetna; and is the founder of Hugo, a personal
474 health information platform. All other authors declare no competing interests.
475

476 **Contributors Statement**

477 LJ and HMK conceived the study and take responsibility for all aspects of it. MS, QZ,

LJ and HMK initially designed the survey, with the support from EM, GAM, XL and JL. Meng Su and QZ wrote the first draft. XB, CW, YL, SSV and AZ provided data management and statistical analysis. LJ, HMK, EM, GAM, MAF, SSV, AZ, KN and YL provided comments and suggestions in critical revision of the article. All authors approved the final version of the article.

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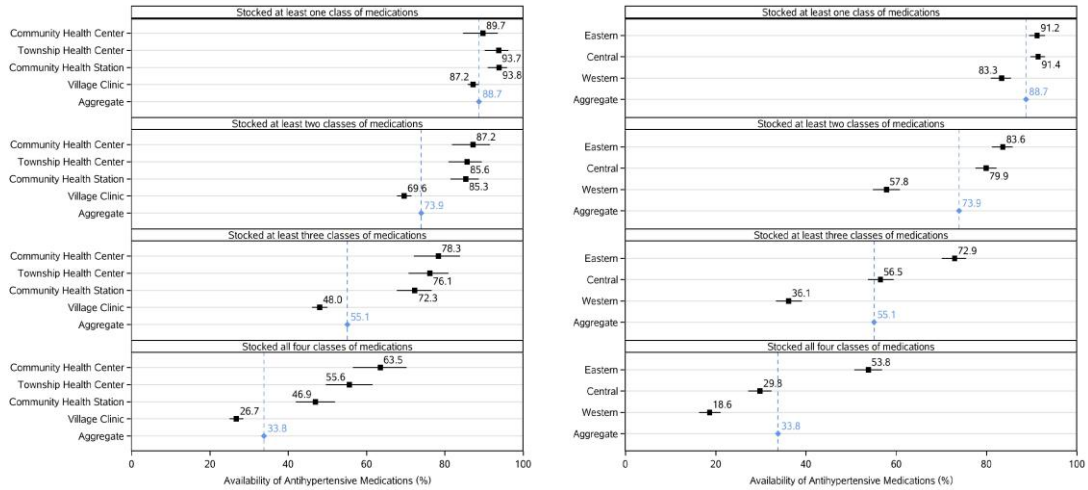


Figure 1: Availability of antihypertensive medicines by type of site and economic region

Note:

Data are shown in point estimates with 95% confidence intervals.

Classification of the three economic regions is shown in Appendix 5.

Figure 2: Availability and prescription of medications, by value quadrants

Note:

x-axis: Chinese Guideline for Hypertension Management in Primary Health Care 2014.

y-axis: Annual cost of medication per patient (RMB).

