Bone Health in the Primary Care Setting

Miami, FL

October 14, 2009
2:00 PM to 3:30 PM

Content Collaborator: National Osteoporosis Foundation
Session 5: Bone Health in the Primary Care Setting Session

Learning Objectives
1. Discuss the current clinical guidelines and strategies to effectively prevent and diagnose osteoporosis, and the impact a primary care clinician can have on the improvement of bone health.
2. Describe a patient specific treatment plan to both prevent and treat osteoporosis through the combined use of proper diet, exercise, monitoring and pharmacologic and non-pharmacologic therapeutic interventions.

Faculty

E. Michael Lewiecki, MD, FACP, FACE
Clinical Assistant Professor of Medicine, University of New Mexico School of Medicine
Director, New Mexico Clinical Research and Osteoporosis Center
Albuquerque, New Mexico

E. Michael Lewiecki, MD, FACP, FACE, is clinical assistant professor of medicine at University of New Mexico School of Medicine and director of New Mexico Clinical Research & Osteoporosis Center. He is a consultant in osteoporosis and metabolic bone disease, supervisor and interpreter of bone density studies at his center, and an educator with a special interest in osteoporosis and bone densitometry. He is principal investigator for the center’s osteoporosis clinical trials and author of many peer-reviewed scientific publications on osteoporosis and bone densitometry. Dr Lewiecki is past-president of the International Society for Clinical Densitometry (ISCD). He is a faculty member for the ISCD educational programs in bone densitometry and vertebral fracture assessment, and is on the Editorial Board of the Journal of Clinical Densitometry.

Faculty Financial Disclosure Statement
The presenting faculty reported the following:

Dr Lewiecki receives research and grant support from Amgen, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, Procter & Gamble, Roche, sanofi-aventis, and Wyeth. He serves on the Scientific Advisory Boards of Amgen, Eli Lilly, Novartis, Roche/GlaxoSmithKline, Upsher-Smith, and Wyeth. He is on the speakers bureaus of Eli Lilly, Novartis, and Roche/GlaxoSmithKline. Dr Lewiecki is a direct stockholder with General Electric, Procter & Gamble, and Teva.

Education Partner Financial Disclosure Statement
The content collaborators at the National Osteoporosis Foundation have reported the following: Audrey Shively and Susan Randall have no relationships to disclose.

Drug List

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
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<tbody>
<tr>
<td>estrogen</td>
<td>various</td>
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<tr>
<td>alendronate PO</td>
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<td>ibandronate IV</td>
<td>Boniva</td>
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<tr>
<td>risedronate PO</td>
<td>Actonel</td>
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<td>zoledronic acid IV</td>
<td>Reclast</td>
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<tr>
<td>calcitonin IN</td>
<td>Fortical, Miacalcin</td>
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<tr>
<td>raloxifene PO</td>
<td>Evista</td>
</tr>
<tr>
<td>teriparatide SC</td>
<td>Forteo</td>
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Investigational

denosumab
lasofoxifene
arzoxifene
basedoxifene
CE/basedoxifene
odanacatib
### Acronym List

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>BMD</td>
<td>bone mineral density</td>
</tr>
<tr>
<td>CRFs</td>
<td>clinical risk factors</td>
</tr>
<tr>
<td>DXA</td>
<td>dual–energy x-ray absorptiometry</td>
</tr>
<tr>
<td>FRAX®</td>
<td>WHO Fracture Risk Assessment Tool</td>
</tr>
<tr>
<td>GIO</td>
<td>glucocorticoid-induced osteoporosis</td>
</tr>
<tr>
<td>ISCD</td>
<td>International Society for Clinical Densitometry</td>
</tr>
<tr>
<td>NOF</td>
<td>National Osteoporosis Foundation</td>
</tr>
<tr>
<td>ONJ</td>
<td>osteonecrosis of the jaw</td>
</tr>
<tr>
<td>PMO</td>
<td>postmenopausal osteoporosis</td>
</tr>
<tr>
<td>VFA</td>
<td>vertebral fracture assessment</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>

