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Comprehensive Evaluation of Treatment Patterns in Postmenopausal Patients with Osteoporosis without Fractures: Insights from Tertiary Care Institutions and Nationwide OMOP-CDM Data

Kyoung Jin Kim[1,*], Dachung Boo[2,3,*], Jimi Choi[1], Hyemin Yoon[4], Chai Young Jung[5], Seong Hee Ahn[6], Namki Hong[3,7], Beom-Jun Kim[8], Ji Seon Oh[4,9], Seng Chan You[2,3]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Korea University College of Medicine; [2]Department of Biomedical Systems Informatics, Yonsei University College of Medicine; [3]Institute for Innovation in Digital Healthcare, Yonsei University; [4]Big Data Research Center, Asan Institute of Life Science, Asan Medical Center, Seoul; [5]Biomedical Research Institute, Inha University Hospital; [6]Division of Endocrinology and Metabolism, Department of Internal Medicine, Inha University Hospital, Inha University College of Medicine, Incheon; [7]Department of Internal Medicine, Endocrine Research Institute, Severance Hospital, Yonsei University College of Medicine; [8]Division of Endocrinology & Metabolism, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine; [9]Department of Information Medicine, Asan Medical Center, Seoul, Korea

Background: Osteoporosis is a global health concern. Despite emerging treatment options for this condition, limited data are available on hospital practices in South Korea. This study addresses the need for a hospital network database that reflects changes in routine clinical practice for osteoporosis in a timely manner.

Methods: We analyzed prescription patterns for anti-osteoporosis medications (AOMs) in postmenopausal women aged ≥50 years diagnosed with osteoporosis between 2012 and 2021 using data from Osteoporosis Analysis and Surveillance Initiative using Standardized data (OASIS) (four tertiary hospitals in South Korea) and a nationwide database from the Health Insurance Review and Assessment (HIRA) Service. AOMs were categorized into antiresorptive and anabolic agents, with a focus on secular changes in the use of oral bisphosphonates, denosumab, selective estrogen receptor modulators (SERMs), and anabolic agents.

Results: In the OASIS cohort, oral bisphosphonates were the most prescribed first-line AOM (49.0%), followed by denosumab (15.7%) and SERMs (18.0%). Denosumab use increased from 2% in 2016 to 40% in 2020, while oral bisphosphonate use declined from 69% in 2012 to 22% in 2021. The use of anabolic agents, including romosozumab and teriparatide, doubled to 6% after 2019. In the HIRA cohort, parenteral bisphosphonates were most common (54.3%), with significant denosumab use (17.3%).

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Corresponding authors: Seng Chan You
Department of Biomedical Systems Informatics, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: +82-2-2228-2500, **Fax:** +82-2-2228-2500, **E-mail:** Chandryou@yuhs.ac

Ji Seon Oh
Department of Information Medicine, Asan Medical Center, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
Tel: +82-2-3010-2530, **Fax:** +82-2-3010-2531, **E-mail:** mdjsoh@amc.seoul.kr

*These authors contributed equally to this work.

Conclusion: Pronounced shifts in AOM prescription patterns were observed in South Korea, marked by a notable increase in denosumab prescriptions and a decline in bisphosphonate use. These trends highlight the impact of policy changes and clinical guidelines on osteoporosis treatment and may inform future management strategies.

Keywords: Osteoporosis, postmenopausal; Practice patterns, physicians'; Drug prescriptions

INTRODUCTION

Osteoporosis is a growing global health issue driven by aging populations. This condition increases fracture risk and imposes a significant social burden, with its prevalence among the elderly in Korea projected to reach 20.3% by 2025 [1-5]. The landscape of anti-osteoporosis medications (AOMs) is evolving rapidly, with new therapies and treatment strategies substantially altering clinical practice [6-8]. In Korea, the approval of denosumab as a first-line treatment in 2019 expanded the range of effective therapies available and led to notable changes in prescribing patterns [9,10]. As treatment options continue to diversify, understanding real-world medication trends is essential for optimizing osteoporosis management.

Nationwide claims databases, such as those from the Health Insurance Review and Assessment Service (HIRA), provide valuable insights into treatment patterns at the national level; however, they have inherent limitations. Their reliance on insurance-covered treatments creates a blind spot by failing to capture the use of non-insured therapies, thus limiting our understanding of the full spectrum of treatment practices [11].

To address these gaps, the Osteoporosis Analysis and Surveillance Initiative using Standardized data (OASIS) system was established at four tertiary care centers in Korea. OASIS leverages the strengths of a federated, standardized data network based on the Observational Medical Outcomes Partnership Common Data Model (OMOP-CDM), enabling extensive investigations of routine clinical practice across multiple institutions using identical study protocols. With this study, we aim to explore changes in AOM prescriptions by comparing data from OASIS and HIRA, thus providing a comprehensive view of osteoporosis medication patterns and capturing shifts in treatment approaches over time in response to evolving therapies and policy changes.

METHODS

Data sources

This study utilized approximately 15 million patient records from the CDM databases of four tertiary care institutions in South Korea [12,13], standardized to version 5.3 of the OMOP-CDM to facilitate consistent network-wide analyses. The institutions included Severance Hospital (6.27 million individuals from January 2006 to August 2023), Asan Medical Center (4.95 million individuals from October 2004 to December 2020), Korea University Anam Hospital (2.18 million individuals from January 2009 to June 2021), and Inha University Hospital (1.98 million individuals from February 2001 to February 2019). Within this standardized data network, we defined the OASIS cohort specifically as a multi-institutional osteoporosis cohort for targeted analysis, enabling an in-depth investigation of osteoporosis treatment patterns.

