Bone Health in Diabetes: An Underrecognized Comorbidity

Screening, Pathophysiology, Drug Selection, & Fracture Prevention

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Learning Objectives

- Explain the "diabetic bone paradox"
- Distinguish skeletal phenotypes of type 1 vs. type 2 diabetes
- Apply diabetes-specific adjustments to fracture risk screening
- Select glucose-lowering agents with bone health in mind
- Implement fall-prevention & lifestyle strategies

Why does bone health belong at a diabetes symposium?

- Fracture is a common but underrecognized diabetes complication
- Increased lifetime fracture risk
  - Increased hip fracture risk
- Morbidity, mortality, & loss of independence

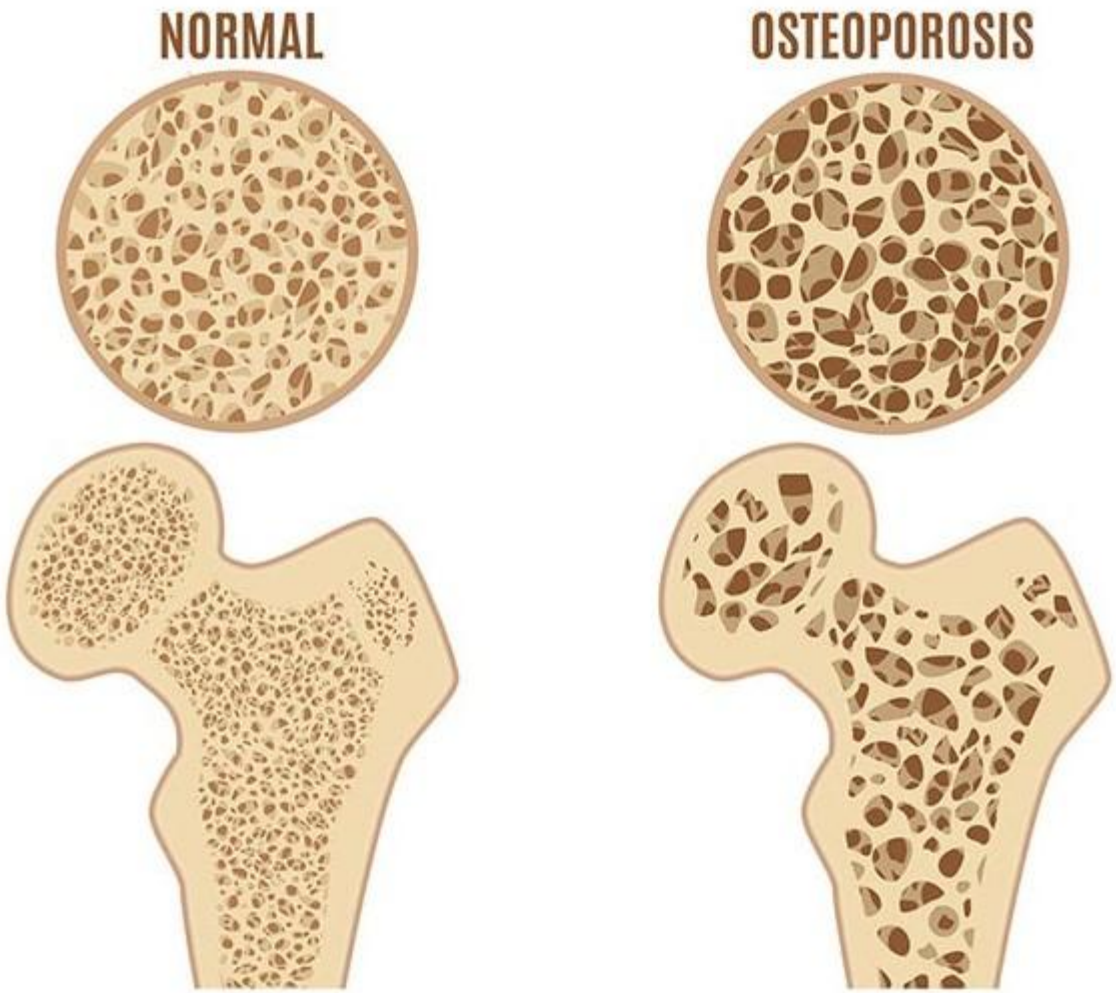
(American Diabetes Association Professional Practice Committee for Diabetes, 2026)

