

# GLP-1 Therapy Associated with Lower Fracture Risk in Patients with Bone Density Disorders

Team A: Kersten Bartelt, RN; Nicholas Volker

Team B: Tony Dunnigan, MD; Eric Barkley

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## Key Findings

- Among patients with type 2 diabetes, GLP-1 use was associated with a 32% lower fracture risk for those with either osteopenia or osteoporosis.
- Among patients without type 2 diabetes, GLP-1 use was associated with a 34% lower fracture risk for those with osteopenia and 38% lower risk for those with osteoporosis.

Glucagon-like peptide-1 receptor agonists (GLP-1s) are commonly prescribed to manage type 2 diabetes and obesity. Prior research has shown that weight loss can affect bone density,<sup>1</sup> so the potential effect of GLP-1s is of growing clinical interest. Early research results on bone health and the use of GLP-1s are mixed, with some randomized trials and meta-analyses suggesting neutral or modestly protective effects on bone density and fracture risk.<sup>2,3</sup> Understanding the real-world relationship between GLP-1 exposure, weight change, and fracture risk can provide additional insight for patients with existing bone density disorders.

We studied adult patients first diagnosed with osteopenia or osteoporosis between 2017 and 2024. Patients were grouped into nondiabetic or type 2 diabetic cohorts, then each patient on a GLP-1 was matched to four patients who were not prescribed a GLP-1 based on age at bone density disorder diagnosis, total observed time with the condition, and number of prior fractures. Patients were excluded if they had GLP-1 exposure of less than six months. We additionally accounted for sex, race, ethnicity, BMI prior to starting the GLP-1, change in BMI upon starting the GLP-1 as well as throughout their usage, use of osteoporosis medications, steroid use, smoking history, and comorbidities including hyperparathyroidism, chronic falls, cancer, CKD, malabsorption, IBD, and eating disorders in our analysis.

Across both diabetic and nondiabetic cohorts, GLP-1s were associated with a meaningfully lower fracture risk. Among patients with type 2 diabetes, GLP-1 use was associated with a 32% lower risk of fracture for those with osteopenia and for those with osteoporosis, as seen in Figure 1. Among patients without diabetes, GLP-1 use was associated with a 34% lower risk of fracture for those with osteopenia and a 38% lower risk for those with osteoporosis.

