Fracture Facts: Real World Osteoporosis Cases

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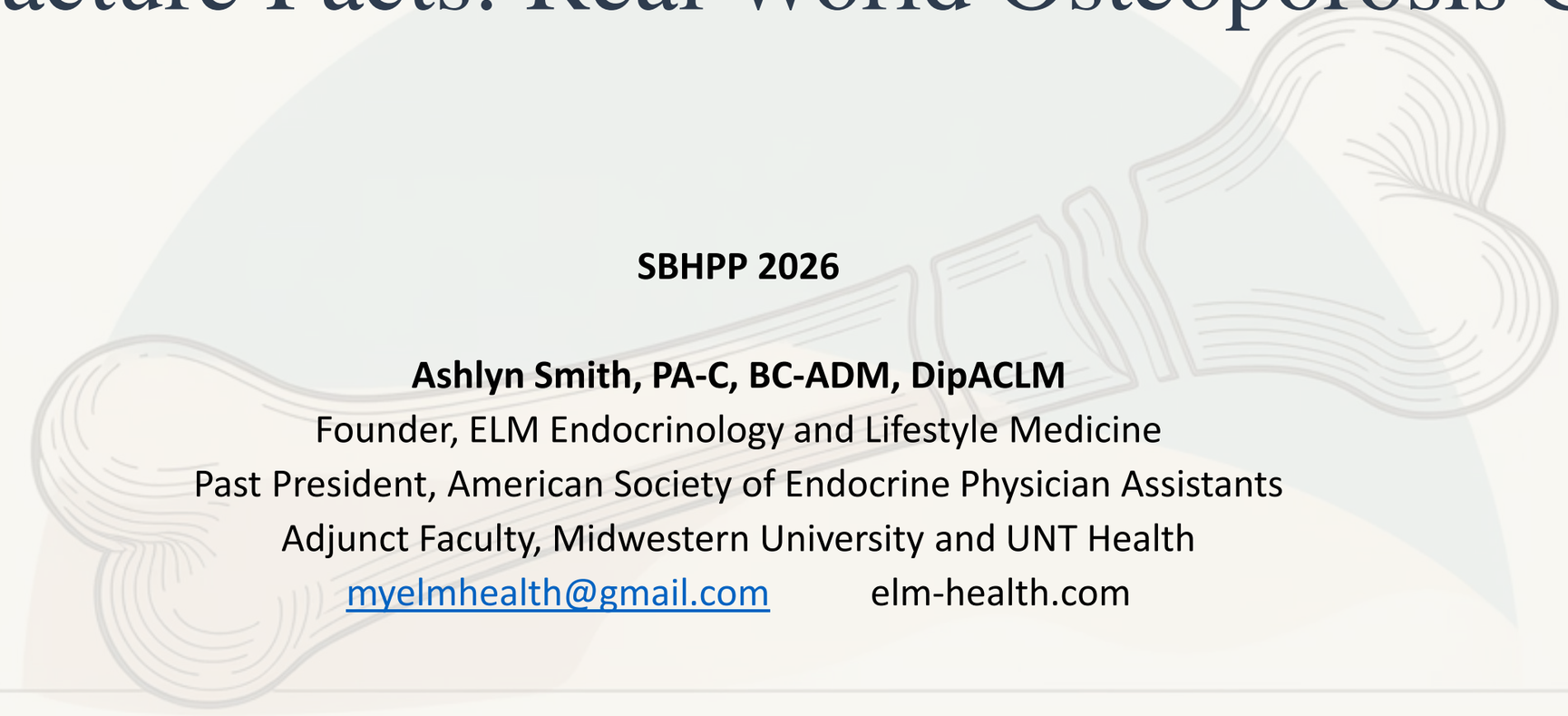


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I have relevant relationships with ineligible companies to disclose within the past 24 months:
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All of the relevant financial relationships listed have been mitigated.