The Diabetic Bone Paradox

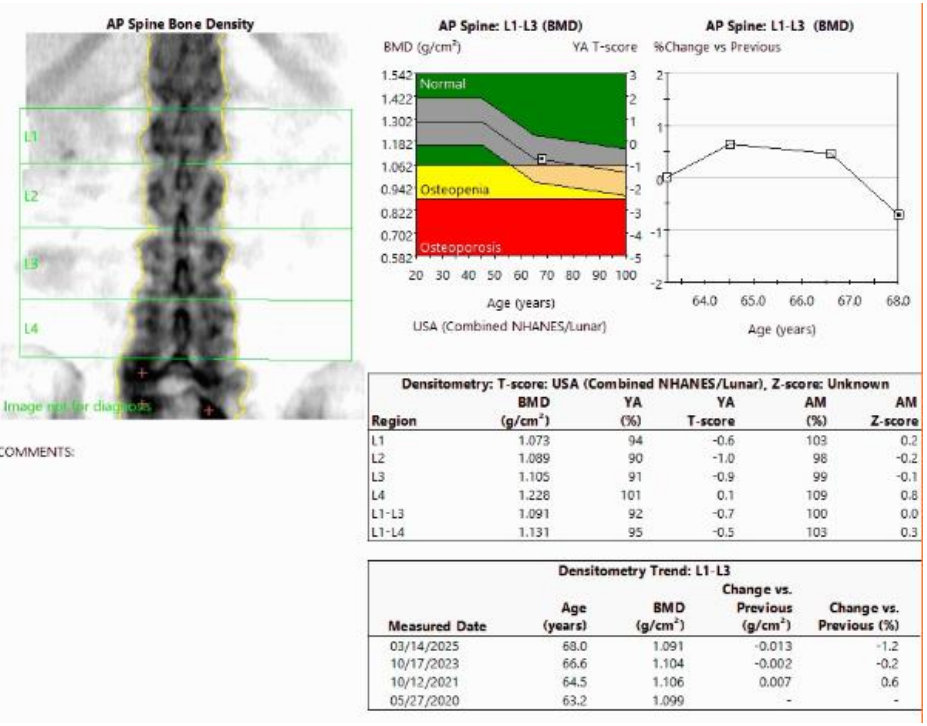
- Type 2 DM patients have 5-10% higher bone mineral density (BMD) yet fracture more often

- Impaired bone quality *not* quantity

(American Diabetes Association Professional Practice Committee for Diabetes, 2026)



(National Institute on Aging, 2022)



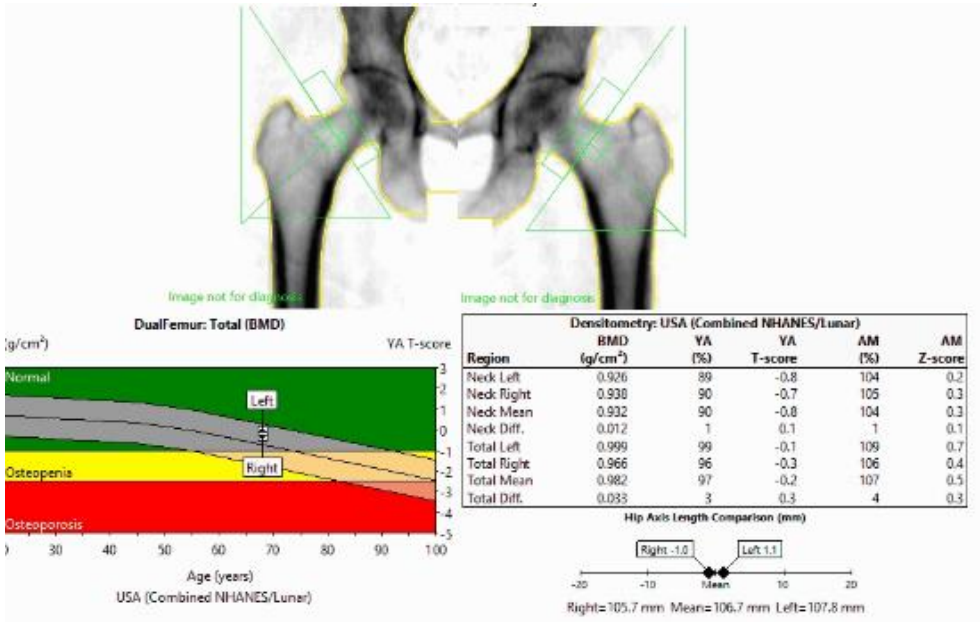
COMMENTS:

Densitometry: T-score: USA (Combined NHANES/Lunar), Z-score: Unknown

Region	BMD (g/cm²)	YA (%)	YA T-score	AM (%)	AM Z-score
L1	1.073	94	-0.6	103	0.2
L2	1.089	90	-1.0	98	-0.2
L3	1.105	91	-0.9	99	-0.1
L4	1.228	101	0.1	109	0.8
L1-L3	1.091	92	-0.7	100	0.0
L1-L4	1.131	95	-0.5	103	0.3

Densitometry Trend: L1-L3

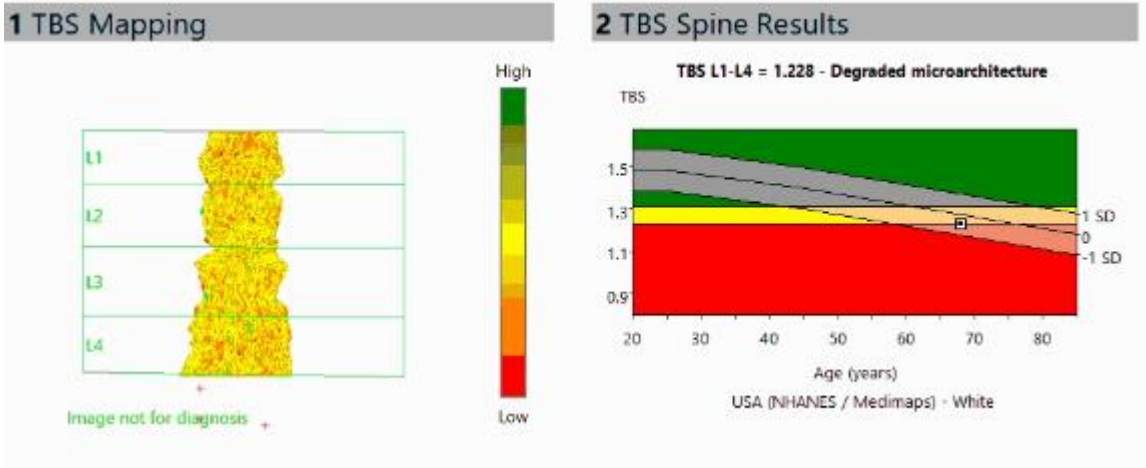
Measured Date	Age (years)	BMD (g/cm²)	Change vs. Previous (g/cm²)	Change vs. Previous (%)
03/14/2025	68.0	1.091	-0.013	-1.2
10/17/2023	66.6	1.104	-0.002	-0.2
10/12/2021	64.5	1.106	0.007	0.6
05/27/2020	63.2	1.099	-	-



Densitometry: USA (Combined NHANES/Lunar)

Region	BMD (g/cm²)	YA (%)	YA T-score	AM (%)	AM Z-score
Neck Left	0.926	89	-0.8	104	0.2
Neck Right	0.938	90	-0.7	105	0.3
Neck Mean	0.932	90	-0.8	104	0.3
Neck Diff.	0.012	1	0.1	1	0.1
Total Left	0.999	99	-0.1	109	0.7
Total Right	0.966	96	-0.3	106	0.4
Total Mean	0.982	97	-0.2	107	0.5
Total Diff.	0.033	3	0.3	4	0.3

