Tipping the Balance: Strategies for Enhanced Detection and Treatment of Osteoporosis in Primary Care

February 7, 2013
Fort Lauderdale, Florida

Educational Partner:

CME • INCITE
Session 5: Tipping the Balance: Strategies for Enhanced Detection and Treatment of Osteoporosis in Primary Care

Learning Objectives

1. Evaluate the risk of developing a fracture using currently available risk-assessment tools.
2. Initiate the treatment of osteoporosis from risk-assessment scores and bone mineral-density measurements.
3. Assess treatment decisions over time based on the benefit-to-risk ratio of long-term therapy for individual patients.

Faculty

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

Dr E. Michael Lewiecki is a clinical assistant professor of medicine at the University of New Mexico School of Medicine and director of the New Mexico Clinical Research & Osteoporosis Center in Albuquerque. His is a consultant in osteoporosis and metabolic bone disease, supervisor and interpreter of bone density studies at the center, and an educator with a special interest in the management of osteoporosis and metabolic bone disease. Principal investigator for the center’s osteoporosis clinical trials, Dr Lewiecki has authored many scientific publications on osteoporosis and bone densitometry.

Dr Lewiecki is past president of the International Society for Clinical Densitometry (ISCD) and a faculty member for the ISCD’s educational programs on bone densitometry, vertebral fracture assessment, and management of osteoporosis. He is senior editor of Clinical Investigation, associate editor of the Journal of Clinical Densitometry, and an editorial board member of Osteoporosis International and other peer-reviewed journals. Dr Lewiecki has received national and international accolades. In 2002, he was named Physician of the Year by the ISCD and, in 2006, was the recipient of both the ISCD Paul D. Miller Service Award and the Laureate Award of the New Mexico Chapter of the American College of Physicians (ACP).

Dr Lewiecki is a fellow of the ACP and the American College of Endocrinology. He is president and founder of the Osteoporosis Foundation of New Mexico, as well as director of its educational activities. In addition, he established and is program director of the annual Santa Fe Bone Symposium.

Dr Lewiecki, who was raised in the Boston area, is a graduate of Amherst College and Northwestern University Medical School. He completed postgraduate medical training at the University of New Mexico Health Sciences Center. He currently resides in Albuquerque.

Michael Maricic, MD
Clinical Associate Professor of Medicine
University of Arizona School of Medicine
Director
Catalina Pointe Clinical Research
Tucson, Arizona

Dr Michael Maricic is a clinical associate professor of medicine at the University of Arizona School of Medicine and director of Catalina Pointe Clinical Research in Tucson.

While at the University of Arizona, Dr Maricic served as head of the section of rheumatology and as program director of both the internal medicine residency and rheumatology fellowship programs. He has chaired both the Curriculum and the Graduate Medical Education Advisory committees. Dr Maricic is the recipient of the Dean’s Teaching Award for Excellence and the Virginia Furrow Award for Excellence in Graduate Medical Education, and was elected Alpha Omega Alpha by the medical student class. The internal medicine house staff named him the Outstanding Attending in both 2003 and 2004.

Dr Maricic is a fellow of the American College of Rheumatology and past chairman of its Educational Materials and Audiovisual Aids committees. He is a member of the American Society for Bone and Mineral Research, a past member of the National Osteoporosis Foundation Newsletter Editorial Board, and an editorial board member of the Journal of Clinical Densitometry, of which he was past associate editor.
Dr Maricic has authored 40 peer-reviewed articles and numerous chapters on osteoporosis and rheumatology and co-edited the textbooks *Decision Making in Internal Medicine*, *Clinical Care in the Rheumatic Diseases*, and *Bone Disease in Rheumatology*.

**Faculty Financial Disclosure Statements**

The presenting faculty reports the following:

Dr Lewiecki receives grant/research support (as principal investigator, funding to New Mexico Clinical Research & Osteoporosis Center) from Amgen Inc., Eli Lilly and Company, GlaxoSmithKline, and Merck and Co., Inc.; is a scientific advisory board member for Amgen Inc., Eli Lilly and Company, and Merck and Co., Inc.; is a speaker for Amgen Inc., Eli Lilly and Company, Novartis Pharmaceuticals Corporation, and Warner Chilcott; and is a consultant for GlaxoSmithKline.

