Osteoporosis Educational Series:
Diagnosis and Management of Osteoporosis in Adults:

Egyptian Academy of Bone Health
and Metabolic Bone Diseases
Objectives:

- At the end of this presentation, attendees will be able to:
  - Characterize the pathophysiology of osteoporosis
  - Identify the clinical diagnosis of osteoporosis
  - Summarize treatment and prevention options
Who needs to be treated for osteoporosis? (Choose one)
T-score between -1.00 to -2.5 at femoral neck, total hip or spine **AND** a FRAX score showing 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20% (FRAX)

a) 10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 20%
b) 10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 10%
c) 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20%
d) 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 30%
Which of the following may be interpreted as improved state of bone turnover after treatment for osteoporosis? (Choose one)

a) A T-score of -1.5 in the spine  
b) Suppression of urine NTX  
c) Improved DXA acquired BMD in both spine and femoral neck regions  
d) Suppressed levels of bone formation and resorption markers
Which of the following would indicate treatment failure, or need to consider alternate treatment for osteoporosis?

a) BMD improved 1% since last DXA done 2 years ago
b) Fracture of femoral shaft while being treated with bisphosphonate for 5 years
c) Increased levels of bone markers since last measure a year ago
d) Femoral neck BMD did not change since last DXA 2 years ago
An 80 year old Caucasian woman with dementia, falls and right hip fracture (1 year ago) while being on bisphosphonate, was referred for evaluation and treatment of osteoporosis. She had a mastectomy, followed by chemotherapy for breast cancer at age 66 and has been cancer free since then. Which of the following would be the best treatment option for her at this time? (Choose one)

a) Ibandronate  
b) Calcitonin  
c) Teriparatide  
d) Denosumab
Selective Estrogen Receptor Modulator (SERM) is one of the first options for osteoporosis treatment.

a) True

b) False
Osteoporosis

- Definition
- Risk Factors
- Screening
- Treatment to prevent fractures
- Monitoring response to treatment
- Special circumstances
- Cases
Osteoporosis: Definition

- Low bone mass and microarchitectural disruption causing weakening of bone which predisposes to fractures
Osteoporosis Organizations

- National Osteoporosis Foundations 2013
- American College of Rheumatology 2010
- US Preventive Services Task Force 2010
- American Association of Clinical Endocrinologists
- North American Menopause Society
Osteoporosis bone
Fig. 1. Complement component 3a (C3a) and collagen triple helix repeat containing 1 (Cthrc1) in the communication between osteoclasts (OC) and osteoblasts (OB). Bone marrow macrophages (BMM) become committed preOC and then mature, multinucleated OC (mOC). C3a is derived from mOC and acts on bone marrow stromal cells (BMSC) to stimulation osteoblastogenesis. Cthrc1 is secreted from mature active OC (maOC) in the middle of bone resorption and stimulates OB differentiation as well as recruitment of BMSC or mesenchymal stem cells (MSC) to resorption lacunae.

J Bone Metab 2014;21:163-167
Bone Remodeling

1. RESTING PHASE:
A bone surface is covered by a protective layer of bone cells - called lining cells.

2. RESORPTION:
During resorption, osteoclasts invade the bone surface and erode it, dissolving the mineral and the matrix.

3. RESORPTION COMPLETE:
A small cavity is created in the bone surface - resorption is complete.

4. FORMATION-REPAIR:
Bone forming cells called osteoblasts begin to fill in the cavity with new bone.

5. REPAIR COMPLETE:
Finally, the bone surface is completely restored.
Osteoporosis Overview

Osteoporosis

“the silent disease”
Overview

- Prevalence: 10 million Americans with osteoporosis
- Affects 18-28% of women and 6-22% of men over the age of 50 years old
- Half of all postmenopausal women and a quarter of men over 50 years old will have an osteoporosis related fracture
Clinical Findings

- Generally patients are asymptomatic even with very low bone densities
- Hip Fractures
- Acute or chronic back pain secondary to vertebral fractures
- Atraumatic or low impact fractures
Fractures

- The main clinical consequence of osteoporosis
- There are more than 1.5 million osteoporosis related fractures per year
  - Hip fractures: 300,000
  - Vertebral fractures: 700,000
  - Wrist fractures: 250,000
  - Other sites: > 300,000
Hip Fracture
Hip Fracture – imaging

Hip Fracture

Hip Fracture – surgical repair c pin
Bone with osteoporosis

Osteoporosis

Normal
Vertebral Fracture- x-ray
Osteoporosis and aging

![Diagram showing a comparison between young and elderly women with osteoporosis](image)
Cost to Society

