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PHARMACOTHERAPY OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN NARRATIVE REVIEW

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ABSTRACT

Background: Postmenopausal osteoporosis is a highly prevalent condition driven by estrogen deficiency that accelerates bone resorption, decreases bone mineral density, and increases the likelihood of fragility fractures. In Central European countries diagnostic coverage for high risk women remains insufficient, and restricted access to modern therapies further limits timely initiation of treatment.

Aims: The aim of this review is to provide an updated clinical assessment of pharmacological treatments used in postmenopausal osteoporosis and to evaluate their efficacy, mechanisms of action, safety profiles, treatment sequencing, adherence factors, and real world limitations related to drug accessibility and national healthcare policies.

Methods: A narrative review of randomized controlled trials, meta analyses, cohort studies, clinical guidelines, and position statements was conducted. The analysis included antiresorptive therapies such as bisphosphonates, denosumab, and selective estrogen receptor modulators, anabolic agents such as teriparatide and romosozumab, and hormone replacement therapy. Special attention was given to safety considerations, adherence, treatment discontinuation, and regional limitations in access to advanced therapies. Foundational trials and recent reviews were included regardless of publication year.

Results: Bisphosphonates, denosumab, teriparatide, romosozumab, and selective estrogen receptor modulators demonstrate clinically proven reductions in vertebral and non vertebral fracture risk and increase bone mineral density. Safety profiles differ substantially between drug classes. Long term bisphosphonate therapy is limited by rare but clinically relevant complications. Denosumab requires carefully structured discontinuation due to the risk of rapid

bone loss and multiple vertebral fractures. Anabolic agents show the strongest improvements in bone parameters and require subsequent antiresorptive therapy to maintain treatment gains. Adherence is a major determinant of treatment success, and complex dosing regimens reduce persistence. Limited access to modern therapies and low diagnostic coverage remain significant barriers in Central European healthcare systems.

Conclusions: Effective management of postmenopausal osteoporosis requires an individualized and clinically reasoned approach that incorporates pathophysiology, proven efficacy and safety, treatment adherence, and healthcare system constraints. Sequential therapy is necessary to maintain benefits achieved with anabolic agents. Improving diagnostic coverage, access to advanced pharmacological treatments, and adherence support programs is essential for reducing fracture risk and achieving better clinical outcomes.

Keywords: osteoporosis postmenopausal, bone density, bisphosphonates, denosumab, teriparatide, romosozumab, selective estrogen receptor modulators, hormone replacement therapy

INTRODUCTION

Postmenopausal osteoporosis is one of the most significant health risks for women after menopause. The reduction in estrogen levels, resulting from the cessation of the menstrual cycle, leads to increased bone resorption, significantly raising the risk of fractures [3,4].

This is a global issue affecting millions of women, and its consequences — such as bone fractures, reduced quality of life, and, in extreme cases, premature mortality — make osteoporosis treatment a matter of major social and medical importance [6,42].

The choice of this topic is driven by the growing need to find effective, safe, and accessible therapies that can improve the quality of life for patients and reduce the burden on healthcare systems associated with osteoporotic fractures [6,21,42]. This is especially relevant in countries such as Poland, where access to advanced osteoporosis therapies remains limited due to reimbursement constraints [39].

Furthermore, current treatment approaches increasingly emphasize individualized therapy based on fracture risk, patient preferences, and long-term safety [36,39]. Cost-effectiveness and healthcare resource optimization have become important considerations in modern clinical practice [40].

This paper analyzes current treatment methods for osteoporosis in postmenopausal women, including pharmacological therapies and integrated approaches involving lifestyle modifications. Additionally, it explores contemporary therapeutic strategies, challenges in treatment access, and recent international guidelines [21,35,39].

RELEVANCE

The relevance of this research is determined by the high prevalence of postmenopausal osteoporosis and the increasing incidence of fragility fractures associated with estrogen deficiency. The condition is one of the major causes of loss of independence in older women and is linked to reduced quality of life and substantially increased mortality after hip fractures and subsequent fractures. The disease also creates a significant burden on healthcare systems due to the costs of surgical treatment, rehabilitation, and long term care. In countries with limited access to modern osteoporosis therapies and restricted availability of early diagnostic methods, including Poland, additional barriers to timely initiation of treatment remain. These factors highlight the need for clinically justified, accessible, and safe pharmacological strategies for postmenopausal patients.

NOVELTY

The novelty of this study lies in a renewed evaluation of contemporary pharmacotherapy for postmenopausal osteoporosis with a focus on clinical aspects that are insufficiently addressed in existing reviews. Particular attention is given to the discrepancy between the strong evidence base supporting antiresorptive and anabolic therapies and the real world limitations related to treatment accessibility, reimbursement constraints, and adherence challenges in Central European healthcare systems. The study aims to identify gaps between the theoretical efficacy demonstrated in clinical trials and the therapeutic outcomes observed in routine practice. Additional attention is devoted to sequential treatment strategies and the clinical considerations related to transitions between drug classes, including the management of therapy discontinuation. This approach enables the development of an updated clinical framework for the management of postmenopausal osteoporosis that integrates pharmacological capabilities with practical healthcare constraints.

