Osteoporosis and Osteopenia Prevention and Treatment - Allaying the Fear Factor

Robin Cornell Creamer, DO, FAAFP

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Robin Cornell Creamer, DO, FAAFP

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Dr. Creamer earned her medical degree from the Chicago College of Osteopathic Medicine, Downers Grove, Illinois, and completed her family medicine residency and geriatric medicine fellowship at AdventHealth (previously Florida Hospital) in Winter Park, Florida. Dr. Creamer has been practicing and teaching family medicine for 25 years. Following her passion for osteoporosis prevention, she leads a National Osteoporosis Foundation (NOF) support group called Central Florida Healthy Bones and has earned her NOF Fracture Liaison Service Certificate. She believes one of family medicine’s critical challenges is to motivate patients to be as physically active as possible.
Learning Objectives

1. Establish screening protocols, using dual-energy x-ray absorptiometry, in accordance to current clinical practice guidelines.

2. Evaluate elderly patients and patients at risk for low bone mass/osteoporosis using the FRAX® algorithm, and consider the impact of fracture risk scores on patient management.

3. Determine appropriate osteoporosis treatment, based on clinical evaluation, side effects of treatment, cost of treatment, diagnostic workup, fracture risk assessments, and BMD measurements.

4. Develop a collaborative prevention and treatment plan for patients at risk for falls, emphasizing exercise, physical therapy, home hazard assessment, and possible withdrawal of medications that increase fall risk.

Associated Sessions

• (PBL) Osteoporosis and Osteopenia Prevention and Treatment: Allaying the Fear Factor
Audience Engagement System

Educational Resources

- National Osteoporosis Foundation: https://www.nof.org
- FRAX: http://www.shef.ac.uk/FRAX or APP
- National Bone Health Alliance: www.nbha.org
- National Institute of Health (NIH); http://www.niams.nih.gov
- Mayo Clinic Shared Decision-Making National Resource Center https://osteoporosisdecisionaid.mayoclinic.org
- University New Mexico. Telementoring Bone Health TeleECHO Clinic. http://www.ofnm.org/project-echo
- AAFP http://familydoctor.org
Osteoporosis

Bone disease marked by reduced bone strength leading to an increased risk of fractures.

Bone Strength = Bone Mass (density) + Bone Quality (microarchitecture)

Impact of Osteoporotic Fractures

Over age 50 up to

1/2 women
1/4 men

will break bone due to osteoporosis

300,000 hip fx/yr

1/4 will die within a year
1/4 end up in nursing homes &
1/2 will need a walking aid

Osteoporotic fractures will likely cost us

$25 billion per year by 2025

After a fracture, Only 1/5 women over 67 are tested or treated for osteoporosis

80% CARE GAP
Vertebral Compression Fractures (VCF)

- Most common osteoporotic fractures
- Wedge fractures most common VCF
- T7-T8; T12-L1 most common sites
- 75% are not clinically evident
- Patients with a spine fracture have a 5-fold future risk of a spine fracture and 2-fold risk of a hip fracture
- Pulmonary: 9% decrease in lung capacity per vertebral fracture
- GI: Constipation, early satiety, wt loss,
- Psychosocial: depression, social isolation

Strong Bones Begin in Childhood

![Graph showing peak bone mass and bone loss over age](image)

- **Peak bone mass**
- **Bone loss due to menopause**
- **Decreasing bone mass with age**

![Image of vertebrae with red arrow indicating fracture](image)
Poll Question 1

USPSTF 2018 recommends screening BMD in all women ≥ 65 years. In addition to FRAX, which of the following tools can be used to screen younger postmenopausal women for increased risk?

