Original Article

Elderly patients with comorbid hypertension who prefer primary care have a lower rate of polypharmacy: A cross-sectional study in Shanghai, China

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SUMMARY   In 2017, the World Health Organization highlighted polypharmacy as one of the key focus areas of the Global Patient Safety Challenge on Medication Safety. According to the experience of developed countries, the provision of primary pharmaceutical care plays a very important role in the intervention of polypharmacy in the elderly. It is necessary to assess the associations between elderly polypharmacy status and primary care in developing countries. The findings of this paper provide the prevalence of polypharmacy in patients with comorbid hypertension, and the factors associated with it. A total of 19,332 elderly patients with hypertension were completed, among which the mean (SD) number of diseases was 4.83 (1.99), the mean (SD) daily maximum number of drugs was 5.13 (2.89), and the rate of polypharmacy was 50.5%. Age, living areas, total number of visits, preference for medical institutions and the number of diseases were associated with polypharmacy. Among them, advanced age, greater number of visits and diseases are the risk factors of polypharmacy for elderly patients with comorbid hypertension. The rate of polypharmacy in patients who intend to seek treatment in community healthcare centers is low. A total of 9,603 pharmaceutical workers worked in Shanghai public hospitals in 2020, among them 52.0% worked in the central city area, and more than 70% worked in secondary and tertiary hospitals. There was a large mismatch between patients' medical preference and the number of pharmaceutical personnel. As a consequence, it is necessary to strengthen the development of community pharmaceutical care in primary medical institutions for elderly polypharmacy management.

Keywords   polypharmacy, the elderly, comorbid hypertension, visit preference, primary pharmaceutical care

1. Introduction

In 2017, the World Health Organization (WHO) highlighted polypharmacy as one of the key focus areas of the Global Patient Safety Challenge on Medication Safety (*1-2*). Due to the decrease of physiological function, the elderly have a high prevalence of chronic diseases, often complicated with multiple underlying diseases, and need to take long-term medication, becoming the key population to deal with the challenge of polypharmacy. Studies have shown that, in the U.S., 20% of Medicare elderly patients have 5 or more chronic diseases, and 50% of them receive 5 or more medications (*3*). In a survey of 2,707 elderly European patients with an average age of 82.2 years, 51% used more than 6 drugs (*4*). According to a survey of 300

thousand Koreans aged 65 and above, 86.4% of them have multiple drug use problems (*5*). Concern regarding possible harm of excessive prescribed medication for comorbid elderly has evolved into a research field covering the term "polypharmacy".

According to the experience of developed countries (Table 1), the important carrier to control the issue of polypharmacy is the two-way referral-based family doctors/pharmacists team, which carries out a comprehensive and systematic assessment of medication status of elderly patients, typically used interventions to reduce overall numbers of drugs or avoid certain categories of drugs thought to be inappropriate, decreasing polypharmacy and improving patient outcomes (*6-9*). This suggests that the provision of primary pharmaceutical care in primary health care

Table 1. Models of polypharmacy management for elderly in typical countries in the world

Country	Model	Content	Reference
the U.S.	Medication Therapy Management Services (MTMS)	Mainly including five core elements: Medication Therapy Review (MTR), Personal Medication Record (PMR), Medication-related Action Plan (MAP), Intervention and/or Referral (I & R) and Documentation and Follow-up (DFU).	Through pharmacists, patients are managed in the whole process of medicine
the UK	NHS pharmaceutical care	Essential Service (Dispensing of drugs, Repeat dispensing, Waste management, Public health, Signposting, Support for self-care and Clinical governance), Advanced Service, Enhanced Service.	Community based, providing continuous services with diversified contents
Germany	Family pharmacy contract	In 2004, the Health Insurance Fund signed a full health contract involving general practitioners, family physicians and family pharmacists, providing health promotion, rational prescription, pharmaceutical care, *etc.*	With the support of laws and regulations, a standardized pharmacist responsibility system has been established to ensure the orderly implementation of pharmaceutical care

(PHC) plays a very important role in the intervention of polypharmacy in the elderly.

