Real-World Osteoporosis Drug Utilization in Patients with Recurrent Osteoporotic Fracture: A Nationwide Cohort Study in South Korea

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INTRODUCTION

- Given the heightened risk of subsequent fractures in the patients with fracture history and the imperative for more effective osteoporosis management in line with treatment guidelines, there is distinct need to establish the real-world evidence of osteoporosis medication[1)2)].
- This study aims to investigate the real-world utilization of first osteoporosis (OP) medication among patients who experienced recurrent osteoporotic fractures (OF).

METHODS

- **Study design**: Longitudinal retrospective cohort study and the detailed study design is described in Figure 1.
- **Data source**: Health Insurance Review and Assessment Service (HIRA) Database covering the entire population in Korea from Jan 2012 to Dec 2017
- **Study population :** Patients aged ≥55 with the first recurrent OF(re-OF) within 2 years after the primary OF in 2013 and the details of cohort selection and exclusion criteria are described in Figure 2.
- **Outcomes of interest**
  - ✓ The median treatment duration of the first treatment episode by types of drug
  - ✓ Medication adherence assessed using medication possession ratio (MPR) and discontinuation rate of the first treatment episode drug by types of drug
- **Operational definitions of study**
  - The first OP medication was defined as the first drug of the initial treatment episode since their first recurrent fracture described in the yellow part in Figure 2.
  - The first treatment episode was defined as the first group of consecutive prescriptions of the initial drug, allowing a 60-day refill gap between prescriptions and the discontinuation of the treatment was defined as the earliest event, either the last date of drug use of the first treatment episode or the latest follow-up date.
  - The MPR was calculated by dividing the duration of prescribing the initial OP medication by two years.

$$MPR = \frac{\textbf{\textit{the duration of prescribing in the first treatment episode}}}{\textbf{\textit{two years}}}$$

- **Statistical analysis**
  - Continuous variables were summarized using medians with ranges and means with standard deviations (SD)and categorical variables were presented as counts and proportions.
  - To assess differences between groups of baseline characteristics, we employed independent t-tests for continuous variables and chi-squared tests for categorical variables.
  - Performed using SAS® Enterprise guide version 9.4, and the statistical significance was set at $P < 0.05$.

Figure 1. Study Design

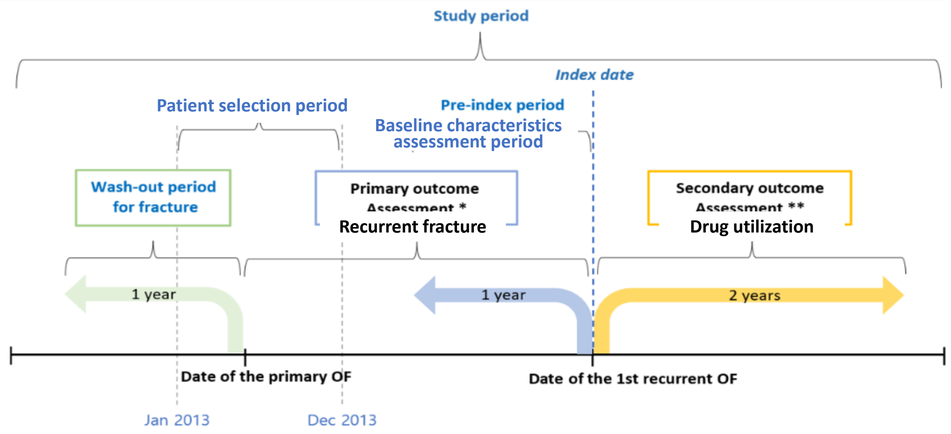
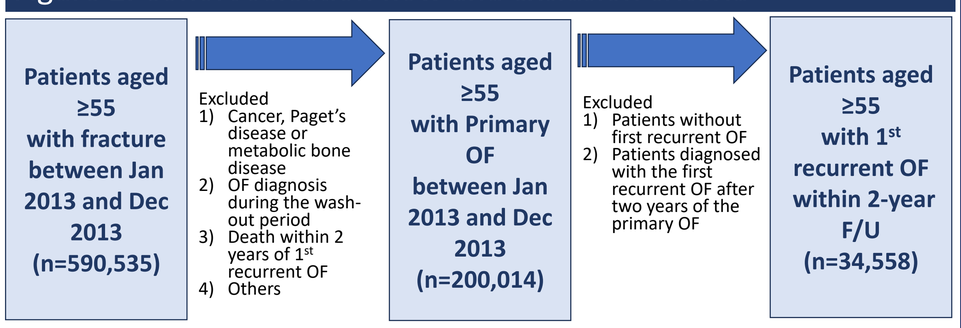


