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Research Article

Continuous Improvement of the Rational Use of Central Nervous System Disease-Related Drugs in Elderly Inpatients

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What Is Known? In elderly inpatients, potential inappropriate medication (PIM) is a prominent prescription challenge. However, there is limited information available regarding PIM in patients with central nervous system (CNS) diseases in China. *Objective*. To evaluate and improve the rational use of drugs for the treatment of CNS diseases in elderly inpatients. *Method*. A retrospective, cross-sectional study was conducted among elderly inpatients (≥65 years) admitted to the Ninth People's Hospital of Zhengzhou in China from March 2020 to March 2021. PIM was identified based on the 2019 Beers criteria at admission and discharge. The patients recruited in March 2020 were considered a baseline group, which was used as a comparison to evaluate PIM of CNS disease-related drugs in June 2020, September 2020, December 2020, and March 2021. *Results*. A total of 1500 patients were included in the evaluation. There was a statistically significant difference in the number of average hospitalization days, drug varieties used, and PIM detection ($p < 0.05$), as determined by X^2 test. A total of 332 cases of PIM were identified, and 226 cases were detected for the interaction with CNS disease dementia. Multifactor logistic regression analysis showed that male, length of stay ≥15 days, and >10 medication types were risk factors for the occurrence of PIM ($p < 0.05$). After clinical supervision and training based on the High-Risk Drug Replacement Program for the Elderly, the rate of irrational medication under medical advice decreased from 34.67% in March 2020 to 14.0% ($p < 0.001$) in March 2021. *What Is New and Conclusion*. There was certain rationality based on the High-Risk Drug Replacement Program for the Elderly, and the rates of selective serotonin reuptake inhibitor, 5-hydroxylamine/norepinephrine re-intake inhibitor, rotenone, quetiapine, and proton pump inhibitor use were improved. These results provide a reference for the continuous improvement of the PIM catalog for elderly patients.

1. What Is Known and Objective

The 2019 Health China Action (2019–2030) released by the National Health and Wellness Commission shows that China has the largest elderly population worldwide, accounting for one-fifth of the global elderly population. Moreover, nearly 180 million of the elderly individuals in China are reportedly affected by chronic diseases [1]. The elderly experience conditions and internal processes with high pathophysiological complexity are affected by multiple comorbidities. Additionally, the pharmacodynamic and pharmacokinetic changes caused by aging render the elderly more prone to drug-drug interactions, adverse drug reactions (ADRs), and other medication risks [2]; thus, elderly individuals are prone to taking potentially inappropriate medication (PIM). PIM refers to medications that are not recommended for use in older adults due to either a high potential for harmful side effects or a lack of evidence supporting their benefits when safer and more effective treatment options are available [3]. Notably, a high prevalence of polypharmacy (≥50%) and PIM use (>30%) in Chinese elderly patients was found [4, 5].

In 1991, Beers, an American geriatrician, organized a meeting of experts in clinical pharmacology, pharmacy-epidemiology, and psychopharmacology who, based on a review of relevant literature, used the Delphi method to

establish Beers criteria, which is a screening tool for PIM in elderly patients [6]. Since then, Beers criteria have been updated periodically, with the latest version released by the American Geriatrics Society (AGS) in January 2019 [7]. Beers criteria play a crucial role in identifying PIM in elderly patients and reducing irrational drug use, providing valuable guidance to clinicians and pharmacists in selecting drug therapy [8]. To further improve medication safety for older adults, the AGS developed the High-Risk Drug Substitution Program for Older Adults based on the AGS Beers criteria [9]. The program offers a list of PIMs for older adults and suggests alternative medications that are safer for older adults when available and is intended to be used by healthcare professionals to improve medication safety. Essentially, the program provides a list of potentially safer alternative medications that can be used instead of the PIMs listed in the Beers criteria.

Hospitalized elderly patients often experience reduced cerebral blood flow and varying degrees of brain tissue atrophy but with increased brain oxygen consumption [10]. In such cases, the brain tissue synthesis of certain proteins is reduced, and neurotransmitters are significantly altered, with a decrease of catecholamines in the brainstem and an increase in the cerebellum [11]. Clinically, elderly people often present with shortened sleep duration, slow movement, emotional indifference, memory loss, and reduced coordination of whole body organ activities [12]. Furthermore, the use of multiple central nervous system (CNS) drugs in combination or in high doses increases the risk of falls [13]. Moreover, drugs with strong anticholinergic effects can aggravate the risk of constipation, dry mucous membranes, delirium, and dementia in the elderly [14].

Although several studies have evaluated PIM of patients with CNS disease [15, 16], no studies are available on the use of 2019 Beers criteria to access and evaluate the rational use of CNS disease-related drugs in elderly inpatients in China. Therefore, we applied the 2019 Beers criteria and the High-Risk Medication Replacement Program for the Elderly to assess, analyze, and intervene in the PIM status of CNS-related medications in hospitalized elderly patients.

2. Method

2.1. Study Design and Setting. This cross-sectional and retrospective study was conducted in China at the Ninth People's Hospital of Zhengzhou, Zhengzhou, Henan, from March 1, 2020, to March 31, 2021. Geriatric inpatients treated for CNS disorders were randomly selected from the hospital information system (HIS) of the geriatric center, neurology ward, and psychology ward of a tertiary general hospital.

