

GLP-1 Use Associated with Lower Osteoporosis Risk in Adults with Type 2 Diabetes but Higher Risk in Adults Without Diabetes

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Key Findings:

- Among adults with type 2 diabetes, osteoporosis risk was lower for patients prescribed a GLP-1 than for patients who were not prescribed a GLP-1, when compared to a baseline of stable-weight patients who were not prescribed a GLP-1.
- Among adults without diabetes, osteoporosis risk was slightly higher for patients prescribed a GLP-1 than for patients prescribed other weight loss medications, compared to a baseline of stable-weight patients who were prescribed weight loss medications other than a GLP-1.

Weight loss can be beneficial for overall health; however, studies have shown weight loss can compromise bone density and bone strength.¹ This concern is especially relevant with the growing use of GLP-1 medications, which are effective for both diabetes glycemic control and obesity management. While prior research has shown GLP-1s influence bone metabolism,^{2,3} the degree to which they alter the osteoporosis risk associated with weight loss remains less clear. We aimed to assess the relationship between GLP-1s and osteoporosis likelihood across different amounts of weight change among patients with and without diabetes.

First, we studied 2 million patients diagnosed with type 2 diabetes who had a healthcare encounter between January 1, 2017, and October 31, 2024. Patients with type 2 diabetes who were prescribed a GLP-1 were compared to those who have never been on a GLP-1 medication. We accounted for age, sex, BMI, smoking history, chronic steroid usage, and weight change over time.

For patients with type 2 diabetes who maintained a stable weight, GLP-1 use was associated with an 8.7% lower osteoporosis risk compared to patients who did not use a GLP-1, as seen in Figure 1. Among groups that lost more weight, osteoporosis risk rose for those with and without GLP-1s, but the increase in risk was consistently smaller among GLP-1 users. Weight gain was associated with increased osteoporosis risk among those not on a GLP-1, while weight gain was not associated with statistically significant change in osteoporosis risk for those on a GLP-1.

Likelihood of Osteoporosis Among Type 2 Diabetics by GLP-1 Usage and Weight Change

