Osteoporosis: Overview

- Definitions
- Risk factors
- Screening and Monitoring
- Treatment
- Emerging Issues

Osteoporosis: Definitions

- Normal: BMD no lower than 1 SD below mean for young adult women
- Osteopenia (Low bone mass): BMD 1.0-2.5 SD below the mean for young adults
  - (T=-1 to -2.5)
- Osteoporosis: BMD more than 2.5 SD below young adult mean
  - (T<-2.5)

Background

- Osteoporotic fractures are increasing as the population ages
- Hip and vertebral fractures are associated with premature mortality
- Any fracture is associated with an increased risk of 5-10 year mortality
- A subsequent fracture is associated with an increased mortality risk for 5 more years
  - Dubbo Osteoporosis Epidemiology study

New Developments in Osteoporosis: Screening, Prevention and Treatment

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Osteoporosis: Definitions

- T scores vs Z scores
- T scores compare the patient with the average young adult female
  - Useful for treatment decisions
- Z scores compare the patient with an age matched female
  - Useful for ruling out secondary causes of bone loss

Risk Factors

- Age
  - Risk of hip fracture increases with age
  - Older women have a much higher fracture rate than younger women with the same bone density
- Vertebral fractures: very high risk
  - Even if asymptomatic
  - 20% risk of new fracture in the year following a fracture

10-Year Fracture Probability
Age vs. Femoral Neck T-score

Adapted from JA Kanis et al, Osteoporos.Int. 2001;12:989-995
Risk Factors in the WHO Risk Factor Assessment Tool

- Age
- Gender
- Personal history of fracture
- Femoral neck BMD
- Low body mass index
- Oral glucocorticoids
- Secondary osteoporosis
- Parental history of hip fracture
- Current smoking
- Alcohol intake of 3 or more drinks per day

Drugs Associated with an Increased Risk of Osteoporosis

- Thyroid hormone (over replacement)
- Aromatase inhibitors
- SSRIs
- PPIs
- Androgen deprivation agents
- Thiazolidinediones
- Anticonvulsants

Screening and Monitoring

Question

Which of the following women would you screen for osteoporosis?

1. 66 year old healthy woman
2. 57 year old healthy woman who does not exercise
3. 55 year old woman whose mother had a hip fracture
4. 1 and 3
5. 1, 2 and 3
Screening for Osteoporosis

- Bone density is the single best predictor of future fracture
  - Hip BMD is best predictor of hip fracture
- Central dual x-ray absorptiometry (DXA) of spine, hip and body most commonly used and preferred when available

NOF 2014 : BMD Screening

- Women age 65 and older, men >70 regardless of risk factors
- Adults who have a low trauma fracture after age 50
- In postmenopausal women age 50 to 64
  - Adults with a condition (e.g., RA) or taking a medication associated with low BMD or bone loss
  - ≥ 5 mg prednisone QD or equivalent for ≥ 3 months
  - Historical height loss of 1.5 inches or more (4 cm)
  - Prospective height loss of 0.8 inches or more (2 cm)


Case

- Bonnie Bony is a 68 year old woman who wants to know when she should have her next bone mineral density test. Her last BMD was 2 years ago and showed osteopenia with a t score of -1.8. What do you tell her?

Choices

1. Let’s schedule it now
2. We should do it in 2 years
3. We should do it in 3 years
4. We should do it in 5 years
5. I have no idea... when do you want to do it?

41% 22% 26% 3% 7%
USPSTF Recommendations

- Screen all women age 65 and older
  - Evidence for screening is indirect
- Screen younger women whose fracture risk is equal to or greater than a 65 year old white woman who has no additional risk factors
- “Evidence is lacking about optimal intervals for repeated screening”
  - A minimum of 2 years may be needed to reliably measure a change in BMD
  - Longer intervals may be needed to improve fracture risk prediction
  - USPSTF 2011

BMD testing

- Medicare pays for BMD every two years regardless of baseline BMD
- Is repeat BMD useful?
- Does change in BMD provide additional information about fracture risk?