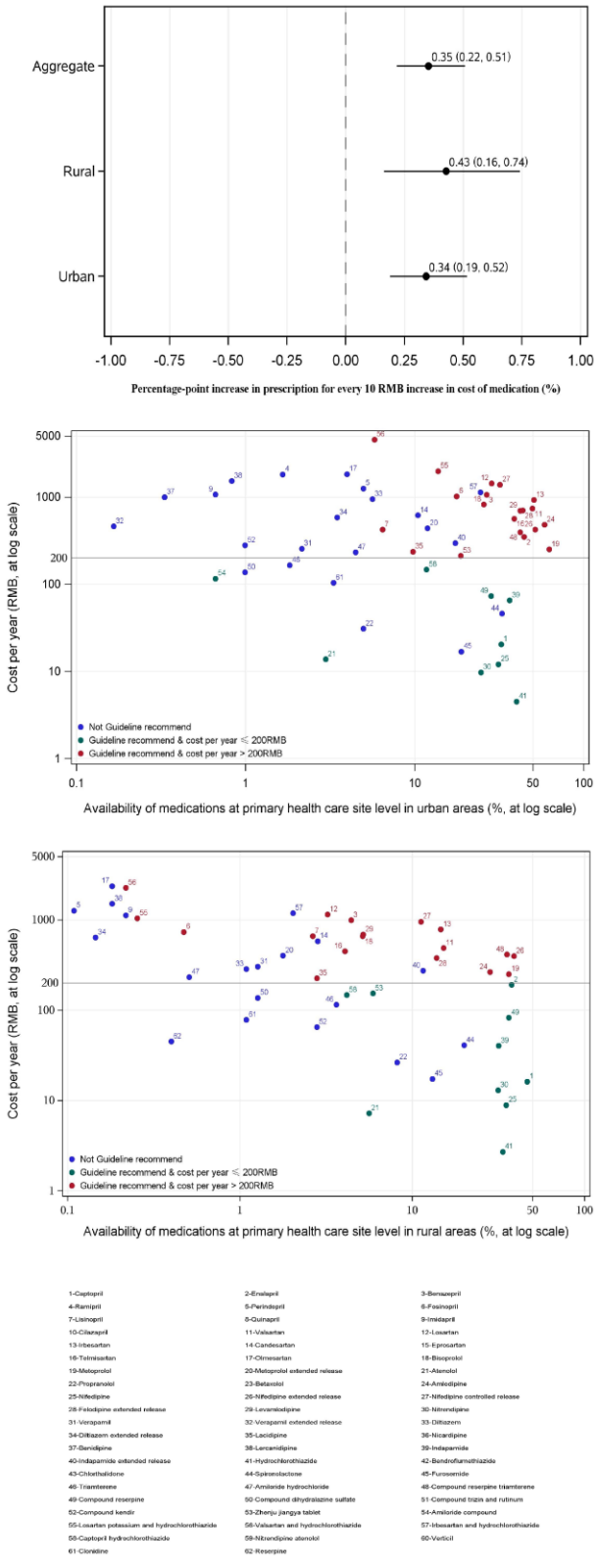


Figure 3: Association of annual cost per patient with availability and prescription pattern of antihypertensive medication

650 **Table 1.** Characteristics of primary health care sites and MPP population included by

651 rural and urban area

	Rural		Urban		Total
	Township health centre	Village clinic	Community health centre	Community health station	
Primary health care site					
N	284	2474	203	401	3362
Region (%)					
Eastern	28·5	27·8	38·9	56·4	31·9
Central	31·0	39·8	29·1	15·7	35·6
Western	40·5	32·4	32·0	27·9	32·5
Linked MPP population (%)					
N	613638		478393		1092031
Age, mean (SD)	56·2 (9·8)		55·8 (9·8)		56·0 (9·8)
Female	59·6		60·9		60·1
Ethnic Han	88.8		93.3		90.8
12-year education or above	9·4		32·3		19·5
Never smoked	11·8		16·3		13·8
No insurance	0·2		1·1		0·6
Last-year income >50K	8·6		18·3		12·8
Hypertensive patients	46·4		44·1		45·4
Awareness*	43·8		48·7		45·9
Treatment*	27·1		34·5		30·3
Control*	5·5		9·8		7·3

652 * Among all hypertensive patients ·

Table 2. Availability of individual and classes of medications among all primary health care sites

Type	Generic name	EM list*			Guidelines			Availability (%) (n=3362)	Class availability (%) (n=3362)	Median annual cost (RMB) per patient (IQR)	Prescription frequency (%)
		WHO	NEM	PSEM	Guideline in primary health care 2014	JNC 8 2014	Chinese guideline 2010				
ACEI	Captopril		✓	1	✓	✓	✓	44·0	62·6	16 (11-43)	2·5
	Enalapril	✓	✓	1	✓	✓	✓	38·9		225 (160-435)	4·2
	Benazepril			13	✓		✓	8·4		1066 (748-1144)	1·2
	Ramipril			1			✓	0·4		1819 (1819-2021)	0
	Perindopril			3			✓	1·0		1255 (1172-1261)	0·2
	Fosinopril			7	✓		✓	3·6		1022 (723-1054)	0·7
	Lisinopril			2	✓	✓	✓	3·3		659 (469-678)	0·1
	Quinapril			1				0·0		1166 (1166-1166)	<0·1
	Imidapril			1			✓	0·3		-	0
	Cilazapril			0			✓	0		-	0
ARB	Valsartan		✓	15	✓	✓	✓	21·4	34·4	663 (340-1028)	7·4
	Losartan			7	✓	✓	✓	7·8		1306 (942-1883)	2·1
	Irbesartan			13	✓	✓	✓	21·1		850 (610-1101)	6·7
	Candesartan			1		✓	✓	4·2		589 (468-751)	1·0
	Eprosartan			0		✓		0		-	0
	Telmisartan			7	✓		✓	10·3		516 (298-801)	4·3
	Olmesartan			0			✓	0·9		1833 (1761-2660)	0·2
ACEI/ARB									69·0	-	
beta-blocker	Bisoprolol	✓	✓	5	✓		✓	8·8	47·2	791 (549-1080)	0·9
	Metoprolol	✓		8	✓	✓	✓	41·0		251 (171-281)	8·0
	Metoprolol extended release			0			✓	3·6		438 (401-440)	0·2
	Atenolol	✓		1	✓	✓	✓	5·1		7 (5-8)	0·2
	Propranolol			2			✓	7·6		26 (16-86)	0·0
	Betaxolol			0			✓	0		-	0
CCB	Amlodipine	✓	✓	23	✓	✓	✓	33·8	75·5	369 (206-565)	16·8
	Nifedipine		✓	16	✓		✓	34·4		9 (5-19)	2·7
	Nifedipine extended release		✓	0	✓		✓	41·2		413 (266-468)	7·4
	Nifedipine controlled-release			0	✓		✓	15·0		1012 (890-1526)	6·0
	Felodipine extended release			15	✓		✓	19·2		425 (313-1049)	3·7
	Levamlodipine			9	✓		✓	11·8		688 (437-904)	7·7
	Nitrendipine		✓	1	✓	✓	✓	30·3		12 (7-44)	1·0