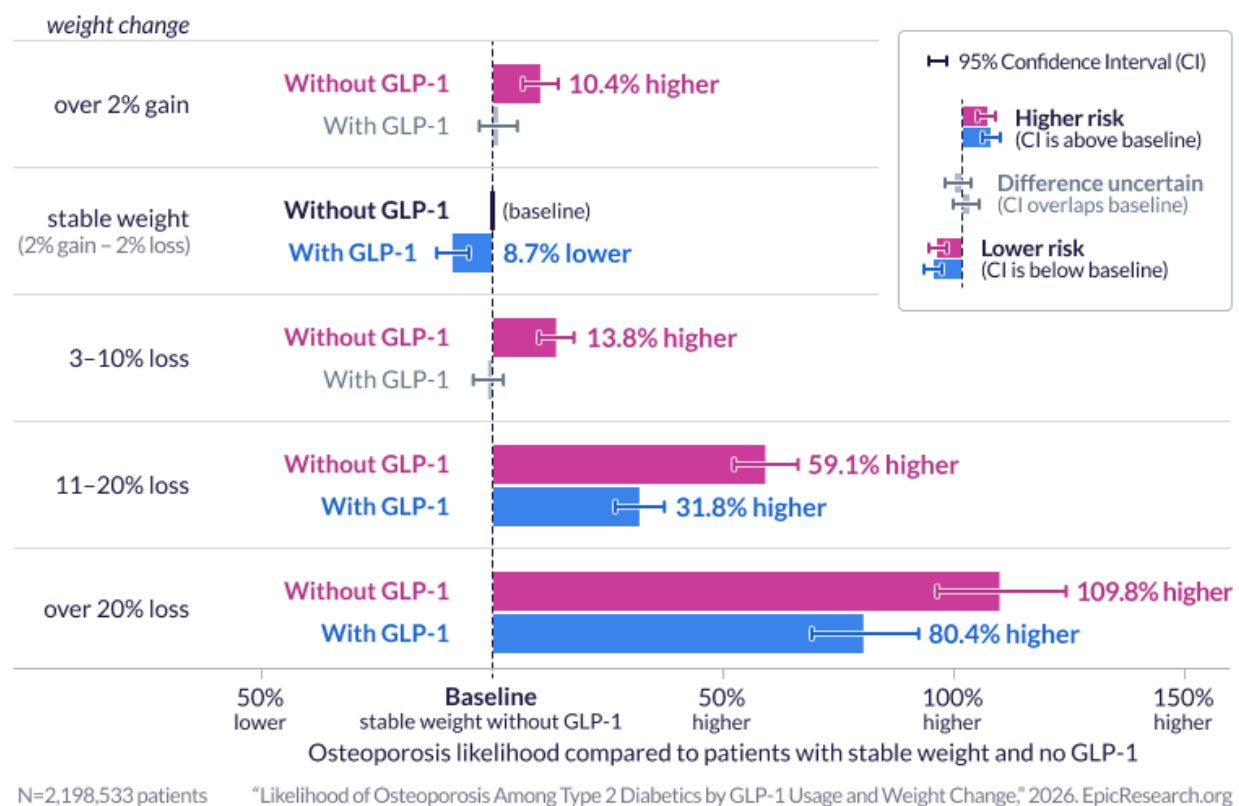


Figure 1. The likelihood of osteoporosis among patients with type 2 diabetes by GLP-1 usage and weight change.

Next, we studied 380,438 patients without diabetes who were prescribed a GLP-1 or other weight loss medication and who had a visit between January 1, 2017, and October 31, 2024. Patients who were prescribed a GLP-1 were compared to those prescribed a different type of weight loss medication. Like the above analysis, we accounted for age, sex, BMI, smoking history, chronic steroid usage, and weight change over time.

Among patients without diabetes, the pattern differed from patients with type 2 diabetes: patients on a GLP-1 who maintained a stable weight had a higher osteoporosis risk relative to those who maintained a stable weight on another weight loss medication (22.0% higher for GLP-1 users). With increasing weight loss, osteoporosis risk increased in both groups, and the GLP-1 risks were generally similar to or higher than the non-GLP-1 weight loss medication risks. Weight gain among patients without diabetes was associated with increased osteoporosis risk in both groups.

Likelihood of Osteoporosis Among Nondiabetics by GLP-1 Usage and Weight Change

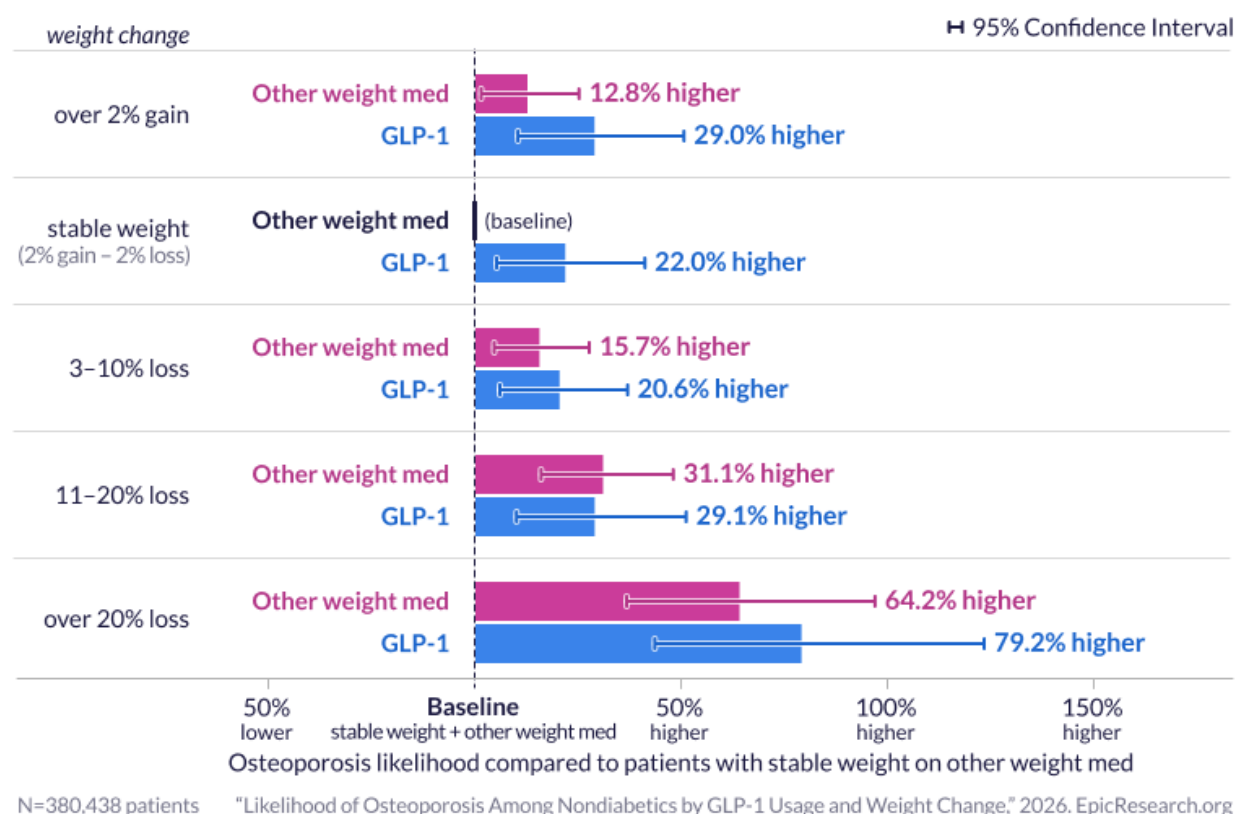


Figure 2. The likelihood of osteoporosis among patients without diabetes by GLP-1 use and weight change.