The News

- Bone-density testing interval and transition to osteoporosis in older women.
  - Gourlay et al. NEJM 2012
- Aim: To determine how the BMD testing interval relates to the timing of the transition from normal BMD or osteopenia to the development of osteoporosis before a hip or vertebral fracture occurs

Methods

- 4,597 women from the Study of Osteoporotic Fractures (SOF)
  - Aged 65 and older, population based
  - Study examinations at year 2, 6, 8, 10 and 16
- Outcome: Estimated interval for 10% of individuals to make transition from normal BMD or osteopenia to osteoporosis before a hip or clinical vertebral fracture or treatment for osteoporosis
Results

• Within each t score range, a percentage of women developed osteoporosis over 15 years
  – Normal 0.8%
  – Mild osteopenia 4.6%
  – Moderate osteopenia 20.9%
  – Advanced osteopenia 62.3%

Results/Competing Risk Analyses

• Adjusted interval between baseline testing and the development of osteoporosis in 10% of study participants
  – Normal BMD 16.8 (11.5-24.6) yrs
  – Mild osteopenia 17.3 (13.9-21.5) yrs
  – Moderate osteopenia 4.7 (4.2-5.2) yrs
  – Advanced osteopenia 1.1 (1.0-1.3) yrs

Conclusions

• Osteoporosis would develop in <10% of individuals during rescreening intervals of 15 years for women with normal BMD or mild osteopenia, 5 years for women with moderate osteopenia and 1 year for women with advanced osteopenia

• Future screening recommendations will probably be based on likelihood of osteoporosis progression based on initial BMD

Take Home Message

• Decisions about when to rescreen should be based on the results of initial screening
• Few women with normal BMD will develop osteoporosis at 15 year follow-up
• Back to Bonnie: Would probably wait at least 5 years from her prior BMD
The News

- Repeat bone mineral density screening and prediction of hip and major osteoporotic fracture.  
- Aim: To determine whether BMD changes after 4 years provide additional information on fracture risk and to quantify the change in fracture risk classification after a second BMD measure

Methods

- Framingham Osteoporosis Study population based cohort of 310 men and 492 women  
  - Two BMD measures from 1987 to 1999
- Outcome: risk of hip or major osteoporotic fracture through 2009 or 12 years after second BMD measure
- Net Reclassification Index (NRI):  
  - Quantifies change in risk classification after a second BMD measure  
  - High risk: Risk of hip fracture 3% or greater or major osteoporotic fracture 20% or greater (vs low risk)

Results

- Mean age 74.8 years
- Mean BMD change -0.6% per year
- Median follow up 9.6 years
- NRI increased proportion classified as high risk by 3.9% and decreased the proportion defined as low risk by 2.2%  
  - Adding BMD change to a model that included baseline BMD did not improve performance of the ROC curve  
  - AUC baseline 0.71 (0.65-0.67) vs 0.72 (0.66-0.79)

ROC Curves for Hip and Major Osteoporotic Fractures

Figure Legend:  
Receiver Operating Characteristic Curves for Models Investigating Fracture in Older Adults From the Framingham Osteoporosis Study. BMD indicates bone mineral density. All models are adjusted for age, sex, body mass index, weight loss (per pound), and history of fracture measured at the time of the second BMD test. Models are defined in the Methods section.
Conclusion and Take Home Message

• In untreated men and women with a mean age of 75, a repeat BMD after 4 years did not meaningfully improve the prediction of major hip or osteoporotic fracture.

• Repeating a BMD after 4 years to improve fracture risk prediction may not be necessary in adults of this age untreated for osteoporosis.

BMD for Monitoring Treatment

• Analysis of data from the FIT study.

• Over 3 year follow-up, comparison of between person variation (treatment) with within person variation (measurement).

• Within person variation was greater than between person variation.

• 97.5% of individuals gained BMD with alendronate treatment.

• Routine monitoring in the first 3 years of bisphosphonate treatment is unnecessary.  
  - BMJ 2009

Monitoring Treatment?

• Treatment should be continued in patients who lose BMD initially.

• Patients who have the largest increases during the first year are more likely to lose or have modest gains during the second year.

• If most women will gain BMD with treatment and since resistance to osteoporosis drugs has not been documented, there may not be value in monitoring BMD during treatment.

• Will monitoring reinforce adherence or change your management?

Monitoring Guidelines

• All recommend follow-up monitoring but no consensus on site and frequency.

• What is “treatment failure?”

• ISCD: DEXA spine and hip when expected change in BMD exceeds LSC expected on bone densitometer.

  – Every 1-2 years and less often when stable.

• AACE: DEXA spine and hip every 1-2 years until stability.

• NAMS: DEXA hip every 2 years.

