Osteoporosis: Diagnosis and Management

Jeri W. Nieves, PhD
Associate Professor of Clinical Epidemiology and Nutrition
Columbia University and Helen Hayes Hospital

NYSOPEP

- Osteoporosis Education Bill (New York State Public Health Law 2707) was signed in 1997.
- This bill established the NYSOPEP program within the New York State Department of Health.
- Helen Hayes Hospital serves as the Statewide Osteoporosis Resource Center
- 845-786-4772
- www.nysopep.org

Objectives

- Identify risk factors for osteoporosis and methods used for diagnosis
- Identify key nutrients for bone health as well as guidelines for physical activity
- Discuss indication for osteoporosis medication, including a discussion of efficacy and safety
Definition of Osteoporosis
A skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Bone strength primarily reflects the integration of bone quality and bone density.

National Institutes of Health (USA)/Consensus Statement on Osteoporosis Prevention, Diagnosis, and Therapy, 2000.

Major Public Health Concern
- In the US, approximately 1 in 2 women and 1 in 4 men over the age of 50 years will have an osteoporosis-related fracture at some point in their life
- Fractures related to osteoporosis in women are more common than heart attack, stroke, and breast cancer combined
- Fracture costs are expected to increase from $19 billion to $25 billion by the year 2025

Osteoporosis is Common In the US
- # of fractures from osteoporosis 1.5 million/ year
- Hospitalizations 500,000/ year
- Trips to the ER 800,000/ year
- Visits to the Doctors office 2.6 million/year
- People placed in nursing homes= 180,000/year
Hip Fractures Can Lead to Disability, Loss of Independence, and Even Death

Hip fracture is associated with increased risk of:

- Disability: 50% never fully recover
- Long-term nursing home care required: 25%
- Increased mortality within 1 year: 30%
- Less than 10% return to full activity
- Chance of another hip fracture is 3 to 4 times greater

Spine Fractures May Cause:

- Pain
- Loss of height
- Stooped posture
- Difficulty breathing
- Stomach pains/digestive discomfort
- Loss of self-esteem
- Increased risk for spine and other non-spine fractures (including hip fracture)

In the year following a vertebral fracture, almost 20% of women will experience another vertebral fracture.

Lindsay, R. Journal of the American Medical Association, Jan 17, 2001
Pathogenesis of Osteoporosis Related Fracture

- LOW PEAK BONE MASS
- POSTMENOPAUSAL BONE LOSS
- AGE-RELATED BONE LOSS

Other Risk Factors

Nonskeletal factors (propensity to fall)

LOW BONE MASS

FRACTURE

Poor bone quality (architecture)

Bone Mass by Age

Peak bone mass:

- GENETIC INFLUENCE

Nutritional factors

PEAK BONE MASS 16-25 yr of age

Hormonal factors

Exercise and environmental factors
Low BMD Is a Strong Predictor of Fracture in PMW

1-Year Fracture Outcomes for 163,935 Women Aged ≥50 Years (NORA Study)

BMD = bone mineral density; PMW = postmenopausal women; NORA = National Osteoporosis Risk Assessment; RR = relative risk.

Who Should get a BMD test?

• All women by the age of 65
• All men by the age of 70
• Postmenopausal women or men who have clinical risk factors
  • Adulthood fractures, kyphosis, family history
  • Chronic diseases that increase risk of osteoporosis
  • Medications that increase risk
  • Active or recent smoking
  • Being very thin
Using T-scores to Define Bone Health

Diagnosis Based on Bone Density Test

<table>
<thead>
<tr>
<th>Osteoporosis</th>
<th>Low Bone Mass</th>
<th>Normal Bone Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>(-2.5 and lower)</td>
<td>(Between -1.0 and -2.5)</td>
<td>(-1.0 and above)</td>
</tr>
<tr>
<td>...-3.5 ...-3.0 ...-2.5 ...-2.4 ...-2.0 ...-1.5 ...-1.1 ...-1.0 ...0.0 ...+1.5 ...+2.0...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pre-menopausal Females and Males under the age of 50

• Z-scores, not T-scores, are preferred. This is particularly important in children.
• A Z-score of -2.0 or lower is defined as “below the expected range for age”, and a Z-score above -2.0 is “within the expected range for age.”
• Z-scores should be population specific where adequate reference data exist. For the purpose of Z-score calculation, the patient's self-reported ethnicity should be used.

