# Practical Pearls for Treating Osteoporosis

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# Disclosures

- None

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# Learning Objective

- Discuss common clinical questions and treatment pearls for osteoporosis

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# Abbreviations Within Presentation

- AACE/ACE: American Association of Clinical Endocrinologists / American College of Endocrinology
- AIDS: Acquired immunodeficiency syndrome
- BMD: Bone mineral density
- BPH: Benign prostatic hyperplasia
- CKD: Chronic kidney disease
- COPD: Chronic obstructive pulmonary disease
- CrCl: Creatinine Clearance
- CV: Cardiovascular
- DM: Diabetes mellitus
- FRAX: Fracture risk assessment tool
- GERD: Gastroesophageal reflux disease
- GFR: Glomerular filtration rate
- GI: Gastrointestinal
- HCP: Health care professional
- HCTZ: Hydrochlorothiazide
- HIV: Human immunodeficiency virus
- HLD: Hyperlipidemia
- HTN: Hypertension
- IU: International units
- IV: Intravenous
- MOA: Mechanism of action
- ONJ: Osteonecrosis of the jaw
- PCP: Primary care provider
- PO: By mouth (oral)
- PTH: Parathyroid hormone
- SCr: Serum creatinine
- SSRI: Selective serotonin reuptake inhibitor
- SGLT2-i: Sodium-glucose cotransporter 2 inhibitor
- Subq: Subcutaneous

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# Baseline Knowledge Expectations

- Definition of Osteoporosis
- Screening for Osteoporosis
- Diagnosis of Osteoporosis
- Vitamin D & Calcium Recommendations
- Pharmacotherapy Treatment Options
- Transitions from Therapeutic Agents

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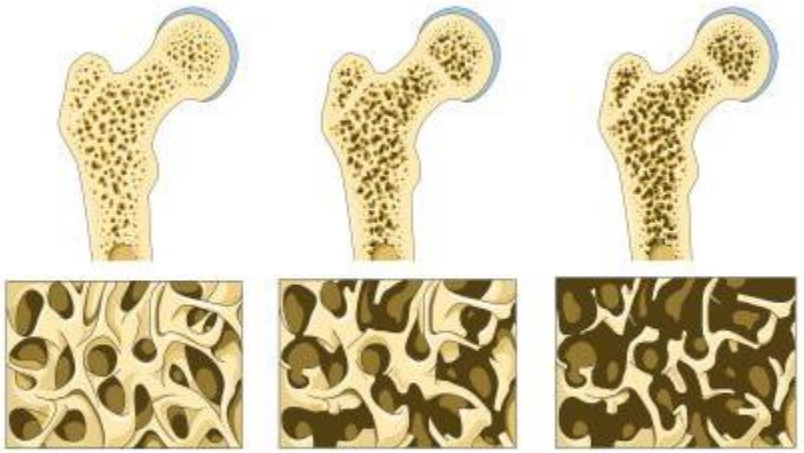
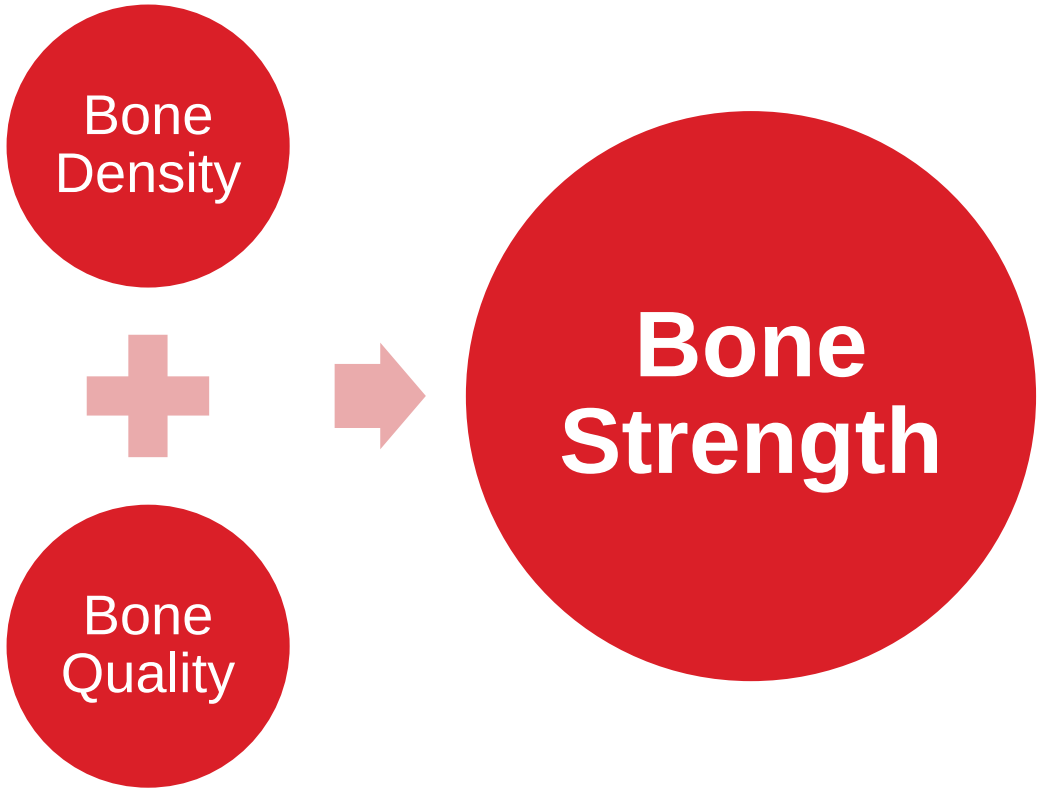
# Osteoporosis Definition