- 432,000 hospitalizations for fracture annually
- $14 billion dollars per year in US related to fractures – includes hospital and nursing home costs
- Estimated to increase to $25.3 billion in 2025
Pathogenesis for osteoporotic fracture
Pathogenesis of Osteoporosis

Normal Bone Remodeling Sequence

Resorption = Formation   No change in bone mass
Unbalanced Remodeling and Osteoporosis

Resorption > Formation → Net bone loss

Influencers:
• Inadequate calcium or vitamin D
• Menopause
• Aging
• Medications or diseases
High Bone Turnover State

Unbalanced Remodeling

Osteoporosis

Normal Bone Structure

Osteoporotic Bone Structure
Risk Factors: non-modifiable

- Age (increasing)
- Low BMI (small, low weight; < 58 kg)
- Ethnicity: Caucasian > Asian/Latino > African American
- Family History of Fracture
- Rheumatoid Arthritis
Risk Factors: Modifiable

- Sex Hormones (low estrogen/testosterone)
- Low calcium and vitamin D
- Inactive lifestyle
- Excessive alcohol
- Cigarette smoking
- Hyperparathyroidism (primary or secondary)
- Hyperthyroidism
- GI conditions which impair adequate nutrition
- Steroids or Cushing’s
- Proton pump inhibitors
Risk Factors for Hip Fracture

- Bone Mineral density
- Fall on hip
- Neuromuscular impairment
- Ethnicity (Caucasians)
- Age
- Multiple falls in last year
- BMI (if lower)
- Vision impairment
- Physical inactivity
X-ray evidence of osteoporosis

May be present and can be clue for further evaluation
Screening

- DEXA scan is the most reliable method
- All women 65 years old and older be routinely screened for osteoporosis.
- Men > 70
- Younger patients (50-64) with equivalent risk of 65 year old woman
- Special populations: glucocorticoids, anti-estrogen, anti-testosterone
DEXA scan

- Dual energy x-ray absorptiometry
- Two photons are emitted from an x-ray tube, gives very precise measurements at clinically important sites with minimal radiation.
- Measures bone mineral density, approximation of bone mass and best predictor of fracture risk
- Measurement: standard deviation of normal young subjects (T-score) and age-matched (Z-score)
DEXA Scan

- Patients lie on exam table for approx 5 minutes while exam is performed.

Cost is $125-200 for this screening test
DEXA-image
### WHO Definition of Osteoporosis Based on BMD

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMD</th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Within 1 SD of the mean level for a young-adult reference population</td>
<td>T-score at -1.0 and above</td>
</tr>
<tr>
<td>Low Bone Mass (Osteopenia)</td>
<td>Between 1.0 and 2.5 SD below that of the mean level for a young-adult reference population</td>
<td>T-score between -1.0 and -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>2.5 SD or more below that of the mean level for a young-adult reference population</td>
<td>T-score at or below -2.5</td>
</tr>
<tr>
<td>Severe or Established Osteoporosis</td>
<td>2.5 SD or more below that of the mean level for a young-adult reference population</td>
<td>T-score at or below -2.5 with one or more fractures</td>
</tr>
</tbody>
</table>

Some experts use Z-score of < -2 to view for secondary causes of osteoporosis; also can be used in young patients to assess for peak bone density.
DEXA scan: uses

- To detect those at risk for bone fracture (those with low bone density)
- To confirm diagnosis of osteoporosis in those with fracture
- To determine rate of bone loss
  - Compare on same machine if possible
    - GE (Bedford, Massachusetts)
    - Hologic (Madison, Wisconsin)
- To determine response to therapy
Table 2 Means and standard deviation of Hologic Apex and GE-Lunar Prodigy BMD in g/cm²