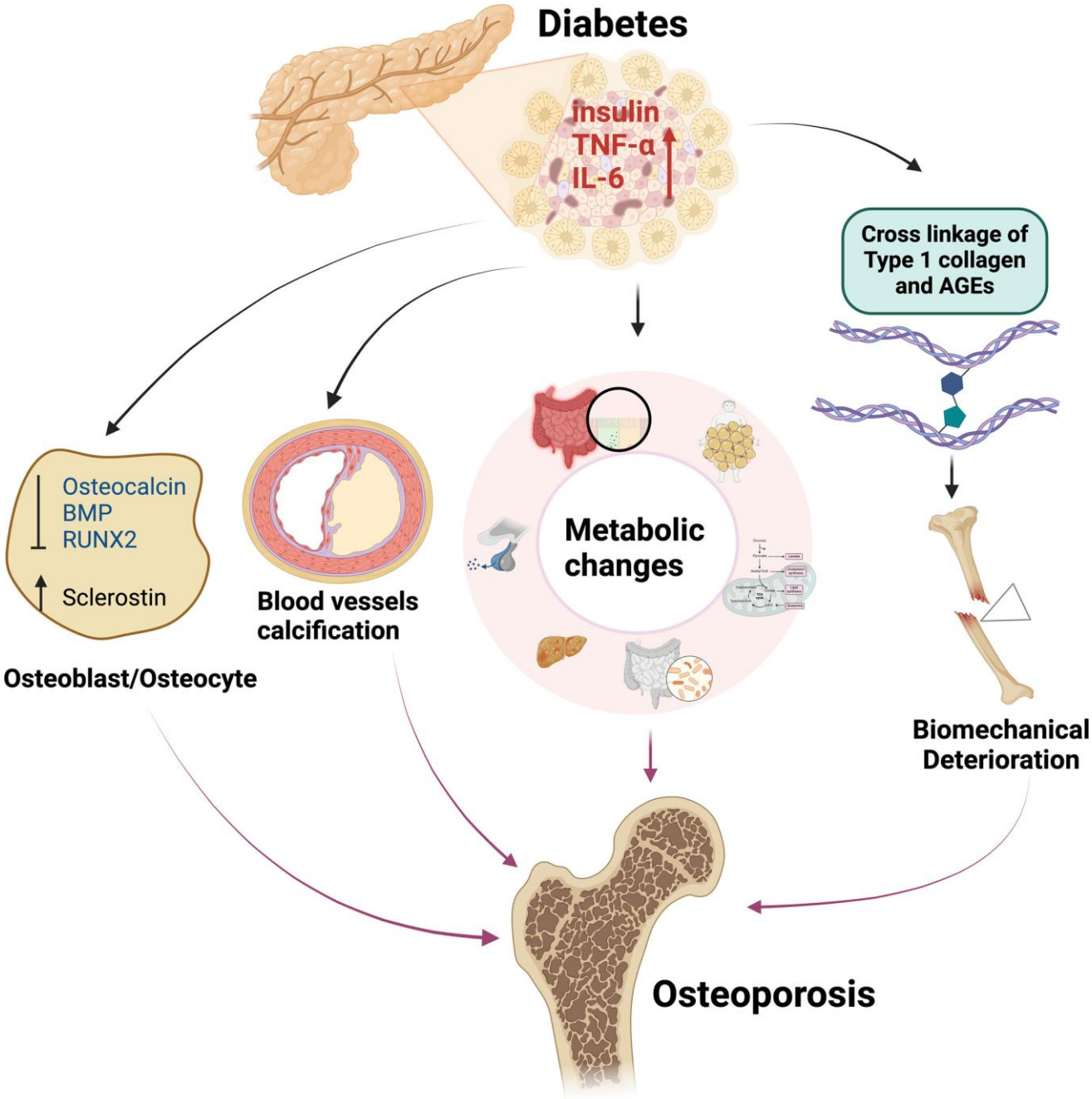
Lowest T-score –0.8 in the left femoral neck but TBS degraded at 1.228 in pt with T2DM & history of 2 fragility fractures



Mechanisms of Skeletal Fragility

- Advanced glycation end products (AGEs) accumulation disrupts collagen
- Increased cortical porosity
- Impaired microarchitecture
- Upregulated sclerostin → inhibits formation, promotes resorption
- Downregulated RUNX2 → impaired bone formation, adipogenesis

(Piccoli et al., 2020; Khosla et al., 2021; Upadhyay & Kumar, 2025)