Type	Generic name	EM list*			Guidelines			Availability (%) (n=3362)	Class availability (%) (n=3362)	Median annual cost (RMB) per patient (IQR)	Prescription frequency (%)
		WHO	NEM	PSEM	Guideline in primary healthcare 2014	JNC 8 2014	Chinese guideline 2010				
	Verapamil			4			✓	1·4		302 (288-360)	0
	Verapamil extended release			0			✓	0·0		-	0
	Diltiazem			11			✓	1·9		507 (269-1117)	0
	Diltiazem extended release			0		✓		0·7		583 (527-869)	0·1
	Lacidipine			7	✓		✓	4·0		228 (225-273)	0·3
	Nicardipine			1			✓	0		-	0
	Benidipine			0			✓	0·1		-	0
	Lercanidipine			0			✓	0·3		-	0
Diuretics	Indapamide		✓	1	✓	✓	✓	32·6	59·9	42 (18-99)	1·2
	Indapamide extended release			0			✓	12·6		279 (197-389)	1·3
	Hydrochlorothiazide	✓		1	✓	✓	✓	34·7		3 (1-5)	1·0
	Bendroflumethiazide			0		✓		0		-	0
	Chlorthalidone			0		✓		0		-	0
	Spironolactone			2			✓	22·3		41 (28-56)	0·5
	Furosemide			1			✓	14·1		17 (16-25)	0·5
	Triamterene			1			✓	3·3		115 (58-158)	0
	Amiloride hydrochloride			0			✓	1·2		232 (232-232)	0
Compound containing TCM ingredients†	Compound reserpine triamterene		✓	1	✓		✓	36·6	55·6	414 (299-435)	2·7
	Compound reserpine		✓	1	✓		✓	34·9		80 (54-158)	0·6
	Compound dihydralazine sulfate			2				1·2		137 (137-158)	<0·1
	Compound trizin and rutinum			1				0·1		-	0
	Compound kendir			1				2·5		65 (63-194)	0
	Zhenju jiangya tablet			7	✓		✓	8·2		178 (130-269)	0·8
Fixed-dose combination	Amiloride compound			2	✓			0·1	10·4	116 (116-116)	<0·1
	Losartan potassium and hydrochlorothiazide			1	✓		✓	2·7		1983 (895-2427	1·6
	Valsartan and hydrochlorothiazide			0	✓		✓	1·2		3750 (1726-4720)	<0·1
	Irbesartan and hydrochlorothiazide			1			✓	6·1		1136 (805-1609)	3·1
	Captopril hydrochlorothiazide			6	✓		✓	5·5		147 (66-197)	0·2
	Nitrendipine atenolol			0	✓		✓	0		-	0
Centrally active	Verticil			1			✓	0·1	2·3	588 (588-588)	0·1
	Clonidine			2			✓	1·5		-	0

Type	Generic name	EM list*			Guidelines			Availability (%) (n=3362)	Class availability (%) (n=3362)	Median annual cost (RMB) per patient (IQR)	Prescription frequency (%)
		WHO	NEM	PSEM	Guideline in primary health care 2014	JNC 8 2014	Chinese guideline 2010				
drugs	Reserpine			15			✓	0·4		45 (45-45)	0·2

Data are number, median (IQR) or %. **IQR:** interquartile ranges

*** Essential lists:**

WHO: WHO Model Lists of Essential Medicines

NEM: National Essential Medicine List

PSEM: provincial supplementary essential medicine lists (value refers to the number of provinces that had this medication in its provincial list)

† **Ingredients per tablet for compound containing TCM:**

Compound reserpine triamterene: reserpine 0·1 mg, triamterene 12·5 mg, hydrochlorothiazide 12·5 mg, dihydralazine 12·5 mg

Compound reserpine: reserpine 0·032 mg, hydrochlorothiazide 3·1 mg, dihydralazine 4·2 mg, promethazine 2·1 mg

Compound dihydralazine sulfate: dihydralazine sulfate 10·0 mg, hydrochlorothiazide 12·5 mg, reserpine 0·1 mg

Compound trizin and rutinum: hydrochlorothiazide 2·0 mg, dihydralazine sulfate 1·5 mg, rutinum 5·0 mg, reserpine 0·03 mg

Compound kendir: kendir 220 mg, dihydralazine sulfate 1·6 mg, hydrochlorothiazide 1·6 mg, promethazine 1·05 mg

Zhenju jiangya tablet: clonidine 0·03 mg, hydrochlorothiazide 5·0 mg

List of Appendices

Appendix 1. Major policies about essential medications' availability and affordability since 2009

Chinese health reform in 2009 introduced the National Essential Medicine Program that was designed to "provide affordable and equitable basic health care for all by 2020." It includes: 1) introduction of a national essential medicine list at primary health care level; 2) establishing province-based competitive-bidding system; 3) dispensing of essential medicines at zero mark-up, and 4) reimbursement mechanism by health insurance. The pharmaceutical policy has also evolved quickly in recent years, major policies about essential medications' availability and affordability since 2009 are shown as follows:

Year	Department	Policy
2009	MOH	Opinion on establishing essential medicine regime
	MOH	National Essential Medicine List (2009)
	CFDA	Notice on strengthening production and quality monitoring in essential medicines
	MIIT	Notice on strengthening in supply of essential medicines
	MOH; NDRC; MOF	Working specification in medicine procurement
2010	State council	The guidance in establishing and normalizing the medicine procurement mechanism among government-sponsored primary health care sites
	MOH	National Essential Medicine List (2012)
2012	MIIT	Fixed-point production in medicines with small dosage but essential for clinical treatment
	8 Ministries[1]	Opinion on ensuring the supply of the commonly-used low-cost medicines
2014	NHFPC	Opinion on strengthening the storage and use of medicines among primary health care sites
	7 Ministries[2]	Notice in promoting the price reform of medicines

Abbreviations:
MOH: Ministry of Health
CFDA: China Food and Drug Administration
MIIT: Ministry of Industry and Information Technology
NDRC: National Development and Reform Commission
NHFPC: National Health and Family Planning Commission
MOF: Ministry of Finance
MHRSS: Ministry of Human Resources and Society Security
MOC: Ministry of Commerce
CFDA: China Food and Drug Administration
SATCM: State Administration of Traditional Chinese Medicine

***Note**: [1]: including NHFPC, NDRC, MIIT, MOF, MHRSS, MOC, CFDA, SATCM; [2]: including NDRC, NHFPC, MHRSS, MIIT, MOF, MOC, CFDA*

Appendix 2. A brief introduction of the health system in China

Organization

Health service institutions in China include hospitals, primary health care (PHC) institutions and specialized public health institutions (Appendix Figure 1). The primary health care system in China is divided into urban and rural components, which are organized differently. Urban areas include community health centres and, one level below them, community health stations (i.e. local clinics). Rural areas include township health centres and, one level below them, village clinics. In 2016, primary health care institutions comprised of 94% of all health care institutions.

