BREAK IT DOWN

Osteoporosis in Primary Care:
Who to screen, who to treat, and how to sequence therapy

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Objectives

1. Apply updated **USPSTF guidelines** for osteoporosis **screening** in practice.
2. Recognize **diagnostic criteria** and work-up for **secondary causes** of osteoporosis.
3. Choose appropriate **first-line pharmacologic** and **sequential therapies** for osteoporosis.
4. Prescribe a safe and effective **exercise program** for patients with osteoporosis.

Epidemiology & Impact

- **Prevalence** of osteoporosis among US residents >= **50 yrs is ~12.6%**
    a. **27.1%** in women and **5.7%** in men >= **65 yrs of age**
- Worldwide, **~1 in 3 women** and **1 in 5 men >= 50 yrs of age** will experience an osteoporosis-related fracture in their remaining lifetime
- **Mortality rate** within **1 year** after hip fracture ranges from **20-36%**
- **40-60%** of people with a hip fracture recover to their **prefracture level of mobility** and **ability to perform ADLs**
- **Economic impact** on health care system: **~25.3 billion per year**

Epidemiology & Impact

Osteoporotic fractures are associated with:

- Psychological distress
- Subsequent fractures
- Loss of independence
- Reduced ability to perform ADLs
- Death

Osteoporosis is a **“Silent Disease”** = opportunity for primary care screening to make a significant impact! 

Definitions:

Osteoporosis:

1. Radiographic criteria: Bone density at hip, femoral neck, or lumbar spine that is defined by a **T-score of <= - 2.5.**

2. Clinical criteria: Presence of **fragility fracture**, particularly at the hip, spine, wrist, shoulder, or pelvis (i.e., major osteoporotic site) *regardless of BMD*.

Fragility Fracture: **fractures** sustained from a fall from **standing height or lower** that would *not* cause a fracture in most healthy individuals.

Osteopenia: **T-score -1.0** to **-2.49**.

Definitions:

- **T-score:** Statistical measure of **bone mineral density** representing the **# of SDs** a patient's **BMD is > or <** the mean BMD of a ***healthy young White female*** reference population.
  - Use for: **post-menopausal women** and **men >=50 yrs**
- **Z-score:** Compares BMD to **age- and sex-matched** reference population
  - Use for: **Premenopausal women, men <50 yrs, children**
  - *Does not define osteoporosis or osteopenia in adults*
  - Z-score <= -2.0 is considered **"below expected range"**--> in the intended populations should prompt evaluation for secondary causes of low bone mass.

Screening

2025 USPSTF Recommendation Statement on Screening for Osteoporosis: Bottom Line

1. **Women ≥65 years:** screen with central DXA BMD, with or without fracture risk assessment.
2. **Postmenopausal women <65 years:** first assess for presence of >=1 risk factor for osteoporosis.
    a. If **>=1 risk factor,** assess for increased fracture risk using a **clinical risk assessment tool**
        i. OST, ORAI, FRAX
    b. If determined to be at increased fracture risk, screen for osteoporosis with **DXA BMD.**
3. **Men:** *insufficient evidence* to recommend for or against screening for osteoporosis in men; clinicians should use their **clinical judgement** regarding whether to screen.
    a. Most guidelines recommend screening men at **>=70 yrs of age,** earlier only if clinical risk factors present

Risk factors to trigger early screening in postmenopausal women <65 yrs

Risk factors include:

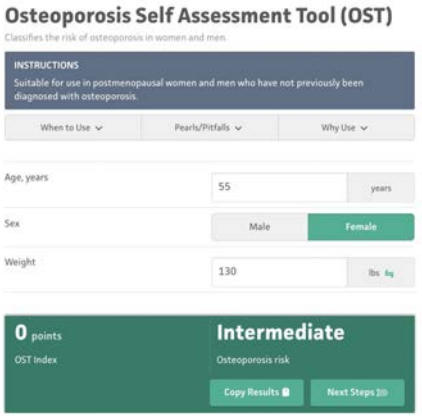
- Previous fragility fracture
- Low body weight/BMI
- Parental hx of hip fracture
- Cigarette smoking
- Use of glucocorticoids
- Excess alcohol consumption
- Rheumatoid Arthritis
- Other secondary causes of osteoporosis (e.g., hyperPTH, CKD, DM, hyperthyroidism, malabsorption, immobility, bariatric surgery, etc.)

