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Opportunistic CT Screening for Osteoporosis in Postmenopausal Women: Background, Challenges, and Evidence Gaps

Shiyu Zhong[1], Ting Zheng[1], Liuqing Yang[2], Xiangrong Deng[3], Bangcai Han[4], Suting Ye[5], Wenmin Li[3], Yinghua Wu[6]*

[1]College of Medical and Life Sciences, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, Sichuan, China
[2]Department of Ultrasound, the First Hospital of Jilin University, Changchun 130021, Jilin, China
[3]Department of Radiology, Chongzhou Traditional Chinese Medicine Hospital, Chengdu 611200, Sichuan, China
[4]Department of Radiology, Suzhou BOE Hospital, Suzhou 130021, Jiangsu, China
[5]Department of Function Inspection, Sichuan Integrative Medicine Hospital, Chengdu 610041, Sichuan, China
[6]PhD Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu 610072, Sichuan, China

***Corresponding author:** Yinghua Wu, wyh@cdutcm.edu.cn

Abstract: Postmenopausal women represent the highest-risk population for osteoporosis (OP), with a prevalence exceeding 32.5%. The resultant fragility fractures are associated with devastating disability, mortality, and a substantial socioeconomic burden. Dual-energy X-ray absorptiometry (DXA), the diagnostic gold standard, is insufficient for large-scale screening due to limited equipment availability, low screening coverage, and poor awareness. Opportunistic screening using CT attenuation values (Hounsfield Units, HU) from routine scans has emerged as a promising alternative, offering the potential for widespread without additional radiation or cost. However, translating this strategy to the core target population of postmenopausal women reveals three critical evidence gaps: (1) a lack of genetic causal evidence specific to postmenopausal women, making it difficult to establish a definitive link between HU decline and osteoporosis; (2) high heterogeneity in diagnostic studies, with a lack of pooled diagnostic parameters exclusive to this group, potentially leading to misclassification with existing general-population thresholds; and (3) the absence of a screening model built entirely on literature parameters from postmenopausal women, hindering individualized risk stratification. This review systematically examines the disease burden of OP in postmenopausal women, the limitations of DXA screening, the principles and progress of opportunistic CT, and critically analyzes these three key gaps to underscore the necessity and urgency for a comprehensive chain of evidence, from causal mechanisms to clinical application.

Keywords: Postmenopausal women; Osteoporosis; Opportunistic screening; CT attenuation value; Hounsfield unit; DXA

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1. Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk. Often termed a "silent epidemic" due to its asymptomatic progression until fracture, its most severe clinical outcome is fragility fractures, typically occurring at the hip, spine, and wrist. Hip fractures, in particular, are associated with mortality rates exceeding 20% within the first year and profound long-term disability in survivors [1,2].

From a public health perspective, identifying an efficient, economical, and widely accessible screening strategy for early identification and intervention in high-risk populations is paramount. This review will first detail the specific burden of osteoporosis in postmenopausal women, then outline the critical failures of current DXA-based screening, before exploring the potential and pitfalls of opportunistic CT. Finally, it will systematically identify and analyze three fundamental evidence gaps that must be addressed to translate this promising technique into effective clinical practice for the highest-risk group

2. Osteoporosis in postmenopausal women: A pressing public health challenge

2.1. Epidemiological burden

Postmenopausal women bear the most significant burden of osteoporosis. According to the 2018 China Osteoporosis Epidemiology Survey, the prevalence of OP in postmenopausal women over 40 was 32.5%, compared to just 6.9% in men of the same age. This disparity widens with age, affecting 51.6% of women over 65. It is estimated that of the approximately 90 million individuals with OP in China, around 70 million (nearly 80%) are women, with postmenopausal women constituting the vast majority [2,3]. This pattern is mirrored globally, where low bone mineral density (BMD) in postmenopausal women contributes significantly to years lived with disability and mortality worldwide [4,5].