AIM OF THE STUDY

The aim of this work is to provide a comprehensive analysis of contemporary pharmacological treatments for postmenopausal osteoporosis, with an evaluation of their efficacy, mechanisms of action, safety profiles, accessibility, and practical applicability.

RESEARCH OBJECTIVES

- To identify the pathophysiological mechanisms of postmenopausal osteoporosis that are relevant for selecting pharmacotherapy.
- To systematize information on the medications used in postmenopausal women, assessing their ability to reduce fracture risk and increase bone mineral density.
- To evaluate the safety profiles of different drugs, taking into account the nature and frequency of adverse effects during long term treatment.
- To analyze factors influencing treatment adherence, including tolerability and dosing convenience.
- To examine clinical approaches to sequential therapy and the rationale for transitioning between medications.
- To assess the impact of drug accessibility, economic constraints, and national guidelines on therapeutic decisions in clinical practice.

MATERIAL AND METHODS

This review was based on a narrative synthesis of the current literature concerning the pharmacological treatment of postmenopausal osteoporosis. The primary objective was to analyze the efficacy, mechanisms of action, safety profiles, and treatment strategies for antiresorptive and anabolic medications, including bisphosphonates, denosumab, selective estrogen receptor modulators (SERMs), hormone replacement therapy (HRT), teriparatide, and romosozumab. Additionally, recent review articles focusing on national and regional treatment accessibility, pharmacoeconomic considerations, and clinical guidelines were analyzed to complement the pharmacological discussion [36–42].

SEARCH STRATEGY AND INCLUSION CRITERIA

A literature search was conducted using international scientific databases, including PubMed, Scopus, and Web of Science, to identify peer-reviewed articles published primarily between 1997 and 2024 , with special attention to review articles from the last five years. . The following keywords and their combinations were used: „postmenopausal osteoporosis", "pharmacotherapy", "bone mineral density (BMD)", "bisphosphonates", "denosumab", "parathyroid hormone", "romosozumab", "selective estrogen receptor modulators (SERM)", "hormone replacement therapy (HRT)", "fracture risk", "therapeutic adherence", "osteoporotic fractures", "patient preferences", "osteoporosis treatment", "long-term effects", "osteoporosis management", "cost-effectiveness", "treatment access", "screening", "clinical guidelines".

INCLUSION CRITERIA:

- Articles in English.
- Studies and reviews concerning postmenopausal women.
- Randomized controlled trials, meta analyses, systematic reviews, cohort studies, and position statements issued by scientific societies.
- Pivotal clinical trials and foundational epidemiological studies relevant to current treatment concepts, regardless of publication year.
- Recent review articles published between 2020 and 2025 that address regional limitations in access to therapy and economic aspects of osteoporosis management.

EXCLUSION CRITERIA:

- Studies focused exclusively on men or pediatric populations.
- Case reports, conference abstracts, and non-peer-reviewed materials.

A total of 42 high-quality sources were selected based on relevance, impact factor of the journal, and clinical applicability. These included guidelines from professional societies such as The North American Menopause Society (NAMS) [7, 14], UK clinical guidelines [39], epidemiological reports [42], and evidence from pivotal trials such as the MORE trial [18], the FIT trial [21], and recent meta-analyses [6, 29–41].

DATA EXTRACTION AND ANALYSIS

Selected studies were manually reviewed, and key data were extracted regarding:

- Mechanism of action and pharmacodynamics of the drugs [15, 17, 20].
- Clinical efficacy in terms of fracture risk reduction and bone mineral density (BMD) improvement [19, 21, 29–32].
- Safety and tolerability profiles, including rare adverse effects [24–26].
- Factors influencing adherence and treatment discontinuation [27–28].
- Guidelines, expert consensus, cost-effectiveness data, and access limitations [34–42]

The results were grouped thematically and discussed in the context of current clinical recommendations and regional implementation challenges. No formal meta-analysis or statistical synthesis was performed, as the review aimed to provide a qualitative and contextual summary of the existing evidence base.

FINDINGS

1. POSTMENOPAUSAL OSTEOPOROSIS – CLINICAL CHARACTERISTICS

1.1. Definition and Classification of Osteoporosis

According to the World Health Organization (WHO) definition from 1994, osteoporosis is a skeletal disorder characterized by decreased bone mass, disruption of the microarchitecture of bone tissue, and increased bone fragility, which raises the risk of fractures, particularly in the spine, wrists, and hips [1].