1. Osteoporosis Self-Assessment Tool (OST)
2. Osteoporosis Risk Assessment Instrument (ORAI)
3. Osteoporosis Index of Risk (OSIRIS)
4. Simple Calculated Osteoporosis Risk Estimate (SCORE)
5. All of the above

DXA Screening Recommendations

- USPSTF 2018:
  - All women ≥ 65 y (B rec.)
  - Younger postmenopausal women at increased risk as determined by a formal clinical risk assessment tool. (B rec.)
  - Men: Evidence is insufficient to recommend screening in men to prevent osteoporotic fractures. (I statement)
    - Note: NOF recommends screening men ≥ 70 y and younger men with risk factors, ie: fracture after 50 y, steroids, et al.
- NCQA HEDIS measure: Number of women ≥ 65 who report ever having a BMD test.
Updated FRAX Risk estimate
65 yo WF w/o major risk factors in U.S.
8.4% MOF (BMI 28.8) instead of 9.3% (BMI 25)

Risk Assessment Tools in addition to FRAX
(1 of 2)

<table>
<thead>
<tr>
<th>Tool</th>
<th>Risk Factors</th>
<th>Scoring</th>
<th>Threshold for Increased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>OST (Osteoporosis Self-Assessment Tool)</td>
<td>Weight (kg) Age (y)</td>
<td>kg·y</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>ORAI (Osteoporosis Risk Assessment Instrument)</td>
<td>Age, y ≥ 75 y 65-74 55-64 45-54 60-69 ≥ 70</td>
<td>15 9 5 0 9 3 0</td>
<td>≥ 9</td>
</tr>
</tbody>
</table>
## Risk Assessment Tools in addition to FRAX (2 of 2)

<table>
<thead>
<tr>
<th>Tool</th>
<th>Risk Factors</th>
<th>Scoring</th>
<th>Threshold for Increased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSIRIS (Osteoporosis Index of Risk)</td>
<td>Age, y</td>
<td>-0.2 x age</td>
<td>&lt; 1</td>
</tr>
<tr>
<td></td>
<td>Weight, Kg</td>
<td>0.2 x kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Current estrogen use</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prior low-impact fracture</td>
<td>-2</td>
<td></td>
</tr>
<tr>
<td>SCORE (Simple Calculated Osteoporosis Risk Estimation)</td>
<td>Non-black race</td>
<td>5</td>
<td>≥ 6</td>
</tr>
<tr>
<td></td>
<td>Rheumatoid arthritis</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prior non-traumatic rib/wrist/hip fx after age 45</td>
<td>4 for each (max 12)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Never used estrogen</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age, y</td>
<td>3 x 1&lt;sup&gt;st&lt;/sup&gt; digit of age</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wt, lb</td>
<td>-1 x (lbs / 10)</td>
<td></td>
</tr>
</tbody>
</table>

### Case: Marilyn

- **73 yo WF, dx osteoporosis age 60.**
- **Fractures:**
  - wrist age 44 fell on ice;
  - elbow age 71 fell on sidewalk;
  - Rib age 72
- **PMHx:** Barrett’s without dysplasia; depression; squamous cell skin CA; Oophorectomy age 40;
- **Meds:** omeprazole 20mg daily (was bid); fluoxetine 10mg x 30 yr; calcium carbonate
Case: Marilyn

- Prior meds: Teriparitide x 1 yr age 60 dc’d due to bone pain; later ibandronate x 3 yrs; then Prolia x 1 injection, stopped due to dental work. No osteoporosis meds in 7 years.
- Social: former smoker; 1 glass wine daily; retired teacher
- Exercise- prior runner; current yoga, walks.
- Family History: Mother- history wrist fracture (no hip).
- BMI 19.6. Lifetime height loss 1” (≥ 1.5” risk of OP)
- Evaluate for additional secondary causes (known low BMI, prior tobacco, early menopause, PPI and SSRI use)
- Order DXA

Case Marilyn : BMD (DXA) result

T scores:
- Lumbar Spine(LS) -2.7
- Left Femoral Neck(LFN) - 2.1
- Left Total Hip (LTH) - 2.2
- Right Femoral neck -1.7
- Right Total hip(RTH) -2.0
- FRAX 10 yr risk of fracture
  - Major osteoporotic fracture (MOF) 18%
  - Hip fracture 4.3%
Current Diagnosis of Osteoporosis

1. Bone Mineral Density as defined by WHO or
2. Fragility fracture of hip or spine

<table>
<thead>
<tr>
<th></th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Equal to -1.0 or higher</td>
</tr>
<tr>
<td>Low Bone Mass (Osteopenia)</td>
<td>Between -1.0 and -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Equal to -2.5 or lower</td>
</tr>
<tr>
<td>Severe Osteoporosis</td>
<td>Equal to -2.5 or lower with fracture</td>
</tr>
</tbody>
</table>