Table 1. Prevalence of osteoporosis in Chinese women by age group

Age Group	Prevalence (%)	Source
40–49	16.0	China OP Epidemiological Survey, 2018
50–59	18.4	China OP Epidemiological Survey, 2018
60–69	37.5	China OP Epidemiological Survey, 2018
70–79	52.9	China OP Epidemiological Survey, 2018
≥ 80	68.0	China OP Epidemiological Survey, 2018

2.2. Catastrophic consequences of fragility fractures

The consequences of fragility fractures are severe. Hip fracture patients face a 20–25% mortality rate within the first year, often due to complications from immobilization such as pneumonia, venous thromboembolism, and infection. Among survivors, approximately 50% experience permanent disability, and only 20% return to their pre-fracture level of function [4]. Vertebral fractures lead to height loss, kyphosis, chronic pain, and reduced quality of life. The economic burden is equally staggering, with the cost of managing osteoporotic fractures projected to reach hundreds of billions in China alone by 2050 [6].

2.3. Core pathophysiology: The role of estrogen deficiency

The fundamental driver of this heightened risk is the sharp decline in estrogen during menopause. Estrogen

plays a crucial role in suppressing bone remodeling and maintaining a balance between osteoblast and osteoclast activity. Its deficiency leads to increased osteoclast activity and accelerated bone resorption, particularly affecting trabecular-rich sites like the vertebrae and distal radius. Bone loss can reach up to 7% per year in the immediate postmenopausal period, far exceeding the gradual decline seen in aging men [7].

3. The screening dilemma: Why DXA fails to meet the need

Despite being the gold standard, DXA-based screening is failing to reach the majority of at-risk postmenopausal women, with testing rates persistently below 10% in many regions, including China [8]. This failure stems from three interconnected barriers.

3.1. Low screening coverage and awareness

Awareness of osteoporosis as a preventable disease is critically low. Many women perceive themselves as healthy in the absence of pain. Studies show low knowledge scores among middle-aged women, which directly correlates with a lack of proactive screening behavior [9]. Unlike established programs for cancers, osteoporosis screening lacks similar policy support and public health infrastructure.

3.2. Severe shortage of DXA equipment

DXA machines are expensive, require specialized operators and facilities, and are therefore concentrated in larger urban hospitals. In rural and primary care settings, where a significant portion of the population resides, DXA availability is extremely limited, often with fewer than one machine per 100,000 elderly individuals [9]. This geographic and financial inaccessibility creates a major bottleneck.

3.3. Limitations of alternative screening tools

While quantitative ultrasound (QUS) is portable and inexpensive, its low sensitivity (< 60%) for detecting asymptomatic OP and its inability to provide a diagnostic T-score limit its utility. An abnormal QUS result still necessitates a confirmatory DXA scan, creating a two-step process that often leads to loss of follow-up [10].

Table 2. Comparison of screening/diagnostic modalities for osteoporosis

Modality	Key Advantages	Key Disadvantages	Role in Screening
DXA	Gold standard; Provides T-score for diagnosis.	High cost, limited availability,requires specialized staff.	Primary diagnostic tool, poor for population screening.
QUS	Portable, low-cost, no radiation.	Low sensitivity for OP; Cannot provide diagnostic T-score.	Triage tool; cannot replace DXA.
Opportunistic CT (HU)	Uses existing scans; No extra cost/radiation; Widely available.	No standardized thresholds; Influenced by technical factors.	High potential for passive population screening.

4. Opportunistic CT attenuation: A new direction for screening

4.1. Scientific basis: HU as a proxy for BMD

CT attenuation values (Hounsfield Units, HU) quantify the radiodensity of tissues. Numerous studies have demonstrated a strong, significant positive correlation between trabecular bone HU in the lumbar vertebrae and BMD measured by DXA or quantitative CT (QCT), with correlation coefficients (r) often exceeding

0.6 for DXA and reaching as high as 0.95 for QCT [10]. This forms the scientific rationale for using HU as a surrogate marker of bone density.