The inclusion criteria were as follows: (i) patients aged ≥65 years; (ii) hospitalization duration ≥3 days and ≤30 days; and (iii) recorded information regarding drugs considered in the 2019 Beers criteria and in the High-Risk Drug Replacement Program. The exclusion criteria were as follows: (i) patients with tumor lesions and (ii) patients who died or were repeatedly admitted (admitted to other hospitals and took medications prescribed by outside providers) to the hospital. We summarized the collected information in March 2020, June 2020, September 2020, December 2020, and March 2021. After exclusion, we collected 300 elderly inpatients in each period. The cases of PIM represent the number of elderly inpatients taking at least one PIM.

The rational use of CNS disease-related drugs was assessed in elderly inpatients in March 2020 as the baseline group and in June 2020, September 2020, December 2020, and March 2021 as the evaluation group (Table 1). Figure 1 illustrates the participant inclusion flowchart.

2.2. Data Collection. The following information was collected from the patients' electronic medical records: name, sex, age, diagnosis, prescribed drugs, dosages, course of treatment, and length of stay and was finally exported in an Excel sheet. To guarantee patient confidentiality, all the data collected were anonymized and stored in a specific database.

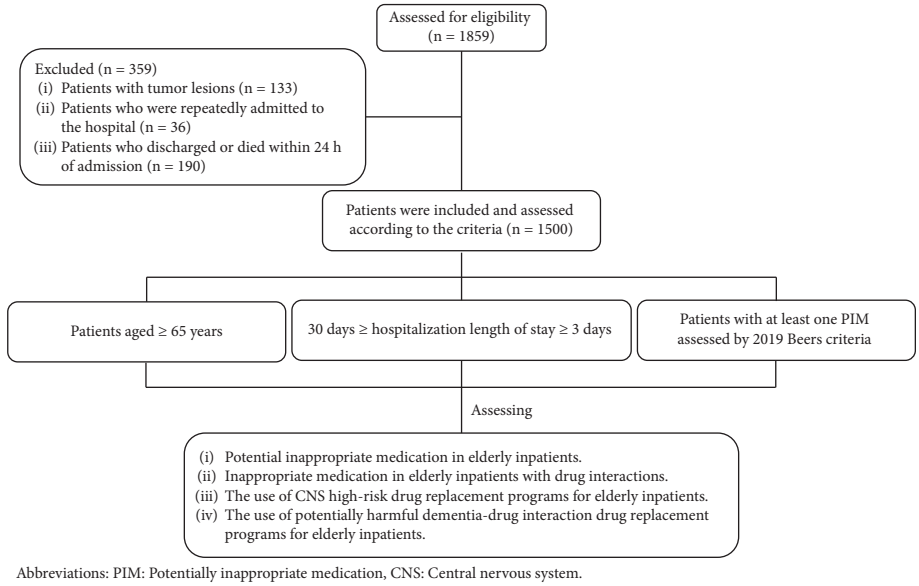
2.3. Evaluation Criteria. The evaluation criteria were as follows: (i) the 2019 Beers criteria were applied to detect the prevalence of PIM in elderly inpatients, with at least one PIM detected for each patient; (ii) inappropriate medication use in elderly inpatients with drug-CNS disease interactions; (iii) use of CNS High-Risk Drug Replacement Programs for Elderly inpatients; and (iv) use of potentially harmful dementia-drug interaction and drug replacement programs for elderly inpatients. We applied Table 2 (PIM use in elderly hospitalized patients), Table 3 (PIM use of CNS drugs in elderly hospitalized patients), Table 4 (PIM use in elderly hospitalized patients due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome), Table 5 (CNS High-Risk Drug Replacement Program for elderly inpatients), and Table 6 (potentially harmful dementia in elderly hospitalized patients-drug interaction drug replacement regimen) of the 2019 Beers criteria to evaluate PIM use in elderly inpatients. The assessment of PIM was performed by two pharmacists (Yinpeng Xu and Yahui Cui) and confirmed by a senior clinical pharmacist (Fang Li).

2.4. Feedback Intervention. During the survey, the system incorporating the PIMs list based on the 2019 Beers criteria and the High-Risk Drug Substitution Program for Older Adults implemented automatic monitoring of drug prescriptions and provided immediate prompts to doctors for any instances of irrational drug prescription. Doctors could modify their prescriptions or submit them for review by pharmacists after self-examination. Pharmacists were able to interact with doctors in real-time during the review process until the prescription was approved, thereby achieving the desired interventional effect of prescription review. The feedback process for individual prescribing errors was completed within a short period of 1 to 3 minutes.

2.5. Ethics Approval. The study protocol was approved by the Ethics Committee of the Ninth People's Hospital of Zhengzhou (LLX001).

Table 1: Patient screening.

		March 2020 (baseline) (*n*)	June 2020 (*n*)	September 2020 (*n*)	December 2020 (*n*)	March 2021 (*n*)
Excluded	Tumor lesions	23	30	22	20	38
	Readmitted	4	8	10	2	12
	Died or discharged	33	59	48	30	20
Included		300	300	300	300	300



Abbreviations: PIM: Potentially inappropriate medication, CNS: Central nervous system.

Figure 1: Flowchart of the study.