In addition, we analyzed a separate cohort from the HIRA database [14]. This nationwide administrative database is standardized to OMOP-CDM version 5.3.1 in South Korea. It represents approximately 20% of the Korean population (9,822,577 patients) and includes data from January 2018 to April 2022. The database contains information on demographics (sex, age, insurance type), visit type (outpatient or hospitalization), medical history (diagnoses, procedures, treatments), examination history, and detailed prescription information. Further descriptions of the methodology and data protocols used in this study are available in a previous publication [14].

This study was approved by the Institutional Review Boards (IRBs) of the four hospitals in accordance with relevant guidelines and regulations (IRB approvals: 2024AN0175, 2023-0860, 2023-06-007, 4-2023-0492, and 4-2023-0798). As this was an observational study utilizing de-identified data, the requirement for informed consent was waived.

Study population and data collection

We examined female patients aged ≥50 years diagnosed with osteoporosis from 2012 to 2021 within the OASIS cohort and from 2018 to 2021 within the HIRA cohort. Osteoporosis was defined using the International Classification of Diseases-10 code M81 (Supplemental Table S1). To focus on primary prevention treatments, patients with code M80 (osteoporosis with fractures) were excluded. Such patients often undergo surgical

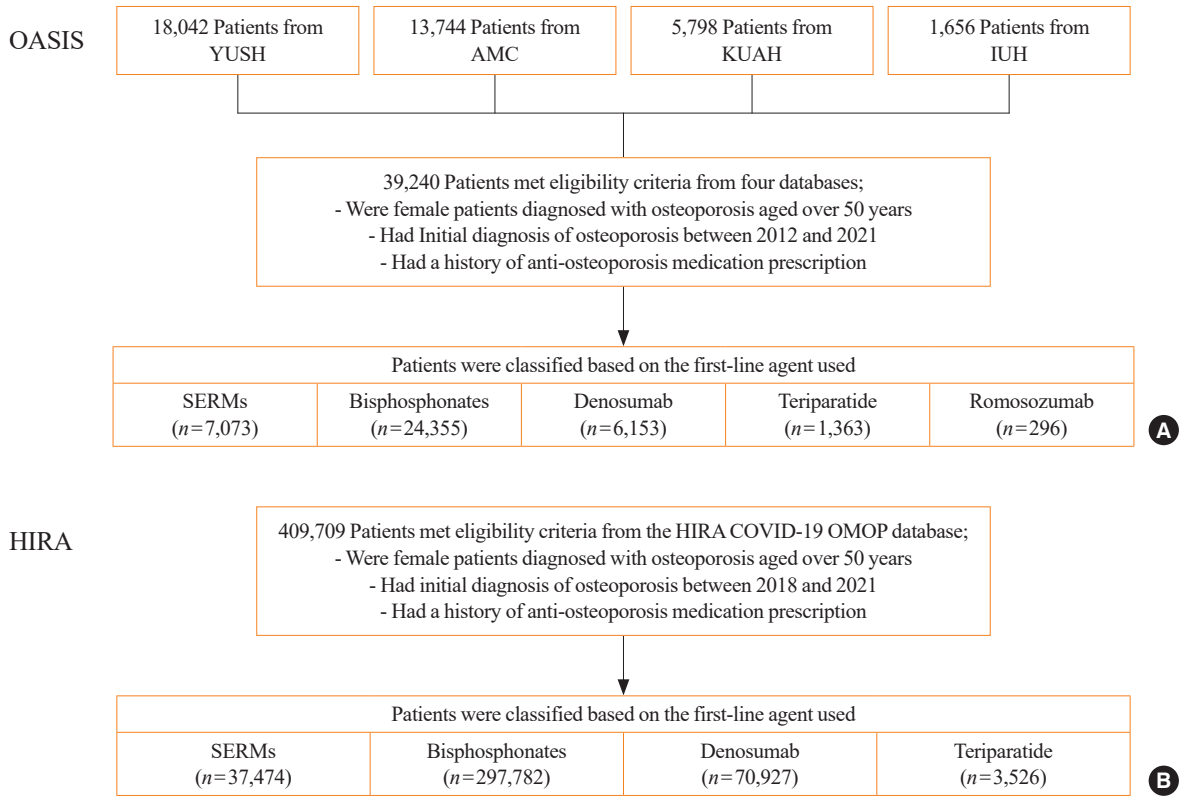

Fig. 1. Study population based on first-line anti-osteoporosis medication. Patients were selected from four Observational Medical Outcomes Partnership Common Data Model (OMOP-CDM) databases: Yonsei University Severance Hospital (YUSH), Asan Medical Center (AMC), Korea University Anam Hospital (KUAH), and Inha University Hospital (IUH) (A), as well as the Health Insurance Review and Assessment Service (HIRA) database (B). Postmenopausal women over 50 years old with osteoporosis diagnosed between 2012 and 2021 and a history of osteoporosis treatment were included. Patients were classified by first-line treatment: selective estrogen receptor modulators (SERMs), bisphosphonates, denosumab, teriparatide, and romosozumab. OASIS, Osteoporosis Analysis and Surveillance Initiative using Standardized data; COVID-19, coronavirus disease 2019.

treatment or aggressive interventions at tertiary hospitals, which could confound the analysis of drug treatment patterns.

