



Analysis of medication treatment for women with osteoporosis: A real-world retrospective study from Chinese tertiary grade A hospital

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ABSTRACT

Purpose: This study aimed to analyze the current medication treatment status for women with osteoporosis (OP) based on real-world prescription data from 2016 to 2021 in Chinese nine cities' tertiary Grade A hospital and systematically describe the medication treatment patterns in women with OP.

Methods: Prescription information for female OP patients in nine cities (Beijing, Shanghai, Guangzhou, Hangzhou, Tianjin, Zhengzhou, Chengdu, Shenyang, Harbin) was extracted from the Hospital Prescription Analysis Collaboration Project Database of the Hospital Pharmacy Professional Committee of the Chinese Pharmaceutical Association. Statistical analysis was conducted to evaluate demographic characteristics and medication treatment patterns.

Results: A total of 669,505 prescriptions for medication treatment of female OP patients were included in this study. The majority of patients were aged 60 to 99 years (69.79 %) followed by 50 to 59 years (18.81 %) and 40 to 49 years (6.69 %). Geographically, the highest concentration of patients was in North China (Beijing, Tianjin) (43.05 %) followed by East China (Shanghai, Hangzhou) (31.43 %). The top three prescribed medications were active vitamin D and its analogs (40.78 %), calcium supplements (32.51 %), and bisphosphonates (18.75 %). The prescription frequency of menopausal hormone therapy (MHT) was 0.31 %. The proportion of female OP patients receiving monotherapy and two drug combinations therapy is equivalent (about 37 %).

Conclusion: The diagnosis and treatment of female OP patients in China showed regional variations. The most commonly prescribed medications for this population were calcitriol, calcium carbonate with vitamin D3, and alendronate sodium with vitamin D3. The use of MHT was relatively limited.

1. Introduction

Osteoporosis (OP) is a systemic metabolic bone disease characterized by reduced bone mass, microstructural damage to bone tissue, increased bone fragility, and susceptibility to fractures. It is often referred to as a “silent killer” because it silently occurs and develops in the body, and once symptoms appear, it often causes irreversible bone damage. In later stages, OP can lead to the deterioration of bone microstructure, skeletal deformities, and even osteoporotic fractures (Qaseem et al., 2023; Endocrinol. Metab. Clin. North Am., 2021).

China, as the world's largest developing country, is experiencing a shift in its population structure towards an aging population (Si et al.,

2015). According to the seventh national census, China has the highest number of elderly individuals globally, with approximately 200 million people exhibiting abnormal bone density. It is estimated that by 2050, this number will increase to 530 million (Jizhe, 2021). The latest epidemiological survey in China has revealed that the prevalence of OP in the population aged 50 years and beyond is 19.2 %, with 32.1 % in females and 6.9 % in males. Among the population aged 65 years and beyond, the prevalence is 32 %, with 51.6 % in females and 10.7 % in males (Chin. J. Osteoporos. Bone Miner. Res., 2022). Therefore, the current situation of decreased bone density in Chinese women, particularly those in perimenopause or postmenopause, is extremely serious. Osteoporosis and related fractures are significant contributors to

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increased rates of mortality and morbidity in postmenopausal women. Interestingly, the lifespan of menopausal women after severe fracture is even shorter than that after breast cancer ([Chinese Journal of Clinical Physicians, 2022](#)). Consequently, OP has emerged as a major public health issue for postmenopausal women in China, necessitating urgent measures for the diagnosis, treatment, and prevention of OP ([Management of Osteoporosis in Postmenopausal Women, 2021](#); [Song et al., 2021](#)).

Drug therapy is one of the primary modalities for the treatment and prevention of OP. Different types of anti-OP drugs are available, and clinicians consider factors such as the patient's age, disease history, and drug accessibility, as well as local economic status, when determining the appropriate treatment approach. Due to limited research on the current status of drug therapy for OP in Chinese women, this study aims to analyze the treatment patterns of OP medications among adult women in nine Chinese cities over a six-year period using real-world prescription data. The objective is to understand the current status of drug therapy for OP in Chinese women.