NOF Clinician's Guide to Prevention and Treatment of Osteoporosis 2014

Calculate FRAX with DXA result

www.shef.ac.uk/FRAX
Used with Permission from International Osteoporosis Foundation
FRAX adjusted with Trabecular Bone Score (TBS)

- FDA approved in 2012, TBS is a Textural index: DXA software that extracts bone texture information from an AP spine DXA scan image
- Shown to be related to bone microarchitecture and fracture risk
- Provides information independent of BMD
- Cannot diagnose osteoporosis
- Can be used to improve fracture risk assessment


Most Fractures in Postmenopausal Women Occur With T scores in Low Bone Density (Osteopenic) Range
NOF Recommendation for Vertebral Fracture Imaging Assessment

Consider Vertebral Imaging tests for the following:

- Women ≥ 70 y and Men ≥ 80 y, if BMD T-score spine, total hip or femoral neck is < -1.0.
- Women 65-69 y and men 70-79 y, if BMD T-score spine, total hip or femoral neck is < -1.5
- Postmenopausal women and men age 50 and older with specific risk factors:
  - Low trauma fracture ≥ 50 y
  - Historical height loss ≥ 1.5 inches (4 cm)
  - Interval height loss ≥ 0.8 inches (2 cm)
  - Glucocorticoid use

NOF Guidelines for Rx Treatment

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Fracture</td>
<td>Hip or Spine</td>
</tr>
<tr>
<td>T-score (DXA)</td>
<td>T-score ≤ -2.5 at spine, hip or femoral neck</td>
</tr>
<tr>
<td>FRAX (osteopenia,low bone mass)</td>
<td>10-year probability of a major fracture (MOF) ≥ 20% 10-year probability of a hip fracture ≥ 3%</td>
</tr>
</tbody>
</table>

National Osteoporosis Foundation’s
Clinician’s Guide to the Prevention and Treatment of Osteoporosis. 2015
Poll Question 2

Medications are recommended for Marilyn based on her Lumbar spine (LS) T-score -2.7. FRAX score isn’t necessary for tx decision.

For patients with T scores in the osteopenic or low bone mass range, which is correct regarding pharmacologic therapy?

1. Therapy not indicated in patients with low bone mass (osteopenia) regardless of FRAX
2. Consider therapy: risk of MOF ≥ 8.4%
3. Consider therapy: risk of MOF ≥ 20%
4. Consider therapy: risk of Hip fracture ≥ 3 %
5. Only answer 3 and 4 are correct

Secondary Causes (1 of 4)

<table>
<thead>
<tr>
<th>Lifestyle factors</th>
<th>Genetic diseases</th>
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<tbody>
<tr>
<td>Alcohol abuse</td>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td>Excessive thinness</td>
<td>Ehlers-Danlos</td>
</tr>
<tr>
<td>Frequent falling</td>
<td>Glycogen storage diseases</td>
</tr>
<tr>
<td>High salt intake</td>
<td>Hemochromatosis</td>
</tr>
<tr>
<td>Inadequate physical activity</td>
<td>Hypophosphatasia</td>
</tr>
<tr>
<td>Low calcium intake</td>
<td>Marfan syndrome</td>
</tr>
<tr>
<td>Vitamin D insufficiency</td>
<td>Osteogenesis imperfecta</td>
</tr>
<tr>
<td>Smoking (active or passive)</td>
<td>Parental history of hip fracture</td>
</tr>
<tr>
<td></td>
<td>Porphyria</td>
</tr>
<tr>
<td></td>
<td>Riley-Day syndrome</td>
</tr>
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</table>

### Secondary Causes (2 of 4)

<table>
<thead>
<tr>
<th>Hypogonadal states</th>
<th>Androgen insensitivity</th>
<th>Anorexia nervosa</th>
<th>Athletic amenorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperprolactinemia</td>
<td></td>
<td>Panhypopituitarism</td>
<td>Premature menopause (&lt;40 yrs)</td>
</tr>
<tr>
<td>Turner’s &amp; Klinefelter’s syndromes</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Endocrine disorders

<table>
<thead>
<tr>
<th>Central obesity</th>
<th>Cushing’s syndrome</th>
<th>Diabetes mellitus (Types 1 &amp; 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperparathyroidism</td>
<td>Thyrotoxicosis</td>
<td></td>
</tr>
</tbody>
</table>

