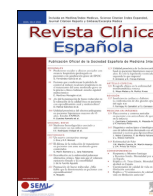




Contents lists available at ScienceDirect

Revista Clínica Española

journal homepage: www.revclinesp.es

Review

Treatment of osteoporosis in clinical practice: when, whom, how, and for how long

*Tratamiento de la osteoporosis en la práctica clínica: cuándo, a quién, cómo y durante cuánto tiempo*R. Arboiro Pinel 

Unidad de Metabolismo Óseo, Servicio de Medicina Interna, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

ARTICLE INFO

Keywords:

Osteoporosis
Fragility fracture
Fracture risk
Bone mineral density
Sequential therapy
Treatment

Palabras clave:

Osteoporosis
Fractura por fragilidad
Riesgo de fractura
Densidad mineral ósea
Tratamiento secuencial
Tratamiento

ABSTRACT

Osteoporosis is a highly prevalent chronic disease associated with an increased risk of fragility fractures and a substantial clinical and socioeconomic burden. Its management is based on fracture risk stratification, integrating clinical risk factors, bone mineral density, and tools such as FRAX[®]. Previous fragility fracture is the strongest predictor of future fractures and, in most cases, indicates the need for pharmacological treatment. In patients at high risk, antiresorptive agents remain the cornerstone of therapy, whereas in those at very high risk, an initial anabolic strategy followed by antiresorptive treatment should be considered. Treatment duration and sequencing require periodic reassessment, particularly with bisphosphonates and denosumab, whose discontinuation must be carefully planned to avoid rebound effects. This practical approach allows individualized clinical decision-making and aims to optimize fracture prevention, treatment adherence, and long-term outcomes in patients with osteoporosis in routine clinical practice settings.

RESUMEN

La osteoporosis es una enfermedad crónica altamente prevalente asociada a un elevado riesgo de fracturas por fragilidad, con importante impacto clínico y sociosanitario. Su manejo se basa en la estratificación del riesgo de fractura, integrando factores clínicos, densidad mineral ósea (DMO) y herramientas como FRAX. La presencia de fractura previa es el principal predictor de nuevas fracturas y, en la mayoría de los casos, indica tratamiento farmacológico. En pacientes con riesgo alto, los fármacos antirresortivos son la base terapéutica, mientras que en aquellos con riesgo muy alto puede considerarse una estrategia inicial con fármacos anabólicos seguida de tratamiento antirresortivo. La duración del tratamiento y su secuenciación requieren reevaluaciones periódicas, especialmente con bisfosfonatos y denosumab, cuya interrupción exige planificación adecuada. Este enfoque práctico permite individualizar decisiones clínicas y optimizar la prevención de fracturas en la práctica clínica habitual y mejorar la adherencia y resultados en pacientes con osteoporosis en la vida real.

Osteoporosis is a highly prevalent chronic disease and one of the leading causes of fragility fractures. Its health care and economic burden is considerable, particularly in the context of population aging. Fragility fractures lead to impaired quality of life and increased mortality, especially hip fractures. The number of hip fractures worldwide is estimated to nearly double by 2050. In Spain, approximately 285,000 fragility fractures occurred in 2019, and an increase of nearly 30% is expected over the next decade. Despite the availability of effective treatments, the dis-

ease remains underdiagnosed and undertreated, highlighting the need to improve the identification of patients at risk.^{1–5}

The management of osteoporosis is based on stratification of the patient's fracture risk by integrating clinical assessment, bone mineral density (BMD), and risk-estimation tools.^{5–7} Most of the available evidence comes from studies in postmenopausal women; consequently, clinical practice guidelines focus on this population and generally recommend a similar approach for men older than 50 years.^{8,9}

This review proposes a practical approach to addressing the main questions in osteoporosis management: when to initiate treatment,

E-mail address: rmarboiro@fjd.es

<https://doi.org/10.1016/j.rceng.2026.502614>

Received 6 April 2026; Accepted 30 May 2026

Available online xxx

0014-2565/© 2026 Elsevier España, S.L.U. and Sociedad Española de Medicina Interna (SEMI). All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Please cite this article as: R. Arboiro Pinel, Treatment of osteoporosis in clinical practice: when, whom, how, and for how long, Revista Clínica Española, <https://doi.org/10.1016/j.rceng.2026.502614>

whom to treat, which strategy to use, and how long treatment should be continued.

Whom to treat and when to initiate treatment

The decision regarding who should receive treatment is based on fracture risk. The timing of treatment initiation depends on the clinical context and is particularly urgent in situations involving a high short-term risk. Current guidelines recommend the combined assessment of clinical factors, BMD measurement, and computerized risk-prediction tools to determine whom and when to treat.^{10–20}

Initial clinical assessment

The medical history is essential for estimating fracture risk. It should include a history of fragility fractures, their location and date, a family history of hip fracture, use of systemic glucocorticoids, comorbidities and treatments associated with bone loss, and risk of falls. Modifiable factors such as smoking, alcohol consumption, physical inactivity, and calcium and vitamin D intake should also be assessed. Height loss or thoracic kyphosis should prompt investigation for vertebral fracture.

A fragility fracture is one that occurs after low-energy trauma or a fall from standing height. Fractures of the hip, vertebra, humerus, and distal radius are considered major osteoporotic fractures, as are asymptomatic vertebral fractures detected on imaging. They are the strongest individual predictor of subsequent fractures and, in most cases, constitute an indication for pharmacologic treatment regardless of BMD.^{21–23}

Furthermore, after a fragility fracture, the risk of a new fracture is particularly high during the following 12–24 months—referred to as imminent fracture risk—supporting early treatment initiation.^{24,25}

Age is a key factor because, for similar BMD values, fracture risk increases with age. Age is also associated with fracture site: distal radius fractures are more prevalent in younger women, whereas vertebral and hip fractures predominate at older ages.²⁶

In this context, fracture liaison services (FLSs), designed to identify and assess patients older than 50 years who experience a first fragility fracture and should receive bone-protective treatment, have demonstrated their usefulness in the secondary prevention of fractures.^{10,27–30}

Bone densitometry and complementary tests

Bone densitometry using dual-energy X-ray absorptiometry (DXA) is the reference technique for assessing BMD. The densitometric criterion for osteoporosis—a T-score ≤ -2.5 —remains valid in current guidelines for postmenopausal women and men aged ≥ 50 years. BMD alone does not identify all patients at high risk.³¹ A substantial proportion of fractures occur in patients with densitometric values outside the osteoporotic range, defined as a T-score > -2.5 .^{32,33} From a practical perspective, BMD may be considered very low when the T-score is < -3.0 , whereas some guidelines reserve a threshold of < -3.5 for very-high-risk categories because of its association with a high fracture risk.^{18,34} BMD, particularly at the hip, is a major determinant of fracture risk.³⁵

