Osteoporosis and Osteopenia Prevention and Treatment: Building Strong Bones for Life

Robin Creamer, DO, FAAFP

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Robin Creamer, DO, FAAFP

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Dr. Creamer is a graduate of the Chicago College of Osteopathic Medicine, Downers Grove, Illinois, and completed her family medicine residency at Florida Hospital in Orlando. She also recently completed a fellowship in geriatric medicine at Winter Park Memorial Hospital, Florida. Dr. Creamer has been practicing and teaching family medicine for more than 20 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, diagnostic workup, fracture risk assessments, and BMD measurements.

4. Develop 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.

Audience Engagement System

Step 1

Step 2

Step 3
Associated Session

- (PBL) Osteoporosis and Osteopenia Prevention and Treatment: Building Strong Bones for Life

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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
\(\frac{1}{2}\) women
\(\frac{1}{4}\) men

will break bone
due to osteoporosis

300,000 hip fx/yr
\(\frac{1}{4}\) will die
within a year
\(\frac{1}{4}\) end up in
nursing homes &
\(\frac{1}{2}\) will need a
walking aid

After a fracture,
Only \(\frac{1}{5}\)
women over 67
are tested or
treated for
osteoporosis

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
Screening for Prevention of Fractures in Older Women (Scoop) study-FRAX reduced hip fx

- RCT compared usual management vs screening by Fracture Risk Assessment Tool (FRAX)
- 12,483 women aged 70-85 years.
- FRAX web-based tool using clinical risk factors with and w/o femoral neck BMD to estimate 10 yr probability of major osteoporotic fractures (MOF) hip, spine, humerus, wrist.
- Treatment recommended on BMD results
- Results- no decrease in MOF, but 28% decrease in hip fractures. Highly cost-effective.

AES 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 Wt, kg &lt; 60 kg 60-69 ≥ 70 No current estrogen use</td>
<td>15 9 5 0 9 3 0 2</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></td>
<td></td>
<td></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 1st 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: Donna

- 65 yo WF here for Wellness Physical. BMI 22.5
- Lifetime height loss 1” (≥ 1.5” risk of OP)
- PMHx: basal cell skin CA so avoids the sun; lactose intolerant
- Meds: no meds.
- Social: no tobacco or ETOH; retired this year from teaching
- Exercise-spinning class twice a week.
- Family History: Mother hip fracture age 78
- Advise Universal Bone Health recommendations & order DXA
Case Donna : BMD (DXA) result

T scores:
- Lumbar Spine (LS) - 2.3
- Femoral Neck (FN) - 2.4
- Total Hip (TH) - 2.2

- FRAX 10 yr risk of fracturing:
  - Major Osteoporotic fracture (MOF)?
  - Hip fracture?

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>

Most Factures in Postmenopausal Women Occur With T scores in Low Bone Density (Osteopenic) Range

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
### NOF Recommendation for Vertebral Fracture Imaging Assessment

Consider Vertebral Imaging tests for the following:

<table>
<thead>
<tr>
<th>Condition</th>
<th>BMD T-score Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women ≥ 70 y and Men ≥ 80 y</td>
<td>&lt; -1.0</td>
</tr>
<tr>
<td>Women 65-69 y and Men 70-79 y</td>
<td>&lt; -1.5</td>
</tr>
<tr>
<td>Postmenopausal women and men age 50 and older with specific risk factors:</td>
<td></td>
</tr>
<tr>
<td>• Low trauma fracture ≥ 50 y</td>
<td></td>
</tr>
<tr>
<td>• Historical height loss ≥ 1.5 inches (4 cm)</td>
<td></td>
</tr>
<tr>
<td>• Interval height loss ≥ 0.8 inches (2 cm)</td>
<td></td>
</tr>
<tr>
<td>• Glucocorticoid use</td>
<td></td>
</tr>
</tbody>
</table>

#### Calculate FRAX with DXA result

![FRAX Calculator Image](https://www.shef.ac.uk/FRAX)

*Used with Permission from International Osteoporosis Foundation*
AES Question #2

T score LS -2.3; FN -2.4; TH -2.2; VFA no vertebral fractures FRAX risk MOF 22%; Hip 2.6%

Which is correct regarding pharmacologic therapy in a patient with low bone mass (osteopenia)?

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

NOF Guidelines for Rx Treatment

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</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>
# Secondary Causes (1 of 4)

<table>
<thead>
<tr>
<th>Lifestyle factors</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Alcohol abuse</td>
<td>Excessive thinness</td>
<td>Excess Vitamin A</td>
</tr>
<tr>
<td>Frequent falling</td>
<td>High salt intake</td>
<td>Immobilization</td>
</tr>
<tr>
<td>Inadequate physical activity</td>
<td>Low calcium intake</td>
<td>Smoking (active or passive)</td>
</tr>
<tr>
<td>Vitamin D insufficiency</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Genetic diseases                   |       |       |
| Cystic fibrosis                    | Ehlers-Danlos | Gaucher’s disease |
| Glycogen storage diseases          | Hemochromatosis | Homocystinuria |
| Hypophosphatasia                   | Marfan syndrome | Menkes steely hair syndrome |
| Osteogenesis imperfecta            | Parental history of hip fracture | Porphyria |
| Riley-Day syndrome                 |       |       |