"a [silent] skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture"



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Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

# Osteoporosis Screening in Women

## AACE/ACE Guidelines

- All postmenopausal women aged ≥ 50 years old should undergo clinical assessment for osteoporosis and fracture risk
  - Includes social & medical history, physical exam, and possibly BMD testing if at increased risk

## U.S. Preventive Services Task Force

- All women aged ≥ 65 years old and younger postmenopausal women with an increased risk should have BMD testing

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# Osteoporosis Diagnosis in Women

## World Health Organization Criteria

| Category | T-Score |
|---|---|
| Normal | -1.0 or above |
| Osteopenia | -1.0 to -2.5 |
| Osteoporosis | -2.5 or below |
| Severe or established osteoporosis | -2.5 or below with fragility fracture |

- Additional Criteria:
  - Low-impact or fragility fracture regardless of bone mineral density (BMD)
  - High FRAX® fracture probability (10-year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%)

Kanis JA, et al. J Bone Miner Res. 1994;9(8):1137–1141.; Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

# Osteoporosis Screening & Diagnosis in Men

## Screening

- Men aged 50-69 years old with risk factors
- Men aged ≥ 70 years old

## Diagnosis

- Men aged < 50 years old:
  - Low BMD (Z-score ≤ 2.0) PLUS fragility fracture
  - Low BMD (Z-score ≤ 2.0) PLUS major risk factor for osteoporosis
- Men aged ≥ 50 years old:
  - BMD T-score ≤ 2.5 OR fragility fracture

## Evaluate for hypogonadism (check testosterone levels)

LeBoff M, et al. Osteoporos Int. 2022;33(10):2049-102. https://doi.org/10.1007/s00198-021-05900-y
Nelson B, et al. J Clin Endo & Metab. 2012;97(6):1802-22. https://doi.org/10.1210/jc.2011-3045

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# Vitamin D Recommendations

- Check serum 25(OH)D
  - Normal (sufficient): ≥ 30 ng/mL
  - Insufficient: 20 to 29 ng/mL
  - Deficient: < 20 ng/mL
- Treat insufficiency or deficiency
  - Cholecalciferol (Vitamin $D_3$) 2000-5000 IU daily x 6-12 weeks (preferred)
  - Ergocalciferol (Vitamin $D_2$) 50,000 IU weekly x 6-12 weeks (alternative)
- Maintenance therapy of 1000-2000 IU daily for all patients
- Additional Considerations
  - Dietary intake and other sources
  - Malabsorption conditions

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Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

# Calcium Recommendations

- Elemental Calcium Supplementation
  - 1000 mg per day for women/men 19-50 y/o & men 50-70 y/o
  - 1200 mg per day for women > 50 y/o and men > 70 y/o
- Formulations
  - Calcium carbonate, 40% elemental calcium (preferred)
  - Calcium citrate, 21% elemental calcium (intolerant to carbonate, achlorhydria)
- Additional Considerations
  - Dietary intake is included in total supplementation
  - 500 – 600 mg per dose for most efficient absorption
  - Common side effects: GI intolerance, constipation
  - Rare side effects: nephrolithiasis, possible CV disease association

Institute of Medicine (IOM). Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academies Press, 2011.
Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