<table>
<thead>
<tr>
<th>Variables</th>
<th>$r^2$ value</th>
<th>BMD results</th>
<th>sBMD results</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Hologic</td>
<td>Prodigy</td>
<td>Difference</td>
</tr>
<tr>
<td>L1-L4 spine</td>
<td>0.99</td>
<td>0.941±0.159</td>
<td>1.110±0.180</td>
<td>-0.169±0.063 (16.5%)**</td>
</tr>
<tr>
<td>L2-L4 spine</td>
<td>0.98</td>
<td>0.970±0.160</td>
<td>1.132±0.190</td>
<td>-0.164±0.048 (15.6%)**</td>
</tr>
<tr>
<td>Left total hip</td>
<td>0.95</td>
<td>0.841±0.124</td>
<td>0.912±0.131</td>
<td>-0.072±0.028 (8.2%)**</td>
</tr>
<tr>
<td>Right total hip</td>
<td>0.96</td>
<td>0.837±0.124</td>
<td>0.905±0.132</td>
<td>-0.068±0.028 (7.8%)**</td>
</tr>
<tr>
<td>Left neck</td>
<td>0.84</td>
<td>0.706±0.108</td>
<td>0.870±0.119</td>
<td>-0.164±0.043 (21.0%)**</td>
</tr>
<tr>
<td>Right neck</td>
<td>0.87</td>
<td>0.711±0.108</td>
<td>0.867±0.118</td>
<td>-0.156±0.038 (20.0%)**</td>
</tr>
</tbody>
</table>

*P<0.05

**P<0.001

GE machines measure higher bone density
Population database difference for T scores
GE: Madison, Wisconsin
Hologic: Bedford, Massachusetts

## FRAX Risk Factors

### Clinical Risk Factors Included in the FRAX Tool

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Associated Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current age</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Gender</td>
<td>Secondary causes of osteoporosis: Type 1 (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated longstanding hyperthyroidism, hypogonadism or premature menopause (&lt;45 years), chronic malnutrition or malabsorption and chronic liver disease</td>
</tr>
<tr>
<td>A prior osteoporotic fracture (including clinical and asymptomatic vertebral fractures)</td>
<td>Parental history of hip fracture</td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>Current smoking</td>
</tr>
<tr>
<td>Low body mass index (BMI, kg/m²)</td>
<td>Alcohol intake (3 or more drinks/d)</td>
</tr>
<tr>
<td>Oral glucocorticoids &gt;5 mg/d of prednisone for &gt;3 months (ever)</td>
<td></td>
</tr>
</tbody>
</table>

National Osteoporosis Foundation
FRAX Score

Threshold for treatment:
- 3% Hip Fracture, 20% Major osteoporotic FX in the next 10 years
Everything is same except on GE-Lunar rather than Hologic
On Hologic FRAX was 1.8% at hip and 7.0 Major Osteoporotic fx.
FRAX Score

Impact of Age on fracture risk: 40 year old instead of 70 year old
70 year old had FRAX of 4.2% hip and 11% major osteoporotic
T-score and Z-score

• **T-score**
  - Postmenopausal women and men
  - Used to determine if patient has osteoporosis and whether treatment is required

• **Z-score**
  - Premenopausal women
  - Used to determine bone mineral density relative to healthy young controls.
  - For same score, risk of fracture is much lower due to age.
  - When considering treatment in patient’s with spontaneous fractures (clinical picture as well), it is important to consider effect of medication on future pregnancy (fetal bone health)
Quantitative CT scan
Vertebral Imaging

<table>
<thead>
<tr>
<th>Consider vertebral imaging tests for the following individuals:***</th>
</tr>
</thead>
<tbody>
<tr>
<td>• All women age 70 and older and all men age 80 and older if BMD T-score at the spine, total hip or femoral neck is ≤ -1.0.</td>
</tr>
<tr>
<td>• Women age 65 to 69 and men age 70 to 79 if BMD T-score at the spine, total hip or femoral neck is ≤ -1.5</td>
</tr>
<tr>
<td>• Postmenopausal women and men age 50 and older with specific risk factors:</td>
</tr>
<tr>
<td>▪ Low trauma fracture during adulthood (age 50)</td>
</tr>
<tr>
<td>▪ Historical height loss of 1.5 inches or more (4 cm)*</td>
</tr>
<tr>
<td>▪ Prospective height loss of 0.8 inches or more (2 cm)**</td>
</tr>
<tr>
<td>▪ Recent or ongoing long term glucocorticoid treatment</td>
</tr>
</tbody>
</table>

* Current height compared to peak height during young adulthood
** Cumulative height loss measured during interval medical assessment
*** If bone density testing is not available, vertebral imaging may be considered based on age alone

National Osteoporosis Foundation
Standard Laboratory Tests

- **CMP (creatinine, calcium, alkaline phosphatase)**
  - Creatinine: assess for renal function for choice of treatment
  - Calcium:
    - if too low consider cause and replete
    - If too high consider hyperparathyroidism
  - Alkaline phosphatase: osteomalacia or Paget’s disease
- **25-OH Vitamin D**
  - Important to replete if low (low vit D can lead to elevated PTH)
- **24-hour Urine calcium**
  - Hypercalciuria: if elevated
  - Malabsorption: if low
Additional Laboratory Tests