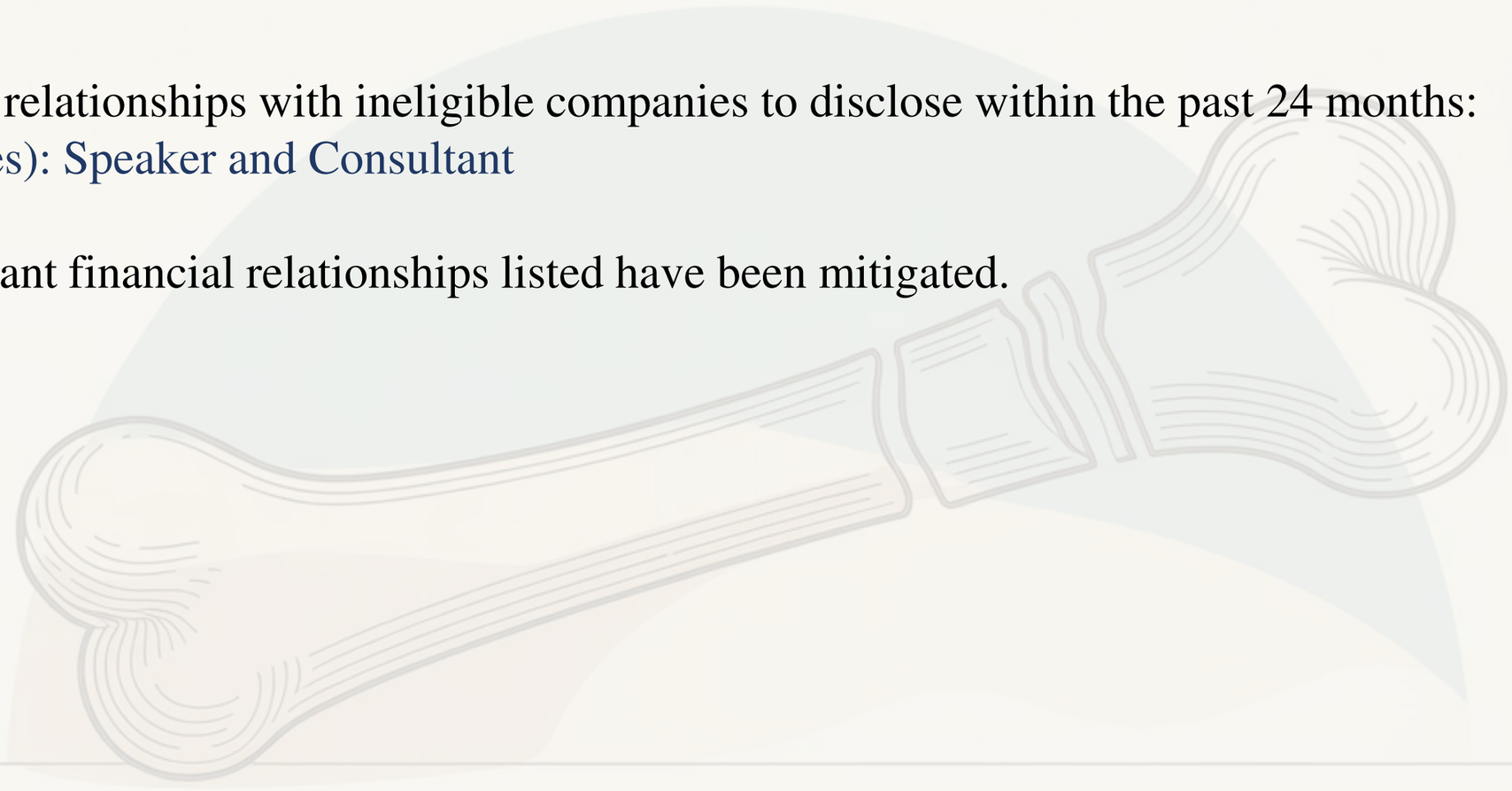


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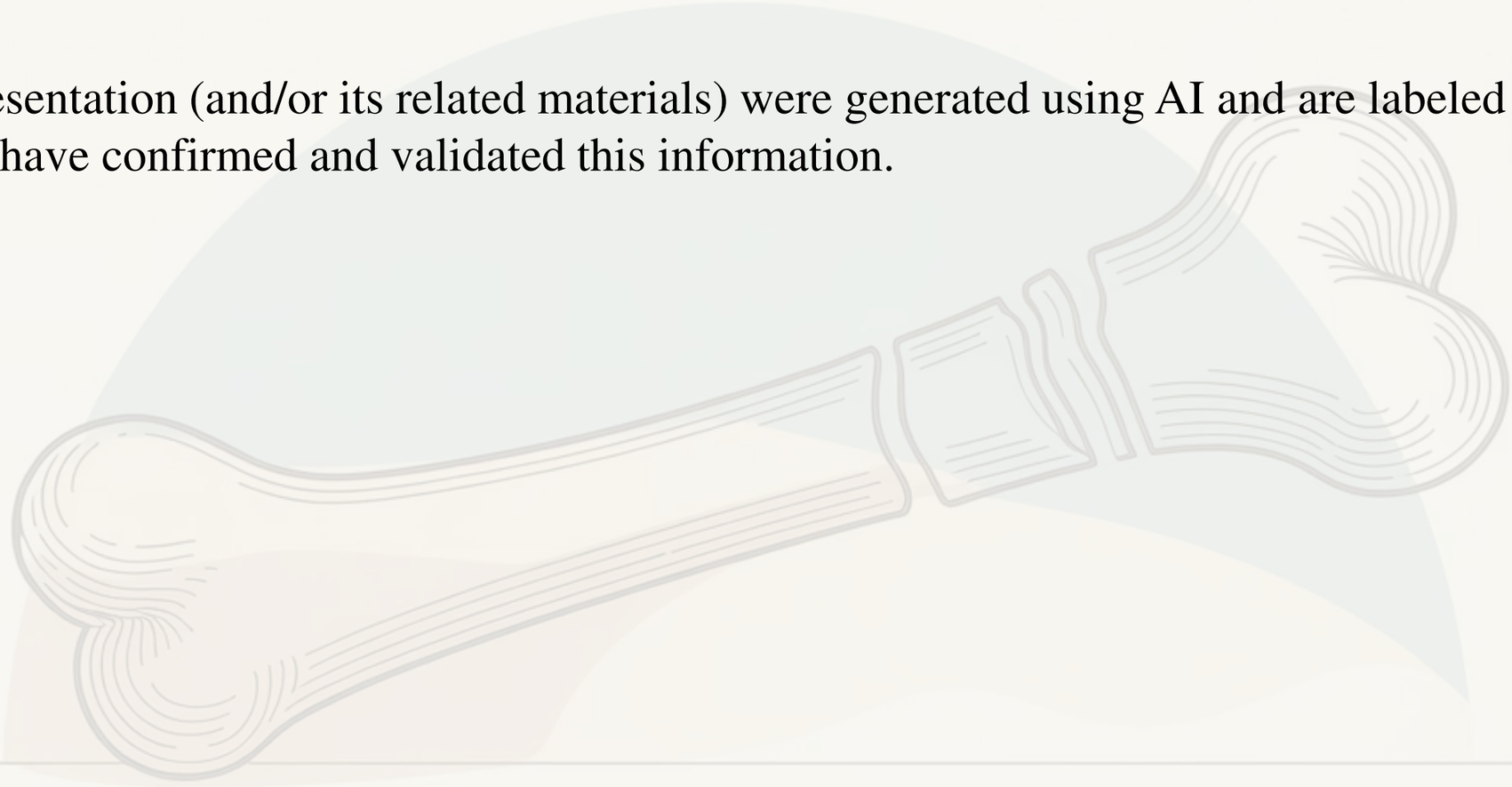


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Learning Objectives

At the conclusion of this activity, participants should be able to:

- Delineate osteoporosis screening guidelines and diagnostic criteria.
- Apply risk stratification techniques to categorize high, versus very high, risk of fracture.
- Develop a comprehensive osteoporosis treatment plan to include lifestyle, nutritional, fall prevention, and pharmacologic interventions.
- Navigate real-world, case-based discussions to individualize osteoporosis care for a diverse patient population.

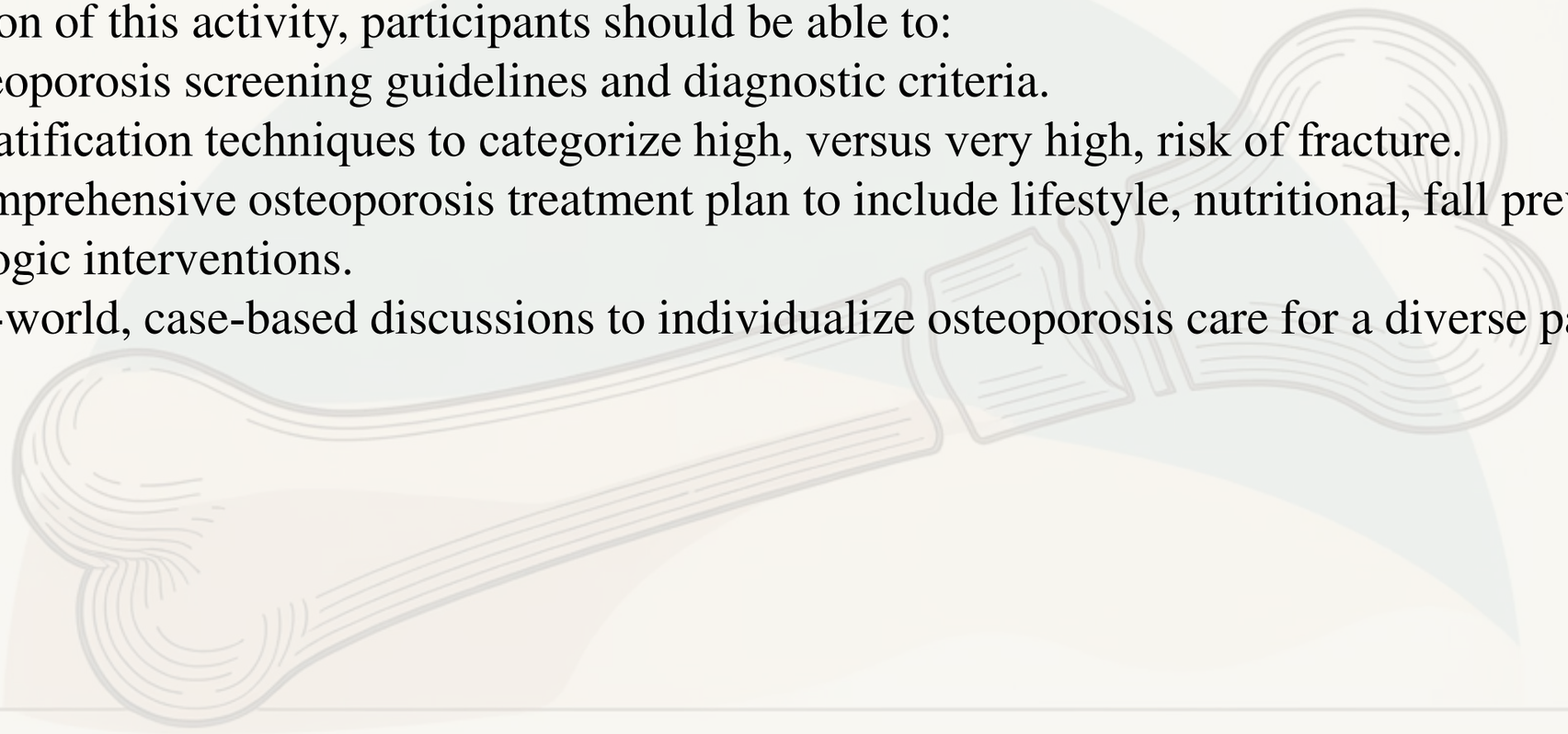


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The Global Impact of Osteoporosis

3

Seconds Between Fractures

Every 3 seconds worldwide, a fracture due to osteoporosis occurs

80%

Treatment Gap

Individuals with fragility fractures never identified or treated

86%

Increased Risk

Risk increase for subsequent fracture after first osteoporosis-related fracture

Osteoporosis represents a *silent epidemic with catastrophic consequences*. Despite the availability of effective therapies and clear guidance on screening, prevention, and treatment, a significant care gap persists.

The condition causes fracture in 1 in 3 women and 1 in 5 men ages 50 years and older globally.

References: International Osteoporosis Foundation. Epidemiology of osteoporosis and fragility fractures. 2019. Kanis JA, et al. SCOPE 2021: a new scorecard for osteoporosis in Europe. Arch Osteoporos. 2021;16(1):82.

