

Impact of a Pharmacist-Implemented Protocol on Calcium Monitoring and Safety Outcomes with Denosumab Use in Ambulatory Patients

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Background

- Denosumab (Prolia[®])
 - 60 mg subcutaneous injection every 6 months
 - Indicated for steroid-induced osteoporosis and osteoporosis/bone loss in men and women
- MOA: Monoclonal antibody which binds to RANKL, preventing osteoclast formation
- Severe ADRs: hypocalcemia, serious infections, atypical femoral fractures, osteonecrosis of the jaw

Prolia [package insert]. Thousand Oaks, CA: Amgen Inc; 2010

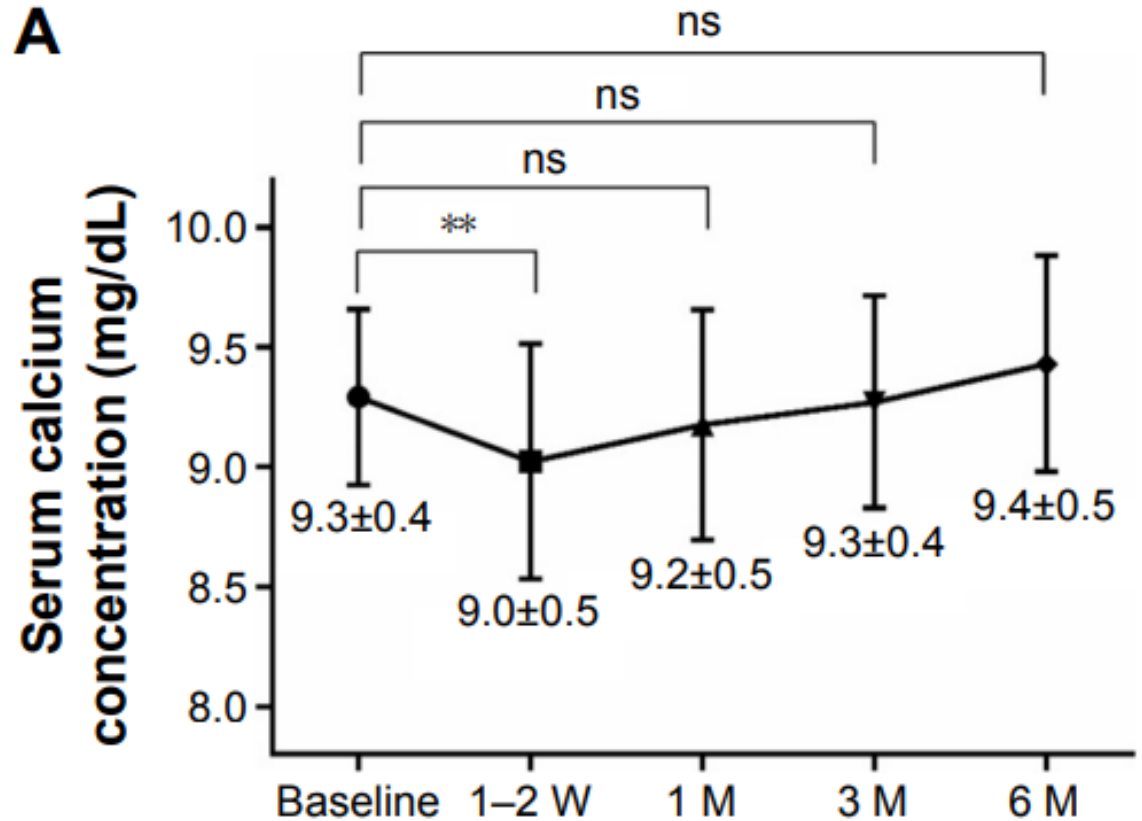
Background

- Hypocalcemia
 - Presentation: tingling fingertips/toes, myalgias, muscle cramps/spasms, tetany, respiratory distress, arrhythmia, seizures, psychiatric symptoms
 - Calcium level nadir typically occurs 10 days post-injection
 - Supplement all patients with calcium 1000 mg daily plus at least vitamin D 400 IU daily
 - Calcium level should be corrected before each injection
 - At-risk patients include: renal impairment/HD, hypoparathyroidism, thyroid surgery, malabsorption syndromes

Background

Retrospective Study

25.9% of patients
experienced hypocalcemia



Ther Clin Risk Manag. 2016;12:1831-1840.