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 1,900 hospitals and more than 42,000 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, in collaboration with a researcher from Johns Hopkins. 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. Cai TT, Li HQ, Jiang LL, et al. Effects of GLP-1 Receptor Agonists on Bone Mineral Density in Patients with Type 2 Diabetes Mellitus: A 52-Week Clinical Study. *Biomed Res Int*. 2021;2021:3361309. Published 2021 Sep 17. doi:10.1155/2021/3361309
3. 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

Data Definitions

Term	Definition
Study period	Index events from 1/1/2017 to 10/31/2024 Follow up through 4/1/2025
Study population: inclusion	Both populations: - Patients must be 30+ years old as of index event - Patients must have at least one weight reading within one year before their index event and one weight reading between three months and one year after their index event Diabetic population: - Patients must have been diagnosed with type 2 diabetes prior to their index event - Control: At least one HbA1c lab within the study period Nondiabetic population: - Patients must have been prescribed a GLP-1 or a weight loss medication for the first time in an outpatient context within the study period
Study population: exclusion	Both populations: Bariatric surgery ever - Use of GLP-1 medication in addition to other weight loss medications or weight loss population control medications - Use of GLP-1 for the first time outside of the study period - Type 1 diabetes: a billing, encounter, or problem list diagnosis with ICD-10-CM code E08*, E09*, E10*, or E13* or SNOMED code 46635009 anywhere on the patient's chart Pregnancy between 1/1/2016 and 10/31/2025 - Diagnosis of type 2 diabetes after the patient's index event date - Diagnosis of osteoporosis before index date Diabetic population: - Use of a non-GLP-1 weight loss medication ever - Use of GLP-1 for the first time before their diabetes diagnosis Nondiabetic population: - Diagnosis of type 1 or type 2 diabetes ever - Use of a non-GLP-1 weight loss medication at any point for the exposure patients
Index event	Diabetes population - Exposed: First GLP-1 medication order start date - Control: Random HbA1c lab within the study period Nondiabetic population - Exposed: First GLP-1 medication order start date - Control: First medication order start date for a weight loss medication, or bariatric surgery start date
Matching	Age in years Legal sex
Censoring	Left censor: The first weight reading between index date plus three months and index date plus one year Right censor: Outcome date or latest face-to-face encounter

Outcomes	Osteoporosis: A billing or encounter diagnosis with ICD-10-CM code M80* or M81*, SNOMED code 64859006, or an order of an osteoporosis medication
Osteoporosis medication	A medication with an order type of prescription, reported, or administered and a simple generic name of one of the following: • Alendronate • Risedronate • Ibandronate • Zoledronic acid • Denosumab • Romosozumab • Teriparatide • Abaloparatide • Raloxifene
Adjustment factors	Legal sex Weight change at least three months after the index date. (This factor is considered time-varying. Between the index date and the first weight change recorded date, the patient is considered unknown in terms of weight change. At each weight change, maximum one per quarter, until their sensor date, they were considered whichever of the categories best describes their weight change compared to a baseline weight before the index date.) • Gained more than 2% • Stable weight: between -2% and 2% change • Slight loss: Lost >2 to 10% • Moderate loss: Lost >10 to 20% • Substantial loss: Lost >20% Initial BMI category • Underweight: <18.5 • Healthy: 18.5 to <25 • Overweight: 25 to <30 • Obese: 30+ Social Vulnerability Index quintile RUCA Age • 30-44 • 45-54 • 55-64 • 65-74 • 75-84 • 85+ History of smoking History of an outcome condition HRT use before censoring Vitamin D deficiency before censoring: a billing, encounter, or problem list diagnosis with ICD-10-CM code E55* or SNOMED code 34713006 Systemic use of steroids before censoring
Type 2 diabetes	A billing, encounter, or problem list diagnosis with ICD-10-CM code E11* or SNOMED code 44054006