2.6. Statistical Analysis. Statistical analysis was performed using SPSS 26.0 software. Count data are expressed as the number of cases (percentage) [*n* (%)], and the X^2 test was used for comparisons between groups. Multifactor logistic regression was utilized to analyze the factors influencing the occurrence of PIM in elderly patients. $p < 0.05$ was considered a significant difference.

3. Results

3.1. Characteristics of the Study Population. A total of 1859 participants were recruited in initial study. Patients were excluded from the study due to tumor lesions ($n = 133$), readmissioned ($n = 36$), and discharged or died within 24 h of admission ($n = 190$) (Figure 1). Table 2 presents the clinical and sociodemographic characteristics of the follow-up study sample in China. Among the remaining 1500 patients, the mean age was 74.97 ± 8.54 years, and 771 (51.40%) patients were male. The average duration of hospital stays and mean total number of medications used during hospitalization were 13.13 ± 8.67 days and 12.42 ± 4.49, respectively. According to the 2019 Beers criteria, 332 out of the 1500 elderly inpatients analyzed (22.14%) were identified as having been prescribed at least one PIM (Table 2). The prevalence of PIM use among male inpatients was 12.47%, while the prevalence among female inpatients was 9.67%. Additionally, there were statistically significant differences in PIM occurrence between groups in terms of sex, number of days in hospital, and total number of medication varieties ($p < 0.05$) (Table 2).

3.2. Multifactorial Logistic Regression Analysis of PIM in Elderly Patients. Logistic regression equations were established using the sex, length of stay, and total number of medications as independent variables and the incidence of PIM as a dependent variable in Table 7. The results showed that male, length of stay ≥15 days, and >10 medication types increased the likelihood of PIM ($p < 0.05$).

3.3. Covariate Diagnosis. A covariance diagnosis was performed for the three variables that were statistically significant in the univariate analysis. The variance inflation factors (VIFs) for sex, length of stay, and total number of medication varieties were 1.025, 1.005, and 1.022, respectively. All VIFs were <10, the variables were independent of each other, and there was no covariance.

3.4. Correlation Analysis of Detected PIM Subgroups with Sex, Days of Hospitalization, and Total Number of Medication Varieties. Spearman's correlation analysis showed that PIM was positively correlated with the sex ($r = 0.053$ and

Table 2: Patient characteristics.

Variable	Total	PIM ($n = 332$)	Non-PIM ($n = 1168$)	X^2	*p value*
Sex					
Male, *n* (%)	771 (51.40%)	187 (12.47%)	584 (38.93%)	4.140	*0.042
Female, *n* (%)	729 (48.60%)	145 (9.67%)	584 (38.93%)		
Age, years					
65–74, *n* (%)	919 (61.27%)	190 (12.67%)	729 (48.60%)		
75–84, *n* (%)	380 (25.33%)	92 (6.13%)	288 (19.20%)	2.963	0.227
≥85, *n* (%)	201 (13.40%)	50 (3.33%)	151 (10.07%)		
Length of stay, days					
≤7, *n* (%)	396 (26.40%)	38 (2.53%)	358 (23.87%)		
8–14, *n* (%)	594 (39.60%)	48 (3.20%)	546 (36.40%)	305.79	***0.00
≥15	510 (34.00%)	246 (16.40%)	264 (17.60%)		
Total number of medications					
≤10	434 (28.93%)	75 (5.00%)	359 (23.93%)	8.343	**0.004
>10	1066 (71.07%)	257 (17.13%)	809 (53.94%)		

Note. PIM: potentially inappropriate medication. Statistical comparisons between sex, length of stay, and total number of medications, according to the X^2 test. $^{*}p < 0.05$, $^{**}p < 0.01$, and $^{***}p < 0.001$.

Table 3: Potentially inappropriate CNS medication cases detected in elderly inpatients based on the 2019 version of the Beers criteria.