Background

Mercy Clinic – Family Medicine (MFM)

- Primary clinical site for the Mercy Family Medicine Residency
 - 18 Medical Residents
- 8-10 Attending Physicians
- Clinical Pharmacist at the clinic since 1992
- Required experience for Mercy PGY-1 Pharmacy Residency Program
- Prior research: pharmacist-physician collaboration improves osteoporosis treatment rates



Ann Pharmacother. 2018;52(9):876-883.

MFM Protocol

Developed in December 2017 by clinical pharmacist

Assess patient to schedule denosumab injection

Calcium level not current

Order BMP

Calcium level current

Normal value
(8.6-10.2 mg/dL)

Schedule injection

Infusion center administration

MFM administration

Abnormal value
(<8.6 or >10.2 mg/dL)

Refer to physician for calcium management

Recheck BMP

Objective

- To determine the impact of a pharmacist-implemented protocol at Mercy Clinic-Family Medicine (MFM) compared to other Mercy East Community clinics on completion of calcium-monitoring and other safety outcomes for patients taking denosumab for osteoporosis

Methods

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none">• Adults \geq 18 years of age• Received denosumab (Prolia[®]) injection between December 13th, 2017 and December 1st, 2019• Patient of the Mercy East Community clinics	<ul style="list-style-type: none">• Patients receiving denosumab for indications other than osteoporosis

Patients identified via EPIC Electronic Medical Record using claims data for denosumab injections

Primary Outcome

Received denosumab for osteoporosis at a Mercy East Community Clinic

Non-MFM patients

Matched in 1:1 ratio
(age & sex)

MFM patients

Calcium level drawn within past 30 days

Calcium level not drawn within past 30 days

Calcium level drawn within past 30 days

Calcium level not drawn within past 30 days

Secondary Outcomes

- Mean days since last calcium level was drawn prior to denosumab injection
- Percentage of:
 - Patients receiving documented calcium plus vitamin D supplementation
 - Patients with correctly-timed denosumab injections 180 to 210 days after the previous administration
- Incidence of:
 - Post-injection hypocalcemia within 30 days
 - Hospital admissions due to hypocalcemia within 30 days post-injection
 - Hospital admissions for infections 30 days post-injection
 - Fractures after injection and prior to next administration