2. Data and methods

2.1. Data source

The data were obtained from the Cooperative Prescription Analysis Project of the Hospital Pharmacy Professional Committee of the Chinese Pharmaceutical Association. The project encompasses data from more than 150 hospitals in nine cities: Beijing, Shanghai, Guangzhou, Hangzhou, Tianjin, Zhengzhou, Chengdu, Shenyang, and Harbin. Electronic prescription data from 10 randomly selected working days were extracted quarterly from the information systems of each hospital, resulting in a total of 40 working days per year and 240 working days over a six-year period. The collected data was compiled and included in the prescription database. The data for this study was sourced from tertiary Grade A hospitals.

2.2. Survey methods

Prescription data of female outpatients aged 18 to 99 years diagnosed with OP between January 1, 2016 and December 31, 2021 were extracted from the database. Osteoporosis diagnosis was performed according to guideline standards based on dual energy X-ray absorptiometry bone density and/or brittle fractures ([Chin. J. Osteoporos. Bone Miner. Res., 2022](#)).

The extracted prescription data consisted of various information, including the region, date of visit, prescription number, department, generic and brand names of drugs, drug specifications, dosage instructions, drug quantities, drug prices, prescription costs, age, and diagnosis. Prescriptions for endocrine diseases that affected calcium metabolism, including malignant tumors, parathyroid adenomas, thyroid tumors, adrenal adenomas, pituitary tumors, and colorectal adenomatosis were excluded. Prescriptions without OP medication treatment were also excluded.

2.3. Statistical methods

Statistical analysis was performed using Microsoft Excel 2019 software. Subgroup analysis of female OP patients was conducted based on age and geographical region in China. The prescription patterns of the therapeutic drugs were analyzed and presented as frequencies or percentages (n, %).

3. Results

3.1. Demographic characteristics

After excluding prescriptions for secondary OP caused by malignant

tumors and endocrine diseases, as well as prescriptions without OP treatment, a total of 669,505 prescriptions were analyzed. The prescription volume experienced a significant decrease of 25.75 % in 2020 compared to 2019. Although there was a slight increase in prescription volume in 2021, it decreased by 9.24 % over the six-year period from 2016 to 2021 ([Table 1](#)).

The majority of patients seeking treatment were aged 60 to 99 years, accounting for 69.79 % of the total number of patients, followed by 50 to 59 years (18.81 %). The third group was patients aged 40 to 49 (6.69 %). The oldest patient among them was 99 years old. Women 50 years of age and beyond constituted the main population seeking treatment for OP. The nine cities included in the study belong to six geographical regions in China: East China (Hangzhou, Shanghai), South China (Guangzhou), Central China (Zhengzhou), North China (Beijing, Tianjin), Southwest China (Chengdu), and Northeast China (Shenyang, Harbin). The distribution of prescriptions across these regions was as follows: East China (31.43 %), South China (12.84 %), Central China (0.22 %), North China (43.06 %), Southwest China (9.77 %), and Northeast China (1.68 %). The majority of patients seeking treatment were concentrated in North China followed by East China ([Table 1](#)). The proportion of female osteoporosis patients taking medication in six regions was as follows: East China (0.56 %), South China (0.49 %), Central China (0.01 %), North China (0.81 %), Southwest China (0.30 %), and Northeast China (0.07 %) ([Table 2](#)).

3.2. Prescription patterns for osteoporosis treatment

From 2016 to 2021, the treatment modalities for female OP patients in the nine cities involved single-drug or combination therapy with five major categories of drugs: basic bone health supplements (calcium, vitamin D), bone resorption inhibitors (bisphosphonates, selective estrogen receptor modulators, calcitonin, menopausal hormone replacement therapy, receptor activator of nuclear factor- κ B ligand[RANKL] inhibitors), bone formation promoters (parathyroid hormone analogs), other mechanism-based drugs (active vitamin D and its analogs, strontium salts), and traditional Chinese medicine (Black Cohosh). Among these therapeutic drugs, the most frequently prescribed drug was active vitamin D and its analogs (40.78 %) followed by calcium supplements (32.51 %) and bisphosphonates (18.75 %). Notably, the prescription rate of MHT for menopausal women accounted for only 0.31 % of the total prescriptions for OP treatment ([Table 3](#)). Among the population aged 50–59, the top three drugs were active vitamin D and its analogues (32.32 %), bisphosphonates (30.19 %) and calcium (29.61 %), however selective estrogen receptor modulators (1.52 %) and MHT were still low (0.98 %).