As one of the countries with the most serious degree of aging, China's 7th National Census shows that the population aged 60 and over totaled 264.02 million, of which about 69% were patients with chronic diseases (*10*). Some studies have found that about 58.24% of elderly out-patients in China have multiple drug use (*11*). A survey of 426 hospitalized elderly patients in China showed that the average number of drugs used in elderly patients was 8, and the highest up to 23 (*12*). A survey on the medication of elderly patients in the Chinese community showed that the average medication types of patients were 10.2±5.6 (*13*). At present, some small-section studies still find that the current situation of multiple drug use among the elderly in China is relatively serious, but there is lack of a large sample size and systematic research data.

Although China issued a number of policy documents at the national level, and began to pay close attention to the rational use of drugs in the elderly, there are still some key issues in elderly polypharmacy management, such as a high degree of specialization, weak consciousness of drug use among the elderly, insufficient quantity and quality of pharmaceutical personnel, low social recognition of pharmaceutical care (especially grass-roots pharmaceutical care), *etc.* (*14*). Given these situations, it is necessary to assess the association between elderly polypharmacy status and primary care. In other words, in the current situation, whether the provision of grass-roots drug services through primary health care still has a positive impact on elderly polypharmacy management.

Shanghai is a province with a mature implementation of the family doctor system in China, which established the "1+1+1" team combination signing service model in 2015, proposing to increase the number of pharmacists in the family doctor team (*15*). In addition, Shanghai has a relatively high economic level and a large amount of aging, so it is more representative for conducting a sampling study on elderly patients with hypertension,

which rank first in common diseases, frequently-occurring diseases and endemic diseases.

The objective of this study was to characterize and determine the prevalence of polypharmacy in patients with comorbid hypertension, and to identify the factors associated with it. In addition, the possible association between polypharmacy and preference for primary care among elderly patients was discussed, through the comparison of patient data (Demand-side) and pharmacists data (Supply-side), in order to provide a reference for policy-making of polypharmacy management for the elderly in China.

2. Methods

2.1. Study design

This is a cross-sectional study conducted in Shanghai by the Department of Health Policy and Management, School of Public Health, Fudan University. Data on outcome measures were obtained from institutions by Shanghai Municipal Health Commission and Shanghai Medical Insurance Administration Center. This study was approved by the Ethics Committee of School of Public Health, Fudan University (International Registration Number: IRB00002408 & FWA00002399).

2.2. Setting and participants

2.2.1. Patients

As of December 31, 2019, the elderly population aged 65 and above in Shanghai was 3,616,600. According to the pre-survey, 2.52% of the elderly in a district of Shanghai (2,956 people surveyed) took more than 6 medicines every day, and the prevalence of hypertension was about 20% in Shanghai. Therefore, according to the sample size calculation formula $N = z_2(\alpha/2) \pi (1-\pi)/\delta_2$, the appropriate sample size is about 20,000. Diagnosis data (outpatient and inpatient diagnosis and records) of 20,000 patients with hypertension in 2019

were randomly extracted from the patient visit database of the information center of Shanghai Municipal Health Commission, and the outpatient medication data of these patients were obtained from Shanghai Medical Insurance Administration Center. After matching, there were 19,332 patients with the effective diagnosis and medication data in 2019 (the effective rate was 96.67%).

2.2.2. Pharmacists in Shanghai

Under the coordination of the Pharmaceutical Administration Office of Shanghai Municipal Health Commission, the information of pharmacists in all public medical institutions (tertiary hospitals, secondary hospitals and community healthcare centers) in Shanghai was provided.

2.3. Definitions and variables

2.3.1. Definitions

Geriatric comorbidity: refers to the phenomenon that two or more chronic diseases coexist in the same elderly patient. This chronic disease refers not only to the common diseases of the elderly (such as hypertension, coronary heart disease, diabetes, *etc.*), but also to the elderly's special syndrome of seniors or old age problems (such as falls, weakness, sleep disorders, malnutrition, urinary incontinence, delirium, depression and drug addiction).

Polypharmacy: at present, there is no recognized definition of polypharmacy in the international academic community, and there are still differences in the number and degree of multiple drug uses (*16-17*). In this study, polypharmacy is defined as simultaneous use of 5 or more drugs (excluding Chinese traditional medicine) or treatment of patients beyond clinical need.

2.3.2. Data

The main contents of institutional data include: *i*) Demand-side: age, gender, living areas, number of visits, number of diseases, maximum number of drugs per day, *etc.*; *ii*) Supply-side: age, gender, working areas, working medical institutions, work experience, specialty, education, professional title, authorized strength, post category, *etc.* The main dependent variable was the rate of polypharmacy in patients.