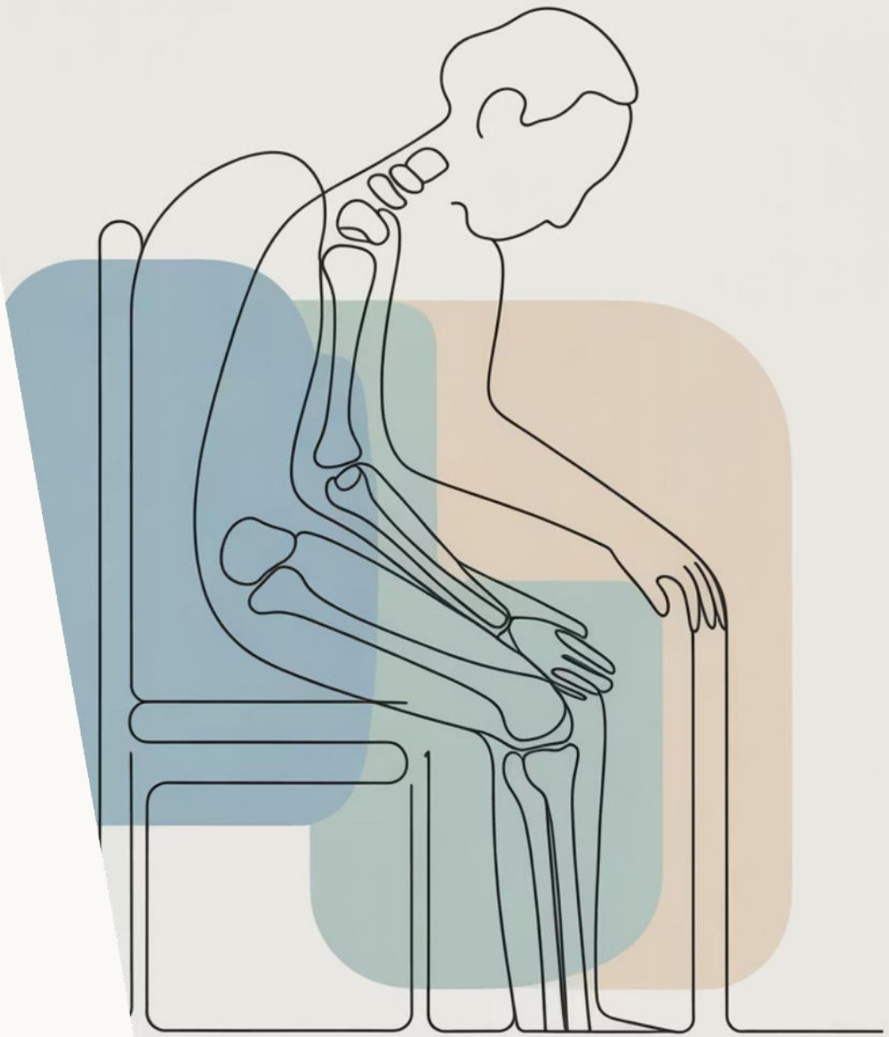


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The Cascade of Consequences

After Hip Fracture

- 40% cannot walk independently
- 60% need help with activities of daily living
- 20-24% die within 1 year

Secondary Fracture Risk

After a fragility fracture, risk of a second fracture triples in the first year. A primary sentinel spine fracture carries the highest risk of secondary fracture, followed by hip, humerus, and forearm fractures.

Each fragility fracture carries risk of hospitalization, high costs associated with care, and the potential for impaired mobility, isolation, and depression. These statistics underscore the critical importance of both *primary prevention* and *timely intervention* when fragility fracture occurs.

References: Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int. 2006;17(12):1726-33. Center JR, et al. Risk of subsequent fracture after low-trauma fracture in men and women. JAMA. 2007;297(4):387-94.

Economic Burden and Healthcare Gap

54 Million Americans

Estimated to have low bone mass or osteoporosis, placing them at increased risk for fractures

$25 Billion by 2025

Annual costs projected to exceed this amount, rising to nearly $57 billion by 2030

80% Untreated

Patients who suffer a fragility fracture are never evaluated or treated for osteoporosis

The economic burden is substantial and growing. This underdiagnosis and undertreatment highlight the crucial role of primary care clinicians in closing the care gap and improving long-term outcomes for patients at risk.

References: Burge R, et al. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. J Bone Miner Res. 2007;22(3):465-75. Singer A, et al. Burden of illness for osteoporotic fractures compared with other serious diseases among postmenopausal women in the United States. Mayo Clin Proc. 2015;90(1):53-62.

Building Strong Bones: Primary Prevention

Prevention of osteoporosis begins in childhood and young adulthood, with peak bone mass achieved in a person's 20s. A comprehensive prevention strategy addresses multiple modifiable risk factors throughout the lifespan.



Calcium & Vitamin D

Appropriate age-based intake ideally obtained through dietary sources, with supplementation considered when dietary goals aren't met



Smoking Cessation

Avoidance and cessation of smoking critical, as exposure is dose-dependent risk factor



Physical Activity

Engagement in routine weight-bearing exercises to maintain and improve bone mineral density



Healthy Body Weight

Maintenance of normal BMI essential for overall health, with specific avoidance of low body weight



Alcohol Limitation

Limit to 2 units/day for females and 3 units/day for males to reduce bone density risk



Hormonal Health

Maintenance of regular menstrual cycles in females, as estrogen promotes bone mineralization

References: Weaver CM, et al. The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. Osteoporos Int. 2016;27(4):1281-386. Heaney RP, et al. Peak bone mass. Osteoporos Int. 2000;11(12):985-1009.

Exercise: The Foundation of Bone Health

- Weight-bearing exercises help directly maintain and even improve bone mineral density
  - Examples: Walking or running, where one bears their body weight.
- Balance and strength training aid with fall prevention
- Activities such as swimming or cycling, while beneficial for cardiovascular health, are not weight-bearing exercises.
- Consider physical therapy with specific experience and training in low bone density intervention:
  - Individuals with mobility limitations
  - Those needing additional guidance can be referred to a physical therapist.
  - Physical therapy programs can tailor exercise regimens to individual abilities and preferences.

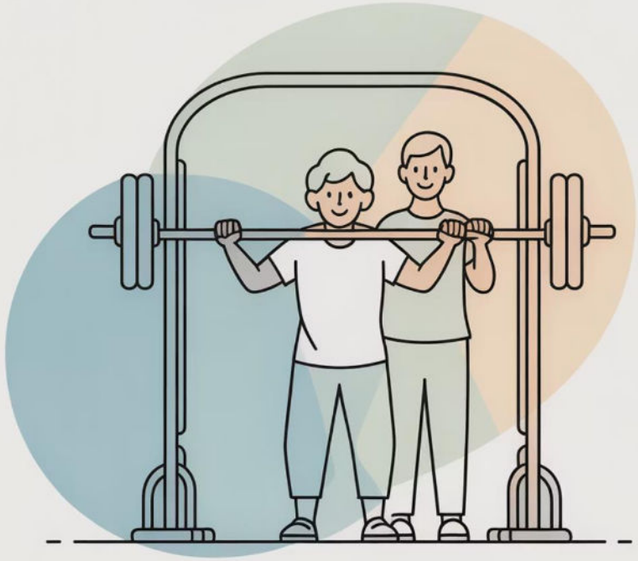


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References: Nikander R, et al. Targeted exercise against osteoporosis: A systematic review and meta-analysis for optimising bone strength throughout life. BMC Med. 2010;8:47. Sherrington C, et al. Exercise to prevent falls in older adults: an updated systematic review and meta-analysis. Br J Sports Med. 2017;51(24):1750-1758.

Hormones and Bone Density

1

Estrogen & Testosterone

Promote bone mineralization throughout life

2

Hormonal Deficiency

Oligomenorrhea, amenorrhea, menopause, hypogonadism increase risk of low bone mineral density (BMD)

3

Clinical Consideration

Hormone replacement therapy can help prevent low BMD but requires shared decision-making

*Prevention, not tx

*Female individuals following menopause are a population known to face increased risk of osteoporosis. While hormone replacement therapy (HRT) is not indicated as a treatment for osteoporosis, it can help prevent low bone mineral density. However, HRT carries specific risks that should be weighed against its benefits, and clinicians should use shared medical decision-making in discussing use with at-risk individuals.

References: Khosla S, et al. Estrogen and the skeleton. Trends Endocrinol Metab. 2012;23(11):576-81. Finkelstein JS, et al. Gonadal steroids and body composition, strength, and sexual function in men. N Engl J Med. 2013;369(11):1011-22.

Risk Factors for Low Bone Mineral Density

Fracture History

- Low-trauma fracture during adulthood
- Parental history of hip fracture
- Hip fracture

Medication Exposure

- Current or past glucocorticoid use >3 months (cumulative)
- Dose ≥5 mg daily prednisolone or equivalent

Physical Changes

- Height loss ≥1.5 inches from peak
- Height loss ≥0.8 inches from previous measurement
- Low body weight

Lifestyle Factors

- Current smoking (dose-dependent)
- Alcohol ≥2 units/day (females) or ≥3 units/day (males)

References: Kanis JA, et al. A meta-analysis of previous fracture and subsequent fracture risk. Bone. 2004;35(2):375-82. Van Staa TP, et al. Use of oral corticosteroids and risk of fractures. J Bone Miner Res. 2005;20(8):1487-94.

Secondary Causes of Osteoporosis

Secondary osteoporosis : bone loss caused by another underlying diagnosis. Identifying these conditions is crucial for comprehensive treatment planning.



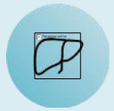
Endocrine Disorders

Eg: Untreated hyperthyroidism, hyperparathyroidism, hypogonadism, premature menopause (age <45 years)



Malabsorption

Eg: Chronic malnutrition, malabsorption syndromes affecting nutrient uptake



Chronic Disease

Eg: Chronic liver disease, rheumatoid arthritis affecting bone metabolism



Genetic Conditions

Eg: Type 1 diabetes, osteogenesis imperfecta in adults

References: Mazziotti G, et al. Drug-induced osteoporosis: mechanisms and clinical implications. Am J Med. 2010;123(10):877-84. Rosen CJ. Clinical practice. Postmenopausal osteoporosis. N Engl J Med. 2005;353(6):595-603.

Screening Guidelines: Who and When

Women

All women ages 65 years and older should receive bone density testing.

Post- or perimenopausal women ages 50 to 65 years with one or more risk factors should also be screened.

Men

BHOF and AACE recommend DXA screening for all men ages 70 years and older, as well as for men ages 50 to 69 years with risk factors including secondary osteoporosis.

USPSTF cites insufficient evidence for routine screening in men.

