

# Osteoporosis

## Who to Screen

The U.S. Preventive Services Task Force (2018):

- Women  $\geq 65$
- Postmenopausal women  $< 65$  years at increased risk using a clinical risk assessment tool<sup>†</sup>
- Insufficient evidence for screening for osteoporosis in men (I)

AACE (2020) and BHOE (2022) - same as USPSTF plus

- Men  $\geq 70$  years
- Younger men with RF

<sup>†</sup> A healthy 65 year old woman has a 10 year fracture risk score of 8.5% (based on FRAX risk calculator)

## Bone Mineral Density\*

Normal	$\geq -1.0$
Osteopenia	Between -1.0 to -2.5
Osteoporosis	$\leq -2.5$

\* BMD should be measured at the forearm (1/3 radius) when:

- The hip and lumbar spine cannot be accurately measured due to structural changes (i.e., osteophytes)
- Weight limitations

FRAX: Major osteoporotic fracture probability  $\geq 20\%$  or hip fracture probability  $\geq 3\%$  is a common treatment threshold.

## Diagnosis

- T score  $< -2.5$
- H/o fragility fracture of hip or spine (regardless of T-score)
- Elevated FRAX Score (or if available TBS adjusted FRAX) **PLUS** Osteopenia
- H/o fracture at proximal humerus, distal forearm or pelvis **PLUS** Osteopenia

## Vertebral Fracture Assessment (VFA)

What is it?

- A diagnostic test using dual-energy X-ray absorptiometry (DXA) to detect vertebral fractures from the thoracic to lumbar spine.
- Provides a low-radiation alternative to traditional spine X-rays.
- Can be performed simultaneously with a DXA scan, allowing both bone density and fracture assessment in one visit.

Why VFA is Important:

- Detects silent vertebral fractures, which often go unnoticed but increase future fracture risk.
- Helps refine fracture risk assessment and guides osteoporosis treatment plans.

When to order:

- Significant Height Loss:
  - Loss of  $>4$  cm historically or  $>2$  cm recently may suggest vertebral fractures.
- History of Fractures or Kyphosis:
  - Patients with previous fractures, especially after age 50, or visible spine curvature.
- Other High Fracture Risk Factors:
  - Conditions like long-term glucocorticoid use, rheumatoid arthritis, or frailty.

## When to Repeat BMD

Initial BMD Result (T-score)	Follow-Up Interval, years	Initial hip fracture risk, %
$\geq -1.0$	$> 10$	$< 0.8$
-1.0 to -1.4	5-10	0.8 to 1.4
-1.5 to -1.9	3-5	1.5 to 2.2

Leslie WD, Crandall CJ. JAMA. 2021 Oct 26;326(16):1622-3.

Parameter	Trabecular Bone Score	DXA (Dual-Energy X-ray Absorptiometry)
Definition	Measure of trabecular bone quality	Standard method for assessing bone mineral density (BMD)
Focus	Bone microarchitecture	Overall bone density
Scoring Range	-2 to +2	T-scores (compared to young adult reference)

## Labs

- AACE 2020: CBC, CMP, vitamin D, PTH, phosphate, 24-hour urine collection for calcium, sodium, creatinine, consider: TSH, celiac Ab, UPEP/SPEP
- The minimum: vitamin D, calcium, creatinine

## When to Repeat BMD once Treatment is Started

No clear consensus

- No need to repeat DEXA until 5 years of treatment (3 yrs if treating w/ Zoledronic acid) (ACP)
- Perform BMD testing 1 to 2 years after initiating or changing medical therapy for osteoporosis and at appropriate intervals thereafter according to clinical circumstances (BHOE 2022)
- 1-2yrs after starting drug holiday (BHOE, AACE)

## Classification

**Primary Osteoporosis** - bone loss not due to underlying medical conditions.

Causes:

- Postmenopausal (estrogen deficiency) or Age-related (senile osteoporosis).
- Risk Factors: Age, gender, family history, low body weight, sedentary lifestyle, smoking, excessive alcohol intake.

**Secondary Osteoporosis** - bone loss due to identifiable medical conditions or medications.

Common Causes:

- Endocrine Disorders: Hyperthyroidism, hyperparathyroidism, Cushing's syndrome.
- Chronic Diseases: Rheumatoid arthritis, chronic kidney disease, multiple myeloma
- Medications: Long-term use of glucocorticoids, certain anticonvulsants.