Disease category	Drug category	Drug name	Reason	Recommendation	Quality of evidence	March 2020, *n* (%)	June 2020, *n* (%)	September 2020, *n* (%)	December 2020, *n* (%)	March 2021, *n* (%)
Central nervous system	Tricyclic antidepressants	Clomipramine	Highly anticholinergic	Avoid	High	2 (0.13%)	1 (0.07%)	0 (0%)	0 (%)	0 (%)
	Antipsychotics	Chlorpromazine	Increased risk of stroke in the elderly, cognitive decline, and increased mortality in patients with dementia	Avoid	Moderate	16 (1.07%)	12 (0.80%)	5 (0.33%)	4 (0.27%)	2 (0.13%)
		Haloperidol				3 (0.20%)	1 (0.07%)	2 (0.13%)	0 (%)	1 (0.07%)
		Sulpiride				3 (0.20%)	2 (0.13%)	0 (0%)	0 (%)	0 (%)
		Perphenazine				1 (0.07%)	0 (0%)	0 (0%)	0 (%)	1 (0.07%)
		Clozapine				6 (0.40%)	3 (0.20%)	2 (0.13%)	1 (0.07%)	1 (0.07%)
		Olanzapine				20 (1.33%)	17 (1.13%)	9 (0.60%)	8 (0.53%)	6 (0.40%)
		Ziprasidone				3 (0.20%)	2 (0.13%)	1 (0.07%)	1 (0.07%)	0 (%)
		Aripiprazole				3 (0.20%)	2 (0.13%)	3 (0.20%)	1 (0.07%)	1 (0.07%)
	Barbiturates	Phenobarbital	Strong physical dependence, with a risk of overdose and poisoning at low doses	Avoid	High	6 (0.40%)	4 (0.27%)	1 (0.07%)	0 (%)	0 (%)
	Benzodiazepines	Alprazolam	All benzodiazepines enhance cognitive impairment, delirium, and the risk of falls and fractures	Avoid	Moderate	10 (0.67%)	7 (0.47%)	3 (0.20%)	2 (0.13%)	4 (0.27%)
		Estazolam				6 (0.40%)	5 (0.33%)	2 (0.13%)	2 (0.13%)	1 (0.07%)
		Lorazepam				4 (0.27%)	4 (0.27%)	4 (0.27%)	3 (0.20%)	2 (0.13%)
		Oxazepam				3 (0.20%)	2 (0.13%)	0 (0%)	0 (%)	0 (%)
		Diazepam				6 (0.40%)	4 (0.27%)	3 (0.20%)	2 (0.13%)	1 (0.07%)
		Clonazepam				4 (0.27%)	1 (0.07%)	0 (0%)	0 (%)	0 (%)
	Benzodiazepine receptor agonist hypnotic	Eszopiclone	Adverse effects in the elderly	Avoid	Moderate	8 (0.53%)	15 (1.0%)	21 (1.40%)	24 (1.60%)	22 (1.47%)

Table 4: Cases of inappropriate medication use in geriatric inpatients with drug-central nervous system disease interactions.

Disease category	Disease	Name of drug	Recommendation	Quality of evidence	March 2020, *n* (%)	June 2020, *n* (%)	September 2020, *n* (%)	December 2020, *n* (%)	March 2021 *n* (%)
Central nervous system	Dementia	Antihistamines (chlorpheniramine, diphenhydramine)	Avoid	Moderate	3 (0.20%)	1 (0.07%)	0 (0%)	0 (%)	2 (0.13%)
		Benzodiazepines			18 (1.20%)	12 (0.80%)	7 (0.47%)	6 (0.40%)	4 (0.27%)
		Benzodiazepine receptor agonist hypnotic			4 (0.27%)	7 (0.47%)	13 (0.87%)	15 (1.0%)	21 (1.40%)
		Antipsychotic drugs (except risperidone and quetiapine)			23 (1.53%)	17 (1.13%)	11 (0.73%)	10 (0.67%)	12 (0.80%)
		H2 receptor antagonist (ranitidine)			18 (1.20%)	11 (0.73%)	5 (0.33%)	4 (0.27%)	2 (0.13%)

Table 5: CNS high-risk drug substitution regimen for elderly inpatients.

Disease category	Category of drugs	High-risk drug	Alternative regimens of drugs	June 2020, *n* (%)	September 2020, *n* (%)	December 2020, *n* (%)	March 2021, *n* (%)
Central nervous system	Tricyclic antidepressants	Clomipramine	Fluoxetine	2 (0.13%)	2 (0.13%)	1 (0.07%)	2 (0.13%)
			Sertraline	3 (0.20%)	22 (1.47%)	18 (1.20%)	24 (1.60%)
			Fluvoxamine	2 (0.13%)	2 (0.13%)	2 (0.13%)	3 (0.20%)
			Escitalopram	8 (0.53%)	9 (0.60%)	7 (0.47%)	8 (0.53%)
			Venlafaxine	2 (0.13%)	4 (0.27%)	3 (0.20%)	1 (0.07%)
			Duloxetine	3 (0.20%)	4 (0.27%)	4 (0.27%)	5 (0.33%)
	Barbiturates	Phenobarbital	Lamotrigine	1 (0.07%)	1 (0.07%)	0 (%)	1 (0.07%)
			Levetiracetam	3 (0.20%)	4 (0.27%)	3 (0.20%)	5 (0.33%)
			Sodium valproate	27 (1.80%)	31 (2.07%)	35 (2.33%)	29 (1.93%)
			Gabapentin	2 (0.13%)	2 (0.13%)	1 (0.07%)	3 (0.20%)
			Oxcarbazepine	2 (0.13%)	3 (0.20%)	3 (0.20%)	4 (0.27%)

Table 6: Potentially harmful dementia in elderly hospitalized patients-drug-drug interactions replacement regimen.