The final study population included patients who had used AOMs for at least 1 month (Fig. 1A for OASIS, Fig. 1B for HIRA). AOMs were categorized into antiresorptive agents (selective estrogen receptor modulators [SERMs]: raloxifene, bazedoxifene; oral bisphosphonates [BPs]: alendronate, risedronate, ibandronate, etidronate; intravenous BPs: ibandronate, zoledronate; and denosumab) and anabolic agents (teriparatide and romosozumab). Abaloparatide was excluded because it is not available in Korea (Supplemental Table S2). The HIRA cohort included no information on romosozumab. Medications were considered only if prescribed after the diagnosis of osteoporosis in women at least 50 years old. The permissible period for continuation of the same drug class was set at 180 days to reflect the long interval between doses. To exclude cases not intended for osteoporosis treatment and to accurately calculate dose duration, we established criteria based on both the quantity and the dosing regimen of the medication (Supplemental Table S2).

To investigate the impact of drug approval and insurance coverage on treatment patterns, the study periods were defined based on changes in the National Health Insurance Service. Denosumab (Prolia) was launched in Korea in November 2016 and approved as a first-line drug for osteoporosis in April 2019. As such, the periods were roughly divided into three segments: before 2017, 2017–2018, and 2019 or later. Comorbidities were considered based on the index date, defined as the time when the osteoporosis diagnosis code was first recorded. Information regarding the concept IDs used in the analyses is summarized in Supplemental Table S2.

Statistical analysis and treatment pathway

Data were expressed as mean±standard deviation for continuous variables and as number (percentage) for categorical vari-

Table 1. Baseline Characteristics by First-Line Medication in the OASIS Cohort

Characteristic	Total	Oral bisphosphonate	Parenteral bisphosphonate	SERMs	Denosumab	Teriparatide	Romosozumab
No. of participants	39,240 (100.0)	19,212 (49.0)	5,143 (13.1)	7,073 (18.0)	6,153 (15.7)	1,363 (3.5)	296 (0.8)
Age group							
50s	10,276 (26.2)	5,780 (30.1)	741 (14.4)	2,495 (35.3)	1,075 (17.5)	109 (8.0)	76 (25.7)
60s	14,209 (36.2)	7,235 (37.7)	1,654 (32.2)	2,744 (38.8)	2,137 (34.7)	337 (24.7)	102 (34.5)
70s	10,503 (26.8)	4,663 (24.3)	1,826 (35.5)	1,434 (20.3)	1,922 (31.2)	586 (43.0)	72 (24.3)
80s and older	4,252 (10.8)	1,534 (8.0)	922 (17.9)	400 (5.7)	1,019 (16.6)	331 (24.3)	46 (15.5)
Comorbidities							
Diabetes mellitus	4,575 (11.7)	2,252 (11.7)	774 (15.0)	646 (9.1)	669 (10.9)	209 (15.3)	25 (8.4)
Hyperlipidemia	6,124 (15.6)	3,099 (16.1)	706 (13.7)	1,295 (18.3)	863 (14.0)	106 (7.8)	55 (18.6)
Hypertensive disorder	9,275 (23.6)	4,262 (22.2)	1,517 (29.5)	1,422 (20.1)	1,555 (25.3)	453 (33.2)	66 (22.3)
Chronic kidney disease	1,260 (3.2)	483 (2.5)	123 (2.4)	230 (3.3)	367 (6.0)	44 (3.2)	13 (4.4)
Rheumatoid arthritis	1,288 (3.3)	613 (3.2)	175 (3.4)	277 (3.9)	182 (3.0)	34 (2.5)	7 (2.4)
Fracture of bone	6,725 (17.1)	2,177 (11.3)	1,424 (27.7)	761 (10.8)	1,443 (23.5)	825 (60.5)	95 (32.1)
Cerebrovascular disease	2,267 (5.8)	1,016 (5.3)	416 (8.1)	357 (5.0)	399 (6.5)	64 (4.7)	15 (5.1)
Coronary arteriosclerosis	725 (1.8)	310 (1.6)	129 (2.5)	105 (1.5)	146 (2.4)	30 (2.2)	5 (1.7)
Heart failure	864 (2.2)	299 (1.6)	179 (3.5)	109 (1.5)	226 (3.7)	38 (2.8)	13 (4.4)
Ischemic heart disease	1,623 (4.1)	615 (3.2)	286 (5.6)	240 (3.4)	379 (6.2)	86 (6.3)	17 (5.7)
Malignant neoplasm of anorectum	158 (0.4)	78 (0.4)	20 (0.4)	29 (0.4)	28 (0.5)	3 (0.2)	0
Malignant neoplastic disease	9,071 (23.1)	5,142 (26.8)	830 (16.1)	1,534 (21.7)	1,445 (23.5)	86 (6.3)	34 (11.5)
Malignant tumor of breast	3,995 (10.2)	2,573 (13.4)	268 (5.2)	389 (5.5)	741 (12)	13 (1.0)	11 (3.7)
Malignant tumor of colon	241 (0.6)	115 (0.6)	38 (0.7)	38 (0.5)	44 (0.7)	5 (0.4)	1 (0.3)
Malignant tumor of lung	368 (0.9)	179 (0.9)	58 (1.1)	41 (0.6)	79 (1.3)	8 (0.6)	3 (1.0)
Malignant tumor of urinary bladder	52 (0.1)	21 (0.1)	11 (0.2)	6 (0.1)	13 (0.2)	1 (0.1)	0
Malignant neoplasm of bone	117 (0.3)	39 (0.2)	30 (0.6)	12 (0.2)	33 (0.5)	3 (0.2)	0
Medication use							
Glucocorticoids	8,567 (21.8)	4,656 (24.2)	744 (14.5)	1,239 (17.5)	1,512 (24.6)	360 (26.4)	56 (18.9)