Although no universal criteria exist, there is general agreement that DXA should be performed when fractures or risk factors strongly associated with osteoporosis are present, such as rheumatoid arthritis, early menopause, malabsorption, or glucocorticoid treatment, or when several factors coexist, including age older than 65 years, low body weight, smoking, alcohol consumption, or a family history of osteoporosis.^{6,16,18,36}

The trabecular bone score may provide information on bone microarchitecture and improve fracture-risk estimation, although its use is not widespread in routine clinical practice.³⁷

Systematic assessment for vertebral fractures using lateral radiography or DXA-based vertebral fracture assessment is indicated in patients with clinical suspicion or risk factors because of their high prevalence

and underdiagnosis. A basic laboratory evaluation should also be performed to rule out secondary causes of osteoporosis, particularly in men, younger patients, or patients with fractures disproportionate to the degree of BMD loss.

Bone turnover markers, including the C-terminal telopeptide of type I collagen and total procollagen type I N-terminal propeptide, are not required for diagnosis but are useful for assessing response and adherence to antiresorptive treatment.¹⁹

Fracture-risk prediction tools

The FRAX[®] algorithm, adapted for each country, estimates the 10-year probability of major osteoporotic and hip fractures and may be calculated with or without BMD. Its main usefulness is to support therapeutic decision-making, particularly in patients without a previous fracture and with BMD in the osteopenic range. It should not be used as the sole decision-making tool because it may underestimate high-risk situations, such as recent or multiple fractures, treatment with high-dose glucocorticoids, or imminent fracture risk.³⁸ It has also not been validated for monitoring treatment response.

In Spain, no fully agreed-upon intervention thresholds have been established. The *Sociedad Española de Reumatología* has proposed indicative FRAX-based intervention thresholds, although their applicability in Spanish clinical practice remains debated and they should be interpreted alongside the overall clinical assessment. In particular, a high risk of hip fracture, defined as $\geq 3\%$, may help identify patients with a greater likelihood of fracture.^{13,14,16,36}

Other predictive models, such as Garvan or QFracture, have limited use in routine clinical practice.

Risk stratification and practical criteria for therapeutic decision-making

Clinical and densitometric assessment allows patients to be classified according to fracture risk and helps identify in whom and when pharmacologic treatment should be initiated. The main international guidelines propose stratification into very-high-, high-, moderate-, and low-risk categories based on clinical criteria, densitometric findings, and FRAX estimates.^{5–7,10–15,17} In Spain, the guidelines of the *Sociedad Española de Investigación Ósea y Metabolismo Mineral* (SEIOMM), updated in 2025, prioritize clinical and densitometric criteria over predictive algorithms.^{18–20} (Table 1).

Very high risk: Current clinical guidelines identify a group of patients with a high probability of new fractures in the short term in whom early treatment initiation should be considered.^{12–15,17,18,20} In practical terms, SEIOMM, in accordance with international guidelines, includes the following in this category:

- Two or more vertebral fractures or equivalent situations, such as the coexistence of a vertebral and a hip fracture, regardless of their timing and BMD.
- A vertebral or hip fracture associated with very low BMD, defined as a T-score < -3.0 .
- Patients without a fracture but with very low BMD, defined as a T-score < -3.5 .

In addition to these criteria, some international clinical practice guidelines consider other situations associated with a particularly high fracture probability, such as a fracture within the previous 12–24 months, treatment with high-dose glucocorticoids—especially ≥ 7.5 mg/day—the occurrence of fractures during treatment with bone-depleting drugs such as glucocorticoids, fracture during bone-protective treatment, high risk of falls, or the coexistence of multiple risk factors.^{12,14,15,17} Additionally, some of these guidelines incorporate very high FRAX estimates as a criterion for very high risk.^{12,14,15,17,31} Classification of these and other situations as very high risk should be

Table 1

Practical stratification of high and very high fracture risk.

Clinical factor	Practical criterion	Risk classification
Severe or multiple fractures	≥2 vertebral fractures or coexistence of a vertebral fracture and a hip fracture	Very high
Very low BMD	T-score < -3.5, regardless of fracture status	Very high
Major fracture plus low BMD	Vertebral or hip fracture with a T-score < -3.0	Very high
Fragility fracture	Other fractures, such as humeral or pelvic fractures, or a hip/vertebral fracture not meeting the criteria for very high risk	High
Densitometric osteoporosis	T-score ≤ -2.5 without a previous fracture	High
FRAX®	High FRAX estimate according to national thresholds ¹	High
Special clinical scenarios	Recent fracture (<2 years) Glucocorticoids (≥5 mg/day) Advanced chronic kidney disease High risk of falls Fracture during osteoporosis treatment	Individualized assessment; may be classified as high or very high risk depending on the clinical context

Risk classification integrates clinical and densitometric factors and risk-estimation tools and should be interpreted in the individual clinical context. The table summarizes the main clinical scenarios.

¹ Indicative thresholds in Spain: FRAX major osteoporotic fracture probability of 10% without BMD or 7.5% with BMD.

individualized according to the clinical context and the coexistence of other risk factors.^{18,20}

In this category, FRAX has limited usefulness for therapeutic decision-making because it may underestimate actual risk and delay treatment initiation.

High risk: Despite differences in densitometric and FRAX thresholds, clinical practice guidelines classify the following patients as being at high risk and recommend treatment:

- A previous fragility fracture, particularly of the vertebra, hip, proximal humerus, or pelvis, even when BMD is > -2.5 or, in some cases of vertebral or hip fracture, even normal.^{6,10,12–20}
- Densitometric osteoporosis, defined as a T-score ≤ -2.5 at any site, even in the absence of previous fractures.^{13,14,16,18,20}
- BMD in the osteopenic range, defined as a T-score between -1.0 and -2.5, associated with a high FRAX risk or relevant clinical factors.^{12–16}

This assessment of risk in osteopenia may include patients without fractures or with other fragility fractures, such as distal radius fractures, which have relevant prognostic implications, although their consideration is less consistent across guidelines than that of vertebral or hip fractures. Moreover, SEIOMM considers treatment in selected patients with osteopenia, particularly those with a T-score < -2.0 associated with relevant clinical factors such as advanced age, prolonged glucocorticoid treatment, hypogonadism, or recurrent falls.^{18,20} In this context, a high FRAX estimate may be useful, although its validity in the Spanish population has limitations.