>=1 risk factor → use **clinical risk assessment tool** to decide on **screening**

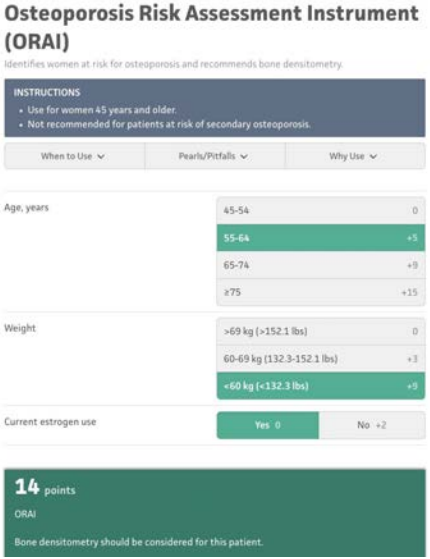
Risk assessment tools

- **Osteoporosis Self-Assessment Tool (OST)**
  - Simple, validated tool that uses easily obtained clinical variables (age, sex, weight) to identify those at increased risk for low BMD
  - Highly sensitivity for detecting BMD-defined osteoporosis
  - Most useful for selecting candidates for DXA testing in younger postmenopausal women
- **Osteoporosis Risk Assessment Instrument (ORAI)**
  - Similar to OST, includes also estrogen use
  - Slightly less sensitive than OST

Most useful when determining **who to screen** with **BMD DXA** in **premenopausal patients with >=1 risk** factor for osteoporosis



Threshold <2



Threshold >=9

Risk assessment tools

FRAX

- Most *widely studied* and *internationally adopted* assessment tool
- Predicts **10-year probability of hip fracture** or **MOF** for individuals **40-90 yrs**
- Includes **demographic** and **clinical factors** +/- BMD
    - Age, sex, BMI, prior fracture, parental hip fracture, glucocorticoid use, RA, secondary osteoporosis, smoking, alcohol intake)
- Calibrated to **country-specific** and **mortality data** improving accuracy
- Most helpful for predicting **future fracture risk**

*Note: FRAX should **not be used** as a mechanistic threshold for screening decisions in postmenopausal women <65 yrs, but may help inform* **clinical judgement**

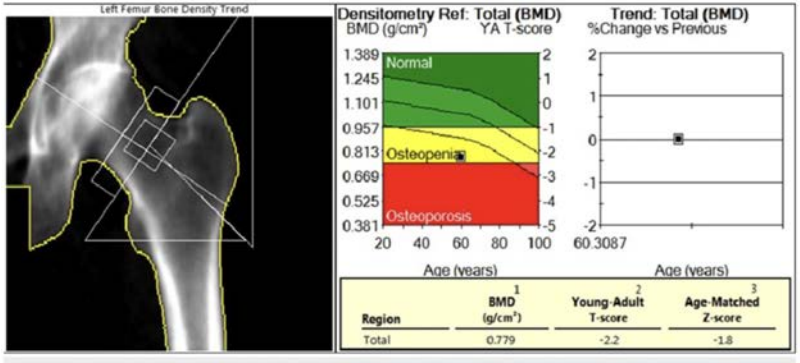
Table 2. Characteristics of Selected Risk Assessment Tools for Osteoporosis or Fracture Risk[a]

