



Trends in Psychotropic Medication Prescriptions in Urban China From 2013 to 2017: National Population-Based Study

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Purpose: Psychotropic medications are commonly used for treating mental disorders; however, there is currently no study on how commonly they are used in China. This study reported the trends in psychotropic medications prescriptions in urban China.

Methods: A national population-based study was conducted using the China Health Insurance Research Association database to estimate the period prescription prevalence of 11 major classes of psychotropic medications annually during 2013–2017. The World Health Organization Anatomical Therapeutic Chemical (ATC) classification codes were used to identify psychotropic medications.

Results: The prescription prevalence of any psychotropic medication increased from 8.110% (8.106–8.114%) in 2013 to 11.362% (11.357–11.366%) in 2017. The prescription prevalence of six classes increased significantly during 2013–2017, including sedatives-hypnotics (from 3.177 to 5.388%), anxiolytics (from 1.436 to 2.200%), antiepileptic drugs (from 1.416 to 2.140%), antipsychotics (from 0.809 to 1.156%), antidepressants (from 0.891 to 1.045%), and psycholeptic polypills (from 0.682 to 0.866%). The prescription prevalence of antidementia drugs increased from 0.069 to 0.122%, and mood stabilizers increased from 0.029 to 0.037%, although not statistically significant. The prescription prevalence of nootropic drugs, attention deficit hyperactivity disorder (ADHD) medications and drugs used in the treatment of addictive disorders was largely stable. Psychotropic medication prescription increased with age for all classes except for ADHD medications and mood stabilizers.

Conclusion: Increasing trends in prescription prevalence were observed for most classes of psychotropic medications in urban China, although the prevalence was still lower than that in most developed countries. Further research is warranted to explore the potential treatment gap between China and most developed countries.

Keywords: psychiatry, psychotropic medication, prescription prevalence, China, population-based, claim data

INTRODUCTION

Mental disorders place a heavy burden on countries all over the world; over 14% of age-standardized years lived with disability (YLDs) across both sexes and all age groups are due to mental disorders (1). In China, the lifetime prevalence of mental disorders increased from 13.2% in 2002 to 16.6% during 2013–2015, which contribute to substantial disease burden (2). In 2017, mental disorders were one of the three leading causes of years lived with disability (YLDs) in China, causing 1,574 YLDs per 100,000 population (3).

Pharmacological treatment is the most commonly used treatment approach for many mental disorders. Data from several countries have shown increasing prescription prevalence of different classes of psychotropic medications during the last few decades (4–9). For example, the prescription prevalence of attention deficit hyperactivity disorder (ADHD) medications increased during the last two decades in studies from different countries (10–13). A rising prescription prevalence of antidepressants was observed among Australian adults during 2007–2015 (7). The prescription prevalence of antipsychotics rose in most European countries during 2005–2014 (8). Moreover, a climbing trend in sedative-hypnotic use was observed among Australian adults during 2007–2015 and American adults during 1999–2010 (7, 9).

An analysis of the patterns of psychotropic medication prescriptions can provide necessary data for the formulation of policies in the context of competing priorities and budgetary constraints. Such data can inform future clinical practice and research in certain population subgroups. In particular, prescription of psychotropic medications in children and adolescents has increased substantially in recent years, reflecting changes in mental health care for this population (14). However, most studies in this regard are from developed countries, with limited information from low- or middle-income countries, especially a national study from China, the country with the largest population in the world. This population-based study, therefore, aimed to evaluate trends in the prescription prevalence of psychotropic medications in China from 2013 to 2017 using nationally representative claim data.

METHODS

Data Sources and Study Population

In China, medical insurance for urban population consists of two main programmes: (1) the Urban Employee Basic Medical Insurance (UEBMI) programme for urban employees and employers (i.e., those working for government agencies and institutions, state-owned enterprises, social organizations, private enterprises, and other private entities) and (2) the Urban Residence Basic Medical Insurance (URBMI) programme for unemployed residents in cities, including children, students, elderly individuals, and other unemployed residents. The medical service records of all insureds are kept in the medical insurance database (i.e., the reimbursement records of the insured population will be kept in the databases if they provide the national insurance card for the medical service, no matter the

proportion they pay for the medical service). By 2014, the two programmes covered ~97.5% of the urban population in China (15). The China Health Insurance Research Association (CHIRA) database is a random sampling database from the UEBMI and URBMI databases (16), with the sampling of beneficiaries performed as follows: (1) 2% from municipalities and provincial cities and (2) 5% from prefecture-level cities. Data sampling is conducted annually. The information in the CHIRA database includes insured individuals' demographic characteristics (birth date, sex, etc.), medical treatment records (medications, surgeries, etc.), and medical expenses. Validation study of the Chinese claim database indicated that the accuracy is relatively high (17). Also, this database has been used to do research regarding the epidemiology of rare diseases (18–20), and also medication utilization (21).

The study population (**Supplementary Table 1**) was all the household-registered population living in the 63 cities included in the CHIRA database during 2013–2017 (**Supplementary Table 2**), which was representative of the urban population in China. The study population was collected from the population census data of the corresponding cities (22). The study was carried out in accordance with the latest version of the Declaration of Helsinki. The study protocol was approved by the ethical review committee of the Peking University Health Science Center (IRB. No: IRB00001052-15045). The requirement for informed consent was waived.

Medication Definition

We identified individuals using psychotropic medications between January 1, 2013 and December 31, 2017 from the CHIRA database. We included 11 major classes of psychotropic medications: sedatives-hypnotics, anxiolytics, antiepileptic drugs, nootropic drugs, antipsychotics, antidepressants, psycholeptic polypills, antidementia drugs, mood stabilizers, ADHD medications, and drugs used in addictive disorders. We used World Health Organization Anatomical Therapeutic Chemical (ATC) classification codes to identify specific psychotropic medications in the CHIRA database. The detailed ATC codes and generic names used are shown in **Supplementary Table 3**. In this study, exclusive classification was used (i.e., each medicine can only be classified into one category). The classification of each medicine was based on the main indication of each medicine in China.