Dr Maricic receives grant/research support from, and/or is a speaker or consultant for Amgen Inc., Eli Lilly and Company, Novartis Pharmaceuticals Corporation, and Roche.

**Education Partner Financial Disclosure Statement**

The content collaborators at CME Incite report the following:

Rose O’Connor, PhD, and Monique Pond, PhD, have no financial relationships to disclose.

**Suggested Reading List**


Tipping the Balance: Strategies for Enhanced Detection and Treatment of Osteoporosis in Primary Care

Michael Maricic, MD
Clinical Associate Professor of Medicine
University of Arizona
Tucson, AZ

E. Michael Lewiecki, MD
Clinical Assistant Professor of Medicine
University of New Mexico School of Medicine
Albuquerque, NM

Drug List

- Estrogen
- Alendronate
- Risedronate
- Ibandronate
- Zoledronate
- Calcitonin
- Raloxifene
- Denosumab
- Teriparatide
- Estrogen
- Fosamax
- Actonel, Atelvia
- Boniva
- Reclast
- Miacalcin, Fortical
- Evista
- Prolia
- Forteo

Learning Objectives

- Evaluate the risk of developing a fracture using currently available risk assessment tools
- Initiate the treatment of osteoporosis from risk assessment scores and bone mineral density (BMD) measurements
- Assess treatment decisions over time based upon the benefit-risk ratio of long-term therapy for individual patients

Demographic Question

Approximately how many patients that you’ve seen in the last 60 days have osteoporosis?

1. None
2. 1-5
3. 6-10
4. 11-20
5. Over 20

Pre-test Question 1

A 56-year-old postmenopausal woman with a T-score of -2.3 at the femoral neck meets the National Osteoporosis Foundation guidelines for pharmacologic treatment to reduce fracture risk in which one of the following cases?

1. Wrist fracture at age 49
2. Mother had hip fracture at age 82
3. FRAX 10-year probability of major osteoporotic fracture is 22%
4. FRAX 10-year probability of hip fracture is 2%

Pre-test Question 2

Which one of the following is a clinical risk factor for input with FRAX to provide a quantitative estimate of the 10-year probability of fracture?

1. Diabetes mellitus
2. Rheumatoid arthritis
3. Proton pump inhibitor therapy
4. Long-term anticonvulsant therapy
Pre-test Question 3

Which one of the following is FDA-approved for the treatment of osteoporosis in both men and women?

1. Ibandronate
2. Calcitonin
3. Raloxifene
4. Denosumab

Pre-test Question 4

A 72-year-old woman with PMO was diagnosed with osteoporosis at age 67, with a femoral neck T-score of -3.2. She has been taking an oral bisphosphonate for the last 5 years, and after an initial increase in BMD, femoral neck T-score has remained stable at -2.8 without any evidence of fracture. What should be your next course of action?

1. Since BMD is no longer improving, switch to teriparatide therapy
2. Since stable BMD on bisphosphonate therapy is associated with a reduction in fracture risk, and the current T-score of -2.8 suggests that fracture risk remains elevated, the benefit of continuing therapy is likely to outweigh the risks
3. Since there is no evidence of benefit after 5 years of therapy, start a “drug holiday” now
4. Switch the patient to another oral bisphosphonate so that she continues to achieve an adequate response to therapy

Case Study 1: Ms. BR

- 60-year-old asthmatic Caucasian woman
- Menopause commenced at age 48 but she never accepted hormone therapy
- She is 5’2”, but says that she used to be 5’3”
- A recent CXR reported a “vertebral deformity” at T8
- Never taken oral glucocorticoids

What would you do next?