2025 USPSTF Update: For individuals younger than 65 years with at least one risk factor, clinicians can consider using osteoporosis risk calculators such as Osteoporosis Risk Assessment Instrument (ORAI) or Osteoporosis Self-Assessment Tool (OST) to determine candidacy for screening with a DXA scan.

References: US Preventive Services Task Force. Screening for osteoporosis to prevent fractures: US Preventive Services Task Force recommendation statement. JAMA. 2018;319(24):2521-2531. Camacho PM, et al. American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis-2020 update. Endocr Pract. 2020;26(Suppl 1):1-46.

The Gold Standard: DXA Scanning

Dual-energy X-ray absorptiometry (DXA) scan with or without fracture risk assessment (FRAX) calculation is the *gold standard for screening for fracture risk*.

01

Standard Sites

Lumbar spine and total hip or femoral neck routinely assessed

02

Additional Sites

Distal third forearm assessed in PTH dysfunction or when spine/hip assessment limited

03

Risk Assessment

Most guidelines recommend including fracture risk assessment with BMD measurement such as FRAX

04

2025 Consideration

USPSTF changed FRAX from recommendation to consideration, citing limitations when applying lens of race

References: Kanis JA, et al. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. Osteoporos Int. 2007;18(8):1033-46. International Society for Clinical Densitometry. 2019 ISCD Official Positions - Adult.

Understanding Your Scores: Z-Score vs T-Score

Z-Score: Age-Matched Comparison

Compares bone density to average of healthy person of *same age*, race, and sex.

Most useful for younger individuals (ages 20-50, premenopausal women, men <50, children).

Z-score ≤-2.0 indicates "below expected range for age."

May underrepresent degree of BMD loss in older adults.

T-Score: Peak Bone Mass Comparison

Compares bone density to healthy *young adult* at peak bone mass, illuminating BMD loss more accurately.

Primary diagnostic tool for adults.

->Normal: -1.0 or above.
->Osteopenia: between -1.0 and -2.5.
->Osteoporosis: -2.5 or below.

References: Looker AC, et al. Updated data on proximal femur bone mineral levels of US adults. Osteoporos Int. 1998;8(5):468-89. Kanis JA, et al. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. Osteoporos Int. 2007;18(8):1033-46.

Three Pathways to Diagnosis

A common misconception is that diagnosis of osteoporosis relies on T-score alone. While T-score is a key marker for fracture risk, it is not the only diagnostic criterion. An individual who meets any one of the following criteria can be diagnosed with osteoporosis:

1

T-Score Criteria

T-score ≤-2.5 at hip, spine, or 33% radius on DXA scan

2

Fragility Fracture

Presence of any low-trauma fracture (e.g., from fall from standing height), *irrespective of T-score*

3

Combined Risk Assessment

Osteopenia +
FRAX ≥20% major osteoporotic fracture or ≥3% hip fracture risk

> An analogy: hyperlipidemia is a marker for cardiovascular disease risk, whereas myocardial infarction is overt evidence of disease. Similarly, low T-score indicates risk, but fragility fracture confirms disease.

1. LeBoff, M. S., et al.. The clinician's guide to prevention and treatment of osteoporosis Consensus Statement. Osteoporosis International (2022) 33:2049–2102
2. Camacho, Pauline MD; et al. "American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis— 2020 UPDATE." ENDOCRINE PRACTICE Vol 26 (Suppl 1) May 2020.

The Critical Window After Fracture

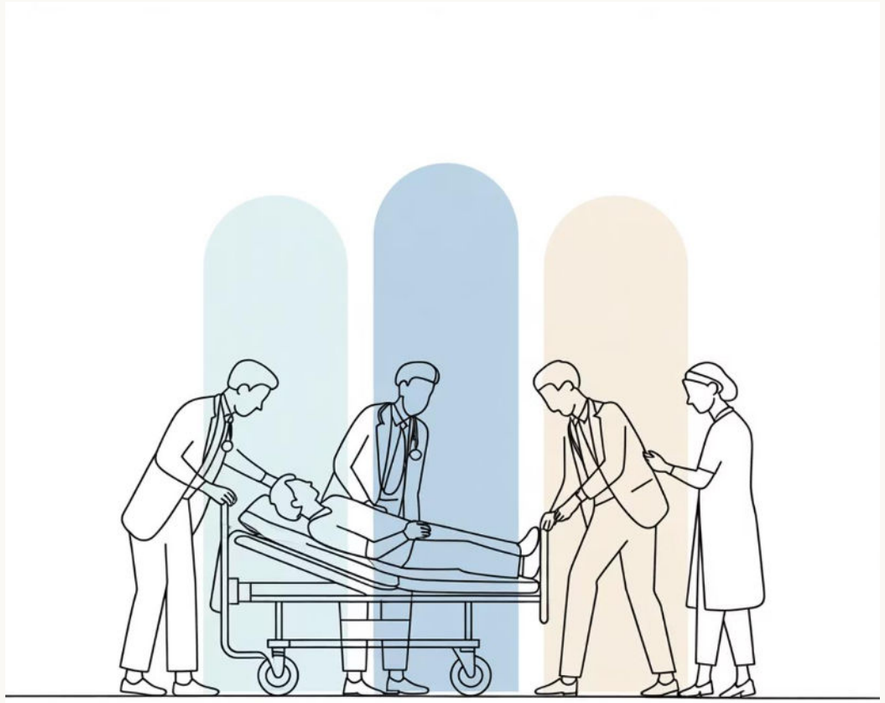


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The period immediately following a fragility fracture is a *critical time* to diagnose and manage osteoporosis.

This window of opportunity can prevent or reduce the associated post-fracture increased risks of subsequent additional fracture, morbidity, mortality, and healthcare costs.

References: Klotzbuecher CM, et al. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. J Bone Miner Res. 2000;15(4):721-39. Bliuc D, et al. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA. 2009;301(5):513-21.

Initial Evaluation: Laboratory Workup

Upon diagnosis of osteoporosis—whether by T-score, FRAX calculation, or presence of fragility fracture—the initial step is an evaluation for secondary causes. This evaluation helps identify underlying conditions that may contribute to bone loss and informs appropriate treatment decisions.

- **Comprehensive Metabolic Panel (CMP) or Basic Metabolic Panel (BMP)**
  - Assesses serum calcium level and renal function.
  - Albumin included to allow for corrected calcium calculation if needed.
  - Renal function important for identifying CKD-MBD and assessing candidacy for certain medications.
- **Serum Phosphate**

  Aids in identifying bone turnover, renal dysfunction, and vitamin D deficiency.
- **Complete Blood Cell (CBC) Count**

  Assesses for signs of malnutrition, malabsorption, and chronic disease that may contribute to bone loss.
- **25-Hydroxyvitamin D Level**

  Assesses for adequate intake and absorption of vitamin D, essential for bone health.

References: Tannenbaum C, et al. Yield of laboratory testing to identify secondary contributors to osteoporosis in otherwise healthy women. J Clin Endocrinol Metab. 2002;87(10):4431-7. Peris P, et al. Guidelines for the diagnosis and treatment of osteoporosis and fragility fractures. Endocrinol Nutr. 2014;61(9):e1-e12.

Additional Workup

Intact Parathyroid Hormone (iPTH)

Assesses for hyperparathyroidism, a common underlying cause of low BMD.

Should be assessed alongside serum calcium and vitamin D level to determine source of parathyroid abnormality.

24-Hour Urine Calcium and Creatinine

Assesses for:

- Excessive calcium excretion (underlying cause of osteoporosis)
- Low calcium excretion, which may suggest familial hypocalciuric hypercalcemia (cause of hypercalcemia without effect on BMD)

Thyroid Stimulating Hormone (TSH)

Assesses for hyperthyroid state, which catabolizes BMD and contributes to bone loss.

Additional tests to consider based on clinical suspicion: Celiac panel (malabsorption), serum and urine protein electrophoresis (malignant cause/hypercalcemia), 24-hour urine sodium (excess calcium excretion), total testosterone (hypogonadism in males).

References: Bilezikian JP, et al. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. J Clin Endocrinol Metab. 2014;99(10):3561-9. Peacock M, et al. Cinacalcet hydrochloride maintains long-term normocalcemia in patients with primary hyperparathyroidism. J Clin Endocrinol Metab. 2005;90(1):135-41.

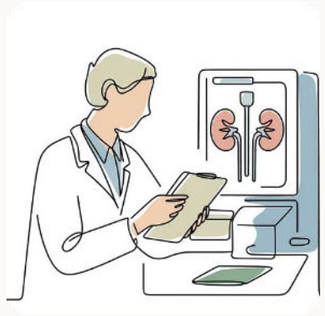
When to Consult Specialists

Should an underlying cause of BMD loss be identified, clinicians should take steps to correct or manage it. Specialist consultation may be needed for comprehensive care.



Endocrinology

For osteoporosis linked to parathyroid disease or hyperthyroidism



Nephrology

For chronic kidney disease–mineral and bone disorder (CKD-MBD)



Gastroenterology

For celiac disease and malabsorption syndromes affecting bone health



Hematology/Oncology

For malignant hypercalcemia and BMD loss related to cancer

References: Rosen CJ, et al. The Official Positions of the International Society for Clinical Densitometry: vertebral fracture assessment. J Clin Densitom. 2013;16(4):482-8. Lewiecki EM, et al. International Society for Clinical Densitometry 2007 Adult and Pediatric Official Positions. Bone. 2008;43(6):1115-21.

