

# Comedication Patterns of Romosozumab Early Adopters Among Medicare Enrollees: An Unsupervised Clustering Approach



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## INTRODUCTION

- Polypharmacy is a major concern in osteoporosis (OP) management, especially in older adults.
- Romosozumab, approved in April 2019, is a parenteral OP medicine for postmenopausal women at high fracture risk, given monthly for 12 months.
- We examined comedication patterns among early romosozumab adopters and their association with treatment adherence.

## METHODS

- Retrospective cohort study using Medicare fee-for-service data (2016-2022)
- Female romosozumab early adopters aged 65 or older who initiated romosozumab in 2019, with  $\geq 4$  years of continuous enrollment, including 3-years pre-initiation. Those with metastatic cancers or Paget's disease were excluded.
- All prescription drugs covering the romosozumab initiation day and selected 8 major medication categories for clustering:

- |                           |             |
|---------------------------|-------------|
| ✓ Anti-hypertensive (HTN) | ✓ Hypnotics |
| ✓ Lipid-lowering          | ✓ NSAIDs    |
| ✓ Anti-diabetic           | ✓ Opioids   |
| ✓ Antidepressants         | ✓ Steroids  |

- We used **hierarchical agglomerative clustering** to identify comedication patterns, with consensus clustering analysis to determine the optimal number of clusters.
- Romo discontinuation was defined as  $\geq 60$  days without injection.
- Cox proportional hazard model, adjusting for demographics, Charlson comorbidity index, fracture history, DXA scan, prior OP treatment history, etc. was used to evaluate the association between comedication pattern and romosozumab treatment discontinuation.

## REFERENCES

1. Saag KG, Petersen J, Brandi ML, Karaplis AC, Lorentzon M, Thomas T, Maddox J, Fan M, Meisner PD, Grauer A. Romosozumab or Alendronate for Fracture Prevention in Women with Osteoporosis. *N Engl J Med*. 2017 Oct 12;377(15):1417-1427. doi: 10.1056/NEJMoa1708322..
2. Liu Y, Arora T, Zhang J, Sodhi SK, Xie F, Curtis JR. The Interruption of Romosozumab Treatment During COVID Lockdown Among U.S. Post-menopausal Women Enrolled in Medicare. *Bone*. 2024 Jan;178:116954. doi: 10.1016/j.bone.2023.116954..

## RESULTS

**Figure 1. Diagnosis panel of Consensus clustering analysis to determine optimal number of clusters (k)**

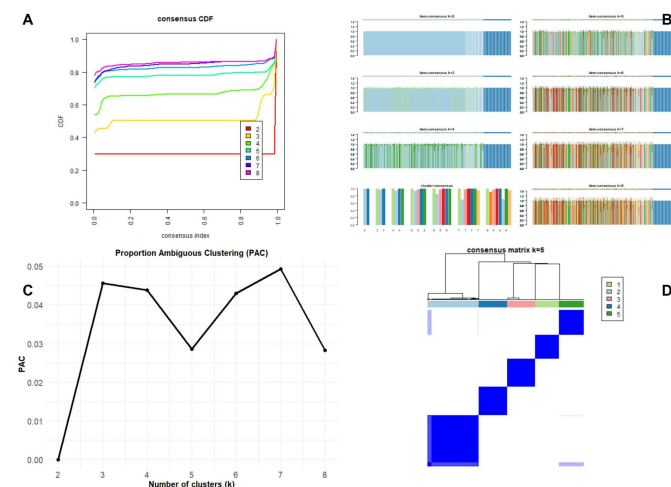


Figure 1. Diagnosis panel of consensus clustering analysis to determine optimal number of clusters (k)  
A: Consensus cumulative distribution function (CDF) plot. B: Item-consensus plot. C: Proportion ambiguous clustering (PAC) plot. D: Consensus matrix at optimal k = 5

- A total of 1,777 romosozumab early users were included (mean age: 77.7 years; 90.9% White). Consensus clustering analysis identified five mutually exclusive comedication pattern groups:

- 1 (N=326). No patients used any pre-specified drugs of interest.
- 2 (N=275). All used anti-HTN only.
- 3 (N=281). All used lipid-lowering drugs, some (67%) also used anti-HTN.
- 4 (N=313). All used antidepressants, some also used anti-HTN (57%) and/or lipid-lowering (41%) drugs.
- 5 (N=582). Various drugs (at least one of the 8 categories, not in other groups).

- Patients in group 2 were the oldest (79.4 years,  $p < 0.001$ ) and had the highest proportion from the South (47.3%,  $p = 0.013$ ).
- Group 5 had the highest Charlson Comorbidity Index (4.8,  $p < 0.001$ ) and the lowest percentage of White patients (88.5%,  $p = 0.001$ ).
- No significant differences in fracture or OP treatment history were observed.
- One-year overall romosozumab discontinuation risk was 32.2% [29.1%, 35.7%].

## CONCLUSIONS

- **Distinct comedication patterns were identified among romosozumab early adopters.**
- **Patients using antidepressants or multiple medication categories had a higher discontinuation risk and needed additional adherence support.**

**Table 1. Adjusted\* Hazard Ratio (HR) and 95% Confidence Interval for 1-year Discontinuation for Each Comedication Pattern Group**

Group	HR [95% CI]
1: No patients used any pre-specified drugs of interest.	REF
2: All used anti-HTN only.	1.22 [0.97 – 1.53]
3: All used lipid-lowering drugs, some also used anti-HTN	1.08 [0.86 – 1.37]
4: All used antidepressants, some also used anti-HTN and/or lipid-lowering drugs.	1.41 [1.14 – 1.76]
5: Various drugs (at least one of the 8 categories, not in other groups).	1.39 [1.14 – 1.69]

Variables adjusted for: age, race, geographic region, Charlson comorbidity score, romosozumab billed in Part D, fracture history within 1-year before romosozumab initiation, received DXA scan within 1-year before romosozumab initiation, osteoporosis treatment adherence/history before romosozumab, had ER visit within 1-year before romosozumab initiation

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