A Case of Osteoporosis…
- 57 year old Caucasian woman with breast cancer s/p left lumpectomy & chemotherapy at 35; then right breast cancer s/p mastectomy and chemotherapy at 40.
- Early menopause started at 40 years of age.
- Normal DEXA at age 45, then diagnosed with osteoporosis by heel scan at age 50 years.
- DEXA May 2012
  - Osteopenia T-score -1.6 to 2.0
- FRAX Score June 2012
  - 1.0% @ hip, 7.6% total

Impact of Fractures
- Fractures caused by osteoporosis affect 1 in 2 women and 1 in 5 men over 50 years of age
- Results in permanent disability in over 30% of those with fracture
- After hip fracture, nearly 20% will die within 1 year
  - Prevalence of death is twice as high in men
- Over 50% of survivors will not return to independent living

Screening

Outlines for Osteoporosis
- Epidemiology
- Guidelines for Screening
- Screening Tools and Pitfalls
- Treatment Options
- Vitamin Supplements & Other Prevention

Figure 1. Epidemiology of osteoporotic fractures in men and women.

Poole, K. E S et al. BMJ 2006;333:1251-1256
Guidelines for Screening for Osteoporosis in Women

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen all women &gt; 65 years regardless of risk</td>
<td>Screen all women at 65 years</td>
<td>Screen all women &gt; 65 years</td>
</tr>
<tr>
<td>Screen all men &gt; 70 years regardless of risk</td>
<td>Screen women at 50 years of age if ↑ risk</td>
<td>Screen women at 60 years if ↑ risk</td>
</tr>
<tr>
<td>Screen postmenopausal women &amp; men 50-69 years with significant risk factors</td>
<td>Screen postmenopausal women age with medical causes of bone loss</td>
<td>Insufficient evidence to support screening younger women</td>
</tr>
</tbody>
</table>

Risk Factors that Prompt Screening

- Personal history of fracture as an adult
- History of fragility fracture in a first-degree relative
- Use of oral corticosteroid therapy for more than 3-6 months
- Estrogen deficiency at an early age
  - (<45 yrs, e.g. Early menopause)

Conditions that Reduce Bone Mineral Density and Prompt Screening

- Cushing disease
- Malabsorption
  - Gastric bypass surgery
  - IBD
  - Pernicious anemia
  - Celiac disease
- Hyperparathyroidism
- Hyperthyroidism
- Vitamin D Deficiency
- Chronic renal disease
  - Impaired Vit D metabolism
- Chronic liver disease
  - Impaired protein synthesis
- COPD or asthma
- Rheumatoid arthritis
- Immobility
- Other Risk Factors To Prompt Screening

- Alcohol in amounts >2 drinks per day
- Current smoking
- Increased fall risk
  - Impaired vision
  - Use of sedatives/hypnotics
  - Frailty
  - History of falls
  - Dementia
- Low body weight (<about 127 lbs = BMI < < 19)
- Low physical activity
- Low calcium intake (lifelong)

Medications that Reduce Bone Mineral Density

- Oral glucocorticoid therapy
  - 3-6 months use
- Aromatase inhibitors
  - Anastrozole (Arimidex), Letrozole (Femara), Exemestane (Aromasin)
- Androgen deprivation therapy
- Anti-convulsants
  - Phenytoin, phenobarbitol
- Heparin
- Cytotoxic agents
- MYTH: Depoprovera

Are we following the guidelines?

Study: 615 women who were screened with DXA between 2007 and 2009

Question 1: Should these women have been screened?
  - 41% did not meet criteria for screening

Question 2: Of those who met criteria for treatment, were they treated?
  - With an indication, 35% were treated
  - With no indication, 18% were treated

Summary: Who To Screen
- All Women >65 years, Men >70 years
- Postmenopausal Women and Men 50-69 years with a risk factor
- Diagnostic DEXA
  - Those with a hip or vertebral fracture to characterize disease severity

Screening Tests

Alternatives to DEXA Scan
- Ultrasound of forearms, heels, & fingers
  - Predictive of vertebral and global fracture risk
  - Less predictive of hip fracture
  - Not validated in men
- Quantitative CT
  - Some limitations in cross site applications
  - Not validated in men
- Quantitative US
  - Predicts hip, vertebral and global risk in postmenopausal women
  - Predicts hip, non-vertebral risk in men >65 years

