Osteoporosis Update:
Review of Current Guidelines, Controversies, and Common Questions

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No disclosures
Goals/Objectives

• Highlight current guidelines (NOF, USPSTF, AACE) to guide diagnosis and management of osteoporosis
• Use case based approach to address common issues that arise when diagnosing and treating osteoporosis.
• Plan to address issues of screening, prevention, and treatment
Triple Aim

• Improve access:
  – Improve access to appropriate screening

• Improve outcomes:
  – Appropriate screening will identify those at risk for osteoporotic fractures and allow treatment to decrease overall fracture burden

• Decrease cost:
  – Detecting and treating those at risk for osteoporotic fracture will decrease cost by reducing hospitalizations, long term care placement, etc.
A quick review: Definitions

- **Normal**
  - T score at -1 and above
- **Low bone mass**
  - T score between -1 and -2.5
- **Osteoporosis**
  - T score at or below -2.5
Case 1

- 63 yo woman with PMH of moderate macular degeneration, HTN, HLD, and RLS presents for her well woman exam. She notes that she had a bone density test in 2005 that showed osteopenia with femoral neck T score of -1.8 and wonders if she needs a repeat DXA.

- Meds: Atenolol, Niacin, Mirapex
- SH: smoker (1 ppd x 30 years)
- Wt 55 kg, Ht 156 cm; BMI 22.6
- What is the next step?
  - A. Calculate FRAX to determine if repeat DXA should be ordered today
  - B. Decline repeat DXA until age 65; Counsel on calcium/vitamin D, smoking cessation, and weight bearing exercise
  - C. Start a bisphosphonate
  - D. Perform a vertebral fracture assessment
National Osteoporosis Foundation (NOF) Screening Recommendations

- Recommended modality: DXA
- Women age ≥ 65 and men age ≥ 70
- Based on risk factor profile for postmenopausal women 50-64 and men 50-69 (if FRAX 10 year risk score is ≥ 9.3%)
- Adults who have had fracture (without trauma) after age 50
- Adults with condition (eg RA) or taking a medication (eg steroids) associated with osteoporosis
The USPSTF recommends (DXA)

- Screening for osteoporosis in women aged 65 years or older
- Screening for younger women whose fracture risk is equal to or greater than that of a 65-year-old white woman who has no additional risk factors. (Frax≥9.3%)
- Grade B

Insufficient evidence to assess the balance of benefits and harms of screening for osteoporosis in men (Grade I)
• Fracture risk can be determined by using FRAX calculator
• Only for postmenopausal women and men ≥50
• FRAX not validated in patients currently or previously treated
• https://www.shef.ac.uk/FRAX/
FRAX Risk Calculator

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth
   - Age: 63
   - Date of Birth: Y: [ ] M: [ ] D: [ ]

2. Sex
   - Male
   - Female

3. Weight (kg)
   - 55

4. Height (cm)
   - 156

5. Previous Fracture
   - No
   - Yes

6. Parent Fractured Hip
   - No
   - Yes

7. Current Smoking
   - No
   - Yes

8. Glucocorticoids
   - No
   - Yes

9. Rheumatoid arthritis
   - No
   - Yes

10. Secondary osteoporosis
    - No
    - Yes

11. Alcohol 3 or more units/day
    - No
    - Yes

12. Femoral neck BMD (g/cm²)
    - T-Score: -1.8

**BMI: 22.6**

The ten year probability of fracture (%)

**with BMD**

- Major osteoporotic: 9.4
- Hip Fracture: 2.0
Case 1

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Vertebral Imaging

• 2 methods
  – Lateral thoracic and lumbar spine x-ray
  – Lateral vertebral fracture assessment (available on most DXA machines)

• Radiographically confirmed vertebral fractures
  – Sufficient to make the diagnosis of osteoporosis
  – Automatically makes the patient a candidate for treatment
  – Increases risk of future vertebral fractures 5-fold and the risk of hip and other fractures 2- to 3-fold
NOF recommendations
• Consider for:
  – All women ≥ 70 and all men ≥ 80 if T score at the spine, total hip or femoral neck is ≤ -1.0
  – Women between 65-69 and men between 75-79 if T score at spine, total hip or femoral neck is ≤ -1.5
  – Postmenopausal woman 50-64 and men 50-69 with specific risk factors:
    • Low trauma fracture
    • Patient report of height loss of 4 cm
    • Measured height loss of 2 cm
    • Recent or ongoing long-term glucocorticoid treatment
Screening Interval