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Lifestyle Interventions: The Cornerstone

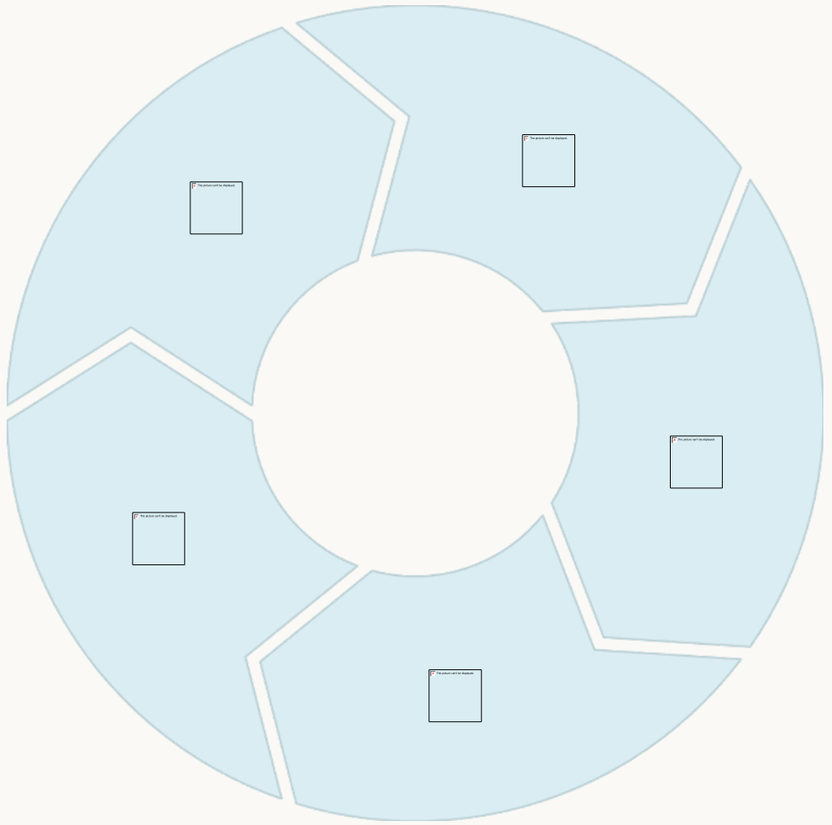
All diagnoses of osteoporosis begin with lifestyle interventions as the cornerstone of management. These interventions mirror the same behaviors that aid in osteoporosis prevention and are essential regardless of pharmaceutical treatment.

Alcohol Limitation

≤2 units/day for females, ≤3 units/day for males

Fall Prevention

Balance training, home safety measures



Smoking Cessation

Higher exposure = higher risk of BMD loss

Weight-Bearing Exercise

Walking, running, add strength training

Nutritional Intervention

Adequate calcium and vitamin D intake

1. Camacho, Pauline MD; et al. “American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diabgnosis and Treatment of Postmenopausal Osteoporosis— 2020 UPDATE.” ENDOCRINE PRACTICE Vol 26 (Suppl 1) May 2020.
2. LeBoff, M. S., et al.. The clinician’s guide to prevention and treatment of osteoporosis Consensus Statement. Osteoporosis International (2022) 33:2049–2102

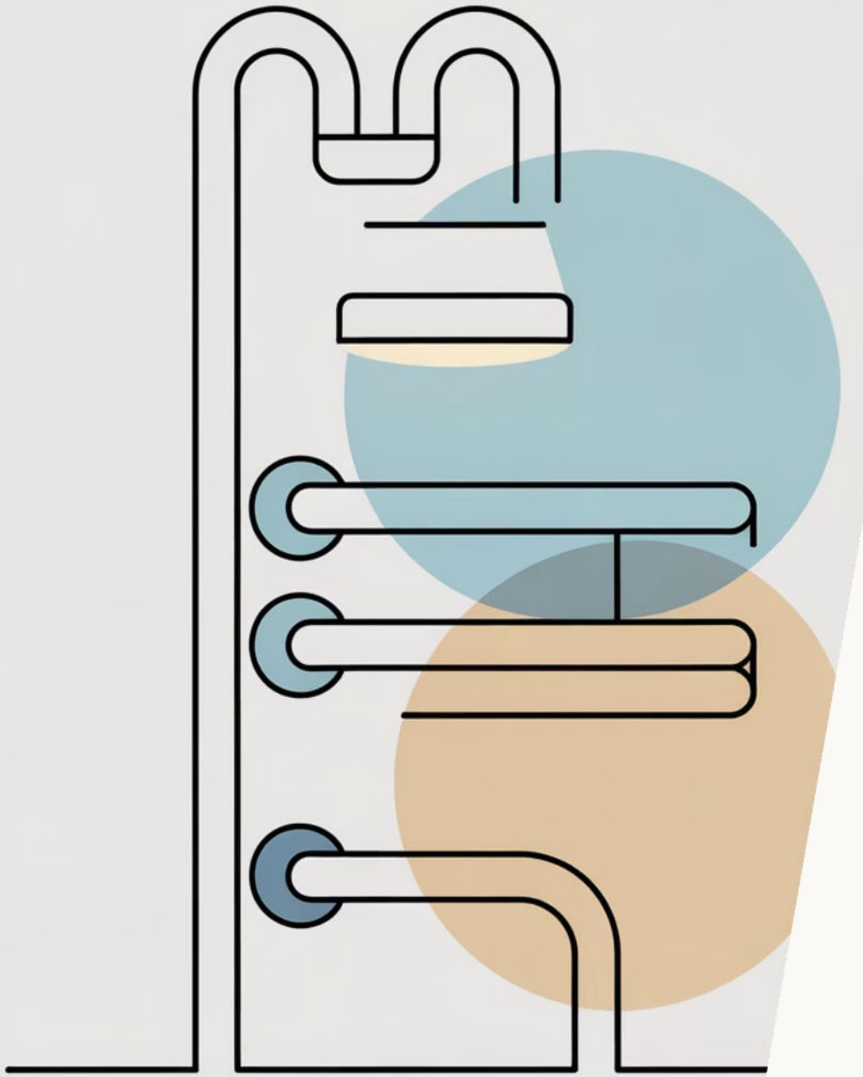


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Fall Prevention Strategies

Patient Actions

- Secure rug corners
- Ensure appropriate lighting in walkways
- Be aware of pets
- Utilize assistive devices near stairs and bathrooms
- Keep mobility devices within reach
- Consider home safety evaluations

Clinician Actions

- Optimize vision
- Monitor and adjust medications
- Avoid overtreatment with antihypertensives
- Dose diuretics to minimize nocturia and volume depletion
- Exercise caution with benzodiazepine receptor agonists
- Identify and correct conditions contributing to falls

Important: Benzodiazepine receptor agonists (e.g., zolpidem, temazepam) have been associated with increased fragility fracture risk and should be prescribed with caution to patients with osteoporosis.

References: Gillespie LD, et al. Interventions for preventing falls in older adults living in the community. Cochrane Database Syst Rev. 2012;(9):CD007146. Tinetti ME, et al. A multifactorial intervention to reduce the risk of falling among elderly people living in the community. N Engl J Med. 1994;331(13):821-7.

Calcium Intake: Diet First, Supplement Second

Nutritional recommendations focus on optimal intake of calcium and vitamin D, with priority placed on dietary intake wherever possible. Additional supplementation with calcium is needed when dietary calcium is suboptimal.



Women ≥50 & Men ≥71

Target daily calcium intake in milligrams



Men Ages 50-70

Target daily calcium intake in milligrams



Maximum Per Dose

Calcium supplements should be divided into doses of 600 mg or less for optimal absorption

> **Clinical Pearl:** Ask patients to track calcium intake for one week while eating their normal diet, then report back. This identifies typical intake and helps patients identify calcium-rich favorite foods to incorporate daily.

References: Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: The National Academies Press; 2011. Weaver CM, et al. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. Osteoporos Int. 2016;27(1):367-76.

Choosing the Right Calcium Supplement

Calcium Carbonate

Pros: Less expensive, fewer tablets needed

Cons: Must be taken with food, requires gastric acid to dissolve, can cause constipation

Calcium Citrate

Pros: Fewer GI considerations, no acid requirement, less constipation

Cons: Lower elemental calcium per tablet, requires more tablets

Alternative Forms

Calcium gluconate, lactate, or phosphate typically contain less absorbable calcium than carbonate or citrate

Although cardiovascular risk of supplemental calcium remains controversial, the cited recommended daily targets are considered safe in osteoporosis treatment.

Importantly, serum calcium level is not a reliable measure of dietary calcium intake, as the body regulates serum calcium closely, including by mobilizing calcium stores in bone.

References: Straub DA. Calcium supplementation in clinical practice: a review of forms, doses, and indications. Nutr Clin Pract. 2007;22(3):286-96. Heaney RP, et al. Absorbability and utility of calcium carbonate and calcium citrate.