Disease	Category of potentially harmful drug	Potentially harmful drug	Replacement proposal	Replacement drug	June 2020, *n* (%)	September 2020, *n* (%)	December 2020, *n* (%)	March 2021, *n* (%)
Dementia	Tricyclic antidepressants	Clomipramine	SSRI and SNRI drugs are used for patients with depression	Fluoxetine	0 (0%)	1 (0.07%)	1 (0.07%)	2 (0.13%)
				Sertraline	1 (0.07%)	1 (0.07%)	2 (0.13%)	3 (0.20%)
				Fluvoxamine	0 (0%)	1 (0.07%)	0 (%)	1 (0.07%)
				Escitalopram	3 (0.20%)	5 (0.33%)	4 (0.27%)	6 (0.40%)
				Venlafaxine	1 (0.07%)	0 (0%)	0 (%)	1 (0.07%)
				Duloxetine	0 (0%)	1 (0.07%)	2 (0.13%)	1 (0.07%)
	Antipsychotics	Chlorpromazine	For behavioral complications associated with dementia, low doses of non-anticholinergic drugs may be used in the short term if nonpharmacological approaches fail/are combined with psychosis/individuals are dangerous to themselves and others	Risperidone	5 (0.33%)	6 (0.40%)	8 (0.53%)	12 (0.80%)
		Haloperidol		Quetiapine	58 (3.87%)	80 (5.33%)	81 (5.40%)	82 (5.47%)
		Sulpiride						
		Perphenazine						
		Clozapine						
		Olanzapine						
		Ziprasidone						
		Aripiprazole						
	H2 receptor antagonist	Ranitidine	PPI drugs are recommended	Omeprazole	3 (0.20%)	5 (0.33%)	5 (0.33%)	6 (0.40%)
				Esomeprazole	14 (0.93%)	17 (1.13%)	24 (1.60%)	21 (1.40%)
				Pantoprazole	2 (0.13%)	2 (0.13%)	2 (0.13%)	1 (0.07%)
				Lansoprazole	1 (0.07%)	2 (0.13%)	2 (0.13%)	3 (0.20%)
				Rabeprazole	3 (0.20%)	5 (0.33%)	4 (0.27%)	3 (0.20%)
	Anticholinergic drugs	Chlorpheniramine	Second generation antihistamines are recommended	Loratadine	1 (0.07%)	2 (0.13%)	2 (0.13%)	4 (0.27%)
		Diphenhydramine		Levocetirizine	3 (0.20%)	4 (0.27%)	7 (0.47%)	7 (0.47%)
	Benzodiazepines	Alprazolam	Buspirone, SSRIs, and SNRIs were used for anxiety patients	Buspirone	2 (0.13%)	4 (0.27%)	5 (0.33%)	3 (0.20%)
		Estazolam		Fluoxetine	1 (0.07%)	1 (0.07%)	1 (0.07%)	0 (%)
		Lorazepam		Sertraline	1 (0.07%)	1 (0.07%)	2 (0.13%)	3 (0.20%)
		Oxazepam		Fluvoxamine	0 (0%)	0 (0%)	0 (%)	1 (0.07%)
		Diazepam		Escitalopram	1 (0.07%)	0 (0%)	0 (%)	1 (0.07%)
				Venlafaxine	2 (0.13%)	2 (0.13%)	0 (%)	3 (0.20%)
				Duloxetine	2 (0.13%)	2 (0.13%)	1 (0.07%)	2 (0.13%)
	Benzodiazepine receptor agonist hypnotic	Eszopiclone		Health behavioral interventions for sleep	7 (0.47%)	13 (0.87%)	15 (1.00%)	19 (1.27%)

Note. SSRIs: selective serotonin reuptake inhibitors; SNRIs: serotonin-norepinephrine reuptake inhibitors; PPI: proton pump inhibitor.

Table 7: Multifactor logistic regression analysis of the occurrence of PIM in elderly patients.

Variable	β	Standard error	$^{\text{Wald}}\chi^a$	p	OR	95% CL
Sex	0.791	0.151	27.328	0.000	2.205	1.639–2.965
Length of stay	2.161	0.195	122.974	0.000	8.681	5.925–12.719
Total number of medications	0.483	0.166	8.513	0.004	1.621	1.172–2.242

$p = 0.042$), days of hospitalization ($r = 0.388$ and $p = 0$), and total number of medication types ($r = 0.075$ and $p = 0.004$).

3.5. Potentially Inappropriate Administration of CNS Drugs in Elderly Hospitalized Patients. Overall, 332 (22.14%) were found to have been prescribed at least one potentially inappropriate medication (PIM) related to CNS drugs according to the 2019 Beers criteria. Of those taking PIMs, 0.20% were prescribed antidepressants, primarily clomipramine, and a tricyclic antidepressant. 4.00% were prescribed antipsychotics, mostly olanzapine. 0.73% were prescribed barbiturates, predominantly phenobarbital. 1.73% were prescribed benzodiazepines, mainly alprazolam. Lastly, 6.0% of those taking PIMs were prescribed benzodiazepine receptor agonist hypnotics, primarily dexzopiclone. Except for dexzopiclone, the usage of all other drugs decreased month-by-month (Table 3).

3.6. Inappropriate Medication Use in Geriatric Inpatients with Drug-CNS Disease Interactions. Of the elderly inpatients taking at least one PIM identified, first-generation antihistamines (chlorpheniramine and diphenhydramine) were used by 0.40% primarily for chronic urticaria with pruritus, but their overall use was low due to the availability of loratadine and levocetirizine. Benzodiazepines were used by 3.13% (47 cases) of the elderly inpatients for anxiety and insomnia, which is considered a PIM due to the high risk of adverse events in older adults. Additionally, 4.0% (60 cases) of the elderly inpatients taking at least one PIM identified were using benzodiazepine agonist hypnotics (dexzopiclone) for insomnia. In 73 cases (4.86%), elderly patients with dementia experienced manic symptoms that required intervention with antipsychotic drugs, excluding risperidone and quetiapine. Finally, 2.66% (40 cases) of the elderly inpatients taking at least one PIM identified were using H2 receptor antagonists (ranitidine), mainly in hospitalized patients with gastrointestinal bleeding and short-term use of nonsteroidal anti-inflammatory drugs (Table 4).