- **PTH (with calcium)**
  - If calcium is elevated
  - If considering using teriparatide (Forteo)
  - Patients with ESRD

- **SPEP/UPEP with immunofixation**
  - In patients with fragility fracture
  - Consider in patients to be placed on teriparatide (Forteo)

- **Testosterone**
  - In men with osteoporosis

- **24 hour urine cortisol**
  - In patients with cushingoid features and unexpected osteoporosis
Bone Markers

Formation

- Serum osteocalcin
- Serum bone specific alkaline phosphatase (BAP)
- Serum pro-collagen type 1 amino-terminal propeptide (P1NP)

Resorption

- Serum C-terminal cross-linking telopeptide of type I collagens (CTX)
- Urine N-terminal cross-linking telopeptide of type I collagen (NTX)
  - 2nd void sample in the AM
Monitoring Treatment Success

DXA Acquired BMD

- Stable or improved BMD
- Loss of BMD <\%CV showing no significant change over mechanical drift from QA report for DXA machine

Bone Markers

- Suppression of Bone markers
  - Both formation and resorption markers
Prevention

• Adequate nutrition, particularly calcium and vitamin D
  - Calcium: 1000 – 1200 mg daily (diet plus supplementation)
  - Vitamin D: goal level of around 30-50 (most 1000 units daily)

• Weight bearing exercise

• Discourage smoking

• Discourage alcohol abuse

• Reduction of risks for falling: consider OT evaluation for home hazards, minimize sedating medications.

• Hip protectors: can be useful if worn properly but often have low compliance.
Who Needs to be Treated?

- Hx of hip fracture
- Other prior fractures and T-score between -1.0 to -2.5 at femoral neck, total hip or spine
- T-score ≤ -2.5 at femoral neck, total hip or spine
- T-score between -1.0 to -2.5 at femoral neck, total hip or spine AND secondary cause ↑ risk of fracture
  - Steroid use, total immobilization
- T-score between -1.0 to -2.5 at femoral neck, total hip or spine AND 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20% (FRAX)
Treatment with medications

- Osteoporosis:
  - Based on DEXA scan (T score < -2.5 in PM Women)
  - Based of FRAX score
    - 10 yr risk for fracture >3% Hip, >20% Major
  - Based on Atraumatic or Low Trauma Fractures

- Osteopenia or osteoporosis plus steroid treatments or anti-estrogen/testosterone therapy.

- Osteopenia and high risk for fracture: on individual basis to decide whether treatment should be given.
## Treatment Options

<table>
<thead>
<tr>
<th>Category</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bisphosphonates</strong></td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td>Alendronate 10 mg daily or 70 mg weekly</td>
</tr>
<tr>
<td></td>
<td>Risedronate 5 mg daily or 35 mg weekly or 150 mg/mo</td>
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<tr>
<td></td>
<td>Ibandronate 150 mg/mo</td>
</tr>
<tr>
<td></td>
<td>Intravenous</td>
</tr>
<tr>
<td></td>
<td>Zoledronic acid 5 mg/yr</td>
</tr>
<tr>
<td><strong>Calcitonin</strong></td>
<td>(no longer used)</td>
</tr>
<tr>
<td><strong>Teriparatide</strong></td>
<td>20 mcg sq daily</td>
</tr>
<tr>
<td></td>
<td>Recombinant human PTH (not &gt;2 yrs)</td>
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<tr>
<td></td>
<td>Contra-indicated in cancer patients</td>
</tr>
<tr>
<td><strong>Denosumab</strong></td>
<td>60 mcg sc/q 6</td>
</tr>
<tr>
<td></td>
<td>Humanized monoclonal antibody</td>
</tr>
<tr>
<td></td>
<td>Usually as a 2\textsuperscript{nd} agent</td>
</tr>
<tr>
<td><strong>Calcium</strong></td>
<td>(1200-1500 mg) + vitamin D (800-1000 IU daily)</td>
</tr>
</tbody>
</table>
Hormones as Treatment Options

**SERM**
(Selective estrogen receptor modulators) – decreased risk for breast cancer)

- Raloxifene – not commonly used because it increases risk of DVT

**Estrogen/Progestin**

- Not encouraged due to increased risk of breast cancer, stroke, DVT and coronary diseases