Vertebral Fracture Assessment (VFA / CPT Code 77086)
Indications for VFA

- When BMD measurement is indicated, performance of VFA should be considered in clinical situations that may be associated with vertebral fractures. Examples include:
  - Documented height loss of greater than 2 cm (0.75 in) or historical height loss greater than 4 cm (1.5 in) since young adult
  - History of fracture after age 50
  - Commitment to long-term glucocorticoid therapy
  - History and/or findings suggestive of vertebral fracture not documented by prior radiologic study

Ten-Year Risk of Hip Fracture by BMD and the Number of Risk Factors

<table>
<thead>
<tr>
<th>Total hip BMD t score</th>
<th>0</th>
<th>1.0</th>
<th>2.0</th>
<th>Number of risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>10.5</td>
<td>5.8</td>
<td>1.4</td>
<td>0 - 1.0</td>
</tr>
<tr>
<td>2.5</td>
<td>23.4</td>
<td>17.9</td>
<td>2.7</td>
<td>2 - 3.0</td>
</tr>
<tr>
<td>3.5</td>
<td>35.0</td>
<td>5.6</td>
<td>5.6</td>
<td>≥ 4</td>
</tr>
</tbody>
</table>

| 10-year risk of hip fracture (%) |
|---------------------|---|
| Total hip BMD t score | 0 | 1.0 | 2.0 |
| ≤ -2.5               | 10.5 | 5.8 | 1.4 |
| -2.5<1.0             | 23.4 | 17.9 | 2.7 |
| ≥ 1.0                | 35.0 | 5.6  | 5.6 |
Independent Risk Factors for Fracture

The WHO has developed a model (FRAX) to estimate the risk of experiencing a fragility fracture over the next decade. Risk factors that are included:

- Age
- BMD of the femoral neck
- Body Mass Index (BMI)
- Personal history of previous fracture
- Family history of fracture
- Smoking and/or alcohol use
- Ever steroid use
- Rheumatoid Arthritis
- Secondary Osteoporosis

Two Patients: Fracture Risk Assessment

<table>
<thead>
<tr>
<th>Mrs. L (Patient 1)</th>
<th>Mrs. R (Patient 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>61 years of age</td>
<td>64 years of age</td>
</tr>
<tr>
<td>T-score –2.8</td>
<td>T-score –1.7</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>Smoker</td>
</tr>
<tr>
<td>155 lb</td>
<td>124 lb</td>
</tr>
<tr>
<td>No family or personal history of fracture</td>
<td>Maternal history of hip fracture</td>
</tr>
<tr>
<td></td>
<td>Prior history of vertebral fracture</td>
</tr>
</tbody>
</table>
**Examples of Diseases/Conditions**

- **Malabsorption**
  - (Crohn's disease, celiac disease, liver disease)
- **Hyperthyroidism** (Overactive thyroid)
- **Diseases associated with immobility or bed rest for more than 6 months**
  - (stroke, Parkinson’s disease)
- **Rheumatoid Arthritis**

**Medications and Bone Loss**

*Higher Risk with Higher Doses/ Longer Duration of Use*

**Examples known to cause bone loss and increase fracture risk**

- Steroid medications (cortisone and prednisone) used for more than 3 months
- Methotrexate
- Excess Thyroid hormone replacement
- Depo-Provera for birth control
- Aromatase inhibitors- Arimidex, Aromasin, Femara
- Antiseizure medications (only some such as Dilantin or phenobarbital)
- Androgen Deprivation Therapy for prostate cancer

**Being studied for bone loss and fracture risk**

- Certain oral medications for diabetes (Actos and Avandia)
- Proton pump inhibitors (PPIs) (Nexium, Prilosec, Prevacid)
- Selective Serotonin Reuptake Inhibitors (Lexapro, Prozac, Zoloft, Paxil, Effexor)
• Individuals should follow a varied nutrient rich diet using the principles of the Dietary Guidelines and ensure adequate calcium and vitamin D intakes.
  • Calcium 1200 mg from diet and supplements combined
  • Vitamin D 800 to 1000 IU per day
• Other nutrients such as potassium, magnesium and vitamin K and C may be important to bone health. Adequate intakes of fruits and vegetables will meet these needs in healthy individuals who consume a nutrient rich diet.

