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OBESITY-ASSOCIATED BONE METABOLIC DYSFUNCTION IN POSTMENOPAUSAL WOMEN: A SYSTEMATIC EVIDENCE REVIEW OF ADIPOKINE SIGNALING, INFLAMMATORY MECHANISMS, AND SKELETAL OUTCOMES (2020–2026)

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ABSTRACT

Background: Obesity is common after menopause, yet its relationship with skeletal health is complex. Greater body mass may increase areal bone mineral density (BMD), while visceral adiposity, inflammation, altered adipokine signaling, and loss of muscle function may adversely affect bone quality and fracture risk.

Objective: To summarize evidence published from 2020 to 2026 on the associations between obesity, adipose-tissue signaling, bone metabolism, bone microarchitecture, and fracture outcomes in postmenopausal women.

Methods: A focused evidence search was undertaken for studies and reviews addressing postmenopausal women, obesity or adiposity, bone health, bone turnover, trabecular bone score (TBS), and fractures. Relevant observational studies, cohort studies, meta-analyses, and mechanistic reviews were narratively synthesized. This document is a PRISMA-informed evidence-review draft; it does not claim completion of a fully reproducible multi-database systematic search, duplicate removal, dual independent screening, or formal risk-of-bias assessment.

Results: Evidence indicates that the relationship between obesity and skeletal outcomes is site- and phenotype-dependent. A meta-analysis of eight cohorts including 671,532 postmenopausal women reported an increased overall fracture risk (RR 1.18, 95% CI 1.09–1.28), with different associations across fracture sites. Studies also associate visceral adiposity with less favorable bone turnover markers and lower TBS. In women with morbid obesity, BMD alone may not fully reflect impaired bone microarchitecture. Sarcopenic obesity appears particularly relevant to falls and fragility fractures.

Conclusion: Obesity should not be considered uniformly protective against postmenopausal osteoporosis. Assessment of central adiposity, muscle status, bone quality, and fracture history may complement BMD. Prospective studies with standardized adiposity and skeletal measures are needed.

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Keywords: postmenopause; obesity; visceral adipose tissue; bone mineral density; trabecular bone score; adipokines; inflammation; fracture; sarcopenic obesity.

1. INTRODUCTION

Postmenopausal bone loss is driven in part by estrogen deficiency, which shifts bone remodeling toward resorption and increases susceptibility to osteoporosis and fragility fractures. Obesity has traditionally been viewed as mechanically protective because greater body mass can increase skeletal loading and areal BMD. However, this simplified view does not account for fat distribution, adipose-tissue endocrine activity, muscle quality, falls, or bone microarchitecture. Adipose tissue is an active endocrine and immune organ. Adipokines and inflammatory mediators may influence osteoblast and osteoclast differentiation, while visceral and bone-marrow adipose depots may have distinct relationships with skeletal metabolism. Consequently, BMI alone may not adequately characterize skeletal risk. The aim of this review is to synthesize recent evidence (2020–2026) on obesity-associated bone metabolic dysfunction in postmenopausal women, emphasizing adiposity distribution, adipokine and inflammatory pathways, BMD, TBS, and fracture outcomes.

2. MATERIALS AND METHODS

This manuscript was prepared as a structured evidence review informed by the PRISMA 2020 framework. The PRISMA 2020 statement provides a 27-item reporting checklist and flow-diagram guidance. The present draft is transparent about the limits of the search work completed and should not be represented as a completed PRISMA systematic review until the full protocol and screening process have been performed. Population: postmenopausal women, or older-adult populations where findings on sarcopenic obesity were relevant but not exclusive to postmenopausal women. Exposure: obesity, visceral adiposity, body composition, sarcopenic obesity, or adipose-tissue signaling. Outcomes: BMD, TBS, bone turnover markers, osteoporosis, falls, and fractures. Eligible evidence included observational studies, cohort studies, meta-analyses, and relevant mechanistic or clinical reviews published in 2020–2026. A focused search of indexed biomedical literature and bibliographic sources was used to identify relevant publications. The evidence was summarized narratively because populations, adiposity definitions, skeletal outcomes, and study designs were heterogeneous. No new pooled effect estimate was calculated. Before submission as a formal systematic review, the authors should document the exact databases searched (e.g., MEDLINE/PubMed, Scopus, Web of Science, and Cochrane Library), complete search strings, search dates, deduplication, independent screening, exclusion reasons, and risk-of-bias methods. This review uses previously published studies and does not report new human-participant recruitment or identifiable patient data. Institutional ethics approval is therefore not applicable to this evidence synthesis.