Risk factors	Scoring
OST (<2 frequently used as threshold to define increased osteoporosis risk)	
Weight, kg	(kg − y) × 0.2
Age, y	
ORAI (≥9 frequently used as threshold to define increased osteoporosis risk)	
Age, y	
≥75	15
65-74	9
55-64	5
45-54	0
Weight, kg	
<60	9
60-69	3
≥70	0
No current estrogen use	2
FRAX (no specific threshold to define increased osteoporosis risk)[b]	
Age, y	Refer to website[c]
Sex	
Weight, kg	
Height, cm	
Previous fracture	
Parental hip fracture	
Current smoking	
Glucocorticoid use	
Rheumatoid arthritis	
Secondary osteoporosis	
Alcohol consumption ≥3 U/d	

Diagnosis

Dual-energy x-ray absorptiometry (DXA)

- **DXA** = gold standard imaging test for **diagnosing osteoporosis** and **assessing fracture risk**
  - Recommended by USPSTF and other major guidelines
- Uses **2 low-dose X-ray beams** to measure BMD at sites most predictive of future fracture (i.e., hip, lumbar spine)
- Results reported as **T-score** and **Z-score**
- Fast, noninvasive, minimal exposure to radiation :)



Treatment

Who to Treat?

Anyone with **Osteoporosis!!!**

1. T-score ≤ -2.5 on DXA BMD
2. OR any low-trauma hip/vertebral fracture

… or **Osteopenia** IF:

- FRAX estimated 10-year hip fracture risk ≥3% or major osteoporotic fracture risk ≥20%.

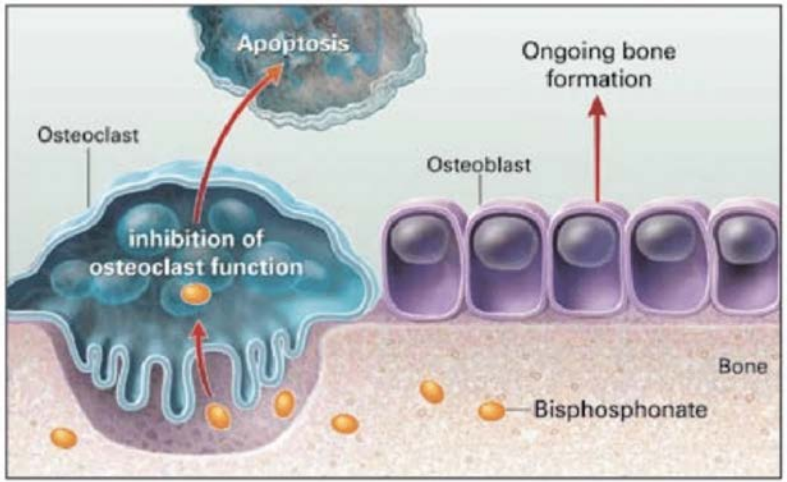
But FIRST… Work-Up for Secondary Causes of Osteoporosis

- When to suspect **secondary causes**
  a. Lab abnormalities (see below)
  b. Age < 50
  c. Unusual fracture sites
  d. Rapid bone loss
- **Basic labs:** CBC, CMP, calcium, phosphate, 25-OH vitamin D, TSH, PTH (if indicated), testosterone in men, celiac serologies if malabsorption suspected.
- *May consider referral to endocrinology*

Pharmacologic Agents

First line: **Bisphosphonates** (alendronate, risedronate, zoledronic acid)

- Mechanism: Antiresorptive agent that binds hydroxyapatite in bone ➜ taken up by osteoclasts ➜ inhibit farnesyl pyrophosphate synthase (FPPS) in the mevalonate pathway ➜ osteoclast apoptosis ➜ reduced bone resorption.