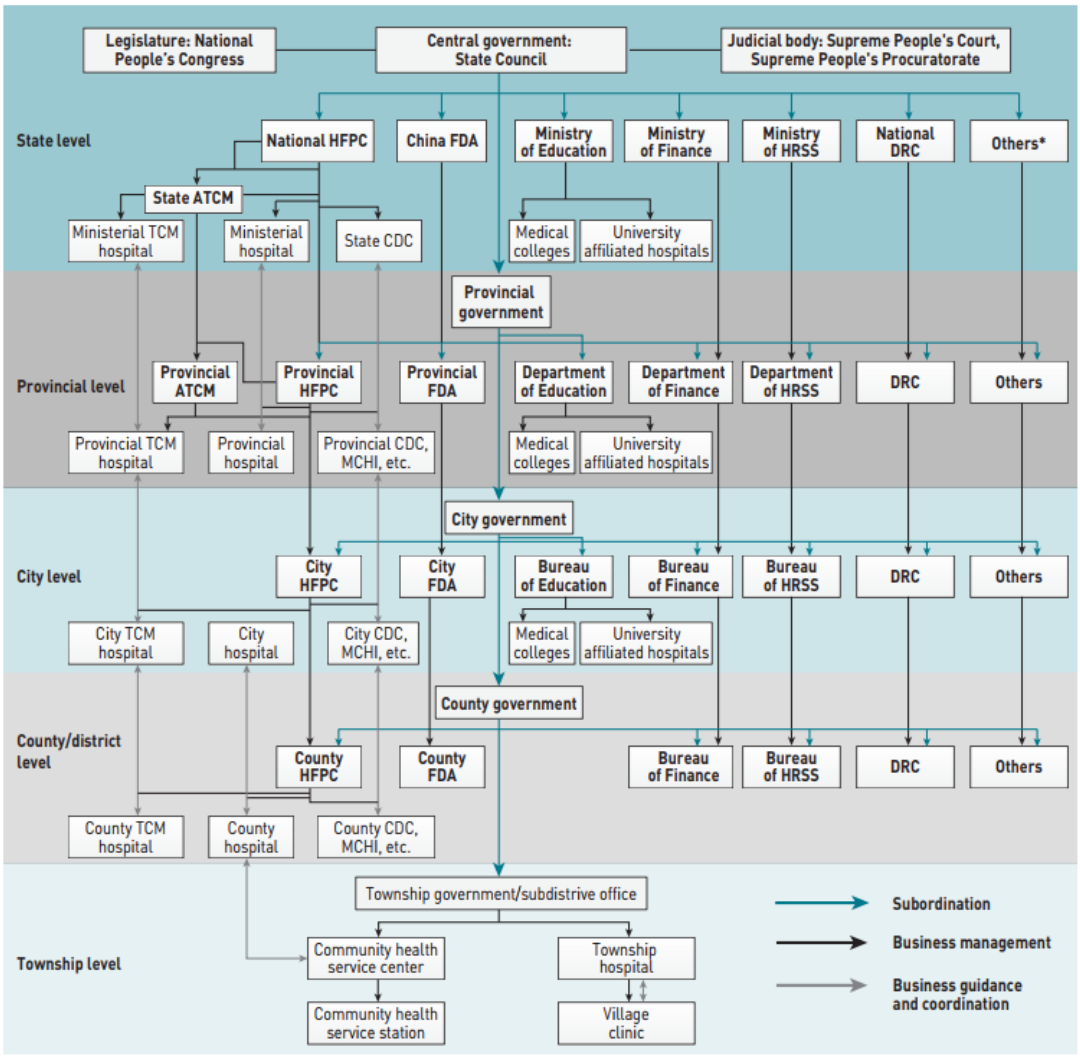
Management

The administration and management relationship between PHC institutions is relatively complex. For example, urban community health stations can either be affiliated with community health centres in the same community, or independent from them; in the latter case, however, the health stations may still receive technical support from the health centres. Similar to health stations in the urban areas, village clinics can be either affiliated with the rural township health centres, or independent from them. In some circumstances, village clinics can be private health institutions that do not fall within the government budget plan. In general, the national and local government health departments supervise and administer the PHC institutions. Professional disease prevention institutions such as the Center for Disease Control and Prevention (CDC) provide technical support and guidance.

Services

Primary health care institutions in China are responsible for providing both basic clinical care and public health services to local residents. In 2015, they provided 4.1 billion outpatient visits and 40.3 million hospitalizations, which accounted for 55.6% and 19.2% of the total utilization in the health care system. They are also the main executor of the National Essential Public Health Service Program aiming to provide 3 categories and 12 subcategories of basic public health services to all residents for free.

Organization of the health system in China



* Others include Ministry of Civil Affaires, Insurance Regulatory Commission, etc.
HFPC: Health and Family Planning Commission;
FDA: Food and Drug Administration;
HRSS: Human Resource and Social Security;
DRC: Development and Reform Commission;
ATCM: Administration of Traditional Chinese Medicine;
CDC: Center of Disease Control;
MCHI: Maternal and Children Health Institution.

***Source**: This figure is cited from Meng Q et al.: People's Republic of China Health System Review; 2015. We used the original figure with the authors' permission.*

Appendix 3a. Definition of six site-specific characteristics

Site-specific characteristics	Definition
Density of healthcare professionals*	Total number of healthcare professionals per 10,000 residents
Licensed physicians	Proportion of primary physicians who are licensed among all healthcare professionals
Physicians with medical bachelor degree	Proportion of physicians who have a medical bachelor degree (i.e. with at least 5-year medical education in medical school)
Physicians took continuing education causes in the last year	Proportion of physicians who have taken continuing education courses in the last year
Social benefits for contracted healthcare professionlas	Number of social benefits for contracted healthcare professionals (i.e. those professionals without permanent position)
Healthcare professionals who use IT system routinely†	Proportion of healthcare professionals who use IT systems† routinly

Note:

*Healthcare professionals include physicians, public health workers and nurses who work in the primary health care setting; †*IT: Information technology*

Appendix 3b. Association of availability with site type, economic region and sit-specific characteristics

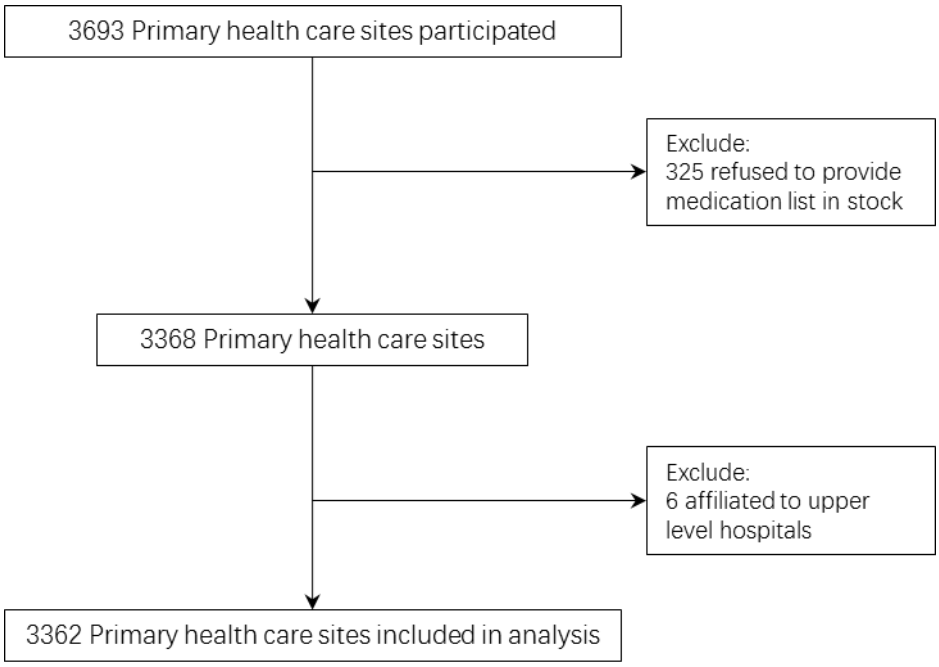
	Adjusted odd ratio (95% CI)
Type of site	
Rural township health centre	1
Urban community health station	0.35 (0.12-1.02)
Urban community health centre	0.15 (0.05-0.40)
Village clinic	0.35 (0.14-0.89)
Region	
Central	1
West	0.34 (0.13-0.89)
East	1.21 (0.47-3.11)
Site characteristics	
Total number of healthcare professionals per 10,000 residents*	1.02 (0.99-1.04)
Proportion of physicians who are licensed	0.98 (0.97-0.99)
Proportion of physicians with medical bachelor degree	0.95 (0.92-0.98)
Proportion of physicians who took continuing education courses in the past year	1.43 (1.24-1.65)
Number of social benefit schemes for contracted healthcare professionals	1.00 (1.00-1.00)
Proportion of healthcare professionals who use IT systems routinely†	1.02 (1.01-1.02)

