

PHARMACOLOGIC THERAPY OF POSTMENOPAUSAL OSTEOPOROSIS: AN UPDATED NARRATIVE REVIEW OF GUIDELINES AND EVIDENCE

ABSTRACT

Postmenopausal osteoporosis is a highly prevalent skeletal disorder that confers a substantial burden of fragility fractures, disability, loss of independence, and mortality. Over the past two decades, several potent antiresorptive and osteoanabolic agents have transformed clinical care. Yet, real-world treatment gaps persist and the optimal choice, sequencing, and duration of therapy remain the subject of evolving guidance. This narrative review synthesizes contemporary international and national guideline recommendations, pivotal randomized trials, and extension studies bearing on the pharmacologic management of postmenopausal osteoporosis. We discuss oral and parenteral bisphosphonates, denosumab, teriparatide and abaloparatide, romosozumab, selective estrogen receptor modulators (SERMs), menopausal hormone therapy, and calcitonin, with emphasis on efficacy against vertebral, nonvertebral, and hip fractures; time to benefit; adverse effects including atypical femoral fractures and osteonecrosis of the jaw; drug holidays; and the increasingly important concepts of sequential and goal-directed therapy. We also highlight updated guideline algorithms for risk stratification, the role of FRAX and recency of fracture, and pragmatic strategies for monitoring response and minimizing rebound phenomena after treatment discontinuation. Evidence supports a tailored approach that aligns drug choice and sequence with absolute fracture risk and patient comorbidity, prioritizing antiresorptives for most high-risk patients and an anabolic-first strategy for the very-high-risk phenotype.

INTRODUCTION

Worldwide, osteoporotic fractures represent a major cause of morbidity, with hip and vertebral fractures carrying the greatest clinical impact. Contemporary guidance from endocrine and bone societies converge on the need to identify high- and very-high-risk women and initiate effective therapy promptly after a fragility fracture, ideally within weeks, to reduce imminent risk. The 2024 UK National Osteoporosis Guideline Group (NOGG) update and recent papers from the International Osteoporosis Foundation (IOF) underscore persistent undertreatment and advocate system-level solutions alongside optimized pharmacotherapy. FRAX® remains central for absolute fracture risk estimation, now calibrated to >80 countries and with adjustments for fracture recency available in FRAXplus®. In clinical practice, treatment thresholds and the choice of first-line therapy depend on age, bone mineral density (BMD), fracture history and recency, glucocorticoid exposure, and comorbidity including cardiovascular disease. [1–6, 16–20, 43].

Risk Stratification and When to Treat

Current guidelines categorize risk on the basis of T-scores, prior fractures, FRAX probabilities, and markers of imminent risk. Women with a recent vertebral or hip fracture, multiple fractures, very low T-scores (e.g., ≤ -3.0), or high glucocorticoid exposure fall into very-high-risk categories wherein anabolic-first strategies or potent parenteral antiresorptives are preferred. Those at high risk without the very-high-risk features often begin with an oral bisphosphonate or yearly intravenous zoledronic acid. FRAX 10-year probabilities guide initiation in women without prior fractures, and country-specific intervention thresholds are recommended. The updated NOGG guidance provides a clear algorithm mapping clinical probabilities to initial therapy and emphasizes early post-fracture intervention within fracture liaison services. [1–5, 16–20].

Overview of Pharmacologic Classes

The principal pharmacologic classes include bisphosphonates (alendronate, risedronate, ibandronate, and zoledronic acid), the RANKL inhibitor denosumab, osteoanabolic agents teriparatide and abaloparatide (PTH analogs) and romosozumab (sclerostin inhibitor with dual anabolic/antiresorptive effects), SERMs (raloxifene and bazedoxifene), menopausal hormone therapy (MHT), and calcitonin with limited contemporary indications. The selection among these agents balances antifracture efficacy at key sites, tolerance and adherence profiles, renal function, injection preferences, concomitant disease, and safety considerations such as cardiovascular risk for romosozumab and rebound risk following denosumab cessation. [1–6, 8–15, 21–44].

(zoledronic acid) extension data, as well as ASBMR task force guidance. [7–10, 22–28, 34–41]. Table 1 describes selected efficacy and characteristics of Bisphosphonates

Table 1. Selected Efficacy and Characteristics of Bisphosphonates

Agent	Regimen	Vertebral fracture reduction	Nonvertebral/hip evidence	Key trials and notes
Alendronate	70 mg weekly oral	Significant	Nonvertebral and hip reduction demonstrated	FIT and FLEX; durable benefit; consider holiday after 5 years in moderate risk [24–26, 28]
Risedronate	35 mg weekly oral	Significant	Hip reduction in osteoporotic elderly women	HIP trial; benefit greatest with low BMD at baseline [24, 27, 29]
Ibandronate	150 mg monthly oral or 3-monthly IV	Significant vertebral reduction	Limited evidence for hip reduction	BONE study; consider spine-predominant risk [24, 30]
Zoledronic acid	5 mg IV yearly	Significant	Significant hip and nonvertebral reduction	HORIZON PFT and extensions; acute-phase reactions manageable [11, 27]

Denosumab

Denosumab, a monoclonal antibody to RANKL, produces potent suppression of bone resorption and increases in BMD with half-yearly subcutaneous dosing. In the pivotal FREEDOM trial, denosumab significantly reduced vertebral, nonvertebral, and hip fractures, with sustained efficacy and safety through 10 years in extension studies. Denosumab is attractive in patients with renal impairment where bisphosphonates are limited, and in those intolerant of oral therapy. The central caveat is the rebound phenomenon upon discontinuation—rapid rise in bone turnover markers, loss of BMD gains within months, and increased risk of multiple vertebral fractures—necessitating planned sequential antiresorptive therapy, typically with zoledronic acid or a potent oral bisphosphonate, timed to the next due dose. Recent reviews refine risk factors and mitigation strategies, though complete prevention of rebound fractures is not guaranteed. Counselling must emphasize adherence to 6-monthly dosing and a structured exit plan. [11–14, 29–33].