**Testosterone**

- If hypogonadism is the cause of osteoporosis
Treatment Options

- 1. Bisphosphonates
- 2. Denosumab (Prolia)
- 3. Teriperatide (Forteo)
- 4. SERMs (Selective estrogen receptor modulators) – decreased risk for breast cancer (raloxifene)
- 5. Hormone replacement therapy
- 6. Calcitonin: no longer used
Treatment

Teriparatide (Forteo)

Denosumab (Prolia)
Bisphosphonates

- generally 1st line
- Medications: alendronate, risendronate, zolendronic acid, ibandronate.
- Suppress resorption by preventing osteoclast attachment to bone matrix
- Cannot be used with eGFR < 30-35%
- Decrease vertebral and nonvertebral in most
  - Reduction in fracture risk by approximately 50%
  - Nonvertebral fx prevention not proven for ibandronate
  - Zolendronic acid: 70% vertebral, 41% hip
- Side effects:
  - Esophagitis (not in IV forms)
  - AVN of Jaw
  - Atypical fragility fractures, delayed fracture healing
Nitrogen containing bisphosphonates
Bisphosphonates

**Figure 1.** Complement component 3a (C3a) and collagen triple helix repeat containing 1 (Cthrc1) in the communication between osteoclasts (OC) and osteoblasts (OB). Bone marrow macrophages (BMM) become committed preOC and then mature, multinucleated OC (mOC). C3a is derived from mOC and acts on bone marrow stromal cells (BMSC) to stimulate osteoblastogenesis. Cthrc1 is secreted from mature active OC (maOC) in the middle of bone resorption and stimulates OB differentiation as well as recruitment of BMSC or mesenchymal stromal cells (MSC) to resorption lacunae.

**Figure 2.** A. Nitrogen-containing bisphosphonates selectively inhibit farnesyl pyrophosphate synthase (FPPS) within osteoclasts. B. Osteoclast endocytosis of bisphosphonate from the bone surface leads to FPPS inhibition and osteoclast apoptosis. BP = nitrogen-containing bisphosphonate; HMG-CoA = 3-hydroxy-3-methylglutaryl coenzyme A.
Bisphosphonates

Alendronate
Increase in bone mineral density (circles)
Decrease in urinary N-telopeptides (squares)
Are All Bisphosphonates The Same?

- **Different pharmacokinetics**
  - Alendronate: long biologic half-life
  - Zolendronic Acid: intermediate biologic half-life
  - Risendronate: short biologic half-life

- **Suggested drug holiday**
  - Alendronate: 3-5 years
  - Zolendronate: 3 years
  - Risendronate: 1 year
Denosumab (Prolia):

- Humanized monoclonal antibody to RANK Ligand
- Prevents formation of active osteoclasts
- Inhibits bone resorption

Lipton A, Smith MR, Ellis GK, Goessl C - Clin Med Insights Oncol (2012)
Denosumab (Prolia):

- Shorter biologic half-life than bisphosphonates
- Reduces Fractures
  - vertebral by 68%
  - Hip by 40%
- Approved for women receiving aromatase inhibitors and men receiving gonadotropin reducing treatment
- Contraindications:
  - current hypocalcemia
  - Pregnancy
  - hypersensitivity
- Potential Adverse Effects
  - Atypical fragility fractures
  - AVN of Jaw
  - Possible increased risk of infections (cellulitis, endocarditis)
  - Suppression of bone turnover (delayed fracture healing)
Denosumab (Prolia):

- Change in bone density over time
SERM

- Selective Estrogen Receptor Molecules: mixed agonists and antagonists of specific estrogen receptors.

- **Raloxifene**:
  - Decrease vertebral fracture by 55% (only 30% in those with history of vertebral fracture)
  - no effect on non-vertebral fractures

- Decreases risk for breast cancer

- Adverse effects:
  - ? Risk for CAD
  - Venous thrombosis – increased risk
  - Hot flashes and leg cramps
Hormone Replacement Therapy: rise and fall

- Estrogens +/- progesterones
- HRT was once considered to be the primary therapy of osteoporosis prevention/treatment
- Blocks cytokine signaling to the osteoclast
- Women’s Health Initiative trial: 34% reduction of hip fracture and vertebral fractures, but increased risk for breast cancer, cardiovascular disease, thrombosis...
- Currently, HRT is not used to treat or prevent osteoporosis alone (often used for other indications such as severe postmenopausal symptoms.)
Teriparatide (Forteo)