Osteoporosis can be classified by cause, age of onset, and mechanism of development. Primary osteoporosis, which develops without an external cause, is divided into type I (postmenopausal) and type II (age-related). Secondary osteoporosis develops as a result of other diseases or medications, such as hyperthyroidism, Cushing's syndrome, or prolonged use of glucocorticoids [1]. Another criterion is the age at which osteoporosis occurs. In children and adolescents, it is rarer and often associated with inherited bone metabolism disorders, such as osteogenesis imperfecta [2]. Osteoporosis can also be classified by the mechanism of development: involutional osteoporosis, related to aging, and idiopathic osteoporosis, occurring in younger individuals without a clear cause [1].

1.2. Pathophysiology of Osteoporosis in Postmenopausal Women

Postmenopausal osteoporosis results from decreased estrogen levels, disrupting the balance between bone resorption and formation. The reduction in estrogen leads to increased activity of osteoclasts (responsible for bone resorption) and decreased activity of osteoblasts (responsible for bone formation). The result is bone mass loss, weakened bone structure, and an increased risk of fractures, especially in the spine, wrists, and hips [3]. Additionally, this process is aggravated by oxidative stress and chronic inflammation, which accelerate bone resorption, as well as the accumulation of senescent cells that affect the bone marrow microenvironment and accelerate resorption processes [4, 5]. Changes in bone structure in postmenopausal women primarily involve the loss of bone mass in trabecular bones, leading to increased bone fragility and a higher risk of fractures, even with minimal trauma [3].

1.3. Epidemiology – Prevalence and Health Impact

Osteoporosis is a common metabolic bone disease affecting millions of people worldwide. It is estimated that over 200 million people suffer from osteoporosis, and approximately one-third of women and one in five men over the age of 50 will experience an osteoporotic fracture in their lifetime [6]. In developed countries, depending on diagnostic methods, osteoporosis affects 2% to 8% of men and 9% to 38% of women [6]. Osteoporosis leads to numerous fractures that have significant health consequences. In 2019, approximately 37 million osteoporotic fractures were registered worldwide in individuals over the age of 55. These fractures significantly worsen quality of life, and hip fractures, particularly in the elderly, may be associated with higher mortality [6].

1.4. Risk Factors

Risk factors for osteoporosis are divided into non-modifiable and modifiable. Genetic factors, such as a family history of osteoporosis, especially in mothers or sisters, increase the risk of developing the disease [7]. White and Asian women are more prone to osteoporosis due to differences in bone structure and metabolism [8]. Smoking increases osteoclast activity, weakening bones, while regular physical activity, especially weight-bearing exercises, increases bone density [9]. Deficiencies in calcium and vitamin D weaken bone structure [10], and low BMI increases the risk of osteoporosis due to lower estrogen production [11]. Regular alcohol consumption weakens bone metabolism, and early menopause (before age 45) accelerates bone mass loss [13]. Women who have had more than six pregnancies are more susceptible to osteoporosis due to hormonal fluctuations [11]. Hyperthyroidism and prolonged use of glucocorticoids also increase the risk of osteoporosis [11, 14].

One of the earliest population-level studies on fracture risk factors emphasized age, family history, low BMI, and

smoking as significant contributors to osteoporotic fractures [12].

2. PHARMACOTHERAPY FOR OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN

2.1. Goals of Pharmacotherapy

The primary goal of pharmacotherapy for osteoporosis in postmenopausal women is to reduce fracture risk, improve bone density, and slow down bone resorption. Medications used in the treatment of osteoporosis, such as bisphosphonates, denosumab, raloxifene, and teriparatide, influence bone metabolism by affecting different mechanisms that regulate bone formation and resorption. The choice of therapy depends on the individual patient's needs, health status, and fracture risk [15].

2.2. Anti-resorptive Medications

Anti-resorptive medications play a crucial role in osteoporosis treatment, as their main goal is to inhibit the process of bone resorption, thus preventing bone loss. These medications help to halt bone mass loss, increase bone mineral density (BMD), and reduce fracture risk, especially in the spine and peripheral bones. Bisphosphonates and denosumab, while working through different mechanisms, both show high effectiveness in treating osteoporosis [21].

2.2.1. Bisphosphonates

AACE/ACE, ACR, NAMS, and the Endocrine Society recommend bisphosphonates (except ibandronate) as the first-line treatment for osteoporosis in postmenopausal women, men, and patients with steroid-induced osteoporosis (GIO). Bisphosphonates inhibit bone resorption by osteoclasts, increasing bone mass and reducing fracture risk. Alendronate, risedronate, and zoledronic acid (IV) are effective in improving BMD. Ibandronate is not the preferred choice despite its effectiveness in reducing vertebral fracture risk.