3.7. Screening the Use of a High-Risk Drug Replacement Regimen in Elderly Hospitalized Patients. According to the High-Risk Drug Replacement Program for the Elderly, the high-risk CNS drugs used in our hospital were tricyclic antidepressants and barbiturates. Selective serotonin reuptake inhibitors (SSRIs) (except paroxetine) and serotonin-norepinephrine reuptake inhibitors (SNRIs) were recommended for the replacement of tricyclic antidepressants (clomipramine) in patients with depression. Tricyclic antidepressants were replaced in 7 cases (0.47%) with fluoxetine, 69 cases (4.47%) with sertraline, 9 cases (0.60%) with fluvoxamine, 32 cases (2.13%) with escitalopram, 10 cases (0.67%) with venlafaxine, and 16 cases (1.07%) with duloxetine; overall, SSRIs (115 cases, 7.67%) were used more often than SNRIs (26 cases, 1.73%), and escitalopram was utilized the most. In patients with epilepsy, it is recommended to replace barbiturates with nonbarbiturates, and the replacement drugs in our hospital were lamotrigine in three cases (0.20%), levetiracetam in 15 cases (1.00%), sodium valproate in 122 cases (8.13%), gabapentin in 8 cases (0.53%), and oxcarbazepine in 12 cases (0.80%). A further review of the cases revealed that sodium valproate was administered most frequently because valproate oral solutions and tablets were available in our hospital (Table 5).

3.8. Potentially Harmful Dementia in Elderly Hospitalized Patients: An Examination of the Use of Drug Interaction and Drug Replacement Regimens. Following the guidelines of the High-Risk Drug Replacement Program for the Elderly, tricyclic antidepressants (clomipramine) were replaced with fluoxetine in 4 cases (0.27%), sertraline in 7 cases (0.47%), fluvoxamine in 2 cases (0.13%), escitalopram in 18 cases (1.20%), venlafaxine in 2 cases (0.13%), and duloxetine in 4 cases (0.27%) of elderly patients with dementia with depressive symptoms. In the presence of manic symptoms, antipsychotics, such as chlorpromazine, haloperidol, and clozapine, were replaced with risperidone in 31 cases (2.07%) and quetiapine in 301 cases (20.07%). A further review of the cases revealed that quetiapine was administered at the highest doses but was used in low doses for a short period of time only in 137 (9.13%) cases. In the presence of gastrointestinal bleeding and short-term nonsteroidal anti-inflammatory drug use, H2 receptor antagonists (ranitidine) were replaced with omeprazole in 19 cases (1.27%), esomeprazole in 76 cases (5.07%), pantoprazole in 7 cases (0.47%), lansoprazole in 8 cases (0.53%), and rabeprazole in 15 cases (1.00%), with esomeprazole being administered at the highest dose. When other symptoms were accompanied by pruritus, first-generation antihistamines were replaced with loratadine in 9 cases (0.60%) and levocetirizine in 21 cases (1.40%); levocetirizine oral solution was used because of the high number of elderly bedridden patients with nasal feeding tubes in our hospital. In the presence of anxiety, benzodiazepines, such as alprazolam and lorazepam, were replaced with buspirone in 14 cases (0.93%), fluoxetine in 3 cases (0.20%), sertraline in 7 cases (0.47%), escitalopram in 2 cases (0.13%), venlafaxine in 7 cases (0.47%), and duloxetine in 7 cases (0.47%), with buspirone being the most used (Table 6).

3.9. Continuous Improvement in the Results Using the High-Risk Drug Replacement Program for the Elderly. A study was conducted in March 2020 to investigate the use of CNS medications in 300 elderly inpatients according to the High-

Table 8: Continuous improvement statistics for use of the High-Risk Drug Replacement Program for the Elderly.

Inspections	Congruent with Beers criteria, (n)	Incongruent with Beers criteria, (n)	Percentage of irrational medication rate (%)	X^2	p value
Control group	196	104	34.67		
Second inspection	218	82	27.33	3.77	0.052
Third inspection	244	56	18.67	19.63	***0.000
Fourth inspection	252	48	16.00	27.63	***0.000
Fifth inspection	258	42	14.00	34.79	***0.000

Note. Statistical comparisons between inspections, according to the X^2 test. $^{*}p < 0.05$ and $^{***}p < 0.001$.

Risk Drug Replacement Program for the Elderly. Subsequent investigations were carried out in June, September, December 2020, and March 2021, with 300 cases examined in each round. The proportion of cases deemed unsuitable for medication was 27.33% in June 2020, 18.67% in September 2020, 16.0% in December 2020, and 14.0% in March 2021, with the results of the first examination serving as the basis for analysis. The results of the control group differed significantly ($p < 0.05$) from those of the second to fifth examinations, as shown in Table 8.

4. Discussion

The 2019 edition of the Beers criteria is the most current evidence-based standard for PIM use [7]. In this study, these criteria were used to analyze data from a geriatric center, mental health center, and neurology department. 332 out of the 1500 elderly inpatients analyzed (22.14%) were identified as having been prescribed at least one PIM related to CNS drugs in this survey. The High-Risk Drug Replacement Program for the Elderly, which is based on Beers criteria for proposing high-risk drug replacement programs for the elderly, used potential CNS drug replacement in 920 cases (67.60%) during the survey.