### Why Is Calcium Needed?

[Diagram showing the relationship between calcium intake, absorption, vitamin D, circulating calcium, PTH, bone remodeling, bone loss, and fracture risk.]

**Recommended Daily Calcium Intake**

(Institute of Medicine, 2010)

<table>
<thead>
<tr>
<th>AGE</th>
<th>Calcium/day in milligrams</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>700</td>
</tr>
<tr>
<td>4-8</td>
<td>1000</td>
</tr>
<tr>
<td>9-18</td>
<td>1300</td>
</tr>
<tr>
<td>Men 19 – 70</td>
<td>1000</td>
</tr>
<tr>
<td>Women 19 - 50</td>
<td>1200</td>
</tr>
<tr>
<td>Women 51- 70</td>
<td>1200</td>
</tr>
<tr>
<td>Men and Women 71+</td>
<td>1200</td>
</tr>
</tbody>
</table>

TUL for men and women age 51+ is 2000 mg
The Information:
“You need 1200 mg of calcium
And 800 IU of vitamin D.”

Typical Action—>

National Osteoporosis Foundation

Calcium Calculator

<table>
<thead>
<tr>
<th>Product</th>
<th>Servings/Day</th>
<th>Calcium (mg)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (8 oz.)</td>
<td>X 300</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Yogurt (6 oz.)</td>
<td>X 200</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Cheese (1 oz. or 1 cubic inch)</td>
<td>X 200</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Fortified Foods/Juices</td>
<td>X 80-1,000</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Estimated total from other foods</td>
<td></td>
<td>= 250</td>
<td></td>
</tr>
<tr>
<td>Total daily calcium intake, in mg</td>
<td></td>
<td>=</td>
<td></td>
</tr>
</tbody>
</table>

Calcium-Rich Foods

Dairy foods (for overall health, fat-free or low-fat)
- Milk- all types including lactose-free
- Yogurt
- Cheese and mixed cheese dishes
- These foods also contain vitamin D, protein, potassium and magnesium

Non-Dairy Foods
- Canned salmon and sardines (with bones)
- Dried figs
- Green leafy vegetables (bok choy, dandelion greens, kale, mustard greens, turnip greens)
- Nuts (almonds, roasted soy nuts)
Meal Makeover
Small Changes Make a Difference
THE BODY USES CALCIUM BEST IN AMOUNTS of 600 mg or less at a time

<table>
<thead>
<tr>
<th>Breakfast (before)</th>
<th>Breakfast (after)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 cup cornflakes (100 mg)</td>
<td>1 cup cornflakes (100 mg)</td>
</tr>
<tr>
<td>½ cup Milk (150 mg)</td>
<td>½ cup Milk (150 mg)</td>
</tr>
<tr>
<td>½ cup OJ (0 mg)</td>
<td>½ cup fortified OJ (175 mg)</td>
</tr>
<tr>
<td><strong>250 mg</strong></td>
<td><strong>425 mg</strong></td>
</tr>
</tbody>
</table>

When is a Calcium Supplement Needed?

Take Recommended Dietary Allowance for Calcium (mg) minus Dietary calcium intake (mg) minus Calcium from multivitamins (mg) minus Calcium from antacids/other medications (mg) equals Calcium needed from supplement (mg)

WHAT IS THE BEST WAY TO TAKE CALCIUM SUPPLEMENTS?

- Take calcium supplements with food - The amount of calcium that the body can use from different calcium compounds is quite similar when supplements are taken with food
- If cannot take calcium with food or if take acid-blocking medication - calcium citrate recommended
- Spread calcium out!
  - 600 mg or less is absorbed best at one time
  - Best to take supplement at a relatively low calcium meal
Fact: More Calcium is Not Better

- It is important to consume the recommended amount of calcium, preferably from food.
- More calcium is not better; excess calcium intake particularly from supplements, consumed on a regular basis may be harmful.
- Tolerable upper limit for calcium was lowered to 2000 mg a day, aim for target of 1200 mg a day from food and supplements if needed.

