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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)

ISSN 2760-4942 (Online) Volume 2, Issue 3, March 2026

https://eurekaoa.com/index.php/5

CONTEMPORARY APPROACHES TO THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS: A NARRATIVE REVIEW WITH REFERENCE TO DATA FROM UZBEKISTAN

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Abstract

Postmenopausal osteoporosis remains a major cause of fragility fractures, loss of independence, and increasing healthcare costs. The aim of this narrative review was to summarize current evidence-based approaches to diagnosis, risk stratification, and treatment of postmenopausal osteoporosis, and to discuss their applicability in Uzbekistan. Sources were searched in PubMed/MEDLINE, PubMed Central, and on the official websites of the Endocrine Society, the International Society for Clinical Densitometry (ISCD), the National Osteoporosis Guideline Group (NOGG), and FRAXplus as of March 18, 2026. The review included clinical guidelines, official position statements, pivotal randomized trials, and Uzbekistan-specific epidemiological data. Contemporary diagnosis should rely on clinical risk factors, DXA, FRAX-based risk estimation, and, in selected cases, trabecular bone score and vertebral fracture assessment. Laboratory evaluation is primarily required to exclude secondary causes of bone loss and to ensure safe treatment selection. Antiresorptive drugs remain the mainstay for women at high fracture risk, whereas early anabolic or dual-action

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treatment followed by antiresorptive consolidation is appropriate for women at very high risk. For Uzbekistan, key priorities include broader access to FRAX and DXA, improved fracture ascertainment, and avoidance of unplanned denosumab discontinuation.

Keywords: Postmenopausal osteoporosis, FRAX, DXA, trabecular bone score, denosumab, romosozumab, narrative review, Uzbekistan.

1. Introduction

Postmenopausal osteoporosis in women is a chronic skeletal disease characterized by reduced bone strength and an increased risk of low-energy fractures, primarily involving the vertebrae, proximal femur, and distal forearm [1, 2]. The pathogenetic basis of the postmenopausal form of the disease is estrogen deficiency, which accelerates bone resorption and disrupts the balance between bone formation and bone resorption [1, 2]. The clinical significance of this problem is determined not only by the frequency of fractures, but also by their consequences: reduced quality of life, increased mortality after hip fracture, and a greater burden on the healthcare system [1, 14].

According to current guidelines, the diagnosis of postmenopausal osteoporosis is not limited solely to the measurement of bone mineral density (BMD). In practice, it requires integration of clinical risk factors, densitometry, fracture probability assessed by FRAX, and, when necessary, additional methods for evaluating bone quality and detecting asymptomatic vertebral compression fractures [1, 4, 5, 15]. This approach is especially important for patients with osteopenia, previous fractures, or multiple risk factors, when the decision to initiate therapy cannot be based on the T-score alone [1, 4, 14].

For Uzbekistan, the problem is of particular relevance. The national FRAX model for Uzbekistan was developed using local epidemiological data, and the projected number of hip fractures is expected to increase from 16,764 cases in 2015 to

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60,272 cases in 2050, that is, by more than threefold [3]. The same study showed that a substantial proportion of hip fractures in the country are not captured in hospital statistics, indicating a problem of underdiagnosis and underreporting of fractures [3]. In this context, the aim of the present review was to critically and rigorously summarize, strictly on the basis of the sources, current evidence-based approaches to the diagnosis and treatment of postmenopausal osteoporosis, with an emphasis on their practical applicability in Uzbekistan.

2. Methods

The present work was conducted as a narrative review. The literature search was performed in PubMed/MEDLINE and PubMed Central, as well as on the official websites of the Endocrine Society, ISCD, NOGG, and FRAXplus. The search was updated as of March 18, 2026. Priority was given to official clinical guidelines, position statements of professional societies, large randomized clinical trials, and regional epidemiological publications.

The review included sources directly related to the diagnosis of postmenopausal osteoporosis, fracture risk assessment, the use of DXA, trabecular bone score (TBS), vertebral fracture assessment (VFA), the role of biochemical markers of bone turnover, as well as the efficacy and safety of bisphosphonates, denosumab, teriparatide, and romosozumab [1–15]. Sources with unclear bibliographic data, unverifiable figures, or inconsistencies between the text and the cited work were not included in this review.