Figure 2. Denosumab Discontinuation: Consolidation Strategy (Flowchart)

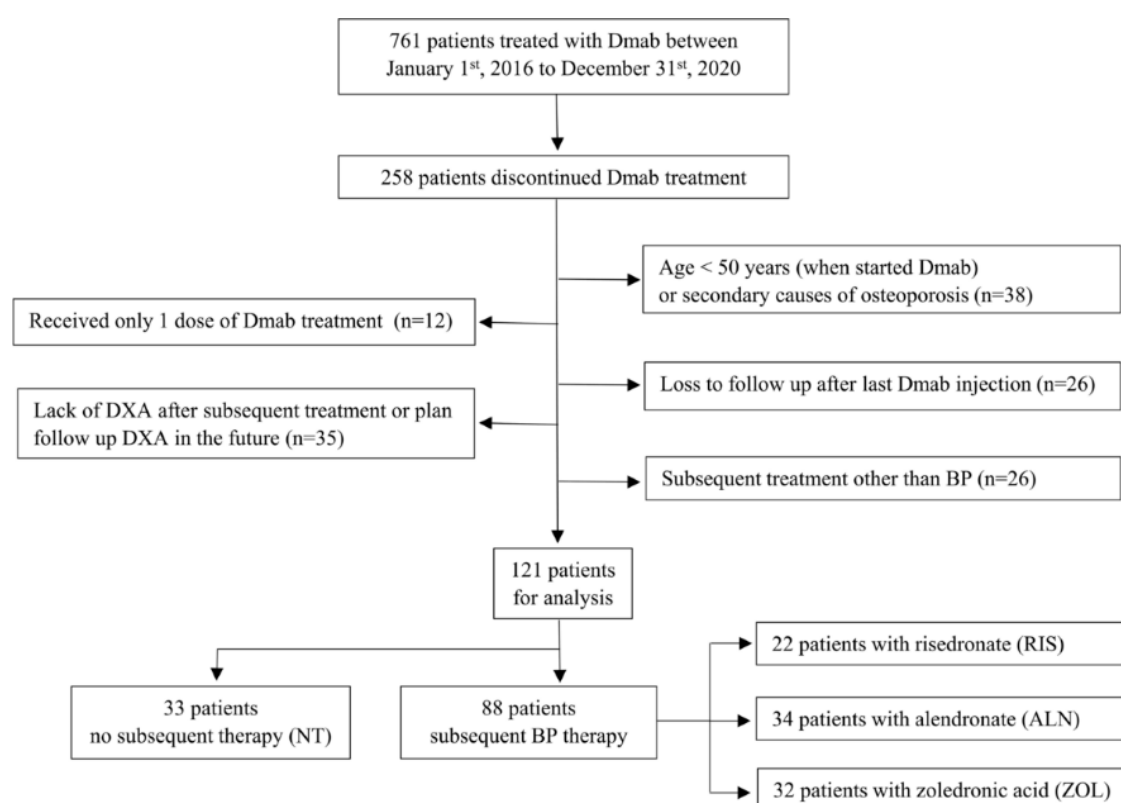


Figure 2 illustrates the clinical pathway following denosumab discontinuation, emphasizing transition to bisphosphonate therapy—particularly intravenous zoledronic acid—to prevent rebound bone loss. It highlights individualized timing based on bone turnover and density monitoring, ensuring ongoing fracture surveillance and optimal skeletal protection after cessation of denosumab therapy.

[29–33],[50]

Osteoanabolic Therapies: Teriparatide and Abaloparatide

Teriparatide (PTH 1–34) and abaloparatide (PTHrPanalog) stimulate bone formation, rapidly increase spine BMD, and reduce vertebral fractures; teriparatide also reduces clinical nonvertebral fractures in high-risk women. The head-to-head VERO trial showed teriparatide superiority over risedronate for vertebral and clinical fractures in women with severe osteoporosis. Abaloparatide in ACTIVE significantly reduced vertebral and nonvertebral fractures compared with placebo, with a lower rate of hypercalcemia than teriparatide, and the ACTIVEExtend sequence demonstrated sustained fracture reduction when followed by alendronate. The approved duration of PTH analog therapy is limited (generally up to 24 months lifetime exposure for teriparatide and 18 months for abaloparatide), after which transition to a potent antiresorptive is essential to preserve gains. Anabolic-first sequencing, particularly for very-high-risk phenotypes with recent vertebral fractures or very low T-scores, achieves larger and faster BMD gains and superior early fracture risk reduction than antiresorptive-first strategies. [18, 21, 35–39]. Table 2 shows osteoanabolic agents along with their efficacy and use.

128 **Table 2. Osteoanabolic Agents: Efficacy and Use**

Agent	Duration	Vertebral	Nonvertebral	Hip	Typical next step
Teriparatide, 20 µg SC daily	Up to 24 mo	Strong reduction	Reduction in clinical fractures; mixed for hip	Limited direct hip data	Follow with zoledronic acid or denosumab
Abaloparatide, 80 µg SC daily	18 mo	Strong reduction	Reduction observed	Limited direct hip data	Follow with alendronate or IV bisphosphonate; ACTIVEExtend support

129 [20, 23, 37–41].

130 **Romosozumab**

131 Romosozumab inhibits sclerostin, producing a dual effect of stimulating bone formation and
132 decreasing resorption. In FRAME and especially ARCH (romosozumab for 12 months
133 followed by alendronate versus alendronate alone), substantial early gains in BMD and
134 greater reductions in vertebral and clinical fractures were observed in women at high fracture
135 risk. Regulatory labeling carries a boxed warning regarding potential increased risk of
136 myocardial infarction, stroke, and cardiovascular death, based primarily on imbalances in the
137 ARCH trial year-1 comparisons to alendronate. Contemporary guidance recommends
138 avoiding initiation in women with MI or stroke in the prior year and caution in those with
139 high cardiovascular risk. After the 12-month romosozumab course, transition to an
140 antiresorptive is required to maintain gains. Ongoing analyses continue to evaluate the
141 cardiovascular signal, but label precautions remain in place. [6, 7, 12, 40–42]. Table 3
142 summarises key points on Romosozumab.