- Stimulates bone remodeling by increasing bone formation
- Moderate to severe osteoporosis:
- Reduction of fractures:
  - Vertebral: 65%
  - Nonvertebral: 53%
- High doses in rats caused osteosarcoma but no cases of osteosarcoma seen in >200,000 patients who received the drug
- Should not be given for more than 2 years
- Side effects: mild hypercalcemia (10.5-11)
- Expensive and subcutaneous administration.
- Should not be given to patients with:
  - Hypercalcemia
  - Multiple Myeloma, bone mets, skeletal tumor
  - Children/teenagers with growing bones
Teriparatide (Forteo)
Response to therapy

- There are no definite guidelines as to when or if to repeat DEXA scans with treatment.
- Generally DEXA scans should not be performed before 2 years of treatment on same machine.
Osteoporosis in Men

- Later onset: approximately 10 years later.
- Often overlooked
- Worse prognosis with fracture
Osteoporosis in Men

Fig. 1. Mortality following fracture in men and women. Reproduced from Center JR, Nguyen TV, Schneider D, Sambrook PN, Eisman JA. Mortality after all major types of osteoporotic fracture in men and women: An observational study. Lancet 1999;353:878-82. Copyright ©1999 with permission from Elsevier.
Osteonecrosis of Jaw

- Can occur with bisphosphonates and denosumab

**Journal Article**
- 30 patients with osteonecrosis of the jaw
  - Preceding: dental extraction 17, trauma 3, none 10
  - 83% healed by 3-52 months
  - Dental extraction average 18 mo, Trauma all by 12 mo
  - 57% with comorbidities: RA, steroids, DMARDs, diabetes

**Journal Article**
- 70 patients with osteonecrosis of the Jaw
  - Mean time on bisphosphonates was 26.53 months
  - 25% with oral bisphosphonates, 75% IV bisphosphonate
  - 68% trigger identified, 48% dental extraction
  - Complete resolution in 58%, average time 16 months
Particular Circumstances

- Lack of response to bisphosphonates
- Drug Holiday
- After fracture – teriparatide (Forteo) favored
- Before surgery: spinal fusion, joint replacement: teriparatide favored
- Dental Extractions planned: favor teriparatide
- Monoclonal Gammopathy – avoid teriparatide (Forteo)
- Metastatic Cancer: avoid teriparatide
- Hyperparathyroidism: avoid teriparatide
- Chronic kidney disease: depends on eGFR
- End stage renal disease: favor denosumab (Prolia)
Particular Circumstances

- Atypical fracture: favor teriparatide (Forteo)
- AVN of Jaw: favor teriparatide (Forteo)
Review

1. Screening
   - All women > 65 years
   - Men > 70
   - Women 50-64 with risk factors
   - Patients on steroids or anti-estrogen/anti-testosterone treatment

2. Prevention with adequate calcium/vitamin D, weight bearing exercise should be advised for all.

3. DEXA scan is the primary screening tool

4. Aggressive therapy should be offered to patients with atraumatic/low-impact fractures and those with osteoporosis, osteopenia with multiple risk factors, patients on steroids, anti-estrogen, and anti-testosterone therapy with abnormal bone densities (T score <-1).
Case 1

- 35 year old female with family history of mother with osteoporosis (mother just had hip fracture at age 70).
- She does not have prior steroid use, PPI use, rheumatoid arthritis, tobacco or alcohol.
- She had fracture of clavicle during high impact motor vehicle accident.
- DEXA scan was done after she requested it when her mother had recent fracture.
- Z score was $-2.6$
- What is the next step?
Case 1

- Check for causes of low bone density
  - Check routine labs including CMP and 25-OH Vit D.
  - Check urinary calcium excretion
    - Can use low dose hydrochlorothiazide if high
  - Check for problems with absorption
    - Such as IBD or Celiac Disease
  - Consider 24 hour urine cortisol if cushingoid
Case 2

- 39 year old premenopausal female with history of lupus who has been on long courses of steroids and has had hip fracture after fall from standing position a year ago. She has chronically been on PPI for GI prophylaxis.
- She does not have family history of fracture/osteoporosis, rheumatoid arthritis, tobacco or alcohol.
- Labs: creatinine 0.9, Calcium normal, 25-OH Vit D 15
- DEXA scan with Z score of -3.5 at spine and -3.3 at hip.
- What are the next steps?
Case 2

- **Replace Vitamin D**
  - 50,000 units weekly for 8-12 weeks, then 1000-2000 units/day
- **Advise Calcium 1000-1400 mg daily (supplement + diet)**
- **Discuss plans regarding pregnancy in the next 5-10 years**
  - If no plans for pregnancy consider bisphosphonate
  - If plan for pregnancy consider teriparatide vs denosumab
- **Teriparatide may be worth considering as initial treatment to increase bone density given several fractures**
Case 3