Data Analysis

The annual period prescription prevalence of psychotropic medications in urban China between 2013 and 2017 was calculated using a three-step approach (10, 20). First, the prescription prevalence of each age group at each city level was calculated. The numerator was the total number of patients prescribed psychotropic medications in the CHIRA database divided by the sampling proportion. The denominator was the urban population of the included cities, which was collected from the population census data (22). The detailed information of the numerator and denominator can be seen in **Supplementary Figure 1**. When calculating the prescription prevalence of a certain type of psychotropic medication, if a

TABLE 1 | Characteristics of the psychotropic medication users from the CHIRA database during 2013–2017.

Characteristic	No. (%)				
	2013	2014	2015	2016	2017
Total	507,240 (100.00)	366,641 (100.00)	430,534 (100.00)	486,161 (100.00)	578,069 (100.00)
Sex					
Male	239,072 (47.13)	171,691 (46.83)	206,094 (47.87)	231,815 (47.68)	272,252 (47.10)
Female	268,168 (52.87)	194,950 (53.17)	224,440 (52.13)	254,346 (52.32)	305,817 (52.90)
Age					
0–14	13,573 (2.68)	10,290 (2.81)	13,250 (3.08)	15,884 (3.27)	22,157 (3.83)
15–64	334,468 (65.94)	220,342 (60.10)	261,278 (60.69)	297,900 (61.28)	350,641 (60.66)
≥65	159,199 (31.38)	136,009 (37.09)	156,006 (36.23)	172,377 (35.45)	205,271 (35.51)

CHIRA, China Health Insurance Research Association.

patient prescribed the same type of medicine many times in a year, the patient only contributed 1 to the numerator of the prescription prevalence in that year. If a patient prescribed different types of medicines many times in a year, the patient contributed 1 to the numerator of the prescription prevalence of different medicines, respectively, in that year. When calculating the prescription prevalence of any psychotropic medication, if a patient prescribed different types of medicines many times in a year, the patient contributed 1 to the numerator of the prescription prevalence of any psychotropic medication in that year. Second, the national prescription prevalence in each age group was calculated by pooling the age-specific prescription prevalence at different city levels using a random-effects meta-analysis to account for heterogeneity across different city levels. Third, the age-specific pooled prescription prevalence was used to calculate the overall annual prescription prevalence in each year, standardized by the national population census data of the corresponding year (22). The prescription prevalence was calculated with 95% confidence intervals (95% CIs) estimated by the Poisson method. The statistical significance level was set at two-sided $P < 0.05$. For CHIRA data used in the study, sex information was available for any participant. The missing rates of age and medication information were 1.60 and 3.08%, respectively. Due to the low missing rates, no data imputation was adopted.

The temporal trend in prescription prevalence was tested through a linear regression model including year, age group (0–14, 15–64, and ≥65) and sex. In addition to temporal trends, the prescription prevalence patterns were evaluated by age group (0–14, 15–64, and ≥65) and by sex. We used Stata 15.0 for data analysis. The prespecified statistical analysis plan is provided in **Supplementary Material**.

RESULTS

There were 507,240, 366,641, 430,534, 486,161, and 578,069 psychotropic medication users in the CHIRA database from 2013 to 2017 (**Table 1**). The prescription prevalence of any psychotropic medication increased from 8.110% (8.106–8.1145%) in 2013 to 11.362% (11.357–11.366%) in

2017, with a higher prevalence in females (12.003, 11.996–12.010%) than males (10.786, 10.779–10.792%). The prevalence among those aged 0–14, 15–64, and ≥65 in 2017 were 2.351% (1.292–3.715%), 9.245% (6.528–12.379%), and 37.970% (25.055–51.817%), respectively.

Temporal Trends

From 2013 to 2017, the period prescription prevalence of the eight classes increased (**Table 2** and **Figure 1**): the prescription prevalence of sedatives-hypnotics, the most commonly used psychotropic medication, changed from 3.177 to 5.388%, with a relative increase of 69.61% (P for trend = 0.007); that of anxiolytics changed from 1.436 to 2.200%, with a relative increase of 53.17% ($P = 0.04$); that of antiepileptic drugs changed from 1.416 to 2.140%, with a relative increase of 51.15% ($P = 0.001$); that of antipsychotics changed from 0.809 to 1.156%, with a relative increase of 42.99% ($P = 0.001$); that of antidepressants changed from 0.891 to 1.045%, with a relative increase of 17.25% ($P = 0.04$); and that of psycholeptic polypills changed from 0.682 to 0.866%, with a relative increase of 27.01% ($P = 0.02$). The prescription prevalence of antidementia drugs changed from 0.069 to 0.122%, with a relative increase of 77.69% ($P = 0.26$), and mood stabilizers changed from 0.029 to 0.037%, with a relative increase of 28.41% ($P = 0.40$), although not statistically significant. The prescription prevalence of nootropic drugs, ADHD medications, and drugs used in addictive disorders ($P > 0.05$) was largely stable (**Figure 1**).

Age and Sex Patterns

In 2017, the prescription prevalence for all psychotropic medications was higher in the older age group (**Table 3**), except that for ADHD medications and mood stabilizers. The prescription prevalence of mood stabilizers was highest among those aged 15–64 years, with a prescription prevalence of 0.047% (0.030–0.069%). ADHD medication prescription was mostly prevalent among those aged 0–14 years, with a prescription prevalence of 0.036% (0.005–0.093%).