2.4. Statistical analysis

IBM SPSS Statistics 23.0 was used for data analysis. The normality of data was tested. The mean ± standard deviation was used to describe data with a normal distribution, quartiles were used to describe data with a non-normal distribution, and the percentage (%) was used to describe numerical data. Logistic regression

analysis was used to analyze influencing factors. A *P* value < 0.05 was considered significant.

3. Results

3.1. Basic characteristics and outcomes of elderly patients with comorbid hypertension

A total of 19,336 elderly patients with hypertension were sampled, among which only 4 patients had a single hypertension disease, and almost all the sampled patients were hypertensive comorbidities (in addition to hypertension, they also had other chronic diseases). Data gathering was completed for these 19,332 patients with comorbid hypertension. Demographic and medical history characteristics of the study participants are presented in Table 2.

Nineteen thousand three hundred and thirty-two patients (men 9,738 [50.4%]; women 9,594 [49.6%]) were enrolled in this study. The mean (SD) age was 75.86 (7.69) years. The degree of aging in Shanghai is relatively high, and the elderly who aged 80 and over with comorbid hypertension account for 31.9%. Seven thousand eight hundred and fourteen patients (40.4%) were living in central city areas.

In terms of the number of visits, the average number of visits in community healthcare centers is higher than that in secondary and tertiary medical institutions. The median number of annual total visits was 21, of which community healthcare centers were the most frequent. In terms of disease and drug use, the mean (SD) number of diseases was 4.83 (1.99), the mean (SD) daily maximum number of drugs was 5.13 (2.89), and the polypharmacy rate was 50.5%.

Table 2. Basic Characteristics and outcomes of elderly patients with comorbid hypertension

Characteristics	*n* = 1,9332
Age	
< 80	13,162 (68.1%)
≥ 80	6,170 (31.9%)
Mean age	75.86 (7.69)
Gender	
Male	9,738 (50.4%)
Female	9,594 (49.6%)
Living areas	
Central city	7,814 (40.4%)
Suburb	7,644 (39.5%)
Countryside	3,874 (20.0%)
The number of visits	
Community healthcare center	11.00 (5.00, 18.00)
Secondary hospital	4.00 (1.00, 10.00)
Tertiary hospitals	1.00 (0.00, 5.00)
Total number of visits	21.00 (13.00, 31.00)
The number of diseases	4.83 (1.99)
Maximum number of drugs per day	5.13 (2.89)
Outcomes	
Polypharmacy	9,769 (50.5%)

3.2 Predictors of polypharmacy among elderly patients with comorbid hypertension

A significant association was observed between polypharmacy and the following variables by multivariate analysis (Table 3): age ≥ 80, living areas, total number of visits, preference for medical institutions and the number of diseases. Among them, advanced age, greater number of visits and diseases are the risk factors of polypharmacy for elderly patients with comorbid hypertension. In addition, compared with patients living in central city areas, patients living in suburb areas and countryside areas are more likely to establish polypharmacy. Compared with patients who prefer to see a doctor in the community healthcare center, patients who prefer secondary and tertiary hospitals are more likely to establish polypharmacy.

Figure 1 intuitively supports and displays the distribution of polypharmacy in different ages and genders of elderly patients with comorbid hypertension living in different urban areas in Shanghai. Patients living in the countryside, those with a higher willingness

Table 3. Predictors of Polypharmacy among elderly patients with comorbid hypertension