- Optimal screening interval would allow detection of low BMD/osteoporosis before the onset of a fragility fracture
- Common practice to screen every 2 years
- National Osteoporosis Foundation
  - Unclear if patients have normal initial screen or in upper low bone mass range and don’t have major risk factors
- USPSTF – No Recommendation
Screening Interval

• AACE, 2010

Guidelines for testing in women who have not received osteoporosis treatment

The frequency of testing depends on the results of the initial test and the likelihood of clinically significant bone loss.

For patients approaching an intervention threshold, retesting every 1–2 years is often appropriate.

For those whose bone mineral density is borderline-low, retesting every 3–5 years is usually sufficient.

Patients who are comfortably above an intervention threshold may not need to undergo reassessment for 5 or 10 years, or ever, unless there is some new indication.
Bone-Density Testing Interval and Transition to Osteoporosis in Older Women

Margaret L. Gourlay, M.D., M.P.H., Jason P. Fine, Sc.D., John S. Preisser, Ph.D., Ryan C. May, Ph.D., Chenxi Li, Ph.D., Li-Yung Lui, M.S., David F. Ransohoff, M.D., Jane A. Cauley, Dr.P.H., and Kristine E. Ensrud, M.D., M.P.H., for the Study of Osteoporotic Fractures Research Group
Figure 2. Unadjusted Cumulative Incidence of Osteoporosis According to Baseline T-Score Range.

The proportion of women who had a transition to osteoporosis is shown as a function of time. The cumulative incidence curves were estimated by means of parametric cumulative incidence models for interval-censored data. The dashed horizontal line marks the 10% threshold for the transition to osteoporosis; where this line intersects each cumulative incidence curve, a vertical dashed line to the x axis marks the estimated testing interval. The analysis of women with osteopenia at baseline is based on three T-score groups and included the 513 women who made the transition from normal BMD to osteopenia and had at least one subsequent examination with BMD recorded.
Conclusion: For untreated men and women with a mean age of 75, repeating DXA after 4 years did not improve fracture risk prediction.
What does Medicare cover?

DXA once every 24 months (more often if “medically necessary”)

No limit on number of total tests

Goal is to find the correct interval to improve quality of care and contain cost

This data suggests that q 2 years may be too frequent for most clinical scenarios.
Bottom lines for screening and interval

- Screen women age ≥ 65 and men ≥70
- Screen younger patients if FRAX 10 year risk score is ≥ 9.3%
- Consider screening adults who have had low trauma fracture after age 50, and those with medical conditions or medications associated with osteoporosis
- Screening interval is unclear, but every 2 years is likely too often for some patients
- Consider baseline BMD and age when considering screening interval
Case 1 (continued)

- Repeat DXA shows a femoral neck T score of -2.1
- Additional history reveals patient is not taking any supplements, but has 1-2 servings of calcium daily. She is sedentary. Which of the following treatments are indicated at this time to prevent falls and fracture risk?
  - A. Start alendronate 10 mg PO daily
  - B. Counsel on adequate calcium/vitamin D intake
  - C. Home safety eval and exercise program
  - D. Start alendronate 70 mg PO weekly
Who should I Treat?

• Hip or vertebral fracture in absence of major trauma
• T score ≤ -2.5 at femoral neck, total hip, or lumbar spine
• Low bone mass/osteopenia (T score between -1 and -2.5) if 10 year hip fracture risk is > 3% or if 10 year major osteoporotic fracture risk is >20% using FRAX
**Questionnaire:**

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   - Date of Birth: ____________

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   - Female

3. Weight (kg)
   - 55

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5. Previous Fracture
   - No
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   - No
   - Yes