The prescription prevalence of sedatives-hypnotics, anxiolytics, and antidepressants was higher in females than males, but the prescription prevalence of ADHD medications was higher in males than females. The prescription prevalence

TABLE 2 | The prescription prevalence of 11 classes of psychotropic medications from 2013 to 2017 in urban China.

Drug	Prevalence of use, % (95% CI)					Relative increase (%) ^a	P ^b
	2013	2014	2015	2016	2017		
Sedatives-hypnotics	3.177 (3.174–3.179)	3.018 (3.016–3.021)	3.292 (3.289–3.294)	4.281 (4.278–4.284)	5.388 (5.385–5.391)	69.61	0.007
Anxiolytics	1.436 (1.435–1.438)	1.315 (1.314–1.317)	1.505 (1.503–1.507)	1.943 (1.941–1.945)	2.200 (2.198–2.202)	53.17	0.036
Antiepileptic drugs	1.416 (1.414–1.417)	1.284 (1.283–1.286)	1.497 (1.496–1.499)	1.836 (1.834–1.837)	2.140 (2.138–2.142)	51.15	0.001
Nootropic drugs	2.378 (2.376–2.380)	2.233 (2.231–2.235)	2.759 (2.757–2.762)	1.645 (1.643–1.646)	2.009 (2.007–2.011)	–15.51	0.49
Antipsychotics	0.809 (0.807–0.810)	0.745 (0.743–0.746)	0.763 (0.762–0.765)	0.987 (0.985–0.988)	1.156 (1.155–1.158)	42.99	0.001
Antidepressants	0.891 (0.890–0.893)	0.742 (0.741–0.743)	0.716 (0.715–0.718)	0.922 (0.921–0.924)	1.045 (1.044–1.047)	17.25	0.042
Psycholeptic polypills	0.682 (0.681–0.683)	0.439 (0.438–0.440)	0.558 (0.557–0.559)	0.810 (0.809–0.811)	0.866 (0.865–0.867)	27.01	0.023
Antidementia drugs	0.069 (0.068–0.069)	0.065 (0.064–0.065)	0.065 (0.065–0.066)	0.103 (0.102–0.103)	0.122 (0.122–0.123)	77.69	0.26
Mood stabilizers	0.029 (0.028–0.029)	0.021 (0.020–0.021)	0.022 (0.022–0.023)	0.029 (0.029–0.029)	0.037 (0.036–0.037)	28.41	0.40
ADHD medications	0.016 (0.016–0.017)	0.013 (0.012–0.013)	0.007 (0.007–0.007)	0.007 (0.007–0.007)	0.008 (0.008–0.008)	–50.28	0.18
Drugs used in addictive disorders	0.004 (0.004–0.004)	0.003 (0.003–0.003)	0.007 (0.007–0.007)	0.002 (0.002–0.002)	0.001 (0.001–0.001)	–65.45	0.15

ADHD, attention deficit hyperactivity disorder.

^aThe relative increase in the prescription prevalence of psychotropic medications in 2017 compared to the prevalence in 2013 was assessed by the formula: Relative increase (%) = $\frac{\text{Prevalence}_{2017} - \text{Prevalence}_{2013}}{\text{Prevalence}_{2013}} \times 100$.

^bThe P-values for the trend in prescription prevalence was from a linear regression model including year, age group (0–14, 15–64, and ≥65), and sex.