### Suggested Reading List


Bone Health in the Primary Care Setting

Osteoporosis
A skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture

Scope of the Problem
In the United States:
- A major health threat for 44 million, or 55% of people 50 years and older
- 10 million with osteoporosis and 34 million with low bone mass (osteopenia)
- 50% lifetime risk of fracture for women; 20% lifetime risk of fracture for men
- Increased risk of death and disability with fractures of hip and spine
- High healthcare expenses

Fracture Incidence
- In the US, 8 million women and 2 million men have established osteoporosis1

The Good News
- Excellent diagnostic tools
- Fracture risk assessment validated
- Effective and safe treatments
- Inexpensive generic drugs
- Better understanding of pathogenesis
- Emerging therapies

The Bad News
- Underdiagnosis: <30% older women screened for osteoporosis1 vs. 70% screened for breast cancer2
- Undertreatment: Only 22% of fracture patients treated compared to 94% of post-MI patients2
- Poor adherence to therapy: About 50% of patients started on therapy are no longer taking it at end of 1 year

2HEDIS measure for 2007.
Indications for BMD Testing

- Women 65 and older and men 70 and older
- Younger postmenopausal women and men 50-69 years old with risk factors
- Women in menopausal transition with risk factors
- Adults who have had a fracture after age 50

Risk Assessment

- Low calcium intake
- Low vitamin D intake
- Alcohol (3 or more drinks /day)
- Inadequate physical activity
- Smoking
- Falling
- Small frame
- Family history of osteoporosis or fracture

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Conditions</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypogonadism</td>
<td>Anorexia</td>
<td>Glucocorticoids</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Alcoholism</td>
<td>Excess thyroxine</td>
</tr>
<tr>
<td>Depression</td>
<td>Hypercalciuria</td>
<td>Antiepileptics</td>
</tr>
<tr>
<td>COPD</td>
<td>Vitamin D deficiency</td>
<td>Depo-Provera</td>
</tr>
<tr>
<td>GI diseases (malabsorption)</td>
<td></td>
<td>GnRH agonists</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td></td>
<td>Aromatase inhibitors</td>
</tr>
<tr>
<td>Cholestatic liver disease</td>
<td></td>
<td>SSRIs</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td></td>
<td>Proton pump inhibitors</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td></td>
<td>TZDs</td>
</tr>
</tbody>
</table>

WHO Diagnostic Criteria

- Normal Bone Density: No pharmacologic treatment
- Low Bone Mass (Osteopenia): Variable
- Osteoporosis: Treat
Treatment Decisions

Osteopenia Challenge
Which one of these women is at higher risk for fracture?
53-year-old smoker with a T-score of -2.0
81-year-old with no prior fracture with a T-score of -1.6

Your answer?
1. 53 year old
2. 81 year old

FRAX® Clinical Risk Factors
Selection Criteria:
- Independent contributor to fracture risk
- Validated in multiple populations
- Readily assessable by primary care practitioners throughout the world
- Contribute to a risk that is amenable to the therapeutic manipulation intended

FRAX®: WHO Fracture Risk Assessment Tool
- Objective: To assess fracture risk in untreated patients
- Input: BMD + clinical risk factors (CRFs)
- Rationale: BMD + CRFs predict fracture risk better than either alone
- Output: 10-year probability of major osteoporotic fracture (hip, spine, wrist, humerus)

Most Women With Fractures Do Not Have T-scores In The Osteoporosis Range
243 women with hip fractures in study of osteoporotic fractures

FRAX®: WHO Fracture Risk Assessment Tool
Age and BMD Are Major Independent Contributors to Fracture Risk


FRAX® Risk Factors

Independent contribution after age and T-score

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior fracture</td>
<td>1.62 (1.30-2.01)</td>
</tr>
<tr>
<td>Parental history of hip fracture</td>
<td>2.28 (1.48-3.51)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.60 (1.27-2.02)</td>
</tr>
<tr>
<td>Systemic corticosteroids</td>
<td>2.25 (1.60-3.15)</td>
</tr>
<tr>
<td>Alcohol intake &gt; 2 units daily</td>
<td>1.70 (1.20-2.42)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1.74 (0.94-3.20)</td>
</tr>
</tbody>
</table>