Bisphosphonates

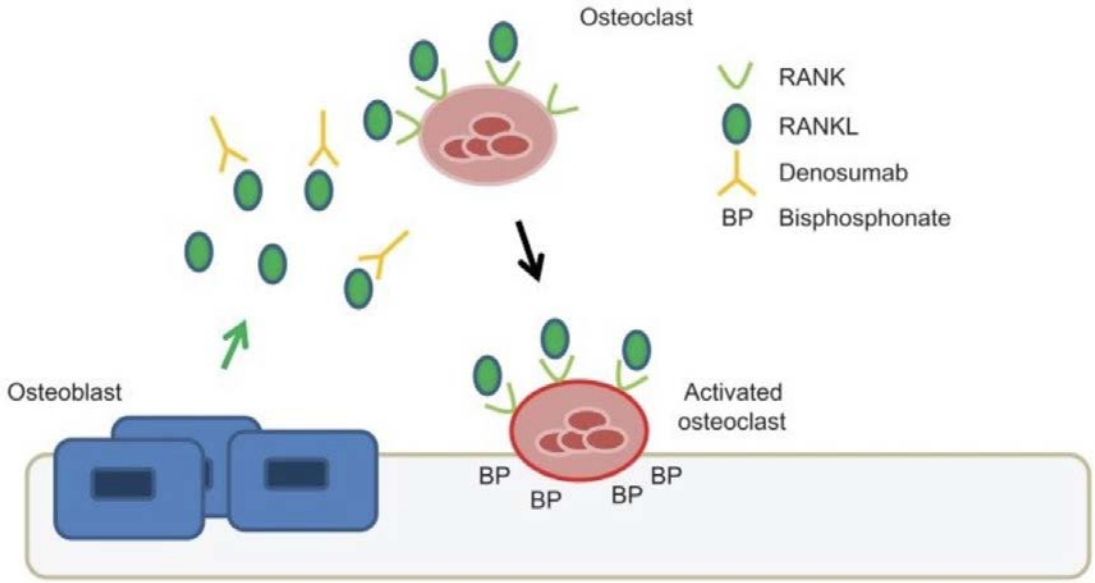
	Route	Frequency	Adverse Effects	Contraindications
Alendronate	PO	Daily **Weekly**	GI irritation, bone pain, rare: atypical femur fractures, ONJ	Esophageal varices/dysmotility, CrCl <30-35, hypocalcemia, bisphosphonate allergy
Risedronate	PO	Daily Weekly **Monthly**	Same as above	Same as above
Zoledronic Acid	**IV**	**Yearly**	Acute-phase rxn, renal impairment, hypocalcemia, AFib, rare: AFF, ONJ	CrCl <35, AKI, hypocalcemia, bisphosphonate allergy; important to ensure vit D sufficiency

Bisphosphonates: Pearls

- Admin: PO bisphosphonates (e.g., alendronate, risedronate) should be taken **first thing in the morning** with a **full glass of water**
  - **30-60 minutes** before food, drink, or other medications
  - Patients should remain **upright** for at least **30 minutes** after administration
  - ➔ decreases risk of esophageal irritation, improves bioavailability
- Drug holidays/sequencing: recommended **1 year medication break** after **5 years of treatment with po** bisphosphonate or **3 years of IV** zoledronic acid in patients who are no longer at high fracture risk (T score > -2.5, no recent fracture)
  - Reduces risk of rare but **serious adverse events** (e.g., atypical femur fracture, ONJ)
  - Fracture risk should be **reassessed every 2-4 yrs**
    - Therapy should be resumed with bisphosphonate or other agent if **BMD declines, bone turnover markers rise, or a new fracture occurs**

Second-line Antiresorptive: **Denosumab**

- Mechanism: monoclonal antibody to RANKL → inhibits RANK-RANKL interaction → decreases osteoclast formation/function → reduces bone resorption.



Denosumab

- Administration: **q6 months subcutaneous injection**
- Duration of treatment: **life-long!** (unless patient-directed discontinuation, side effects, contraindications)
- Adverse effects: bone pain, skin infections, rashes, hypocalcemia, rebound bone loss and fractures after stopping, rare: AFF, ONJ
- Contraindications: hypocalcemia, hypersensitivity; important to ensure vitamin D sufficiency
- **Sequencing: Rapid offset in drug levels after discontinuation — must bridge to bisphosphonate to prevent rapid rebound bone loss and vertebral fractures**.