J Am Coll Nutr. 1999;18(5):435-41.

Vitamin D: Supplement Based on Serum Level

Vitamin D plays a crucial role in calcium absorption and bone health. Deficiency is common, particularly in older adults, those with limited sun exposure. Regular monitoring ensures adequate levels for optimal bone health.

Vitamin D supplementation is based on an individual's serum vitamin D level, not a specific amount of dietary or supplemental intake. The 25-hydroxyvitamin D level should be measured and supplementation adjusted accordingly.



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If a patient has difficulty tracking or obtaining sufficient nutritional intervention, referral to a registered dietitian nutritionist can be considered for personalized guidance.

References: Holick MF, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911-30. Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: The National Academies Press; 2011.



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Pharmacologic Management: Risk-Stratified Approach

Any diagnosis of osteoporosis indicates high risk of fracture; therefore, pharmaceutical intervention is strongly recommended.

Treatment options can broadly be divided into anti-resorptive and anabolic agents, with choice depending on severity of fracture risk.

1

Anti-Resorptive Agents

Decrease bone turnover by *slowing bone resorption*, interfering with natural downward trajectory of BMD

2

Anabolic Agents

Promote bone regrowth by stimulating osteoblastic activity, helping reverse degree of bone loss

1. Camacho, Pauline MD; et al. “American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diabgnosis and Treatment of Postmenopausal Osteoporosis—2020 UPDATE.” ENDOCRINE PRACTICE Vol 26 (Suppl 1) May 2020.
2. LeBoff, M. S., et al.. The clinician’s guide to prevention and treatment of osteoporosis Consensus Statement. Osteoporosis International (2022) 33:2049–2102

First-Line Therapy for High Risk

First-line agents for patients with osteoporosis at high risk of fracture are the *antiresorptive* agents. These medications have been shown to reduce vertebral, hip, and non-vertebral fractures by 40% to 50% over 3 years.

Alendronate Oral bisphosphonate, proven efficacy, cost-effective first	**Risedronate** Oral bisphosphonate, alternative to alendronate with similar efficacy
Zoledronic Acid IV bisphosphonate given once yearly, option for GI contraindications	**Denosumab** Alternative first-line agent if other options not preferred or contraindicated

Note: Ibandronate is not a first-line agent, as its effect on fracture risk reduction is specific to the spine only.

1. Camacho, Pauline MD; et al. “American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diabgnosis and Treatment of Postmenopausal Osteoporosis—2020 UPDATE.” ENDOCRINE PRACTICE Vol 26 (Suppl 1) May 2020.
2. LeBoff, M. S., et al.. The clinician’s guide to prevention and treatment of osteoporosis Consensus Statement. Osteoporosis International (2022) 33:2049–2102

Identifying Very High Risk Patients

All individuals with osteoporosis are at high risk of fracture. However, certain factors indicate elevated concern due to very high risk of fracture, requiring more aggressive treatment approaches.

Recent Fracture

Fracture within the past 12 months significantly increases immediate risk

Fracture on Treatment

Fracture while on osteoporosis treatment indicates treatment failure

Medication-Related Fractures

Fractures while on drugs detrimental to bone health

Multiple Fractures

History of multiple fractures compounds risk exponentially

Fall Risk

At risk for falls or history of injurious falls

Very Low T-Score

T-score less than -3.0 indicates severe bone loss

Very High FRAX Score

Major osteoporosis fracture risk >30% or hip fracture risk >4.5%

1. Camacho, Pauline MD; et al. “American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diabgnosis and Treatment of Postmenopausal Osteoporosis—2020 UPDATE.” ENDOCRINE PRACTICE Vol 26 (Suppl 1) May 2020.
2. LeBoff, M. S., et al.. The clinician’s guide to prevention and treatment of osteoporosis Consensus Statement. Osteoporosis International (2022) 33:2049–2102

First-Line Therapy for *Very* High Risk

First-line agents for patients at very high risk of fracture are the *anabolic* agents. These medications promote bone formation and can reverse bone loss more effectively than anti-resorptive therapy alone.



Teriparatide

PTH analog
Daily injection
50-65% fracture risk reduction after 18 months



Abaloparatide

PTH analog
Daily injection
Similar efficacy to teriparatide



Romosozumab

Sclerostin inhibitor
Monthly injection
70% fracture risk reduction at one year

Alternatively, anti-resorptive therapy can be considered in very high-risk patients if anabolic therapy is not preferred or is contraindicated. However, anabolic agents offer superior bone-building capacity for those at greatest risk.

1. Camacho, Pauline MD; et al. “American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diabgnosis and Treatment of Postmenopausal Osteoporosis—2020 UPDATE.” ENDOCRINE PRACTICE Vol 26 (Suppl 1) May 2020.
2. LeBoff, M. S., et al.. The clinician’s guide to prevention and treatment of osteoporosis Consensus Statement. Osteoporosis International (2022) 33:2049–2102

Bisphosphonates: Benefits and Precautions

Benefits

- Reduce fracture risk by ~50% over 3 years
- Available in weekly, monthly, or yearly dosing
- Cost-effective first-line option
- Extensive safety and efficacy data

Dosing Options

Oral preparations (alendronate, risedronate) or once-yearly IV zoledronic acid for patients with GI contraindications or barriers to oral medication

Precautions

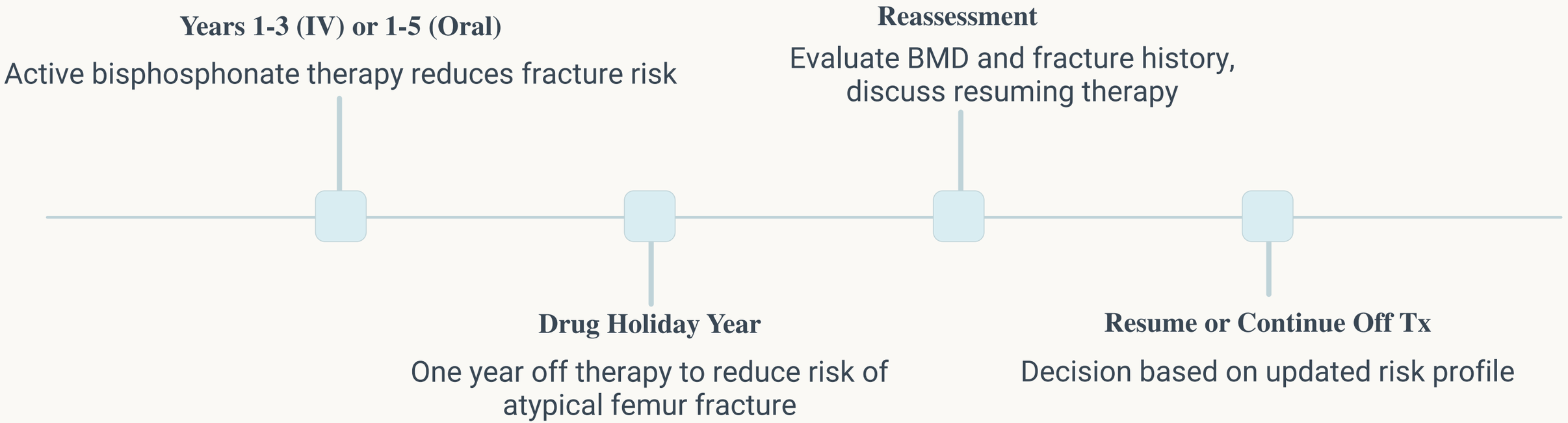
- Oral agents can cause gastric reflux
- Precluded in gastroesophageal disease
- Require creatinine clearance ≥35 mL/min
- Risk of osteonecrosis of jaw (ONJ)
- Risk of atypical femur fracture (AFF) with prolonged use

Dental Care

Dental clearance prior to initiation and routine dental checks advised to reduce ONJ risk, highest following dental injuries or invasive procedures

References: Shane E, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2014;29(1):1-23. Khosla S, et al. Bisphosphonate-associated osteonecrosis of the jaw: report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2007;22(10):1479-91.

The Drug Holiday: Balancing Benefit and Risk



Although bisphosphonate therapy reduces the risk of fragility fracture, prolonged use increases the risk of atypical femur fracture not associated with low BMD. To reduce this risk, patients are recommended to take one year off therapy after 3 consecutive years on IV bisphosphonate or 5 sequential years on oral bisphosphonate. Following a drug holiday, bisphosphonate therapy can be resumed. Alternative treatment during a drug holiday can be considered based on individual risk category.

References: Adler RA, 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(1):16-35. Black DM, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). J Bone Miner Res. 2012;27(2):243-54.

Denosumab: A Unique Alternative

Mechanism & Efficacy

- Monoclonal antibody RANK ligand inhibitor
- Injectable every 6 months
- Reduces fx risk over 3 years: 68% vertebral, 40% hip, 20% non-vertebral

Key Advantages

- No renal dose adjustment or creatinine clearance requirement
- Lower risks of ONJ and AFF compared to bisphosphonates

Critical Warnings

- Boxed warning for severe hypocalcemia in advanced renal disease (2024)
- Rebound vertebral fxs as soon as 7 months post-injection BMD returns to baseline after 2 years if stopped.