4.1. Analysis of PIM Use of CNS-Related Drugs in Elderly Hospitalized Patients. The dosage of clomipramine used in the mental health center to treat depression was low for two reasons: firstly, the high anticholinergic and sedative effects of tricyclic antidepressants [17], which can cause postural hypotension [18], and secondly, the availability of SSRI and SNRI analogues for replacement in our hospital. Olanzapine was used primarily for the treatment of schizophrenia and manic episodes by the mental health and geriatric centers, respectively. Olanzapine and risperidone increase the risk of stroke in elderly patients, cognitive decline in patients with dementia, and mortality [19, 20]. Phenobarbital was used primarily by the neurology and geriatric centers for the treatment of epilepsy, which can cause physical dependence and resistance and is associated with an increased risk of toxicity at low doses [21]. In our hospital, phenobarbital was mostly administered for short-term treatment. Alprazolam was mainly used by the mental health and geriatric centers for anxiety disorders and insomnia, respectively. However, the metabolism of long-acting alprazolam is reduced in the elderly [22], which increases the risk of cognitive dysfunction, delirium, falls, and fractures [23, 24]. Dexzopiclone is predominantly used in mental health centers, geriatric centers, and neurology departments, for the treatment of insomnia. The abovementioned drugs have similar adverse effects to benzodiazepines, which increase the risk of emergencies and hospitalizations in elderly patients [25]. However, as the relevant domestic guidelines state that they have fewer adverse effects than benzodiazepines, many patients using benzodiazepines are converted to dexzopiclone [14].

4.2. Analysis of Inappropriate Medication Use in Elderly Hospitalized Patients with Drug-Dementia Interactions in CNS Diseases. The use of certain medications should be avoided in elderly patients with CNS diseases, including first-generation antihistamines (chlorpheniramine and diphenhydramine) [26], benzodiazepines [27], benzodiazepine receptor agonist hypnotics, antipsychotics (except risperidone and quetiapine) [28], and H2 receptor antagonists (ranitidine) [29]. First-generation antihistamines have anticholinergic effects, which can lead to confusion, dry mouth, and constipation [26]. Moreover, benzodiazepines increase the risk of cognitive impairment, delirium, falls, and fractures in older adults, although they may be indicated for seizures or severe generalized anxiety [7]. Benzodiazepine receptor agonist hypnotics are associated with a lower risk of drug dependence than traditional benzodiazepines and are safe and effective for the treatment of insomnia [30]. Additionally, they were the only drugs whose dosage increased month-by-month because they are recommended by the relevant domestic guidelines [31]. Antipsychotics (except risperidone and quetiapine) increase the risk of stroke, cognitive decline, and mortality in patients with dementia and should only be used when behavioral intervention therapy fails or when patients cause serious harm to themselves or others [32]. H2 receptor antagonists can cause adverse drug reactions in the CNS and are inappropriate for use in elderly patients with CNS diseases [4].

4.3. Analysis of Utilization Screening of a High-Risk Drug Replacement Program for the CNS in Elderly Hospitalized Patients. According to the High-Risk Drug Replacement Program for the Elderly, tricyclic antidepressants (clomipramine) can be replaced with SSRIs (except paroxetine) and SNRIs for the treatment of depression in the elderly. Tricyclic

antidepressants are not usually preferred because of their anticholinergic and other adverse effects and their tendency to induce seizures and postural hypotension [33]. Paroxetine is the most potent among the SSRIs due to its high capacity to inhibit the reuptake of 5-hydroxytryptamine, block the recycling of norepinephrine, and produce powerful anticholinergic effects [34]. Moreover, the blood levels of paroxetine are 78% higher in the elderly than in young individuals, and the probability of delirium is greater [35]. SSRIs are a first-line treatment for depression in the elderly, with good tolerability, long half-life, stable action, and good compliance [36]. SSRIs also have easy access to the CNS via the blood-brain barrier, as well as high bioavailability and high overall safety [37]. SNRIs, as an alternative treatment to SSRIs, can better relieve anxiety and depression symptoms in elderly patients and improve somatic symptoms, such as pain [38]. For elderly patients with epilepsy, phenobarbital, as a hepatic metabolizing enzyme inducer, may interact with many other drugs [39]. The guidelines mention that elderly patients, especially postmenopausal women, are prone to osteoporosis, and it is recommended to avoid hepatic enzyme-inducing antiepileptic drugs as much as possible and to supplement with vitamin D and calcium [40]. Furthermore, phenobarbital is highly addictive, prone to drug resistance, and associated with a risk of overdose, even at low doses [41]. Therefore, we used lamotrigine, levetiracetam, gabapentin, and oxcarbazepine as alternatives to phenobarbital for the treatment of geriatric epilepsy. Among these drugs, sodium valproate is available in an oral liquid form, which is convenient to ingest and has a clear effect; thus, it is used in the largest amount and is more appropriate.