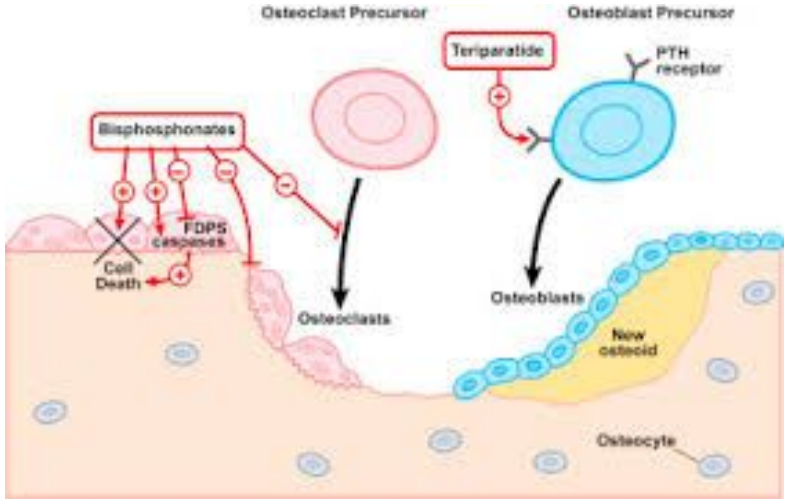
“Very high fracture risk”: indication for anabolic therapies

Presence of >=1 of the following:

1. T-score < -3.0
2. Recent spine or hip fracture in a patient with a T score of <= -2.5 at lumbar spine or hip
3. Multiple spine or fragility fragility fractures
4. Fracture within the previous 12 months
5. Fracture occurring during therapy
6. Fracture while receiving drugs that cause bone less (e.g., long-term glucocorticoid therapy)
7. High risk of falling
8. Very high fracture probability according to FRAX (e.g., major osteoporotic fracture risk >30%, hip fracture risk >4.5%, or advanced age)

Anabolics: **PTH analogs** (teriparatide, abaloparatide)

- Mechanism: Intermittent PTH receptor activation → increases osteoblast activity and new bone formation (anabolic window).



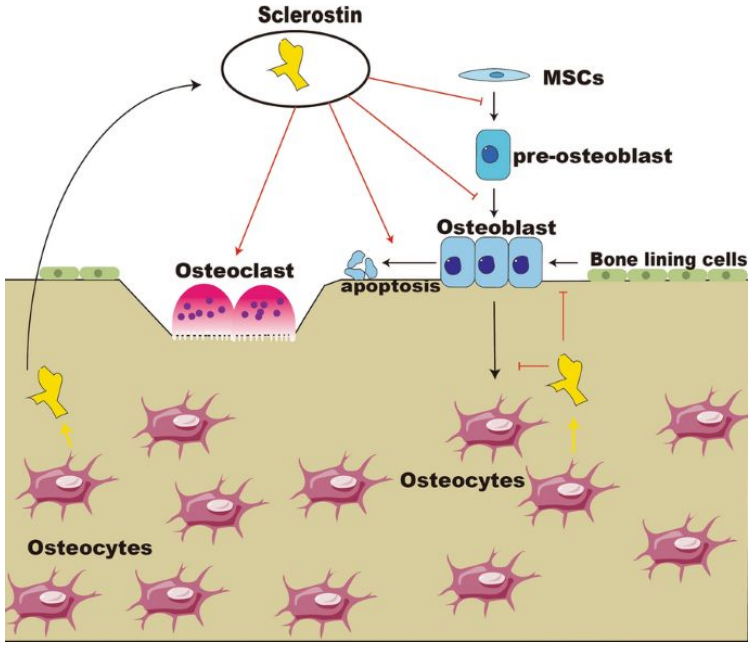
*Indicated in patients with **very high** fracture risk