Quantifying Fracture Risk

- **Prior fracture**: Denotes previous adult fracture occurring with little or no trauma—fractures of face, fingers, toes excluded.
- **Parental history of hip fracture**: Parents only—impact of hip fractures in other family members not known.
- **Current smoking**: Assumes “average use”, but amount not specified. Higher intake associated with higher fracture risk.
- **Systemic corticosteroids**: Ever use of oral steroids—best applies to current or long-term past use (≥ 5mg/day prednisone equiv.)
- **Alcohol intake > 2 units daily**: 1.5 oz liquor; 10 oz beer; 3-4 oz wine.
- **Rheumatoid arthritis**: Reliance on patient report problematic unless there is evidence to support diagnosis.

Answering Risk Factor Questions in FRAX®

- **Prior fracture**: Denotes previous adult fracture occurring with little or no trauma—fractures of face, fingers, toes excluded.
- **Parental history of hip fracture**: Parents only—impact of hip fractures in other family members not known.

FRAX® Caveat

Entering Bone Density Data

- Use femoral neck BMD only.
Bone Density Data for FRAX®

Enter DXA manufacturer and BMD (g/cm²)

Fracture Risk Assessment in Clinical Practice

Quantifying Fracture Risk

NOF Guide: What's New?

NOF Treatment Guidelines

Postmenopausal Women and Men ≥ 50

Initiation of pharmacological therapy recommended in presence of any one of:

- Osteoporosis (Fracture)
  A vertebral or hip fracture

- Osteoporosis (T-score)
  T-score ≤ –2.5 at femoral neck or spine

- Osteopenia + FRAX®
  10-year probability of major osteoporotic fracture ≥ 20%
  10-year probability of a hip fracture ≥ 3%

NOF Treatment Guidelines
Shift Treatment Away From Younger Women

2008 Guidelines
Ten-year probability of a major osteoporotic fracture in average white women without prior fracture or other risk factors

<table>
<thead>
<tr>
<th>AGE</th>
<th>50</th>
<th>55</th>
<th>60</th>
<th>70</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-score</td>
<td>2.0</td>
<td>4.9</td>
<td>6.5</td>
<td>8.9</td>
<td>12</td>
</tr>
<tr>
<td>2.5</td>
<td>5.7</td>
<td>7.6</td>
<td>10</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>3.0</td>
<td>6.9</td>
<td>9.1</td>
<td>12</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td>3.5</td>
<td>7.1</td>
<td>11</td>
<td>15</td>
<td>20</td>
<td>27</td>
</tr>
</tbody>
</table>

Estimating Fracture Risk
Which woman is at high risk and meets NOF criteria for pharmacotherapy?
53 year old smoker with a T-score of -2.0
10 year risk of hip fracture = 2.4%
major osteoporotic fracture = 9%

81 year old with no prior fracture with a T-score of -1.6
10 year risk of hip fracture = 3.5%
major osteoporotic fracture = 20%

Your answer?
1. 53 year old
2. 81 year old

NOF Clinician’s Guide
• Recommendations are not intended as rigid standards of practice
• Specific treatment decisions must be individualized
• An estimate of the patient’s 10-year fracture risk should facilitate shared decision-making

Making Treatment Decisions
Case Study: 53 year old woman
Mild vasomotor symptoms since menopause 5 years ago; weighs 140 pounds; no fractures; concerned about osteoporosis, but also worried about taking medication

<table>
<thead>
<tr>
<th>Age</th>
<th>53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Neck T-score</td>
<td>-2.0</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>smoking</td>
</tr>
<tr>
<td>10 yr Major Fracture Risk</td>
<td>9%</td>
</tr>
</tbody>
</table>