Osteoporosis

Diagnosis and Screening

Michael Maricic, MD
Clinical Associate Professor of Medicine
University of Arizona
Tucson, AZ

Osteoporosis

NIH Consensus Statement 2000

- ... a skeletal disorder characterized by compromised bone strength predisposing a person to increased risk of fracture
- Bone strength primarily reflects integration of bone quality and bone density

Bone mass + bone quality = Bone strength

Normal Bone Remodeling

1. Osteoclast Resorption
2. Osteoblast Recruitment
3. New Bone Formation
4. Osteoblast Apoptosis/Osteocyte Transition

Postmenopausal Bone Loss

1. Increased Osteoclast Resorption
2. Increased Osteoblast Recruitment
3. Inadequate Osteoblast Osteoid Production
4. Net Bone Loss Osteocyte transition

Impact of Osteoporosis

- 44 million Americans have low bone mass
- 10 million have osteoporosis
  - Increasing to 12 million by end of 2012
  - Increasing to >14 million by end of 2020
- 50% of Caucasian women and 25% of men aged >50 will suffer ≥1 osteoporotic fracture in their lifetimes
- Prevalence of osteoporosis will rise with increases in elderly population

Postmenopausal Bone Loss

- 44 million Americans have low bone mass
- 10 million have osteoporosis
  - Increasing to 12 million by end of 2012
  - Increasing to >14 million by end of 2020
- 50% of Caucasian women and 25% of men aged >50 will suffer ≥1 osteoporotic fracture in their lifetimes
- Prevalence of osteoporosis will rise with increases in elderly population


![Prevalence of Health Conditions in US Women](image)

Distribution of Osteoporotic Fractures: Combined Total for Men and Women

![Distribution of Osteoporotic Fractures](image)

Consequences of Fractures

- Increased risk of future fractures
- Chronic pain
- Loss of height
- Impaired pulmonary function
- Medical expenses/lost income
- Hospitalization
- Surgery
- Need for rehabilitation
- Nursing home
- Loss of self-esteem
- Depression
- Loss of independence
- Disability
- Death

High Economic Burden

Estimated $17 billion/year spent related to osteoporosis in 2005

- Inpatient care ($9.7 billion)
- Long-term care ($5.1 billion)
- Outpatient care ($2.2 billion)

2.5 million office visits, ~200,000 nursing home admissions, ~400,000 hospitalizations annually
**Vertebral Fractures (VFs)**

- Most common fractures
- **Only 1/3 of VFs are clinically apparent**
- Progressive
- Associated with
  - Deformity, height loss, back pain
  - Morbidity and mortality
- Predict future vertebral and non-vertebral fractures

---

**Incident Vertebral Fracture Rapidly Increases Risk of Next Vertebral Fracture**

<table>
<thead>
<tr>
<th>Incidence During Study Year 0-1 (n=2570)</th>
<th>Incidence Within 1 Year Following First Fracture (n=381)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.6%</td>
<td>19.2%</td>
</tr>
</tbody>
</table>

Presence of ≥1 VF at baseline increased risk of additional VF 5-fold during Study Year 1

---

**Prevalent Vertebral Fracture Predicts Risk of Future Hip Fracture**

- N=6459 postmenopausal women
- Aged 55-81 years
- Followed for average of 3.8 years

---

**Relative Risk of Death Following Clinical Fractures**

<table>
<thead>
<tr>
<th>Fracture Intervention Trial (FIT):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Symptomatic</td>
</tr>
<tr>
<td>Non-spine</td>
</tr>
<tr>
<td>Hip</td>
</tr>
<tr>
<td>Spine</td>
</tr>
<tr>
<td>Forearm</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age-Adjusted Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Symptomatic</td>
</tr>
<tr>
<td>Non-spine</td>
</tr>
<tr>
<td>Hip</td>
</tr>
<tr>
<td>Spine</td>
</tr>
<tr>
<td>Forearm</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

---

**Clinical Evaluation**

- History
  - Assessment of risk factors for low bone mass falls and fractures
- Physical exam
- Laboratory tests
- Measurement of bone density
Clinical Risk Factors