Moderate risk: SEIOMM includes in this category postmenopausal women < 65 years with densitometric osteoporosis at the lumbar spine, defined as a T-score between -2.5 and -3.0, and a hip T-score > -2.0, without fractures or other risk factors. In these patients, treatment with selective estrogen receptor modulators is recommended.¹⁸ Some international clinical practice guidelines place patients with a T-score > -2.5, a low FRAX estimate, and no major fractures in non-high-risk categories, in whom periodic reassessment or treatment according to the clinical context may be considered.¹³

Low risk: In patients without a previous hip, vertebral, proximal humerus, or pelvic fracture, with BMD > -1.0, a low FRAX estimate, and no relevant clinical factors, management focuses on nonpharmacologic measures: adequate calcium and vitamin D intake, tailored physical exercise, fall prevention, and correction of modifiable risk factors such as smoking or alcohol consumption. Periodic risk reassessment is recommended.^{13,18}

In clinical practice, pharmacologic treatment is indicated in patients at high or very high risk of fracture. In those at very high risk, par-

ticularly after a recent fracture, early treatment initiation should be considered because of the high short-term fracture risk.^{13,15,17}

How should treatment be selected?

Once the indication for treatment has been established, the therapeutic strategy should be selected according to the level of fracture risk, the patient's clinical characteristics, and the balance between efficacy, safety, and therapeutic feasibility. The primary endpoint is to reduce fracture risk, prioritizing higher-impact strategies in patients with the greatest likelihood of clinical benefit, particularly during the period of imminent risk.^{19,31,34,39} (Fig. 1).

All patients should receive an adequate calcium intake, preferably through the diet, of 1000–1200 mg/day, and vitamin D, 800–1000 IU/day, particularly in the presence of deficiency, institutionalization, or antiosteoporotic treatment.

Patients at high risk

In patients at high risk, bisphosphonates are the treatment of choice in most cases.^{5,6,13–16,18}

Both oral bisphosphonates, including risedronate and alendronate, and IV bisphosphonates, including zoledronic acid, as well as denosumab, have consistently demonstrated efficacy in reducing vertebral and nonvertebral fractures.^{40–43} The choice among antiresorptive agents should be individualized according to factors such as renal function, GI tolerance, expected adherence, and patient preferences.⁴⁴ From a practical perspective, oral bisphosphonates are generally the first option in patients with good expected adherence, a low risk of GI problems, and preserved renal function, particularly those younger than 75 years. Zoledronic acid may be preferable when adherence problems or GI intolerance are present. Denosumab is an effective alternative in patients with contraindications to or poor tolerance of bisphosphonates, provided that a transition strategy is planned from the outset in case treatment is discontinued.

In patients > 75 years with a hip fracture who are classified in this group, treatment is generally parenteral, using denosumab or zoledronic acid if adherence to denosumab cannot be assured.¹⁸

Patients at very high risk

In this group, the primary endpoint is to achieve a rapid reduction in fracture risk. For this purpose, international clinical practice guidelines recommend initiating anabolic treatment in patients at very high fracture risk.^{13–17,34} These treatments have demonstrated a more rapid

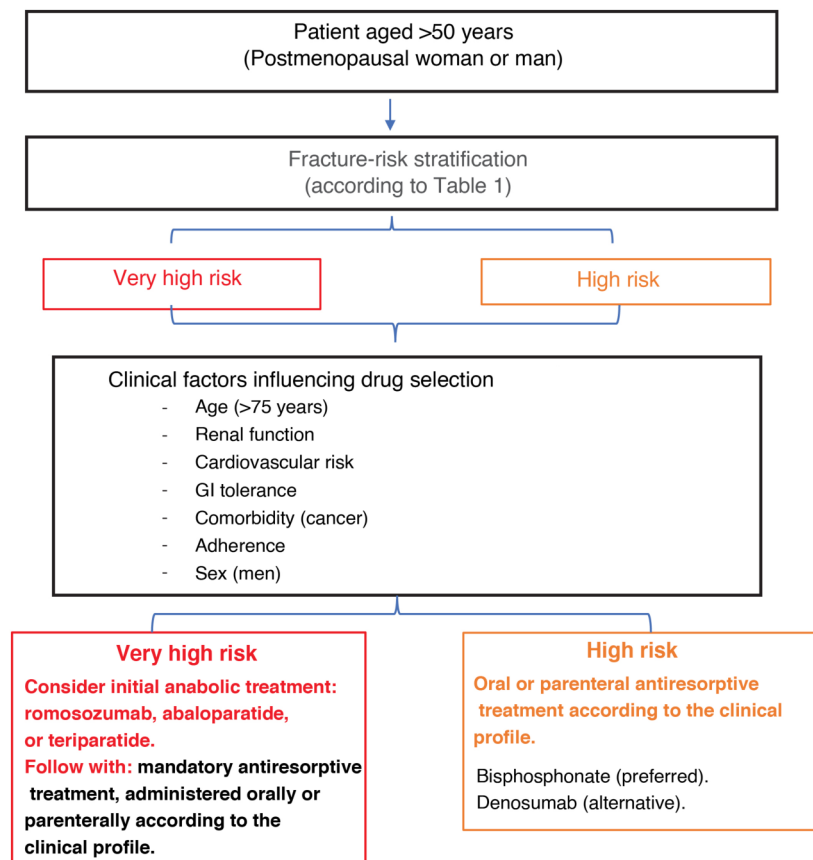


Fig. 1. Practical strategy for initial treatment selection in osteoporosis. Practical strategy for guiding initial treatment in postmenopausal women and men older than 50 years classified as being at high or very high risk (Table 1), adapted from the 2025 SEIOMM recommendations. Treatment selection should be individualized according to conditioning factors such as renal function, cardiovascular risk, gastrointestinal tolerance, fall risk, expected adherence, and the feasibility of oral or parenteral administration.

reduction in fracture risk and a greater increase in BMD than antiresorptive agents.^{45–48}

Three anabolic agents are currently available: teriparatide, abaloparatide, and romosozumab. No direct comparative studies between these agents are available, and indirect comparisons should be interpreted cautiously because the clinical trials differ in terms of populations, comparators, and outcome measures. Accordingly, current clinical guidelines do not establish an absolute hierarchy among anabolic treatments and recommend individualizing the choice according to the clinical profile, predominant fracture type, comorbidities, and safety profile.