Note:

**Healthcare professionals include physicians, public health workers and nurses who work in the primary health care setting*

†IT: Information technology

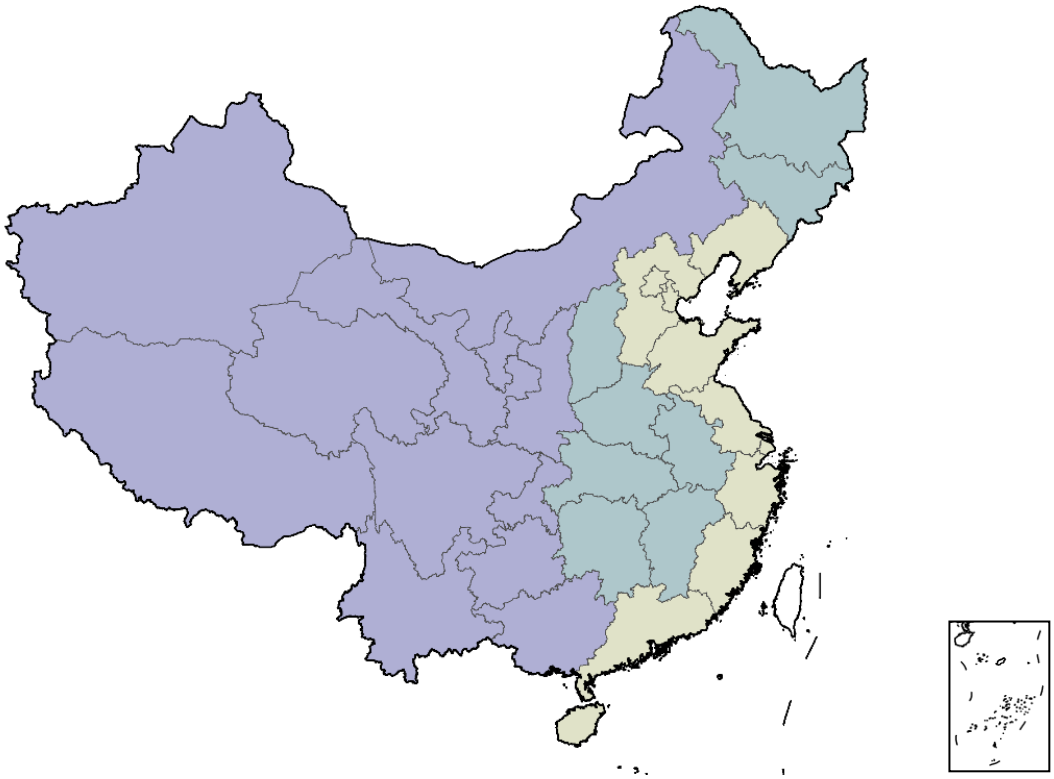
Appendix 4. Flowchart of study participant selection



Appendix 5. List of provinces by economic regions

Eastern region includes 11 provinces and municipalities: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan.
Central region includes 8 provinces: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan.
Western region includes 12 provinces, autonomous regions and municipalities: Inner-Mongolia, Chongqing, Guangxi, Sichuan, Guizhou, Yunnan, Tibet, Shannxi, Gansu, Qinghai, Ningxia, and Xinjiang.