(Upadhyay & Kumar, 2025)

Type 1 vs. Type 2: Two Distinct Phenotypes

- **Type 1 DM**
  - Truly low BMD
  - High hip fracture risk
  - Insulin/IGF-1 deficiency
  - Low peak bone mass
  - Marrow adiposity
- **Type 2 DM**
  - Normal/high BMD
  - Poor bone quality
  - Neuropathy
  - Microvascular disease
  - Sarcopenia

(Cortet et al., 2019)

Glycemic Control as a Fracture Risk Modifier

- Each 1% rise in HbA1c → 8% higher fracture risk
- Poor control (HbA1c >9%) over 2 years → 29% higher risk
- Hypoglycemia increases fracture risk → falls
- Diabetes duration >10 years

(American Diabetes Association Professional Practice Committee for Diabetes, 2026)

FRAX Underestimates Risk

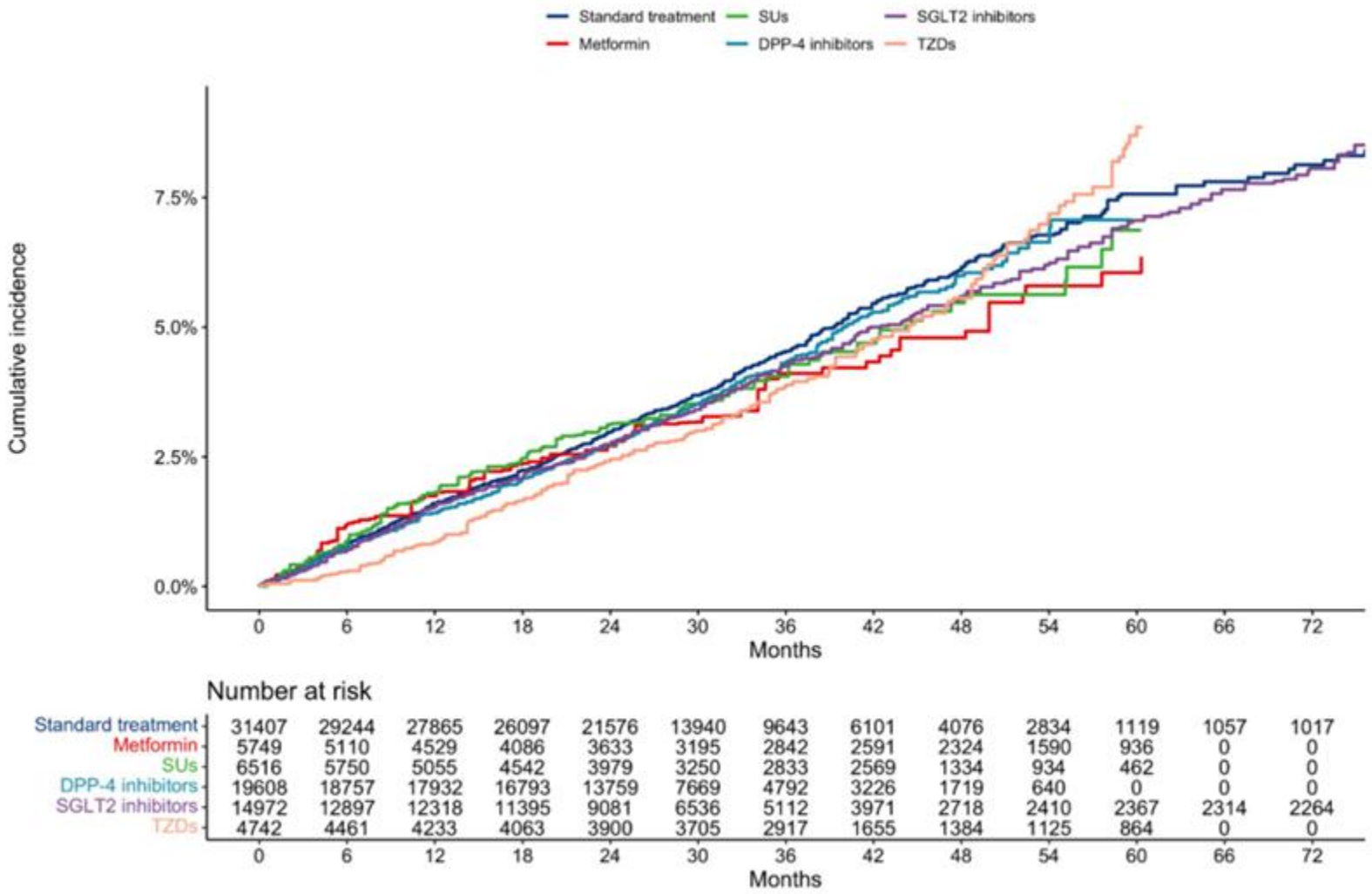
- FRAX does not include T2DM & underestimates hip fracture risk
- ADA 2026 workarounds
  - T-score adjustment –0.5
  - Use rheumatoid arthritis input
  - Add 10 years to age
  - Apply TBS adjustment
- DXA screening
  - ≥65 years
  - >50 years with risk factors
  - Every 2-3 years