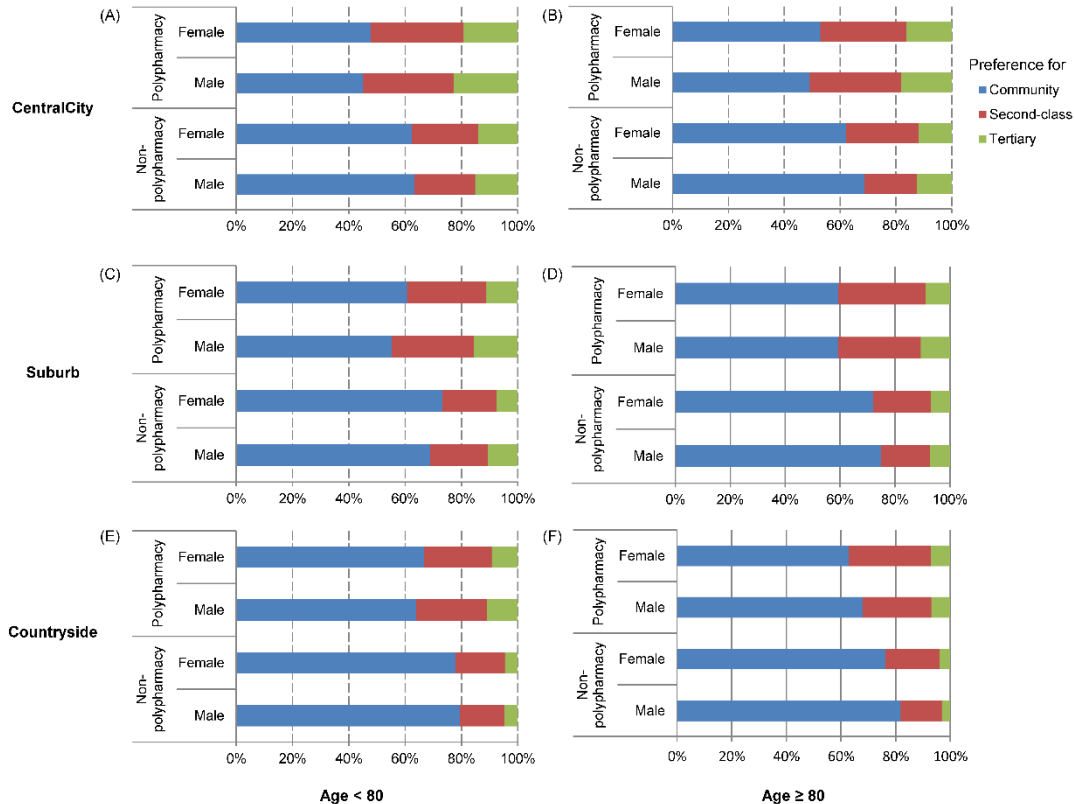| Clinical Characteristic	Polypharmacy cases	Univariate *P*-value	OR (95%CI)	Multivariate *P*-value	OR (95%CI)
Age ≥ 80	3,648 (37.3%)	< 0.0001	1.66 (1.56-1.77)	< 0.0001	1.68 (1.57-1.79)
Male	4,905 (50.2%)	0.65	0.99 (0.93-1.04)	-	-
Living areas					
CentralCity	3,888 (39.8%)	-	-	-	-
Suburb	4,071 (41.7%)	< 0.0001	1.15 (1.08-1.23)	< 0.0001	1.35 (1.26-1.44)
Countryside	1,810 (18.5%)	< 0.0001	0.89 (0.82-0.96)	< 0.0001	1.14 (1.05-1.24)
Total number of visits	27.96 (16.43)	< 0.0001	1.04 (1.04-1.05)	< 0.0001	1.04 (1.04-1.05)
Preference for medical institutions					
Community healthcare center	1,418 (14.5%)	-	-	-	-
Secondary hospital	2,913 (29.8%)	< 0.0001	1.83 (1.71-1.96)	< 0.0001	2.06 (1.91-2.21)
Tertiary hospitals	5,438 (55.7%)	< 0.0001	1.84 (1.68-2.01)	< 0.0001	2.25 (2.04-2.48)
The number of diseases	5.06 (2.07)	< 0.0001	1.13 (1.11-1.15)	< 0.0001	1.09 (1.08-1.11)

Figure 1. The distribution of polypharmacy among elderly patients with comorbid hypertension. The study visually shows the distribution of polypharmacy in different ages and genders of elderly patients with comorbid hypertension living in different urban areas. Gender had no significant effect on the distribution of polypharmacy. The rate of polypharmacy was higher in elderly patients. Patients living in the countryside, had a higher willingness to seek medical care in the community healthcare center, and a lower rate of polypharmacy than those who prefer secondary and tertiary hospitals.

to seek medical care in the community healthcare center, have a lower rate of polypharmacy than those who prefer secondary and tertiary hospitals. Overall, gender had no significant effect on the distribution of polypharmacy, and the rate of polypharmacy was higher in elderly patients aged over 80.