In practical terms, parathyroid hormone analogues—abaloparatide and teriparatide—may be particularly appropriate in patients with predominant vertebral involvement, such as multiple or severe vertebral fractures or very low spinal BMD. Romosozumab may be considered particularly useful in patients at very high risk of nonvertebral fractures, especially after a hip fracture or when cortical involvement predominates, as indicated by very low hip BMD.⁴⁹

In all cases, the sequence of initial anabolic treatment followed by an antiresorptive agent is the most effective strategy for consolidating bone gain and maintaining long-term fracture-risk reduction.^{50–52}

Nevertheless, treatment selection should be individualized, and not all patients at very high risk are candidates for initial anabolic treatment.

Clinical factors in treatment selection

In addition to the level of risk, treatment selection requires assessment of clinical factors that may influence the choice. In this regard, it should be remembered that neither age, sex, nor the presence of

comorbidities is associated with a poorer response to antiosteoporotic treatment.⁵³ (Fig. 1).

Renal function: Bisphosphonates, teriparatide, and abaloparatide are not recommended in patients with advanced renal impairment, defined as an estimated glomerular filtration rate <30–35 mL/min. Specifically, the caution threshold is <35 mL/min for alendronate and zoledronic acid and <30 mL/min for risedronate. Denosumab may be used in these patients because it is not eliminated by the kidneys, although close monitoring is required because of the risk of hypocalcemia. In advanced chronic kidney disease, adynamic bone disease should be excluded before antiresorptive treatment is initiated. Management in this patient profile should be individualized and requires specialist assessment.

Cardiovascular risk: Romosozumab is contraindicated in patients with a recent history of myocardial infarction or stroke—or unstable angina or transient ischemic attack—and in those with uncontrolled high vascular risk. This restriction reflects the safety warning issued by regulatory agencies after a slight imbalance in serious cardiovascular events was observed in the pivotal ARCH trial.^{48,54}

Cancer and radiotherapy: Teriparatide and abaloparatide are contraindicated in patients at risk of osteosarcoma, those who have received skeletal radiotherapy, and patients with Paget disease.⁵⁵ They are not recommended in patients with malignancies with potential bone involvement, including known or suspected bone metastases, because of the lack of evidence regarding their safety in this setting.⁴⁹ In patients with breast or prostate cancer receiving hormonal therapies, such as aromatase inhibitors or androgen-deprivation therapy, antiresorptive agents—bisphosphonates or denosumab—are the preferred option.

Nephrolithiasis and calcium metabolism: Parathyroid hormone analogues, including teriparatide and abaloparatide, may increase urinary

calcium excretion. Therefore, in patients with active or recurrent nephrolithiasis, an individualized assessment of recurrence risk is recommended before their use. These agents are not indicated in patients with hypercalcemia or primary hyperparathyroidism.

GI tolerance: Oral bisphosphonates should be avoided in patients with clinically relevant esophageal disease, such as esophagitis, achalasia, or stenosis, or with significant GI intolerance. In these cases, parenteral alternatives should be considered.

Age and functional status: Advanced age is not a contraindication to osteoporosis treatment, including anabolic treatment, because gains in BMD and reductions in fracture risk are similar to those observed in other age groups. Although data in patients > 85–90 years are limited, the cost–benefit balance is particularly important in these patients.^{49,56} Nevertheless, life expectancy, fall risk, frailty, and the ability to adhere to treatment should be considered when selecting the most appropriate therapeutic option.

Men with osteoporosis: The treatment strategy should focus on bisphosphonates, denosumab, and teriparatide, whereas romosozumab and abaloparatide are not yet approved for men in Spain.

How long should treatment be continued, and how should it be sequenced?

Treat-to-target strategies and periodic reassessment of fracture risk and therapeutic response have gained importance in recent international documents when determining treatment duration.^{13,18,57–59} (Fig. 2).

Bisphosphonates

Scientific evidence supports mandatory reassessment after 5 years of treatment with oral bisphosphonates or 3 years of treatment with zoledronic acid.^{5,6,13–18} At this clinical milestone, management depends on whether the risk persists:

- **Persistent risk:** In high-risk patients who continue to have a femoral-neck T-score < –2.5, have experienced a fragility fracture within the previous 3–5 years, have a history of vertebral fracture—particularly 2 or more fractures—or hip fracture, or remain on glucocorticoid treatment, continuation of the bisphosphonate is recommended, up to a total of 10 years for oral agents or 6 years for zoledronic acid.^{14–16,18} Some experts also recommend treatment for longer than 5 years in patients who were > 70 years when treatment was initiated.^{15,16}
- **Controlled risk:** In patients who do not meet the above criteria, a drug holiday may be considered. This temporary interruption, usually lasting 1–3 years, is possible because bisphosphonates bind to the bone matrix and maintain a residual effect after discontinuation. During the treatment pause, clinical and densitometric follow-up—usually annually—should be maintained, and treatment should be restarted if new fractures occur, BMD declines significantly, such as a return to the osteoporotic range, or the patient returns to a high-risk category.^{14–16,18}

The decision to continue or interrupt treatment should be individualized and reassessed periodically. It is important to emphasize that evidence regarding efficacy and safety beyond 10 years of oral treatment or 6 years of zoledronic acid is limited. In these situations, the decision to discontinue or continue bisphosphonates should be individualized by weighing whether the residual fracture risk justifies continued treatment against the possibility of rare adverse events, such as atypical femoral fracture or osteonecrosis of the jaw, or the need to sequence treatment to a bone-forming agent.^{6,18}

Denosumab

Denosumab cannot be interrupted without therapeutic planning. Its discontinuation, as well as delayed administration, is associated with