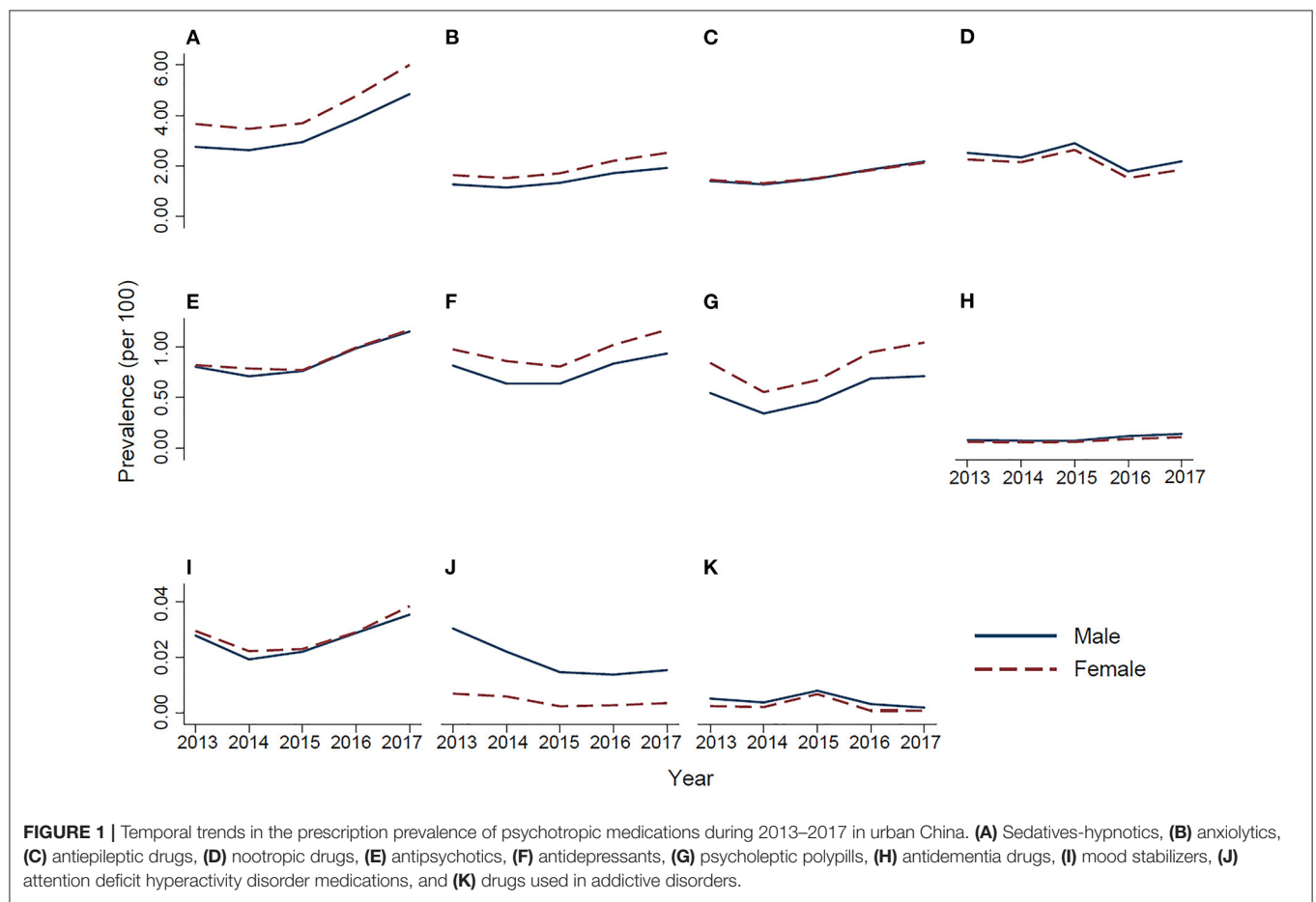


FIGURE 1 | Temporal trends in the prescription prevalence of psychotropic medications during 2013–2017 in urban China. (A) Sedatives-hypnotics, (B) anxiolytics, (C) antiepileptic drugs, (D) nootropic drugs, (E) antipsychotics, (F) antidepressants, (G) psycholeptic polypills, (H) antidementia drugs, (I) mood stabilizers, (J) attention deficit hyperactivity disorder medications, and (K) drugs used in addictive disorders.

TABLE 3 | The prescription prevalence of 11 classes of psychotropic medications in 2017 in urban China by age group.

Drug	Prevalence of use, % (95% CI)		
	0–14	15–64	≥65
Sedatives-hypnotics	0.984 (0.583–1.488)	4.662 (3.331–6.204)	16.457 (12.381–20.987)
Anxiolytics	0.217 (0.128–0.330)	1.733 (1.256–2.285)	8.066 (5.712–10.785)
Antiepileptic drugs	1.140 (0.500–2.036)	1.844 (1.043–2.867)	5.476 (3.133–8.423)
Nootropic drugs	0.138 (0.074–0.221)	1.128 (0.615–1.792)	10.317 (5.821–15.913)
Antipsychotics	0.086 (0.060–0.115)	1.146 (0.756–1.616)	2.800 (1.963–3.779)
Antidepressants	0.016 (0.010–0.023)	1.005 (0.852–1.171)	2.812 (1.934–3.848)
Psycholeptic polypills	0.002 (0.001–0.003)	0.761 (0.605–0.935)	2.801 (1.833–3.966)
Antidementia drugs	NA ^a	0.037 (0.031–0.044)	0.838 (0.549–1.186)
Mood stabilizers	0.001 (0.000–0.002)	0.047 (0.030–0.069)	0.023 (0.015–0.032)
ADHD medications	0.036 (0.005–0.093)	0.003 (0.001–0.005)	0.001 (0.000–0.004)
Drugs used in addictive disorders	NA ^a	0.001 (0.000–0.003)	0.003 (0.001–0.006)

ADHD, attention deficit hyperactivity disorder.

^aNo users of the corresponding drugs in the age group.

patterns in 2013, 2014, 2015, and 2016 (data not shown) were similar to those in 2017.

DISCUSSION

Based on nationally representative claim data, this study firstly reported the prescription prevalence of psychotropic medications in China. During 2013–2017, upward trends were observed in the period prescription prevalence of sedatives-hypnotics, anxiolytics, antiepileptic drugs, antipsychotics, antidepressants, psycholeptic polypills, antidementia drugs, and mood stabilizers. Among them, psycholeptic polypills were mostly used by patients with anxiety and depression in China, but relevant evidence regarding the utilization of psycholeptic polypills were limited worldwide. In 2017, 11.362% of individuals has used at least one class of psychotropic medication. Considering the 810 million urban population in China, it corresponds to 92 million psychotropic medication users. Prescription of psychotropic medication increased with age for all classes except for ADHD medications and mood stabilizers. The prescription prevalence of sedatives-hypnotics, anxiolytics, and antidepressants was markedly higher in females than in males.

One of the key findings in this study was the upward trends in prescription prevalence of eight classes of psychotropic medications from 2013 to 2017. In contrast, the prevalence of most of their main indications remained relatively stable during the last decade. For instance, the prevalence of schizophrenia in urban China fluctuated from 0.8% in 2010 to 0.6% in 2013 (2, 23), and the prevalence of depression in China varied from 6.8% in 2013 to 4.0% in 2017 (24). Therefore, the rising prescription prevalence of these psychotropic medications may largely reflect the increased attention to mental health in China during the study period. For example, from 2013 to 2017, the number of psychiatric hospitals/institutions and practitioners increased by 46 and 40%, respectively (**Supplementary Figure 2**). During the same period, the relative increase in the prescription prevalence of sedatives-hypnotics, anxiolytics, and antipsychotics ranged

from 43 to 70%, which largely matched the increase in psychiatric hospitals/institutions and practitioners. In 2015, China released the National Mental Health Work Plan (2015–2020) (25), which aimed to improve the mental health prevention, treatment, and rehabilitation service system; improve the security system for patient information; create a social atmosphere of understanding, accepting, and caring for patients; and improve the public awareness of mental disorders. Additionally, in the same year, the second edition of Chinese guidelines related to the prevention and treatment of mental disorders were published. Thus, the rising trend, to some extent, reflects the growth in mental health care in China in the past decade, although other factors may have contributed as well.