3. Results

3.1. Diagnosis and Stratification of Fracture Risk

DXA remains the basic tool for diagnosing osteoporosis in postmenopausal women. According to the official positions of the ISCD, the T-score is used for diagnostic classification in postmenopausal women, and a diagnosis of osteoporosis is established when the T-score is <= -2.5 at the lumbar spine,

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femoral neck, total hip, or the 33% radius if forearm assessment is indicated [4]. At the same time, low BMD does not capture the full extent of skeletal fragility: a substantial proportion of fractures occur in women who do not fall within the densitometric range of osteoporosis, especially when clinical risk factors are present [1, 14].

Therefore, modern risk assessment should include clinical risk factors and probabilistic models. The FRAX algorithm is used to calculate the 10-year probability of major osteoporotic fractures and hip fracture; the calculation can be performed with or without femoral neck BMD data if densitometry is unavailable [14, 15]. Uzbekistan has its own national FRAX model based on local data on hip fractures and mortality [3, 15]. This makes FRAX particularly valuable in settings where access to DXA is uneven and allows more rational selection of patients for densitometry and treatment [3, 14, 15].

Additional methods help refine risk assessment in borderline patients. TBS, derived from DXA images of the lumbar spine, is regarded as an indicator reflecting features of trabecular microarchitecture. Official ISCD positions emphasize that TBS improves fracture risk assessment and may be used as an adjunct to BMD and FRAX, but it should not be used as an independent diagnostic criterion for establishing osteoporosis [5]. Similarly, VFA makes it possible to detect morphometric vertebral fractures, which are often asymptomatic but substantially increase the risk of subsequent fractures and influence treatment choice [4]. Therefore, in clinical practice, the most informative strategy is a combined approach: clinical risk profile, DXA, FRAX, and targeted use of TBS or VFA in patients with uncertain or intermediate risk [1, 4, 5, 14].

3.2. Laboratory Assessment and Monitoring

Laboratory tests are not an independent criterion for the diagnosis of osteoporosis; however, they are necessary to exclude secondary causes of low

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bone mass and to ensure safe treatment selection [1, 2, 14]. At the initial stage, in patients with suspected postmenopausal osteoporosis, it is advisable to assess at minimum calcium, renal function, 25(OH)D concentration, and, when clinically indicated, parathyroid hormone, thyroid function tests, complete blood count, and other tests aimed at identifying secondary causes of the disease [1, 14]. This scope of evaluation makes it possible to distinguish primary postmenopausal osteoporosis from conditions in which low BMD is secondary to other endocrine, inflammatory, renal, or gastrointestinal disorders [1, 2].

Biochemical markers of bone turnover play a special role in monitoring, but their use requires cautious interpretation. International expert documents recommend serum PINP and beta-CTX as reference markers of bone formation and bone resorption in research and clinical monitoring [6]. Their main value lies not in establishing the diagnosis, but in assessing the biological response to therapy and adherence to treatment, especially during the first months after initiation of antiresorptive or anabolic therapy [6, 7, 14]. At the same time, absolute “normal” values for these markers depend on the assay method, timing of blood sampling, menopausal status, and the individual laboratory; therefore, universal rigid reference intervals should not be used without reference to a specific analytical system [6, 7].

Correction of vitamin D deficiency and обеспечение adequate calcium intake remain essential components of patient management, but the modern approach avoids universal application of controversial thresholds to all clinical situations. The NOGG guidelines emphasize adequate calcium intake preferably through diet, the use of supplements when intake is insufficient, as well as correction of vitamin D deficiency before initiation of certain treatment regimens and in patients at risk of deficiency [14]. Thus, in the modern model, laboratory assessment serves not to “confirm” osteoporosis by a single biochemical indicator, but to support safe and individualized patient management [1, 14].