3.3. Associations between polypharmacy and preference for primary care

The demographic characteristic and working conditions of pharmacists in Shanghai public hospitals in 2020 are summarized in this study (Table 4). A total of 9,603 pharmaceutical workers were enrolled in this study, most of whom were female (72.2%). The mean (SD) age was 36.13 (8.42) years and the average (SD) working years was 12.79 (9.44) years. More pharmacists work in secondary and tertiary hospitals in the central city area,

Table 4. Basic Characteristics of pharmacists in Shanghai, China in 2020

Characteristics	$n = 9,603$
Working areas	
Central city	4,996 (52.0%)
Suburb	3,038 (31.6%)
Countryside	1,569 (16.3%)
Working medical institutions	
Community healthcare center	2,794 (29.1%)
Secondary hospital	3,411 (35.5%)
Tertiary hospital	3,398 (35.4%)
Gender	
Male	2,667 (27.8%)
Female	6,935 (72.2%)
Mean age	36.13 (8.42)
Work experience	12.79 (9.44)
Specialty	
Pharmacy	7,627 (79.4%)
Traditional Chinese pharmacology	1,688 (17.6%)
Medicine	16 (0.2%)
Nursing	17 (0.2%)
Management related	62 (0.6%)
Others	193 (2.0%)
Highest Education	
Junior college or below	2,602 (27.1%)
Bachelor degree	6,049 (63.0%)
Master degree	778 (8.1%)
Doctoral degree	174 (1.8%)
Education when entering the institution	
Junior college or below	6,150 (64.0%)
Bachelor degree	2,621 (27.3%)
Master degree	695 (7.2%)
Doctoral degree	137 (1.4%)
Professional title	
Primary	5,656 (58.9%)
Intermediate	3,272 (34.1%)
Advanced	384 (4.0%)
Unqualified	291 (3.0%)
Authorized strength	6,758 (70.4%)
Post category	
Dispensing pharmacist	4,402 (45.8%)
Prescription-checking pharmacist	2,813 (29.3%)
Clinical pharmacist	1,574 (16.4%)
Administrative management	83 (0.9%)
Others	731 (7.6%)

what the data result of this study shows 4,996 (52.0%) worked in the central city area, and more than 70% worked in secondary and tertiary hospitals. From the perspective of major, 79.4% of pharmacists majored in pharmacy, 17.6% in traditional Chinese pharmacology, and some other pharmacists majored in clinical medicine, nursing and management. From the perspective of the highest degree, 6,049 (63%) had Bachelor degree, which has doubled from the proportion of majors at the beginning of employment. In terms of post category, nearly half were dispensing pharmacists, while only 16.4% were clinical pharmacists. From the perspective of suppliers, the proportion of clinical pharmacists working in community healthcare centers is high.

From the perspective of supply-demand matching (Figure 2): most patients' preferences do not match the number of pharmaceutical staff in institutions. Most patients prefer to see a doctor in tertiary medical institutions, especially in countryside areas. However, most pharmacists in the central city area are concentrated in tertiary hospitals; while in countryside areas, the majority of pharmacists work in community healthcare centers. This is related to the high degree of specialization of medical institutions, and also intuitively reflects the mismatch between patients' medical preference and the number of pharmaceutical personnel.

4. Discussion

With the improvement of living conditions and the progress of medical technology, China's population life expectancy is rising rapidly, and the process of population aging is accelerating, much faster than many low-income and high-income countries (*18-19*). One of the main problems related to population aging is the increasing burden of chronic diseases, with high incidence and coexistence of chronic diseases, which seriously affect the health status and quality of life of the elderly (*20*). The prolonged survival time of chronic diseases leads to increased risk of lifelong medication and multiple medications for many patients. In 2017, WHO proposed Medication Safety as the third Global Patient Safety Challenge. For governments of all countries, it is urgent to take measures to solve medication safety problems such as polypharmacy for the elderly and strengthen medication management for the elderly (*21-22*).