Bisphosphonates are available as oral tablets or intravenous injections, administered at long intervals. The dosing schedule depends on the treatment objective. Bisphosphonates are excreted by the kidneys, which may cause toxicity in patients with renal impairment. They should be taken on an empty stomach while remaining upright for 30 minutes after ingestion to avoid esophageal irritation.

Adverse effects include gastrointestinal issues, osteonecrosis of the jaw (ONJ), and atypical femur fractures (AFF) with long-term use. The FDA recommends treatment holidays, especially in patients with moderate or low fracture risk. Studies such as the Fracture Intervention Trial (FIT) have shown that alendronate effectively reduces vertebral fracture risk, and 5 years of treatment may be sufficient to maintain therapeutic benefits. Women with low BMD may benefit from longer treatment [21].

2.2.2. Denosumab

Denosumab is a monoclonal biological drug used to treat osteoporosis in patients at high fracture risk and those unable to use oral therapies. It works by inhibiting RANKL, reducing osteoclast activity and bone loss.

The drug is FDA-approved for treating osteoporosis in postmenopausal women, breast cancer patients receiving aromatase inhibitors, and men with prostate cancer. Denosumab reduces fracture risk in the spine, hip, and peripheral bones, and increases BMD.

It is administered subcutaneously every six months at a dose of 60 mg and is well-tolerated, though side effects may include infections, skin reactions, musculoskeletal pain, and hypocalcemia. It does not require dose adjustment in patients with renal or hepatic impairment but should be used cautiously in those with severe renal impairment. According to AACE/ACE guidelines, treatment holidays are not recommended, as discontinuation leads to a decrease in BMD [21].

2.3. Anabolic Medications

Anabolic medications in osteoporosis treatment focus on stimulating bone formation, reducing fracture risk, and improving bone health. Two widely used drugs in osteoporosis therapy are teriparatide and romosozumab. Although their mechanisms of action differ, both aim to reduce fracture risk, particularly in high-risk osteoporosis patients.

2.3.1. Teriparatide

Teriparatide, a fragment of parathyroid hormone, is an anabolic drug that stimulates osteoblasts to produce new bone tissue, leading to increased BMD and improved bone structure.

Studies show that teriparatide effectively reduces vertebral fracture risk by up to 65% and improves spinal bone density, especially in women with prior fractures [19]. It also reduces the risk of fractures in other bones, such as the hip.

Teriparatide is mainly used in short-term therapy, usually for up to two years, due to the risk of bone weakening and

osteosarcoma with long-term use. After therapy, continuation with other drugs, such as bisphosphonates, is recommended.

2.3.2. Romosozumab

Romosozumab is an anabolic drug that blocks sclerostin, increasing osteoblast activity and stimulating new bone formation while reducing bone resorption. It is one of the most effective medications in osteoporosis treatment.

Recent data confirm that romosozumab significantly increases BMD and reduces vertebral and clinical fractures in postmenopausal women with high fracture risk [20].

Studies have shown that romosozumab is more effective than alendronate in preventing vertebral and peripheral fractures. Its use for 12 months leads to significant increases in BMD. Romosozumab is used in short-term therapy, after which it is typically necessary to switch to other treatments.

It is particularly recommended for patients with high fracture risk who have not achieved expected results with bisphosphonates [20].

2.4. Selective Estrogen Receptor Modulators (SERM) – Raloxifene

Raloxifene is a selective estrogen receptor modulator (SERM) used in the treatment of osteoporosis in postmenopausal women. It acts as an agonist in tissues such as bones and as an antagonist in others, such as the breasts and endometrium, making it an attractive alternative to traditional hormone replacement therapy (HRT) [17].

Raloxifene increases BMD in the spine and hip, contributing to a reduced risk of vertebral fractures in postmenopausal women [3]. Additionally, clinical studies have shown that raloxifene reduces the risk of breast cancer by 65%, particularly in estrogen-dependent tumors [18].

2.5. Hormone Replacement Therapy (HRT)

Hormone replacement therapy (HRT) is used to treat osteoporosis in postmenopausal women, particularly those with menopausal symptoms. Estrogens, such as estradiol, inhibit bone resorption, reducing fracture risk, especially in the spine and hips.

Studies suggest that HRT can reduce body fat post-menopause, but it does not significantly affect BMD compared to untreated women. HRT is not recommended as first-line therapy and should be considered in women with menopausal symptoms or when other methods are contraindicated or ineffective [16]. The decision to start therapy should be individualized, weighing the benefits and risks.

2.6. Contemporary Treatment Strategies and Therapeutic Challenges in Poland and Europe

Modern approaches to the pharmacological management of postmenopausal osteoporosis increasingly emphasize not only the selection of an individual drug but also long-term therapeutic strategy — including treatment sequencing, duration, and continuity. Recent reviews highlight the effectiveness of sequential therapy, where anabolic agents are used initially, followed by antiresorptive maintenance treatment. This strategy has been shown to yield better improvements in bone mineral density (BMD) and greater fracture risk reduction compared to monotherapy [36,37,41].