• Question: What are you going to do?
OSTEOPOROSIS

Absolute Risk Assessment

WHO Fracture Risk Algorithm

- FRAX
- Calculate the 10 year probability of a hip fracture and the 10 year probability of any osteoporotic fracture
- Includes femoral neck BMD and risk factors
- Can be used only in previously untreated patients
- Can be used with or without BMD
- Algorithm adapted for the U.S.
- Available as an I phone app

www.shef.ac.uk/FRAX
WHO Fracture Risk Algorithm

- Most useful in identifying individuals in the osteopenic range who are most likely to benefit from treatment
- Treat when there is a 10 year risk of hip fracture ≥3% or a 10 year risk of a major osteoporosis-related fracture that is ≥20% based on the U.S. adapted WHO algorithm
- In the future some BMD machines may be able to provide a report with absolute fracture risk

OSTEOPOROSIS

TREATMENT

Question

Mrs. P is a 66 year old woman who has no previous fracture or other risk factors. Her hip BMD t score is -2.3. She is on no medications. What are your next steps?

1. Discuss Calcium and Vitamin D intake
2. Start raloxifene 60 mg per day
3. Start alendronate 70 mg per week
4. 1 and 3

NOF 2014 Treatment Guidelines

Prior hip or vertebral fracture
Other prior bone fracture, or
Secondary medical condition, or
Elevated 10 year fracture risk
No Risk Factors

0 -1.0 -1.5 -2.0 -2.5 -3.0
T-Score
**NOF 2014: Vertebral Imaging**

- Vertebral fractures indicate very high risk
- Consider in women age 70 and over and men aged 80 and over with BMD T score ≤-1.0
- Consider in women aged 65-69 and men aged 70-79 with BMD T score ≤-1.5
- Consider
  - Low trauma fracture during adulthood
  - Long term glucocorticoid use
  - Height loss
    - Historical ≥ 1.5 inch
    - Prospective ≥ 0.8 inch
- No evidence for treatment initiation based on these criteria

**NOF: Osteoporosis Prevention**

- Preventive measures for everyone:
  - Calcium: diet alone or with supplements
    - 1,000 to 1,200 mg a day
  - Vitamin D intake of 800-1,000 IU a day
  - Weight bearing and muscle strengthening exercise to improve agility, strength, posture and balance, increase bone density and avoid falls and fractures
  - Assess fall risk and appropriate modifications
  - Avoid tobacco and excessive alcohol
  - Hip protectors for some at risk?

*Revised 2014 NOF Guidelines

**Calcium/Vitamin D**

- Women should ideally get RDA for calcium and Vitamin D from diet
- Previous studies have suggested that calcium/Vitamin D are necessary but not sufficient
  - Even if a woman is receiving adequate calcium and Vitamin D, she may still be at risk for fracture
  - Additional therapies (eg anti-resorptive therapies) may also be necessary

**USPSTF Recommendations February, 2013**

- Evidence is insufficient to assess balance of benefits and harms
  - Vitamin D with or without calcium for cancer prevention
  - Vitamin D and calcium for primary prevention of fractures in postmenopausal women or men
  - Daily supplementation with >400 IU of Vitamin D3 and 1,000 mg of calcium for fracture prevention
- Recommends against daily supplementation with <400 IU of Vitamin D3 and 1,000 mg calcium for primary prevention of fractures in noninstitutionalized postmenopausal women
Vitamin D and Falls

• USPSTF concluded that Vitamin D supplementation is effective in preventing falls in community dwelling adults aged 65 and older who are at increased risk for falls
  – Ages 51-70: 600 IU daily
  – Older than aged 70: 800 IU daily

What do you most commonly use for treatment of osteoporosis?

1. Weekly bisphosphonate
2. Monthly bisphosphonate
3. Annual bisphosphonate
4. Selective estrogen receptor modulator
5. PTH
6. Denosumab

FDA Approved Pharmacologic Therapies

• Estrogen
• Bisphosphonates
• Calcitonin
• SERMs
• Parathyroid hormone
• Denosumab

Estrogen

• 50% reduction in hip and other non-spine fractures in observational studies
• In two RCTs of women with vertebral fractures, estrogen reduced the risk of new vertebral fractures by half
• Women’s Health Initiative
  – Reduced hip fracture risk by 34%
  – No overall benefit even in women at high risk for osteoporosis
• Approved non-estrogen treatments should first be carefully considered
**Estrogen**