Figure 2. Cohort selection flow and exclusion criteria



RESULTS

Table 1. Baseline characteristics of cohorts and OP medication rate

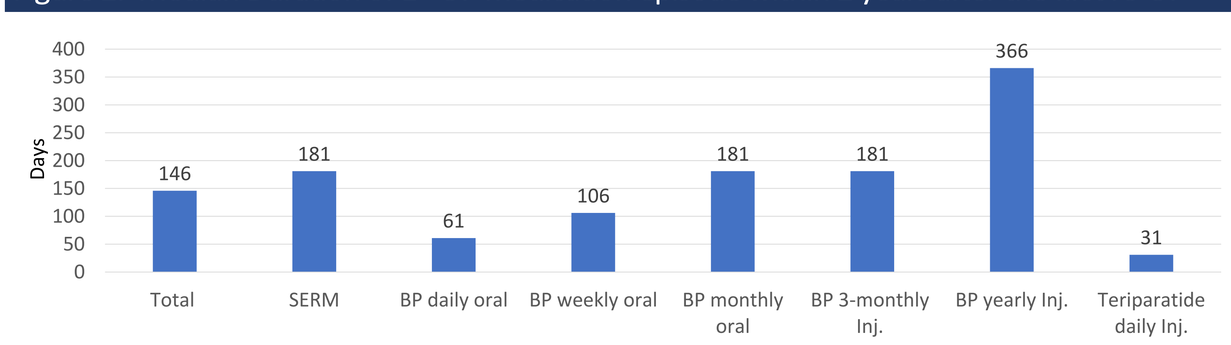
	Total N (%) or mean (SD)	Male N (%) or mean (SD)	Female N (%) or mean (SD)	*P* value [a]
No. cohort	34,558 (100)	5,261 (15.22)	29,297 (84.78)	<0.001
Age(years)	73.3 (9.31)	70.37 (9.41)	73.82 (9.20)	<0.001
No. cohort by age group				
55 ≤ Y < 65	7,306 (21.14)	1,734 (32.96)	5,572 (19.02)	<0.001
65 ≤ Y < 75	10,826 (31.33)	1,662 (31.59)	9,164 (31.28)	0.650
75 ≤ Y < 85	12,358 (35.79)	1,461 (27.77)	10,897 (37.19)	<0.001
85 ≤ Y	4,068 (11.77)	404 (7.68)	3,664 (12.51)	<0.001
CCI scores				
0	6,703 (19.40)	1,194 (22.70)	5,509 (18.80)	<0.001
1	8,017 (23.20)	1,155 (21.95)	6,862 (23.42)	0.020
2	7,012 (20.29)	996 (18.93)	6,016 (20.53)	0.008
≥ 3	12,826 (37.11)	1,916 (36.42)	10,910 (37.24)	0.260
Previous OP medication history				
N	20,141 (58.46)	4,324 (82.55)	15,817 (54.14)	<0.001
Y	14,313 (41.54)	914 (17.45)	13,399 (45.86)	<0.001
Type of previous OP medication [b]				
SERM	1,175 (8.21)	0 (0.00)	1,175 (8.77)	<0.001
BP oral	10,188 (71.18)	887 (97.05)	9,301 (69.42)	<0.001
BP Injection	2,950 (20.61)	27 (2.96)	2,923 (21.82)	<0.001
Treatment rate	18,462 (53.42)	1,247 (23.70)	17,215 (58.76)	<0.001
55 ≤ Y < 65	2,467 (33.77)	180 (10.38)	2,252 (41.04)	<0.001
65 ≤ Y < 75	6,368 (58.82)	387 (23,29)	5,862 (65.27)	<0.001
75 ≤ Y < 85	7,749 (62.70)	550 (37.65)	7,053 (66.06)	<0.001
85 ≤ Y	1,878 (46.17)	130 (32.18)	1,707 (47.71)	<0.001

CCI, the Charlson Comorbidity Index; OF, Osteoporotic Fracture; OP, Osteoporosis; SD, Standard deviation; BP, Bisphosphonate

[a] *Comparison between males and females. The chi-squared test was used for categorical variable analysis, and the Student's t-test was used for continuous variable analysis.*