Another emerging clinical issue involves treatment discontinuation. In particular, sudden withdrawal of denosumab without subsequent therapy can lead to rapid BMD loss and a sharp increase in vertebral fractures, known as the "rebound effect" [37,38]. Therefore, transition planning — often involving bisphosphonates — is essential.

The 2024 UK clinical guidelines recommend individualized treatment based on fracture risk, age, comorbidities, patient preferences, and drug availability [39]. In Poland, however, the implementation of such personalized care is hindered by limited access to novel therapies. For example, romosozumab is currently not reimbursed by the national health system, which significantly restricts its use in outpatient settings. Compared to other EU countries, treatment options in Poland are often constrained by financial and systemic barriers.

According to the International Osteoporosis Foundation (IOF), over 25% of postmenopausal women in Central Europe, including Poland, are at high risk of fragility fractures [42]. It is estimated that approximately 2.1 million women in Poland are affected by osteoporosis, with over 120,000 osteoporotic fractures annually, most commonly involving the hip, spine, and wrist. Despite the scale of the problem, Poland still lacks a population-based screening program for osteoporosis. Access to dual-energy X-ray absorptiometry (DXA) and public awareness of early diagnostics remain insufficient.

Economic considerations are also gaining importance. Pharmacoeconomic analyses suggest that effective pharmacological prevention of fractures in high-risk patients is cost-saving in the long term, by reducing hospitalizations, long-term care needs, and loss of independence [40].

Finally, hormonal therapies — including estrogens and selective estrogen receptor modulators (SERMs) — continue to be considered in selected patients. However, their use requires careful evaluation of cardiovascular and thromboembolic risks [6].

These considerations underline the complexity of osteoporosis management in real-world settings, particularly in Central and Eastern Europe, where access, cost-effectiveness, and policy decisions shape therapeutic outcomes.

3. CRITERIA FOR ASSESSING THE EFFECTIVENESS OF OSTEOPOROSIS TREATMENT

The effectiveness of osteoporosis treatment is assessed based on several key criteria, which include both biomarkers and clinical outcomes. It is important to note that treatment efficacy depends not only on improvements in bone mineral density (BMD) but also on fracture risk reduction, therapy tolerance, and the frequency and convenience of medication administration.

3.1. Bone Mineral Density (BMD) – Measurement and Interpretation

Bone mineral density (BMD) is a key indicator used to assess the effectiveness of osteoporosis treatment. The most commonly used method for measuring BMD is dual-energy X-ray absorptiometry (DXA), which accurately determines bone density in areas such as the lumbar spine and hip. An increase in BMD after therapy is strong evidence of reduced fracture risk. Studies, such as Osteoporosis: Clinical Evaluation, confirm that DXA is considered the gold standard for assessing BMD, and its results are widely used for monitoring treatment effects and fracture risk assessment [22].

3.2. Fracture Risk – Clinical Assessment Methods

Fracture risk in postmenopausal women is assessed using the FRAX tool (Fracture Risk Assessment Tool), which takes into account key risk factors such as age, body mass, fracture history, smoking, alcohol consumption, and the use of glucocorticoids. FRAX allows for the estimation of a 10-year fracture risk, providing valuable support in making therapeutic decisions.

Additionally, it is essential to regularly monitor changes in BMD and measure bone turnover markers such as CTX (C-terminal cross-linked telopeptide) and BSAP (bone-specific alkaline phosphatase), which can provide information on treatment effectiveness and support patients in continuing therapy [23].

3.3. Side Effects and Therapy Tolerance

The effectiveness of osteoporosis treatment is not only determined by the action of medications but also by their tolerance by patients. Adverse effects such as gastrointestinal issues, musculoskeletal pain, flu-like symptoms, osteonecrosis of the jaw, and atypical bone fractures may hinder the continuation of therapy. Long-term use of bisphosphonates also increases the risk of heart rhythm disorders, particularly atrial fibrillation.

Poor therapy tolerance is a major reason for premature treatment discontinuation, with about 20-30% of patients discontinuing therapy within the first year. To improve adherence, it is important to educate patients about potential side effects, adjust treatment regimens, and regularly monitor both efficacy and adverse effects. Psychological support can also help patients continue therapy. Adherence to osteoporosis treatment is critical for treatment success, and poor adherence, particularly with oral bisphosphonates, can hinder treatment outcomes [24, 25, 26]. Traditional dosing regimens, such as daily or weekly administration, can be difficult to maintain, with around 50% of patients discontinuing therapy in the first year [27]. Less frequent dosing regimens, such as monthly or quarterly, improve adherence and may lead to better treatment outcomes [28]. Patient preferences regarding dosing frequency significantly impact adherence to therapeutic recommendations [27].