#### Gastrointestinal disorders

<table>
<thead>
<tr>
<th>Celiac disease</th>
<th>Gastric bypass</th>
<th>Gastrointestinal surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory bowel disease</td>
<td>Malabsorption</td>
<td>Pancreatic disease</td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
<td></td>
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</tbody>
</table>

#### Hematologic disorders

<table>
<thead>
<tr>
<th>Hemophilia</th>
<th>Leukemia and lymphomas</th>
<th>Monoclonal gammopathies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple myeloma</td>
<td>Sickle cell disease</td>
<td>Systemic mastocytosis</td>
</tr>
<tr>
<td>Thalassemia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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### Secondary Causes (3 of 4)

#### Rheumatologic and autoimmune diseases

<table>
<thead>
<tr>
<th>Ankylosing spondylitis</th>
<th>Other rheumatic and autoimmune diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>Systemic lupus</td>
</tr>
</tbody>
</table>

#### Neurological and musculoskeletal risk factors

<table>
<thead>
<tr>
<th>Epilepsy</th>
<th>Multiple sclerosis</th>
<th>Muscular dystrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinson’s disease</td>
<td>Spinal cord injury</td>
<td>Stroke</td>
</tr>
</tbody>
</table>

#### Miscellaneous conditions and diseases

<table>
<thead>
<tr>
<th>AIDS/HIV</th>
<th>Alcoholism</th>
<th>Amyloidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic metabolic acidosis</td>
<td>Chronic obstructive lung disease</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Depression</td>
<td>End stage renal disease</td>
<td>Hypercalciuria</td>
</tr>
<tr>
<td>Idiopathic scoliosis</td>
<td>Post-transplant bone disease</td>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>Weight loss</td>
<td></td>
<td></td>
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</tbody>
</table>

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Secondary Causes (4 of 4)

<table>
<thead>
<tr>
<th>Medications</th>
<th>Anticoagulants (heparin)</th>
<th>Anticonvulsants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum (in antacids)</td>
<td>Barbiturates</td>
<td>Cancer chemotherapeutic drugs</td>
</tr>
<tr>
<td>Aromatase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depo-medroxyprogesterone (premenopausal contraception)</td>
<td>Glucocorticoids (≥ 5 mg/d prednisone or equivalent for ≥ 3 months)</td>
<td>GnRH (Gonadotropin releasing hormone) agonists</td>
</tr>
<tr>
<td>Lithium Cyclosporine A and tacrolimus</td>
<td>Methotrexate</td>
<td>Parental nutrition</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>Selective serotonin reuptake inhibitors</td>
<td></td>
</tr>
<tr>
<td>Tamoxifen® (premenopausal use)</td>
<td>Thiazolidinediones (such as Actos® and Avandia®)</td>
<td>Thyroid hormones (in excess)</td>
</tr>
</tbody>
</table>

Labs to Consider for Secondary Causes

- Chemistry (calcium, renal, phosphorus, Mg)
- Liver function tests
- CBC
- TSH, PTH
- 25(OH)Vitamin D
- Testosterone younger men
- 24-hour urinary calcium

Selected cases:
- SPEP/UPEP
- Celiac disease-(tTG)
- Iron and ferritin
- Homocysteine
- Tryptase
- Prolactin
- Bone turnover markers
Case: Marilyn

- 73 yo who stopped osteoporotic medications in past due to fear of side effects.
- Labs normal including
  - Vit D 52, calcium 9.3; creat 0.54, TSH 1.65; Hgb 12.8;
- Changed to calcium citrate to meet RDA 1200 mg calcium/day
- Remains on SSRI, PPI
- Exercise-Agrees to PT to optimize her posture/exercise routine
- Agrees to medication to treat her osteoporosis.