Over the six-year period, approximately 37 % of female OP patients received monotherapy or combination therapy with two drugs respectively ([Table 4](#)). Among the monotherapy prescriptions, the top five prescribed drugs were calcitriol, alfacalcidol, alendronate sodium, carbocalcitonin and calcitonin ([Table 5](#)). Among the two-drug treatments, the top five combinations were calcium carbonate with vitamin D₃, alendronate sodium with vitamin D₃, calcitriol combined with calcium carbonate, calcitriol combined with calcitonin, in the fifth place, the first three years was alfacalcidol with alendronate sodium, and the last three years was calcium acetate combined with calcitriol ([Table 6](#)). Among the three-drug combination treatments, the top five combinations were Calcitriol + Calcium carbonate with vitamin D₃, Alfacalcidol + Calcium carbonate with vitamin D₃, Alendronate sodium with vitamin D₃ + Calcitriol, Alfacalcidol + Alendronate sodium with vitamin D₃ and Alendronate sodium + Calcium carbonate with vitamin D₃ over the six years. ([Table 7](#)).

4. Discussion

This study provided insights into the current status of drug therapy for female OP patients in China based on real-world outpatient

Table 1
Demographic Characteristics of female OP patients from 2016 to 2021.

Demographic characteristics	Particular year						Total n =	Percentage (%)
	2016(n = 117,026)	2017(n = 115,209)	2018(n = 120,770)	2019(n = 120,682)	2020(n = 89,609)	2021(n = 106,209)		
Age							669,505	100
18–39	5230	5186	5946	5923	4371	4913	31,569	4.71
40–49	6798	7116	8124	8362	6677	7685	44,762	6.69
50–59	22,387	20,792	21,467	22,264	17,689	21,337	125,936	18.81
60–99	82,611	82,115	85,233	84,133	60,872	72,274	467,238	69.79
Geographical region								
East China	33,591	36,385	39,568	37,732	28,558	34,573	210,407	31.43
South China	14,894	14,488	14,953	16,796	14,501	17,037	92,669	13.84
Central China	163	213	180	228	317	395	1496	0.22
North China	60,217	54,224	53,255	50,303	32,050	38,204	288,253	43.06
Southwest China	7085	8521	10,846	13,296	12,168	13,498	65,414	9.77
Northeast China	1076	1378	1968	2327	2015	2502	11,266	1.68

Note: N is the number of OP prescriptions included in the analysis in the current year.

Table 2
Population statistics of female osteoporosis patients in different regions.

Physical geography	Number of patients visited	Population size (10,000 people)	Proportion (%)
East China	210,407	3739	0.56
South China	92,669	1882	0.49
Central China	1496	1282	0.01
North China	288,253	3549	0.81
Southwest China	65,414	2140	0.30
Northeast China	11,266	1533	0.07

prescription data. The data collected from tertiary Grade A hospitals in nine big cities in China. The material life of Chinese people has been improved, residents in suburban and rural areas tends to seek medical treatment in tertiary Grade A hospitals in big cities (Shihan et al., 2021), so the prescription data in our study can represent the current level of medical development in different regions of China.

4.1. Patient demographic characteristics

The number of OP prescriptions exhibited an increasing trend from 2016 to 2019 in tertiary Grade A hospital. However, in 2020, the COVID-19 pandemic had a significant impact, leading to a decrease in OP consultations due to patients' fear of COVID-19 and adherence to infectious disease control measures. The number of prescriptions dropped by 25.75 % compared to 2019. In 2021, the number of prescriptions increased, but it did not reach pre-pandemic levels.

The consultation rate for female OP patients was found to be

Table 3
Frequency and percentage of prescription of treatment drugs for female OP patients from 2016 to 2021.

Drug categories	Drug	Frequency of prescription (n)						Total Percentage (%)	
		2016	2017	2018	2019	2020	2021		
Basic bone health supplements	Calcium	56,013	54,306	55,671	55,353	42,766	51,565	315,674	32.51
	Vitamin D	837	688	1102	1619	1472	3180	8898	0.92
Bone resorption inhibitors	Bisphosphonates	32,143	31,911	34,234	33,223	23,923	26,575	182,009	18.75
	Selective estrogen receptor modulators	2087	2130	2683	2926	2000	1556	13,382	1.39
	Calcitonin	9386	9979	9533	8801	5318	7334	50,351	5.19
Bone formation promoters	Menopausal hormone therapy	488	446	559	553	395	531	2972	0.31
	RANKL inhibitors	0	0	0	0	0	1206		0.12
Other mechanism-based drugs	Parathyroid hormone analogs	26	31	55	72	47	37	268	0.03
	Active vitamin D and its analogs	67,580	67,201	71,214	72,192	53,981	63,734	395,902	40.78
Traditional Chinese medicine	Strontium salts	4	0	0	0	0	0	4	0.0004
	Black cohosh	16	11	13	19	19	26	104	0.01
Total		168,610	166,741	175,096	174,758	129,921	155,744	970,870	100