Values are expressed as number (%).
OASIS, Osteoporosis Analysis and Surveillance Initiative using Standardized data; SERM, selective estrogen receptor modulator.

ables. The chi-square test and analysis of variance were used to compare categorical and continuous variables, respectively. Treatment pathway analysis can be used to identify treatment patterns and utilization by summarizing initial prescriptions and subsequent therapy changes, thus providing insights into prevalent treatments, such as discontinuation and switching rates. Prescriptions for each medication event were extracted for each patient after the index date and ranked by exposure. We summarized and visualized sequential medication patterns using sunburst plots. In this study, combination therapies were excluded to align with the strategies for osteoporosis treatment. A limit of three treatment sequences was applied. R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria) was used, employing the Feature Extraction package (version 4.0.1) to extract baseline characteristics. The full source code for the analyses is available online (https://github.com/ohdsi-studies/OsteoporosisTreatmentPathways).

RESULTS

Characteristics of the study population

The baseline characteristics of the study participants are summarized in Table 1 for the OASIS cohort and Table 2 for the HIRA cohort. The baseline characteristics for each institution

Table 2. Baseline Characteristics by First-Line Medication in the HIRA Cohort

Characteristic	Total	Oral bisphosphonate	Parenteral bisphosphonate	SERMs	Denosumab	Teriparatide
No. of participants	409,709 (100.0)	75,209 (18.4)	222,573 (54.3)	37,474 (9.1)	70,927 (17.3)	3,526 (0.9)
Age group						
50s	61,900 (15.1)	13,873 (18.4)	28,666 (12.9)	7,418 (19.8)	11,650 (16.4)	293 (8.3)
60s	143,991 (35.1)	28,067 (37.3)	75,544 (33.9)	14,542 (38.8)	25,044 (35.3)	794 (22.5)
70s	132,861 (32.4)	22,342 (29.7)	77,777 (34.9)	10,833 (28.9)	20,614 (29.1)	12,95 (36.7)
80s and older	70,957 (17.3)	10,927 (14.5)	40,586 (18.2)	4,681 (12.5)	13,619 (19.2)	11,44 (32.4)
Comorbidities						
Diabetes mellitus	93,147 (22.7)	14,460 (19.2)	51,590 (23.2)	6,754 (18.0)	19,241 (27.1)	1,102 (31.3)
Hyperlipidemia	228,958 (55.9)	39,828 (53.0)	12,2491 (55.0)	19,972 (53.3)	44,571 (62.8)	2,096 (59.4)
Hypertensive disorder	203,058 (49.6)	33,888 (45.1)	113,930 (51.2)	15,987 (42.7)	37,053 (52.2)	2,200 (62.4)
Chronic kidney disease	6,382 (1.6)	740 (1.0)	2,532 (1.1)	465 (1.2)	2,545 (3.6)	100 (2.8)
Rheumatoid arthritis	13,277 (3.2)	1,979 (2.6)	6,997 (3.1)	1,109 (3.0)	3,020 (4.3)	172 (4.9)
Fracture of bone	100,584 (24.6)	12,294 (16.3)	51,036 (22.9)	6,399 (17.1)	27,508 (38.8)	3,347 (94.9)
Cerebrovascular disease	31,898 (7.8)	4,570 (6.1)	17,813 (8.0)	2228 (5.9)	6,889 (9.7)	398 (11.3)
Coronary arteriosclerosis	5,125 (1.3)	724 (1.0)	2,660 (1.2)	336 (0.9)	1,332 (1.9)	73 (2.1)
Heart failure	26,202 (6.4)	3,565 (4.7)	14,609 (6.6)	1,623 (4.3)	6,011 (8.5)	394 (11.2)
Ischemic heart disease	40,196 (9.8)	5,715 (7.6)	22,872 (10.3)	2,811 (7.5)	8,290 (11.7)	508 (14.4)
Malignant neoplasm of anorectum	886 (0.2)	140 (0.2)	488 (0.2)	51 (0.1)	195 (0.3)	12 (0.3)
Malignant neoplastic disease	26,350 (6.4)	4,911 (6.5)	11,407 (5.1)	2,333 (6.2)	7,524 (10.6)	175 (5.0)
Malignant tumor of breast	6,666 (1.6)	1,610 (2.1)	1,954 (0.9)	386 (1)	2,696 (3.8)	20 (0.6)
Malignant tumor of colon	1,884 (0.5)	274 (0.4)	1,034 (0.5)	125 (0.3)	430 (0.6)	21 (0.6)
Malignant tumor of lung	699 (0.2)	105 (0.1)	323 (0.1)	26 (0.1)	242 (0.3)	3 (0.1)
Malignant tumor of urinary bladder	498 (0.1)	80 (0.1)	253 (0.1)	32 (0.1)	129 (0.2)	4 (0.1)
Malignant neoplasm of bone	492 (0.1)	40 (0.1)	79 (0.0)	12 (0.0)	357 (0.5)	4 (0.1)
Medication use						
Glucocorticoids	226,685 (55.3)	35,315 (47.0)	127,356 (57.2)	15,932 (42.5)	45,687 (64.4)	2,395 (67.9)