143

144 **Table 3. Romosozumab: Key Points**

Feature	Evidence summary
Rapid BMD gains at spine and hip within 6–12 months	Consistent across trials; larger than antiresorptives over the same period [6, 12]
Greater reduction in vertebral and clinical fractures versus alendronate over 24 months in ARCH	Supports anabolic-first in very-high-risk patients [6, 12]
CV boxed warning	Avoid initiation within 1 year of MI/stroke; weigh risks in high CV risk [40–42]
Mandatory follow-on antiresorptive	Maintains BMD and antifracture benefits [6]

145

146 **SERMs and Menopausal Hormone Therapy**

Raloxifene and bazedoxifene reduce vertebral fractures and can be considered in younger postmenopausal women with spine-predominant risk and low absolute hip risk, especially where breast cancer risk reduction is desirable. They do not convincingly reduce hip fractures and increase the risk of venous thromboembolism. MHT reduces fractures in the Women's Health Initiative but is limited by risks that outweigh benefits for primary fracture prevention in older women. It may be considered in recently menopausal, symptomatic women at low cardiovascular and breast cancer risk where fracture risk reduction is an ancillary benefit rather than the primary indication. [30–33, 44–48]. Table 4 describes various SERMs and MHT in Postmenopausal Osteoporosis.

Table 4. SERMs and MHT in Postmenopausal Osteoporosis

Class	Fracture efficacy	Typical candidate
Raloxifene	Vertebral reduction; no proven hip reduction	Postmenopausal women with spine-predominant risk and desire for breast cancer risk reduction; avoid if high VTE risk [44–47]
Bazedoxifene	Vertebral reduction; possible nonvertebral benefit in higher-risk subgroups	Similar to raloxifene; international availability varies [46–47]
MHT	Reduces fractures; risk-benefit unfavorable in older women	Symptomatic, recently menopausal, low CV/breast cancer risk; osteoporosis prevention as secondary objective [48]

Calcitonin

Intranasal salmon calcitonin formerly held an indication for postmenopausal osteoporosis with vertebral pain, but concerns about modest efficacy and potential cancer risk signals have led to restricted use in many regions. It is not a first-line therapy in contemporary guidelines and, where available, is mainly reserved for short-term analgesia after acute vertebral fracture rather than long-term antifracture therapy. [1–3].

Safety Considerations: AFF and ONJ

AFFs and ONJ represent rare but serious complications occurring predominantly with long-term antiresorptive use. The absolute AFF risk remains very low relative to the number of typical osteoporotic fractures prevented by bisphosphonates, particularly within the first 3–5 years of therapy. ONJ risk is higher with oncology-dose antiresorptives than with osteoporosis doses; in the latter setting it remains uncommon, although dental risk factors, poor oral hygiene, denture use, invasive dental procedures, and prolonged exposure increase risk. Shared decision-making should include these risks, but the benefit-to-risk balance strongly favors treatment in appropriately selected patients. Drug holidays with bisphosphonates may mitigate cumulative AFF risk; in contrast, drug holidays are contraindicated with denosumab due to rebound vertebral fracture risk. [34–41].

Duration, Drug Holidays, and Monitoring

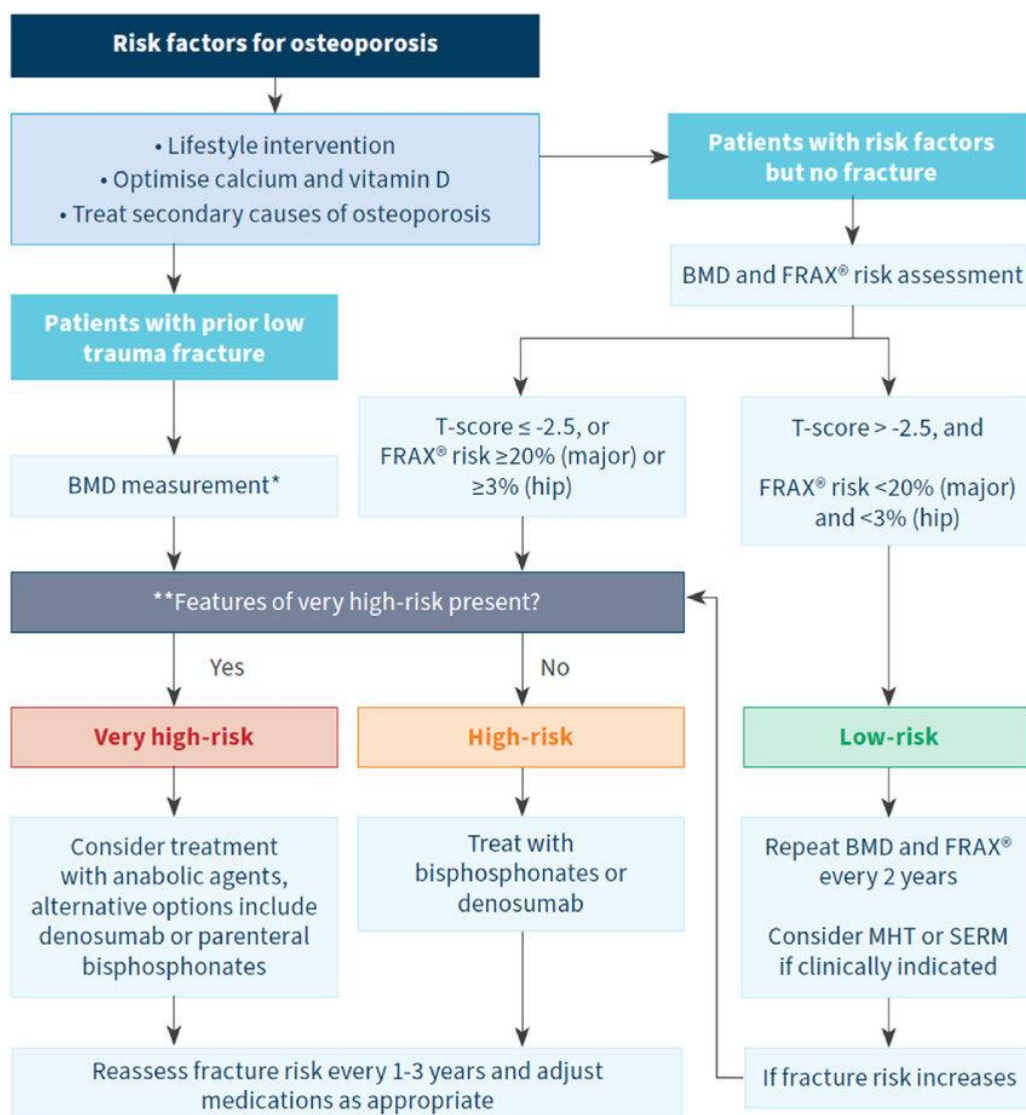
Guidelines recommend periodic reassessment after 3–5 years of oral bisphosphonates or 3 years of IV zoledronic acid to determine whether to continue therapy or institute a holiday in