4. COMPARISON OF THE EFFECTIVENESS OF SELECTED MEDICATIONS

4.1. Review of Clinical Trials and Meta-Analyses

The treatment of osteoporosis in postmenopausal women includes various groups of medications, including bisphosphonates, denosumab, parathyroid hormone, selective estrogen receptor modulators (SERM), and hormone therapy. Clinical studies and meta-analyses assessing the efficacy and safety of these therapies provide important insights for clinical practice.

Bisphosphonates: Drugs such as alendronate, risedronate, and zoledronic acid are widely used in the treatment of osteoporosis. Meta-analysis has shown that bisphosphonates reduce the risk of vertebral, hip, and wrist fractures in postmenopausal women [29].

Denosumab: This monoclonal antibody inhibits osteoclast activation. Studies indicate that denosumab effectively reduces fracture risk and improves bone mineral density (BMD) in postmenopausal women [30].

Parathyroid hormone (teriparatide): This anabolic drug stimulates the formation of new bone tissue. Studies have shown that teriparatide significantly reduces the risk of vertebral and non-vertebral fractures in women with severe osteoporosis [31].

Selective Estrogen Receptor Modulators (SERM): Raloxifene is an example of a SERM, which acts similarly to estrogen in certain tissues, including bones. Meta-analysis has shown that raloxifene increases BMD and reduces the risk of vertebral fractures [32].

Hormone Therapy (HT): Estrogen therapy is effective in preventing bone mass loss and reducing fracture risk in postmenopausal women. However, its use is associated with the risk of adverse effects, such as increased risk of breast cancer and cardiovascular diseases [33].

4.2. Discussion of Treatment Outcome Differences

The differences in efficacy and safety of various therapies stem from their mechanisms of action and patient profiles. Bisphosphonates and denosumab are effective in preventing bone mass loss and reducing fracture risk, but bisphosphonates require long-term use and may be associated with the risk of osteonecrosis of the jaw. Denosumab, though effective, requires regular injections every 6 months.

Parathyroid hormone (teriparatide) acts anabolically, stimulating the formation of new bone tissue, making it effective in treating severe osteoporosis. However, its use is limited to a 2-year period.

Raloxifene, a selective estrogen receptor modulator, increases BMD and reduces the risk of vertebral fractures but may increase the risk of thrombosis.

Hormone therapy (HT) is effective in preventing bone mass loss and reducing fracture risk, but it is associated with higher risks of adverse effects, such as breast cancer and cardiovascular diseases.

The selection of therapy for osteoporosis in postmenopausal women should be individualized, taking into account age, health status, fracture risk, patient preferences, and the presence of other conditions. Younger women without menopausal symptoms are preferred candidates for bisphosphonates or denosumab, while older women with fractures or low bone density are recommended parathyroid hormone or romosozumab [34].

Women with a high risk of fractures may benefit from anabolic therapies, such as parathyroid hormone or romosozumab [34]. It is important to consider patient preferences to improve adherence to treatment, such as selecting therapies that require less frequent administration.

In the case of cardiovascular or oncological diseases, hormone therapy should be avoided, with bisphosphonates, denosumab, or parathyroid hormone being preferred. Often, a combination of pharmacological therapies with lifestyle modifications, such as a diet rich in calcium and vitamin D and physical activity, is used [34, 35].

Table 1. Comparison of key pharmacologic therapies for postmenopausal osteoporosis by mechanism, efficacy in fracture risk reduction, adverse effects, route of administration, and dosing frequency.

Drug	Mechanism	Efficacy (Fracture Reduction)	Notable Risks	Route	Dosing Frequency
Bisphosphonates	Anti-resorptive (osteoclasts)	★★★★☆ Vertebral & Hip	GI irritation, ONJ (Osteonecrosis of the Jaw), atypical fractures	Oral / IV	Weekly / Yearly
Denosumab	RANKL inhibitor	★★★★★ Vertebral & Hip	Hypocalcemia, rebound fractures	Subcutaneous	Every 6 months
Teriparatide	Anabolic (PTH analog)	★★★★★ Severe osteoporosis	Osteosarcoma (theoretical risk)	Subcutaneous	Daily (max 2 years)

Romosozumab	Sclerostin inhibitor	★★★★★ Very high fracture risk	Cardiovascular events (possible), injection site reaction	Subcutaneous	Monthly (up to 12 months)
Raloxifene	SERM	★★☆☆☆ Vertebral only	Thrombosis, hot flashes	Oral	Daily
HRT	Estrogen replacement	★★★☆☆ Vertebral & Hip	Breast cancer, stroke, MI	Oral / Transdermal	Daily

RESULTS

The analysis of selected clinical studies and reviews demonstrates notable differences in the efficacy, mechanisms of action, and safety profiles of the main pharmacological groups used in postmenopausal women with osteoporosis [21, 29–32, 35–41].