7. Current Smoking
   - No
   - Yes

8. Glucocorticoids
   - No
   - Yes

9. Rheumatoid arthritis
   - No
   - Yes

10. Secondary osteoporosis
    - No
    - Yes

11. Alcohol 3 or more units/day
    - No
    - Yes

12. Femoral neck BMD (g/cm²)
    - T-Score: -2.1

**BMI: 22.6**

The ten year probability of fracture (%)

with BMD

- Major osteoporotic: 11
- Hip Fracture: 2.7
Prevention

NOF recommendations
• Weight bearing and strengthening exercises
• Fall risk assessment and risk modification
• Adequate calcium and vitamin D
• Tobacco cessation
• Identify and treat alcoholism
• Measure height annually
Fall Prevention/Exercise

- **2012 Cochrane review**
  - 159 trials; 80,000 subjects
  - Group and home exercise programs reduced risk of falling as well as risk of fall related fractures
  - Home safety evaluations/interventions reduced rate and risk of falls.
    - More effective when delivered by an occupational therapist.
  - Vitamin D supplementation did not prevent falls*
- **2012 USPSTF**
  - Recommends exercise or physical therapy (B)
  - Recommends vitamin D supplementation (B)
NOF recommendations

• Calcium
  – 1200 mg daily for women > 50 and men >70
  – 1000 mg daily for men 50-70

• Vitamin D
  – 800-1000 IU daily
  – Consider check levels in those at risk for deficiency and supplementing as necessary

• If adequate dietary calcium cannot be obtained, dietary supplementation is indicated up to the recommended daily intake.
Prevention: Calcium/Vitamin D

USPSTF, 2013

- Recommend **against** daily supplementation with 400 IU or less of vitamin D and 1000 mg or **less** of calcium for the primary prevention of fractures in **non-institutionalized postmenopausal women**. (D)

- Insufficient evidence to assess the balance of the benefits and harms of combined vitamin D and calcium supplementation for the primary prevention of fractures in **premenopausal women or in men**. (I)

- Insufficient evidence to assess the balance of the benefits and harms of daily supplementation with **greater** than 400 IU of vitamin D3 and greater than 1000 mg calcium for the primary prevention of fractures in **non-institutionalized postmenopausal women**. (I)
Bottom Line: Calcium/Vitamin D

• Highly controversial area of ongoing research

• Advocate for getting RDI of calcium/D through food

• Not great evidence for prevention of osteoporosis/fractures with supplements, but good studies are limited

• Risk of CVD is not compelling, but modest increase in urinary tract stones
Case 2

- 70 year old postmenopausal woman with PMH of GERD, hypothyroidism, and depression has a routine DXA as part of a well woman assessment. Her chronic medical conditions are well controlled, though she is due for a TSH. Her T score at the femoral neck is -2.7 and -3.2 at the L spine. She has no history of fractures.
- BMI 24.1
- Meds: omeprazole 20 mg daily, levothyroxine 100 mcg daily, and citalopram 10 mg daily

Which of the following statements is true?
- A. Bisphosphonates are contraindicated because of her h/o GERD
- B. All of the medications this patient takes can adversely affect bone health.
- C. Vertebral imaging would help to guide your management of this patient.
- D. The first line therapy for this patient would be estrogen.
<table>
<thead>
<tr>
<th>Drug class</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucocorticoids</td>
<td>Decreased bone formation</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>Decreased bone formation, increased resorption</td>
</tr>
<tr>
<td>Aromatase inhibitors</td>
<td>Reduced estrogen production</td>
</tr>
<tr>
<td>Gonadotropin-releasing hormone agonists</td>
<td>Hypogonadism</td>
</tr>
<tr>
<td>Medroxyprogesterone acetate (depot)</td>
<td>Reduced estrogen levels</td>
</tr>
<tr>
<td>Excessive thyroid hormone replacement</td>
<td>Increased bone resorption</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Possible decreased bone formation</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>Possible decreased calcium absorption</td>
</tr>
<tr>
<td>Serotonin selective reuptake inhibitors</td>
<td>Inhibition of serotonin transporter</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Calcineurin inhibitors</td>
<td>Uncertain</td>
</tr>
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</table>
Case 2 (revisit)

70 year old postmenopausal woman with PMH of GERD, hypothyroidism, and depression has a routine DXA with T score at the femoral neck is -2.7 and -3.2 at the L spine. She has no history of fractures. Her TSH is normal.