3. RESULTS

A meta-analysis of eight cohort studies involving 671,532 postmenopausal women and 40,172 fractures reported a higher overall fracture risk among women with obesity (RR 1.18, 95% CI 1.09–1.28). Associations differed by fracture site: vertebral fracture risk was

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increased (RR 1.154, 95% CI 1.020–1.305), whereas pelvic fracture risk was lower (RR 0.575, 95% CI 0.470–0.702); hip and humerus outcomes did not show statistically significant differences in that analysis. Considerable heterogeneity was reported for the overall estimate. In a cross-sectional study of 76 obese postmenopausal women, visceral adipose tissue was an independent negative determinant of CTX-1 and osteocalcin. The study also reported associations between visceral fat and BMD after adjustment for BMI, supporting the concept that fat distribution may provide information beyond total body mass. A clinical study comparing 250 postmenopausal women across non-obese, obese, and morbidly obese groups reported lower femoral-neck BMD and lower TBS in the morbid-obesity group than in the obese comparison group. These findings illustrate why BMD should not be interpreted as a complete measure of bone strength in people with severe obesity. In a cross-sectional study of 1,007 postmenopausal women, possible sarcopenic obesity was associated with lower odds of densitometric osteoporosis but higher odds of fragility fracture (OR 2.29, 95% CI 1.31–4.00) and lower TBS. A broader systematic review in older adults also found increased fall risk in sarcopenic obesity compared with controls. These observations suggest that muscle function and fall propensity may modify fracture risk independently of BMD. A population-based cohort of women aged 66 years followed for approximately 7.7 years found that the association between body composition and fracture varied according to baseline BMD. In women with osteoporosis, severe obesity was associated with higher vertebral fracture risk (adjusted HR 3.45, 95% CI 2.99–3.97), demonstrating that high BMI does not guarantee protection in women with compromised bone. A 2025 study of 118 postmenopausal women found an inverse association between visceral adipose tissue mass and TBS in a multivariable model. A 2026 systematic review and meta-analysis of GLP-1 receptor agonists across broad populations found no clear adjusted effect on BMD or fracture outcomes, while reporting reductions in lean or fat-free mass; these findings are not specific to postmenopausal women and should be interpreted cautiously.

Table 1. Selected quantitative findings from recent evidence

Study	Design / sample	Main finding	Interpretation
Liu et al., 2023	Meta-analysis; 8 cohorts, 671,532 women	Overall fracture RR 1.18 (95% CI 1.09–1.28)	Obesity is not uniformly fracture-protective
Sharma et al., 2020	Cross-sectional; n=76	Visceral fat negatively associated with CTX-1 and osteocalcin	Central adiposity may relate to altered turnover
Jose et al., 2021	Cross-sectional; n=250	Morbid obesity group had lower femoral-neck BMD and TBS than obese group	BMD alone may not capture bone quality
Lin & Teng, 2022	Cross-sectional; n=1,007	Sarcopenic obesity: fragility fracture OR	Muscle phenotype may influence

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		2.29 (1.31–4.00)	fracture risk
Lee et al., 2023	Population cohort; women aged 66	Severe obesity with osteoporosis: vertebral fracture aHR 3.45 (2.99–3.97)	Baseline BMD modifies obesity-fracture association
Chondrogianni et al., 2025	Cross-sectional; n=118	Visceral fat inversely associated with TBS (β=-0.415)	VAT may be relevant to bone microarchitecture

FIGURES

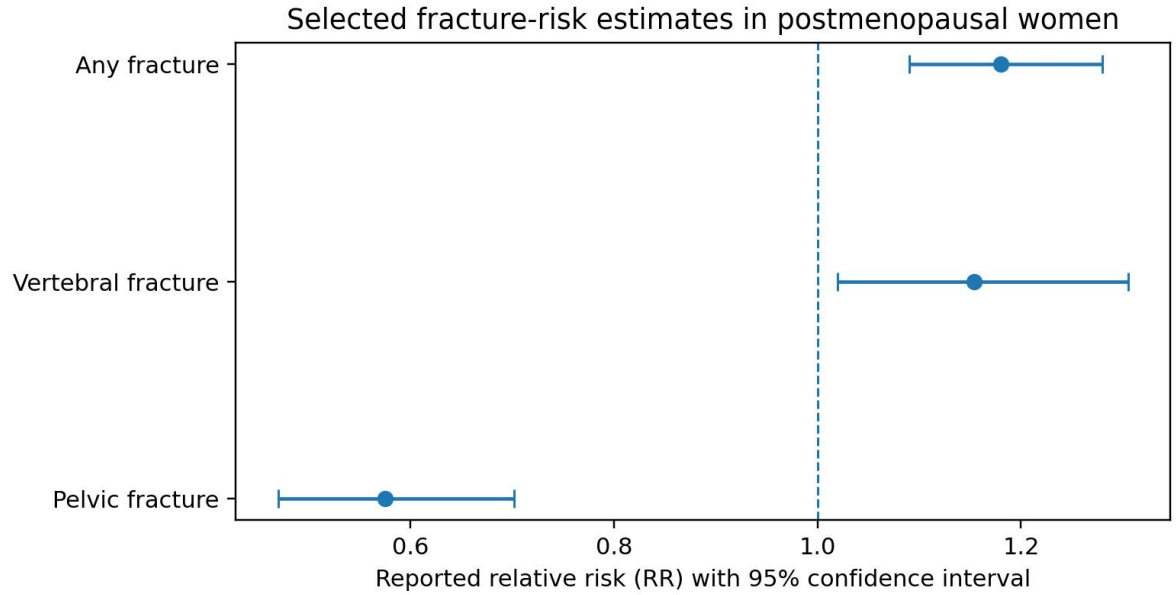


Figure 1. Selected relative-risk estimates reported in the cited meta-analysis. These are published estimates, not a new analysis.

