

Some Bone Density Treatments Linked to Increased Likelihood of Heart Attack and Atrial Fibrillation

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Key Findings:

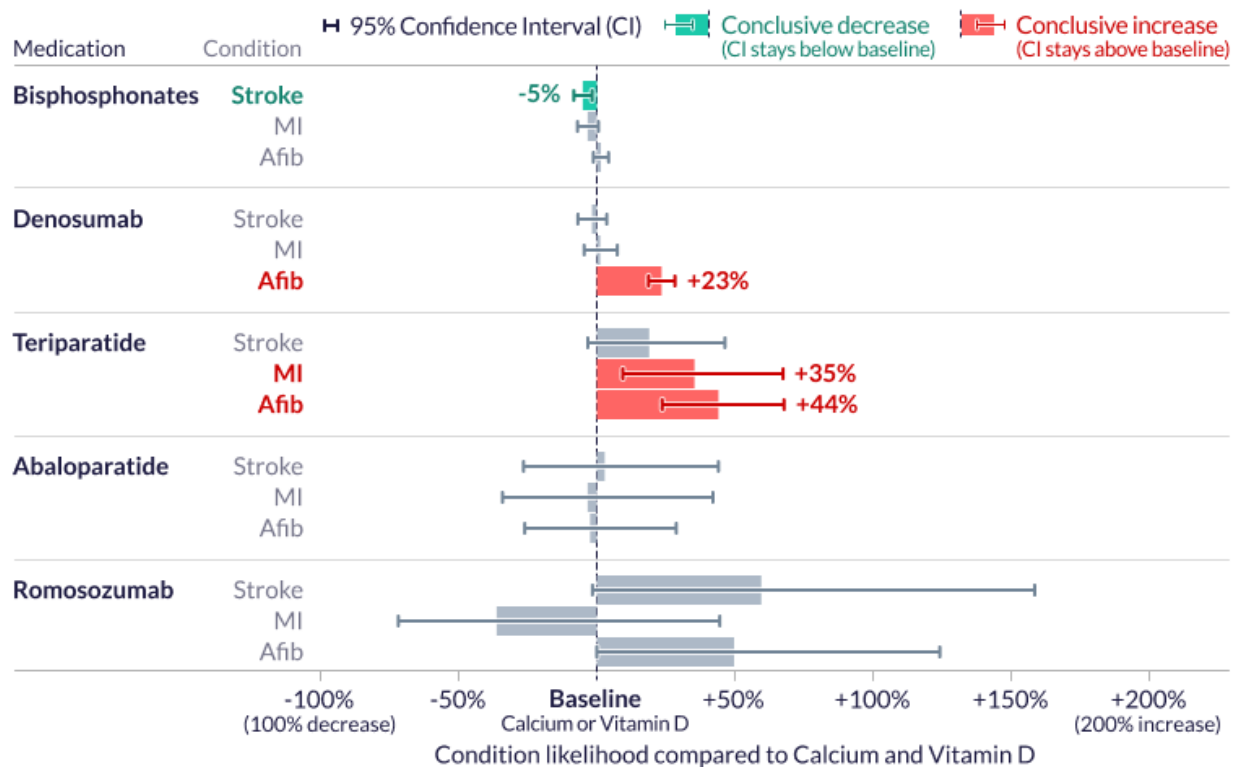
- Patients with bone density disorders prescribed bisphosphonates are 5% less likely to experience an ischemic stroke than those prescribed calcium or vitamin D.
- Patients with bone density disorders prescribed teriparatide are 35% more likely to experience a heart attack, also known as myocardial infarction (MI), than those prescribed calcium or vitamin D.
- Patients with bone density disorders prescribed teriparatide or denosumab are 44% and 23% more likely, respectively, to experience atrial fibrillation (AFib) than those prescribed calcium or vitamin D.

Osteoporosis medications are used to treat loss of bone density and prevent fractures. Despite their benefits, some studies have raised potential concerns about the use of these treatments increasing the risk of cardiovascular conditions.^{1,2} Standard first-line therapies for bone density disorders include denosumab and bisphosphonates. In severe cases, or if initial treatment is unsuccessful, doctors may prescribe alternative therapies such as romosozumab, teriparatide, or abaloparatide.³

To explore the relationship between osteoporosis medications and cardiovascular events, we studied 447,208 patients with osteoporosis or osteopenia. We factored in patient age, sex, BMI, smoking status, and histories of hyperlipidemia, diabetes, chronic kidney disease, and cardiovascular disease. Patients prescribed more than one of the studied medications within the follow-up period were excluded.

We found that patients prescribed bisphosphonates were slightly less likely to experience an ischemic stroke compared to patients prescribed calcium or vitamin D. Patients prescribed denosumab were 23% more likely to be diagnosed with AFib, while patients prescribed teriparatide were 44% more likely to be diagnosed with AFib and 35% more likely to experience an MI than patients prescribed calcium or vitamin D. Patients prescribed romosozumab or abaloparatide were not conclusively more or less likely to experience the conditions studied compared to those prescribed calcium or vitamin D.