No Drug Holiday

- Drug holiday NOT recommended
- If discontinued, transition to alternative osteoporosis agent to prevent rebound fractures
- Careful patient selection and adherence education essential

References: Cummings SR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med. 2009;361(8):756-65. Bone HG, 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(7):513-523.

PTH Analogs: Building Bone Back

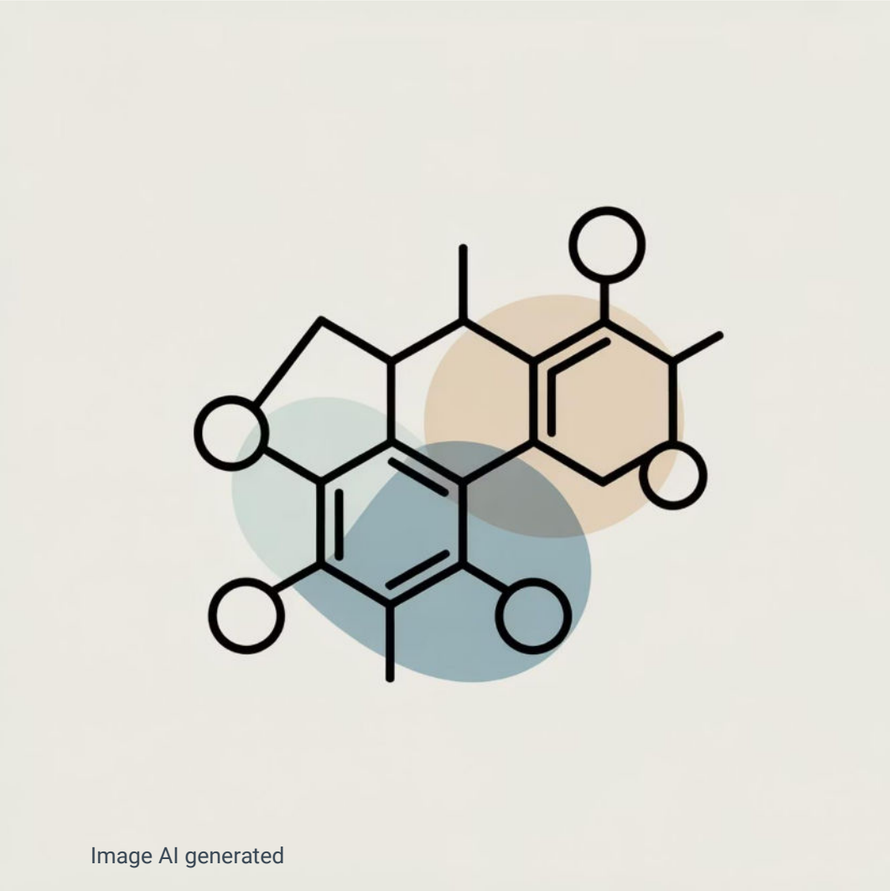


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50% to 65% reduction in fracture risk after 18 months of therapy

These agents mimic endogenous PTH to promote bone formation, offering powerful bone-building capacity for very high-risk patients.

Important Limitations: *2-year lifetime limitation*

Use generally limited to 2 years in a lifetime (unless under specialist direction) due to osteosarcoma signal in rats. The 2 years are cumulative and need not be consecutive. Use should be avoided in Paget disease and prior skeletal radiation.

Critical Consideration: *Sequential therapy is key*

When PTH analog is stopped, sequential therapy with another osteoporosis agent is key to preserve bone density regained. Without consecutive therapy, bone loss after discontinuation can be rapid.

References: Neer RM, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med. 2001;344(19):1434-41. Miller PD, et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial. JAMA. 2016;316(7):722-33. Vahle JL, et al. Skeletal changes in rats given daily subcutaneous injections of recombinant human parathyroid hormone (1-34) for 2 years and relevance to human safety. Toxicol Pathol. 2002;30(3):312-21.

Romosozumab: The Newest Anabolic Option

Mechanism of Action

Sclerostin inhibitor opposes osteocyte-derived inhibitor of bone formation

Superior Efficacy

Reduces fracture risk by ~70% at one year, 50% further reduction beyond alendronate in head-to-head comparison

Treatment Duration

One year of therapy (based on efficacy without increased safety signals), given as monthly injections

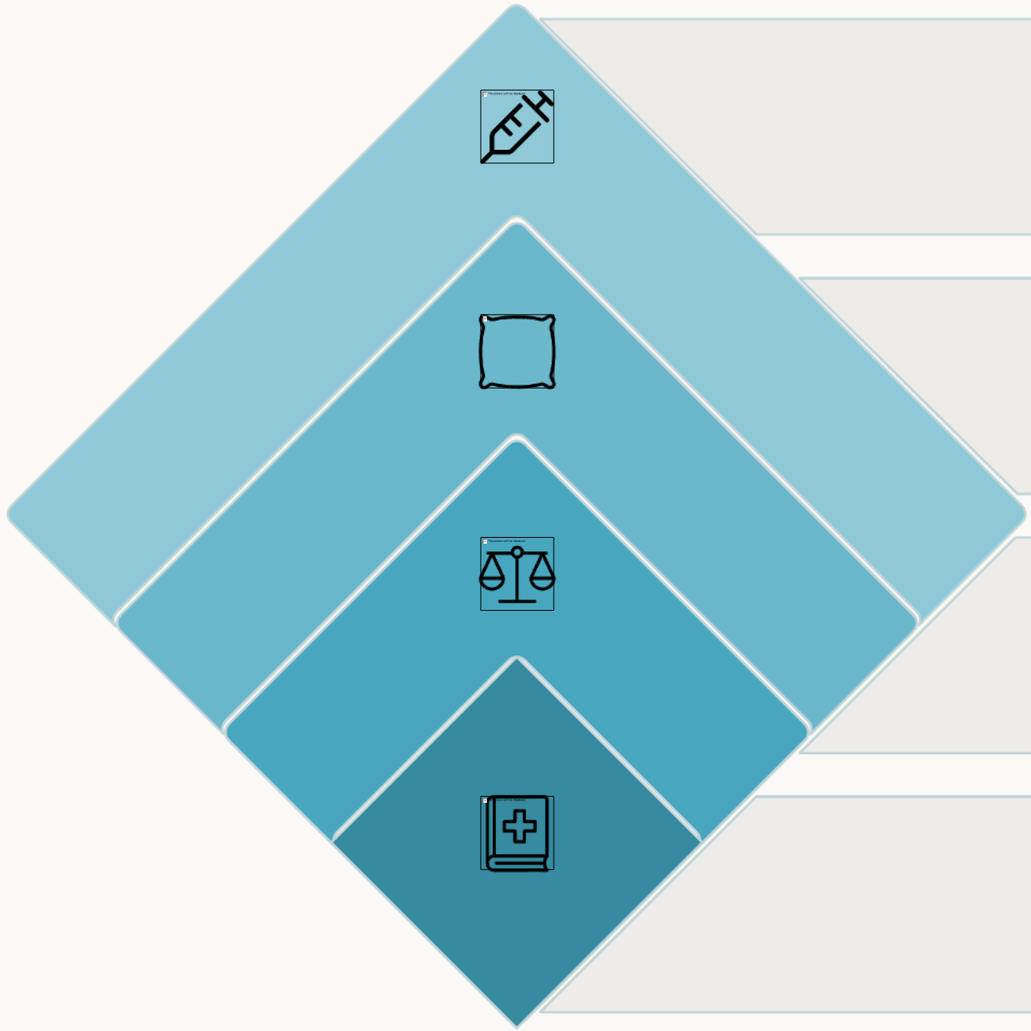
Sequential Therapy

Must be followed by antiresorptive therapy to maintain gains

Important Restrictions: Currently restricted to females. Boxed warning for individuals with history of MI or stroke within last year. Postmarket information suggests increased risk of ONJ; dental clearance and precautions similar to bisphosphonates and denosumab.

References: Cosman F, et al. Romosozumab treatment in postmenopausal women with osteoporosis. N Engl J Med. 2016;375(16):1532-1543. Saag KG, et al. Romosozumab or alendronate for fracture prevention in women with osteoporosis. N Engl J Med. 2017;377(15):1417-1427.

Treatment Selection Pathway



Very High Risk

Anabolic agents first-line

High Risk

Anti-resorptives: bisphosphonates or denosumab

Risk Stratify

High risk vs very high

Diagnosis

Confirm osteoporosis

Monitoring and Assessing Treatment Response

After initiation of pharmaceutical intervention, monitoring with DXA scan every 1 to 2 years is generally recommended, with consideration for less frequent monitoring once bone density is stable.

Adequate Response

As the natural trajectory of BMD is downward, stable BMD is one indicator of response to osteoporosis intervention. Continued monitoring ensures sustained benefit.

Treatment Failure

Significant bone mineral density decline or a new fragility fracture indicates treatment failure and need to switch therapy. Fracture despite therapy is an indication of very high risk of fracture.

Escalation Strategy

Treatment failure warrants transition to anabolic therapy for 1 to 2 years depending on medication class, patient preference, and clinical picture. Sequential therapy using anti-resorptive agents following anabolic agents maintains BMD improvement.