The sex patterns in the prescription prevalence of different classes of psychotropic medications was similar to the findings from developed countries, i.e., the prescription prevalence of antidepressants, sedatives-hypnotics, and anxiolytics was higher in females (9, 26, 27), but the prescription prevalence of ADHD medications was lower in females (10).

With regard to specific medications, the prescription prevalence of antipsychotics in this study, the primary pharmacotherapy for schizophrenia, was 1.156% in China in 2017. A multinational study indicated that the prescription prevalence of antipsychotics in most European or American countries was higher than that in China (8). However, the age-standardized point prevalence of schizophrenia in China was highest on a global scale according to the GBD 2016 (28). All the above evidence suggests a non-negligible gap between the prevalence of schizophrenia and the prescription prevalence of antipsychotics in China. The poorer awareness and higher public stigma associated with schizophrenia in developing countries might be an explanation for this phenomenon (29). Another possible explanation was the relative shortage of mental health resources and services in China (30). In 2015, China had ~1.5 psychiatrists and 1.7 psychiatric beds per 100,000 population (30), while in 2011, upper-middle-income countries had ~2.0 psychiatrists and 2.7 psychiatric beds per 100,000

population (30). Also, different prescribing patterns might contribute to the difference between countries, for example, in some countries, antipsychotics are used for depression treatment.

We found that the prescription prevalence of antidepressants in China in 2017 was 1.045%, lower than that in European or American countries, which ranged from 2 to 16% during 2010–2012 (27, 31). A number of factors may explain the observed difference: First, the difference may be due to the lower prevalence of depression in China (2) than in Europe or America (32). Second, similar to other types of mental disorders, the difference may be explained by the public stigma associated with seeking mental care, the unawareness of depressive symptoms or the shortage of local mental health services (29, 30). Third, some Chinese patients with depression may choose traditional Chinese medicine (TCM) treatments (33), which were not considered in this study. Fourth, another factor that could not be ignored is the variation in medication duration and adherence, as the antidepressant discontinuation rate among East Asian patients (i.e., patients from mainland China, Hong Kong, Taiwan, Malaysia, Singapore, and South Korea) with major depressive disorder was 56%, while the antidepressant discontinuation rates in Western populations ranged from 22 to 42% (34).

The prescription prevalence of antidementia drugs among the Chinese urban population aged 65 years and older in 2017 was 0.838%. According to the German Health Interview and Examination Survey for Adults 2008–2011, antidementia drugs were used by 4.2% of the population aged 60–79 years (35). In Japan, the prescription prevalence of antidementia drugs among those aged 65 years and older was 5.1% during 2015–2016 (36). The prevalence of dementia among the population aged 65 years and older was 5.6% in mainland China from 2013 to 2015 (2), 9.3% in Germany in 2009 (37), and ~6–10% in Japan in 2015 (38). Therefore, the prescription prevalence of antidementia drugs of <1% in China was relatively lower, which may be caused by the fact that the rate of undetected dementia was higher in middle-income Asian countries (i.e., Thailand and China) (93.2%) than in North America (62.9%) and Europe (53.7%) (39). Also, vascular dementia, as the second most common type of dementia, accounted for 15–20% of dementia cases in North America and Europe but more (roughly 27%) in China (40, 41). The symptoms of vascular dementia can be misdiagnosed as symptoms of stroke (40). Moreover, some Chinese patients with dementia may choose TCM (42). Reimbursement differences in different countries may also play a role in the differences of prescription prevalence of antidementia drugs in different countries.

In this study, the prescription prevalence of mood stabilizers was 0.037% in 2017. Mood stabilizers are mainly used as pharmacotherapies for bipolar disorder. The age-standardized prevalence of bipolar disorder in China is similar to that in other countries, with the age-standardized prevalence remaining at 0.7% between 1990 and 2013 globally (43). However, the prescription prevalence of lithium in some European countries, such as Italy and France (~0.1%), was higher than that in China (44, 45). The relatively lower prescription prevalence of lithium in China may be due to the lack of knowledge regarding bipolar disorder in China. As reported, Eastern countries had poorer recognition of bipolar disorder than Western societies

(46). Another possible explanation may be that the proportion of patients who received lithium was lower in China (~40%) than in European or American countries (~60–80%) because of the relatively higher proportion of patients who received other drugs in China (44, 47, 48).

The prescription prevalence of ADHD medications was 0.036% among those aged 0–14 years in 2017 in China. A systematic review reported that the prevalence of ADHD among Chinese children and adolescents was 6.5% (49), similar to that in European or American countries (50, 51). However, according to a multinational study (covering Asia and Australia, North America, northern Europe, and western Europe) (10), the lowest prescription prevalence of ADHD medications was 0.27% in France among children aged 3–18 years in 2010, which was still ~7 times higher than our estimate in China. There are a few possible explanations for the lower prescription prevalence among Chinese children. First, there was a lack of training in ADHD treatment among clinical practitioners (52). Second, the control of possibly addictive medications such as stimulants was strict in China (52). Third, some Chinese parents of the patients with ADHD were reluctant to use ADHD medications since they think ADHD is bad behavior rather than a disease that requires medication. Fourth, given the potential side effects of ADHD medications, many Chinese parents turn to TCM (52). Fifth, the cessation of Ritalin production by Chinese pharmaceutical enterprises in 2009 might result in an increased economic burden on patients' families to purchase imported ADHD medications, which may also explain the stable or relatively reduced trend in the prescription prevalence of ADHD medications. Sixth, the differences in the medications available for ADHD in different countries may also contribute to it (53).

To our knowledge, this is the first national study in China to describe the trends in the prescription of major classes of psychiatric medications. A large, nationally representative sample of the Chinese mainland population was used to ensure robust estimations of the prescription prevalence of psychiatric medications. Our results identified two gaps: one between the prescription prevalence of psychiatric medications and the prevalence of mental disorders in China and the other between the prescription prevalence of psychiatric medications in China and that in developed countries.