moderate-risk patients. Continuation is favored in those with very low hip BMD, prior vertebral or hip fracture, or fractures on therapy, given evidence from FLEX and HORIZON extensions that continuation reduces morphometric vertebral fractures and better maintains BMD. During a drug holiday, patients should undergo clinical surveillance, BMD monitoring approximately every 2–3 years, and earlier re-initiation if fractures occur, BMD declines substantially, or risk escalates. For denosumab, there is no safe holiday; stopping requires timely administration of a potent bisphosphonate with monitoring of bone turnover markers to ensure adequate suppression. [22–27, 29–33].

Sequential and Goal-Directed Therapy

Emerging guidance endorses “goal-directed” management, aligning therapy choices and sequences to reach explicit treatment targets (e.g., femoral neck T-score thresholds) and minimize time spent at very high risk. An anabolic-first strategy with romosozumab or a PTH analog followed by a potent antiresorptive is particularly compelling for women with recent vertebral fractures, multiple fractures, or profoundly low BMD, as early, large BMD gains correlate with greater fracture risk reduction. Conversely, most high-risk patients without very-high-risk features can begin with a bisphosphonate or denosumab and transition according to response and tolerability. The choice between denosumab-based and bisphosphonate-based sequences should consider renal function, adherence, dental risk, and the necessity to plan for denosumab consolidation therapy to avoid rebound. [5, 6, 12, 19]. Figure 3 summarises Sequential Therapy while treating postmenopausal osteoporosis.

Figure 3. “Sequential Therapy Playbook” (Schematic)



Interpretation:

This schematic outlines phenotype-driven sequencing in postmenopausal osteoporosis therapy, aligning initial treatment intensity with fracture risk. It emphasizes individualized transition between anabolic and antiresorptive agents, renal and cardiovascular safety considerations, and the “lock-in” principle ensuring sustained skeletal protection after anabolic or denosumab discontinuation.[51]

Practical Considerations: Implementation and Adherence

Fragility fracture pathways and fracture liaison services improve treatment initiation and persistence. Achieving calcium and vitamin D adequacy, educating about correct oral bisphosphonate administration, scheduling on-time denosumab injections, and arranging timely transition after finite anabolic or romosozumab courses are essential operational steps. NOGG 2024 emphasizes streamlined assessment, early parenteral therapy post-fracture, and systematic follow-up. Utilization of FRAXplus® adjustments for fracture recency or multiple prior fractures can refine risk estimation and increase the appropriateness of anabolic-first strategies where warranted. [1–3, 16–20].