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ISSN 2760-4942 (Online) Volume 2, Issue 3, March 2026

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Table 1. Baseline Laboratory Evaluation for Suspected Postmenopausal Osteoporosis

Parameter	Purpose of the test
Serum calcium	Exclusion of hypercalcemia and hypocalcemia
Creatinine / estimated GFR	Assessment of renal function; determination of the feasibility of bisphosphonate therapy
25(OH)D	Detection of vitamin D deficiency
Parathyroid hormone (when indicated)	Exclusion of primary and secondary hyperparathyroidism
TSH (when indicated)	Exclusion of thyrotoxicosis as a cause of secondary bone loss
Complete blood count	Screening for systemic and hematologic diseases
P1NP, β-CTX (for monitoring)	Assessment of the biological response to therapy; not for the diagnosis of osteoporosis [6, 7]

Note. Reference intervals for bone turnover markers depend on the analytical method and the laboratory [6, 7]; universal “normal” values are not provided without reference to a specific system.

3.3. Pharmacotherapy and Treatment Sequencing

In women at high fracture risk, antiresorptive agents remain the cornerstone of pharmacotherapy [1, 2, 14]. In current NOGG and Endocrine Society guidelines, bisphosphonates are regarded as first-line therapy for most high-risk patients, whereas denosumab is considered an effective alternative when supported by appropriate clinical indications and organizational capacity [2, 14]. The efficacy of zoledronic acid was confirmed in the randomized HORIZON-PFT trial: annual intravenous infusion reduced the risk of vertebral, hip, and nonvertebral fractures

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in postmenopausal women [8]. In the FREEDOM trial, denosumab also significantly reduced the risk of vertebral, hip, and nonvertebral fractures when administered at a dose of 60 mg subcutaneously once every 6 months [9].

In patients at very high fracture risk, with multiple vertebral fractures or extremely low BMD, current guidelines allow preferential use of an anabolic strategy or a dual-action strategy followed by antiresorptive consolidation [2, 14]. Teriparatide has demonstrated the ability to reduce the risk of vertebral and nonvertebral fractures in postmenopausal women [10]. In the FRAME trial, romosozumab reduced the risk of new vertebral fractures compared with placebo, and subsequent transition to denosumab allowed preservation and further improvement of gains in BMD and fracture risk reduction [11]. In the ARCH trial, among high-risk patients, romosozumab followed by alendronate was superior to alendronate alone in preventing new vertebral, clinical, nonvertebral, and hip fractures [12].

The sequence of therapy is of fundamental importance. After completion of a course of teriparatide or romosozumab, subsequent administration of an antiresorptive agent is necessary; otherwise, part of the BMD gain is lost [2, 11, 12, 14]. This principle is especially important in denosumab therapy: the drug should not be discontinued without a preplanned transition to another antiresorptive agent, because withdrawal of denosumab is associated with rapid reactivation of bone resorption, loss of BMD, and an increased risk of multiple vertebral fractures [13, 14]. Therefore, the choice of therapy should take into account not only the baseline fracture risk, but also the feasibility of maintaining treatment continuity, monitoring, and adherence to the schedule of injections or infusions [2, 13, 14].

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Table 2. Main pharmacological agents for the treatment of postmenopausal osteoporosis

Drug	Mechanism of action	Key study	Main proven effects	Important considerations for use
Zoledronic acid (5 mg IV once yearly)	Antiresorptive (bisphosphonate)	HORIZON-PFT [8]	Reduction in the risk of vertebral, hip, and nonvertebral fractures	Requires adequate renal function; drug holidays may be possible
Denosumab (60 mg SC once every 6 months)	Antiresorptive (anti-RANKL)	FREEDOM [9]	Reduction in the risk of vertebral, hip, and nonvertebral fractures	Discontinuation only with transition to a bisphosphonate [13]
Teriparatide (20 µg SC daily, up to 24 months)	Anabolic (PTH 1-34)	Neer et al. [10]	Reduction in the risk of vertebral and nonvertebral fractures	Duration of therapy is limited; subsequent antiresorptive therapy is required
Romosozumab (210 mg SC once monthly, for 12 months)	Dual-action (anti-sclerostin)	FRAME [11], ARCH [12]	Reduction in vertebral fracture risk; superiority over alendronate (ARCH)	Cardiovascular risk should be taken into account; transition to an antiresorptive agent is mandatory