Values are expressed as number (%).
HIRA, Health Insurance Review and Assessment Service; SERM, selective estrogen receptor modulator.

are further detailed in Supplemental Tables S3-S6. The OASIS cohort included 39,240 participants. The distribution of first-line AOMs was as follows: oral BPs (49.0%), parenteral BPs (13.1%), SERMs (18.0%), denosumab (15.7%), teriparatide (3.5%), and romosozumab (0.8%) (Fig. 1A). Oral BPs were the most common, particularly among individuals in their 50s and 60s. SERMs were frequently used in patients in their 50s, while denosumab was more prevalent among those in their 60s and 70s. Parenteral BPs and teriparatide were mainly prescribed to older patients. Comorbidities such as diabetes mellitus (11.7%), hyperlipidemia (15.6%), and hypertension (23.6%) were common. BPs were often prescribed to patients with diabetes and hypertension, whereas denosumab was preferred for those with renal impairment (3.2%). Patients with fractures (17.1%) commonly received teriparatide and romosozumab (Table 1). In the HIRA cohort, 409,709 participants were included. The distribution of first-line AOMs was as follows: oral BPs (18.4%), parenteral BPs (54.3%), SERMs (9.1%), denosumab (17.3%), and teriparatide (0.9%) (Fig. 1B). Parenteral BPs were the most frequently prescribed, followed by oral BPs. Denosumab was widely used among individuals in their 60s and 70s. SERMs and teriparatide were less frequently prescribed, with teriparatide predominantly used in older age groups. The HIRA cohort had higher rates of chronic conditions such as diabetes mellitus

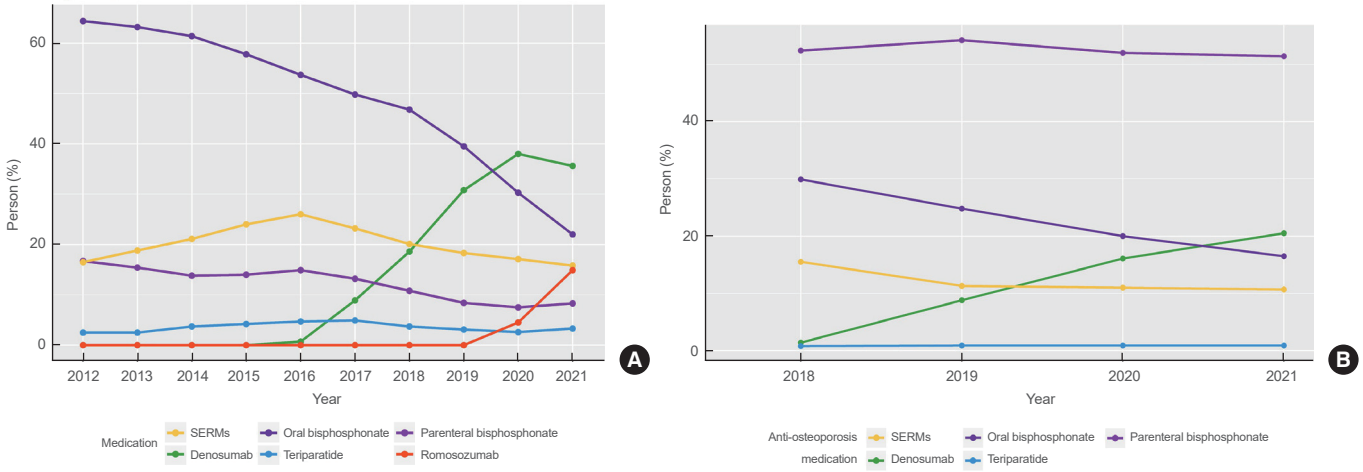

Fig. 2. Trends in anti-osteoporosis medication prescriptions over time. (A) Osteoporosis Analysis and Surveillance Initiative using Standardized data (OASIS) (2012–2021) and (B) Health Insurance Review and Assessment Service (HIRA) (2018–2021) cohort data showing the proportions of postmenopausal women prescribed selective estrogen receptor modulators (SERMs), oral and parenteral bisphosphonates, denosumab, teriparatide, and romosozumab. Prescription trends highlight shifts in medication use over time.