## Fracture Risk by GLP-1 Usage

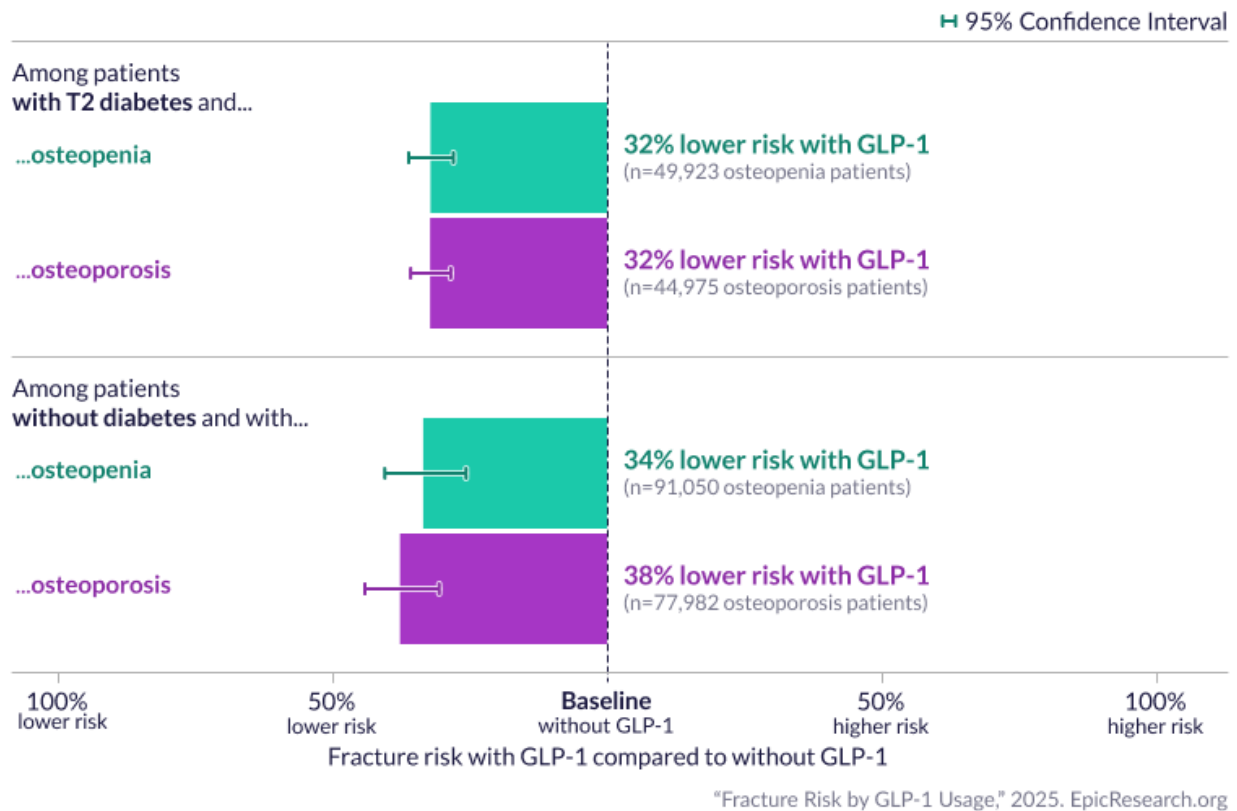


Figure 1. The risk of a patient with a pre-existing bone density disorder experiencing a fracture by whether they were prescribed a GLP-1.

The magnitude of risk reduction was slightly greater among non-diabetic patients, suggesting that the difference in fracture risk might be independent of glycemic control. However, this study did not assess bone mineral density (DEXA) results or lifestyle factors such as physical activity and nutrition, which might moderate fracture risk.

*These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,800 hospitals and more than 41,000 clinics from all 50 U.S. states, Canada, 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. Paccou J, Compston JE. Bone health in adults with obesity before and after interventions to promote weight loss. *Lancet Diabetes Endocrinol.* 2024;12(10):748-760. doi:10.1016/S2213-8587(24)00163-3
2. Tan Y, Liu S, Tang Q. Effect of GLP-1 receptor agonists on bone mineral density, bone metabolism markers, and fracture risk in type 2 diabetes: a systematic review and meta-analysis. *Acta Diabetol.* 2025;62(5):589-606. doi:10.1007/s00592-025-02468-5
3. Su B, Sheng H, Zhang M, et al. Risk of bone fractures associated with glucagon-like peptide-1 receptor agonists' treatment: a meta-analysis of randomized controlled trials. *Endocrine.* 2015;48(1):107-115. doi:10.1007/s12020-014-0361-4