Mayo Shared Decision Aid
https://osteoporosisdecisionaid.mayo Clinic.org

Used with permission from Victor Montori, M.D., Mayo Clinic
Advise Universal Recommendations for Bone Health Regardless of Bone Density

• Advise adequate dietary calcium intake, supplement if diet is insufficient
• Advise adequate Vitamin D intake, supplement if diet is insufficient
• Avoid Tobacco and excess alcohol
• Recommend exercise program for strength, posture and balance
• Fall Prevention

USPSTF 2018 Recommendation: Vit D, Calcium, or Combined Supplementation for the Primary Prevention of Fractures in Community-Dwelling Adults

1. Asymptomatic men and premenopausal women: Current evidence is insufficient to assess the balance of the benefits and harms of Vit D and calcium supplementation, alone or combined. (I statement)

2. Postmenopausal women: Current evidence is insufficient to assess the balance of benefits and harms of daily supplementation with doses greater than 400 IU of vit D and greater than 1000 mg of calcium. (I statement)

3. Postmenopausal women: Advises against daily supplementation with 400 IU or less of vitamin D and 1000 mg or less of calcium. (D recommendation)

4. These recommendations do not apply to persons with a history of osteoporotic fractures, increased risk for falls, or a diagnosis of osteoporosis or vitamin D deficiency.
Institute of Medicine: Dietary Reference Intakes for Calcium and Vitamin D -- 2011

<table>
<thead>
<tr>
<th>YEARS</th>
<th>CALCIUM (mg/d) Recommended Dietary Allowance</th>
<th>VITAMIN D (IU/d) Recommended Dietary Allowance</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-50 y M/F</td>
<td>1,000</td>
<td>600</td>
</tr>
<tr>
<td>51-70 y Males</td>
<td>1,000</td>
<td>600</td>
</tr>
<tr>
<td>51-70 y Females</td>
<td>1,200</td>
<td>600</td>
</tr>
<tr>
<td>&gt;70 y M/F</td>
<td>1,200</td>
<td>800</td>
</tr>
</tbody>
</table>

Too Fit To Fracture Recommendations

**For preventing bone loss and falls, recommend a combination of:**
- Strength training for major muscle groups ≥ 2x/week
- Balance challenges daily
- Moderate-to-vigorous aerobic physical activity ≥ 150 min/week, or 20-30 min per day

**To reduce spine loads, recommend:**
- Exercises for back extensor muscles daily
- Spine sparing strategies – hip hinge for bending, step-to-turn instead of twisting, holding loads close to body

Physical Therapy for Bone Health
Allaying the Fear of Fracture and the Fear of Falling

• Physical Therapy
  • Medicare accepts Physical Therapy ICD 10 diagnosis code of Osteopenia (M85.80) or Osteoporosis (M81.0)
  • 1-3 sessions usually all that is needed for osteopenia to review posture and exercise routine.
  • Rx: Osteoporosis/ Osteopenia: Physical Therapy to evaluate, treat and instruct in spine safe posture and exercise to optimize strength and balance. Minimize fall risk.
  • VCF- decreases risk of subsequent VCF’s

Poll Question 3

AAFP recommends considering oral bisphophonates as first line, but considering to Marilyn’s GERD and hx of Barret’s esophagus, which of the following would be appropriate?

1. Alendronate orally for 5 years, then consider a drug holiday
2. Zoledronic acid IV for 3 yrs, then consider a drug holiday
3. Denosumab SC injections for 5 years, then consider a drug holiday
4. Anabolic agent teriparatide or abaloparatide SC injections for 2 yr, then consider a drug holiday.
AAFP Endorsed 2017 - ACP Guideline Update:
Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women

1. Treat with alendronate, risedronate, zoledronic acid or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis (grade: strong rec; high-quality evidence)

2. Treat osteoporotic women with pharmacological therapy for 5 years. (Grade: weak rec; low-quality evidence)

3. Treat with bisphosphonates to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis. (Grade: weak rec; low-quality evidence)

AAFP Endorsed 2017 - ACP recommendations continued:

4. Against bone density monitoring during the 5-yr period pharmacologic treatment period for osteoporosis in women. (Grade: weak rec; low quality evidence).

5. Against using menopausal estrogen therapy or menopausal estrogen plus progestogen therapy or raloxifene for the treatment of osteoporosis in women. (Grade: strong rec; mod-quality evidence).