There are still several limitations to be considered when interpreting the findings of the study. First, due to the age categories in the Chinese population census, it is impossible to obtain a more detailed age pattern in the prescription prevalence of psychotropic medications (7, 8). Second, we cannot follow individuals longitudinally in the CHIRA database to evaluate individual prescription patterns of psychotropic medications over time, and further work could examine the prescription of psychotropic medications at the individual level. Third, rural residents were not included in this study because they are covered under different health insurance programmes, although the urban population makes up the largest segment (~60% in 2017) of the Chinese population (22). Fourth, exclusive classification of psychotropic medications was used in this study, which may overestimate the prescription prevalence of the classification for the medicines treating main indication, and underestimate the

prescription prevalence of the classification for the medicines treating secondary indications. Fifth, since in medical electronic big data, it was hard to obtain the detailed information of patients' medication use, collected prescriptions were used to reflect medication use in this study. Although prescriptions cannot completely reflect the medication use, in many previous high-quality articles from other countries, prescriptions were used to roughly reflect the medication use in the whole population when using electronic big data as well (10, 54, 55).

As the first national population-based study in China, our study reported increasing trends in the prescription prevalence of eight classes of psychotropic medications. Although the prescription prevalence of psychotropic medications was still lower in China than in most European or American countries, the large absolute number of psychotropic medication users suggests a heavy burden from mental disorders and the necessity to further improve mental health care in China. Future research is warranted to explore the potential treatment gap between China and most developed countries.

DATA AVAILABILITY STATEMENT

Summarized health data about psychiatric medications can be accessed by contacting the National Insurance Claims for Epidemiological Research (NICER) Group, School of Public Health, Peking University. Contact email: 0016163159@bjmu.edu.cn.

ETHICS STATEMENT

The study protocol was approved by the ethical review committee of the Peking University Health Science Center (IRB. No: IRB00001052-15045). The requirement for informed consent was waived.

REFERENCES

- James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. (2018) 392:1789–858. doi: 10.1016/S0140-6736(18)32279-7
- Huang Y, Wang Y, Wang H, Liu Z, Yu X, Yan J, et al. Prevalence of mental disorders in China: a cross-sectional epidemiological study. *Lancet Psychiatry*. (2019) 6:211–24. doi: 10.1016/S2215-0366(18)30511-X
- Zhou M, Wang H, Zeng X, Yin P, Zhu J, Chen W, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. (2019) 394:1145–58. doi: 10.1016/S0140-6736(19)30427-1
- Pincus HA, Tanielian TL, Marcus SC, Olfson M, Zarin DA, Thompson J, et al. Prescribing trends in psychotropic medications: primary care, psychiatry, and other medical specialties. *JAMA*. (1998) 279:526–31. doi: 10.1001/jama.279.7.526
- Olfson M, Marcus SC. National patterns in antidepressant medication treatment. *Arch Gen Psychiatry*. (2009) 66:848–56. doi: 10.1001/archgenpsychiatry.2009.81
- Olfson M, Blanco C, Wang S, Laje G, Correll CU. National trends in the mental health care of children, adolescents, and

AUTHOR CONTRIBUTIONS

LX and XL contributed to the acquisition, analysis and interpretation of data, drafting the manuscript, and the statistical analysis. HW, ShZ, and XY contributed to the acquisition, analysis, and interpretation of data. QL, SG, and SD contributed to the administrative, technical, and material support. SW, ZC, and SiZ contributed to the study concept and design, the acquisition, analysis, and interpretation of data, and the administrative, technical, or material support. All authors contributed to the critical revision of the manuscript for important intellectual content.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsy.2021.727453/full#supplementary-material>

- adults by office-based physicians. *JAMA Psychiatry*. (2014) 71:81–90. doi: 10.1001/jamapsychiatry.2013.3074
- Brett J, Karanges EA, Daniels B, Buckley NA, Schneider C, Nassir A, et al. Psychotropic medication use in Australia, 2007 to 2015: changes in annual incidence, prevalence and treatment exposure. *Aust N Z J Psychiatry*. (2017) 51:990–9. doi: 10.1177/0004867417721018
- Hálfðánarson Ó, Zoëga H, Aagaard L, Bernardo M, Brandt L, Fusté AC, et al. International trends in antipsychotic use: a study in 16 countries, 2005-2014. *Eur Neuropsychopharmacol*. (2017) 27:1064–76. doi: 10.1016/j.euroneuro.2017.07.001
- Bertisch SM, Herzig SJ, Winkelman JW, Buettner C. National use of prescription medications for insomnia: NHANES 1999-2010. *Sleep*. (2014) 37:343–9. doi: 10.5665/sleep.3410
- Raman SR, Man KKC, Bahmanyar S, Berard A, Bilder S, Boukhris T, et al. Trends in attention-deficit hyperactivity disorder medication use: a retrospective observational study using population-based databases. *Lancet Psychiatry*. (2018) 5:824–35. doi: 10.1016/S2215-0366(18)30293-1
- Stuhec M, Locatelli I. Age-related pharmacotherapy of attention deficit hyperactivity disorder in Slovenia in children and adolescents: a population-based study. *Eur Psychiatry*. (2017) 42:129–33. doi: 10.1016/j.eurpsy.2017.01.002
- Schubert I, Köster I, Lehmkuhl G. The changing prevalence of attention-deficit/hyperactivity disorder and methylphenidate prescriptions: a study of data from a random sample of insureds of the AOK Health Insurance