4.2. The concept of opportunistic CT

Formalized by Pickhardt et al. [9], opportunistic CT screening refers to the practice of leveraging existing CT scans (performed for reasons such as abdominal pain, trauma, or oncology follow-up) to measure vertebral HU and assess osteoporosis risk. Its transformative potential lies in its ability to generate significant public health value from existing clinical data at no additional cost or radiation exposure to the patient. It represents a form of "passive" screening on a massive scale [11].

4.3. Technical considerations and confounders

For reliable and reproducible measurements, several technical factors must be standardized:

(1) Scan Parameters: Tube voltage (kVp) significantly affects HU. Lower kVp results in higher HU. Consistency is key, and kVp-specific thresholds may be needed.

(2) Region of Interest (ROI): Measurements should be taken from the trabecular bone in the mid-vertebral body, carefully avoiding the cortex, posterior venous plexus, bone islands, or focal lesions like hemangiomas or fractures [12]. Inclusion of cortical bone or osteophytes will falsely elevate HU values.

(3) Contrast Media: Intravenous contrast significantly increases measured HU values, making it unsuitable for direct application of thresholds derived from non-contrast scans. If contrast scans must be used, correction factors are required [13].

(4) Patient Factors: Bone marrow composition, particularly increased fatty infiltration in postmenopausal women, can lower HU values, a factor that must be considered when applying general thresholds [14].

5. Critical research gaps and the rationale for this study

While the potential of opportunistic CT is immense, a systematic review of the literature reveals three interconnected evidence gaps that specifically hinder its application to postmenopausal women. Addressing these gaps requires a comprehensive research approach.

(1) Gap 1: Lack of Causal Genetic Evidence in Postmenopausal Women

All current studies correlating HU with BMD or fractures are observational, which are susceptible to confounding and cannot prove causality. Mendelian randomization (MR) uses genetic variants as instrumental variables to strengthen causal inference. While MR studies have confirmed a causal link between low BMD and osteoporosis using genome-wide association study (GWAS) data [14], they have not specifically focused onspine CT attenuation values in postmenopausal women. Although genetic correlations exist between BMD at different skeletal sites (e.g., heel and spine), directly extrapolating findings to this specific phenotype and population is methodologically unsound. A targeted MR study is needed to provide robust causal evidence that genetically predicted lower spinal HU is a direct cause of osteoporosis risk in this group.

(2) Gap 2: Heterogeneity in Diagnostic Studies and Lack of Pooled Data for Postmenopausal Women

Existing diagnostic meta-analyses on CT values for osteoporosis typically pool data from mixed populations (men, premenopausal women, postmenopausal women) [13]. The pooled sensitivity, specificity, and derived thresholds are therefore not optimized for postmenopausal women. Their

unique pathophysiology, particularly increased marrow fat, likely means their HU distribution differs. Applying a generic threshold could lead to systematic over- or under-diagnosis. A dedicated diagnostic meta-analysis,strictly limited to studies reporting data on postmenopausal women, is required to generate pooled diagnostic accuracy parameters and propose an evidence-based HU threshold specific to this population.

(3) Gap 3: Absence of a Screening Model Built on Postmenopausal Women-Specific Parameters

Current fracture risk assessment tools (e.g., FRAX, Garvan) are derived from general population cohorts and lack variables critical to postmenopausal women, such as age at menopause, years since menopause, or parity [12]. Models incorporating CT values are similarly built on mixed cohorts. An ideal, personalized screening model for this group should be constructed using epidemiological parameters (e.g., baseline prevalence, risk factor effect sizes) derivedexclusively from postmenopausal women. It should integrate key variables—including CT attenuation value, age, years since menopause, prior fracture history, and low BMI—to provide accurate, individualized risk stratification. No such model currently exists.