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# Osteoporosis Treatments

| Drugs | Dosage (Treatment of osteoporosis) | FDA-Labeled Renal Cutoff | Effect on Bone | Effect on Mineral Metabolism |
|---|---|---|---|---|
| Alendronate* | 10 mg PO daily or 70 mg PO weekly | CrCl < 35mL/min | Antiresorptive | ↓ serum $Ca^{2+}$, ↓ serum $PO^{4-}$ |
| Risedronate* | 5 mg PO daily, 35 mg PO weekly, or 150 mg PO monthly | CrCl < 30mL/min | Antiresorptive | ↓ serum $Ca^{2+}$, ↓ serum $PO^{4-}$ , ↑ PTH levels |
| Ibandronate# | 150 mg PO monthly | CrCl < 30mL/min | Antiresorptive | Unknown |
| Zoledronate* | 5 mg IV q12months** | CrCl < 35mL/min | Antiresorptive | ↓ serum $Ca^{2+}$, ↓ serum $PO^{4-}$ |
| Denosumab* | 60 mg subcutaneous q6months** | None | Antiresorptive | ↓ serum $Ca^{2+}$, ↓ serum $PO^{4-}$ |
| Abaloparatide | 80 mcg subcutaneous daily | None | Anabolic | ↑ serum $Ca^{2+}$, ↑ urine $Ca^{2+}$ |
| Teriparatide* | 20 mcg subcutaneous daily | None | Anabolic | ↑ serum $Ca^{2+}$, ↓ serum $Ca^{2,}$, ↑ urine $Ca^{2+}$ |
| Romosozumab | 210 mg subcutaneous monthly** | None | Antiresorptive and anabolic | Unknown |

*FDA approved for use in men with osteoporosis; **Administered by health care professional;
#Ibandronate is generally not a preferred bisphosphonate due to lack of direct evidence for prevention of hip or nonvertebral fractures.

UpToDate, Inc.; 2021. https://online.lexi.com. Accessed August 26, 2021.;
LexiComp Online, Lexi-Drugs Online. Waltham, MA.; Khairallah P, et al. Clin J Am Soc Nephrol. 2018;13:962-969.

# Transitions from Therapeutic Agents

| Bisphosphonate (IV: ≤ 3 years; PO: ≤ 5 years) | Denosumab (≤ 5-10 years) | Teriparatide, Abaloparatide (≤ 2 years, lifetime max) | Romosozumab (≤ 12 months) |
|---|---|---|---|
| • Drug Holiday<br>• Continue bisphosphonate (additional ≤ 3-5 yrs)<br>• Denosumab<br>• Anabolic Agent<br>• Romosozumab | Bisphosphonate only | Antiresorptive Agent (denosumab, bisphosphonate) | Antiresorptive Agent (denosumab, bisphosphonate) |

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# Patient Case #1

MR is a 67yoF (height 67 in, weight 170 lbs) who presents to her primary care doctor for a follow-up appointment. She recently had a DEXA scan and was diagnosed with osteoporosis.

- PMH: T2DM, HLD, COPD, osteoarthritis
- Medications: semaglutide, metformin, rosuvastatin, budesonide/glycopyrrolate/formoterol inhaler, diclofenac gel

- Laboratory Values: SCr 0.85, eGFR 67, Ca 8.8, 25(OH)D 40
- DEXA Scan: Hip: -2.9, Femoral Neck: -2.7, Spine: -2.6
- FRAX Score (10 yr risk): 4.9% (major osteoporotic fracture); 0.1% (hip fracture)
- Social History:
  - Smokes 1 pack/day of cigarettes
  - Consumes 3 glasses of wine every night
  - Limited physical activity

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# Patient Case #1 – Questions to Consider

- What is the patient's risk level for a fracture?
- Does the patient have any modifiable risk factors?
- What are preferred treatment options?
- What are pertinent medication counseling points?
- How is treatment efficacy assessed?

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# High Risk of Osteoporotic Fracture

- Osteoporosis based on T-score ≤ -2.5
  - No history of fractures
- Osteopenia with high FRAX Score
  - 10-year major fracture risk ≥ 20%
  - Hip fracture risk ≥ 3%

## First Line

- Alendronate (Fosamax)
- Risedronate (Actonel, Atelvia)
- Zoledronic Acid (Reclast)
- Denosumab (Prolia)

## Alternate Therapy*

- Ibandronate (Boniva)
- Raloxifene (Evista)

*Not first line due to lack of evidence for direct prevention of hip or non-vertebral fractures