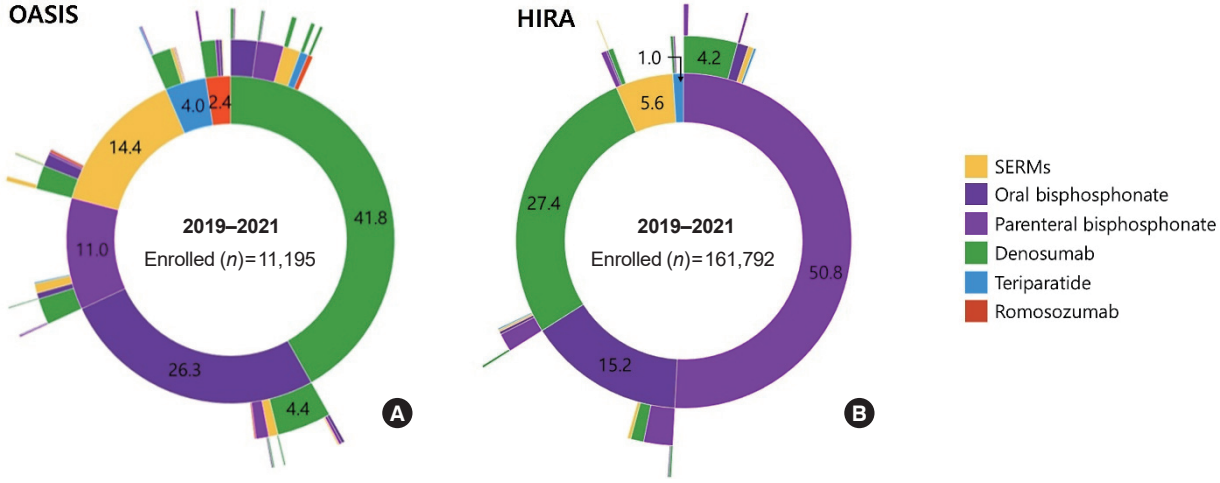

Fig. 3. Anti-osteoporotic treatment pathways for the (A) Osteoporosis Analysis and Surveillance Initiative using Standardized data (OASIS) and (B) Health Insurance Review and Assessment Service (HIRA) cohorts from 2019 to 2021. The sunburst plots display first-line therapies in the center and second- and third-line therapies in the outer rings. Medications include selective estrogen receptor modulators (SERMs), bisphosphonates, denosumab, teriparatide, and romosozumab.

(22.7%), hyperlipidemia (55.9%), and hypertension (49.6%). However, the prevalence of severe diseases such as chronic kidney disease (CKD, 1.6%) and malignant neoplastic diseases (6.4%) was lower, reflecting a closer representation of the general population compared to the OASIS cohort (Table 2).

Secular trends in pharmacological treatment of postmenopausal osteoporosis

Fig. 2 illustrates trends in AOM prescriptions from 2012 to 2021. In the OASIS cohort, denosumab prescriptions exhibited a rapid increase, surging from around 2% in 2016 to approximately 40% by 2020. In contrast, the use of oral BPs decreased from 69% in 2012 to 22% in 2021. Romosozumab prescriptions began around 2019, reaching about 14% by 2021. Meanwhile, the use of other medications, such as SERMs, parenteral BPs, and teriparatide, remained relatively stable with only minor fluctuations. The secular trends in AOMs at each institution are illustrated in Supplemental Fig. S1.

In the HIRA cohort, trends from 2018 to 2021 exhibited similar patterns. The use of oral BPs declined from 18.4% to 14.5%,

while denosumab prescriptions increased sharply. The proportion of patients using SERMs remained relatively stable, and the use of parenteral BPs stayed nearly constant throughout the study period.

AOM treatment patterns by cohort

Fig. 3 presents the AOM patterns derived from a cohort pathway analysis spanning 2019 to 2021 for the OASIS and HIRA cohorts. In the OASIS cohort, the selection of first-line drugs was diverse, reflecting the tertiary care setting. Denosumab emerged as the most frequently used first-line drug, accounting for 41.8% of prescriptions, followed by oral BPs at 26.3%. Anabolic agents, including teriparatide and romosozumab, were actively employed as first-line therapies, comprising 6.4% of prescriptions. This distribution reflects the higher fracture risk and more aggressive treatment strategies used in tertiary care settings. The HIRA cohort exhibited different prescription patterns, with parenteral BPs predominating at 50.8% of first-line prescriptions and denosumab accounting for 27.4%. The use of anabolic agents was limited, with teriparatide comprising only 1% of prescriptions.

Supplemental Fig. S2A illustrates the AOM prescription patterns in the OASIS cohort from 2012 to 2021. Over this period, oral and parenteral BPs collectively accounted for approximately 62.1% of prescriptions. SERMs and denosumab were also commonly used, while anabolic agents were less frequently prescribed. The use of denosumab increased markedly after 2019, reaching 41.8%, whereas BP usage decreased to 37.3%. Anabolic agents, including teriparatide and romosozumab, comprised 6% of prescriptions by 2021. In the HIRA cohort, from 2018 to 2021, the prescription rate of denosumab increased significantly following its approval as a first-line drug (Supplemental Fig. S2B). In 2018, oral BPs accounted for 20.4% of prescriptions, parenteral BPs for 56.6%, and SERMs for 11.5%. By 2019–2021, oral BPs had decreased to 15.2%, parenteral BPs to 50.8%, and SERMs to 5.6%, highlighting a shift toward denosumab and a decline in SERM usage. The treatment pattern figures for AOMs at each institution are also shown in Supplemental Figs. S3-S6.