- BMI 24.1
- Meds: omeprazole 20 mg daily, levothyroxine 100 mcg daily, and citalopram 10 mg daily

What class of medication should we start?
- A. Calcitonin
- B. HRT
- C. Bisphosphonate
- D. Teriparatide
<table>
<thead>
<tr>
<th>Drug</th>
<th>Postmenopausal osteoporosis</th>
<th>Glucocorticoid-induced osteoporosis</th>
<th>In men</th>
</tr>
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<tbody>
<tr>
<td>estrogen (multiple formulations)</td>
<td>Multiple regimens</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>calcitriol (Miacalcin, Fortical)</td>
<td>... 200 IU intranasally once daily, or 100 IU SQ qod</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>denosumab (Prolia)</td>
<td>... 60 mg SQ every 6 mo</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>raloxifene (Evista)</td>
<td>60 mg PO daily</td>
<td>60 mg PO daily</td>
<td>...</td>
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<tr>
<td>ibandronate (Boniva)</td>
<td>2.5 mg PO daily 150 mg PO monthly</td>
<td>2.5 mg PO daily 150 mg PO monthly</td>
<td>...</td>
</tr>
<tr>
<td>alendronate (Fosamax)</td>
<td>5 mg PO daily 35 mg PO weekly</td>
<td>10 mg PO daily 70 mg PO weekly 70 mg + D&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 mg PO daily 10 mg PO daily 70 mg PO weekly</td>
</tr>
<tr>
<td>risendronate (Actonel)</td>
<td>5 mg PO daily 35 mg PO weekly 150 mg PO monthly</td>
<td>5 mg PO daily 5 mg PO daily 5 mg PO daily 35 mg PO weekly 150 mg PO monthly</td>
<td>5 mg IV once yearly 5 mg IV once yearly 5 mg IV once yearly 5 mg IV once yearly</td>
</tr>
<tr>
<td>zoledronic acid (Reclast)</td>
<td>5 mg IV every 2nd y</td>
<td>5 mg IV once yearly</td>
<td>5 mg IV once yearly</td>
</tr>
<tr>
<td>teriparatide (Forteo)</td>
<td>... 20 µg SQ daily</td>
<td>...</td>
<td>20 µg SQ daily</td>
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</tbody>
</table>

* Please review the package inserts for specific prescribing information. IV = intravenously; PO = orally; qod = every other day; SQ = subcutaneously.

<sup>a</sup> Fosamax 70 mg is available as both a tablet and a unit dose liquid. Alendronate (generic Fosamax) is available.

<sup>b</sup> Fosamax Plus D is a tablet containing 70 mg of alendronate and 2,800 IU or 5,600 IU of vitamin D for weekly administration.

<sup>c</sup> The approved dosage of alendronate for treatment of glucocorticoid-induced osteoporosis in men and in estrogen-replete women is 5 mg daily.

<sup>d</sup> The approved dosage of alendronate for treatment of glucocorticoid-induced osteoporosis in estrogen-deficient women is 10 mg daily.

★ Have demonstrated decreased vertebral, nonvertebral, and hip fractures when compared to placebo.
Bisphosphonates (BPs)

- Alendronate*
  - Reduced vertebral and hip fractures by ~ 50 % over 3 years
- Risendronate
  - Reduced vertebral fractures by 41-49%; Reduced other fractures by 36% over 3 years
- Ibandronate
  - Reduced vertebral fractures by ~ 50% over 3 years; **no effect on non-vertebral fractures**
- Zoledronic acid
  - Reduced vertebral fractures by 70%; Reduced hip fractures by 41%; other fracture reduction 25% over 3 years
Bisphosphonates

- Side effects: difficulty swallowing, esophageal erosions/inflammation, gastric ulcer, bone/joint pain, osteonecrosis of jaw, hypocalcemia, low trauma atypical femur fracture
- Can have flu like syndrome after IV infusions
- Can affect renal function –
  - check creatinine/GFR first
  - Not recommended if GFR < 30
Bisphosphonates

- Empty stomach
- First thing in the morning
- Stay upright for 30-60 minutes
- 8 oz water
- Can pretreat with acetaminophen before IV meds
Osteonecrosis of the Jaw