- USPSTF does not recommend the use of estrogen for the treatment of any chronic disease
- Some women may be taking estrogen for other reasons

**Bisphosphonates**

- Four approved: alendronate, risedronate, ibandronate, zolendronate
- Bind to bone and inhibit osteoclastic resorption
- Increase BMD by 3% per year
- Reduce fracture risk
  - All reduce vertebral fracture
  - All but ibadronate reduced nonvertebral fracture (including hip fracture)
- Therapeutic effects with 10 year use of alendronate
- Gradual loss of effect with discontinuation of medication

**Bisphosphonates: Adverse Effects**

- Atrial fibrillation
  - Seen in some trials (zolendronic acid and alendronate) but not others
  - Could be spurious
- Osteonecrosis of the jaw
- Femoral shaft fractures

**Potential Long-term Side Effect of Bisphosphonates?**
Osteonecrosis of the Jaw

- Associated with potent bisphosphonate use:
  - 94% treated with IV bisphosphonates
  - 4% of cases have OP, most have cancer
  - 60% caused by tooth extraction. Other risk factors unknown. Infection?
- Key points: extremely rare, importance of treatment duration unclear
  - Estimated risk in those treated for osteoporosis
    - 1/10,000 to 1/100,000 person years
- Dental exam recommended before Rx, but no need to stop for dental procedures
  
  Woo et al; Ann Intern Med, 2006
  ADA Guidelines, 2011

Atypical Femoral Fractures (AFF)

- Long-term BP users (and others)
- Transverse not spiral, cortical thickening, minimal trauma
- Often bilateral, prodromal pain, abn. imaging (x-ray, bone scan/MR)
- ASBMR Task Force (2013)
  Stress fractures. Microdamage?
  Clinical studies: RR for BPs= 2-50
  Risk goes up with longer use and down 1 year after stopping

Re-analysis of Data in 3 RCTs

- 284 hip or femur fractures in 14,195 women
  - 12 were atypical
- Relative hazards
  - RH 1.03 (95% C.I. 0.06, 16.46) for alendronate in FIT
  - RH 1.50 (95% C.I. 0.25, 9.00) for zoledronic acid in HORIZON-PFT
  - RH 1.33 (95% C.I. 0.12, 14.67) for continued alendronate in FLEX
- Conclusions
  - Fracture of subtrochanteric or diaphyseal femur was rare even in women on bisphosphonates for up to 10 years
  - No significant increase in risk but wide confidence intervals

  Black et al NEJM 2010

Impact for Practice

- Small risk of atypical fracture associated with bisphosphonate use must be weighed against the population benefits of overall reduction in hip fractures with bisphosphonates in women with osteoporosis
**Long-term Efficacy of Bisphosphonates?**

- Long half-life also suggests that life-long treatment may not be necessary
- Best study design: re-randomize treated individuals to continue or stop
- FIT Long-term Extension (FLEX) study
  - 1099 ALN-treated FIT subjects
  - Randomized to ALN or PBO for 5 yr.

Black DM, Jama, 2006

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**Cumulative Incidence of Fractures During FLEX**

<table>
<thead>
<tr>
<th>Type</th>
<th>PBO (N = 437)</th>
<th>ALN (N = 662)</th>
<th>RR (95% CI)</th>
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<tbody>
<tr>
<td>Non-spine</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Non-vertebral</td>
<td>20%</td>
<td>19%</td>
<td>1.0 (0.8, 1.4)</td>
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<tr>
<td>Hip</td>
<td>3%</td>
<td>3%</td>
<td>1.1 (0.5, 2.3)</td>
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<tr>
<td>Vertebral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphometric</td>
<td>11%</td>
<td>10%</td>
<td>0.9 (0.6, 1.2)</td>
</tr>
<tr>
<td>Clinical</td>
<td>5%</td>
<td>2%</td>
<td>0.5 (0.2, 0.8)</td>
</tr>
</tbody>
</table>

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**FDA View of Long-term Bisphosphonate Use (Sept. 2011)**

- Independent review of epidemiologic studies to date and all bisphosphonate trial data...
- FDA conclusions about atypical fractures
  - “conflicting results...causality uncertain”
  - “no agreement on effects of duration or cumulative dose”
- FDA conclusions about ONJ
  - “some evidence that risk increases after 4 yr.”
  - “causality not established”

www.fda.gov, 2011
Discontinuation of Bisphosphonates After 3-5 Years?