6. Treat osteopenic women 65 yrs age and older who are at a high risk for fracture based on a discussion of pt preferences, fracture risk profile, and benefits, harms, and costs of medications. (Grade: weak rec.; low-quality evidence)
Pharmacology

- **Antiresorptive**
  - Bisphosphonates
    - Alendronate
    - Ibandronate
    - Risedronate
    - Zoledronic Acid
  - Denosumab
  - Raloxifene
  - Estrogen
  - Calcitonin

- **Anabolic (Bone Forming)**
  - Teriparatide (PTH 1-34)
  - Abaloparatide (hPTHrP)
  - Rozosumab (Evenity)

**Fracture Data Postmenopausal**

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>SPINE</th>
<th>HIP</th>
<th>NON-VERT</th>
<th>DOSE/ADMIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>70 mg po weekly</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>✓</td>
<td></td>
<td></td>
<td>150 mg po monthly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 mg IV every 3 mo.</td>
</tr>
<tr>
<td>Risedronate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>35 mg po weekly</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>150 mg po monthly</td>
</tr>
<tr>
<td>Zoledronic Acid</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>5 mg IV yearly</td>
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</table>
Fracture Data Postmenopausal

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>SPINE</th>
<th>HIP</th>
<th>NON-VERT</th>
<th>DOSE/ADMIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denosumab (Prolia)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>60 mg SC every 6 month</td>
</tr>
<tr>
<td>SERM-Raloxifene</td>
<td>✓</td>
<td></td>
<td></td>
<td>Not recommended due to adverse effects</td>
</tr>
<tr>
<td>Estrogen</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Not recommended due to adverse effects</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>✓</td>
<td></td>
<td></td>
<td>Not recommended due to adverse effects</td>
</tr>
<tr>
<td>PTH 1-34 Teriparatide</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>20 mcg SC daily for max 2 yrs</td>
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<tr>
<td>PTHrP Abaloparatide</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>80 mcg SC daily for max 2 yrs</td>
</tr>
<tr>
<td>Romosozumab (Evenity)</td>
<td>✓</td>
<td></td>
<td></td>
<td>2 injections monthly x 12 mo.</td>
</tr>
</tbody>
</table>

Bisphosphonates (BP)

- PMW, men, steroid induced osteoporosis
- Fx Reduction RR in Postmenopausal women from RCTs:
  - Spine ~50% alendronate, risedronate, zoledronic acid & ibandronate
  - Hip ~ 40% with all except ibandronate
- Short term (3-5 yrs) benefits far exceed risks
- Long term (>5 yrs) benefits smaller, risks higher
- Oral alendronate first line due to efficacy, safety data, cost $7/month.
- Specific dosing regime due to adverse effects of esophagitis
- IV-Zoledronic acid, if unable to follow oral dosing or GI intol
- Caution: CrCl <35; Hypocalcemia-monitor Ca, Mg, PO4
Atypical Femoral Fractures (AFF) & Osteonecrosis of Jaw (ONJ)

Rare serious adverse effects: Bisphosphonates

• AFF: Associated with long-term use >5 yrs.
  Evaluate for Drug holiday after 5 yrs of treatment
  Rare <0.1% or absolute risk 5 cases/10,000 pt tx yrs
  Inquire about thigh or groin pain
  Evaluate any pain for stress fracture with bil femur x-rays

• ONJ: Rare 1/10,000 to 1/100,000 risk
  Consider dental exam prior to starting
  Recommend good oral hygiene

<table>
<thead>
<tr>
<th>Medication</th>
<th>NNT</th>
<th>%</th>
<th>NNH</th>
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</thead>
<tbody>
<tr>
<td>Bisphosphonate in PMW with prior fractures or very low BMD</td>
<td>1/20 prevent vertebral fracture</td>
<td>94% saw no benefit after 3 years of treatment</td>
<td>A small number were harmed</td>
</tr>
<tr>
<td></td>
<td>1/100 prevent hip fracture</td>
<td>5% avoided a vertebral fracture</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1% avoided a hip fracture</td>
<td></td>
</tr>
<tr>
<td>BP meds for 5 years to prevent death, MI, stroke</td>
<td>1 in 125 were helped (prevented death)</td>
<td>97% saw no benefit</td>
<td>1 in 10 were harmed</td>
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<tr>
<td></td>
<td>1 in 67 were helped (prevented stroke)</td>
<td>0.8% were helped by preventing death</td>
<td>(medication side effects, stopping the drug)</td>
</tr>
<tr>
<td></td>
<td>1 in 100 were helped (prevented heart attack*)</td>
<td>1.5% were helped by preventing stroke</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0% were helped by preventing heart attack</td>
<td></td>
</tr>
</tbody>
</table>