82% of fractures are not in women with osteoporosis on DEXA

Diagnosis

WHO Risk Model: FRAX®

Diagnostic Criteria by WHO

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>BMD Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>BMD w/ 1 SD of the T-score</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>BMD b/t -1 &amp; -2.5 SD below the T-score</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>BMD at least -2.5 below the T-score</td>
</tr>
<tr>
<td>Severe Osteoporosis</td>
<td>Fracture &amp; BMD &lt;-2.5</td>
</tr>
</tbody>
</table>

- Z-score=age matched adult mean BMD
- T-score=young adults ages 25 to 45 year olds mean BMD

WHO Risk Model: FRAX®

No validation in men

![WHO Risk Model: FRAX®](https://www.shef.ac.uk/FRAX)

Only valid for people who are untreated, only >50 years, and post menopausal
When to Re-Screen for Osteoporosis

<table>
<thead>
<tr>
<th>DEXA Result</th>
<th>T-Score</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Osteopenia</td>
<td>-1.0 or higher</td>
<td>15 years</td>
</tr>
<tr>
<td>Mild Osteopenia</td>
<td>-1.5 to -1.0</td>
<td>15 years</td>
</tr>
<tr>
<td>Moderate Osteopenia</td>
<td>-1.5 to -1.99</td>
<td>5 years</td>
</tr>
<tr>
<td>Severe Osteopenia</td>
<td>-2.0 to -2.49</td>
<td>1 year</td>
</tr>
</tbody>
</table>


When to Treat Osteoporosis

- **Osteoporosis by BMD**: > -2.5 SD away from T-score mean
- **Osteopenia +FRAX® Model Output**
  - women and men >50 years of age with 10-year risk of hip fracture >3% or any fracture >20%
- **Fracture of the hip or vertebra**
- **History of low-impact fracture**
- **Loss of height > 1.5 inches regardless of BMD**

Osteoporosis Prevention & Treatment with Bisphosphonates

<table>
<thead>
<tr>
<th>Medication</th>
<th>Regimen</th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>35 mg/week</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>(Fosamax)</td>
<td>70 mg/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risedronate</td>
<td>150 mg/month</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>(Actonel)</td>
<td>35 mg/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibandronate</td>
<td>150 mg/month</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>(Boniva)</td>
<td>2.5 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 mg IV/q3 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoledronic Acid*</td>
<td>5 mg IV/q12 mo</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>(Reclast)</td>
<td>5 mg IV/q24 mo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 3 years MAX

Bisphosphonate Dosing Factoids

- All have equivalent efficacy for reducing vertebral and non-vertebral fractures
- Take on empty stomach with 8 oz water, then sit upright for 30 minutes
  - Risk for erosive esophagitis
- WEEKLY dosing has BEST adherence
- Ideal duration UNCLEAR: 5 -10 years?
- Renal dosing required if CLcr <30 mL/min

Osteoporosis Prevention & Treatment with Other Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Regimen</th>
<th>Prevent’n</th>
<th>Treat’n</th>
<th>Frx ↓</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raloxifene*</td>
<td>60 mg/day</td>
<td>√</td>
<td>√</td>
<td>Vertebral</td>
</tr>
<tr>
<td>(Evista)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denosumab (Prolia)</td>
<td>60 mg SC q6 mo</td>
<td></td>
<td>√</td>
<td>Vertebral</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>200 IU SC/day</td>
<td></td>
<td>√</td>
<td>Vertebral</td>
</tr>
<tr>
<td></td>
<td>100 IU SC/qod</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTH (Forteo)</td>
<td>20 mcg SC/day</td>
<td></td>
<td>√</td>
<td>Vertebral</td>
</tr>
</tbody>
</table>

*anti-estrogen effects on uterus and breast, † VTE, CVA

Renalized
Osteoporosis Prevention with Estrogen Preparations

- Oral Estrogens
  - Estradiol, Estrogen, Estropipate, CEE
- Oral Estrogen-Progestin Combinations
  - Estradiol + estriol or norgestrel
  - CEE+medroxyprogesterone
- Transdermal Estrogens
  - Estradiol
- Transdermal Estrogen-Progestin Combinations
  - Estradiol + levonorgestrel