Figure 4. Site-Tailored Therapeutic Alignment in Postmenopausal Osteoporosis

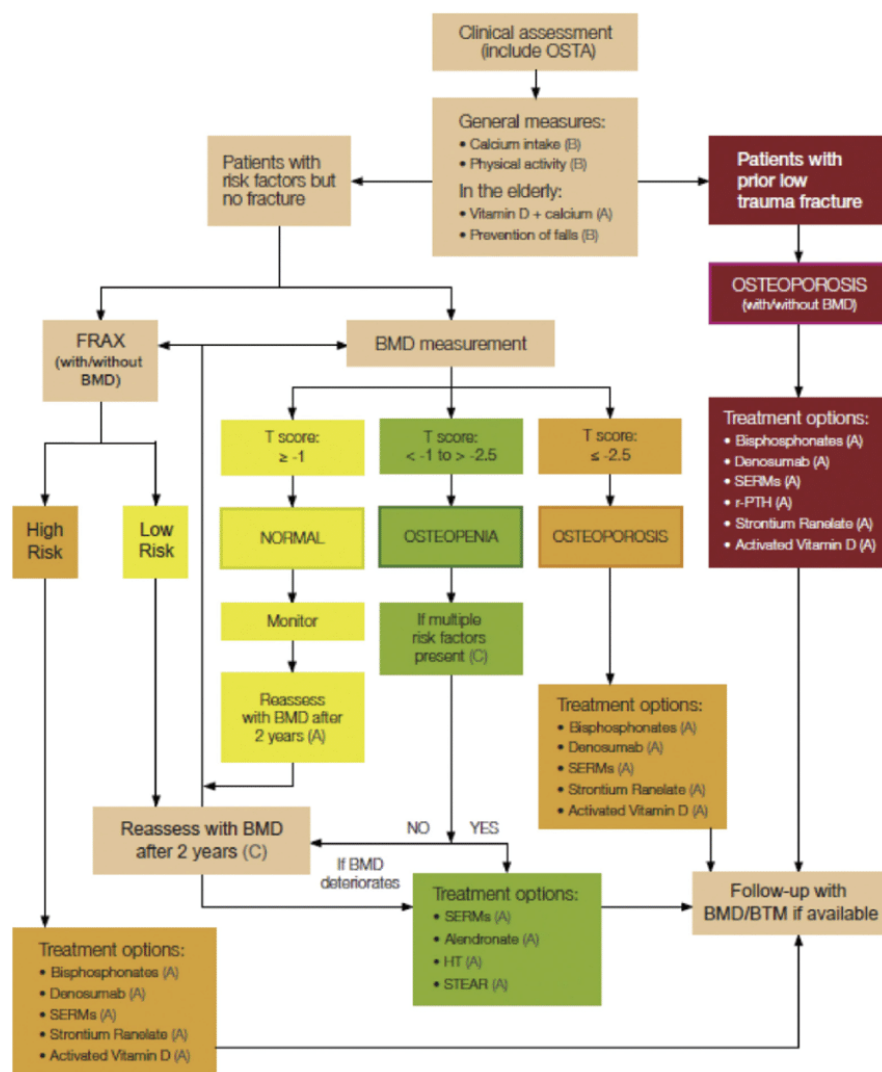


Figure 4 illustrates treatment individualization based on skeletal site predominance of fracture risk. It emphasizes aligning pharmacologic choice with spine versus hip vulnerability, integrating anabolic and antiresorptive strategies to optimize both vertebral and nonvertebral protection while ensuring consolidation therapy to preserve bone mass and reduce recurrent fracture risk. [6, 9, 12, 18, 21]

Monitoring Response and When to Switch

Clinical endpoints include incident fractures and changes in BMD by DXA at 1.5–2-year intervals. Lack of expected BMD gain or new fractures on therapy prompts evaluation of adherence, secondary causes (e.g., hyperparathyroidism, malabsorption), and, in some cases, intensification or a mechanistic switch (from antiresorptive to anabolic or vice versa). Bone turnover markers can aid in assessing bisphosphonate adherence or denosumab rebound but should complement, not replace, clinical outcomes and BMD. A goal-directed approach encourages switching if targets are not met within reasonable intervals. [5, 19].

Conclusion

Pharmacologic therapy for postmenopausal osteoporosis is highly effective when matched to risk and delivered in sequences that preserve structural gains. For most high-risk women, bisphosphonates or denosumab remain appropriate initial options with strong vertebral,

nonvertebral, and hip fracture efficacy. In women at very high risk—especially those with recent vertebral fractures, multiple fractures, or very low T-scores—an anabolic-first strategy with romosozumab or a PTH analog followed by a potent antiresorptive maximizes early risk reduction and long-term durability. Denosumab requires planned consolidation to avoid rebound vertebral fractures upon discontinuation; bisphosphonates permit risk-stratified drug holidays. The 2024 NOGG guidance and contemporary positions from endocrine and bone societies, along with FRAXplus® refinements, support a pragmatic, goal-directed approach that integrates site-specific efficacy, patient preferences, comorbidity, and systems that close the persistent treatment gap. [1–7, 9–12, 15–19, 21–48].

UNDER PEER REVIEW IN IJAR

1. Gregson CL, Armstrong DJ, Bowden J, Cooper C, Edwards J, Gittoes NJL, Harvey N, Kanis J, Leyland S, Low R, McCloskey E, Moss K, Parker J, Paskins Z, Poole K, Reid DM, Stone M, Thomson J, Vine N, Compston J. UK clinical guideline for the prevention and treatment of osteoporosis. *Arch Osteoporos*. 2022 Apr 5;17(1):58. doi: 10.1007/s11657-022-01061-5. Erratum in: *Arch Osteoporos*. 2022 May 19;17(1):80. doi: 10.1007/s11657-022-01115-8. PMID: 35378630; PMCID: PMC8979902.
2. Rozenberg S, Al-Daghri N, Aubertin-Leheudre M, Brandi ML, Cano A, Collins P, Cooper C, Genazzani AR, Hillard T, Kanis JA, Kaufman JM, Lambrinoudaki I, Laslop A, McCloskey E, Palacios S, Prieto-Alhambra D, Reginster JY, Rizzoli R, Rosano G, Trémollières F, Harvey NC. Is there a role for menopausal hormone therapy in the management of postmenopausal osteoporosis? *Osteoporos Int*. 2020 Dec;31(12):2271-2286. doi: 10.1007/s00198-020-05497-8. Epub 2020 Jul 8. PMID: 32642851; PMCID: PMC7661391..
3. Yang J, Guo X, Cui Z, Guo H, Dong JN. Efficacy and safety of denosumab and teriparatide versus oral bisphosphonates to treat postmenopausal osteoporosis: a systematic review and meta-analysis. *Front Endocrinol (Lausanne)*. 2024 Sep 2;15:1431676. doi: 10.3389/fendo.2024.1431676. PMID: 39286276; PMCID: PMC11402677.
4. Ko SS, Jordan VC. Treatment of osteoporosis and reduction in risk of invasive breast cancer in postmenopausal women with raloxifene. *Expert OpinPharmacother*. 2011 Mar;12(4):657-74. doi: 10.1517/14656566.2011.557360. Epub 2011 Feb 7. Retraction in: *Expert OpinPharmacother*. 2012 May;13(7):1081. doi: 10.1517/14656566.2012.677336. PMID: 21294695; PMCID: PMC3085345.
5. Cortet B, Guañabens N, Brandi ML, Siggekkow H. Similarities and differences between European guidelines for the management of postmenopausal osteoporosis. *Arch Osteoporos*. 2024 Sep 5;19(1):84. doi: 10.1007/s11657-024-01441-z. PMID: 39235671; PMCID: PMC11377466.
6. Wong P, Chen W, Ewald D, Girgis C, Rawlin M, Tsingos J, Waters J. 2024 Royal Australian College of General Practitioners and Healthy Bones Australia guideline for osteoporosis management and fracture prevention in postmenopausal women and men over 50 years of age. *Med J Aust*. 2025 May 19;222(9):472-480. doi: 10.5694/mja2.52637. Epub 2025 Mar 25. PMID: 40134107; PMCID: PMC12088310.
7. Hanley DA, Adachi JD, Bell A, Brown V. Denosumab: mechanism of action and clinical outcomes. *Int J Clin Pract*. 2012 Dec;66(12):1139-46. doi: 10.1111/ijcp.12022. Epub 2012 Sep 12. PMID: 22967310; PMCID: PMC3549483..
8. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, Harris ST, Hurley DL, Kelly J, Lewiecki EM, Pessah-Pollack R, McClung M, Wimalawansa SJ, Watts NB. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS-2020 UPDATE. *EndocrPract*. 2020 May;26(Suppl 1):1-46. doi: 10.4158/GL-2020-0524SUPPL. PMID: 32427503..
9. Silva BC, Madeira M, d'Alva CB, Maeda SS, de Holanda NCP, Ohe MN, Szejnfeld V, Zerbini CAF, de Paula FJA, Bandeira F. Definition and management of very high fracture risk in women with postmenopausal osteoporosis: a position statement from the Brazilian Society of Endocrinology and Metabolism (SBEM) and the Brazilian Association of Bone Assessment and Metabolism (ABRASSO). *Arch Endocrinol*