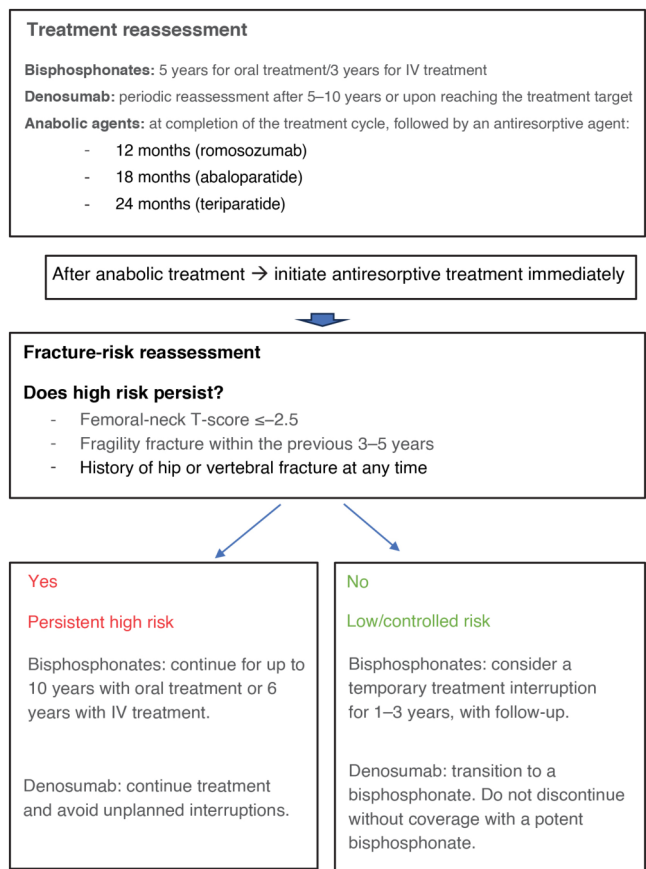


Fig. 2. Practical framework for long-term follow-up and decision-making in osteoporosis. Practical strategy for long-term follow-up and therapeutic decision-making in osteoporosis. Treatment duration and decisions regarding continuation or therapeutic transition should be individualized according to treatment response, residual fracture risk, and patient characteristics. Discontinuation of denosumab always requires a transition strategy using potent bisphosphonates to prevent the rebound effect and the occurrence of multiple vertebral fractures.

increased bone turnover, rapid BMD loss, and a higher risk of multiple vertebral fractures. Therefore, all clinical practice guidelines agree that it should not be discontinued without a transition strategy involving a potent bisphosphonate.^{13–18,60–62} Continuous use for 5–10 years is recommended, although robust evidence beyond this period is lacking. The decision to continue or discontinue treatment should be carefully assessed. Some experts suggest considering a total-hip T-score above –1.5 as an indicative treatment target when planning treatment duration, although this threshold is not a formal clinical guideline recommendation.^{5,34,63,64}

Anabolic agents

Anabolic treatments have a limited treatment-cycle duration according to their approved product information: 18 months for abaloparatide, 24 months for teriparatide—currently limited to a single treatment cycle in Spain—and 12 months for romosozumab. At the end of this period, antiresorptive treatment must be initiated immediately to consolidate the gain in bone mass; otherwise, the benefits are progressively lost.

Therapeutic sequencing: practical principles

The chronic nature of the disease and the limitations of prolonged treatments make it essential to understand therapeutic sequencing op-

tions that can achieve the objective of fracture-risk reduction. This is currently one of the central principles of osteoporosis management.⁶⁵

- **Anabolic-to-antiresorptive sequence:** This is the strategy most strongly supported by evidence in patients at very high risk, especially those with imminent fracture risk, to maximize fracture reduction.^{17,51,52,66}
- **Denosumab-to-bisphosphonate sequence:** When denosumab is discontinued after the therapeutic target has been achieved, administration of a potent bisphosphonate is mandatory to prevent the rebound effect. If denosumab treatment lasted < 2.5 years, it may be followed by oral alendronate for 2 years. If treatment lasted longer, IV zoledronic acid should be administered 6 months after the last denosumab dose, and the need for subsequent doses should be assessed according to increases in bone turnover markers, or additional doses may be administered at 6 and 12 months.^{18,67}
- **Direct switching from denosumab to an anabolic agent,** such as teriparatide or romosozumab, is not recommended: This sequence does not control the rebound increase in bone turnover after denosumab discontinuation and is associated with rapid and substantial loss of the BMD gained, particularly at cortical sites.^{52,68,69}
- **Bisphosphonate-to-anabolic and bisphosphonate-to-denosumab sequences:** These are not contraindicated when considered necessary to reduce fracture risk.^{18,66}

Overall, treatment duration and sequencing should be understood as a continuous, personalized process guided by periodic reassessment of fracture risk and integration of the best available evidence.

How should treatment be monitored?

Follow-up of patients with osteoporosis aims to assess treatment efficacy, verify adherence and safety, and periodically reassess fracture risk. The intensity of follow-up should be adapted to the level of risk and the type of treatment (Fig. 2).

- **Clinical assessment:** New fractures, vertebral pain, fall risk, and new or modifiable risk factors should be evaluated, together with confirmation of correct administration and treatment adherence.
- **DXA:** Assessment is recommended 12–24 months after treatment initiation or modification, particularly in patients at high or very high risk. In stable, low-risk patients, assessments may be performed at longer intervals, provided that changes are interpreted within the context of technical and biological variability.^{13,14,16}
- **Bone turnover markers:** These may be useful as early indicators of response and adherence, particularly with antiresorptive agents, although their use is not mandatory in all patients.^{13,14,16,18}

Clinical practice guidelines consider treatment response adequate when no new fractures occur and BMD increases, although the degree of increase has not been defined in absolute terms.^{13,14,16} Therapeutic failure is considered to have occurred when several successive fractures develop during treatment or when a new fracture occurs along with significant BMD loss or the absence of expected changes in bone turnover markers, provided that adherence has been confirmed and secondary causes have been excluded.^{18,70} The occurrence of a single fracture does not necessarily imply treatment failure, but it should prompt reassessment of treatment and risk factors, particularly in patients at very high risk who may require adjustment of the therapeutic strategy.

Antiresorptive agents have a clearly favorable benefit–risk profile in patients at high risk but require monitoring for very rare yet potentially serious adverse events.^{71–74}

- **Osteonecrosis of the jaw:** Periodic dental assessment is recommended.
- **Atypical femoral fractures:** The development of groin or thigh pain should prompt radiologic evaluation.

- **Hypocalcemia:** This is a risk with denosumab and zoledronic acid in patients with vitamin D deficiency or advanced renal impairment.

The use of teriparatide was initially limited because of a theoretical risk of osteosarcoma observed in rats. Human surveillance studies conducted over more than 15 years have not shown an increased incidence, although the drug remains contraindicated in patients with bone metastases or previous radiotherapy as a precaution.

Special clinical considerations

In premenopausal women and young men with a fragility fracture or low BMD, a secondary cause should always be excluded. Treatment of the underlying cause should be prioritized, and pharmacologic therapy should be reserved for selected cases.