- 75 year old female with multiple myeloma who has had multiple compression fractures and was on alendronate for 5 years, then off for 3 years; she had a hip fracture 10 months ago.
- She has family history of fracture and bone density shows decline in T score compared to prior 2 years ago.
- DEXA scan with T-score of -3.6 at lumbar spine and -2.9 at femoral neck.
- Creatinine 0.7, 25-Vit D 55, calcium normal, PTH normal
- What is the next step?
Case 3

- Restart osteoporosis treatment with denosumab (Prolia) since the patient is having ongoing fractures and has decreasing bone density.
- Avoid Teriparatide given diagnosis of multiple myeloma.
Case 4

- 80 year old male with end stage kidney disease with osteoporosis with T score of -3.1 at lumbar spine and -2.9 at femoral neck.
- He has kyphosis with vertebral compression fractures on x-ray of thoracic spine.
- Estimated GFR 20, 25-OH-Vit D 40, calcium normal, PTH mildly elevated.
- What is the treatment choice?
Case 4

- Denosumab (Prolia)
- Cannot use bisphosphonates given low eGFR.
- Avoid Teriparatide given elevated PTH
- For men, in general would be worth to check testosterone level and consider replacement therapy.
Case 5

- 70 year old female with osteoporosis with T score of -2.1 at lumbar spine and -2.6 at femoral neck.
- She has not had any fractures and does not have any other risk factors; no history of tumors.
- She does have frequent falls
- FRAX with 10 year hip fracture risk of 3.6%
- Labs with creatinine 0.9, vitamin D 8, normal calcium, elevated PTH
- What is the treatment?
Case 5

- Replete vitamin D since it is low
- Elevated PTH is likely secondary to low vitamin D level
- Bisphosphonates would generally be treatment of choice in this case.
References

- Up to Date
# Risk factors for Osteoporosis

<table>
<thead>
<tr>
<th>Lifestyle factors</th>
<th>Genetic diseases</th>
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</thead>
<tbody>
<tr>
<td>Alcohol abuse</td>
<td>Cystic fibrosis</td>
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<tr>
<td>Excessive thinness</td>
<td>Ehlers-Danlos</td>
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<tr>
<td>Excess Vitamin A</td>
<td>Gaucher’s disease</td>
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<tr>
<td>Frequent falling</td>
<td>Glycogen storage diseases</td>
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<tr>
<td>High salt intake</td>
<td>Hemochromatosis</td>
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<tr>
<td>Immobilization</td>
<td>Homocystinuria</td>
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<tr>
<td>Inadequate physical activity</td>
<td>Hypophosphatasia</td>
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<tr>
<td>Low calcium intake</td>
<td>Marfan syndrome</td>
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<tr>
<td>Smoking (active or passive)</td>
<td>Menkes steely hair syndrome</td>
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<tr>
<td>Vitamin D insufficiency</td>
<td>Osteogenesis imperfecta</td>
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<td>Parental history of hip fracture</td>
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<td>Porphyria</td>
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<td>Riley-Day syndrome</td>
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</tbody>
</table>
TABLE 1: Conditions, Diseases and Medications That Cause or Contribute to Osteoporosis and Fractures (Continued)