- Metab. 2022 Nov 11;66(5):591-603. doi: 10.20945/2359-3997000000522. Epub 2022 Oct 3. PMID: 36191263; PMCID: PMC10118822.
10. Zhou X, Long H, Wang JH, Huang Z, Cao L. Clinical outcomes and safety of combined calcitriol and bisphosphonates in treating postmenopausal osteoporosis: a retrospective cohort study. *J Orthop Surg Res.* 2025 Apr 9;20(1):359. doi: 10.1186/s13018-025-05714-2. PMID: 40205415; PMCID: PMC11983753.
 11. Lewiecki EM. Intravenous zoledronic acid for the treatment of osteoporosis: The evidence of its therapeutic effect. *Core Evid.* 2010 Jun 15;4:13-23. doi: 10.2147/ce.s6011. PMID: 20694061; PMCID: PMC2899787.
 12. Thomasius F, Kurth A, Baum E, Drey M, Maus U, Schmidmaier R. Clinical Practice Guideline: The Diagnosis and Treatment of Osteoporosis. *DtschArztebl Int.* 2025 Jan 10;122(1):12-18. doi: 10.3238/arztebl.m2024.0222. PMID: 39803994; PMCID: PMC12416032.
 13. Rizzoli R, Reginster JY, Boonen S, Bréart G, Diez-Perez A, Felsenberg D, Kaufman JM, Kanis JA, Cooper C. Adverse reactions and drug-drug interactions in the management of women with postmenopausal osteoporosis. *Calcif Tissue Int.* 2011 Aug;89(2):91-104. doi: 10.1007/s00223-011-9499-8. Epub 2011 Jun 3. PMID: 21637997; PMCID: PMC3135835.
 14. Liu R, Liu J, Yang J, Sun Z, Yan H. Comparative analysis of ChatGPT-4o mini, ChatGPT-4o and Gemini Advanced in the treatment of postmenopausal osteoporosis. *BMC MusculoskeletDisord.* 2025 Apr 16;26(1):369. doi: 10.1186/s12891-025-08601-3. PMID: 40241048; PMCID: PMC12001388.
 15. Clunie G. Update on postmenopausal osteoporosis management. *Clin Med (Lond).* 2007 Jan-Feb;7(1):48-52. doi: 10.7861/clinmedicine.7-1-48. PMID: 17348575; PMCID: PMC4953548.
 16. Alam F, Alsaed O, Abdulla N, Abdulmomen I, Lutf A, Al Emadi S. Guidelines for fracture risk assessment and management of osteoporosis in postmenopausal women and men above the age of 50 in Qatar. *Arch Osteoporos.* 2024 May 2;19(1):34. doi: 10.1007/s11657-024-01389-0. PMID: 38698101; PMCID: PMC11065783.
 17. Jiang X, Hou S, Deng X, Hu L, Wang J, Hou D. Sequential treatment from bisphosphonate to denosumab improves lumbar spine bone mineral density in postmenopausal osteoporosis patients: A meta-analysis of randomized controlled trials. *Medicine (Baltimore).* 2024 Nov 15;103(46):e40594. doi: 10.1097/MD.00000000000040594. PMID: 39560527; PMCID: PMC11576034.
 18. Räkel A, Boucher A, Ste-Marie LG. Role of zoledronic acid in the prevention and treatment of osteoporosis. *Clin Interv Aging.* 2011;6:89-99. doi: 10.2147/CIA.S7282. Epub 2011 Mar 28. PMID: 21594000; PMCID: PMC3095556.
 19. Wells GA, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, Coyle D, Tugwell P. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database Syst Rev.* 2008 Jan 23;(1):CD001155. doi: 10.1002/14651858.CD001155.pub2. Update in: *Cochrane Database Syst Rev.* 2025 Jan 27;1:CD001155. doi: 10.1002/14651858.CD001155.pub3. PMID: 18253985.
 20. Hsieh SC, Kibret T, Hamid JS, Kelly SE, Peterson J, Zheng C, Tugwell P, Wells GA, Singh JA. Bisphosphonates for postmenopausal osteoporosis: a network meta-analysis. *Cochrane Database Syst Rev.* 2023 Sep 28;2023(9):CD015008. doi: 10.1002/14651858.CD015008. PMCID: PMC10535791.
 21. Shevroja E, Reginster JY, Lamy O, Al-Daghri N, Chandran M, Demoux-Baiada AL, Kohlmeier L, Lecart MP, Messina D, Camargos BM, Payer J, Tuzun S, Veronese N, Cooper C, McCloskey EV, Harvey NC. Update on the clinical use of trabecular bone