DISCUSSION

This study provides a comprehensive analysis of AOM treatment patterns among postmenopausal women in South Korea using the OASIS cohort and the HIRA database. In the OASIS cohort, which comprises data from four tertiary hospitals, denosumab emerged as the most frequently prescribed first-line AOM from 2019 to 2021, reflecting the higher fracture risk and more aggressive treatment strategies typical of tertiary care settings. Additionally, the use of anabolic agents as first-line treatments approximately doubled following the introduction of romosozumab in 2019. Conversely, the HIRA cohort—representing a broader population sourced from primary and secondary institutions—exhibited predominant use of parenteral BPs and significant use of denosumab, likely influenced by its compliance benefits. These results demonstrate the impact of national health insurance policies and the introduction of new medications on prescribing practices, indicating a shift towards denosumab and a decline in SERMs and oral BPs over time. The findings underscore the importance of considering institutional characteristics and policy changes when analyzing osteoporosis treatment.

According to major clinical guidelines, oral BPs (including alendronate and risedronate) are generally recommended as the first-line treatment for postmenopausal osteoporosis in patients at high risk of fracture [6,7,15]. Denosumab is also recommended as a first-line therapy for these patients; this aligns with our findings that denosumab was widely used as a first-line agent (15.7%), reflecting its acceptance in clinical practice. In our study, BPs were more commonly prescribed to patients with multiple comorbidities. Despite its efficacy, denosumab can be challenging to discontinue abruptly [16,17], whereas BPs are often preferred for their residual effects, ensuring ongoing benefits even if treatment is interrupted [18]. Additionally, denosumab, as a RANK ligand monoclonal antibody that does not undergo renal excretion, is preferred for patients with CKD [19,20]. This is supported by our findings, in which many patients with CKD were included in the denosumab first-line treatment group. Anabolic agents like teriparatide and romosozumab are typically prescribed to elderly patients and those with a history of previous fractures, reflecting their utility in cases with high fracture risk [21-23]. However, their use remains limited among patients with fractures, possibly due to obstacles such as insurance coverage, cost limitations, and compliance issues. These factors highlight the challenges of prescribing anabolic agents in real-world settings.

In the OASIS cohort, romosozumab was prescribed even to patients without prior fractures (M81). This trend in tertiary institutions may reflect several factors: (1) greater familiarity with newer therapeutic options among specialists; (2) institutional protocols that support more aggressive treatment approaches; and (3) different patient populations with varying risk factors

that were not captured in our database [21]. However, without individual-level risk assessments or clinical outcome data, we cannot conclusively attribute these prescribing behaviors to personalized treatment strategies. Instead, the observed diversification in first-line AOM prescriptions over time should be interpreted primarily as an indication of evolving clinical practices rather than definitive evidence of treatment individualization.

In contrast, the limited use of anabolic agents in the HIRA cohort underscores the influence of policy and economic barriers. The absence of reimbursement for anabolic agents as first-line therapies likely restricts their broader adoption in primary and secondary care settings, despite strong guideline support. Addressing these disparities through expanded reimbursement policies could facilitate greater use of anabolic agents in patients at high risk across all healthcare levels. Furthermore, policy changes may mitigate the challenges associated with sequential treatment strategies, wherein administering antiresorptive agents before anabolic agents can reduce the efficacy of the latter [24].

Our study revealed a significant shift in treatment patterns for postmenopausal osteoporosis, mirroring global trends. Specifically, we observed a decline in BP use and an increase in denosumab prescriptions, a pattern also noted in countries such as the United States and France [25,26]. Several factors have contributed to the decline in BP use, including potential adverse effects such as gastrointestinal issues, complex administration regimens, and compliance concerns [27]. Additionally, rare but serious side effects like osteonecrosis of the jaw and atypical femoral fractures have raised concerns among both the public and physicians, further reducing BP prescriptions [28]. Notably, the long-lasting effects of BPs allow patients to benefit even after discontinuation. Conversely, denosumab use has increased due to its convenient administration as a biannual subcutaneous injection and its efficacy in increasing bone density and reducing fracture risk [29]. This trend, observed in studies from several countries, reflects a growing preference for denosumab among patients and healthcare providers [25,26,30]. Our findings align with previous research in Korea, which has reported similar shifts in medication trends [30]. Overall, this shift highlights an international pattern in which convenience, patient compliance, and evolving clinical guidelines drive the choice of osteoporosis treatment.

Our study also highlights the influence of policy changes and clinical guidelines on AOM prescription patterns. The expansion of insurance coverage for denosumab—especially since its approval as a first-line treatment in 2019—has led to a marked increase in its use, underscoring the powerful role of policy decisions in shaping treatment practices. In Korea, similar patterns have emerged, with increased denosumab prescriptions following broader insurance coverage. This trend emphasizes how policy changes may facilitate the adoption of newer therapies. Growing evidence indicates that anabolic agents, such as teriparatide, abaloparatide, and romosozumab, are more effective than antiresorptive agents in increasing bone mineral density and preventing fractures [6,31]. Administering anabolic agents before antiresorptive agents has been shown to be more effective than providing antiresorptives before anabolic therapies [24]. Although these treatments are typically short term (1 to 2 years), their benefits can be maintained with subsequent antiresorptive therapy, significantly reducing long-term fracture risk [32]. This paradigm shift supports the use of anabolic therapies as first-line treatments rather than salvage therapy, emphasizing the importance of identifying patients who would benefit most from this approach, particularly in an aging population like that of Korea.