Bisphosphonates remain the most consistently validated first line therapy. Randomized trials have shown that alendronate, risedronate, and zoledronic acid reduce the risk of vertebral and non vertebral fractures and increase bone mineral density. Their effectiveness is supported by the FIT trial and other large clinical studies [21, 29].

Denosumab has demonstrated fracture risk reduction comparable to bisphosphonate based regimens. Large studies confirm increases in bone mineral density at the lumbar spine and hip with long term therapy [30, 31]. Its twice yearly administration improves adherence compared with oral regimens [27, 28]. However, discontinuation is associated with rapid loss of bone mineral density and a risk of multiple vertebral fractures, as documented in recent reviews, which has led to the requirement for mandatory transition to antiresorptive agents after stopping denosumab [38, 41].

Anabolic agents, including teriparatide and romosozumab, show pronounced clinical efficacy in women with severe osteoporosis or very high fracture risk. Teriparatide reduces vertebral and non vertebral fractures, particularly in women with previous fractures [19]. Romosozumab exerts a dual effect by stimulating bone formation and decreasing bone resorption, and comparative studies show that it is more effective than alendronate in preventing vertebral fractures [20].

Selective estrogen receptor modulators increase bone mineral density primarily at the spine and reduce vertebral fracture risk, which has been confirmed in multiple studies [17, 18, 32]. Their effect on hip fracture risk remains limited. A further clinical advantage is the reduction of estrogen dependent breast cancer risk [15], which makes them suitable for certain patient groups.

Hormone therapy slows bone loss and reduces fracture risk but its use is limited by the risk of cardiovascular and oncological complications, as noted in contemporary clinical guidelines [16, 33].

Treatment adherence remains a key determinant of pharmacotherapy effectiveness. Multiple studies have shown that a significant proportion of women discontinue treatment within the first year. Adherence is influenced by dosing regimen, treatment tolerability, and patient awareness [24–28].

Overall, the analysis confirms the need for individualized pharmacotherapy tailored to clinical risk, severity of osteoporosis, comorbidities, and patient preferences. Bisphosphonates and denosumab have the broadest evidence base, while anabolic agents provide the most pronounced benefit in women with severe disease [34–37]. Non pharmacological measures, including adequate calcium and vitamin D intake and regular physical activity, enhance the clinical effectiveness of treatment [6, 34, 35].

DISCUSSION

INTERPRETATION OF RESULTS

Postmenopausal osteoporosis, driven by estrogen deficiency, disrupts the balance between bone formation and resorption, resulting in accelerated bone loss and increased susceptibility to fragility fractures in the spine, hip, and wrist [3,4]. The reviewed therapeutic classes, including bisphosphonates, denosumab, parathyroid hormone analogs such as teriparatide, romosozumab, and selective estrogen receptor modulators, consistently demonstrate the ability to increase bone mineral density and reduce fracture incidence across different groups of postmenopausal women [19,20,21,29–32].

Hormone replacement therapy provides an effective option for bone preservation in women with concurrent menopausal symptoms; however, its use is limited by safety concerns, notably cardiovascular complications and hormone dependent malignancies, which require careful risk stratification before initiation [16,33].

Denosumab, administered every six months, and anabolic agents such as teriparatide and romosozumab show particular advantage in women with high or very high fracture risk. These therapies demonstrate greater gains in bone mineral density and more robust fracture protection in populations with severe osteoporosis. Their selection should be guided by comprehensive risk evaluation, comorbidities, patient preference regarding mode and frequency of administration, and the need for structured follow up to ensure safe continuation or transition of therapy [30,31,34].

Access and reimbursement continue to influence real world treatment patterns. The availability of recently approved agents such as romosozumab varies widely between healthcare systems. In several Central and Eastern European countries, including Poland, restricted reimbursement and limited access to innovative treatments impede personalization of therapy and may negatively affect fracture outcomes at the population level [38,42].

LIMITATIONS OF AVAILABLE DATA AND THIS REVIEW

Although numerous randomized trials and meta analyses support the efficacy of current osteoporosis treatments, several limitations affect both the evidence base and the present review. Many pivotal studies are of short to medium duration, which restricts understanding of long term safety and the durability of treatment effects [29,35]. Variability in outcome measures, including differences in fracture definitions, bone mineral density assessment techniques such as DXA, and clinical risk evaluation tools such as FRAX, may contribute to heterogeneity and inconsistency across published results [22,23].

Important evidence gaps remain in several clinical domains. Long term effects of anabolic therapies, real world adherence patterns, and comparative effectiveness in older patients with multimorbidity are insufficiently represented in the literature. Many trials exclude frail or very elderly women, limiting generalizability of the findings.