References: Watts NB, et al. Osteoporosis in men: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012;97(6):1802-22. Lewiecki EM, et al. Official positions of the International Society for Clinical Densitometry. J Clin Endocrinol Metab. 2004;89(8):3651-5.

Special Populations: Unique Considerations

Specific populations may be at high risk of bone mineral density loss or have poorly understood bone health dynamics, requiring individualized approaches to screening and treatment.



Eating Disorders

Malnutrition and hormonal disruption significantly impact bone health; requires multidisciplinary care



Premature Ovarian Failure

Hormone therapy recommended until natural menopause age to protect bone, per guidelines



Type 1 & Type 2 Diabetes

Fracture risk elevated even with normal BMD due to poor bone quality; requires heightened vigilance



Bariatric Surgery

Malabsorption following surgery affects calcium and vitamin D uptake; close monitoring essential



Male Individuals

Often underdiagnosed; approved agents include alendronate, risedronate, zoledronic acid, denosumab, teriparatide, abaloparatide



Transgender Individuals

Bone health depends on hormone use and duration of hypogonadism; research remains limited

Further study of osteoporosis occurrence, impact, pathophysiology, and potential pharmacologic approaches in these populations is needed to optimize care.

References: Golden NH, et al. Optimizing bone health in children and adolescents. Pediatrics. 2014;134(4):e1229-43. Misra M, et al. Anorexia nervosa and bone metabolism. Psychoneuroendocrinology. 2004;29(7):949-64. Yu EW, et al. Bone metabolism after bariatric surgery. J Bone Miner Res. 2014;29(7):1507-18.

Case Study 1: Treatment Failure and Escalation

01

Initial Diagnosis

Postmenopausal woman diagnosed with osteoporosis at high risk of fracture on screening DXA scan

02

First-Line Treatment

Started on oral bisphosphonate but develops gastric reflux despite proper administration; transitioned to IV bisphosphonate

03

Initial Response

After one year, repeat DXA shows stable BMD; continued on IV bisphosphonate for second infusion

04

Treatment Failure

Six months later, patient sustains hip fragility fracture following trip and fall

05

Recognition & Escalation

Fracture on therapy indicates treatment failure and very high risk; clinician recommends transition to anabolic therapy based on shared decision-making

> Recognize treatment failure and appropriately escalating care to prevent subsequent fractures and their devastating consequences.

References: Diez-Perez A, et al. Treatment failure in osteoporosis. Osteoporos Int. 2012;23(12):2769-74. Adler RA, 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(1):16-35.

Case Study 2: Successful Drug Holiday

-> Imagine the same patient had not sustained a hip fragility fracture. Instead, her annual BMD at year two continued to be stable, indicating high risk of fracture rather than very high risk.

Year 1

IV bisphosphonate initiated, BMD stable at 1 year

Year 2

Second IV infusion, BMD remains stable

Year 3

Third IV infusion, continued stable BMD

Year 4

Drug holiday recommended; lifestyle and nutritional interventions maintained

Year 5

BMD and fracture history reassessed; discuss resuming therapy based on updated risk profile

- After three sequential years of IV bisphosphonate therapy, the clinician recommends one year off therapy (drug holiday), while maintaining lifestyle and nutritional interventions.
- Following one year off therapy, BMD and fracture history are reassessed, and resuming IV bisphosphonate therapy or continuing off pharmaceutical treatment is discussed based on updated risk profile.

References: Black DM, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). J Bone Miner Res. 2012;27(2):243-54. McClung MR, et al. Bisphosphonate therapy for osteoporosis: benefits, risks, and drug holiday. Am J Med. 2013;126(1):13-20.

Closing the Care Gap: A Call to Action

Clinicians across many specialties may encounter patients at risk for osteoporosis

- Multiple opportunities for timely screening and diagnosis
- potentially causing confusion over *which specialty takes* ownership of the condition

Care teams can help prevent this confusion—and the resultant healthcare gap—by clearly communicating amongst each other and with their patients

- The phrase *"own the bone"* emphasizes the importance of every clinician taking responsibility for identifying and managing osteoporosis within their patient population

Approximately 80% of individuals who have sustained a fragility fracture are not identified as having osteoporosis nor treated for the condition. This represents a critical opportunity for intervention.



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Key Teaching Points: Screening & Diagnosis

1

Screening is critical but underutilized

Despite clear guidelines, ~80% of patients with fragility fractures are never evaluated or treated for osteoporosis

2

USPSTF 2025 update

Screening recommended for all women ≥65 and postmenopausal women 50-64 with risk factors; for men, evidence limited, but AACE/BHOF recommend screening ≥70 or ≥50 with risk factors

For adults under 65 with risk factors, consider tools like ORAI or OST to assess need for DXA screening.

3

Diagnostic criteria are broader than T-score

Osteoporosis diagnosed by: T-score ≤-2.5, fragility fracture, or osteopenia + FRAX (≥20% major, ≥3% hip)

4

Fragility fractures predict future fractures

Prior fracture increases risk by 86%; risk triples in first year. Hip and spine fractures carry greatest morbidity and mortality

Key Teaching Points: Treatment & Monitoring

1 **Identify very high-risk patients**

Features include recent fracture (≤12 months), fracture on therapy, multiple fractures, very low T-score (<-3.0), or very high FRAX (>30% major, >4.5% hip)

2 **Lifestyle is the foundation**

Adequate calcium/vitamin D (diet first, supplement if needed), weight-bearing and balance exercise, smoking cessation, alcohol moderation essential

3 **Pharmacologic therapy is stratified by risk**

High risk → first-line antiresorptives (alendronate, risedronate, zoledronic acid, denosumab).
Very high risk → anabolic therapy (teriparatide, abaloparatide, romosozumab) followed by antiresorptive maintenance

4 **Drug holidays and monitoring**

Bisphosphonates require drug holiday after 5 years oral or 3 years IV.
No drug holiday for denosumab; if stopped, start alternative agent.
DXA every 1-2 years; stable BMD = adequate response

Comprehensive Management: A Dynamic Process

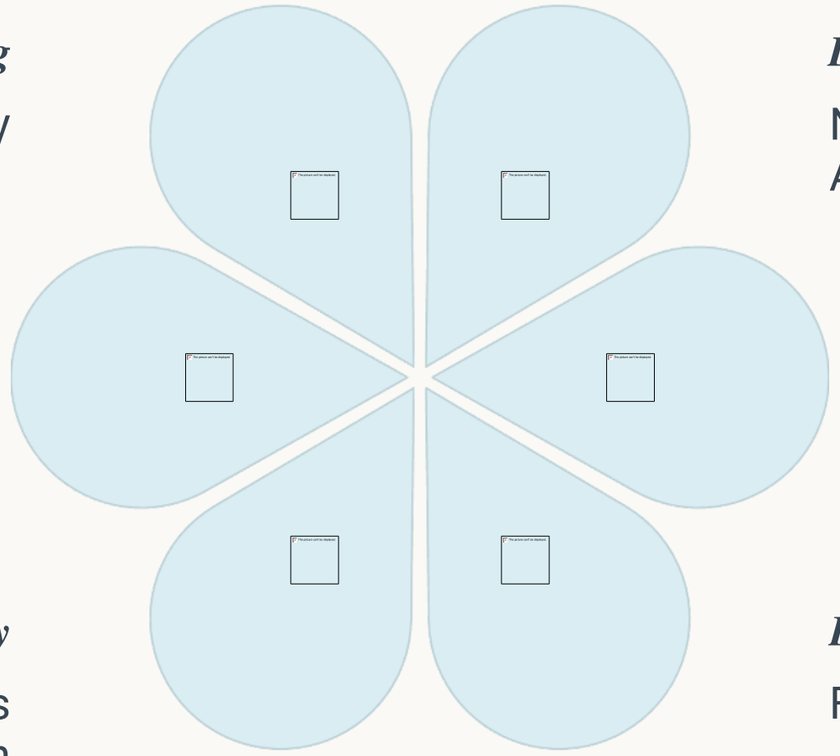
Osteoporosis management is a dynamic process requiring consistent monitoring and assessment/reassessment of fracture risk stratification alongside the overall clinical picture to optimize patient outcomes.

Screening

Identify at-risk individuals early

Diagnosis

Not just T-score
Assess fx hx and FRAX



Monitoring

Regular assessment and adjustment

Risk Stratification

Distinguish high vs very high risk

Pharmacotherapy

All dx of osteoporosis
Risk-stratified medication selection

Lifestyle Intervention

Foundation of all treatment plans

Primary prevention is key to reducing the significant risks of mortality, loss of mobility, subsequent fracture, isolation, and depression that accompany low-trauma fractures.

Call to Action



Identify those at risk for osteoporosis



Screen and diagnose using T-score, fx hx, and/or fracture risk assessment



Risk-stratify all cases of osteoporosis



Tx recommendations based on risk category:

➔ High risk: anti-resorptive

➔ Very high risk: anabolic



Nutritional and lifestyle intervention for all dx of osteoporosis



Osteoporosis is dynamic, requiring consistent monitoring and risk reassessment

Questions?

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