The 2019 reimbursement of denosumab as a first-line therapy exemplifies the key role of policy changes in facilitating medication adoption [24]. Similar policy adjustments to expand reimbursement coverage for anabolic agents could replicate this success, aligning real-world practices with guideline recommendations. Such changes would improve access to effective therapies for patients at very high risk, optimize treatment sequences, and enhance overall clinical outcomes. The increased use of anabolic agents, driven by guideline recommendations and insurance coverage, reflects the substantial influence of clinical guidelines on prescribing patterns [24]. In the OASIS cohort, the use of anabolic agents doubled after the introduction of romosozumab in 2019, reflecting the recommendation for anabolic agent use in patients with very high fracture risk. Similarly, in the HIRA cohort, we observed a slight increase in the use of the anabolic agent teriparatide since 2019, indicating adherence to guidelines. Previous research has shown that changes in reimbursement policies and clinical guidelines can significantly affect prescription rates of diagnostic tests and treatments for osteoporosis [10]. For instance, Australia's Medicare reimbursement for dual-energy X-ray absorptiometry (DXA) tests led to an increase in test referrals, albeit with limited impact on fracture incidence. Similarly, policy changes in Ontario, Canada, were found to affect DXA test rates and influence osteoporosis management [33]. In this regard, our findings illustrate that policy and guideline changes are pivotal in shaping AOM prescription patterns, as seen in the increase in denosumab use

following expanded insurance coverage and the rise in romosozumab prescriptions.

The limitations of our study are multifaceted and warrant careful consideration. First, the retrospective design may have introduced selection bias and limited causal inferences. Data standardization can result in the loss of specific details from the original datasets. Differences between the OASIS and HIRA cohorts may restrict the generalizability of our findings across diverse populations and healthcare settings, and the inconsistent study periods further complicate the assessment of long-term outcomes. Additionally, the study did not account for medication adherence, a critical factor in osteoporosis management, and the HIRA cohort lacked certain data (such as romosozumab prescriptions). Moreover, while our study highlights a shift in prescription patterns, these changes cannot be directly interpreted as improvements in clinical outcomes due to the absence of patient-specific clinical data. The lack of key clinical metrics—such as T-scores, DXA results, and fracture risk assessments—prevents us from evaluating whether these prescribing trends translate into optimized or individualized treatment outcomes and limits our ability to fully assess osteoporosis severity. Future longitudinal studies are recommended to explore the relationship between prescription trends and clinical outcomes in patients with osteoporosis without fractures. Incorporating detailed clinical data—such as bone mineral density measurements, fracture risk assessments, and patient adherence information—will be essential to determine whether these evolving prescribing patterns reflect more optimized, individualized care.

Furthermore, this study did not include variables related to socioeconomic status (SES), such as household income or private insurance coverage, which may influence access to high-cost therapies like anabolic agents. The absence of such data in the OASIS and HIRA cohorts precluded a thorough analysis of the economic factors affecting prescribing patterns, particularly for primary prevention in osteoporosis without fractures. Lastly, the use of two datasets with distinct characteristics—OASIS, reflecting tertiary care, and HIRA, more broadly representing primary and secondary care—could have introduced bias when comparing treatment patterns. Differences in available data, such as the inclusion of newer therapies like romosozumab in OASIS but not in HIRA, may have yielded variations that were driven by database structure rather than clinical practice. While this approach highlights complementary trends, it also necessitates caution when interpreting results across these datasets. Future studies should consider integrating SES-related information and harmonizing data collection processes to provide a more thorough understanding of the interplay between economic status, healthcare setting, and osteoporosis treatment patterns.

Nevertheless, the innovative use of two distinct databases, OASIS and HIRA, also represents a key strength of this study. This choice enabled a comprehensive, multifaceted analysis of osteoporosis treatment patterns within a single country. By utilizing the OMOP-CDM, we aggregated and standardized data from multiple large institutions, providing a broad and diverse patient sample. This approach included medications not typically covered in national insurance-based studies, thereby increasing the reliability and scope of our findings. The combination of institutional data (OASIS) and nationwide claims data (HIRA) enabled the analysis of treatment practices across various healthcare settings, thus mitigating regional biases and increasing generalizability. Our study identified distinct prescription patterns between tertiary care institutions, at which denosumab and anabolic agents were more frequently prescribed due to higher fracture risk and more aggressive treatment strategies, and primary/secondary care institutions, where parenteral BPs predominated, reflecting different patient profiles and compliance factors. By incorporating datasets with differing characteristics, the study not only highlights the complementary strengths of these sources but also provides insights into prescribing patterns both within and beyond the boundaries of insurance coverage. This dual perspective offers a more complete understanding of real-world practices and treatment disparities across levels of care. These findings underscore the impacts of healthcare settings, patient characteristics, and policy changes on AOM prescription patterns, providing valuable insights into the real-world management of osteoporosis.

In conclusion, this study demonstrates how policy changes and clinical guidelines have shaped AOM prescription patterns in postmenopausal women in South Korea, with increased use of newer medications—including denosumab and romosozumab—and a decline in BPs and SERMs. By utilizing both the OASIS and HIRA databases, our study offers a thorough analysis of osteoporosis treatment patterns by combining detailed institutional data with nationwide trends. This dual-database approach highlights the impact of diverse healthcare settings on optimizing osteoporosis management and improving patient outcomes.

CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

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ORCID

Kyoung Jin Kim *https://orcid.org/0000-0001-7925-2515*
Dachung Boo *https://orcid.org/0000-0002-6855-3723*
Ji Seon Oh *https://orcid.org/0000-0002-0205-6492*
Seng Chan You *https://orcid.org/0000-0002-5052-6399*

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