positively correlated with age. As individuals age, degenerative changes in bone structure, declining body functions, and abnormal bone metabolism occur, leading to reduced calcium absorption and progressive bone mass loss, thus resulting in OP (Cedeno-Veloz et al., 2022). The risk factors for OP in the elderly population include reduced outdoor physical activity, limited sunlight exposure, and gastrointestinal disorders (Xiao et al., 2022). A study has shown that women reach peak bone density between the ages of 20 and 29 followed by a gradual decline, with a more significant decline after the age of 40. This decline is associated with a decrease in ovarian function and a sharp decline in estrogen secretion (Santoro et al., 2021). Thus, early screening for bone density in females is crucial for early diagnosis, prevention, and treatment.

China's vast territory and local factors, such as certain customs and geographical regions, also influence the treatment of OP. Research indicates that populations living at higher altitudes tend to have lower bone density compared to those living at lower altitudes. Furthermore,

Table 4
Percentage of prescriptions of treatment drugs with monotherapy or combination therapy for female OP patients from 2016 to 2021.

Prescription Patterns	Percentage of prescriptions(%)					
	2016	2017	2018	2019	2020	2021
Monotherapy	38.3	37.49	36.6	37.49	36.78	37.38
Two-drug combinations	37.42	35.63	38.38	36.2	36.88	35.93
Three-drug combinations	17.53	20.02	19.11	20.78	20.38	20.58
Others	6.75	6.86	5.91	5.53	5.96	6.11

Table 5
Frequency of prescription of treatment drugs with monotherapy for female OP patients from 2016 to 2021.

Drug	2016		2017		2018		2019		2020		2021	
	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug
Calcitriol	20,196	Calcitriol	21,827	Calcitriol	22,556	Calcitriol	23,718	Calcitriol	17,493	Calcitriol	20,402	Calcitriol
Alfacalcidol	8452	Alfacalcidol	8024	Alfacalcidol	8302	Alfacalcidol	8101	Alfacalcidol	6401	Alfacalcidol	7189	Alfacalcidol
Alendronate sodium	7552	Alendronate sodium	5304	Alendronate sodium	3534	Alendronate sodium	2976	Alendronate sodium	1891	Alendronate sodium	2450	Alendronate sodium
Carbocalcitonin	2294	Calcitonin	2459	Calcitonin	2378	Carbocalcitonin	2229	Calcitonin	1470	Calcitonin	1748	Calcitonin
Calcitonin	2260	Carbocalcitonin	2388	Carbocalcitonin	2254	Calcitonin	2130	Carbocalcitonin	1203	Carbocalcitonin	1561	Carbocalcitonin
Calcium carbonate	1143	Calcium carbonate	1052	Calcium carbonate	1051	Calcium carbonate	1152	Raloxifene	804	Raloxifene	1379	Vitamin D2
Raloxifene	721	Raloxifene	829	Raloxifene	1008	Raloxifene	1137	Calcium acetate	790	Calcium acetate	1141	Calcium acetate
Zoledronic acid	679	Zoledronic acid	618	Calcium acetate	769	Calcium acetate	901	Zoledronic acid	736	Zoledronic acid	789	Calcium carbonate
Risedronate sodium	305	Risedronate sodium	403	Zoledronic acid	730	Zoledronic acid	864	Zoledronic acid	651	Calcium carbonate	691	Zoledronic acid
Vitamin D2	262	Calcium acetate	341	Risedronate sodium	710	Risedronate sodium	836	Risedronate sodium	604	Vitamin D2	686	Raloxifene
Others	954	Others	784	Others	913	Others	1195	Others	917	Others	1670	Others