Another limitation concerns the diagnostic landscape. In many regions, including Central and Eastern Europe, osteoporosis remains underdiagnosed, and a substantial proportion of fragility fractures occur in women without a prior osteoporosis diagnosis. This diagnostic gap complicates the interpretation of real world treatment outcomes and reduces the applicability of clinical trial results to routine care.

For denosumab, most long term studies do not fully address the clinical consequences of treatment discontinuation. Evidence on rebound associated multiple vertebral fractures remains largely derived from observational data, which limits the strength of conclusions about long term management strategies.

Data regarding therapy in women with advanced chronic kidney disease also remain limited. Differences in pharmacokinetics and safety profiles restrict the use of certain drug classes, yet evidence supporting optimal treatment choices in this population is scarce.

The present review focused primarily on pharmacological interventions with established regulatory approval and clinical relevance. Non pharmacological strategies such as nutritional optimization, physical activity, fall prevention, and adequate vitamin D and calcium intake, although essential components of osteoporosis management, were not examined in depth [6,21]. Future research should integrate pharmacologic therapy with behavioral, educational, and system level interventions to improve outcomes and address the gaps in diagnostic coverage, treatment adherence, and access to innovative therapies [27,34].

PRACTICAL IMPLICATIONS FOR PHYSICIANS AND PATIENTS

Effective management of postmenopausal osteoporosis requires personalized therapeutic strategies tailored to patient characteristics, risk factors, and treatment goals. The selection between bisphosphonates, denosumab, and anabolic agents should consider fracture risk, comorbidities, renal function, and patient adherence potential [16,21,34].

Medication adherence is a major determinant of clinical effectiveness. Adverse effects (e.g., gastrointestinal intolerance with bisphosphonates) and complex dosing regimens remain key reasons for premature discontinuation [24,25,26]. Less frequent administration (e.g., semiannual injections) and improved patient education may enhance long-term compliance [26–28]. Sequential antiresorptive therapy is required after completing a course of anabolic treatment to maintain gained bone mineral density and sustain fracture risk reduction.

Physicians should involve patients in shared decision-making, highlighting treatment benefits, risks, and expected outcomes. Importantly, pharmacotherapy should be supported by education on lifestyle modifications, such as weight-bearing exercise, smoking cessation, and fall risk reduction, which together may amplify the benefits of medical treatment.

A comprehensive, patient-centered approach that integrates pharmacotherapy, lifestyle interventions, and consideration of healthcare system constraints is essential to optimize outcomes and reduce the burden of osteoporosis-related fractures.

CONCLUSIONS

Postmenopausal osteoporosis arises from estrogen deficiency, which disrupts the balance between bone formation and bone resorption. Understanding these pathophysiological mechanisms allows for a rational selection of pharmacological strategies and helps identify patient groups most vulnerable to loss of bone mineral density and fractures.

The analysis of pharmacological options shows that bisphosphonates, denosumab, teriparatide, romosozumab, and selective estrogen receptor modulators provide clinically meaningful reductions in vertebral and non-vertebral fracture risk and increase bone mineral density. Their clinical usefulness depends on baseline fracture risk, comorbidities, previous fractures, renal function, and individual tolerability.

Safety profiles differ substantially between therapeutic classes. Long term therapy with bisphosphonates is limited by rare but clinically significant complications. Denosumab is effective but requires carefully planned discontinuation to prevent rapid loss of bone mineral density and the risk of multiple vertebral fractures. Anabolic agents provide the most pronounced improvement in bone parameters but require subsequent antiresorptive therapy to maintain the achieved effect. These distinctions confirm the need for individualized risk based assessment.

Treatment adherence remains a central determinant of long term outcomes. Adverse effects, complex dosing regimens, and limited patient understanding contribute to early treatment discontinuation. Simplified dosing schedules and educational support improve persistence and clinical results.

Sequential therapy is essential for sustaining improvements achieved with anabolic agents and for maintaining long term fracture risk reduction. Decisions regarding transitions between therapeutic classes must take into account clinical risk, age, comorbidities, and medication tolerability.

Access to therapy significantly influences real world treatment patterns. Limited availability of modern medications and lack of reimbursement, particularly in Central European countries, reduce the possibility of personalized therapy and affect actual clinical outcomes. These constraints highlight the need to improve access to diagnostic methods and contemporary pharmacologic treatments.

Taken together, the findings of this review demonstrate that effective management of postmenopausal osteoporosis requires a comprehensive, individualized, and clinically grounded approach that incorporates the pathophysiological mechanisms of the disease, proven efficacy and safety of medications, treatment adherence, and healthcare system limitations.

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USE OF AI

The authors declare that no artificial intelligence tools were used to generate, analyze, or interpret scientific content in this manuscript. AI assisted only in grammar checking and formatting without influencing the scientific conclusions.

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