Table 3. Summary of key evidence gaps and proposed research directions

Research Gap	Specific Problem in Postmenopausal Women	Proposed Research Direction
1. Causal Evidence	Lack of proof that low spinal HUcausesOP in this group.	Perform a two-sample Mendelian randomization study using GWAS data specific to spinal BMD/OP in women.
2. Diagnostic Threshold	No pooled diagnostic parameters (sensitivity/ specificity) or HU threshold exists for this group.	Conduct a diagnostic meta-analysis of studies limited to postmenopausal women to derive a pooled threshold.
3. Screening Model	No risk stratification model is built using parameters solely from this population.	Develop and validate a new screening model using predictor variables and baseline risk from postmenopausal female cohorts.

6. Conclusion and future directions

Opportunistic CT screening for osteoporosis in postmenopausal women holds tremendous promise to overcome the significant limitations of current DXA-based approaches. By harnessing ubiquitous imaging data, it offers a path towards truly large-scale, passive identification of at-risk individuals. However, the strategy cannot be responsibly implemented in this specific population until the three key evidence gaps identified in this review are addressed.

A systematic research program is urgently needed. First, causal evidence must be established using genetic epidemiology methods like Mendelian randomization. Second, rigorous diagnostic synthesis through a population-specific meta-analysis must provide a reliable, evidence-based HU threshold. Finally, this foundational evidence must be integrated into a novel, clinically useful screening model that provides individualized risk probabilities for postmenopausal women. Filling these gaps is not merely an academic exercise; it is a critical prerequisite for translating a promising concept into a safe, effective, and equitable public health strategy to combat the devastating burden of osteoporosis in the highest-risk population.

7. Analytical pathway

To systematically address the three interconnected evidence gaps hindering the clinical translation of

opportunistic CT screening for osteoporosis in postmenopausal women, we propose a sequential, three-phase analytical pathway. This design moves from establishing causal mechanism, to synthesizing diagnostic evidence, and finally to developing a clinical application tool.

7.1. Phase 1: Causal validation

(1) Objective: To determine if genetically predicted lower spinal CT attenuation values are a causal risk factor for osteoporosis in women.

(2) Methodology: A two-sample Mendelian Randomization (MR) study will be conducted.

(3) Data Source: The largest available genome-wide association study (GWAS) summary statistics for 1) lumbar spine bone mineral density (as a proxy for HU) and 2) osteoporosis (fracture) will be utilized. Preference will be given to datasets stratified by or predominantly composed of women.

(4) Analysis: The inverse-variance weighted (IVW) method will be the primary analysis, with sensitivity analyses (MR-Egger, weighted median) to test for and correct potential pleiotropy.

(5) Expected Outcome: Confirmation of a significant causal effect, providing the genetic etiological foundation for using spinal attenuation as a screening target in this population.

7.2. Phase 2: Diagnostic synthesis

(1) Objective: To derive a pooled, evidence-based diagnostic threshold (HU value) for identifying osteoporosis specifically in postmenopausal women.

(2) Methodology: A comprehensive diagnostic test accuracy (DTA) meta-analysis will be performed.

(3) Inclusion Criteria: Studies must report HU measurements (index test) and DXA T-scores (reference standard) specifically for a postmenopausal female population, or provide disaggregated data for this subgroup.

(4) Analysis: A bivariate random-effects model will be used to pool sensitivity, specificity, and construct a summary receiver operating characteristic (SROC) curve. Meta-regression will explore sources of heterogeneity (e.g., CT technical parameters).

(5) Expected Outcome: A statistically robust, population-specific HU threshold with corresponding pooled sensitivity and specificity, offering a reliable diagnostic benchmark for clinical use.

7.3. Phase 3: Model development

(1) Objective: To construct and internally validate a clinical screening model for individualized osteoporosis risk prediction in postmenopausal women.

(2) Methodology: A prediction model study will be developed using data from a large, well-characterized cohort of postmenopausal women.

(3) Predictors: The model will integrate the HU threshold identified in Phase 2 with key clinical risk factors prevalent in this population (e.g., age, years since menopause, BMI, prior fracture history).