- score (TBS) in the management of osteoporosis: results of an expert group meeting organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO), and the International Osteoporosis Foundation (IOF) under the auspices of WHO Collaborating Center for Epidemiology of Musculoskeletal Health and Aging. *Osteoporos Int.* 2023 Sep;34(9):1501-1529. doi: 10.1007/s00198-023-06817-4. Epub 2023 Jul 1. PMID: 37393412; PMCID: PMC10427549.
22. Vondracek SF, Linnebur SA. Diagnosis and management of osteoporosis in the older senior. *Clin Interv Aging.* 2009;4:121-36. doi: 10.2147/cia.s4965. Epub 2009 May 14. PMID: 19503775; PMCID: PMC2685234.
23. Kendler DL, Cosman F, Stad RK, Ferrari S. Denosumab in the Treatment of Osteoporosis: 10 Years Later: A Narrative Review. *Adv Ther.* 2022 Jan;39(1):58-74. doi: 10.1007/s12325-021-01936-y. Epub 2021 Nov 11. PMID: 34762286; PMCID: PMC8799550..
24. Ardelean A, Tit DM, Furau R, Todut O, Bungau GS, Pavel RMS, Uivaraseanu B, Bei DA, Furau C. Beyond Bone Mineral Density: Real-World Fracture Risk Profiles and Therapeutic Gaps in Postmenopausal Osteoporosis. *Diagnostics (Basel).* 2025 Aug 6;15(15):1972. doi: 10.3390/diagnostics15151972. PMID: 40804936; PMCID: PMC12346389.
25. Gourlay ML, Overman RA, Ensrud KE. Bone Density Screening and Re-screening in Postmenopausal Women and Older Men. *Curr Osteoporos Rep.* 2015 Dec;13(6):390-8. doi: 10.1007/s11914-015-0289-5. PMID: 26408154; PMCID: PMC4623874.
26. Akbar A, Zaheer A, Kharal MM, Komel A, Khan MH, Ahsan A, Singh AK. Evolving strategies for osteoporosis management in postmenopausal women: From tradition to innovation. *Medicine (Baltimore).* 2025 Feb 14;104(7):e41605. doi: 10.1097/MD.00000000000041605. PMID: 39960896; PMCID: PMC11835067.
27. Wells GA, Hsieh SC, Zheng C, Peterson J, Tugwell P, Liu W. Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database Syst Rev.* 2022 May 3;5(5):CD004523. doi: 10.1002/14651858.CD004523.pub4. PMID: 35502787; PMCID: PMC9062986.
28. Vandenbroucke A, Luyten FP, Flamaing J, Gielen E. Pharmacological treatment of osteoporosis in the oldest old. *Clin Interv Aging.* 2017 Jul 6;12:1065-1077. doi: 10.2147/CIA.S131023. PMID: 28740372; PMCID: PMC5505539.
29. Li S, Chen B, Chen H, Hua Z, Shao Y, Yin H, Wang J. Analysis of potential genetic biomarkers and molecular mechanism of smoking-related postmenopausal osteoporosis using weighted gene co-expression network analysis and machine learning. *PLoS One.* 2021 Sep 23;16(9):e0257343. doi: 10.1371/journal.pone.0257343. PMID: 34555052; PMCID: PMC8459994.
30. Nunkoo S, Krissheeven M, Chitravanshi A, Ramanah M, Robinson J, Banerjee I. Clinical Efficacy and Safety of Teriparatide Versus Alendronate in Postmenopausal Osteoporosis: A Systematic Review of Randomized Controlled Trials. *Cureus.* 2024 Nov 5;16(11):e73068. doi: 10.7759/cureus.73068. PMID: 39640163; PMCID: PMC11620021.
31. Gates M, Pillay J, Thériault G, Limburg H, Grad R, Klarenbach S, Korownyk C, Reynolds D, Riva JJ, Thombs BD, Kline GA, Leslie WD, Courage S, Vandermeer B, Featherstone R, Hartling L. Screening to prevent fragility fractures among adults 40 years and older in primary care: protocol for a systematic review. *Syst Rev.* 2019 Aug 23;8(1):216. doi: 10.1186/s13643-019-1094-5. PMID: 31443711; PMCID: PMC6706906.