- FDA conclusions about long-term efficacy
  - Pooled FLEX, HORIZON Extension, and smaller risedronate studies
  - No non-spine fracture benefit after 3-5 years but did not address vertebral fractures
- Driven by lack of non-spine fracture benefit after 5 years, not high risk of harm

FDA Perspective, NEJM, 2012

Bisphosphonates: Duration of Use

- “Bisphosphonates may be safely discontinued in some patients without compromising therapeutic gains but no adequate clinical trials have yet delineated how long the drugs' benefits are maintained after cessation.”
- New “Important Limitation of Use Statement”
  - Optimal duration of use has not been determined
  - Periodic re-evaluation of continued need

Impact for practice

- Patients at “low risk” may safely have bisphosphonates discontinued
  - Younger, no fracture history, med was started for osteopenia, BMD approaching normal?
- Patients at “increased risk” may benefit from continued therapy
  - Older, history of fracture, BMD remaining in osteoporotic range?
- Decisions about when to restart?
  - Role of BMD and bone marker turnovers

When to Stop?

- Stop if treatment was not indicated...
  - Definitely: Pre-treatment hip BMD>-2.5, no fractures, no other risk factors
  - Probably: Pre-treatment hip BMD>-2.5, no fractures but other risk factors (FH, smoking, etc)
  - Unclear: Pre-treatment hip BMD>-2.5, previous non-spine fractures
- Consider assessment for vertebral fracture before stopping (x-ray or DXA lateral spine scan)
- What about those who had clear treatment indication?
What Should Clinicians Do?

- Consider stopping after 3 yr. (zolendronic acid) or 5 yr. (alendronate) in older women
  - Applies to other bisphosphonates? Men?
  - Continue in high risk up to 10 yr.? Longer?
- No evidence on optimal duration to withhold therapy
- Short-term monitoring (BMD or markers) after discontinuation of ALN does not predict fracture
  - Hip bone loss >3% after 2-3 yr may be helpful
- Re-assess fracture risk 3-5 years after stopping? Incorporate FRAX calculation?

2014 Summary: Who Should Be Treated and When to Stop?

- Suggested treatment thresholds:
  - Existing hip or vertebral fracture? Yes!
  - T-score < -2.5? Yes!
  - “Low bone mass” + FRAX score that exceeds absolute threshold? Probably not
- Drug holiday after 3-5 years of bisphosphonate? Consider
  - No hip/vertebral fracture; no fracture on therapy
  - BMD T-score > -2.5 before stopping
  - Re-evaluate after 3-5 years off therapy

Question: Choice of Drugs

Bea Brittle is a 67 year old woman with a hip BMD with a t score of -2.8. She has severe GI side effects with weekly bisphosphonates. She is otherwise healthy, but had a DVT at the age of 33 when she was on birth control pills. What would you choose as the next step?

1. Start ibandonate monthly
2. Start yearly intravenous zolendronate
3. Start raloxifene 60 mg per day
4. Start daily subcutaneous PTH
5. Start intranasal calcitonin

Raloxifene

- Selective Estrogen Receptor Modulators
- Ideally maximize bone and cardiovascular protective effects of estrogen, while minimizing negative effects (endometrial and breast cancers)
Raloxifene

- Raloxifene reduces vertebral fractures, but has not been shown to reduce the risk of hip fracture
- Increased risk of thromboembolic events
- Effect similar to tamoxifen in preventing breast cancer
- No effect on vaginal bleeding/endometrial cancer

Calcitonin

- FDA approved for women who are at least 5 years postmenopausal
- Intranasal spray
- Increased BMD 10-15% in two years
- Fracture data limited and inconclusive
- Analgesic effect
- Oral calcitonin in studies
  - Possible increased cancer risk

Parathyroid Hormone

- Pulsatile vs constant effect
  - Anabolic vs anti-resorptive
- PTH 1-34 and PTH 1-84
- Reduces vertebral fractures by 65% and nonvertebral fractures by 53% after 18 months
- FDA approved for postmenopausal women at high risk for fracture
- Safety and efficacy has been shown for 2 years
  - Most BMD gains occur in first few months
- Daily subcutaneous injection

PTH vs Bisphosphonates

- They have not been compared head to head in a trial that evaluated fracture outcomes
- PTH increased BMD more than alendronate
- PTH is much more expensive
- Long term safety of PTH?
**PTH: Adverse Effects**