(American Diabetes Association Professional Practice Committee for Diabetes, 2026)

Glucose Lowering Drugs & Bone

- TZDs "-glitazones" increase fracture risk
  - Risk doubles after 1-2 years of use
  - Decreases after discontinuation
- Sulfonylureas accelerate bone loss & increase fall risk due to hypoglycemia
- Insulin associated with doubling of hip fracture risk
- SGLT2 inhibitors, DPP-4 inhibitors, metformin neutral

(American Diabetes Association Professional Practice Committee for Diabetes, 2026; Hofbauer et al., 2022; Shen et al.; 2024)



(Shen et al., 2024)

Glucose Lowering Drugs & Bone, cont.

- **GLP1s**
  - Neutral to beneficial at low/standard doses
  - Data lacking for higher doses
  - Substantial weight loss may accelerate bone turnover and reduce BMD
  - Semaglutide associated with lower fracture risk in obesity and T2DM
  - Importance of pairing weight loss with resistance exercise to preserve lean muscle mass

(Al Refai et al., 2025; American Diabetes Association Professional Practice Committee for Diabetes, 2026; Anastasilakis et al., 2025; Huang et al., 2026; Hofbauer et al., 2022; Karam et al., 2025; Shen et al.; 2024)

Treatment

- Strongly consider treatment at T-score −2.0 to −2.5 due to underestimated risk
- No specific trials for use of osteoporosis drugs in diabetes
- First line antiresorptives
- Anabolic therapy for high-risk patients
- T2DM low turnover, poor bone quality state
  - Observational data, post-hoc analysis, & pilot studies indicate abaloparatide/teriparatide improve BMD & TBS
  - Romosozumab appealing given high sclerostin but caution regarding CV risk
- Denosumab modestly improves BMD

(American Diabetes Association Professional Practice Committee for Diabetes, 2026; Hofbauer et al., 2022; Shen et al.; 2024)

Further Considerations

- Denosumab
  - Rebound vertebral fractures if dose is missed
  - Hypocalcemia risk in advanced CKD (eGFR <30)
- Bisphosphonates showed similar gains & safety in diabetic patients
  - Select when adherence is a concern
- **ALWAYS** follow anabolic therapy with antiresorptive to preserve gains
- Refer to Monument Health Osteoporosis & Fracture Prevention Clinic

(American Diabetes Association Professional Practice Committee for Diabetes, 2026; Hofbauer et al., 2022)

Fall Prevention & Lifestyle

- Falls amplified by neuropathy, retinopathy, hypoglycemia, sarcopenia
- Individualize glucose targets to minimize hypoglycemia
- Exercise: weight bearing, resistance, balance training
- Calcium 1000-1200 mg daily
- Vitamin D goal ≥30 ng/mL
- Adequate protein
- Smoking cessation

(American Diabetes Association Professional Practice Committee for Diabetes, 2026; Hofbauer et al., 2022; Shen et al.; 2024)

Key Takeaways

- Despite preserved BMD, bone fragility is a diabetes complication
- Adjust screening tools
- Standard FRAX misleads
- Choose glucose-lowering therapy with skeletal impact in mind
- Optimize diabetes control
- Prevent falls
- Treat proactively

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Questions?

Thank you!