longer annual sunlight hours and average sunlight hours under standard illumination in the afternoon are associated with a lower rate of OP (Zuo et al., 2022; Liu et al., 2021). In flat areas of land, the population's bone density is positively correlated with sunlight exposure (Manoj et al., 2023). Chengdu, situated in the Sichuan Basin, has the fewest annual sunlight hours and average sunlight hours under standard illumination of the nine surveyed cities, leading to a higher prevalence of vitamin D deficiency among its residents (Tang et al., 2016). However, the prescription rate for OP treatment in Chengdu was only 9.77 %. On the other hand, regions in North China, with Beijing having the highest annual sunlight hours and average sunlight hours under standard illumination, exhibited the highest prescription rate, indicating a greater awareness of OP and a proactive attitude towards medication use. The prescription frequency in Central China and Northeast China only accounts for 0.22 % and 1.68 %. This may be related to the population size. As shown in Fig. 1, the population of the three cities in Central China (Zhengzhou) and Northeast China (Shenyang, Harbin) is only 12.82 million, 9.84 million, and 5.49 million, far lower than the population size of other regions. A study has highlighted the challenges of OP treatment and prevention, which include high rates of prevalence but low rates of awareness, diagnosis, and treatment in China. Additionally, significant disparities exist in the diagnosis and treatment of OP among different regions and between urban and rural areas (Chin. J. Osteoporos. Bone Miner. Res., 2022). The prescription data from this study align with these challenges, illustrating notable regional differences in OP treatment rates, with higher rates in first-tier cities such as Beijing and Shanghai in North and East China.

4.2. Prescription patterns for osteoporosis treatment

4.2.1. Treatment drug selection

Calcium/vitamin D is the fundamental component of bone health. Supplementing with calcium and vitamin D is an important basic strategy for preventing and treating osteoporosis. The common serious complication of osteoporosis is fractures. A meta-analysis conducted by the National Osteoporosis Foundation in the United States in 2016 concluded that taking calcium and vitamin D supplements could serve as intervention measures to reduce the risk of fractures in middle-aged and elderly people (Weaver et al., 2016). From this study, calcium/vitamin D accounted for 33 %, other anti OP drugs accounted for 67 %. For further analysis, the most commonly prescribed drugs were active vitamin D and its analogs (40.78 %) followed by calcium (32.51 %) and bisphosphonates (18.75 %). Active vitamin D and its analogs are hydroxylated forms of vitamin D that can exert their effects without requiring hydroxylation by 1 α -hydroxylase in the kidneys. These drugs are particularly suitable for patients with renal insufficiency, and those with a reduced level or a lack of 1 α -hydroxylase. Active vitamin D and its analogs have been shown to increase bone density, reduce falls, and lower fracture risk (Veldurthy et al., 2016).

Among the active vitamin D analogs, calcitriol has emerged as the most frequently prescribed drug since 2016. Studies have reported that calcitriol monotherapy can improve the density of bone, markedly reduce the turnover of bone markers, and lower the risk of falls. Common adverse reactions to calcitriol include hypercalcemia and hypercalciuria, whereas gastrointestinal adverse reactions and abnormalities in the liver and kidneys are less common (Palacios et al., 2021; Kong et al., 2022; Zhang et al., 2019). In the Chinese population, the low incidence of hypercalcemia may be attributed to the use of low-dose calcitriol (Liao et al., 2019; American College of Obstetricians and Gynecologists' Committee on Clinical Practice Guidelines–Gynecology, 2021).

Bisphosphonates are recommended as first-line drugs for the treatment and prevention of OP by organizations such as the American College of Obstetricians and Gynecologists and the American Association of Clinical Endocrinologists. In our study, alendronate sodium ranked third among the prescribed drugs. Alendronate sodium with

Table 6
Frequency of prescription of treatment drugs with two-drug combinations for female OP patients from 2016 to 2021.