4. Discussion

This narrative review shows that the modern model of postmenopausal osteoporosis management is based on the integration of several levels of risk assessment. Diagnosis by DXA remains fundamental, but clinical decision-making should also take into account prior fractures, age, accompanying risk factors, and fracture probability according to FRAX [1, 4, 14, 15]. Additional methods such as TBS and VFA do not replace densitometry; however, they improve the accuracy of risk stratification in some patients, especially when BMD values are intermediate or the clinical profile is uncertain [4, 5].

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Particular attention should be paid to the trend toward earlier use of anabolic therapy or dual-action therapy in patients at very high risk. Whereas clinical practice previously often followed a “bisphosphonate for everyone” approach, current guidelines allow a different sequence: first, a drug capable of rapidly increasing bone formation or substantially altering remodeling, followed by an antiresorptive agent to consolidate the result [2, 11, 12, 14]. This is especially important for women with recent vertebral fractures, multiple fractures, or extremely low BMD values, in whom delay of effective therapy may lead to new fracture events within the coming months [2, 14].

At the same time, clinical rigor requires avoiding oversimplification. Biochemical markers of bone turnover are useful for monitoring, but they should not replace densitometry or clinical risk assessment [6, 7]. Likewise, vitamin D, calcium, and renal function parameters are important for safety and for correction of accompanying abnormalities, but they are not isolated criteria for selecting the entire treatment strategy [1, 14]. It is equally important to avoid unjustified discontinuation of denosumab, since organizational gaps in long-term therapy are themselves a source of preventable complications [13, 14].

For Uzbekistan, the data discussed here have direct practical significance. The national FRAX model [3, 16] provides a basis for standardizing risk assessment, but by itself it does not solve the problem of underdetection of fractures, limited access to DXA, or weak referral pathways after the first fracture [3]. Given the projected more than threefold increase in the number of hip fractures by 2050 [3], expansion of primary risk assessment should be regarded as a task not only for specialized care, but also for primary healthcare. In practical terms, this implies early referral for DXA in patients with high clinical risk, broader use of FRAX in settings where densitometry is limited, targeted use of TBS and VFA to refine risk in patients with osteopenia [4, 5, 14, 16], as well as organizational strengthening of the post-fracture care pathway. NOGG recommends a coordinator-based Fracture Liaison Service as a model of effective secondary prevention [14]; for

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Uzbekistan, where a proportion of hip fractures remain outside hospital statistics, such an approach may be as important as expanding access to pharmacologic treatment [3, 14].

This review has limitations. It is not a systematic review or meta-analysis and therefore does not claim to provide exhaustive coverage of all publications. In addition, the regional evidence base for Uzbekistan remains much more limited than the international one, and many organizational conclusions must be extrapolated from international guidelines to local conditions [3, 14]. Nevertheless, source selection in this work was intentionally restricted to verifiable guidelines, official positions, and key randomized studies, which increases the reliability of the practical conclusions.

5. Conclusion

Modern management of postmenopausal osteoporosis should be based on the integration of clinical risk factors, DXA, and probabilistic fracture assessment using FRAX, and in selected patients, the use of TBS and VFA [1, 4, 5, 14, 15]. Laboratory evaluation is necessary to exclude secondary causes of low bone mass and to ensure safe prescription of therapy, rather than to replace densitometry or clinical assessment [1, 6, 7, 14]. In high-risk patients, antiresorptive agents remain the foundation of treatment, whereas in those at very high risk, early use of anabolic therapy or dual-action therapy is justified, with mandatory subsequent antiresorptive consolidation [2, 8–14]. For Uzbekistan, the priority areas are expanding access to the national FRAX model, improving fracture detection, ensuring a pathway for secondary prevention, and preventing uncoordinated discontinuation of denosumab [3, 13–15].

Conflict of Interest

The author declares no conflict of interest.

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Funding

This work received no external funding.

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