Would you recommend pharmacologic therapy to this patient?
1. Yes
2. No

Benefits of FRAX®
• Avoid giving medication to those with little to gain
  ▪ Expense
  ▪ Potential side-effects
  ▪ Poorer compliance with multiple medications
• Reassurance for clinician and patient to use nonpharmacologic therapy first
  ▪ Monitor to determine if bone loss is being prevented

Nonpharmacological Approach for Everyone
• Calcium (1200 mg/day)
• Vitamin D (800-1000 IU/day)
• Exercise
• Lifestyle (smoking cessation, limit alcohol)
• Fall Prevention
Calcium & Vitamin D

- Calcium and vitamin D slow or prevent bone loss
- Vitamin D
  - 26% reduction in hip and nonvertebral fractures with dose of 700-800 IU/d (meta-analysis)
  - Improves balance, muscle strength; reduces falls
- Higher vitamin D levels associated with:
  - Lower risk of prostate, breast, colon cancer
  - Lower risk of some autoimmune diseases
  - Improved immune function

Vitamin D Recommendations

- Recommended intake for postmenopausal women and men ≥ 50 = 800-1000 IU daily
- Higher doses often needed (dark skin; obesity; gastric surgery; GI disease; elderly)
- Current consensus for minimum desirable 25-OH-D is 30 ng/ml (75 nmol/l)
- Rules of thumb:
  - Up to 2000 IU safe
  - 1000 IU needed to raise 25-OH-D by ~10 ng/ml

FRAX® Caveat

FRAX® is intended only for untreated patients
- Fracture risk decreases after initiation of therapy before significant change in BMD
- Fractures reduced even if bone density does not change with therapy
- FRAX® will overestimate fracture risk in patients on pharmacotherapy
- FRAX® cannot be used to monitor therapy

FRAX® can underestimate fracture risk in some patients
- Failure to enter all risk factors into FRAX®
- The impact of some risk factors (steroids; spine fractures) is underestimated
- Some risk factors not included in FRAX®: anticonvulsants, diabetes, COPD, SSRIs, immobilization, falls

FRAX® Caveat

FRAX® and NOF guidelines should not be used for premenopausal women or men under age 50
- Little known about the relationship between BMD and fracture risk: not the same in the young
- Fracture risk will be overestimated

FRAX® Caveat

60 yo postmenopausal woman with history of hyperlipidemia and past smoking; feels she is shorter now than in the past, but has no back pain; takes calcium supplement and 1000 IU vitamin D daily

<table>
<thead>
<tr>
<th>Age</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-score</td>
<td>-1.8</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>None</td>
</tr>
<tr>
<td>10 Year Risk</td>
<td>None</td>
</tr>
<tr>
<td>Major fracture</td>
<td>13%</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>1%</td>
</tr>
</tbody>
</table>

Should pharmacologic therapy be prescribed?
1. Yes
2. No
3. Don't know: need more information
60-Year-Old Postmenopausal Woman
2” loss from young adult height

Vertebral Fracture Assessment (VFA)

Effect of Prevalent Fracture on FRAX® Calculations

<table>
<thead>
<tr>
<th>Age</th>
<th>65</th>
<th>65</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-score</td>
<td>-1.8</td>
<td>-1.8</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>None</td>
<td>2 vertebral compression fractures</td>
</tr>
<tr>
<td>10 Year Risk Major fracture</td>
<td>13%</td>
<td>&gt;22%</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>1.3%</td>
<td>&gt;2.1%</td>
</tr>
</tbody>
</table>

NOF recommends treatment for all postmenopausal women and men ≥ 50 years old with spine or hip fractures

Be On The Lookout For Vertebral Fractures

- Most common fracture type
- Most are unrecognized by patients and clinicians
- Indicate high risk for future spine and hip fractures

Measure height yearly in women and men >50 yo
Order spine imaging if:
- Height loss from peak (>1.6” in women; >2.4” in men)
- Prospective height loss (>0.8” in women; >1.2” in men)

Fracture Risk Assessment and Treatment Guidelines Summary

- FRAX® is a statistically robust fracture risk prediction tool for clinical practice
- Use of FRAX® and the NOF guidelines can improve clinical decision making in patients with low bone mass
- Knowledge of fracture risk can facilitate discussions with patients to encourage treatment in high risk patients and reassure the “worried well”