- Age
- Previous low trauma fracture
- Current cigarette smoking
- Rheumatoid arthritis
- High alcohol intake (>2 units/day)
- Parental history of hip fracture
- Prior or current glucocorticoid use

Clinical Evaluation: Physical Exam

- Height loss >1.5 inches
- Kyphosis

Clinical Evaluation: Laboratory Tests

- Serum calcium, phosphorus, and alkaline phosphatase
- Creatinine
- 25-OH Vitamin D
- 24 hour urine calcium
- TSH (in women receiving thyroid supplementation)

The above tests identify 92% of patients with secondary causes

Bone Density Measurement: DXA Is the “Gold Standard”

- Widely used in epidemiological studies from which prevalence data is derived
- WHO criteria based on BMD measured by DXA
- Correlation with fracture risk
- Low radiation
- Excellent precision

2010 NOF Guidelines Indications for BMD Testing

- Women ≥65, men ≥70 regardless of risk factors
- Younger postmenopausal women and men aged 50-70 with risk factors
- Adults with fracture after age 50
- Adults with conditions such as rheumatoid arthritis or taking medications (such as glucocorticoids ≥5 mg/day ≥3 months) associated with low bone mass or bone loss
- Anyone being treated or being considered for treatment for osteoporosis
- Postmenopausal women discontinuing estrogen therapy

Should We Further Evaluate Ms. BR?

- Over age 50
- Loss of only 1 inch in height
- “Vertebral deformity” noted on CXR
- No history of glucocorticoid use

WHO=World Health Organization. DXA=Dual-energy X-ray absorptiometry.

NOF=National Osteoporosis Foundation.
5 Categories of Medicare-Covered Services

- Estrogen-deficient women at clinical risk for osteoporosis
- Individuals with vertebral abnormalities
- Individuals receiving long-term glucocorticoid therapy
- Individuals with primary hyperparathyroidism
- Individuals being monitored to assess the response to or efficacy of an FDA-approved osteoporosis drug therapy

\[ \text{Bone Mass Measurement Act} \]
\[ \text{July 1, 1998} \]

WHO Classification of BMD

<table>
<thead>
<tr>
<th>Classification</th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>-1.0 or greater</td>
</tr>
<tr>
<td>Low Bone Mass (Osteopenia)</td>
<td>Between -1.0 and -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>-2.5 and below</td>
</tr>
<tr>
<td>Severe Osteoporosis</td>
<td>-2.5 with history of fragility fracture</td>
</tr>
</tbody>
</table>


5 Categories of Medicare-Covered Services

- Estrogen-deficient women at clinical risk for osteoporosis
- Individuals with vertebral abnormalities
- Individuals receiving long-term glucocorticoid therapy
- Individuals with primary hyperparathyroidism
- Individuals being monitored to assess the response to or efficacy of an FDA-approved osteoporosis drug therapy

\[ \text{WHO Classification of BMD} \]

<table>
<thead>
<tr>
<th>Classification</th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>-1.0 or greater</td>
</tr>
<tr>
<td>Low Bone Mass (Osteopenia)</td>
<td>Between -1.0 and -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>-2.5 and below</td>
</tr>
<tr>
<td>Severe Osteoporosis</td>
<td>-2.5 with history of fragility fracture</td>
</tr>
</tbody>
</table>


Diagnosis in Postmenopausal Women and in Men Aged ≥50

- Osteoporosis may be diagnosed in postmenopausal women and in men aged 50 and older if the T-score of the lumbar spine, total hip, or femoral neck is -2.5 or less
- In certain circumstances the 33% radius (also called 1/3 radius) may be utilized

*Note: Other hip regions of interest, including Ward's area and the greater trochanter, should not be used for diagnosis. Application of recommendation may vary according to local requirements.