PTH analogs (teriparatide, abaloparatide)

- Administration: **Daily subcutaneous injection**
- Duration of treatment: **18-24 months**
- Adverse effects: hypercalcemia, muscle cramps, nausea, headache, dizziness, hypotension
- Contraindications: Bone mets, skeletal cancers, hx skeletal radiation, increased risk of osteosarcoma, Paget's disease, hypercalcemic disorders, unexplained elevated alk phos, hypersensitivity
- **Sequencing: follow course of PTH analog with antiresorptive agent (bisphosphonate or denosumab) to preserve anabolic gains in BMD and reduce subsequent fracture risk.**

Anabolics: **Sclerostin inhibitors** (Romosozumab)

- Mechanism: monoclonal antibody against sclerostin ➜ increases bone formation and decreases resorption (dual effect).



*Indicated in patients with **very high** fracture risk

Sclerostin inhibitors (Romosozumab)

- Administration: **monthly subcutaneous injection**
- Duration of treatment: **12 months**
- Adverse effects: arthralgia, headache, bone pain, hypocalcemia, CV events, rare: AFF, ONJ
- Contraindications: **Recent stroke or MI; other CV risks**, hypocalcemia, hypersensitivity; important to ensure vitamin D sufficiency
- **Sequencing: follow course of PTH analog with antiresorptive agent (bisphosphonate or denosumab) to preserve anabolic gains in BMD and reduce subsequent fracture risk**

Sequencing review: High yield points

1. **High/very-high fracture risk:** consider **anabolic** (romosozumab or teriparatide/abaloparatide) first for **rapid BMD gain → transition to antiresorptive** (denosumab or bisphosphonate).
2. **Denosumab-specific note:** if stopping, must transition to **bisphosphonate** soon after last dose to **reduce rebound vertebral fracture risk.**
3. **Bisphosphonate holidays:** for low-to-moderate risk after 3–5 years depending on agent and baseline fracture risk.

Monitoring

- **DXA**
  a. Repeat **q1-2 years** after **initiation of therapy** until **BMD is stable**
     i. May consider longer intervals once stability is achieved
     ii. Monitoring should occur at **same facility** with the **same DXA machine** to minimize measurement variability
  b. A significant **decrease in BMD** or occurrence of **new fractures** should prompt evaluation of **secondary causes, compliance to medication,** and **consideration of alternative therapy**
- **Labs**
  a. Recommended at **baseline** (exclude secondary causes of osteoporosis) and **periodically** (e.g., q6 months) to monitor for **treatment response** and possible **adverse effects.**
  b. Serum calcium, urine calcium, 25-hydroxyvitamin D, BMP (eGFR, creatinine, lytes), Phos, TSH, PTH, markers of bone turnover (e.g., urine N-telopeptide)

Non-Pharmacologic Treatment

Cornerstones of Non-Pharmacologic Management

- **Calcium + Vitamin D:**
  a. Evidence for fracture reduction is **limited** and benefit appears most pronounced for **hip fractures** when calcium and Vitamin D are combined
  b. **Ensure adequate** intake of both **Calcium** and **Vitamin D** in patients with osteoporosis
  c. Total daily intake of **1000-1200 mg Calcium**, **400-1000 IU vit D**
  d. Emphasize meeting nutritional needs primarily through **dietary intake**, supplement only when dietary intake is insufficient
     i. Calcium-rich foods and vitamin D from diet/safe sun exposure when appropriate
- **Fall prevention:** home safety, vision correction, med review.
- **Lifestyle:** smoking cessation, limit alcohol, weight-bearing exercise.

Exercise Prescription for Bone Health

- **Why:** modest BMD improvements + clear reduction in falls and improved function.
- **Key principles:** progressive loading, weight-bearing, resistance training, balance, posture/extension work.
- **Safety:** avoid loaded spinal flexion/forward bending and high-risk movements in frail patients.