Data Analysis

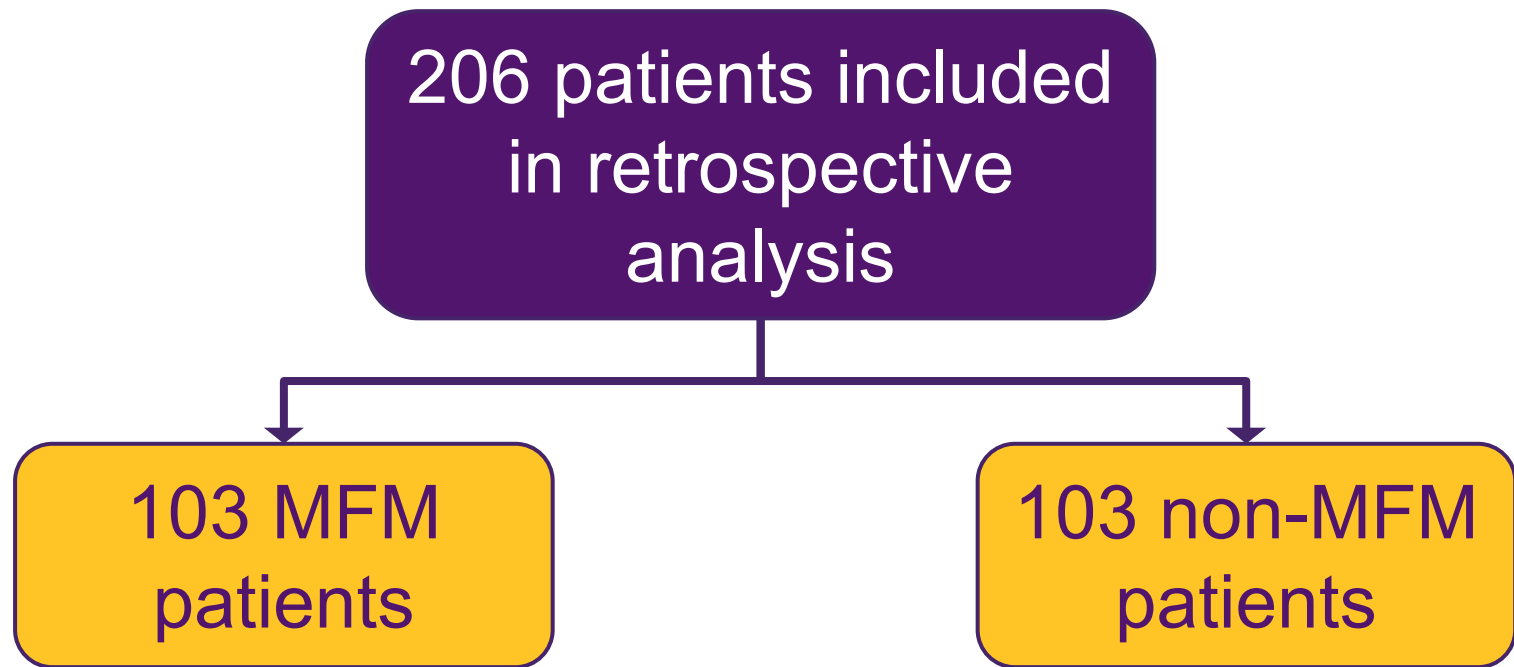
Chi-squared or Fisher's exact tests

- **Primary Outcome:** Calcium level drawn within past 30 days
- **Secondary Outcomes:** Post-injection hypocalcemia, hospital admission for hypocalcemia or infection, incidence of fracture, on-time injections, calcium and/or vitamin D supplementation

Student's t-test

- **Secondary Outcome:** Days since last calcium was drawn

Enrollment

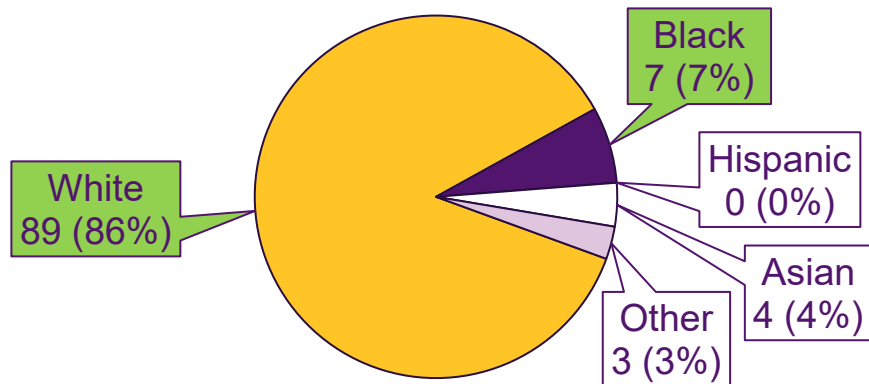


Baseline Characteristics

	MFM (n = 103)	Non-MFM (n = 103)	p-value
Age – yr	75.2 ± 9.8	75.3 ± 9.8	0.98
Female – n (%)	98 (95.1)	98 (95.1)	1.00
Height – in	62.7 ± 2.7	63.0 ± 3.0	0.42
Weight – kg	63.0 ± 10.8	67.1 ± 15.1	0.03

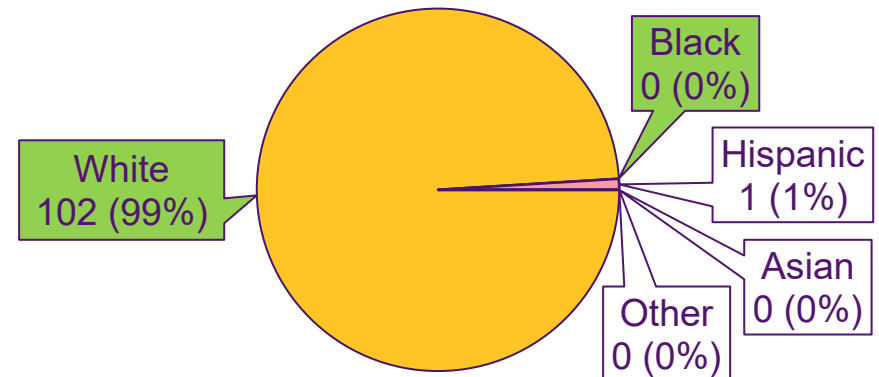
Baseline Characteristics

MFM (n = 103)