Choosing Pharmacologic Therapy In Clinical Practice

- Efficacy and safety
  - Nonskeletal risks/benefits
- Patient factors
  - Comorbidities
  - Expected compliance with therapy
  - Patient beliefs and preferences
  - Insurance coverage / affordability

Bone Remodeling

FDA Indications for Osteoporosis

<table>
<thead>
<tr>
<th>Drug</th>
<th>PMO Prevention</th>
<th>PMO Treatment</th>
<th>GIO (Women, Men) Prevention</th>
<th>GIO (Women, Men) Treatment</th>
<th>Men Prevention</th>
<th>Men Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate PO</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risedronate PO</td>
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<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibandronate PO</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibandronate IV</td>
<td>✓</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Zoledronic Acid IV</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>Calcitonin IN</td>
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<td></td>
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<td></td>
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<tr>
<td>Raloxifene PO</td>
<td>✓</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teriparatide SC</td>
<td>✓</td>
<td></td>
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</tbody>
</table>

PMO = Postmenopausal Osteoporosis; GIO = Glucocorticoid Induced Osteoporosis

Fracture Risk Reduction in RCTs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Spine</th>
<th>Nonvertebral</th>
<th>Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risedronate daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibandronate daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoledronic Acid yearly</td>
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<td></td>
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</tr>
<tr>
<td>Calcitonin</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Raloxifene daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teriparatide</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Bisphosphonates

Oral
- Alendronate 5 or 10 mg daily, 35 or 70 mg weekly
- Risedronate 5 mg daily, 35 mg weekly, 75 mg x 2 days monthly or 150 mg monthly
- Ibandronate 150 mg monthly

Injectable
- Ibandronate 3 mg IV quarterly
- Zoledronic acid 5 mg IV annually
- Zoledronic acid IV every two years for prevention

Absorption and Tolerability of Oral Bisphosphonates
- Only ~1% of oral dose is absorbed
  - Coffee or juice reduce absorption by as much as 60%\(^1\)
  - Calcium supplements can completely block absorption\(^2,3\)
  - GI side effects more likely if dosing not followed\(^1,3\)
  - Even when instructions are given, 25% - 50% of patients disregard at least one requirement\(^4\)

Compliance and Persistence with Chronic Therapy
- Up to 1 in 5 patients never redeem prescriptions\(^3\)
- Only half of patients persist with long-term therapy\(^1,2\)
- Most stop within first 3-4 months
- Patients with asymptomatic chronic diseases have little motivation to comply with therapy\(^4\)

When to Consider an Injectable Bisphosphonate
- Intolerance to oral bisphosphonate
- Contraindication to oral bisphosphonate
- Malabsorption of oral bisphosphonate
- Poor response to oral bisphosphonate
- Poor compliance to oral bisphosphonate

Compliance and Persistence with Chronic Therapy
- Up to 1 in 5 patients never redeem prescriptions\(^3\)
- Only half of patients persist with long-term therapy\(^1,2\)
- Most stop within first 3-4 months
- Patients with asymptomatic chronic diseases have little motivation to comply with therapy\(^4\)


**Refill Compliance and Fracture Protection**

![Graph showing compliance over 2 years and fracture protection](image)

*Over 24 months for bisphosphonate-treated patients

### Bisphosphonate Selection Issues

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pro</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>Weekly dosing, generic</td>
<td>Complex administration and GI effects with oral dosing;</td>
</tr>
<tr>
<td>Risedronate</td>
<td>Weekly/monthly dosing Monthly oral</td>
<td></td>
</tr>
<tr>
<td>Ibandronate</td>
<td>Q3M IV dosing</td>
<td>Logistics of IV dosing and acute phase reaction with IV;</td>
</tr>
<tr>
<td>Zoledronic Acid</td>
<td>Annual IV dosing</td>
<td>Not to be used if CrCl&lt; 30 or 35ml/min</td>
</tr>
</tbody>
</table>