2016		2017		2018		2019		2020		2021	
Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription
Calcium carbonate with vitamin D3	23,445	Calcium carbonate with vitamin D3	20,566	Calcium carbonate with vitamin D3	21,178	Calcium carbonate with vitamin D3	20,125	Calcium carbonate with vitamin D3	15,736	Calcium carbonate with vitamin D3	18,022
Alendronate sodium with vitamin D3	6590	Alendronate sodium with vitamin D3	8351	Alendronate sodium with vitamin D3	10,809	Alendronate sodium with vitamin D3	10,801	Alendronate sodium with vitamin D3	7485	Alendronate sodium with vitamin D3	7771
Calcitriol + Calcium carbonate	4112	Calcitriol + Calcium carbonate	3729	Calcitriol + Calcium carbonate	3013	Calcitriol + Calcium carbonate	2525	Calcitriol + Calcium carbonate	1642	Calcitriol + Calcium carbonate	2016
Alendronate sodium + Calcitriol	2499	Alendronate sodium + Calcitriol	1943	Alendronate sodium + Calcitriol	1618	Alendronate sodium + Calcitriol	1371	Alendronate sodium + Calcitriol	838	Alendronate sodium + Calcitriol	1050
Alfacalcidol + Alendronate sodium	1588	Alfacalcidol + Alendronate sodium	1214	Alfacalcidol + Alendronate sodium	1121	Calcium acetate + Calcitriol	947	Calcium acetate + Calcitriol	653	Calcium acetate + Calcitriol	910
Calcitriol + Carbocalcitonin	662	Calcitriol + Calcitonin	697	Calcitriol + Calcitonin	776	Alfacalcidol + Alendronate sodium	849	Alfacalcidol + Alendronate sodium	547	Calcitriol + Calcitonin	762
Calcitriol + Calcitonin	609	Calcitriol + Carbocalcitonin	545	Calcium acetate + Calcitriol	695	Calcitriol + Calcitonin	747	Alfacalcidol + Calcium acetate	480	Alfacalcidol + Alendronate sodium	706
Alfacalcidol + Calcium carbonate	553	Alfacalcidol + Raloxifene	376	Calcitriol + Carbocalcitonin	450	Calcitriol + Carbocalcitonin	504	Calcitriol + Calcitonin	456	Alfacalcidol + Calcium acetate	452
Calcitriol + risedronate sodium	359	Calcitriol + risedronate sodium	372	Calcitriol + Raloxifene	425	Calcitriol + Raloxifene	478	Calcitriol + risedronate sodium	394	Calcitriol + risedronate sodium	421
Alfacalcidol + Raloxifene	357	Alfacalcidol + Calcium carbonate	370	Alfacalcidol + Raloxifene	413	Alfacalcidol + Calcium acetate	440	Calcitriol + Raloxifene	337	Calcitriol + Carbocalcitonin	310
Others	3014	Others	6192	Others	5850	Others	4219	Others	4479	Others	5740

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Table 7
Frequency of prescription of treatment drugs with three-drug combinations for female OP patients from 2016 to 2021.