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# Bisphosphonates

MOA: Inhibits osteoclast activity, antiresorptive

Alendronate
Risedronate
Zoledronic Acid
Ibandronate

Dosing:

- Oral: daily, weekly, or monthly available
- IV: q12 months (treatment), q24 months (prevention)
- Renal dose adjustment needed once CrCl < 30 to 35 mL/min (agent dependent)

Oral Administration:

- Must be taken after a prolonged fast (typically in the morning)
- Must be taken with a full glass of water
- Must wait at least 30 minutes before consuming other medications, food, or beverages other than water

Monitoring: SCr, Serum $Ca^{2+}$, Serum $PO^{4-}$, Mag

**Must correct hypocalcemia before starting treatment**

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# Bisphosphonates

Adverse Effects:

- Common: GI issues (i.e. abdominal pain, indigestion, constipation, diarrhea, flatulence)
- Rare: ONJ, atypical femur fracture, esophageal or GI ulcers/perforation

**Do NOT use ORAL bisphosphonate with:** esophageal disorders or abnormalities (i.e. achalasia, stricture), GI malabsorption issues (i.e. history of gastric bypass, Crohn's disease), inability to follow administration instructions

Duration of Therapy: up to 3 years IV, up to 5 years oral

- Could consider an additional 3-5 years of treatment
- Could consider a drug holiday

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# Lifestyle Counseling

## Make lifestyle changes

Modifications in lifestyle and habits that can regulate the body's metabolism and reduce the risk of bone density loss and fracture include:

Quitting smoking

Avoiding excessive alcohol use

Increasing Vitamin D intake

Consuming plenty of calcium

## Participate in weight-bearing exercise

Regularly performing weight-bearing activities can help build and maintain bone mass. Simple ways to engage in weight-bearing exercise include:

Going for a walk or jog

Climbing stairs or doing bench steps

Doing resistance or strength training

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# Treatment Goals & Monitoring

## Goal to **reduce fractures** through

- Improving bone strength
- Preventing falls
- Reducing the impact force of falls

## Monitor with **serial BMD screenings**

- Frequency is individualized
- Typically testing every 1 to 2 years is appropriate

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# Treatment Success or Failure

**Treatment Success**

- Stable or increasing BMD
- Higher T-Score
- Lower FRAX probability

**Treatment Failure***

- Significant decrease in BMD
- Recurrent fracture

*Fracture during treatment is not necessarily a treatment failure!*
*Reconsider risk factors and possibly change treatment strategies*

***Only if patient is compliant to therapy**

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# Patient Case #1 – Summary

Lifestyle Modifications

- Decrease or stop smoking
- Decrease or stop consuming alcohol
- Increase weight-bearing and balance exercises

Medication Therapy

- Calcium carbonate 600 mg / Vitamin D3 800 IU twice daily
- Alendronate 70 mg once weekly
    - Counsel on correct administration instructions!

Follow-Up

- Ongoing and as needed assessment of fracture risk
- 3 months to assess medication tolerability and compliance
- 1-2 years to repeat DEXA scan

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# Patient Case #2

LM is a 55yoF (height 62 in, weight 130 lbs) who presents to her primary care doctor after discharging from a skilled nursing facility where she was in rehab post-hip fracture which occurred after a fall.  She was instructed to follow-up with her PCP about getting on a medication to "make her bones stronger."

- PMH: hypertension, hypothyroidism, depression, GERD, rheumatoid arthritis
- Medications: lisinopril, levothyroxine, sertraline, omeprazole, etanercept, prednisone

- Laboratory Values: SCr 0.68, eGFR 90, Ca 9.7, 25(OH)D 22
- DEXA Scan: No results at this time
- FRAX Score (10 yr risk): Unable to calculate due to no DEXA Scan

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# Patient Case #2 – Questions to Consider

- What risk factors did the patient have for a fracture?
- Can the patient be diagnosed with osteoporosis with the information provided?
- What are preferred treatment options?
- What are pertinent medication counseling points?
- How do we know if the treatment is working?