White Black Hispanic Asian Other

Non-MFM (n = 103)



White Black Hispanic Asian Other

MFM versus non-MFM	p-value
White	<0.001
Black	0.01

Baseline Characteristics

	MFM (n = 103)	Non-MFM (n = 103)	p-value
Smoking Status – n (%)			
Current	8 (7.8)	6 (5.8)	0.78
Past	41 (39.8)	44 (42.7)	0.67
Alcohol use* – n (%)	5 (4.9)	1 (1.0)	0.21
Hx of CKD – n (%)	27 (26.2)	23 (22.3)	0.52
CrCl – mL/min	51.9 ± 25.0	53.6 ± 18.6	0.58
<30 mL/min – n (%)	17 (16.5)	9 (8.7)	0.14
≥30 mL/min – n (%)	86 (83.5)	94 (91.3)	0.14

* ≥ 3 drinks/day

Baseline Characteristics

	MFM (n = 103)	Non-MFM (n = 103)	p-value
Hx steroid use* – n (%)	9 (8.7)	3 (2.9)	0.13
Hx bisphosphonate use – n (%)	78 (75.7)	55 (53.4)	<0.001
Admin Location – n (%)			
Primary care clinic	99 (96.1)	99 (96.1)	1.00
Infusion center	4 (3.9)	0 (0)	0.12
Specialty care clinic	0 (0)	4 (3.9)	0.12
10-year FRAX score – %			
Major osteoporotic fracture	21.2 ± 12.1	20.0 ± 11.0	0.46
Hip fracture	8.4 ± 8.5	8.6 ± 9.4	0.62

* Prednisone 5 mg/day or equivalent for > 90 days

Results

Primary Outcome	MFM (n = 103)	Non-MFM (n = 103)	p-value
Calcium drawn in last 30 days – n (%)	88 (85.4)	49 (47.6)	<0.001

Secondary Outcomes	MFM (n = 103)	Non-MFM (n = 103)	p-value
Time since last calcium level – days	24.3 ± 46.1	97.8 ± 110.7	<0.001
Calcium supplement – n (%)	76 (73.8)	65 (63.1)	0.10
Vitamin D supplement – n (%)	89 (86.4)	80 (77.7)	0.10
	(n = 77)	(n = 85)	p-value
Correctly timed injections* - n (%)	56 (72.7)	59 (69.4)	0.64

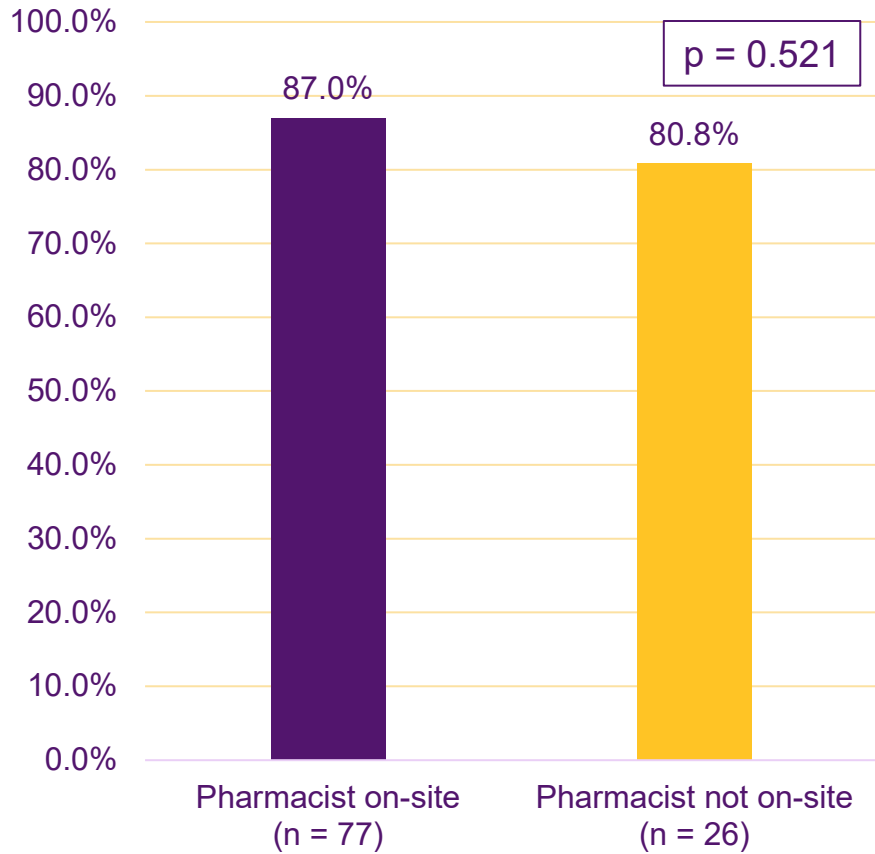
* Within 180 to 210 days from previous injection