### Lifestyle Interventions

- 1200mg of calcium (BHOFF)
- Vitamin D 800-1000 IU (50mcg – BHOFF)
- Exercise: 2 days strength
- Fall risk
- Consider PT
- Limit drinking
- Quit smoking

### Medication Classes

#### Anti-resorptives

- Bisphosphonates
- RANKL-i: Prolia or denosumab
- SERM/estrogen

#### Anabolics

- PTH Analogs (Forteo or teriparatide, Tymlos or abaloparatide)
- Sclerostin Inhibitors (Evenity or romusosumab)

### Treatment of Osteoporosis – First Line: Bisphosphonates

#### Mechanism of Action:

- Inhibit osteoclast-mediated bone resorption, leading to increased bone density and decreased fracture risk.

#### Common Medications:

- Alendronate (Fosamax): Oral, weekly (preferred)
- Risedronate (Actonel): Oral, weekly or monthly.
- Ibandronate (Boniva): Oral monthly or IV every 3 months (\*no proven reduction of hip fractures)
- Zoledronic acid (Reclast): IV, once yearly.

Side effects: GI upset, esophageal irritation, ONJ (rare), AFF (rare)

Consider a drug holiday after 3-5 years in low-risk patients.

### Treatment of Osteoporosis – Second Line: Denosumab

#### Mechanism of Action:

- Monoclonal antibody that inhibits RANK ligand, preventing the formation and activity of osteoclasts, reducing bone resorption and increasing bone density.

#### Administration:

- Subcutaneous injection every 6 months (60 mg).
- Administered by healthcare providers in a clinical setting.

#### Efficacy:

- Proven to significantly reduce the risk of vertebral, hip, and nonvertebral fractures.
- Increases bone mineral density (BMD) at the spine, hip, and forearm.

#### Side Effects:

- Hypocalcemia: Monitor calcium levels, especially in patients with renal impairment.
- Osteonecrosis of the jaw (ONJ) and atypical femur fractures (AFF) are rare but possible (similar to bisphosphonates).

#### Discontinuation Risks:

- Rapid bone loss after stopping; consider transitioning to another therapy (e.g., bisphosphonates) after discontinuation to maintain bone density.

### Treatment of Osteoporosis - Very High Risk

Medication	Mechanism of Action	Indications	Dosing	Efficacy	Side Effects/Warnings
<b>Teriparatide (Forteo)</b>	Parathyroid hormone analog	Severe osteoporosis, high fracture risk	Daily subcutaneous injection (20 mcg) for up to 2 years	Increases BMD, reduces vertebral and non-vertebral fractures	Hypercalcemia, leg cramps, dizziness
<b>Abaloparatide (Tymlos)</b>	PTH-related peptide analog	Severe osteoporosis in postmenopausal women, high fracture risk	Daily subcutaneous injection (80 mcg) for up to 2 years	Reduces vertebral fractures, increases BMD in spine and hip	Dizziness, nausea, increased uric acid levels
<b>Romozosumab (Evenity)</b>	Sclerostin inhibitor	Severe osteoporosis, previous fractures, high fracture risk	Monthly subcutaneous injections (210 mg) for 12 months	Reduces vertebral, hip, and non-vertebral fractures, significantly increases BMD	Cardiovascular events (stroke, heart attack risk), avoid in stroke patients

<b>SERMs (e.g., raloxifene)</b>	- Reduces vertebral fracture risk in postmenopausal women. - May reduce breast cancer risk (selective estrogen modulation)	- Limited efficacy for hip fracture reduction. - Increases risk of VTE and hot flashes.	- Postmenopausal women with mild osteoporosis or those at increased breast cancer risk
<b>Estrogen</b>	- Reduces vertebral and hip fractures. - May provide relief from menopausal symptoms (hot flashes, vaginal dryness).	- Increased risk of breast cancer, stroke, VTE, and cardiovascular disease. - Often used only short-term.	- Postmenopausal women with osteoporosis and significant menopausal symptoms; often as short-term therapy
<b>Calcitonin</b>	- Reduces vertebral fracture risk. - May provide short-term pain relief in acute vertebral fractures.	- Limited overall fracture efficacy (not shown to reduce hip fractures). - Potential increased risk of cancer with long-term use.	- Rarely used; may be considered for acute pain relief in recent vertebral fractures

### ACP Guidelines

First Line -----> bisphosphonates

Second-Line -----> denosumab

High-Risk\* Postmenopausal Women -----> romosozumab or teriparatide, followed by bisphosphonate

\* High-risk: Multiple spine fracture and T-score ≤ -2.5, fracture during treatment for osteoporosis, fracture while taking medications that cause skeletal harm (e.g., long-term glucocorticoids), T-score < -3.0, FRAX > 4.5% for hip fracture or > 30% for major osteoporotic fracture