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# Secondary Causes of Osteoporosis

| Endocrine or Metabolic Causes | Nutritional or GI Conditions | Drugs | Disorders of Collagen Metabolism | Other |
|---|---|---|---|---|
| Acromegaly<br>Diabetes mellitus (T1 & T2)<br>Growth hormone deficiency<br>Hypercortisolism<br>Hyperparathyroidism<br>Hyperthyroidism<br>Hypogonadism<br>Hypophosphatasia<br>Porphyria<br>Pregnancy | Alcoholism<br>Anorexia nervosa<br>Calcium deficiency<br>Chronic liver disease<br>Malabsorption syndromes / malnutrition (celiac disease, cystic fibrosis, Crohn's disease, gastric resection/bypass)<br>Total parenteral nutrition<br>Vitamin D deficiency | Anti-epileptic drugs<br>Aromatase inhibitors<br>Chemotherapy/ immunosuppressants<br>Medroxyprogesterone acetate<br>Glucocorticoids<br>Gonadotropin-releasing hormone agents<br>Heparin<br>Lithium<br>Proton pump inhibitors<br>SSRIs<br>SGLT2-inhibitors<br>Thiazolidinediones<br>Thyroid hormone (in supraphysiologic doses) | Ehler-Danlos syndrome<br>Homocystinuria due to cystathionine deficiency<br>Marfan syndrome<br>Osteogenesis imperfecta | AIDS/HIV<br>Ankylosing spondylitis<br>COPD<br>Gaucher disease<br>Hemophilia<br>Hypercalciuria<br>Immobilization<br>Major depression<br>Myeloma and some cancers<br>Organ transplantation<br>Renal insufficiency/failure<br>Renal tubular acidosis<br>Rheumatoid arthritis<br>Systemic mastocytosis<br>Thalassemia |

For this case:

- Conditions: Rheumatoid arthritis, depression
- Medications:
  - Glucocorticoid – Dose & duration dependent (≥ 2.5mg daily for ≥ 3 months)
  - Selective Serotonin Reuptake Inhibitor
  - Proton Pump Inhibitor

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Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

# Osteoporosis Diagnosis in Women

## World Health Organization Criteria

| Category | T-Score |
|---|---|
| Normal | -1.0 or above |
| Osteopenia | -1.0 to -2.5 |
| Osteoporosis | -2.5 or below |
| Severe or established osteoporosis | -2.5 or below with fragility fracture |

- Additional Criteria:
  - **Low-impact or fragility fracture regardless of bone mineral density (BMD)**
  - High FRAX® fracture probability (10-year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%)

Kanis JA, et al. J Bone Miner Res. 1994;9(8):1137–1141.; Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

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# Very High Risk of Osteoporotic Fracture

- Fracture within previous 12 months
- Fracture on approved osteoporosis therapy
- Multiple fractures
- Fractures while on drugs causing skeletal harm (e.g. long-term glucocorticoids)
- T-score less than -3.0
- High risk for falls or history of injurious falls
- FRAX® score of major osteoporosis fracture >30% or hip fracture >4.5%

## First Line

- Zoledronic Acid (Reclast)
- Denosumab (Prolia)
- Teriparatide (Forteo)
- Abaloparatide (Tymlos)
- Romosozumab (Evenity)

## Alternate Therapy

- Alendronate (Fosamax)
- Risedronate (Actonel, Atelvia)

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# Anabolic Agents vs Antiresorptive Agents

- Anabolic agents should be used as first line for very high risk patients to optimize the anabolic effect
- Studies have demonstrated anabolic agents are superior over antiresorptive agents in increasing BMD
- In patients with a prior fracture, risk of a second major fracture is highest immediately following the first fracture

| Anabolic | Antiresorptive |
|---|---|
| Promotes new bone formation | Suppresses bone resorption |
| Increases osteoblast activity | Decreases osteoclast activity |

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Hassan N, et al. Fac Rev. 2021; 10: 44. doi: 10.12703/r/10-44.

# Abaloparatide (Tymlos) & Teriparatide (Forteo)

Anabolic Agents

MOA: recombinant PTH; anabolic agents



Dosing:

- Abaloparatide: 80 mcg subq daily
- Teriparatide: 20 mcg subq daily
  - No renal dose adjustment needed for either medication
  - Teriparatide has specific indications for glucocorticoid-induced osteoporosis and osteoporosis in men

Administration & Storage:

- Subcutaneously into the periumbilical region, rotate injection site
- Sit or lay down for first several doses (due to risk of orthostatic hypotension)
- After first use can be stored at room temperature for up to 30 days

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# Abaloparatide (Tymlos) & Teriparatide (Forteo)

Anabolic Agents

Monitoring: Serum $Ca^{2+}$, PTH, 25(OH)D, Serum $PO^{4-}$

Adverse Effects:

- Common: nausea, leg cramps, orthostatic hypotension
  - Have patients sit following administration for first few doses
- Rare: hypercalcemia, usually mild and asymptomatic
- Boxed Warning: osteosarcomas (in rats with high doses)
  - Do not use in patients at increased risk