Use Clinical Judgement

- T-score ≤-2.5 does not always mean that osteoporosis is present
  - Primary disease may be something else (eg, hyperparathyroidism, osteomalacia, or multiple myeloma)
- T-score >-2.5 does not eliminate the possibility of osteoporosis
  - Clinical diagnosis of osteoporosis may be made in the presence of a fragility fracture

Consider FRAX

Diagnosis of Osteoporosis

- Densitometric diagnosis
  - DXA
  - WHO criteria
- Clinical diagnosis
  - Fragility fracture

Vertebral Fracture Assessment (VFA)

- Recognition of vertebral fracture may...
- Change diagnostic classification
- Change estimate of fracture risk
- Change treatment decisions
Combined Effect of Bone Density and Prevalent Fractures


Problem: Most Women With Fracture Have T-score >-2.5

Study of Osteoporotic Fractures in 243 Women With Hip Fractures
National Osteoporosis Research Assessment 239 Women With Osteoporotic Fractures

Current Status of Care

- 3% of wrist fracture patients receive BMD testing
- Only 12% of vertebral fractures are diagnosed and 2% are treated
- Only 3% to 5% of hip fracture patients are diagnosed for osteoporosis and treated

Unmet Needs

- Underdiagnosis
- Undertreatment
- Poor adherence to treatment

Undertreatment of Osteoporosis in Men and Women Who Have Experienced a Hip Fracture


Real-World Persistence to Daily and Weekly Bisphosphonate Therapies

Fracture Risk Assessment and Treatment of Osteoporosis

E. Michael Lewiecki, MD
Clinical Assistant Professor of Medicine
University of New Mexico School of Medicine
Albuquerque, NM

Summary

- Osteoporosis results in great cost, morbidity, and mortality to both men and women
- Prevalence of osteoporosis and fractures is rising worldwide
- Only 1/3 of VF s are clinically apparent
- Presence of ≥1 VF increases risk of subsequent vertebral and non-vertebral fractures
- Combination of BMD testing and presence of clinical risk factors is better predictor of fracture risk than BMD or CRF alone

Fracture Risk Assessment:
BMD, VFA, CRFs, FRAX

Intervention Thresholds

Treatment

Follow-up

Age Is an Independent Risk Factor for Osteoporotic Fractures

Probability of Major Osteoporotic Fracture

10-Year Fracture Probability (%)

Femoral Neck T-score

Prior Fracture Increases Relative Risk of Subsequent Fractures

<table>
<thead>
<tr>
<th>Site of Prior Fracture</th>
<th>Site of Subsequent Fracture</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist</td>
<td>Wrist</td>
<td>3.3</td>
</tr>
<tr>
<td>Vertebra</td>
<td>Vertebra</td>
<td>1.7</td>
</tr>
<tr>
<td>Hip</td>
<td>Hip</td>
<td>1.9</td>
</tr>
<tr>
<td>Wrist</td>
<td>Vertebra</td>
<td>1.4</td>
</tr>
<tr>
<td>Vertebra</td>
<td>Hip</td>
<td>4.4</td>
</tr>
<tr>
<td>Hip</td>
<td>NA</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.3</td>
</tr>
</tbody>
</table>

FRAX: to Assess Fracture Risk in Untreated Patients From Age 40 to 90

- Access: http://www.shef.ac.uk/FRAX
- Input: BMD + clinical risk factors (CRF)
- Rationale: BMD + CRF predict fracture risk better than either alone
- Output: 10-year fracture probability

Predicting Hip Fractures: Relative Risk vs Fracture Probability

<table>
<thead>
<tr>
<th>Age* (years)</th>
<th>Hip T-score</th>
<th>Relative Risk(^1) (2.6)(^{1/2})</th>
<th>10-Year Fracture Probability(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>-2.5</td>
<td>17.6</td>
<td>1.9%</td>
</tr>
<tr>
<td>80</td>
<td>-2.5</td>
<td>17.6</td>
<td>19.4%</td>
</tr>
</tbody>
</table>

Relative Risk = (RR per SD)\(^{T-score or Z-score Difference from 11 study populations including 90,000 person years of observation time}
10-year probability from Swedish National Bureau of Statistics

*Postmenopausal women.