- Risk very small in those treated for osteoporosis
- 0.001 to 0.1% risk with oral BPs
- 0.8-20% risk with high-dose IV BPs for > 2 year
- Risk increases with treatment duration and higher doses
- Oral exam with xrays indicated to evaluate jaw heaviness, tingling, pain, loose teeth or oral ulceration
Atypical femur fractures

• Absolute risk is low (3.2-50 cases per 100,000 patient years)
  – Miniscule when compared to risk of osteoporotic fractures

• Risk increases with treatment duration

• Usually precipitated by pain in groin/thigh

• Check x-rays, MRI, bone scan if suspected
Other FDA Approved Therapies

- Calcitonin
- Estrogen Agonist/Antagonist: Raloxifene
- Parathyroid hormone: Teriparatide
- RANKL/RANKL inhibitor: Denosumab
Teriparatide

- Synthetic parathyroid hormone stimulates osteoblasts to form bone (anabolic), increases calcium absorption
- Reduces risk of vertebral fractures by 65%; non-vertebral fractures by 53% over 18 months
- Daily SQ injection
- Side effects: leg cramps, nausea, dizziness, increased osteosarcoma in rats
- Only approved for use for 2 years, usually followed by a bisphosphonate
• Monoclonal Ab that prevents Receptor Activator of Nuclear Factor kappa-B (RANK) and RANK ligand from interfacing
• RANK/RANKL interaction critical for osteoclast function
• Reduces vertebral fractures 68%, hip fractures 40%, and other fracture 20% over 3 years
• SQ injection q 6 months
• Side effects: hypocalcemia, skin rash and infection, osteonecrosis of jaw, atypical femur fractures
Monitoring treatment

• Repeating DXA sooner than 2 years is not likely to show significant change
  – Stability of or increase in BMD is considered a good response
  – Even those with decreased BMD show fracture risk reduction

• Good evidence on the utility of DXA for monitoring is lacking, controversial area

• Looking for non-responders and noncompliance
Monitoring treatment

- **NOF guidelines:**
  - Clinical assessment: review med side effects and compliance, risk factors, fall prevention measures, calcium/vitamin d intake, exercise
  - 1-2 years after starting therapy, the q 2 years thereafter
  - Vertebral imaging – only repeat if ht loss, new back pain
  - Bone Turnover Markers

- **AACE**
  - Repeat DXA every 1-2 years until BMD is stable, then reduce testing frequency

- **NIH, UK, and Canada** do not offer recommendation
Case 2 (continued)

• The patient asks she will have to take a bisphosphonate for the rest of her life? How do you counsel her?
  • A. Lifelong treatment is warranted
  • B. 1-2 years of treatment
  • C. 3-5 years of treatment
  • D. 10 years of treatment
Duration of treatment

• FLEX study, 2006
  – Demonstrated that taking alendronate > 5 years did not provide additional fracture protection for nonvertebral fractures
  – Did lower clinical vertebral fracture risk

• FLEX 2, 2010
  – Alendronate for > 5 years may be beneficial in those women with femoral neck T ≤ -2.5, unlikely to be beneficial in those with ≥ 2

• Reassess risk after 3-5 years
  – Interval fracture history, new meds/conditions, height measurement, BMD, and vertebral imaging (if there has been documented height loss ≥ 2 cm)
  – If low risk of fracture:
    • Consider stopping oral therapy after 5 years
    • Consider stopping IV therapy (zoledronic acid) after 3 years

• No consensus on how to monitor after treatment is stopped and if you should restart meds
Bottom Line for Treatment

• Bisphosphonates are first line
• Monitoring is controversial, but generally check for response 2 years after initiating treatment
• Consider contributing causes/secondary work up if patient isn’t responding as expected
• Consider stopping treatment after 3-5 years
Take Home Points: Screening

• Screen women ≥ 65 and men ≥ 70
• Screen younger patients if FRAX 10 year risk score is ≥ 9.3%
• Consider screening adults who have had low trauma fracture after age 50, and those with medical conditions or medications associated with osteoporosis
• Consider baseline BMD and age when considering screening interval
Take Home Points: Prevention

- Fall Prevention:
  - Group or home exercise programs/physical therapy
  - Home safety evaluations
  - Consider vitamin D

- Calcium and Vitamin D
  - Controversial
  - Best through food
Take Home Points: Treatment

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Questions/Comments???


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