Duration of Therapy: up to 2 years

- **After stopping treatment BMD declines quickly**
- Start antiresorptive treatment immediately
  - No need for a "washout period" or "drug holiday"

Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.
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# Romosozumab (Evenity)

Anabolic Agent

MOA: monoclonal antibody against sclerostin; anabolic and antiresorptive agent

Dosing: 210 mg subq monthly

- No renal dose adjustment needed


Administration: Must be administered by a HCP

Monitoring: Serum $Ca^{2+}$, 25(OH)D

**Must correct hypocalcemia before starting treatment**

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# Romosozumab (Evenity)

Anabolic Agent

Adverse Effects:

- Common: arthralgias, headache, injection site reactions
- Rare: ONJ, atypical femur fracture
- Boxed Warning: increased risk of cardiovascular events

**Do NOT use romosozumab in:** patients with MI or stroke in the past year

Duration of Therapy: up to 1 year

- **After stopping treatment BMD declines quickly**
- Start antiresorptive treatment immediately
    - No need for a "washout period" or "drug holiday"

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# Fall Prevention Strategies

- Anchor rugs
- Minimize clutter
- Remove loose wires
- Use nonskid mats
- Install handrails in bathrooms, halls, and long stairways
- Light hallways, stairwells, and entrances
- Wear sturdy, low-heeled shoes

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Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

# Patient Case #2 – Summary

Medication Therapy

- Calcium carbonate 600 mg twice daily
- Vitamin D3 5000 IU daily x 12 weeks – *Need to treat insufficiency*
- Teriparatide 20 mcg subq daily
    - Counsel on injection technique and side effect of hypotension!

Follow-Up

- Ongoing and as needed assessment of fracture risk
- 3 months to recheck vitamin D level;
  assess medication tolerability and compliance
- 1-2 years to repeat DEXA scan
- 2 years or before to plan for treatment change

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# Patient Case #3

AJ is a 69yoM (height 68 in, weight 160 lbs) who presents to his primary care doctor complaining of excessive fatigue, low libido, and night sweats.

- PMH: HTN, HLD, COPD, wrist fracture (8 months ago)
- Medications: Losartan-HCTZ, atorvastatin, umeclidinium/vilanterol inhaler

**What labs and/or screening tests should be done?**

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# Osteoporosis Screening & Diagnosis in Men

## Screening

- Men aged 50-69 years old with risk factors
- Men aged ≥ 70 years old

**Risk Factors include (but not limited to):**

- Hx of fracture after age 50
- Secondary causes of osteoporosis

## Diagnosis

- Men aged < 50 years old:
  - Low BMD (Z-score ≤ 2.0) PLUS fragility fracture
  - Low BMD (Z-score ≤ 2.0) PLUS major risk factor for osteoporosis
- Men aged ≥ 50 years old:
  - BMD T-score ≤ 2.5 OR fragility fracture

## Evaluate for hypogonadism (check testosterone levels)

LeBoff M, et al. Osteoporos Int. 2022;33(10):2049-102. https://doi.org/10.1007/s00198-021-05900-y
Nelson B, et al. J Clin Endo & Metab. 2012;97(6):1802-22. https://doi.org/10.1210/jc.2011-3045

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# Patient Case #3

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- PMH: HTN, HLD, COPD, wrist fracture (8 months ago)
- Medications: Losartan-HCTZ, atorvastatin, umeclidinium/vilanterol inhaler

- Lab Values: SCr 1.3, CrCl 50, Ca 9.2, 25(OH)D 14, total testosterone 172
- DEXA Scan (T-score): Hip: -2.8, Femoral Neck: -2.5, Spine: -1.9
- FRAX Score (10 yr risk): 16% (major osteoporotic fracture); 5.1% (hip fracture)

**AJ has hypogonadism and osteoporosis**

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# Patient Case #3 – Questions to Consider

- How does hypogonadism effect osteoporosis in men?
- Should the patient receive an osteoporosis medication in addition to testosterone?
- What osteoporosis medications are indicated in men?