In patients on chronic glucocorticoid treatment, preventive treatment with bisphosphonates should be considered at lower BMD thresholds. Postmenopausal women and men older than 50 years receiving prednisone at doses ≥ 5 mg/day for ≥ 3 months should be treated throughout the period of exposure. In younger patients, the decision should be individualized according to the presence of previous fractures, BMD, and glucocorticoid dose.¹⁸

Conclusions

The management of osteoporosis should be based on individualized fracture-risk stratification. The presence of a fragility fracture and very high risk, particularly after recent vertebral or hip fractures, identify patients who should be prioritized for treatment. Antiresorptive agents remain the therapeutic cornerstone for most patients, whereas initial anabolic strategies may be considered in situations of very high risk. Treatment duration and sequencing require periodic reassessment and individualized planning, particularly with bisphosphonates and denosumab.

Declaration of Generative AI and AI-assisted technologies in the writing process

ChatGPT was used for the final review of the manuscript to detect typographical errors or grammatical inconsistencies and improve the readability of the text in its original language (Spanish).

Funding

None declared.

Declaration of competing interest

The author declares having received payments for lectures, scientific activities, or travel grants from Gedeon Richter, UCB, Amgen, Stada, Sanofi, Italfarmaco, and Rubió.

References

1. Borgström F, Karlsson L, Orsäter G, et al. Fragility fractures in Europe: burden, management and opportunities. *Arch Osteoporos*. 2020;15:59, doi:10.1007/s11657-020-0706-y.
2. Sing CW, Lin TC, Bartholomew S, et al. Global epidemiology of hip fractures: secular trends in incidence rate, post-fracture treatment, and all-cause mortality. *J Bone Miner Res*. 2023;38:1064–1075, doi:10.1002/jbmr.4821.
3. Nan FJ, Gui ZC, Hua LB, Yan ZS, Feng WS, Li SC. Global burden of hip fracture: the Global Burden of Disease Study. *Osteoporos Int*. 2024;35:41–52, doi:10.1007/s00198-023-06907-3.
4. Kanis JA, Norton N, Harvey NC, et al. SCOPE 2021: a new scorecard for osteoporosis in Europe. *Arch Osteoporos*. 2021;16:82, doi:10.1007/s11657-020-00871-9.
5. Hoong CWS, Saul D, Khosla S, Sfeir JG. Advances in the management of osteoporosis. *BMJ*. 2025;390:e081250, doi:10.1136/bmj-2024-081250.
6. Morin SN, Leslie WD, Schouboe JT. Osteoporosis: a review. *JAMA*. 2025;334:894–907, doi:10.1001/jama.2025.6003.