Results

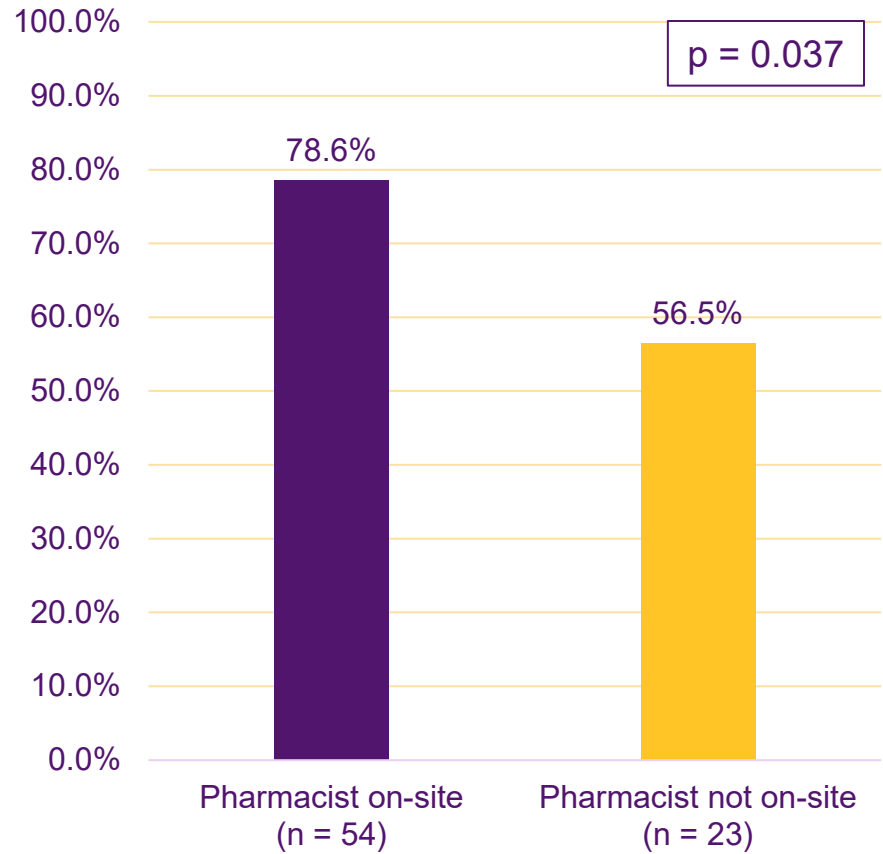
	MFM (n = 103) n (%)	Non-MFM (n = 103) n (%)	p-value
Post-injection hypocalcemia	4 (3.9)	6 (5.8)	0.75
Post-injection hospitalization for hypocalcemia	1 (1.0)	4 (3.9)	0.37
Post-injection hospitalization for infection	0 (0)	3 (2.9)	0.25
Fracture	2 (1.9)	6 (5.8)	0.28

Results

Calcium drawn in last 30 days



Correctly-timed injections



Discussion

Strengths

- Similar baseline characteristics between groups
- Assess benefit of clinical pharmacist involvement and success of clinic protocols

Limitations

- Small study population limits analysis of rare safety outcomes
- Post-injection hypocalcemia difficult to capture
- No pharmacist at MFM from August 2018 to February 2019

Conclusions

- The pharmacist-implemented protocol at MFM significantly improved the frequency of calcium monitoring before denosumab administration
- This difference was not shown in secondary safety outcomes
- Pharmacists can have a significant impact on the appropriate monitoring of denosumab

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