www.thennt.com
Bisphosphonate Drug Holiday

- After 5 yr of oral bisphosphonates (BP) or 3 yr of intravenous (IV) BP
- DXA and Vertebral Fracture Assessment (VFA)
- VFA: No vertebral fractures. No thigh or groin pain
- Women not at high fracture risk after 5 yr of oral (3 yr IV) bisphosphonate treatment, a drug holiday of upto 5 yrs can be considered.
- If drug holiday initiated reassess need for tx q 2-4y. Consider resuming tx in pts w/fracture or significant BMD loss.
- Remember “Drug Holiday ≠ Drug Retirement”

High-risk patients may benefit from BP treatment >5 yrs

- FLEX trial alendronate extended 5 →10 yrs. Continued prevention of vertebral fractures, but no effect on non-vertebral fracture risk.
- The risk of AFF, but not ONJ, clearly increases with BP therapy duration, but such rare events are outweighed by vertebral fracture risk reduction in high-risk patients.
- High- risk patients include:
  - Femoral Neck T score ≤ -2.5
  - Vertebral fractures prior to or during therapy
  - Older women, high FRAX risk

Task Force of the ASBMR. Bone Miner Res. 2016 Jan;31(1)16:-35
Poll Question 4

Which is correct regarding the discontinuation of denosumab (Prolia)?

1. "Drug holiday” is a bisphosphonate specific concept, not appropriate for denosumab (Dmab).
2. Denosumab discontinuation is associated with rapid loss of BMD and severe rebound vertebral fractures.
3. Treatment with a bisphosphonate before or after taking denosumab reduces risk of vertebral fractures.
4. All of the above are correct.

Denosumab –DMab (Prolia)

- Monoclonal antibody, RANKL inhibitor, potent antiresorptive
- Approved for use in postmenopausal women, men.
- Approved for cancer induced bone loss from hormone ablation tx.
- Administer: SQ injection 60 mg every 6 months
- Reduces the incidence of vertebral, non-vertebral, and hip fractures
- Cost estimate: $1,000/ injection
- Caution: CrCl <30; Hypocalcemia-monitor Ca, Mg, PO4 periodically
- Adverse: Infection skin. Rare complications include AFF and ONJ
- FREEDOM Extension Study 10 y- low rates of adverse events, low fracture incidence and continued increases in BMD without plateau
DMab Discontinuation: Rapid loss of BMD and Rebound-Associated Vertebral Fractures

- Extension trial, 82 women, 42 no f/u med
  - After 8 yr DMab: LS + 16.8%, Hip +6.2%
  - 1 yr w/o DMab: LS – 7.4%, Hip – 7.8%
  - w/in 9-10 months after last Dmab
    - 8 of 82 (9.8%) total had VCF
    - 6 of 42 with no f/u med had VCF (14.3%)
  - Possibly disruption of trabecular microarchitecture + low BMD → rebound increase VCFs.
- Do not stop Dmab(or switch to teriparatide) w/o transition to a bisphosphonate.


Estrogen with or without Progestin; or Raloxifene

- Recommend AGAINST for treatment of osteoporosis in women.
  - ACP Grade: strong recommendation against
  - Increased risk of stroke and thromboembolic events
  - Consider Raloxifene if independent need for breast cancer prophylaxis

- Estrogen + Bazedoxifene = (Duavee)
  - FDA indication for prevention of osteoporosis
  - No RCT with primary fracture outcomes
Calcitonin

- FDA-approved for postmenopausal women when alternative treatments are not suitable.
- Reduces vertebral fractures 30% in those with prior vertebral fractures.
- Not been shown to reduce non-vertebral or hip fractures.
- **Administer:** 200 IU intranasal spray. SQ available
- **Adverse effects:** suggested increased risk of malignancies

Anabolic Therapy: PTH1 Receptor ligands
Teripаратide (PTH 1-34) and Abaloparatide (PThrP)