# Secondary Causes (2 of 4)

| Hypogonadal states                |       |       |
| Androgen insensitivity            | Anorexia nervosa | Athletic amenorrhea |
| Hyperprolactinemia                | Panhypopituitarism | Premature menopause (<40 yrs) |
| Turner’s & Klinefelter’s syndromes|       |       |

| Endocrine disorders               |       |       |
| Central obesity                   | Cushing’s syndrome | Diabetes mellitus (Types 1 & 2) |
| Hyperparathyroidism               | Thyrotoxicosis    |       |

| Gastrointestinal disorders        |       |       |
| Celiac disease                   | Gastric bypass | Gastrointestinal surgery |
| Inflammatory bowel disease        | Malabsorption  | Pancreatic disease |
| Primary biliary cirrhosis         |       |       |

| Hematologic disorders            |       |       |
| Hemophilia                        | Leukemia and lymphomas | Monoclonal gammopathies |
| Multiple myeloma                  | Sickle cell disease | Systemic mastocytosis |
| Thalassemia                       |       |       |
### Secondary Causes (3 of 4)

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

<table>
<thead>
<tr>
<th>Neurological and musculoskeletal risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>Muscular dystrophy</td>
</tr>
<tr>
<td>Parkinson's disease</td>
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<tr>
<td>Spinal cord injury</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
</tbody>
</table>

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

### Secondary Causes (4 of 4)

<table>
<thead>
<tr>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum (in antacids)</td>
</tr>
<tr>
<td>Anticoagulants (heparin)</td>
</tr>
<tr>
<td>Anticonvulsants</td>
</tr>
<tr>
<td>Aromatase inhibitors</td>
</tr>
<tr>
<td>Barbiturates</td>
</tr>
<tr>
<td>Cancer chemotherapeutic drugs</td>
</tr>
<tr>
<td>Depo-medroxyprogesterone (premenopausal contraception)</td>
</tr>
<tr>
<td>Glucocorticoids (≥ 5 mg/d prednisone or equivalent for ≥ 3 months)</td>
</tr>
<tr>
<td>GnRH (Gonadotropin releasing hormone) agonists</td>
</tr>
<tr>
<td>Lithium Cyclosporine A and tacrolimus</td>
</tr>
<tr>
<td>Methotrexate</td>
</tr>
<tr>
<td>Parental nutrition</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitors</td>
</tr>
<tr>
<td>Tamoxifen® (premenopausal use)</td>
</tr>
<tr>
<td>Thiazolidinediones (such as Actos® and Avandia®)</td>
</tr>
<tr>
<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: Donna returns office visit 1 month

- 65 yo WF, risks parental hip fx, lactose intolerant
- DXA:T- score LS -2.2; FN -2.4; TH -2.2.
- FRAX risk scores: MOF 22%; Hip 2.6%
- Labs: 25(OH) Vit D insufficient, replenish, then Vit D3 2,000 u/day
- CMP, CBC, TSH, iPTH, Mg, Phosphorous all normal
- Diet: well rounded; lactose alternative sources of calcium.
  - Meets minimum of 1200 mg calcium daily in diet
- Exercise-Agrees to PT to optimize her posture/exercise routine
- Pharmacologic Therapy is recommended, but she declines, concerned of side effects, asks to wait until her next DXA in 2 yrs
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)

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

3. 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


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**Physical Therapy for Osteoporosis and Osteopenia Prevention and Treatment**

- 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
Case: Follow-Up

- At 9 months, follow up after ED visit:
  - She became entangled in her dog’s leash,
  - Fell, fractured her ankle (distal fibula fracture)
  - Recalculate FRAX with fracture

Case: FRAX after fracture

- BMI: 22.5
- The ten year probability of fracture (%)
  - with BMD
    - Major osteoporotic: 33
    - Hip Fracture: 5.2

Used with Permission from International Osteoporosis Foundation
AES Question #3

T scores: LS -2.3; FN -2.4; TH -2.2
FRAX MOF 33%; Hip 5.2%

Donna agrees to pharmacologic therapy. Which medication is recommended to consider as first line?

1. Pharmacologic therapy for 5 years with alendronate
2. Pharmacologic therapy for 5 years with ibandronate
3. Pharmacologic therapy for 5 years with denosumab
4. Pharmacologic therapy for 5 years with raloxifene

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; moderate 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)
### 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><strong>Bisphosphonates</strong></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 3 mg IV every 3 mo.</td>
</tr>
<tr>
<td>Risedronate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>35 mg po weekly 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>

<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 6month</td>
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<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>
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<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>
</tr>
<tr>
<td>PTHrP Abaloparatide</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>80 mcg SC daily for max 2 yrs</td>
</tr>
</tbody>
</table>
**Bisphosphonates (BP)**

- Postmenopausal women, men, steroid induced osteoporosis
- Fracture 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, et al.
- IV-Zoledronic acid, if unable to follow oral dosing or GI intolerance
- Caution: CrCl <35; Hypocalcemia-monitor Ca, Mg, PO4 periodically.

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

**Bisphosphonate Drug Holiday**

- After 5 yr of oral bisphosphonates (BP) or 3 yr of intravenous (IV) BP
- DXA and Vertebral Fracture Assessment (VFA)
- Donna’s T- scores:  
  - Lumbar Spine (LS) -2.3 -1.9  
  - Femoral neck (FN) -2.4 -1.9  
  - Total Hip (TH) -2.2 -1.8  
- VFA: No vertebral fractures. No thigh or groin pain
- Women not at high fracture risk after 5 yr of BP treatment, a drug holiday of 2-3 yr can be considered
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

AES 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

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**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 \(\rightarrow\) 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
Teriparatide (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.

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
• Develop collaborative post-fracture care coordination
• Encourage patients to exercise to decrease their fracture and fall risk.

Questions
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References

References

• Kanis JA, on behalf of the World Health Organization Scientific Group. Assessment of osteoporosis at the primary health care level. WHO Collaborating Centre for Metabolic Bone Diseases, University of Sheffield 2007.
• National Bone Health Alliance. http://www.nbha.org/resources
Educational Resources

– National Osteoporosis Foundation (NOF) Professional Learning Center; Clinicians Guidelines www.cme.nof.org/Resources.aspx
– 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