Rare high profile side effects: chronic muscle and bone pain, ONJ, uveitis/scleritis/iritis, hypocalcemia, subtrochanteric fractures, esophageal cancer, atrial fibrillation

### Nonbisphosphonate Selection Issues

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pro</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen</td>
<td>Relieves menopausal symptoms, cholesterol, LDL, HDL</td>
<td>Uterine bleeding, DVT, breast cancer, stroke, coronary disease, estrogen sensitive tumors, triglyceride, breast tenderness, fluid retention</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>Reduction in risk of invasive breast cancer</td>
<td>Hot flashes, DVT, leg cramps, fatal stroke</td>
</tr>
<tr>
<td>Salmon Calcitonin</td>
<td>Ease of administration, Analgesic effect (?)</td>
<td>Nasal irritation, epistaxis</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>↓ Back pain</td>
<td>Daily injection, refrigeration, expense , 24 month limit, hypercalcemia, nausea, leg cramps; osteosarcoma in rats</td>
</tr>
</tbody>
</table>

### Which Drug to Use?

**Case Study:** 58-year-old estrogen deficient Hispanic woman

DXA: lumbar spine T-score = -2.5 and femoral neck T-score = -2.1

- Only occasional vasomotor symptoms
- She smokes 2 cigarettes per day after dinner
- No other risk factors for fracture
- NOF Guide: Treat (No need to use FRAX®)

### Which Drug Would You Use?

1. Estrogen
2. Oral bisphosphonate
3. IV bisphosphonate
4. Raloxifene
5. Salmon calcitonin

### Case Study

**72-Year-Old Woman With History Of Wrist Fracture and Recurrent Deep Venous Thrombosis**

<table>
<thead>
<tr>
<th>Age</th>
<th>72</th>
</tr>
</thead>
<tbody>
<tr>
<td>FN T-score</td>
<td>-2.0</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>Wrist fracture at 65</td>
</tr>
<tr>
<td>10 year risk</td>
<td></td>
</tr>
<tr>
<td>Major fractures</td>
<td>25%</td>
</tr>
<tr>
<td>Hip fractures</td>
<td>5%</td>
</tr>
</tbody>
</table>

She is afraid to take a bisphosphonate because her dentist says that it will cause her jaw to rot!

**What would you do now?**

1. Prescribe raloxifene
2. Prescribe teriparatide
3. Use calcium and vitamin D alone
4. Use FRAX® to try to convince her to take the bisphosphonate
10-Year Probabilities of ONJ on Bisphosphonate and Other Adverse Outcomes

<table>
<thead>
<tr>
<th>Probability</th>
<th>ONJ</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>0.15%</td>
</tr>
<tr>
<td>10%</td>
<td>0.06%</td>
</tr>
<tr>
<td>15%</td>
<td>0.007%</td>
</tr>
</tbody>
</table>

Fracture risk typical of patient with osteoporosis; MVA and murder data from the CDC at http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_10.pdf; ONJ estimate for the ADA at JADA. 2006;137:1144-1150.

Case Study
72-Year-Old with Wrist Fracture

As you are writing her prescription for an oral bisphosphonate, she tells you she has had trouble swallowing in the past.

What would you prescribe now?
1. Oral bisphosphonate
2. IV Ibandronate q 3 months
3. IV Zoledronic Acid q year
4. Teriparatide

Improving Therapy Compliance and Persistence

- Before starting therapy:
  - assure patient understanding of seriousness of disease and importance of RX
  - address patient concerns and discuss AEs that are common, serious, or high profile
- Consider injectable therapy (?)
- Ongoing communication
- Monitoring

Evaluating Response to Therapy in Clinical Practice

Serial BMD Testing

- DXA must be performed and interpreted at a qualified facility with known Least Significant Change (LSC)
- Stability or increase in BMD is predictive of fracture risk reduction
- Guidelines often recommend repeat 1-2 years after starting therapy
- Widely available and generally affordable