(4) Analysis: Multivariable logistic regression will be used to develop the model. Performance will be assessed through calibration (Hosmer-Lemeshow test, calibration plot) and discrimination (Area Under the Curve, AUC). Internal validation will be performed using bootstrapping techniques.

(5) Expected Outcome: A user-friendly, evidence-based screening tool (e.g., a nomogram or risk score) that provides an individual's absolute probability of having osteoporosis, enabling targeted DXA referral and intervention.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Ardelean A, Tit DM, Furau R, et al., 2025, Beyond Bone Mineral Density: Real-World Fracture Risk Profiles and Therapeutic Gaps in Postmenopausal Osteoporosis. Diagnostics, 15(15): 1972.

[2] Zhao W, Wu Q, Liu Q, et al., 2025, Government-Implemented Population Osteoporosis Screening in Rural China: Achieving Universal Coverage with Portable DXA. BMC Geriatrics, 25(1): 815.

[3] Zeng Q, Li N, Wang Q, et al., 2019, The Prevalence of Osteoporosis in China, A Nationwide, Multicenter DXA Survey. Archives of Osteoporosis, 14(1): 39–48.

[4] Kanis JA, Cooper C, Rizzoli R, et al., 2019, European Guidance for the Diagnosis and Management of Osteoporosis in Postmenopausal Women. Osteoporosis International, 30(1): 3–44.

[5] Özmen S, Kurt S, Timur HT, et al., 2024, Prevalence and Risk Factors of Osteoporosis: A Cross-Sectional Study in a Tertiary Center. Medicina, 60(12): 2109.

[6] Heaton TB, Behrens NF, Eyring JB, et al., 2026, Language Barriers as a Driver of Health Disparity in Bone Density Screening Among the Aging Population. American Journal of Preventive Medicine, 70(5): 108263.

[7] Hans D, Hartl F, Krieg M, 2020, Quantitative Ultrasound for Osteoporosis Detection: A Meta-Analysis. Journal of Bone and Mineral Research, 35(9): 1677–1684.

[8] Pongchaiyakul C, Songpattanasilp T, 2024, Barriers to Osteoporosis Care in Rural Thailand. Archives of Osteoporosis, 19: 12.

[9] Pickhardt PJ, Pooler BD, Lauder T, et al., 2013, Opportunistic Screening for Osteoporosis Using Abdominal Computed Tomography Scans Obtained for Other Indications. Annals of Internal Medicine, 158(8): 588–595.

[10] Majumdar SR, Leslie WD, 2013, Conventional Computed Tomography Imaging and Bone Mineral Density: Opportunistic Screening or "Incidentaloporosis"? Annals of Internal Medicine, 158(8): 630–631.

[11] Vermue H, Garibaldi R, Alshoaibi Y, et al., 2025, Opportunistic CT-Based Osteoporosis Screening of the Hip: A Systematic Review of Diagnostic Accuracy. Archives of Orthopaedic and Trauma Surgery, 145(1): 506.

[12] Gausden EB, Nwachukwu BU, Schreiber JJ, et al., 2017, Opportunistic Use of CT Imaging for Osteoporosis Screening and Bone Density Assessment: A Qualitative Systematic Review. Journal of Bone and Joint Surgery American Volume, 99(18): 1580–1590.

[13] Zhu Y, Triphuridet N, Yip R, et al., 2021, Opportunistic CT Screening of Osteoporosis on Thoracic and Lumbar Spine: A Meta-Analysis. Clinical Imaging, 80: 382–390.

[14] UK Biobank, 2025, Mapping the Role of Macro and Micronutrients in Bone Mineral Density: A Comprehensive Mendelian Randomization Study. UK Biobank, London.

[15] Scientific Reports, 2025, MR Analysis Reveals No Causal Association Between Mitochondrial DNA Copy Number and Osteoporosis. Scientific Reports, 15: 22286.