Vitamin D

What are the Skeletal Health Indicators for Vitamin D?

![Graph showing skeletal health indicators for Vitamin D](image)

Daily Vitamin D Recommendations
Institute of Medicine 2010

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Vitamin D (IU/daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 1 year</td>
<td>400 IU</td>
</tr>
<tr>
<td>Age 1 to 70</td>
<td>600 IU</td>
</tr>
<tr>
<td>Age 71 or older</td>
<td>800 IU</td>
</tr>
</tbody>
</table>

- More may be recommended for at risk for low vitamin D levels or those with certain medical conditions or for other health benefits
- TUL ages 9+ is 4000 IU
Vitamin D Sources

- Sunlight - not reliable
- Diet - minor
  - Natural Sources
  - Fortified sources
- Supplements readily available, inexpensive, needed by all breastfed infants, many children and adults

Natural Sources of Vitamin D

- High Vitamin D (400 IU or more in a 3 ounce serving or in a tsp oil)
  - Eel
  - Trout
  - Swordfish
  - Catfish
  - Mackerel
  - Shiitake mushrooms, sun-dried
  - Cod liver oil (but not recommended as a source of vitamin D)
- Moderate Vitamin D (100 IU to 300 IU in a 3 ounce serving)
  - Salmon
  - Tuna (light)
  - Halibut
  - Sardines
  - Flounder or Sole
- Some Vitamin D (Less than 100 IU in a serving)
  - Tuna (3 ounces white or yellowfin)
  - Egg (1 egg eaten with yolk)
  - Shiitake Mushrooms (per cup)
Foods that May be Fortified with Vitamin D

- Almond, coconut, rice, and soy beverages—most
- Orange juice—some, other juice—few
- Infant formulas—most
- Yogurt—few
- Tofu—few
- Cereal—some
- Bread and grain products—few
- Butter—most, but little added
- Egg substitutes—most
- Margarine—few

Vitamin D from Supplements

<table>
<thead>
<tr>
<th>Source (D2 or D3)</th>
<th>Vitamin D content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamins</td>
<td>varies, 400-1000 IU</td>
</tr>
<tr>
<td>Calcium + vitamin D</td>
<td>varies, 100 to 400 IU per tablet</td>
</tr>
<tr>
<td>Vitamin D *</td>
<td>varies, 400 IU, 800, 1000, 2000, and 5000 IU</td>
</tr>
<tr>
<td>Prescription-strength vitamin D</td>
<td>50,000 IU D2 or 8000 IU D2 /ml liquid</td>
</tr>
</tbody>
</table>

* Look for vitamin D supplements that are not combined with vit A

Populations at Highest Risk for Vitamin D Deficiency

- Breastfed babies not receiving vitamin supplements
- People with osteoporosis or hyperparathyroidism
- Older adults
- People with darker skin
- Patients with malabsorption syndromes
  - (Crohn's disease, celiac disease, bariatric surgery)
- Patients with liver or kidney diseases
- Patients taking medications that interfere with vitamin D metabolism
  - (eg steroids >3 months and certain anti-seizure medications)
- Obese individuals (BMI above 30)
Medications for Osteoporosis

Who do we consider treating with osteoporosis medication?

- Patients with fragility fracture (usually at the hip or spine)
- Patients with a T-score of -2.5 or less at the femoral neck, total hip, or lumbar spine
- Patients with a 10-year probability of a hip fracture of 3% or greater or a 10-year probability of a major osteoporosis-related fracture of 20% or more based on the US-adapted WHO algorithm/FRAX.

Medications

Osteoporosis medications fall into two classes based on their effects.