2016		2017		2018		2019		2020		2021	
Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription	Drug	Frequency of prescription
Calcitriol + Calcium carbonate with vitamin D3	11,033	Calcitriol + Calcium carbonate with vitamin D3	10,881	Calcitriol + Calcium carbonate with vitamin D3	11,117	Calcitriol + Calcium carbonate with vitamin D3	12,022	Calcitriol + Calcium carbonate with vitamin D3	9243	Calcitriol + Calcium carbonate with vitamin D3	11,413
Alfacalcidol+ Calcium carbonate with vitamin D3	3649	Alfacalcidol+ Calcium carbonate with vitamin D3	3765	Alfacalcidol+ Calcium carbonate with vitamin D3	4662	Alfacalcidol+ Calcium carbonate with vitamin D3	4808	Alfacalcidol+ Calcium carbonate with vitamin D3	4175	Alfacalcidol+ Calcium carbonate with vitamin D3	4860
Alendronate sodium with vitamin D3+ Calcitriol	1700	Alendronate sodium with vitamin D3+ Calcitriol	2323	Alendronate sodium with vitamin D3+ Calcitriol	2891	Alendronate sodium with vitamin D3+ Calcitriol	3065	Alendronate sodium with vitamin D3+ Calcitriol	2177	Alendronate sodium with vitamin D3+ Calcitriol	2441
Alfacalcidol+ Alendronate sodium with vitamin D3	1421	Alfacalcidol+ Alendronate sodium with vitamin D3	1678	Alfacalcidol+ Alendronate sodium with vitamin D3	1811	Alfacalcidol+ Alendronate sodium with vitamin D3	1614	Alfacalcidol+ Alendronate sodium with vitamin D3	1124	Alfacalcidol+ Alendronate sodium with vitamin D3	967
Alendronate sodium + Calcium carbonate with vitamin D3	816	Alendronate sodium + Calcium carbonate with vitamin D3	669	Alendronate sodium + Calcium carbonate with vitamin D3	584	Alendronate sodium + Calcium carbonate with vitamin D3	476	Alendronate sodium + Calcium carbonate with vitamin D3	377	Alendronate sodium + Calcium carbonate with vitamin D3	467
Alendronate sodium+ Calcitriol+ Calcium carbonate	526	Alendronate sodium+ Calcitriol+ Calcium carbonate	313	Calcitriol + Calcitonin + Calcium carbonate	238	Calcitriol + Calcitonin + Calcium carbonate	198	Alendronate sodium + Calcitriol + Calcium carbonate	101	Alendronate sodium + Calcitriol + Calcium carbonate	123
Calcitriol + Calcitonin + Calcium carbonate	243	Calcitriol + Calcitonin + Calcium carbonate	213	Alendronate sodium+ Calcitriol+ Calcium carbonate	235	Alendronate sodium+ Calcitriol+ Calcium carbonate	184	Alendronate sodium + Calcium acetate + Calcitriol	78	Calcitriol + Calcitonin + Calcium carbonate	122
Calcitriol + Calcium carbonate + Carbocalcitonin	126	Calcitriol + Risedronate sodium + Calcium carbonate	133	Alfacalcidol+ Alendronate sodium + Calcium carbonate	86	Alfacalcidol+ Alendronate sodium + Calcium carbonate	144	Calcitriol + Calcitonin + Calcium carbonate	56	Alendronate sodium + Calcium acetate + Calcitriol	96
Calcitriol + Risedronate sodium + Calcium carbonate	121	Calcitriol + Calcium carbonate + Carbocalcitonin	117	Alfacalcidol + Risedronate sodium + Calcium carbonate	65	Alfacalcidol + Risedronate sodium + Calcium acetate + Calcitriol	117	Calcitriol + Risedronate sodium + Calcium carbonate	50	Alfacalcidol+ Alendronate sodium + Calcium carbonate	70
Calcitriol + Risedronate sodium + Calcium carbonate	77	Alendronate sodium+ Calcitriol+ Calcitonin	53	Alendronate sodium + Calcium acetate + Calcitriol	65	Alendronate sodium + Calcium acetate + Calcitriol	65	Alfacalcidol+ Alendronate sodium + Calcium carbonate	49	Calcium acetate + Calcitriol + Calcitonin	54
Others	811	Others	848	Others	1329	Others	1423	Others	836	Others	1241



Fig. 1. Geographical Region and Population Size Map.

vitamin D3 is a combined preparation of bisphosphonates and vitamin D3. Vitamin D3 enhances calcium absorption in the body, and when it is used in conjunction with bisphosphonates, it effectively regulates blood calcium levels, improves phosphate excretion, and promotes bone formation and resorption (Zhang et al., 2015). Compared to alendronate alone, alendronate sodium with vitamin D3 further enhances calcium absorption, reduces adverse drug reactions, improves patient quality of life, and meets the needs of OP treatment (Dominguez et al., 2021). Alendronate sodium with vitamin D3 significantly improves the treatment experience and increases bone density at various sites, especially in elderly OP patients (Liao et al., 2018). Although RANKL inhibitors and bone formation promoters only account for 0.12 % and 0.03 %, for patients with high fracture risk, the guidelines recommend the use of denosumab and teriparatide for treatment (Chin. J. Osteoporos. Bone Miner. Res., 2022). From other literature, Oral bisphosphonates and zoledronic acid are also most commonly used for preventing fractures of women patient in other countries. In more recent years, anabolic agents, including teriparatide, abaloparatide and romosozumab have been a treatment for women at very high fracture risk suggested to consider for sequential treatment (Lorentzon et al., 2022).

It is worth noting that MHT accounted for only 0.31 % of the total prescriptions for OP treatment drugs. Female OP patients aged between 60 and 99 years followed by those aged between 50 and 59 years primarily sought medical attention. The prevalence of OP was significantly higher among women 60 years of age and beyond, indicating that this age range associates with a high-risk of the disease. Menopausal hormone therapy, a primary preventive measure for postmenopausal OP,