Bone Turnover Markers

- Potentially helpful
- No clinical practice guidelines
- Many uncertainties
  - Biological and analytical variability
  - LSC in clinical practice
  - Best marker for which drug
  - Insurance coverage
**Case Study**

**Bone Loss on Therapy**

- 65-year-old retired university professor has osteoporosis (L1-L4 T-score = -3.3)
- Treatment with oral bisphosphonate results in a significant BMD increase at L1-L4 one year later
- Next DXA shows BMD loss
- He sees you for evaluation of nonresponse to therapy

**Quiz: What do you do?**

1. Change therapy to an injectable bisphosphonate
2. Stop alendronate and start teriparatide
3. Order lab studies to evaluate factors contributing to bone loss
4. Other

**L1-L4 Scans**

Baseline: 0.729 g/cm²

Follow-up #1: +0.038 (+5.3%)

Follow-up #2: -0.037 (-5.1%)

Mislabeled vertebral bodies

**Quantitative Comparison**

- Same instrument at same facility (unless cross-calibration has been done)
- Compare "apples with apples," e.g., same skeletal site, same bone area
- Precision assessment and least significant change (LSC) known

**Managing Poor Responders**

- 62-year-old woman with osteoporosis has been treated with an oral bisphosphonate for 2 years
- DXA on same instrument as baseline shows a BMD decrease of 0.036 g/cm² (LSC = 0.030 g/cm²)
- A careful review shows that this is a valid comparison
- What do you now?

**Managing Poor Responders**

What do you do now?

1. Tell patient that BMD is stable and to continue same treatment
2. Tell her there is a significant decrease in BMD and that further evaluation is necessary
3. Change from oral to IV bisphosphonate
4. Start teriparatide
Managing Poor Responders

You decide further evaluation is necessary. What would you do?

1. Ask her if she is taking her drug and how she is taking it
2. Ask about calcium and vitamin D intake
3. Ask about other medications she is taking
4. Order lab tests to evaluate for diseases and conditions that could contribute to poor response to therapy
5. All of the above

Common Causes Of Secondary Osteoporosis

- Vitamin D deficiency
- Hypercalciuria
- Malabsorption
- Hypogonadism (men)

Occur in 40-60% of patients who present with what appears to be primary osteoporosis

Laboratory Evaluation in Patients with Osteoporosis

Minimum Testing:
- Chemistries (Ca, Phosphorus, Alk Phos, LFTs, Creatinine)
- CBC
- 24 hour urine calcium (and creatinine, sodium)
- 25-OH-D (not 1,25 vitamin D)
- TSH if symptomatic, elderly or on thyroxine

Other Possible Tests

- PTH
- SPEP
- Immunofixation/ urine light chains
- Celiac disease antibodies
- 24 hour urine cortisol
- Testosterone (in men)
- Bone turnover markers
- Bone biopsy (rarely used in clinical practice)

Management of a Nonresponder

- Evaluate and address contributing factors
- Consider change to IV bisphosphonate in a patient with poor response to oral bisphosphonate
- Consider switch to teriparatide if poor response to anti-resorptive agent and at high risk for fracture
- Consider no change in therapy and re-evaluate in 1 year

How Long to Treat?
Offset of Effect

- Estrogen, raloxifene, calcitonin
  - Short half-life
  - Rapid offset of effect when stopped
- Teriparatide
  - Short half-life
  - Limited to 24 months by FDA
  - Must be followed by anti-resorptive to preserve gains
- Bisphosphonates
  - Long skeletal-retention time
  - Persistence of effect probably varies by drug

Total Hip BMD Change in FLEX Population*

- Significant change in BMD over 5 years

FLEX: Incidence of Spine Fractures

- ALN for 5 yrs/PLB (n=437)
- ALN for 10 yrs (n=662)

FLEX
Continuing Alendronate for Years 5-10 Reduces NVFs in Women with Osteoporotic T-scores

Treatment Summary

- Many pharmacological agents have been proven to reduce fracture risk
- Drug selection should be based on risk/benefit evaluation for each individual patient
- Follow-up care to assure compliance, persistence, and therapeutic effect is important