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<thead>
<tr>
<th>Hypogonadal states</th>
<th>Anorexia nervosa</th>
<th>Athletic amenorrhea</th>
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<tr>
<td>Androgen insensitivity</td>
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<tr>
<td>Hyperprolactinemia</td>
<td>Panhypopituitarism</td>
<td>Premature menopause (&lt;45 yrs)</td>
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<tr>
<td>Turner’s &amp; Klinefelter’s syndromes</td>
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<tr>
<td><strong>Endocrine disorders</strong></td>
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<tr>
<td>Central obesity</td>
<td>Cushing’s syndrome</td>
<td>Diabetes mellitus (Types 1 &amp; 2)</td>
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<tr>
<td>Hyperparathyroidism</td>
<td>Thyrotoxicosis</td>
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<td><strong>Gastrointestinal disorders</strong></td>
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<tr>
<td>Celiac disease</td>
<td>Gastric bypass</td>
<td>Gastrointestinal surgery</td>
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<td>Inflammatory bowel disease</td>
<td>Malabsorption</td>
<td>Pancreatic disease</td>
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<td>Primary biliary cirrhosis</td>
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<tr>
<td><strong>Hematologic disorders</strong></td>
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<tr>
<td>Hemophilia</td>
<td>Leukemia and lymphomas</td>
<td>Monoclonal gammopathies</td>
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<tr>
<td>Multiple myeloma</td>
<td>Sickle cell disease</td>
<td>Systemic mastocytosis</td>
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<td>Thalassemia</td>
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<td><strong>Rheumatologic and autoimmune diseases</strong></td>
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<tr>
<td>Ankylosing spondylitis</td>
<td>Other rheumatic and autoimmune diseases</td>
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<tr>
<td>Rheumatoid arthritis</td>
<td>Systemic lupus</td>
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<tr>
<td><strong>Neurological and musculoskeletal risk factors</strong></td>
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<tr>
<td>Epilepsy</td>
<td>Multiple sclerosis</td>
<td>Muscular dystrophy</td>
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<td>Parkinson’s disease</td>
<td>Spinal cord injury</td>
<td>Stroke</td>
</tr>
<tr>
<td><strong>Miscellaneous conditions and diseases</strong></td>
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<tr>
<td>AIDS/HIV</td>
<td>Alcoholism</td>
<td>Amyloidosis</td>
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<tr>
<td>Chronic metabolic acidosis</td>
<td>Chronic obstructive lung disease</td>
<td>Congestive heart failure</td>
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<tr>
<td>Depression</td>
<td>End stage renal disease</td>
<td>Hypercalciuria</td>
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<td>Idiopathic scoliosis</td>
<td>Post-transplant bone disease</td>
<td>Sarcoidosis</td>
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<td>Weight loss</td>
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<tr>
<td><strong>Medications</strong></td>
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<tr>
<td>Aluminum (in antacids)</td>
<td>Anticoagulants (heparin)</td>
<td>Anticonvulsants</td>
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<tr>
<td>Aromatase inhibitors</td>
<td>Barbiturates</td>
<td>Cancer chemotherapeutic drugs</td>
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<tr>
<td>Depo-medroxyprogesterone (premenopausal contraception)</td>
<td>Glucocorticoids (≥ 5 mg/d prednisone or equivalent for ≥ 3 months)</td>
<td>GnRH (Gonadotropin releasing hormone) agonists</td>
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<tr>
<td>Lithium Cyclosporine A and tacrolimus</td>
<td>Methotrexate</td>
<td>Parental nutrition</td>
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<tr>
<td>Proton pump inhibitors</td>
<td>Selective serotonin reuptake inhibitors</td>
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<tr>
<td>Tamoxifen* (premenopausal use)</td>
<td>Thiazolidinediones (such as Actos® and Avandia®)</td>
<td>Thyroid hormones (in excess)</td>
</tr>
</tbody>
</table>

From: The Surgeon General’s Report*, with modification
Response to therapy

Alendronate

- Medscape: Long Term Safety of bisphosphonates
Who needs to be treated for osteoporosis? (Choose one)
T-score between -1.00 to -2.5 at femoral neck, total hip or spine **AND** a FRAX score showing 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20% (FRAX)

a)  10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 20%
b)  10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 10%
c)  10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20%
d)  10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 30%
Which of the following may be interpreted as improved state of bone turnover after treatment for osteoporosis? (Choose one)

a) A T-score of -1.5 in the spine
b) Suppression of urine NTX
c) Improved DXA acquired BMD in both spine and femoral neck regions
d) Suppressed levels of bone formation and resorption markers
Which of the following would indicate treatment failure, or need to consider alternate treatment for osteoporosis?

a) BMD improved 1% since last DXA done 2 years ago
b) Fracture of femoral shaft while being treated with bisphosphonate for 5 years
c) Increased levels of bone markers since last measure a year ago
d) Femoral neck BMD did not change since last DXA 2 years ago
An 80 year old Caucasian woman with dementia, falls and right hip fracture (1 year ago) while being on bisphosphonate, was referred for evaluation and treatment of osteoporosis. She had a mastectomy, followed by chemotherapy for breast cancer at age 66 and has been cancer free since then. Which of the following would be the best treatment option for her at this time? (Choose one)

a) Ibandronate  
b) Calcitonin  
c) Teriparatide  
d) Denosumab
Selective Estrogen Receptor Modulator (SERM) is one of the first options for osteoporosis treatment.

a) True
b) False
Osteoporosis Educational Series:
Diagnosis and Management of Osteoporosis in Adults:

Thank you

Egyptian Academy of Bone Health and Metabolic Bone Diseases