- Company in the German State of Hesse, 2000–2007. *Dtsch Arztebl Int.* (2010) 107:615–21. doi: 10.3238/arztebl.2010.0615
13. Treceño C, Martín Arias LH, Sáinz M, Salado I, García Ortega P, Velasco V, et al. Trends in the consumption of attention deficit hyperactivity disorder medications in Castilla y León (Spain): changes in the consumption pattern following the introduction of extended release methylphenidate. *Pharmacoepidemiol Drug Saf.* (2012) 21:435–41. doi: 10.1002/pds.2348
 14. Correll CU, Kratochvil CJ, March JS. Developments in pediatric psychopharmacology: focus on stimulants, antidepressants, and antipsychotics. *J Clin Psychiatry.* (2011) 72:655–70. doi: 10.4088/JCP.11r07064
 15. Xiong X, Zhang Z, Ren J, Zhang J, Pan X, Zhang L, et al. Impact of universal medical insurance system on the accessibility of medical service supply and affordability of patients in China. *PLoS One.* (2018) 13:e0193273. doi: 10.1371/journal.pone.0193273
 16. Yang Y, Zhou X, Gao S, Lin H, Xie Y, Feng Y, et al. Evaluation of electronic healthcare databases for post-marketing drug safety surveillance and pharmacoepidemiology in China. *Drug Saf.* (2018) 41:125–37. doi: 10.1007/s40264-017-0589-z
 17. Sun Y, Zhou G, Feng J, Chen L, Liu G, Wang J, et al. Incidence and prevalence of moyamoya disease in urban China: a nationwide retrospective cohort study. *Stroke Vasc Neurol.* (2021). doi: 10.1136/svn-2021-000909. [Epub ahead of print].
 18. Xu L, Chen L, Wang S, Feng J, Liu L, Liu G, et al. Urban prevalence of multiple sclerosis in China: a population-based study in six provinces. *Eur J Neurol.* (2021) 28:1636–44. doi: 10.1111/ene.14764
 19. Zhang C, Feng J, Wang S, Gao P, Xu L, Zhu J, et al. Incidence of and trends in hip fracture among adults in urban China: a nationwide retrospective cohort study. *PLoS Med.* (2020) 17:e1003180. doi: 10.1371/journal.pmed.1003180
 20. Xu L, Chen L, Wang S, Feng J, Liu L, Liu G, et al. Incidence and prevalence of amyotrophic lateral sclerosis in urban China: a national population-based study. *J Neurol Neurosurg Psychiatry.* (2020) doi: 10.1136/jnnp-2019-322317
 21. Wei G, Wu M, Zhu H, Han S, Chen J, Zhai C, et al. Off-label use of antineoplastic drugs to treat malignancies: evidence from China based on a nationwide medical insurance data analysis. *Front Pharmacol.* (2021) 12:616453. doi: 10.3389/fphar.2021.616453
 22. National Bureau of Statistics. *China Statistical Yearbook.* (2020). Available online at: <http://www.stats.gov.cn/tjsj/ndsj/> (accessed April 12, 2020) (in Chinese).
 23. Chan KY, Zhao F-F, Meng S, Demaio AR, Reed C, Theodoratou E, et al. Prevalence of schizophrenia in China between 1990 and 2010. *J Glob Health.* (2015) 5:010410. doi: 10.7189/jogh.05.010410
 24. Ren X, Yu S, Dong W, Yin P, Xu X, Zhou M. Burden of depression in China, 1990–2017: findings from the global burden of disease study 2017. *J Affect Disord.* (2020) 268:95–101. doi: 10.1016/j.jad.2020.03.011
 25. Hua F, Zhao C. China's National Mental Health Working plan. *Lancet.* (2015) 386:1442. doi: 10.1016/S0140-6736(15)00404-3
 26. Van der Heyden JHA, Gisle L, Hesse E, Demarest S, Driessens S, Tafforeau J. Gender differences in the use of anxiolytics and antidepressants: a population based study. *Pharmacoepidemiol Drug Saf.* (2009) 18:1101–10. doi: 10.1002/pds.1827
 27. Lewer D, O'Reilly C, Mojtabei R, Evans-Lacko S. Antidepressant use in 27 European countries: associations with sociodemographic, cultural and economic factors. *Br J Psychiatry.* (2015) 207:221–6. doi: 10.1192/bjp.bp.114.156786
 28. Charlson FJ, Ferrari AJ, Santomauro DF, Diminic S, Stockings E, Scott JG, et al. Global epidemiology and burden of schizophrenia: findings from the Global Burden of Disease Study 2016. *Schizophr Bull.* (2018) 44:1195–203. doi: 10.1093/schbul/sby058
 29. Ganasen KA, Parker S, Hugo CJ, Stein DJ, Emsley RA, Seedat S. Mental health literacy: focus on developing countries. *Afr J Psychiatry (Johannesbg).* (2008) 11:23–8. doi: 10.4314/ajpsy.v11i1.30251
 30. Wang Q, Tian W. Prevalence, awareness, and treatment of depressive symptoms among the middle-aged and elderly in China from 2008 to 2015. *Int J Health Plann Manage.* (2018) 33:1060–70. doi: 10.1002/hpm.2581
 31. Kantor ED, Rehm CD, Haas JS, Chan AT, Giovannucci EL. Trends in prescription drug use among adults in the United States from 1999–2012. *JAMA.* (2015) 314:1818–31. doi: 10.1001/jama.2015.13766
 32. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. *Annu Rev Public Health.* (2013) 34:119–38. doi: 10.1146/annurev-publhealth-031912-114409
 33. Li C, Huang J, Cheng Y-C, Zhang Y-W. Traditional Chinese medicine in depression treatment: from molecules to systems. *Front Pharmacol.* (2020) 11:586. doi: 10.3389/fphar.2020.00586