Woman, Caucasian, 0.578, no CRFs: 11%, 2.2%

Women Risk Assessment

Intervention Thresholds:

Osteoporosis
- T-score ≤ -2.5 at FN or LS after evaluation for secondary causes, or
- Hip or vertebral (clinical or morphometric) fracture

Osteopenia
- T-score between -1.0 and -2.5 at FN or LS, and
- FRAX 10-year probability of hip fracture ≥ 3% or major osteoporotic fracture ≥ 20%

NOF Treatment Guidelines

Postmenopausal women and men aged ≥50 with the following should be considered for treatment, after evaluation for secondary causes of osteoporosis:

**NOF Intervention Thresholds**

- **Benefits**
  - Provides objective criteria for making treatment decisions
  - Directs limited healthcare resources to those most likely to benefit
- **Limitations**
  - Based on cost-effectiveness analysis using obsolete assumptions
  - Does not consider individual patient factors
  - Not a substitute for good clinical judgment

**Universal Recommendations**

- Regular weight-bearing exercise
- Fall prevention
- Avoid tobacco use and excess alcohol
- Identification and treatment of risk factors for fracture
- Elemental calcium at least 1200 mg/day
  - IOM: RDA 1000-1200 mg, UL 2000 mg
  - Vitamin D 800-1000 IU/day, target ≥30 ng/mL
    - IOM: RDA 600-800 IU, target >20 ng/mL, UL 4000 IU

**Treatment Decisions**

- Individual patient factors
  - Efficacy and safety for individual patient
  - Nonkeletal risks and benefits
  - Comorbidities
  - Expected adherence to therapy
  - Patient beliefs, concerns, preferences
  - Insurance coverage/affordability
  - Risk communication, shared decision-making

**FDA-Approved Medications: Indications**

<table>
<thead>
<tr>
<th>Drug</th>
<th>PMO</th>
<th>GIO (Women &amp; Men)</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prevention</td>
<td>Treatment</td>
<td>Prevention</td>
</tr>
<tr>
<td>Estrogen</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate PO</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Risedronate PO</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Risedronate Delayed Release PO</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>ibandronate PO</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>ibandronate IV</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Zoledronate</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Calcitonin IN</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raloxifene PO</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denosumab SC</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Teriparatide SC</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

**FDA-Approved Medications: Efficacy**

<table>
<thead>
<tr>
<th>Medication</th>
<th>BMD</th>
<th>BTM</th>
<th>Fracture Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Alendronate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Risedronate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>ibandronate PO</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Zoledronate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>~</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Raloxifene</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Denosumab</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Teriparatide</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

PMO=post-menopausal osteoporosis. GIO=glucocorticoid-induced osteoporosis.

Injectable Osteoporosis Therapy

1. [Link to source]

Bisphosphonate Safety Issues: Balancing Benefits and Risks

- Combination therapy
- Oversuppression of bone turnover
- Osteonecrosis of the jaw
- Atypical femur fractures
- Atrial fibrillation
- Esophageal cancer
- Impaired fracture healing
- Drug holidays

Risk Communication

[10-year probabilities]

80-year-old Woman With FN T-Score = -3.3

- Includes 0.01% Atypical Femur Fracture Risk
- Includes 0.5% Atypical Femur Fracture Risk

Clinical Challenges After Beginning Treatment

- Motivating patient to fill prescription and take it correctly, regularly, and for a sufficient length of time to provide benefit
- Determining how (or if) to follow and monitor the patient to assure that benefit is achieved
- Managing nonresponders/suboptimal responders
- Deciding when (if ever) to stop or change therapy
- Knowing when (if ever) to restart, if treatment is stopped
- Managing side effects, perceived side effects, and fear of side effects

Improving Adherence to Therapy

- Risk communication
- Shared decision making
- Longer dosing intervals
- Less complex administration
- Injectable therapy
- Patient education
- Follow-up contact
Monitoring in Clinical Practice: Assess Long-term Benefit: Risk Ratio

- BMD (DXA)
  - Measure 1-2 years after starting therapy
  - Goal is stability or increase
- BTM (NTX, CTX, BSAP, P1NP, etc)
  - Measure ~3 months after starting therapy or when BMD response is not as expected
  - Goal - significant decrease with antiresorptive agent and increase with anabolic agent
- Cause for concern and further evaluation
  - Significant loss of BMD
  - Lack of expected change in BTM
  - Fracture while receiving therapy

NTX=N-telopeptide of collagen type 1. CTX=C-telopeptide of collagen type 1. BSAP=bone–specific alkaline phosphatase. P1NP=N-terminal serum type 1 procollagen.