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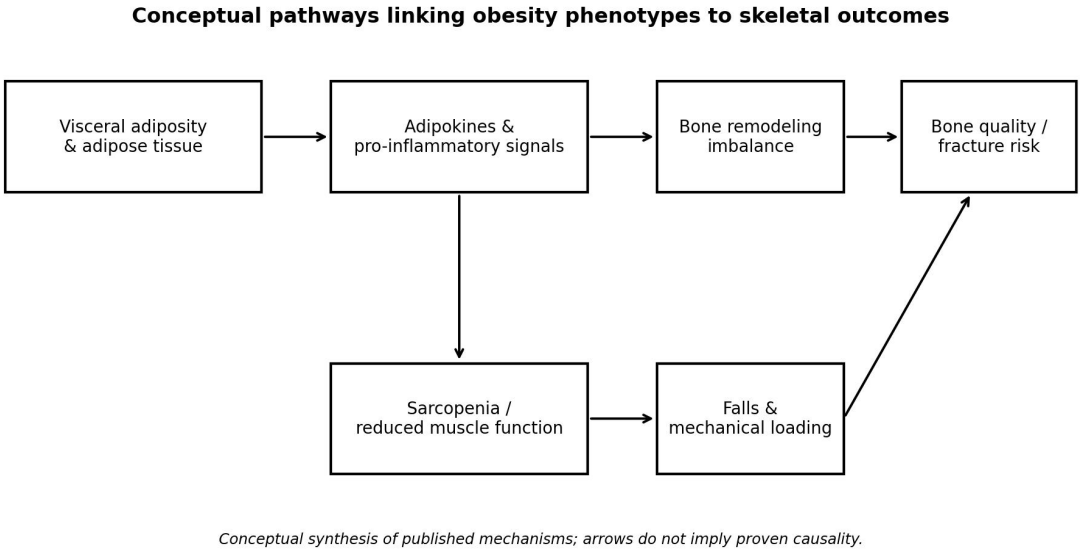


Figure 2. Conceptual pathways connecting visceral adiposity, inflammatory/adipokine signaling, muscle dysfunction, and skeletal outcomes.

4. DISCUSSION

The evidence synthesized here challenges the assumption that obesity protects the postmenopausal skeleton. Increased mechanical loading can be associated with higher areal BMD, but fracture outcomes depend on more than bone mass. Visceral fat, altered adipokine signaling, chronic low-grade inflammation, impaired bone microarchitecture, reduced muscle quality, and falls may offset or exceed any mechanical benefit. The endocrine activity of adipose tissue provides a plausible biological link between obesity and skeletal remodeling. Leptin, adiponectin, and inflammatory cytokines such as TNF-α and IL-6 have been implicated in pathways regulating osteoblast and osteoclast activity. Bone-marrow adipose tissue may also interact with the hematopoietic and skeletal niches. Nevertheless, mechanistic pathways are complex, and observational associations do not establish causality. The distinction between general obesity and sarcopenic obesity is clinically important. A person may have a high BMI while having reduced muscle mass or function. Such a phenotype may increase fall risk and compromise physical loading, balance, and functional reserve. In postmenopausal women, assessment of muscle function and body composition may therefore complement DXA-derived BMD. This review has limitations. The evidence base is heterogeneous, several studies are cross-sectional, and not all included populations are exclusively postmenopausal. The search process represented in this draft is focused rather than a fully reproducible systematic search across all major databases. No formal risk-of-bias assessment or independent duplicate screening is claimed. The quantitative results are taken from the cited publications and have not been recalculated. Clinical assessment should avoid using BMI as a surrogate for skeletal protection. In postmenopausal women with obesity, clinicians may consider fracture history, fall history, central adiposity, muscle strength and performance, vitamin D status

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when indicated, and standard osteoporosis evaluation. TBS or other measures of bone quality may be useful in selected patients where available. These considerations do not replace established clinical guidelines or individualized medical assessment.

5. CONCLUSION

Obesity-associated skeletal effects in postmenopausal women are heterogeneous. Higher body mass may coexist with impaired bone microarchitecture, altered bone turnover, sarcopenia, and increased risk of selected fracture types. Visceral adiposity and sarcopenic obesity appear to be important phenotypes that BMI alone cannot adequately describe. Future prospective studies should integrate adipose distribution, adipokines, inflammatory markers, muscle function, BMD, TBS, and adjudicated fracture outcomes.

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