Exercise Breakdown

- **Resistance training: 2–3x/week** targeting **major muscle groups; multi-joint**; **8–12 reps** to near fatigue; **progressive overload**.
- **Impact/weight-bearing aerobic activity:** brisk walking, stair climbing, dancing; include short higher-impact in low-risk individuals.
    a. 30-40 minutes, **3-4x per week**
- **Balance & functional training:** Tai Chi, yoga, single-leg stance, tandem walking.
- **Postural extension exercises:** scapular retraction, thoracic extension exercises to reduce kyphosis and vertebral compression.

Red Flags & Modifications

- **Acute severe back pain** after movement ➔ evaluate for **new vertebral fracture**
- Caution if **frail/severe osteoporosis** or **recent vertebral fracture**
    a. **Avoid** exercises that include:
        i. **Spinal flexion (e.g., sit-ups, toe-touches)**
        ii. **Rotation**
        iii. **Heavy axial loading**
    b. Prioritize **supervised rehab**
- **Always consider PT referral!!**

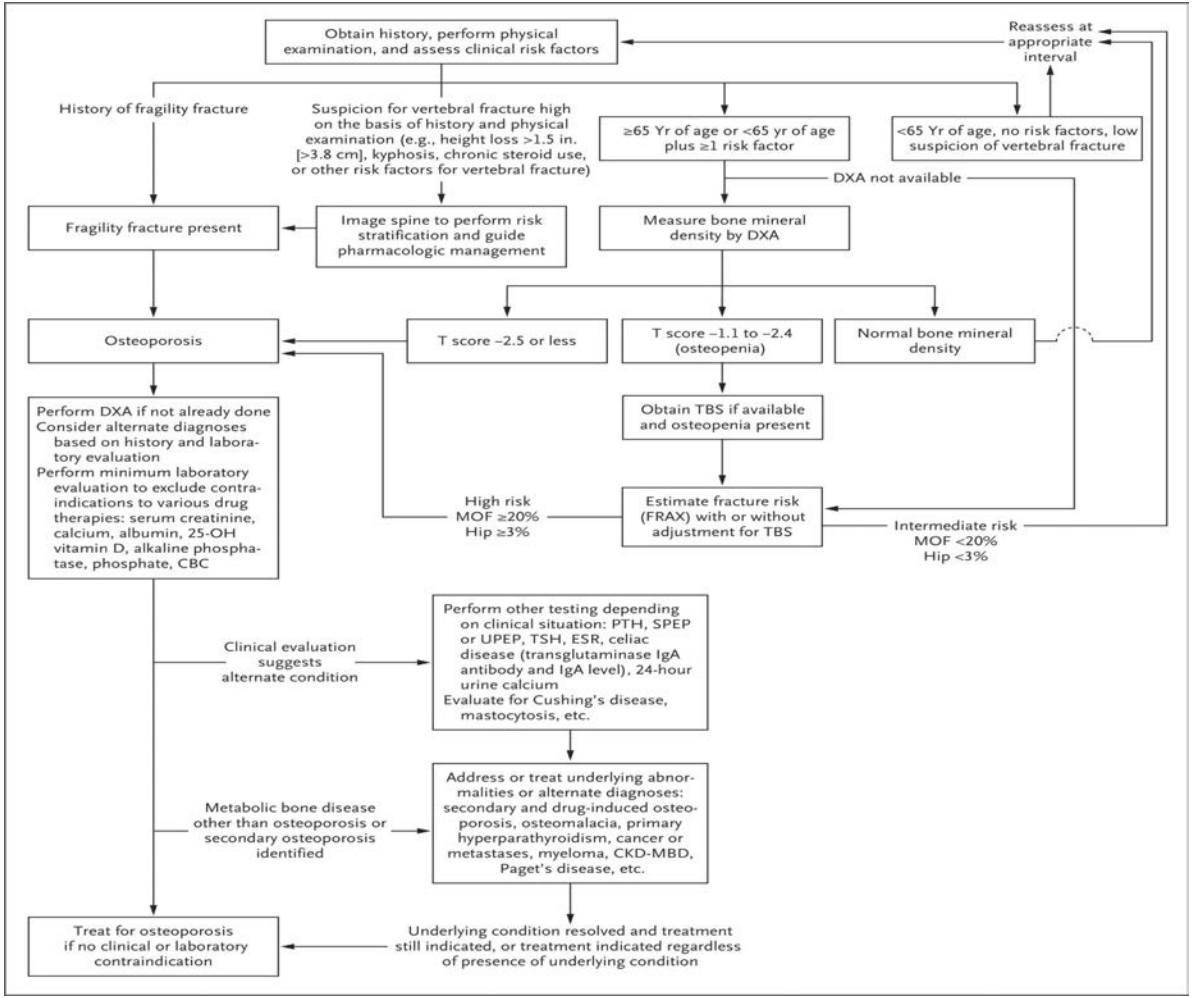
Sample 7-day Program

Goal: 2-3 days strength, 3-5 days weight-bearing aerobic, daily balance/posture

Day 1	**Resistance (lower body focus)** + **balance** 10 min
Day 2	**Weight-bearing aerobic** 30 min (brisk walk/stairs) + **posture** 10 min
Day 3	**Resistance (upper body/hips)** + **posture** 10 min
Day 4	**Balance/flexibility** (Tai Chi or modified yoga)
Day 5	**Weight-bearing intervals** (stairs or brisk uphill walk)
Day 6	**Full-body resistance** + **balance** 10 min
Day 7	**Weight-bearing aerobic** 30 min (brisk walk/stairs) + **posture** 10 min

Key Takeaways

1. **Screen women ≥65, younger postmenopausal women** with **risk factors**.
2. **Diagnose osteoporosis** based on **T-score** or **fragility fracture**.
3. **Treat** with **lifestyle** + **targeted pharmacology**.
4. **Exercise prescription** = cornerstone for **fracture prevention** and **quality of life.**


Obtain history, perform physical examination, and assess clinical risk factors