## Data Definitions

Term	Definition
Study period	2017 to 2024
Study population: inclusion	Adult patients with: <ul style="list-style-type: none"> <li>• A diagnosis of <b>osteopenia</b> or <b>osteoporosis</b></li> <li>• At least two <b>outpatient face to face visits</b> prior to the onset of <b>osteopenia</b> or <b>osteoporosis</b></li> </ul>
Study population: exclusion	Prescription for a <b>GLP-1</b> for less than six months History of <b>GLP-1</b> use before the inclusion diagnosis occurred
Censoring	Date of death Last <b>face-to-face visit</b> Patients at the point of the onset of following conditions: <ul style="list-style-type: none"> <li>• <b>Osteopenia:</b> Censor at <b>fracture, osteoporosis, or other bone conditions</b></li> <li>• <b>Osteoporosis:</b> Censor at <b>fracture or other</b></li> </ul>
Osteopenia	A billing, encounter, or problem list diagnosis with ICD-10-CM M85.8* or SNOMED code 312894000
Osteoporosis	A billing, encounter, or problem list diagnosis with ICD-10-CM M81* or SNOMED code 64859006
Other bone conditions	A diagnosis with any of: <ul style="list-style-type: none"> <li>Osteomalacia: A billing, encounter, or problem list diagnosis with ICD-10-CM M83*, SNOMED CT 4598005</li> <li>Paget's: A billing, encounter, or problem list diagnosis with ICD-10-CM M88*, SNOMED CT 2089002</li> <li>Osteogenesis Imperfecta: A billing, encounter, or problem list diagnosis with ICD-10-CM Q78.0, SNOMED CT 78314001</li> <li>Osteomyelitis: A billing, encounter, or problem list diagnosis with ICD-10-CM M86*, SNOMED CT 60168000</li> <li>Bone Cancer: A billing, encounter, or problem list diagnosis with ICD-10-CM C41*, V79.5*, SNOMED CT 428281000</li> </ul>
Face-to-face visit	An encounter of type "Office Visit," "Follow-up," "Telemedicine," "Walk-in," "Routine Prenatal," "Postpartum Visit," or "Fetal Care Consult"
Type 2 diabetes	A billing, encounter, or problem list diagnosis with ICD-10-CM code E11*
GLP-1	A medication order with a type of prescription, historical, or administered and a pharmaceutical class of "ANTI-OBESITY GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST," "ANTIHYPERGLYCEMIC – INCRETIN MIMETICS COMBINATION," or containing "GLP-1"
Fracture	A billing, encounter, or problem list diagnosis with ICD-10-CM S[0-9]2* or M80* or SNOMED code 125605004
Confounders	Evaluated sex Age on index date: <50, 50-64, 65-79, 80+ Race: Asian, Black, Hispanic, other, White BMI nearest index date: <18.5, 18.5-25, 25-30, 30-40, 40+ Osteoporosis medication: A medication order that has a type of prescription, historical, or administered in the <b>study period</b> or prior (simple generic name): <ul style="list-style-type: none"> <li>• Bisphosphonates</li> <li>• Alendronate</li> </ul>

	<ul style="list-style-type: none"> <li>• Risedronate</li> <li>• Ibandronate</li> <li>• Zoledronic acid</li> <li>• Denosumab</li> <li>• Romosozumab</li> <li>• Teriparatide</li> <li>• Abaloparatide</li> </ul> <p><b>Steroid</b> use greater than 30 days</p> <p>History of smoking</p> <p>Comorbidities:</p> <ul style="list-style-type: none"> <li>• Hyperparathyroidism and related: A billing, encounter, or problem list diagnosis with ICD-10-CM code E21* or SNOMED code 66999008</li> <li>• Chronic falls: A billing, encounter, or problem list diagnosis with ICD-10-CM code R29.6 or SNOMED code 279992002</li> <li>• Cancer: A billing, encounter, or problem list diagnosis with ICD-10-CM code C* (excluding C41* and C79.5*) or SNOMED code 363346000 (excluding 428281000)</li> <li>• CKD: A billing, encounter, or problem list diagnosis with ICD-10-CM code N18* or SNOMED code 90708001</li> <li>• Intestinal malabsorption: ICD-10-CM code K90* or SNOMED code 197476001</li> <li>• IBD: A billing, encounter, or problem list diagnosis with ICD-10-CM code K50*-K52* or SNOMED code 24526004</li> <li>• Eating disorder: A billing, encounter, or problem list diagnosis with ICD-10-CM code F50* or SNOMED code 72366004</li> </ul>
<b>Race and ethnicity</b>	Patients were classified into exclusive groups by self-reported race and ethnicity values mapped to standards: Hispanic, single race Asian, single race Black, single race White, or multiracial/another race
<b>Steroid</b>	A medication order that has a type of prescription, historical, or administration and a pharmaceutical class or pharmaceutical subclass of "GLUCOCORTICIDS" and a route of "injection," "intra-articular," "intramuscular," "intravenous," or "oral"
<b>Model specifications</b>	<p>Matching 1:4 on:</p> <ul style="list-style-type: none"> <li>• Duration between condition start and censoring (6-month bands)</li> <li>• Age at condition start (5-year bands)</li> <li>• Number of fractures documented on the patient as of 60 days after the first bone condition diagnosis</li> </ul> <p>Observation period starts 6 months after the start of the <b>GLP-1</b> in the exposure patients, which was the same observation window applied to the matched non-exposure patients.</p> <p>We conducted a negative-control analysis using benzonatate and ibuprofen, medications not expected to influence fracture risk. When we applied the same methods used in the GLP-1 analysis, these drugs showed no difference in fracture risk between the exposure and non-exposed patients. This suggests that the GLP-1 findings are unlikely to be an artifact of the study's design.</p>