- Hypercalcemia and hypercalcuria
- Concern for osteosarcoma
  - Higher doses for longer duration increased risk in rats
  - Case reports of co-existing osteosarcoma in patients with primary hyperparathyroidism
  - Only one reported case in post-menopausal woman on PTH
- FDA currently recommends limiting PTH therapy to two years
  - Post-marketing surveillance is ongoing

**Combination Treatment**

- PTH plus bisphosphonates
  - No additional benefit
  - Bisphosphonate may impair PTH stimulation of new bone formation
- PTH plus SERMs
  - Does not suppress BMD response to PTH
  - No evidence that adding SERM is beneficial
- PTH plus hormone therapy
  - Small studies show an increase in BMD with combined therapy
- PTH plus denosumab
  - Increased BMD more than either agent alone and more than reported with other approved therapies

**After PTH...**

- PTH is recommended to be used for two years
- Some BMD decline after discontinuing PTH
- Some anti-resorptive therapy should be added after PTH discontinuation
  - Bisphosphonate
  - Raloxifene is an alternative

**PTH: Summary**

- Big impact on BMD
- Reduces spine and non-spine fractures compared with placebo
  - Hip fracture?
- Long term safety issues
- Daily injection of an expensive drug
- Consider use in severe osteoporosis when other agents have failed
Denosumab: FREEDOM Trial

- Human monoclonal antibody against RANKL
  - RANKL is a cytokine essential to osteoclast function
  - Inhibits osteoclast mediated bone resorption
- 7,868 women with osteoporosis received denosumab 60 mg or placebo subcutaneously every 6 months for 36 months
- Endpoints: new vertebral fractures at 6 months and time to first hip and non-vertebral fractures
  » Cummings SR et al., NEJM 2009: 361: 756-65

Denosumab: FREEDOM Trial

- Reduced risk of vertebral fractures
  - 2.3% in denosumab group vs 7.2% in placebo group
  - (Risk ratio: 0.32: 95% C.I. 0.26 to 0.41)
- Reduced risk of hip fracture
  - 0.7% in denosumab group vs 1.2% in placebo group
  - (Hazard ratio 0.60: 95% C.I. 0.37, 0.97)
- Reduced risk of nonvertebral fracture
  - 6.5% vs 8.0% in placebo group
  - (Hazard ratio 0.80: CI 0.67 to 0.95)
- Increased risk of cellulitis in denosumab group
  - No significant differences in overall infection or cancer

On the Horizon

- Sclerostin is an osteocyte-derived inhibitor of osteoblast activity
- Individuals with hereditary deficiency of sclerostin have high bone mass and resistance to fractures
- Monoclonal antibody romosozumab binds to sclerostin and increases bone formation
- In Phase 2 trial of 419 postmenopausal women, romosozumab increased BMD at multiple sites more than placebo, alendronate or PTH
  - No fracture outcomes yet
  - Stay tuned

McClung, NEJM 2014

Denosumab

- FDA approved for the following groups
  - High risk for fracture including androgen deprivation therapy for prostate cancer and aromatase inhibitor therapy for breast cancer
  - Treatment for osteoporosis in postmenopausal women at high risk for fracture
There is currently no compelling reason for her to switch from a bisphosphonate to any other osteoporosis therapy.

Summary: Osteoporosis Prevention

- Avoid or quit smoking and avoid excess alcohol use
- Regular weight bearing and muscle strengthening exercise
- Calcium and vitamin D
- Fall prevention

Summary

- Measure bone mineral density in women aged 65 and older
- Consider risk factors in measuring BMD in younger postmenopausal women
- WHO FRAX tool is useful for absolute risk assessment especially in women with low bone mass
- BMD monitoring frequency should be based on initial BMD and impact on management

Choice of Pharmacologic Therapies

- The bisphosphonates have been studied most extensively and should remain first line agents
  - Consider stopping after 5 years in “low risk” patients
  - Guidelines about when or whether to stop bisphosphonates remain in evolution
- Raloxifene, calcitonin and PTH should remain second line agents
  - Raloxifene can reduce breast cancer risk
Choice of Pharmacologic Therapies

- Calcitonin may be an option for women who decline or cannot tolerate other options or who desire analgesic effect
- PTH may be an option for women who have failed other treatments
  - Treatment for 2 years should be followed by an antiresorptive therapy
- Denosumab FDA approved for women with breast cancer on AIs and for postmenopausal women with osteoporosis

Questions?