Reassess at appropriate interval
History of fragility fracture
Suspicion for vertebral fracture high on the basis of history and physical examination (e.g., height loss >1.5 in. [>3.8 cm], kyphosis, chronic steroid use, or other risk factors for vertebral fracture)
≥65 Yr of age or <65 yr of age plus ≥1 risk factor
<65 Yr of age, no risk factors, low suspicion of vertebral fracture
DXA not available
Fragility fracture present
Image spine to perform risk stratification and guide pharmacologic management
Measure bone mineral density by DXA
Osteoporosis
T score −2.5 or less
T score −1.1 to −2.4 (osteopenia)
Normal bone mineral density
Perform DXA if not already done
Consider alternate diagnoses based on history and laboratory evaluation
Perform minimum laboratory evaluation to exclude contraindications to various drug therapies: serum creatinine, calcium, albumin, 25-OH vitamin D, alkaline phosphatase, phosphate, CBC
Obtain TBS if available and osteopenia present
High risk
MOF ≥20%
Hip ≥3%
Estimate fracture risk (FRAX) with or without adjustment for TBS
Intermediate risk
MOF <20%
Hip <3%
Clinical evaluation suggests alternate condition
Perform other testing depending on clinical situation: PTH, SPEP or UPEP, TSH, ESR, celiac disease (transglutaminase IgA antibody and IgA level), 24-hour urine calcium
Evaluate for Cushing's disease, mastocytosis, etc.
Metabolic bone disease other than osteoporosis or secondary osteoporosis identified
Address or treat underlying abnormalities or alternate diagnoses: secondary and drug-induced osteoporosis, osteomalacia, primary hyperparathyroidism, cancer or metastases, myeloma, CKD-MBD, Paget's disease, etc.
Treat for osteoporosis if no clinical or laboratory contraindication
Underlying condition resolved and treatment still indicated, or treatment indicated regardless of presence of underlying condition

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