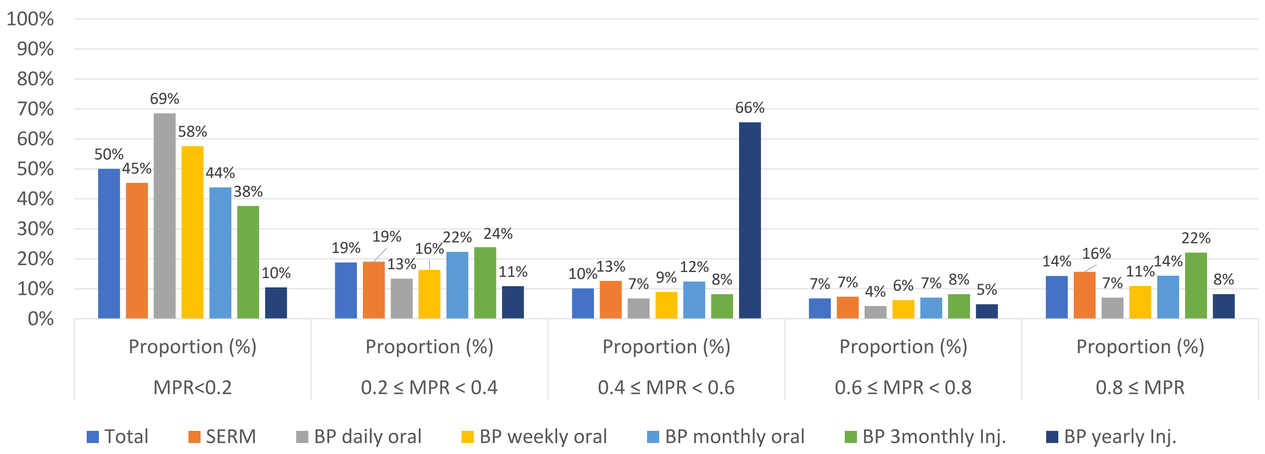
[b] *the latest OP medication before the first recurrent OF. Since the assessment period was before the approval of teriparatide, denosumab, and romosozumab, there were no patients who were prescribed those medications.*

Figure 2. Median Duration of 1st OP medication episode within 2 years after the first re-OF



- Figure 3 illustrates a gradual decline in OP medication adherence with increasing follow-up time, along with a tendency toward better adherence for drugs administered over the long term, as assessed by MPR, in accordance with the findings presented in Figure 2.

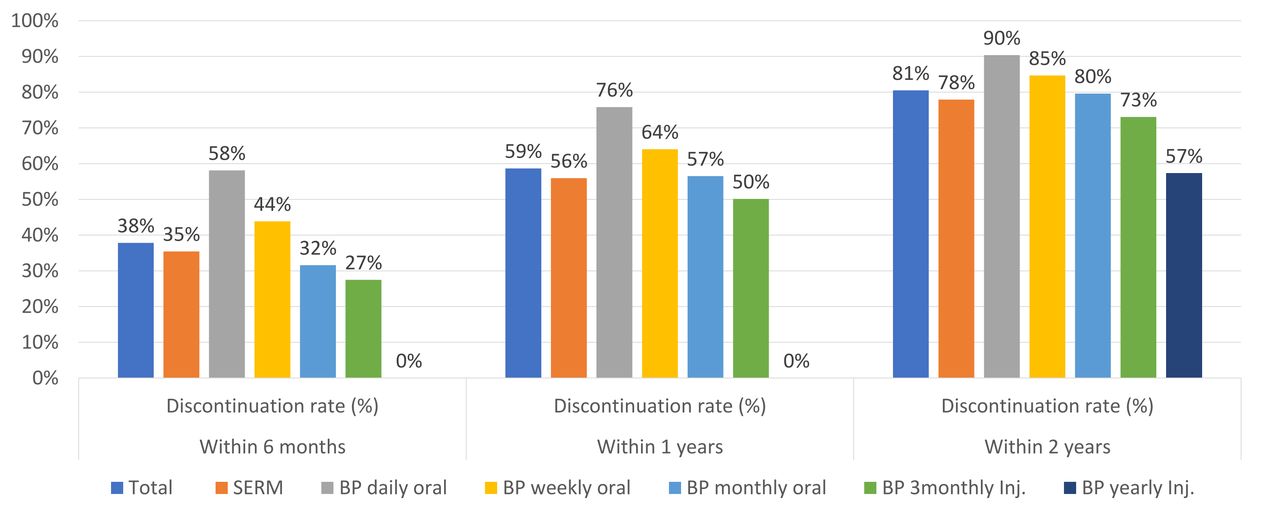
Figure 3. MPR of 1st OP medication episode within 2 year after 1st re-OF



BP, Bisphosphonate
Note: The number of teriparatide user was too small and the results was not included in this figure.

- Figure 4 demonstrates that the majority of re-OF patients discontinue their OP medication within one year, with most of them discontinuing OP treatment within two years of follow-up after the re-OF.

Figure 4. Discontinuation rate of OP medication within 2 years follow-up after 1st re-OF



BP, Bisphosphonate
Note: The number of teriparatide user was too small and the results was not included in this figure.

CONCLUSIONS

- **Although patients with recurrent fractures require intensive osteoporosis management, our results revealed significantly low utilization rates of osteoporosis drugs among the high-risk OP patient with re-OF.**
- Hence, adopting strategic treatment guidelines and refining reimbursement criteria are essential to address osteoporosis treatment gaps in high-risk patients with recurrent OFs.

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- HH, MK, DP, and HSS have no conflict of interest.
- EW and MJK are an employee of Amgen Korea Inc.

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