FRAX used to assess fracture risk in untreated patients from age 40 to 90
- Inclusion of the following CRFs improves qualitative assessment
  - Previous fracture, parental hip fracture, smoking status, glucocorticoid use, diagnosis of rheumatoid arthritis
- NOF recommends pharmacotherapy be considered in postmenopausal women and men ≥50 years of age in each scenario:
  - T-score ≤-2.5
  - Presence of hip or vertebral fracture
  - T-score between -1.0 and -2.5 at FN or LS and FRAX 10-year probability of hip fracture ≥3% or major osteoporotic fracture ≥20%
- Many therapeutic options available for PMO women
  - Alendronate, risendronate, zoledronate, denosumab, and teriparatide also indicated for osteoporosis treatment in men
  - Treatment decisions must consider all available information and good clinical judgment

Osteoporosis Case Study

- 64-year-old Caucasian woman
- Healthy, active, feels fine
- Weight 116 lbs, height 5’2”
- Physical exam normal
- Takes no medications, vitamins, or supplements
- Only known fracture is to forearm falling off school jungle gym at age 10
- Mother had hip fracture at age 87

ARS Question

Is bone density testing indicated?

1. No, because she is under age 65
2. No, because fracture risk is low
3. Yes, according to standard guidelines
4. Yes, because she takes no calcium supplements

Mrs. CS

- DXA shows femoral neck T-score = -2.3 and lumbar spine T-score = -2.1
- Laboratory studies normal except for serum 25-OH-D = 18 ng/mL
- Further review of vital signs shows she had lost about 1½ inches in height since historical maximum
What is the diagnosis?

1. Normal bone density
2. Osteopenia
3. Osteoporosis
4. Severe osteoporosis

What is her fracture risk?

1. Normal
2. High
3. Low
4. Need more information

Does she meet the NOF guidelines for pharmacological therapy to reduce fracture risk now?

1. Yes
2. No
A 56-year-old postmenopausal woman with a T-score of -2.3 at the femoral neck meets the National Osteoporosis Foundation guidelines for pharmacologic treatment to reduce fracture risk in which one of the following cases?

1. Wrist fracture at age 49
2. Mother had hip fracture at age 82
3. FRAX 10-year probability of major osteoporotic fracture is 22%
4. FRAX 10-year probability of hip fracture is 2%

Which one of the following is a clinical risk factor for input with FRAX to provide a quantitative estimate of the 10-year probability of fracture?

1. Diabetes mellitus
2. Rheumatoid arthritis
3. Proton pump inhibitor therapy
4. Long-term anticonvulsant therapy

Which one of the following is FDA-approved for the treatment of osteoporosis in both men and women?

1. Ibandronate
2. Calcitonin
3. Raloxifene
4. Denosumab

A 72-year-old woman with PMO was diagnosed with osteoporosis at age 67, with a femoral neck T-score of -3.2. She has been taking an oral bisphosphonate for the last 5 years, and after an initial increase in BMD, femoral neck T-score has remained stable at -2.8 without any evidence of fracture. What should be your next course of action?

1. Since BMD is no longer improving, switch to teriparatide therapy
2. Since stable BMD on bisphosphonate therapy is associated with a reduction in fracture risk, and the current T-score of -2.8 suggests that fracture risk remains elevated, the benefit of continuing therapy is likely to outweigh the risks
3. Since there is no evidence of benefit after 5 years of therapy, start a “drug holiday” now
4. Switch the patient to another oral bisphosphonate so that she continues to achieve an adequate response to therapy