HbA1c	A lab with LOINC code 17856-6, 17855-8, 4548-4, or 4549-2
Pregnancy	Pregnancy episode started during the study period Birth record with a gestational age zero date during the study period A billing, encounter, or problem list diagnosis with ICD-10-CM code O* during the study period
Systemic steroids	More than one order of glucocorticoids: Medication with a pharmaceutical class of "GLUCOCORTICOIDS" or pharmaceutical subclass of "Glucocorticoids" and a route of "injection," "intra-articular," "intramuscular," "intravenous," or "oral"
Bariatric surgery	A procedure with CPT code 43644, 43645, 43659, 43770, 43771, 43772, 43773, 43774, 43775, 43845, 43846, 43847, 43848, 43886, 43887, 43888, 43842, or 43843
HRT	A medication with a simple generic name of "testosterone;" "testosterone cypionate;" "testosterone cypionate, micro;" "testosterone enanthate;" "testosterone micronized;" "testosterone propionate;" or "testosterone undecanoate" A medication with RxNorm code 4083, 261472, 214549, 4099, 4103, 33747, 197679, 197680, or 4124, pharmaceutical class of "ESTROGENIC AGENTS" or "ESTROGEN/ANDROGEN COMBINATIONS," pharmaceutical subclass of "Estrogens" or "Vaginal Estrogens," or simple generic name of "TESTOSTERONE ENAN/ESTRADIOL;" "ESTROGEN,ESTER/ME-TESTOSTERONE;" "ESTRADIOL/NORETHINDRONE ACET;" "ESTRADIOL/LEVONORGESTREL;" "ESTRADIOL/NORGESTIMATE;" "ESTRADIOL CYPIONATE;" "ESTRADIOL VALERATE;" "ESTRADIOL;" "ESTRONE;" "ESTROGENS, CONJUGATED;" "ESTROGENS,ESTERIFIED;" "ETHINYL ESTRADIOL;" "ESTROPIRATE;" "ESTROGENS,CONJ.,SYNTHETIC A;" "ESTRADIOL MICRONIZED;" "ESTRADIOL ACETATE;" "ESTROGENS,CONJ.,SYNTHETIC B;" or "DROSPIRENONE/ESTRADIOL" A medication with RxNorm code 1251327, a pharmaceutical class of "ESTROGEN AND PROGESTIN COMBINATIONS" or "ESTROGEN-PROGESTIN WITH ANTIMINERALCORTICOID COMB," a pharmaceutical subclass of "ESTROGEN-PROGESTIN," or a simple generic name of "ESTROGEN,CON/M-PROGEST ACET"
Other weight loss medications	Orders with one of the following pharmaceutical classes and not associated with any GLP-1 : "ANTI-OBESITY SEROTONIN 2C RECEPTOR AGONISTS;" "ANTI-OBESITY-OPIOID ANTAG-NOREPI,DOPAMINE RU INHIB;" "ANTI-OBESITY - ANOREXIC AGENTS;" or "ANTI-OBESITY - MELANOCORTIN 4 RECEPTOR AGONISTS"
GLP-1	Medication order with a pharmaceutical class or subclass like "GLP-1," or a pharmaceutical class exactly matching "ANTI-OBESITY GLUCAGON-LIKE PEPTIDE-1 RECEPT AGONIST;" "ANTIHYPERGLYCEMIC - INCRETIN MIMETICS COMBINATION;" "ANTIHYPERGLY,INCRETIN MIMETIC(GLP-1 RECEPT.AGONIST);" or "ANTIHYPERGLY,INSULIN,LONG ACT-GLP-1 RECEPT.AGONIST"
Methodology	Cox PH survival analysis with a time-varying factor for weight change after at least three months

Table 1. Likelihood of Osteoporosis Among Type 2 Diabetics by GLP-1 Usage and Weight Change

Factor	Hazard Ratio	95% CI Low	95% CI High
No GLP: >2% gain	1.10	1.07	1.14
On GLP: >2% gain	1.01	0.97	1.05
No GLP: stable (baseline)	-	-	-
On GLP: stable	0.91	0.88	0.95
No GLP: 3-10% loss	1.14	1.10	1.18
On GLP: 3-10% loss	0.99	0.96	1.02
No GLP: 11-20% loss	1.59	1.52	1.66
On GLP: 11-20% loss	1.32	1.27	1.37
No GLP: >20% loss	2.10	1.96	2.24
On GLP: >20% loss	1.80	1.69	1.92

Table 2. Likelihood of Osteoporosis Among Nondiabetics by GLP-1 Usage and Weight Change

Factor	Hazard Ratio	95% CI Low	95% CI High
No GLP: >2% gain	1.13	1.02	1.25
On GLP: >2% gain	1.29	1.10	1.51
No GLP: stable (baseline)	-	-	-
On GLP: stable	1.22	1.05	1.41
No GLP: 3-10% loss	1.16	1.05	1.28
On GLP: 3-10% loss	1.21	1.06	1.37
No GLP: 11-20% loss	1.31	1.16	1.48
On GLP: 11-20% loss	1.29	1.10	1.51
No GLP: >20% loss	1.64	1.37	1.97
On GLP: >20% loss	1.79	1.44	2.23