Distribution of three economic regions is shown as the following figure:



Note:

Eastern region (grey); Central region (navy); Western region (mazarine)

Appendix 6. Treatment pattern by type of primary health care site

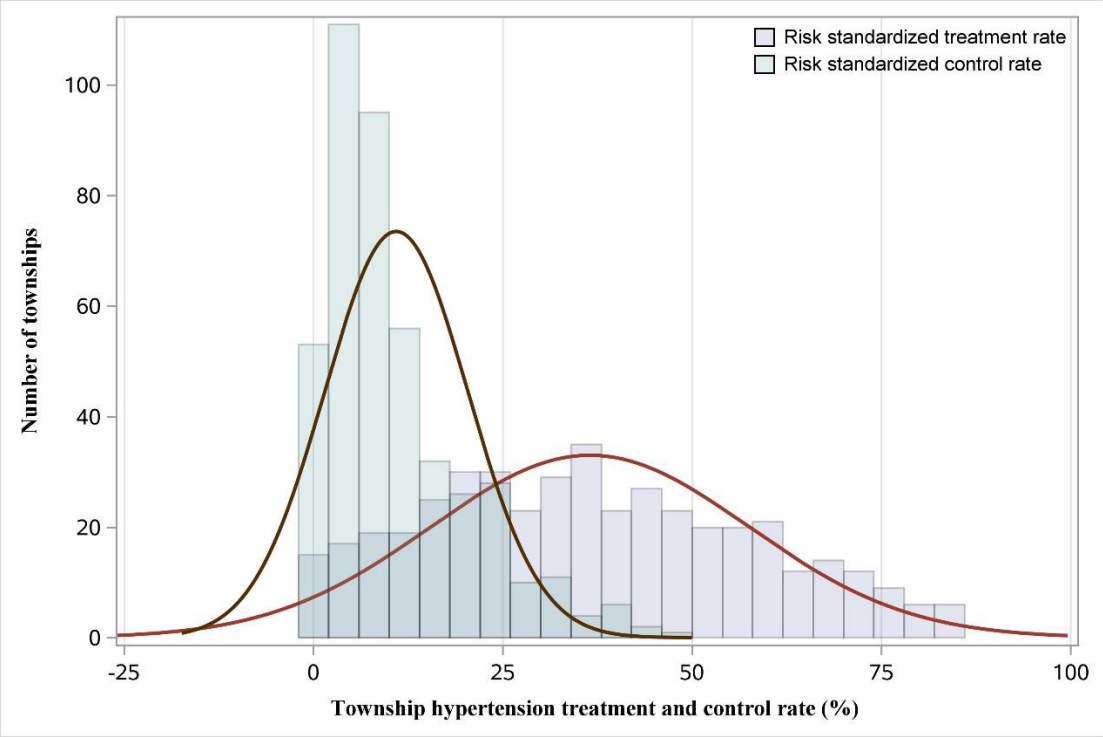
	Total	Township health centre	Community health centre
Anti-HTN medication record number	29,171	18,993	10,178
Overall (%)*			
ACEI	9·1	6·0	14·9
ARB	21·7	24·7	163
β-blocker	9·4	10·4	7·6
CCB	45·6	46·8	43·4
Diuretic	4·7	3·1	7·7
Compound containing TCM	4·2	2·2	8·0
Fixed-dose combination	4·9	6·9	1·3
CAD	0·3	0·0	0·9
HTN prescription number	26,159	17,752	8407
Monotherapy (%)†	86·2	88·2	81·9
ACEI	7·9	5·7	12·7
ARB	23·5	26·4	16·9
β-blocker	9·3	10·6	6·4
CCB	49·8	51·9	45·2
Diuretic	4·2	3·0	7·0
Compound containing TCM	4·9	2·5	10·5
CAD	0·4	0·0	1·2
Two medicines (%)†	13·0	11·2	16·8
ACEI plus CCB	18·3	8·1	32·8
ARB plus CCB	17·0	12·4	23·5
ACEI plus Diuretic	2·2	0·8	4·2
ARB plus Diuretic	2·1	1·3	3·3
CCB plus Diuretic	3·5	1·5	6·2
CCB plusβ-blocker	9·3	7·9	11·4
Fixed-dose combination	38·9	61·9	6·4
ACEI plus ARB	0·4	0·3	0·6
Three or more medicines (%)†	0·8	0·6	1·3
ACEI/ARB plus CCB plus Diuretic	12·7	8·6	16·8
ACEI/ARB plus CCB+Diuretic plusβ-blocker	2·8	1·9	3·7

Note:

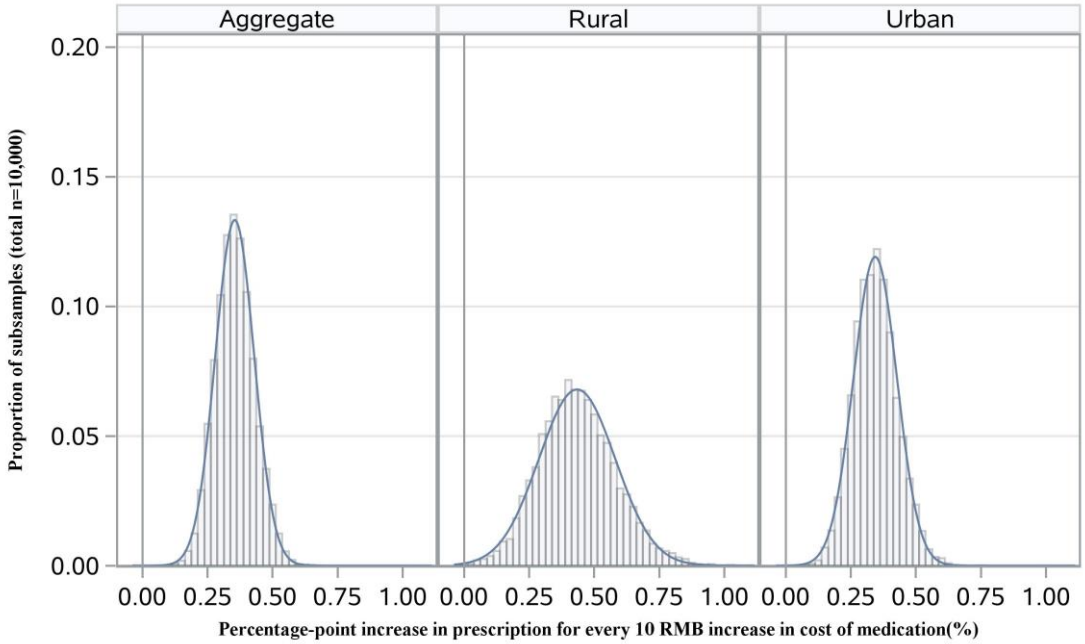
** Use Anti-HTN medication record number as denominator. The results of the following subcategory of medication use were the proportion among in certain treatment pattern*

† Use HTN prescription number as denominator. The results of the following subcategory of medication use were the proportion in this certain treatment pattern

Appendix 7. Distribution of risk-standardized treatment and control rates



Appendix 8. Distribution of coefficients in Figure 3a



Note: Analysis is based on 10,000 times of simulation.

Appendix 9. The Members of Provincial Coordinating Office in China PEACE Million Persons Project

Beijing Center for Diseases Prevention and Control: Chun Huang, Bo Jiang; **Tianjin Chest Hospital**: Zhigang Guo, YingYi Zhang; **Hebei Center for Diseases Prevention and Control**: Jingbo Zhai, Yuhuan Liu; **Shanxi Center for Diseases Prevention and Control**: Zhikai Chai, Yaqing Meng; **Inner Mongolia Center for Diseases Prevention and Control**: Namuheng, Yunfeng Xi; **Liaoning Center for Diseases Prevention and Control**: Chunming Lu, Ning Li, Leilei Pan; **Jilin Center for Diseases Prevention and Control**: Jianwei Liu, Yao Fu, Ting Liu; **Heilongjiang Center for Diseases Prevention and Control**: Shichun Yan, Lin Zhan; **Shanghai Center for Diseases Prevention and Control**; **Jiangsu Center for Diseases Prevention and Control**: Jinyi Zhou, Yu Qin; **Zhejiang Hospital**: Wei Yu, Xiaoling Xu, Li Yang; **Anhui Center for Diseases Prevention and Control**: Zhirong Liu, Luan Zhang; **Fujian Center for Diseases Prevention and Control**: Shuguang Lin, Xin Fang; **Jiangxi Center for Diseases Prevention and Control**: Liping Zhu, Yan Xu; **Shandong Center for Diseases Prevention and Control**: Xiaolei Guo, Junli Tang; **Henan Center for Diseases Prevention and Control**: Gang Zhou, Lei Fan; **Hubei Center for Diseases Prevention and Control**: Shuzhen Zhu, Junfeng Qi; **Hunan Center for Diseases Prevention and Control**: Biyun Chen, Li Yin; **Guangdong Center for Diseases Prevention and Control**: Yingqing Feng, Xida Li; **The First Affiliated Hospital of Guangxi Medical University**: Hong Wen; **Hainan Center for Diseases Prevention and Control**: Dan Wang, Puyu Liu; **Chongqing Center for Diseases Prevention and Control**: Wenge Tang, Xianbin Ding; **Sichuan Center for Diseases Prevention and Control**: Ying Deng, Jun He, Xiaoqi Gao; **The People's Hospital of Guizhou Province**: Guie Liu, Chenxi Jiang; **Yunnan Center for Diseases Prevention and Control**: Shun Zha, Cangjiang Yang; **Tibet Center for Diseases Prevention and Control**: Guoxia Bai, Yue Yu; **Shaanxi Center for Diseases Prevention and Control**: Jingang Ma, Rong Liu; **Gansu Center for Diseases Prevention and Control**: Xinhua Wang, Tingcai Wang; **Qinghai Center for Diseases Prevention and Control**: Minru Zhou, Xiaoping Li; **Ningxia Center for Diseases Prevention and Control**: Jianhua Zhao, Shaoning Ma; **The First Affiliated Hospital of Xinjiang Medical University**: Yitong Ma, Ying Huang, Yuchen Zhang; **Xinjiang Corps Center for Diseases Prevention and Control**: Fanka Li, Jiacong Shen.