Institute of Medicine
Vitamin D and Calcium

Calcium
- Adults 19-50 years 1000 mg/day
- Men >50 years of age 1000 mg/day
- Women >50 years of age 1200 mg/day
Vitamin D
- Adults up to age 70 years 600 IU/day
- Adults above age 70 years 800 IU/day

NOTE:
- Consider calcium citrate because less dependent on stomach acid for absorption (NOF, 2008)
- Adherence of about 80% shows best BMD (WHI)

Vitamin D and Calcium: Low Doses

- WHI-Vitamin 36,000 women 59 to 70 years
  - 7 year follow-up
  - Vitamin D 200IU + Calcium 500mg
  - No difference in hip, total fracture rate or BMD
  - Sub-group analysis on women with > 80% adherence showed PROTECTION
- WHI-RCT 36,000 women 59 to 70 years
  - 7 year follow-up
  - Vitamin D 400IU + Calcium 1000mg
  - No difference in fracture rate, Increased BMD
  - Low dose of Vitamin D

Vitamin D and Calcium: High Doses as Monotherapy

- RCT-1460 women >70 years old for 5 years
  - 1200 mg calcium only
  - Sub-group analysis on women with > 80% adherence showed PROTECTION
- Meta-analysis 700-800 IU vitamin D only
  - Hip fracture reduction by 26% RR=0.74 (95% CI, 0.61–0.88)
  - Non-vertebral fracture reduction by 23% RR=0.77 (95% CI, 0.68–0.87)
    - Bischoff-Ferrari, 2005

Meta-Analysis: Hip Fracture Rates

Evidence for Calcium
Doses 1000mg or more

Boonen, J Internal Med, 2008
Meta-Analysis: Hip Fracture Rates

Evidence for Vitamin D does 700-800IU

Boonen, J Internal Med, 2006

Calcium and Vitamin D Associated with Risk for CHD

- WHI: Calcium and Vitamin D Supplementation Study
- Followed 32,282 women for 7 years
- RCT: Calcium 1000mg and Vitamin D 400 IU versus personal supplementation
  - Risk of MI
    HR 1.14 (p=0.05)
  - Risk of CVA plus MI
    HR 1.22 (p=0.04)

Reducing Falls Reduces Fracture Risk...

- 90% of fractures associated with a fall event
  - Alcohol intake reduction
  - Poor vision
  - Physical therapy
  - Weight-baring exercise
  - Impaired transferring
  - Home safety evaluation
  - Treat pain, go easy on the sedatives

A Clinical Case…Part 1

- 57 year old Caucasian woman with the following
  - Diagnosed with DCIS 1991 (age 35)
    s/p Left lumpectomy, chemotherapy & radiation
  - Diagnosed with second primary 1995 (age 40)
    s/p right mastectomy with chemotherapy
  - Early menopause since age 40 years

When should this woman be screened for osteoporosis? And why?

A clinical case…Part 2

- 57 year old Caucasian woman with breast cancer & chemotherapy twice with early menopause from age 40 years.
- She reports a loss of height ≥ 1.5 inches

Does this change your management?

Would isolated height loss without the other risks make you screen her?

A clinical case…Part 3

- 57 year old Caucasian woman with breast cancer & chemotherapy twice with early menopause from age 40 years.
- Diagnosed with osteoporosis by heel scan in 2005 at age 50 years.

Would you treat her based on this information?

If yes, then for how long?
A clinical case... Part 4

- 57 year old Caucasian woman with breast cancer & chemotherapy twice with early menopause from age 40 years.
- DEXA May 2012
  - Osteopenia T-score -1.6 to 2.0)
- FRAX Score June 2012
  - 1.0% @ hip, 7.6% total

Should she be treated now?
When should she be re-screened?

Summary

- Screen women > 65 years, Men > 70 years
- Risk stratify younger women
- Treat women with bisphosphonates when indicated
- Give ENOUGH vitamin supplementation
- REDUCE fall risk

Fracture Calculators

- FRAX from the UN
  - www.shef.ac.uk/FRAX/tool.jsp
- Hip Calculator
  - http://hipcalculator.fhcrc.org
- UK population based
  - http://www.qfracture.org

References

2. North American Menopause Society
3. US Preventive Health Services Task Force