**Antiresorptive** — prevent bone loss
- Evista, Duavee, Fosamax, Actonel, Boniva, Atelvia, Reclast, Prolia

**Anabolic** — build new bone
- Forteo
Medication Targets

Biochemical or Bone Turnover Markers

Urine test – 2nd morning fasting void:
- N-Telopeptide (NTx)

Blood tests – fasting morning sample:
Resorption
- Collagen Crosslinks (C-telopeptide or CTx)
- N-telopeptide

Formation
- Osteocalcin
- Bone Specific Alkaline Phosphatase (BSAP/BAP)

Medications

- When a medication is FDA-approved for osteoporosis, it means that the medication has been tested and it has been proven that the medication reduces bone loss, may increase bone density, and reduces fracture risk (in at least one site) in a person with osteoporosis.
Raloxifene
- Brand name Evista
- One pill daily
- Mild antiresorptive
- Confers protection against invasive breast cancer

Bazedoxifene/conjugated estrogens
- Brand name Duavee
- One pill daily
- Mild antiresorptive
- Confers protection against invasive breast cancer
- Estrogen component combats post-menopausal symptoms

Cautions with Evista & Duavee
- History of heart attack, stroke, or blood clot
- Bleeding or clotting disorder
- Any breast, uterine, or hormone-dependent cancer
- Age >75
- Severe osteoporosis
Oral bisphosphonates
(alendronate, risedronate, ibandronate)

- Brand names: Fosamax, Actonel, Atelvia, Boniva
- A pill taken once a week or once a month
- Stronger antiresorptive than Evista/Duavee

Cautions with oral bisphosphonates

- History of Barrett’s esophagitis, gastric or esophageal ulcers
- Swallowing problems
- Decreased kidney function
- Low serum calcium
- Length of therapy

Intravenous bisphosphonates
(ibandronate, zolendronic acid)

- Brand names: Boniva, Reclast
- Boniva is given as an IV infusion every three months
- Reclast is given as an IV infusion every one or two years
- Reclast is proven to decrease re-fracture in patients who have already had a hip fracture
Cautions with IV bisphosphonates

- Low serum calcium
- Decreased kidney function
- Length of therapy

Denosumab

- Brand name: Prolia
- An injection given every six months
- Strong antiresorptive

Cautions with Prolia

- Low serum calcium
- Length of therapy
- Side effects – muscle aches, joint pain, rash, cellulitis
Rare Side Effects
Bisphosphonates and Prolia
~ Osteonecrosis of the jaw
~ Atypical femur fracture

Teriparatide
• Brand name: Forteo
• A daily injection
• Promotes bone growth
• Shows the greatest reduction in risk for vertebral fractures

Cautions with Forteo
• High serum calcium
• History of radiation therapy
• History of bone cancer or a bone disease other than osteoporosis
• Hyperparathyroidism
• History of kidney stones
Sequential therapy

- When either Forteo or Prolia therapy is stopped, bone loss can be rapid and alternative agents should be considered to maintain bone density
- Often a one-time Reclast infusion is used to lock in the gains

Pearls

- Hormone replacement therapy provides protection against bone loss, but is not a first-line therapy for osteoporosis.
- Length of antiresorptive therapy
- Traveling – Evista, Duavee, Forteo
- Sequential therapy
- Monitoring effectiveness with CTX, annual BMD testing

Non-medical recommendations

- Dietary calcium
- Calcium supplementation only as needed
- Vitamin D
- Physical activity
- Stop smoking
- Limit alcohol intake
- Prevent falls
Summary

- Osteoporosis is a major public health concern.
- The best way to diagnose osteoporosis, before a fracture occurs, is to measure BMD.
- There are many risk factors for osteoporosis and fracture that are independent of BMD.
- Calcium and vitamin D play a clear role in bone health and in cases of low intakes, supplementation may be needed.
- Treatment is recommended in patients with a spine or hip fracture, in patients with a T-score of -2.5 or less or a FRAX score exceeding 3% for hip or 20% for other fractures.
- There are several approved anti-resorptive therapies and one currently approved anabolic therapy.
- It is important to monitor RX effectiveness with CTX and BMD testing.

Conclusions

Osteoporosis is a major public health concern. Osteoporosis can be prevented through education and providing effective diagnosis and treatment with the goal of preventing fractures.