7. Cortet B, Guàñabens N, Brandi ML, Siggekow H. Similarities and differences between European guidelines for the management of postmenopausal osteoporosis. *Arch Osteoporos*. 2024;19:84, doi:10.1007/s11657-024-01441-z.
8. Beaudart C, Demonceau C, Sabico S, et al. Efficacy of osteoporosis pharmacological treatments in men: a systematic review and meta-analysis. *Aging Clin Exp Res*. 2023;35:1789–1806, doi:10.1007/s40520-023-02478-9.
9. Fuggle NR, Beaudart C, Bruyère O, et al. Evidence-based guideline for the management of osteoporosis in men. *Nat Rev Rheumatol*. 2024;20:241–251, doi:10.1038/s41584-024-01094-9.
10. Kanis JA, Cooper C, Rizzoli R, Reginster JY. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int*. 2019;30:3–44, doi:10.1007/s00198-018-4704-5.
11. Kanis JA, Cooper C, Rizzoli R, Reginster JY. Executive summary of the European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Calcif Tissue Int*. 2019;104:235–238, doi:10.1007/s00223-018-00512-x.
12. Kanis JA, Harvey NC, McCloskey E, et al. Algorithm for the management of patients at low, high and very high risk of osteoporotic fractures. *Osteoporos Int*. 2020;31:1–12, doi:10.1007/s00198-019-05176-3.
13. Shoback D, Rosen CJ, Black DM, Cheung AM, Murad MH, Eastell R. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society guideline update. *J Clin Endocrinol Metab*. 2020;105:dga048, doi:10.1210/clinem/dga048.
14. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologist/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis-2020 Update. *Endocr Pract*. 2020;26:1–46, doi:10.4158/GL-2020-0524SUPPL.
15. Gregson CL, Armstrong DJ, Bowden J, et al. UK clinical guideline for the prevention and treatment of osteoporosis. *Arch Osteoporos*. 2022;17:58, doi:10.1007/s11657-022-01061-5.
16. LeBoff MS, Greenspan SL, Insogna KL, et al. The clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2022;33:2049–2102, doi:10.1007/s00198-021-05900-y.
17. Curtis EM, Reginster JY, Al-Daghri N, et al. Management of patients at very high risk of osteoporotic fractures through sequential treatments. *Aging Clin Exp Res*. 2022;34:695–714, doi:10.1007/s40520-022-02100-4.
18. Riancho J, Peris P, González-Macías J, Pérez-Castrillón J. Guías de práctica clínica en la osteoporosis postmenopáusica, glucocorticoidea y del varón (actualización 2022). *Rev Osteoporos Metab Miner*. 2022;14:13–33, doi:10.4321/S1889-836X2022000100003.
19. Riancho JA, Peris P, González-Macías J, et al. Resumen ejecutivo de las Guías de práctica clínica en la osteoporosis postmenopáusica, glucocorticoidea y del varón (actualización 2022). *Rev Osteoporos Metab Miner*. 2022;14:5–12, doi:10.4321/s1889-836x2022000100002.
20. Riancho JA, Martín Millán M, Peris P, Martínez G. Actualización de las guías de manejo de la osteoporosis de la SEIOMM: abalaparitada. *Rev Clin Esp*. 2025;225:502338, doi:10.1016/j.rce.2025.502338.
21. Kanis JA, Johansson H, McCloskey EV, et al. Previous fracture and subsequent fracture risk: a meta-analysis to update FRAX. *Osteoporos Int*. 2023;34:2027–2045, doi:10.1007/s00198-023-06870-z.
22. Vandenput L, Johansson H, McCloskey EV, et al. A meta-analysis of previous falls and subsequent fracture risk in cohort studies. *Osteoporos Int*. 2024;35:469–494, doi:10.1007/s00198-023-07012-1.
23. Conley RB, Adib G, Adler RA, et al. Secondary fracture prevention: consensus clinical recommendations from a Multistakeholder Coalition. *J Bone Miner Res*. 2020;35:36–52, doi:10.1002/jbmr.3877.
24. Johansson H, Siggeirsdóttir K, Harvey NC, et al. Imminent risk of fracture after fracture. *Osteoporos Int*. 2017;28:775–780, doi:10.1007/s00198-016-3868-0.
25. Wong RMY, Wong PY, Liu C, et al. The imminent risk of a fracture-existing worldwide data: a systematic review and meta-analysis. *Osteoporos Int*. 2022;33:2453–2466, doi:10.1007/s00198-022-06473-0.
26. Geusens P, van den Bergh J, Roux C, et al. The fracture phenotypes in women and men of 50 years and older with a recent clinical fracture. *Curr Osteoporos Rep*. 2024;22:611–620, doi:10.1007/s11914-024-00885-z.
27. Eisman JA, Bogoch ER, Dell R, et al. Making the first fracture the last fracture: ASBMR task force report on secondary fracture prevention. *J Bone Miner Res*. 2012;27:2039–2046, doi:10.1002/jbmr.1698.
28. Javadi MK, Sami A, Lems W, et al. A patient-level key performance indicator set to measure the effectiveness of fracture liaison services and guide quality improvement: a position paper of the IOF Capture the Fracture Working Group, National Osteoporosis Foundation and Fragility Fracture Network. *Osteoporos Int*. 2020;31:1193–1204, doi:10.1007/s00198-020-05377-1.
29. Wu CH, Chen CH, Chen PH, et al. Identifying characteristics of an effective fracture liaison service: systematic literature review. *Osteoporos Int*. 2018;29:1023–1047, doi:10.1007/s00198-017-4370-z.
30. Wu CH, Kao LJ, Hung WC, et al. Economic impact and cost-effectiveness of fracture liaison services: a systematic review of the literature. *Osteoporos Int*. 2018;29:1227–1242, doi:10.1007/s00198-018-4411-2.
31. Kanis JA, McCloskey EV, Harvey NC, et al. Intervention thresholds and diagnostic thresholds in the management of osteoporosis. *Aging Clin Exp Res*. 2022;34:3155–3157, doi:10.1007/s40520-022-02216-7.
32. Pasco JA, Seeman E, Henry MJ, Merriman EN, Nicholson GC, Kotowicz MA. The population burden of fractures originates in women with osteopenia, not osteoporosis. *Osteoporos Int*. 2006;17:1404–1409, doi:10.1007/s00198-006-0135-9.
33. Kadri A, Binkley N, Daffner SD, Anderson PA. Clinical risk factor status in patients with vertebral fracture but normal bone mineral density. *Spine J*. 2022;22:1634–1641, doi:10.1016/j.spinee.2022.05.019.
34. Cosman F, Lewiecki EM, Eastell R, et al. Goal-directed osteoporosis treatment: ASBMR/BHOF task force position statement 2024. *J Bone Miner Res*. 2024;39:1393–1405, doi:10.1093/jbmr/zjae119.
35. Schini M, Lui LY, Vilaca T, et al. The relationship between baseline bone mineral density and fracture incidence in the placebo groups of randomized controlled trials using individual patient data from the FNIH-ASBMR-SABRE project. *J Bone Miner Res*. 2025;40:307–314, doi:10.1093/jbmr/zjae201.
36. Naranjo Hernández A, Díaz del Campo Fontecha P, Aguado Acín MP, et al. Recomendaciones de la Sociedad Española de Reumatología sobre osteoporosis. *Reumatol Clin*. 2019;15:188–210, doi:10.1016/j.reuma.2018.09.004.
37. Shevroja E, Reginster JY, Lamy O, et al. 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;34:1501–1529, doi:10.1007/s00198-023-06817-4.
38. Schini M, Johansson H, Harvey NC, Lorentzon M, Kanis JA, McCloskey EV. An overview of the use of the fracture risk assessment tool (FRAX) in osteoporosis. *J Endocrinol Invest*. 2024;47:501–511, doi:10.1007/s40618-023-02219-9.
39. Pérez Castrillón JL. Sequential therapy and stratified risk of osteoporotic fracture. *Rev Osteoporos Metab Miner*. 2026;18:1–2, doi:10.20960/RevOsteoporosMetab-Miner.00108.
40. Cummings SR, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures results from the fracture intervention trial. *JAMA*. 1998;280:2077–2082, doi:10.1001/jama.280.24.2077.
41. Harris ST, Watts NB, Genant HK, et al. Effects of risenedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. Vertebral Efficacy With Risedronate Therapy (VERT) Study Group. *JAMA*. 1999;282:1344–1352, doi:10.1001/jama.282.14.1344.
42. Black DM, Delmas PD, Eastell R, et al. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. *N Engl J Med*. 2007;356:1809–1822, doi:10.1056/NEJMoa067312.
43. Bone HG, Wagman RB, Brandi ML, et al. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomised FREEDOM trial and open-label extension. *Lancet Diabetes Endocrinol*. 2017;5:513–523, doi:10.1016/S2213-8587(17)30138-9.
44. Nogués X, Carbonell MC, Canals L, Lizán L, Palacios S. Current situation of shared decision making in osteoporosis: a comprehensive literature review of patient decision aids and decision drivers. *Health Sci Rep*. 2022;5:e849, doi:10.1002/hsr2.849.
45. Brown JP, Engelke K, Keaveny TM, et al. Romosozumab improves lumbar spine bone mass and bone strength parameters relative to alendronate in postmenopausal women: results from the Active-Controlled Fracture Study in Postmenopausal Women With Osteoporosis at High Risk (ARCH) trial. *J Bone Miner Res*. 2021;36:2139–2152, doi:10.1002/jbmr.4409.
46. Kendler DL, Marin F, Zerbin C, et al. Effects of teriparatide and risenedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy, randomised controlled trial. *Lancet*. 2018;391:230–240, doi:10.1016/S0140-6736(17)32137-2.
47. Leder BZ, Mitlak B, Hu MY, Hattersley G, Bockman RS. Effect of abaloparatide vs alendronate on fracture risk reduction in postmenopausal women with osteoporosis. *J Clin Endocrinol Metab*. 2020;105:938–943, doi:10.1210/clinem/dgz162.
48. Saag KG, Petersen J, Brandi ML, et al. Romosozumab or alendronate for fracture prevention in women with osteoporosis. *N Engl J Med*. 2017;377:1417–1427, doi:10.1056/NEJMoa1708322.
49. Cosman F, Dempster DW. Anabolic agents for postmenopausal osteoporosis: how do you choose? *Curr Osteoporos Rep*. 2021;19:189–205, doi:10.1007/s11914-021-00663-1.
50. Cosman F, Oates M, Betah D, et al. Romosozumab followed by denosumab versus denosumab only: a post hoc analysis of FRAME and FRAME extension. *J Bone Miner Res*. 2024;39:1268–1277, doi:10.1093/jbmr/zjae116.
51. McClung MR. Sequential and long-term therapy for osteoporosis. *Curr Osteoporos Rep*. 2025;23:15, doi:10.1007/s11914-025-00909-2.
52. Cosman F, Langdahl B, Leder BZ. Treatment sequence for osteoporosis. *Endocr Pract*. 2024;30:490–496, doi:10.1016/j.eprac.2024.01.014.
53. Coco Martín MB, Leal Vega L, Blázquez Cabrera JA, et al. Comorbidity and osteoporotic fracture: approach through predictive modeling techniques using the OSTeOMED registry. *Aging Clin Exp Res*. 2022;34:1997–2004, doi:10.1007/s40520-022-02129-5.
54. Cummings SR, McCulloch C. Explanations for the difference in rates of cardiovascular events in a trial of alendronate and romosozumab. *Osteoporos Int*. 2020;31:1019–1021, doi:10.1007/s00198-020-05379-z.
55. Krege JH, Gilsenan AW, Komacko JL, Kellier Steele N. Teriparatide and osteosarcoma risk: history, science, elimination of boxed warning, and other label updates. *JBMR Plus*. 2022;6:e10665, doi:10.1002/jbm4.10665.
56. Fuggle N, Laslop A, Rizzoli R, et al. Treatment of osteoporosis and osteoarthritis in the oldest old. *Drugs*. 2025;85:343–360, doi:10.1007/s40265-024-02138-w.
57. Adler RA, El-Hajj Fuleihan G, Bauer DC, et al. 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;31:16–35, doi:10.1002/jbmr.2708.
58. Nogués X, Nolla JM, Casado E, et al. Spanish consensus on treat to target for osteoporosis. *Osteoporos Int*. 2018;29:489–499, doi:10.1007/s00198-017-4310-y.
59. Lewiecki EM. Operationalizing treat-to-target for osteoporosis. *Endocrinol Metab (Seoul)*. 2021;36:270–278, doi:10.3803/EnM.2021.970.