This study is the first large-scale survey on medication use of hypertensive comorbidities in China. More than half of the elderly patients with comorbid hypertension have polypharmacy in Shanghai, which as a city has a relatively high economic level and a deep degree of aging. Although this polypharmacy rate is similar to other studies, due to Chinese traditional medicine is excluded from the statistics of drug types in this study the results of the research data are actually far underestimated (*23-24*). In reality, the polypharmacy
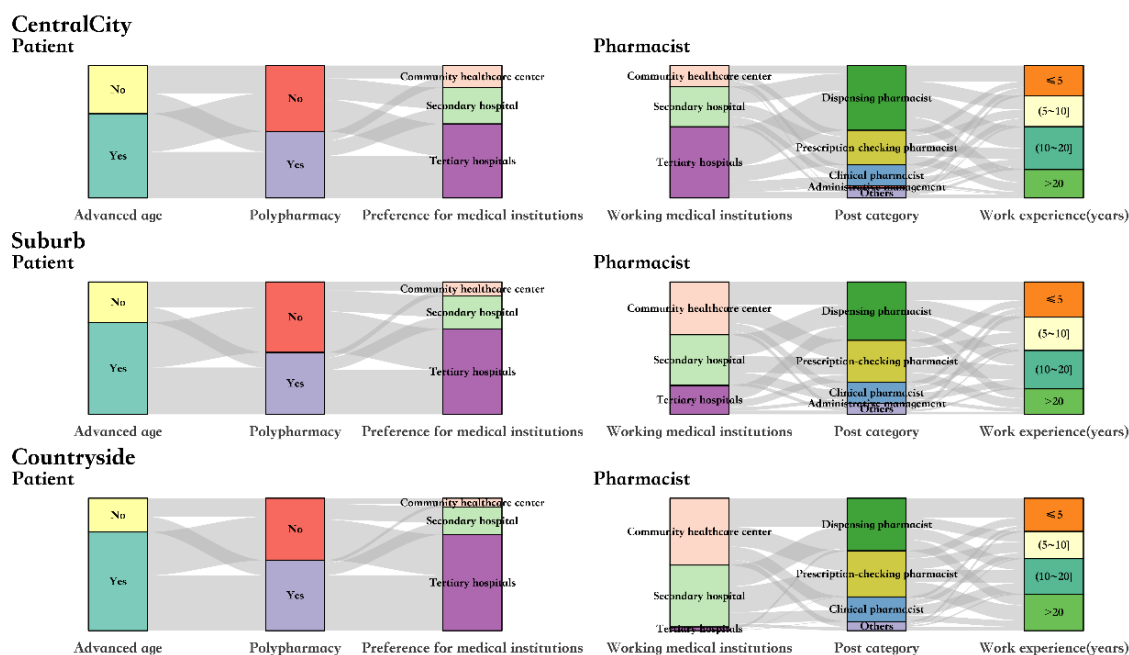
Figure 2. The distribution of the drug-related characteristics of elderly patients and pharmacists in a Sankey diagram. From the perspective of supply-demand matching, most patients' preferences do not match the number of pharmaceutical staff in institutions. Most patients prefer to see a doctor in tertiary medical institutions, especially in countryside areas. However, most pharmacists in the central city area are concentrated in tertiary hospitals; while in countryside areas, the majority of pharmacists work in community healthcare centers. This is related to the high degree of specialization of medical institutions, and also intuitively reflects the mismatch between patients' medical preference and the number of pharmaceutical personnel.

rate of elderly patients with comorbid hypertension in Shanghai is even more alarming. The data from this current study shows that in areas with a high degree of aging, the demand for medication management is much greater (*25-26*).

In order to improve the medication status of the elderly, influencing factors should be clarified first. Advanced age is a significant risk factor for multiple medications due to the decline in physical function associated with aging (*27*). It is worth noting that the variables of living in the central city areas, which was a protective factor in the univariate analysis, became a risk factor in the multivariate analysis. This is to consider that there is a potential protective factor, and most of the people with this factor are concentrated in the countryside area, so the countryside area will show a protective effect when there is only one factor. After the inclusion of multiple factors, this factor was isolated, and the protective effect of the countryside area was no longer significant. This suggests that we need to continue to expand subsequent studies and analyze the protective factors that can play a role in living in the countryside areas.