4.4. Potentially Harmful Dementia in Elderly Inpatients: An Analysis of the Use of Drug Interaction and Drug Replacement Programs for Screening. When treating elderly patients with dementia and depressive symptoms, it is recommended to use antidepressants such as SSRIs (fluoxetine, sertraline, fluvoxamine, and escitalopram) or SNRIs (venlafaxine and duloxetine) [32]. The use of antipsychotics in these patients can increase the risk of stroke and death, according to Beers criteria [7]. However, some studies suggest that risperidone and quetiapine have fewer adverse effects at low doses [42, 43]. If a patient experiences central anticholinergic effects such as impaired cognitive function, sweating, or tremors, the medication should be reduced or stopped and the patient treated symptomatically [44]. Low doses of risperidone and quetiapine are preferred when treating patients with dementia [45]. H2 receptor antagonists may cause drug resistance and discontinuation can lead to rebound symptoms such as hallucinations and mania [46, 47]. Proton pump inhibitors (PPIs) are more effective in increasing gastric pH and reducing the risk of bleeding associated with stress ulcers [48]. The effect of PPIs on reducing the risk of bleeding associated with stress ulcers is significantly better than that of H2 receptor antagonists [49]. Therefore, it was reasonable to administer PPIs in significant excess of H2 receptor antagonists in our institution. First-generation antihistamines are commonly used in our clinic. However, according to the relevant guidelines [50], first-generation antihistamines are prone to cause falls in the elderly due to their obvious central inhibitory effects, while their anticholinergic effects can aggravate adverse effects, such as glaucoma, cardiac arrhythmia, constipation, and difficulty in urination in the elderly; thus, second-generation antihistamines should be preferred.

Second-generation antihistamines do not usually require dose adjustment unless the patient has severe hepatic or renal impairment [51]. As benzodiazepines have adverse effects, buspirone, SSRIs, and SNRIs are considered better options for elderly patients with anxiety [52, 53]. SSRIs and SNRIs should be started at 1/2 to 1/3 of the usual dose and slowly increased, while monitoring for efficacy and tolerability [54]. Beers criteria suggest that nonbenzodiazepine sleep aids have similar risks to benzodiazepines. Health behavioral interventions may be offered to elderly patients with sleep problems. However, most elderly patients with dementia do not respond to these interventions, and benzodiazepine use has decreased, while nonbenzodiazepine use (e.g., dexzopiclone) has increased with pharmacy department supervision and adherence to guidelines [55]. Nonbenzodiazepine hypnotics represent an alternative to benzodiazepines for treating sleep difficulties due to having fewer side effects and being less addictive [56]. Nonbenzodiazepine hypnotics are safe and effective for treating insomnia, improving sleep, and reducing daytime dysfunction in the elderly [57].

This study has several limitations that warrant discussion. Firstly, because the research was conducted at a single institution and center, our findings may have limited generalizability. Nevertheless, the findings indirectly reflect the status of several nursing institutions because we analyzed preadmission medications of patients transferred from various nursing facilities. Secondly, we only have data on medications that were prescribed within the outpatient health system that was studied, which may be missing medications prescribed by outside providers. Thirdly, COVID-19 may have impacted our findings given that it complicates the clinical management of elderly populations. Elderly individuals are more susceptible to COVID-19 infection due to having a weakened immune system and underlying health conditions, such as cardiovascular disease, diabetes, and respiratory illness [58]. Additionally, the pandemic has disrupted healthcare systems, leading to delays in routine medical care and preventative screenings, which can lead to complications and worsen pre-existing conditions, resulting in more severe outcomes for elderly patients [59]. The COVID-19 pandemic has also led to social isolation and loneliness, which lead to depression, anxiety, and cognitive decline, exacerbating pre-existing health conditions [60]. Indeed, a study found statistically significant increases in the use of antipsychotics, benzodiazepines, antidepressants, anticonvulsants, and opioids following the onset of the COVID-19 pandemic, although the absolute differences were small, which might diminish the significance of our analysis [61]. Therefore, to internationally validate these results, similar assessment and prospective studies should be repeated in other cohorts of elderly people in different regions.

5. What Is New and Conclusion

The elderly population often has multiple chronic conditions that require various drug treatments. However, as physiological functions decline with age, drug pharmacodynamics and pharmacokinetics undergo changes that may result in drug accumulation and ADRs. Therefore, it is crucial to monitor medication use in hospitalized elderly patients. Recently, the Chinese government released guidance to strengthen medication protection and guidance for the elderly. Here, we utilized the 2019 Beers criteria and the High-Risk Drug Replacement Program for the Elderly to reduce inappropriate medication use in hospitalized elderly patients with CNS disorders. Through hospital-wide training, supervisory inspections, and communication with clinical staff, the rate of inappropriate CNS-related medication use decreased by a factor of 2.31 over a 6-month period, while clinician awareness of the standardized protocols also significantly improved. These findings provide a reference for improving the PIM catalog for elderly patients in China and underscore the importance of developing individualized medication regimens based on their physiological functional conditions.

Data Availability

The datasets are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Fang Li contributed to the research idea, study design, and statistical analysis. Yinpeng Xu and Yingli Zhu were responsible for drafting, submitting, and revising the manuscript. Yinpeng Xu, Yahui Cui, and Ying Yang were involved in data collection and interpretation. Yaling Wang conducted the statistical analysis. Min Li and Hong Hao provided critical revisions to the manuscript. All authors reviewed and commented on the manuscript.

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