60. Cummings SR, Ferrari S, Eastell R, et al. Vertebral fractures after discontinuation of denosumab: a post hoc analysis of the randomized placebo-controlled FREEDOM trial and its extension. *J Bone Miner Res.* 2018;33:190–198, doi:10.1002/jbmr.3337.
61. Bone HG, Bolognese MA, Yuen CK, et al. Effects of denosumab treatment and discontinuation on bone mineral density and bone turnover markers in postmenopausal women with low bone mass. *J Clin Endocrinol Metab.* 2011;96:972–980, doi:10.1210/jc.2010-1502.
62. Tsourdi E, Zillikens MC, Meier C, et al. Fracture risk and management of discontinuation of denosumab therapy: a systematic review and position statement by ECTS. *J Clin Endocrinol Metab.* 2020:dga756, doi:10.1210/clinem/dga756.
63. Cosman F, Lewiecki EM, Ebeling PR, et al. T-Score as an indicator of fracture risk during treatment with romosozumab or alendronate in the ARCH trial. *J Bone Miner Res.* 2020;35:1333–1342, doi:10.1002/jbmr.3996.
64. Ferrari S, Libanati C, Lin CJF, et al. Relationship between bone mineral density T-score and nonvertebral fracture risk over 10 years of denosumab treatment. *J Bone Miner Res.* 2019;34:1033–1040, doi:10.1002/jbmr.3722.
65. Sølling AS, Langdahl BL, Cosman F. Recent advances in osteoporosis therapeutics. *Annu Rev Med.* 2026;77:433–448, doi:10.1146/annurev-med-050124-040555.
66. Han YX, Mo YY, Wu HX, et al. Safety and efficacy of sequential treatments for postmenopausal osteoporosis: a network meta-analysis of randomised controlled trials. *eClinicalMedicine.* 2024;68:102425, doi:10.1016/j.eclinm.2024.102425.
67. Kumar S, Wang M, Kim AS, Center JR, McDonald MM, Girgis CM. Denosumab discontinuation in the clinic: implications of rebound bone turnover and emerging strategies to prevent bone loss and fractures. *J Bone Miner Res.* 2025;40:1017–1034, doi:10.1093/jbmr/zjaf037.
68. Leder BZ, Tsai JN, Uihlein AV, et al. Denosumab and teriparatide transitions in postmenopausal osteoporosis (the DATA-Switch study): extension of a randomised controlled trial. *Lancet.* 2015;386:1147–1155, doi:10.1016/S0140-6736(15)61120-5.
69. Langdahl B. Treatment of postmenopausal osteoporosis with bone-forming and antiresorptive treatments: combined and sequential approaches. *Bone.* 2020;139:115516, doi:10.1016/j.bone.2020.115516.
70. Diez-Perez A, Adachi JD, Agnusdei D, et al. Treatment failure in osteoporosis. *Osteoporos Int.* 2012;23:2769–2774, doi:10.1007/s00198-012-2093-8.
71. Ayers C, Kansagara D, Lazur B, Fu R, Kwon A, Harrod C. Effectiveness and safety of treatments to prevent fractures in people with low bone mass or primary osteoporosis: a living systematic review and network meta-analysis for the american college of physicians. *Ann Intern Med.* 2023;176:182–195, doi:10.7326/M22-0684.
72. Black DM, Condra K, Adams AL, Eastell R. Bisphosphonates and the risk of atypical femur fractures. *Bone.* 2022;156:116297, doi:10.1016/j.bone.2021.116297.
73. Xiao Y, Chen Y, Huang Y, Xiao Y. Atypical femur fracture associated with common anti-osteoporosis drugs in FDA adverse event reporting system. *Sci Rep.* 2023;13:10892, doi:10.1038/s41598-023-37944-x.
74. Watts NB, Grbic JT, Binkley N, et al. Invasive oral procedures and events in postmenopausal women with osteoporosis treated with denosumab for up to 10 years. *J Clin Endocrinol Metab.* 2019;104:2443–2452, doi:10.1210/jc.2018-01965.