reduces the incidence of all fractures, including vertebral and hip fractures, and is an effective modality to decrease fracture incidence in perimenopausal and postmenopausal women (US Preventive Services Task Force et al., 2022; The 2022 Hormone Therapy Position Statement of The North American Menopause Society Advisory Panel, 2022). The Menopause Study Group of the Chinese Medical Association of Obstetrics and Gynecology proposes that “early initiation of MHT after menopause or at any stage of estrogen deficiency yields greater benefits and achieves primary prevention of osteoporotic fractures” (Chinese Menopause Society, 2023). Similarly, the American Association of Clinical Endocrinologists recommends that “for patients under 60 years of age, less than 10 years since menopause, with a low risk of venous thrombosis, and experiencing menopause-related symptoms but not using MHT, MHT can be given after adequate evaluation” (Shoback et al., 2022). Additionally, the Osteoporosis Branch of the Chinese Geriatrics Society states that “MHT can prevent bone loss in perimenopausal and early postmenopausal women, increase or maintain bone density in women, and has beneficial effects on the skin, cartilage, and other connective tissues” (Chinese Journal of Clinical Physicians, 2022). Therefore, clinicians should pay attention to the bone health of perimenopausal women and recommend MHT for women aged 50 to 60 years or within 10 years of menopause to prevent OP and fractures.

4.2.2. Drug treatment patterns

From 2016 to 2021, The proportion of female OP patients in nine cities across the country received monotherapy and combination therapy with two drugs are both approximately 37 %. Among the

combination therapy regimens in this study, the top two prescription frequency were calcium carbonate with vitamin D3 and Calcitriol + Calcium carbonate with vitamin D3. According to the literature, this regimen can significantly increase bone density in the lumbar spine, femoral neck, greater tuberosity, and hip bone (Dai et al., 2018).

Calcium carbonate D3 tablets are a combined preparation containing calcium, which can supplement calcium in the body. Vitamin D3 promotes calcium precipitation and absorption in the bones, providing the conditions for bone formation. However, vitamin D3 is metabolized in the liver and kidneys and converted into an active substance that promotes calcium absorption, which poses certain limitations in the treatment of elderly patients. Calcitriol, a vitamin-like drug and an important active metabolite of vitamin D3, directly binds to receptors and promotes calcium absorption. In addition, calcitriol plays a key role in regulating the calcium balance and providing a good pharmacological basis for the treatment of OP, including the stimulation of osteoblast activity in the bones and the correction of hypocalcemia (Vieth, 2022; Tilyard et al., 1992).

Given that OP is a chronic disease with high incidence and serious consequences, it requires the use of multiple effective drugs for long-term combination or sequential therapy to increase bone density and reduce fracture risk. Both national and international guidelines emphasize that the treatment of OP should be based on adequate calcium and vitamin D supplementation as well as the use of drugs that inhibit bone resorption or promote bone formation to improve bone density and prevent fracture risk. During treatment, attention should be paid to the therapeutic benefits and potential adverse effects of the medications. The combination of drugs with different mechanisms of action should be grounded on evidence-based medicine and take into consideration the impact of pharmacoeconomics. Additionally, the treatment regimen should be personalized based on the patient's fracture risk, clinical condition, and other factors (Endocrinol. Metab. Clin. North Am., 2021; Chin. J. Osteoporos. Bone Miner. Res., 2022).

5. Conclusion

This study provides insights into the current status of drug treatment and the treatment patterns for female OP patients in nine cities in China from 2016 to 2021 based on a multicenter real-world prescription database. The most used drugs for OP treatment were calcitriol, calcium carbonate D3, and alendronate sodium with vitamin D3. More than 74 % of patients received monotherapy and two-drug combination therapy. However, the utilization of MHT for the treatment or prevention of OP in postmenopausal or 50–59 years' old female patients remains low, indicating relatively low popularity and acceptance of MHT in China at this stage.

6. Limitations

There are several limitations in our study. First, the prescription data used in this study were randomly sampled within 10 working days of each quarter, which may not completely reflect the overall situation. Second, the analyzed prescriptions were from major cities or provincial capitals in China, and the prescription patterns in economically-weaker regions may differ due to medical and economic factors. Third, the analyzed prescriptions were all from Chinese tertiary Grade A hospitals, not including community medical institutions. Fourth, the prescription data lacked patient medical histories, and the limited information restricted the evaluation of rational drug use. In the future, it is necessary to collect prescription samples with more complete information and broader geographical coverage.

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Ethics statement

This study protocol was approved by the Ethics Committee of the Obstetrics and Gynecology Hospital of Fudan University (approval number: 2023–01).

CRediT authorship contribution statement

Xiaolei Liu: Writing – original draft, Visualization, Validation, Formal analysis. **Zhenling Zhu:** Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Xianli Wang:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Data availability

Data will be made available on request.

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