The rate of polypharmacy in patients intending to visit community healthcare centers was low (*P* < 0.0001). From the perspective of medical institutions' medical preference, compared with patients who prefer to seek treatment in community healthcare centers, patients who prefer to seek treatment in secondary and tertiary medical institutions are more likely to take multiple medications. This is similar to the experience of classic

countries. Providing pharmaceutical care in primary medical institutions can better manage the whole process of drug use for patients, carry out drug integration and reduce polypharmacy. Certainly, the increase of the number of diseases and visits are risk factors, which may be due to the fact that patients have higher disease grades and need to visit medical institutions several times, or they have higher willingness to seek medical care. There may be an effect of the degree of disease, but the research group conducted interviews with some patients and found that advanced medical institutions can provide more drug choices for patients. This means that the degree of disease has a limited impact on the preference of medical institutions. In the case of a high degree of specialization in medical institutions, many patients choose to go to high-level hospitals even if they have common diseases.

Medical institutions equipped with sufficient professional pharmaceutical technicians is the basis of pharmaceutical care, however, in fact, most patients' preferences do not match the number of pharmaceutical staff in institutions in this current study. According to the *Provisions on Pharmaceutical Administration of Medical Institutions in China*, the number of pharmaceutical professional and technical personnel in medical institutions shall not be less than 8% of the number of health technical personnel in the institutions. However, the number of pharmaceutical personnel, especially clinical pharmacists, is seriously insufficient at present (*28*). As of 2018, the number of pharmacists (physicians) in China was only 460,000 (*29*), far less

than licensed (assistant) physicians (3.607 million) and registered nurses (physicians) (4.099 million). A survey of 415 tertiary medical institutions in China found that 50.1% of them had less than 5 clinical pharmacists (*30*). Another study of 39 medical institutions found that the average number of clinical pharmacists per 100 beds was only 0.43 (*31*). Especially in community healthcare centers and other basic institutions, the number of pharmaceutical staff is insufficient, and it is very common for doctors or nurses to exercise the duties of pharmacists part-time. The poor enthusiasm of pharmacists, high staff mobility and unstable teams are not conducive to the development of polypharmacy management (*32*). It is thus obvious that enhancing the quantity and quality of grassroots pharmaceutical staff is the key to reduce the multiple drug use of the elderly.

Polypharmacy is a complex phenomenon, which require to distinguish a drug use for real health needs from not necessary use. Polypharmacy involves multiple links and stakeholders, including doctors' prescription issuance and delivery, pharmacists' prescription review and dispensing, drug storage, medication compliance of the elderly, *etc.* Factors leading to polypharmacy exist in all links, which is a complex engineering system requiring multi-link cooperation and integration. The final support point for elderly health improvement is the family doctor team in community healthcare centers, including pharmaceutical staff. Chinese government vigorously promotes community pharmaceutical care, and this study also confirmed that the preference of community primary care has a positive effect on the polypharmacy management of elderly comorbidities. However, it is very difficult to implement community pharmaceutical care at the present stage, with deeply specialized medical institutions, in China. But if it is done, there is a long-term benefit, which is the efficiency of the process.

Based on this study, comprehensive measures to deal with the problem of polypharmacy were proposed: *i*) Increase the input of pharmaceutical care related resources, especially the input of talent training in pharmaceutical education transformation and upgrading; *ii*) Establish a pharmaceutical service price system to ensure reasonable remuneration for pharmacists; *iii*) Strengthen the development of community pharmaceutical care in primary medical institutions, such as home pharmaceutical care, medication management of elderly patients with chronic diseases, the use of Internet to empower polypharmacy management publicity, *etc.*

Several limitations of this study should be acknowledged. This study is a larger sample survey, which only collects the most basic demographic and medical history characteristics, and lacks the sociological characteristics of elderly patients. Therefore, the possible protective or risk factors cannot be explored in depth during the analysis of influencing factors. In addition, data on patients' medication used in the study were institutional data, rather than the actual medication use data of patients, which may constitute a bias. However, since the institutional data only included public medical institutions and did not include the data of private institutions such as private pharmacies, the impact of such deviation is limited.

5. Conclusion

In conclusion, the rate of polypharmacy among elderly patients with comorbid hypertension was 50.5% in Shanghai. Age, living areas, total number of visits, preference for medical institutions and the number of diseases were associated with polypharmacy. The rate of polypharmacy in elderly patients who intend to seek treatment in community healthcare centers is low. And this study also confirmed that the preference of community primary care has a positive effect on the polypharmacy management of elderly comorbidities in developing countries. As a consequence, obtaining better medication outcomes based on primary pharmaceutical care is necessary.

Conflict of Interest: The authors have no conflicts of interest to disclose.

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