 34. Novick D, Montgomery W, Moneta V, Peng X, Brugnoli R, Haro JM. Antidepressant medication treatment patterns in Asian patients with major depressive disorder. *Patient Prefer Adherence.* (2015) 9:421–8. doi: 10.2147/PPA.S68432
 35. Du Y, Wolf I-K, Knopf H. Psychotropic drug use and alcohol consumption among older adults in Germany: results of the German Health Interview and Examination Survey for Adults 2008–2011. *BMJ Open.* (2016) 6:e012182. doi: 10.1136/bmjopen-2016-012182
 36. Okumura Y, Sakata N. Antidementia drug use in Japan: bridging the research-to-practice gap. *Int J Geriatr Psychiatry.* (2018) 33:1286–7. doi: 10.1002/gps.4892
 37. Doblhammer G, Fink A, Fritze T. Short-term trends in dementia prevalence in Germany between the years 2007 and 2009. *Alzheimers Dement.* (2015) 11:291–9. doi: 10.1016/j.jalz.2014.02.006
 38. Fukawa T. Prevalence of dementia among the elderly population in Japan. *Health Prim Car.* (2018) 2:1–6. doi: 10.15761/HPC.1000112
 39. Lang L, Clifford A, Wei L, Zhang D, Leung D, Augustine G, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. *BMJ Open.* (2017) 7:e011146. doi: 10.1136/bmjopen-2016-011146
 40. Wolters FJ, Ikram MA. Epidemiology of vascular dementia. *Arterioscler Thromb Vasc Biol.* (2019) 39:1542–9. doi: 10.1161/ATVBAHA.119.311908
 41. Jia L, Du Y, Chu L, Zhang Z, Li F, Lyu D, et al. Prevalence, risk factors, and management of dementia and mild cognitive impairment in adults aged 60 years or older in China: a cross-sectional study. *Lancet Public Health.* (2020) 5:e661–e71. doi: 10.1016/S2468-2667(20)30185-7
 42. Jia J, Zuo X, Jia X-F, Chu C, Wu L, Zhou A, et al. Diagnosis and treatment of dementia in neurology outpatient departments of general hospitals in China. *Alzheimers Dement.* (2016) 12:446–53. doi: 10.1016/j.jalz.2015.06.1892
 43. Ferrari AJ, Stockings E, Khoo J-P, Erskine HE, Degenhardt L, Vos T, et al. The prevalence and burden of bipolar disorder: findings from the Global Burden of Disease Study 2013. *Bipolar Disord.* (2016) 18:440–50. doi: 10.1111/bdi.12423
 44. Parabiaghi A, Barbato A, Riso P, Fortino I, Bortolotti A, Merlino L, et al. Lithium use from 2000 to 2010 in Italy: a population-based study. *Pharmacopsychiatry.* (2015) 48:89–94. doi: 10.1055/s-0034-1398506
 45. Verdoux H, Pambrun E, Cortaredona S, Coldefy M, Le Neindre C, Tournier M, et al. Geographical disparities in prescription practices of lithium and clozapine: a community-based study. *Acta Psychiatr Scand.* (2016) 133:470–80. doi: 10.1111/acps.12554
 46. Gong AT, Furnham A. Mental health literacy: public knowledge and beliefs about mental disorders in mainland China. *Psych J.* (2014) 3:144–58. doi: 10.1002/pchj.55
 47. Depp C, Ojeda VD, Mastin W, Unützer J, Gilmer TP. Trends in use of antipsychotics and mood stabilizers among Medicaid beneficiaries with bipolar disorder, 2001–2004. *Psychiatr Serv.* (2008) 59:1169–74. doi: 10.1176/ps.2008.59.10.1169
 48. Li S, Jiang T, Han M. Investigation on the drug use of bipolar disorder patients. *J Qiqihar Med Univ.* (2018) 39:556–9 (in Chinese).
 49. Liu A, Xu Y, Yan Q, Tong L. The prevalence of attention deficit/hyperactivity disorder among Chinese children and adolescents. *Sci Rep.* (2018) 8:11169. doi: 10.1038/s41598-018-29488-2
 50. Akmatov MK, Steffen A, Holstiege J, Hering R, Schulz M, Bätzing J. Trends and regional variations in the administrative prevalence of attention-deficit/hyperactivity disorder among children and adolescents in Germany. *Sci Rep.* (2018) 8:17029. doi: 10.1038/s41598-018-35048-5
 51. Xu G, Strathearn L, Liu B, Yang B, Bao W. Twenty-year trends in diagnosed attention-deficit/hyperactivity disorder among US children and adolescents, 1997–2016. *JAMA Netw Open.* (2018) 1:e181471. doi: 10.1001/jamanetworkopen.2018.1471
 52. Himshaw SP, Scheffler RM, Fulton BD, Aase H, Banaschewski T, Cheng W, et al. International variation in treatment procedures

- for ADHD: social context and recent trends. *Psychiatr Serv.* (2011) 62:459–64. doi: 10.1176/ps.62.5.pss6205_0459
53. Stuhec M, Locatelli I, Svab V. Trends in attention-deficit/hyperactivity disorder drug consumption in children and adolescents in Slovenia from 2001 to 2012: a drug use study from a national perspective. *J Child Adolesc Psychopharmacol.* (2015) 25:254–9. doi: 10.1089/cap.2014.0071
54. Zito JM, Safer DJ, dosReis S, Gardner JE, Boles M, Lynch F. Trends in the prescribing of psychotropic medications to preschoolers. *JAMA.* (2000) 283:1025–30. doi: 10.1001/jama.283.8.1025
55. Keshwani S, Grande I, Maguire M, Goodin A, Vouri SM, Hincapie-Castillo JM. Trends in use of prescription nonsteroidal anti-inflammatory medications before vs after implementation of a florida law restricting opioid prescribing for acute pain. *JAMA Netw Open.* (2021) 4:e2113383. doi: 10.1001/jamanetworkopen.2021.13383

Conflict of Interest: QL and SG were employed by Beijing Brainpower Pharma Consulting Co., Ltd.

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