**Table 1: GLP Fracture Risk with Osteopenia and Type 2 Diabetes**

Coefficient	Odds Ratio	CI Low	CI High
GLP-1 Exposure	0.68	0.64	0.72
Past Fractures-One	1.83	1.71	1.96
Past Fractures-Multiple	2.81	2.54	3.11
Age Under50	0.93	0.82	1.06
Age 65-79	1.02	0.96	1.09
Age 80+	1.52	1.33	1.75
Race Black	0.69	0.63	0.76
Race Hispanic	0.83	0.75	0.93
Race Other	0.88	0.81	0.96
Female	1.01	0.93	1.08
BMI Underweight	0.93	0.56	1.56
BMI Overweight	1.02	0.92	1.13
BMI Obese	1.08	0.97	1.19
BMI Severely Obese	1.12	0.99	1.25
Early 10+ Gain	1.23	1.05	1.44
Early 2-9 Gain	1.08	1.00	1.17
Early 2-9 Loss	1.01	0.94	1.08
Early 10+ Loss	1.00	0.89	1.12
Secondary 10+ Gain	0.96	0.85	1.08
Secondary 2-9 Gain	0.98	0.90	1.06
Secondary 2-9 Loss	0.88	0.82	0.95
Secondary 10+ Loss	0.67	0.61	0.73
Osteoporosis Med Exposure	1.02	0.92	1.13
Steroid Exposure	1.05	0.99	1.12
Hyperparathyroidism	0.89	0.81	0.98
Chronic Falls	1.57	1.44	1.71
Cancer	1.00	0.94	1.06
CKD	1.08	1.02	1.15
Intestinal Malabsorption	0.84	0.73	0.97
IBD	1.00	0.93	1.07
Eating Disorder	0.99	0.80	1.23
Ever Smoker	1.19	1.12	1.26

**Table 2: GLP Fracture Risk with Osteoporosis and Type 2 Diabetes**

Coefficient	Odds Ratio	CI Low	CI High
GLP-1 Exposure	0.68	0.64	0.71
Past Fractures-One	2.08	1.96	2.20
Past Fractures-Multiple	3.18	2.94	3.44
Age Under50	0.88	0.77	1.01
Age 65-79	1.06	1.00	1.12
Age 80+	1.33	1.18	1.48
Race Black	0.66	0.60	0.72
Race Hispanic	0.91	0.83	1.00
Race Other	0.82	0.76	0.88
Female	1.06	0.98	1.14
BMI Underweight	1.09	0.84	1.40
BMI Overweight	0.98	0.91	1.07
BMI Obese	0.97	0.90	1.05
BMI Severely Obese	0.92	0.84	1.02
Early 10+ Gain	1.25	1.10	1.43
Early 2-9 Gain	1.08	1.01	1.16
Early 2-9 Loss	1.04	0.97	1.10
Early 10+ Loss	1.26	1.14	1.39
Secondary 10+ Gain	0.75	0.67	0.84
Secondary 2-9 Gain	0.93	0.86	1.00
Secondary 2-9 Loss	0.85	0.79	0.91
Secondary 10+ Loss	0.67	0.62	0.73
Osteoporosis Med Exposure	1.10	1.04	1.15
Steroid Exposure	0.98	0.93	1.04
Hyperparathyroidism	0.92	0.85	1.00
Chronic Falls	1.55	1.44	1.66
Cancer	0.97	0.92	1.03
CKD	1.02	0.97	1.08
Intestinal Malabsorption	1.09	0.98	1.21
IBD	1.02	0.96	1.09
Eating Disorder	1.19	0.98	1.44
Ever Smoker	1.10	1.04	1.16