32. Burstein HJ, Lacchetti C, Anderson H, Buchholz TA, Davidson NE, Gelmon KA, Giordano SH, Hudis CA, Solky AJ, Stearns V, Winer EP, Griggs JJ. Adjuvant Endocrine Therapy for Women With Hormone Receptor-Positive Breast Cancer: ASCO Clinical Practice Guideline Focused Update. *J Clin Oncol*. 2019 Feb 10;37(5):423-438. doi: 10.1200/JCO.18.01160. Epub 2018 Nov 19. PMID: 30452337.
33. Chandran M. The why and how of sequential and combination therapy in osteoporosis. A review of the current evidence. *Arch Endocrinol Metab*. 2022 Nov 11;66(5):724-738. doi: 10.20945/2359-3997000000564. PMID: 36382762; PMCID: PMC10118820.
34. Patel D, Gorrell C, Norris J, Liu J. A narrative review of the pharmaceutical management of osteoporosis. *Ann Jt*. 2023 Jun 20;8:25. doi: 10.21037/aoj-23-2. PMID: 38529240; PMCID: PMC10929303.
35. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, Delmas P, Zoog HB, Austin M, Wang A, Kutilek S, Adami S, Zanchetta J, Libanati C, Siddhanti S, Christiansen C; FREEDOM Trial. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med*. 2009 Aug 20;361(8):756-65. doi: 10.1056/NEJMoa0809493. Epub 2009 Aug 11. Erratum in: *N Engl J Med*. 2009 Nov 5;361(19):1914. PMID: 19671655.
36. Wang J, Wang Y, Li L, Cai S, Mao D, Lou H, Zhao J. Network pharmacology-based pharmacological mechanism prediction of Lycii Fructus against postmenopausal osteoporosis. *Medicine (Baltimore)*. 2023 Dec 1;102(48):e36292. doi: 10.1097/MD.00000000000036292. PMID: 38050297; PMCID: PMC10695557.
37. Hayes KN, Baschant U, Hauser B, Burden AM, Winter EM. When to Start and Stop Bone-Protecting Medication for Preventing Glucocorticoid-Induced Osteoporosis. *Front Endocrinol (Lausanne)*. 2021 Dec 15;12:782118. doi: 10.3389/fendo.2021.782118. Erratum in: *Front Endocrinol (Lausanne)*. 2022 Mar 14;13:877512. doi: 10.3389/fendo.2022.877512. PMID: 34975756; PMCID: PMC8715727.
38. Kanis JA, Harvey NC, Cooper C, Johansson H, Odén A, McCloskey EV; Advisory Board of the National Osteoporosis Guideline Group. A systematic review of intervention thresholds based on FRAX : A report prepared for the National Osteoporosis Guideline Group and the International Osteoporosis Foundation. *Arch Osteoporos*. 2016 Dec;11(1):25. doi: 10.1007/s11657-016-0278-z. Epub 2016 Jul 27. PMID: 27465509; PMCID: PMC4978487.
39. Hiligsmann M, Ronda G, van der Weijden T, Boonen A. The development of a personalized patient education tool for decision making for postmenopausal women with osteoporosis. *Osteoporos Int*. 2016 Aug;27(8):2489-96. doi: 10.1007/s00198-016-3555-1. Epub 2016 Apr 5. PMID: 27048388; PMCID: PMC4947108.
40. Laurent MR, Goemaere S, Verroken C, Bergmann P, Body JJ, Bruyère O, Cavalier E, Rozenberg S, Lapauw B, Gielen E. Prevention and Treatment of Glucocorticoid-Induced Osteoporosis in Adults: Consensus Recommendations From the Belgian Bone Club. *Front Endocrinol (Lausanne)*. 2022 Jun 9;13:908727. doi: 10.3389/fendo.2022.908727. PMID: 35757436; PMCID: PMC9219603.
41. Xiao J, Yu Z, Han Q, Guo Y, Ye J, Lian H, Wang L, Ma Y, Liu M. The Mechanism of Action and Experimental Verification of Narenmandula in the Treatment of Postmenopausal Osteoporosis. *Comb Chem High Throughput Screen*. 2024;27(15):2249-2259. doi: 10.2174/0113862073264965231116105323. PMID: 38178685; PMCID: PMC11348460.
42. Fiani B, Newhouse A, Sarhadi KJ, Arshad M, Soula M, Cathel A. Special Considerations to Improve Clinical Outcomes in Patients with Osteoporosis

- Undergoing Spine Surgery. *Int J Spine Surg.* 2021 Apr;15(2):386-401. doi: 10.14444/8050. Epub 2021 Apr 5. PMID: 33900998; PMCID: PMC8059385.
43. Lee TH, Song YJ, Kim H, Sung YK, Cho SK. Intervention Thresholds for Treatment in Patients with Glucocorticoid-Induced Osteoporosis: Systematic Review of Guidelines. *J Bone Metab.* 2020 Nov;27(4):247-259. doi: 10.11005/jbm.2020.27.4.247. Epub 2020 Nov 30. PMID: 33317228; PMCID: PMC7746480.
44. Niznik JD, Gilliam MA, Colón-Emeric C, Thorpe CT, Lund JL, Berry SD, Hanson LC. Controversies in Osteoporosis Treatment of Nursing Home Residents. *J Am Med Dir Assoc.* 2022 Dec;23(12):1928-1934. doi: 10.1016/j.jamda.2022.09.013. Epub 2022 Nov 3. PMID: 36335990; PMCID: PMC9885478..
45. Adler RA, El-Hajj Fuleihan G, Bauer DC, Camacho PM, Clarke BL, Clines GA, Compston JE, Drake MT, Edwards BJ, Favus MJ, Greenspan SL, McKinney R Jr, Pignolo RJ, Sellmeyer DE. Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research. *J Bone Miner Res.* 2016 Jan;31(1):16-35. doi: 10.1002/jbmr.2708. Erratum in: *J Bone Miner Res.* 2016 Oct;31(10):1910. doi: 10.1002/jbmr.2918. PMID: 26350171; PMCID: PMC4906542.
46. Wells GA, Hsieh SC, Peterson J, Zheng C, Kelly SE, Shea B, Tugwell P. Etidronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database Syst Rev.* 2024 Apr 9;4(4):CD003376. doi: 10.1002/14651858.CD003376.pub4. PMID: 38591743; PMCID: PMC11003221.
47. Kirazlı Y, AtamazÇalış F, El Ö, GökçeKutsal Y, Peker Ö, Sindel D, Tuzun Ş, Gogas Yavuz D, Durmaz B, Akarirmak Ü, Bodur H, Hamuryudan V, Inceboz U, Öncel S. Updated approach for the management of osteoporosis in Turkey: a consensus report. *Arch Osteoporos.* 2020 Aug 29;15(1):137. doi: 10.1007/s11657-020-00799-0. PMID: 32860546; PMCID: PMC7456410.
48. El Miedany Y, Paruk F, Kalla A, Adebajo A, El Gaafary M, El Maghraoui A, Ngandeu M, Dey D, Gadallah N, Elwy M, Moosajee F, Abu-Zaid MH, Galal S, Miladi S, Hassan W, Fadlelmola A, Saber S. Consensus evidence-based clinical practice guidelines for the diagnosis and treat-to-target management of osteoporosis in Africa: an initiative by the African Society of Bone Health and Metabolic Bone Diseases. *Arch Osteoporos.* 2021 Nov 18;16(1):176. doi: 10.1007/s11657-021-01035-z. PMID: 34792646; PMCID: PMC8598938.