Likelihood of Cardiovascular Condition Within Three Years by Osteoporosis Medication



N=447,208 patients "Likelihood of Cardiovascular Condition Within Three Years by Osteoporosis Medication," 2025. EpicResearch.org

Figure 1. The likelihood of experiencing an ischemic stroke, myocardial infarction, or atrial fibrillation within three years of starting treatment by osteoporosis medication.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 298 million patient records from 1,700 hospitals and more than 39,000 clinics from all 50 states, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Azeez TA. Osteoporosis and cardiovascular disease: a review. Mol Biol Rep. 2023;50(2):1753-1763. doi:10.1007/s11033-022-08088-4
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3. Osteoporosis treatment: Medications can help. Mayo Clinic. Published August 28, 2024. <https://www.mayoclinic.org/diseases-conditions/osteoporosis/in-depth/osteoporosis-treatment/art-20046869>. Accessed September 13, 2024.

Data Definitions

Term	Definition
Study period	1/1/2017 to 7/15/2024

Study population	<p>Patients diagnosed with osteoporosis or osteopenia who were prescribed an osteoporosis medication in the study period.</p> <p>Excluding patients:</p> <ul style="list-style-type: none"> • With a diagnosis of a cardiovascular event before their osteo diagnosis • With a diagnosis of a cardiovascular event between their osteo diagnosis date and the start of the osteoporosis medication • With more than one category of cardiovascular event • With a family history of cardiovascular events • With multiple osteoporosis medication types within the first three years of their medication start date • Without a visit in each of the three calendar years following their osteoporosis medication start
Osteoporosis	A diagnosis with ICD-10-CM code M80* & M81*
Osteopenia	A diagnosis with ICD-10-CM code M85.8
Osteoporosis medications	<p>Prescription with a simple generic name of:</p> <ul style="list-style-type: none"> • Bisphosphonates <ul style="list-style-type: none"> ○ Alendronate ○ Risedronate ○ Ibandronate ○ Zoledronic acid • Denosumab • Romosozumab • Teriparatide • Abaloparatide <p>Control patients were prescribed calcium or vitamin D without any of the above medications. We selected patients with a calcium or vitamin D prescription to increase the certainty around the potential for use of over-the-counter medications.</p>
Cardiovascular event	<p>A diagnosis within three years of starting an osteoporosis medication of:</p> <ul style="list-style-type: none"> • MI: ICD-10-CM code I21*, I22*, or I23* • Ischemic stroke: ICD-10-CM code I63* • AFib: ICD-10-CM code I48.0*, I48.1*, I48.2*, or I48.91, ICD-9-CM code 427.31, or SNOMED CT code 49436004
Family history of cardiovascular events	A diagnosis with ICD-10-CM code Z82.49*
Confounders	<p>BMI classification:</p> <ul style="list-style-type: none"> • Underweight: <18.5 • Normal: 18.5 to <25 • Overweight: 25 to <30 • Class 1 obesity: 30 to <35 • Class 2 obesity: 35 to <40 • Class 3 obesity: 40+ <p>Family history of cardiovascular events</p> <p>Age:</p> <ul style="list-style-type: none"> • <50 • 50-59 • 60-64 • 65-69

	<ul style="list-style-type: none"> • 70-74 • 75+ <p>Smoking status</p> <ul style="list-style-type: none"> • Anywhere the patient indicated current or former smoking status prior to the cardiovascular event or three years from their first osteoporosis medication <p>Legal sex</p> <p>Diabetes: ICD-10-CM code E11*</p> <p>Hyperlipidemia: ICD-10-CM code E78.2*-E78.5*</p> <p>Essential hypertension: ICD-10-CM code I10</p> <p>CKD: ICD-10-CM code N18*</p> <p>CVD: ICD-10-CM code I24*-I26*, I30*-I49*, I51*, or I70*-I79*</p> <ul style="list-style-type: none"> • I48* is conditionally excluded when AFib was the outcome
Model specifications	Logistic Regression for outcome within three years of presence of osteoporosis medication

Table 1: Likelihood of Cardiovascular Condition Within Three Years by Osteoporosis Medication

Med	Condition	Odds Ratio	Lower CI	Upper CI
Bisphosphonates	Stroke	0.95	0.92	0.98
	MI	0.97	0.93	1.01
	Afib	1.01	0.99	1.04
Denosumab	Stroke	0.98	0.93	1.04
	MI	1.01	0.95	1.07
	Afib	1.23	1.19	1.28
Teriparatide	Stroke	1.19	0.97	1.46
	MI	1.35	1.09	1.67
	Afib	1.44	1.24	1.68
Abaloparatide	Stroke	1.03	0.73	1.44
	MI	0.97	0.66	1.42
	Afib	0.98	0.74	1.29
Romosozumab	Stroke	1.60	0.98	2.59
	MI	0.64	0.28	1.45
	Afib	1.50	1.00	2.24