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# Hypogonadal Men and Osteoporosis

Low testosterone can cause low BMD and increased fracture risk

Testosterone levels <200 ng/dL and symptoms of androgen deficiency should be treated with testosterone therapy

## Fracture Risk

| Modest to Borderline Risk: | High Risk: |
| --- | --- |
| Testosterone alone may be sufficient | Add an agent with proven antifracture efficacy to testosterone |

**Men *<u>without</u>* hypogonadism but high risk of fractures (e.g. osteoporosis) should be treated with pharmacologic therapy**

LeBoff M, et al. Osteoporos Int. 2022;33(10):2049-102. https://doi.org/10.1007/s00198-021-05900-y
Nelson B, et al. J Clin Endo & Metab. 2012;97(6):1802-22. https://doi.org/10.1210/jc.2011-3045

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# Osteoporosis Treatment in Men

(Bone Health and Osteoporosis Foundation and Endocrine Society Guidelines)

## Osteoporosis Medications Indicated in Men

- Alendronate (Fosamax)
- Risedronate (Actonel, Atelvia)
- Zoledronic Acid (Reclast)
- Teriparatide (Forteo)

Choice of medication is patient-specific

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# Patient Case #3 – Summary

Medication Therapy

- Calcium carbonate 500 mg twice daily
- Vitamin D2 50,000 units weekly x 12 weeks – *Need to treat deficiency*
- Testosterone cypionate 200 mg IM q2weeks
- Alendronate 70 mg po weekly

Follow-Up

- Ongoing and as needed assessment of fracture risk
- 3 months to recheck testosterone level and vitamin D level; assess medication tolerability and compliance
- 1-2 years to repeat DEXA scan

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# Patient Case #3 (Part 2) – 3 years later

AJ is a 72yoM (height 68 in, weight 152 lbs) who presents for a chronic care follow-up with his PCP. He was hospitalized for a COPD exacerbation and pneumonia a few months ago where his kidney function declined and has not recovered.

4 months ago: SCr 1.7 (CrCl 36); Today: SCr 2.0 (CrCl 30)

- PMH: HTN, HLD, COPD, hypogonadism, osteoporosis
- Medications: Losartan-HCTZ, atorvastatin, fluticasone/umeclidinium/vilanterol inhaler, testosterone, alendronate, calcium-vitamin D

- Lab Values (today): SCr 2.0, CrCl 30, Ca 8.9, 25(OH)D 30, testosterone 363
- DEXA Scan (6 months ago): Hip: -2.6, Femoral Neck: -2.2, Spine: -1.7
- FRAX Score (10 yr risk): 18% (major osteoporotic fracture); 7.4% (hip fracture)

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# Patient Case #3 (Part 2) – Questions to Consider

- How does the patient's renal function change his therapy?
- What osteoporosis medications can be used with poor renal function?

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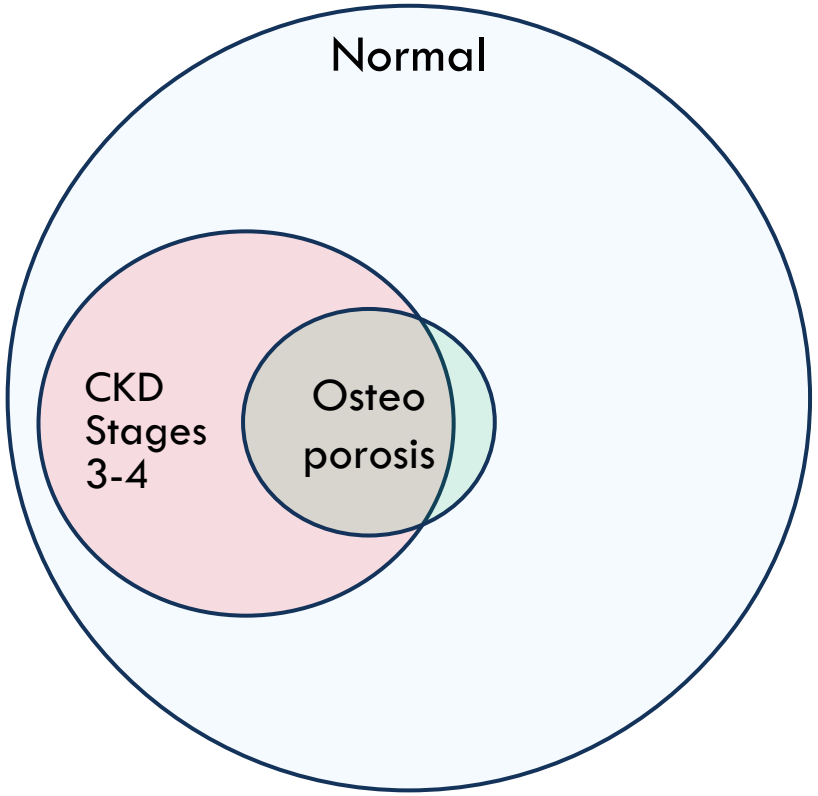
# CKD and Osteoporosis

- Osteoporosis is very common in patients with CKD
- > 2 times higher fracture rate in CKD compared to age-matched individual without CKD
- Higher risk of vitamin D deficiency
- Osteoporosis treatment is the same as the general population EXCEPT if there is evidence of CKD Mineral and Bone Disorder (CKD-MBD)




KDIGO CKD-MBD Workgroup. Kidney International. 2009:76(Suppl 113):S22-S49.;
Klawansky S, et al. Osteoporos Int. 2003; 14: 570–576.; Khairallah P, et al. Clin J Am Soc Nephrol. 2018;13:962-969.