**Table 3: GLP Fracture Risk with Osteopenia**

Coefficient	Odds Ratio	CI Low	CI High
GLP-1 Exposure	0.66	0.59	0.74
Past Fractures-One	1.74	1.65	1.84
Past Fractures-Multiple	2.78	2.56	3.02
Age Under50	0.90	0.83	0.98
Age 65-79	1.07	1.02	1.13
Age 80+	1.91	1.70	2.15
Race Black	0.75	0.67	0.83
Race Hispanic	0.90	0.80	1.01
Race Other	0.86	0.81	0.93
Female	0.91	0.85	0.97
BMI Underweight	1.19	1.00	1.41
BMI Overweight	0.99	0.94	1.05
BMI Obese	1.03	0.98	1.10
BMI Severely Obese	1.09	0.99	1.21
Early 10+ Gain	1.31	1.17	1.48
Early 2-9 Gain	1.09	1.03	1.15
Early 2-9 Loss	1.09	1.03	1.15
Early 10+ Loss	1.23	1.10	1.38
Secondary 10+ Gain	0.72	0.65	0.79
Secondary 2-9 Gain	0.91	0.86	0.96
Secondary 2-9 Loss	0.91	0.86	0.96
Secondary 10+ Loss	0.77	0.71	0.84
Osteoporosis Med Exposure	0.98	0.91	1.06
Steroid Exposure	1.07	1.02	1.12
Hyperparathyroidism	0.85	0.76	0.96
Chronic Falls	1.83	1.66	2.00
Cancer	0.94	0.90	0.99
CKD	0.99	0.95	1.04
Intestinal Malabsorption	1.08	0.96	1.21
IBD	1.09	1.03	1.16
Eating Disorder	1.21	0.99	1.48
Ever Smoker	1.22	1.16	1.27

**Table 4: GLP Fracture Risk with Osteoporosis**

Coefficient	Odds Ratio	CI Low	CI High
GLP-1 Exposure	0.62	0.56	0.69
Past Fractures-One	2.15	2.06	2.25
Past Fractures-Multiple	3.20	3.00	3.40
Age Under50	0.92	0.84	1.01
Age 65-79	1.08	1.04	1.13
Age 80+	1.77	1.62	1.94
Race Black	0.69	0.63	0.76
Race Hispanic	0.77	0.68	0.86
Race Other	0.89	0.84	0.95
Female	0.96	0.90	1.02
BMI Underweight	1.26	1.15	1.39
BMI Overweight	1.01	0.96	1.05
BMI Obese	1.06	1.01	1.12
BMI Severely Obese	1.12	1.01	1.23
Early 10+ Gain	1.31	1.19	1.45
Early 2-9 Gain	1.10	1.05	1.15
Early 2-9 Loss	1.09	1.04	1.14
Early 10+ Loss	1.23	1.11	1.35
Secondary 10+ Gain	0.81	0.74	0.87
Secondary 2-9 Gain	0.90	0.85	0.94
Secondary 2-9 Loss	0.93	0.89	0.98
Secondary 10+ Loss	0.75	0.70	0.81
Osteoporosis Med Exposure	1.01	0.97	1.05
Steroid Exposure	1.08	1.04	1.13
Hyperparathyroidism	0.94	0.87	1.02
Chronic Falls	1.49	1.39	1.61
Cancer	0.95	0.91	0.99
CKD	1.03	0.99	1.07
Intestinal Malabsorption	0.99	0.90	1.08
IBD	1.02	0.97	1.08
Eating Disorder	1.11	0.93	1.31
Ever Smoker	1.25	1.20	1.29