Teriparatide (Forteo) and Abaloparatide (Tymlos)
- Postmenopausal Women at high risk for fracture (h/o of fx or multiple risk factors) or who have failed or intolerant to other therapies.
- Reduce vertebral and non-vertebral fractures
- Daily SQ injection. Cost estimate: $1,500 to 3,000/ month
- Limited to 2 years in lifetime
- Contraindicated: in patients with increased risk of osteosarcoma
  - Paget’s disease, prior radiation therapy skeleton, bone metastases, hypercalcemia, or a history of skeletal malignancy

Teriparatide- also indicated for men at high fx risk; steroid induced OP
Abaloparatide- lower incidence of hypercalcemia.
Romosozumab “Evenity”

- FDA approved April 2019
- Indication: PMW at high risk
- monoclonal AB to sclerostin
- 2 Injections monthly x 12 months
- Primarily anabolic
- Follow by an antiresorptive
  Increase risk of CV events
- Serious Reactions: MI, CVA, CV death, hypocalcemia, ONJ, AFF

Sequencing of Anabolic and Antiresorptive Therapies

- Anabolic agents shown to have greater BMD gains when used prior to an antiresorptive agent.
- Anabolic response may be blunted for a period of time after bisphosphonate (longer time) or Dmab (shorter time).
- Consider anabolic agents as initial therapy in very high risk women and men who have had OP fracture.
- Follow 2 yr anabolic tx with antiresorptive (BP or DMab) to maintain BMD gains.
Interval Care for During Treatment

- Patients taking medications need to be evaluated annually
  - Calcium, diet, exercise, lifestyle, new meds or chronic diseases
  - Inquire if any thigh or groin pain
  - Exam: height. 2 cm (0.8 in) loss, repeat VFA.
  - Labs: creatinine, calcium, Mg, Vit D

- DXA interval BMD testing during treatment- no RCT
  - ACP- recommends against testing during 5 yr treatment.
    - Reduced fractures with treatment even if BMD did not increase
  - NOF: recommends every 2 yrs
  - ISCD: If stable or increased, repeat at 5 years.
  - If BMD decrease ≥ 5%
    • Inquire about non-compliance; assess for secondary causes.
    • If poor absorption of oral BP, consider switch to IV bisphosphonate

Healthy Bones for Life: Primary Prevention

- NCQA HEDIS measure: Number of women ≥ 65 yrs who report ever having a BMD test.
- Repeat DXA interval depends on initial BMD. If no risk factors:
  - Normal DXA T score > -1.49, repeat 10-15 yrs or more
  - T score -1.50 to -1.99, repeat in 3-5 years
  - T score -2.0 or less, repeat in 2 years
- Patient education is the foundation of care
  - Provide referral to Physical Therapy, Registered Dietician
  - Consider utilizing CPT code 99490 Chronic Care Management
  - Consider starting an NOF Support Group / Lecture Series
Improving Bone Health after a Fracture

- NCQA HEDIS measure: Number of women ≥ 65-85 yrs who suffered a fracture and who had either BMD or a prescription for a drug to treat osteoporosis.

- In adults ≥ 50 y, after a fracture, assess FRAX for DXA
- Care coordination programs after fracture
  - National Bone Health Alliance (NBHA)
    - Fracture Liaison Service (FLS) resources
  - American Orthopedic Assoc.: Own the Bone
  - IOF recognition program: Capture the Fracture

USPSTF Recommendations 2018
Fall prevention in community-dwelling ≥ 65 y

- Exercise intervention to prevent falls (B recommendation)
- Multifactorial interventions to prevent falls (C recommendation)
  - medications, medical conditions, environmental hazards
  - ie: CDC STEADI Program
- Vitamin D supplementation not recommended
  - (D recommendation)

✈ These apply to community-dwelling adults NOT known to have osteoporosis or Vitamin D insufficiency or deficiency.
Practice Recommendations

• Actively counsel patients on the prevention of osteoporosis
• Use a Formal Risk Assessment Tool to identify patients for screening and treatment of osteoporosis
• Evaluate and treat adults with fragility fractures for their underlying osteoporosis
• Address patients fear of medications, fractures and falls.
• Encourage patients to exercise to decrease their fracture and fall risk.

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Family Medicine Residency and Geriatric Medicine Fellowship

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Questions

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