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# CKD and Osteoporosis

- If CKD Mineral and Bone Disorder (CKD-MBD) is present with low BMD:
  - **Refer to nephrology if CKD-MBD suspected**
  - Address biochemical abnormalities (including secondary hyperparathyroidism)
  - Complete bone turnover assessment
  - *May* consider osteoporosis medications

KDIGO CKD-MBD Workgroup. Kidney International. 2009:76(Suppl 113):S22-S49.;
Klawansky S, et al. Osteoporos Int. 2003; 14: 570–576.; Khairallah P, et al. Clin J Am Soc Nephrol. 2018;13:962-969.

# Renal Considerations with Osteoporosis Medications

- Bisphosphonates should NOT be used with severe renal dysfunction
  - CrCl <35 mL/min: alendronate and zoledronic acid
  - CrCl <30 mL/min: risedronate and ibandronate

- Non-bisphosphonate medications are not renally cleared and can be used in renal dysfunction
  - Denosumab, teriparatide, abaloparatide, romosozumab

- Patients with CKD are at higher risk of hypocalcemia

- Antiresorptive agents can cause hypocalcemia

LexiComp Online, Lexi-Drugs Online. Waltham, MA.;
Khairallah P, et al. Clin J Am Soc Nephrol. 2018;13:962-969.

# Denosumab (Prolia)

- MOA: RANKL inhibitor; Antiresorptive agent


- Dose: 60 mg subcutaneous q6 months
  - Must be administered by HCP
  - No renal dose adjustments recommended

- Monitoring:
  - SCr,  Serum $Ca^{2+}$, Serum $PO^{4-}$ and Mg
    - Especially within the first 14 days of therapy or during the first weeks of therapy initiation

**Must correct hypocalcemia before starting treatment**

LexiComp Online, Lexi-Drugs Online. Waltham, MA.;
Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

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# Denosumab (Prolia) - continued

- Adverse Effects:
  - Common: Flu-like syndrome (≤ 3 days of admin)
    - Fever, chills, flushing, bone pain, arthralgia, and myalgia
  - Uncommon: Increased incidence of infection
  - Rare: ONJ and atypical fractures

- Duration of Therapy: up to 10 years
  - Could consider indefinite therapy
  - Must transition to bisphosphonate upon discontinuation

**Possible rapid bone loss with delayed administration or discontinuation**

LexiComp Online, Lexi-Drugs Online. Waltham, MA.;
Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

# Transitions from Therapeutic Agents

| Bisphosphonate (IV: ≤ 3 years; PO: ≤ 5 years) | Denosumab (≤ 5-10 years) | Teriparatide, Abaloparatide (≤ 2 years, lifetime max) | Romosozumab (≤ 12 months) |
|---|---|---|---|
| • Drug Holiday<br>• Continue bisphosphonate (additional ≤ 3-5 yrs)<br>• Denosumab<br>• Anabolic Agent<br>• Romosozumab | Bisphosphonate only | Antiresorptive Agent (denosumab, bisphosphonate) | Antiresorptive Agent (denosumab, bisphosphonate) |

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Camacho PM, et al. Endocr Pract. 2020;26(Suppl 1):1-46.

# Patient Case #3 (Part 2) – Summary

Medication Therapy

- Discontinue alendronate
- Start denosumab 60 mg subcutaneous q6 months – *Indefinite therapy?*
- Continue testosterone and calcium-vitamin D

Follow-Up

- Refer to nephrology; evaluate for CKD-MBD
- 1-2 weeks to recheck SCr, Serum $Ca^{2+}$, Serum $PO^{4-}$ and Mg; assess medication tolerability and compliance
- 1 year to recheck testosterone level, vitamin D level
- 1-2 years to repeat DEXA scan
- Ongoing and as needed assessment of fracture risk

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# *QUESTIONS?*

## Practical Pearls for Treating Osteoporosis

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