WHAT IS OSTEOPOROSIS?

Osteoporosis is a disease characterized by low bone density, deterioration of bone tissue, disrupted bone microarchitecture, compromised bone strength, and risk of fracture.

Osteoporosis is the most common metabolic bone disease. It is a subclinical condition until complicated by fracture(s). These fractures place an enormous medical and personal burden on individuals who suffer from them and take a significant economic toll. Any new fracture in an adult aged 50 years or older signifies an elevated risk for subsequent fractures, particularly in the year following the initial fracture. Osteoporosis is a risk factor for fracture, just as hypertension is for stroke and hypercholesterolemia is for heart disease.

Approximately 1 in 2 women and up to 1 in 4 men aged 50 and older will break a bone due to osteoporosis or low bone mass.
### EVALUATION/DIAGNOSIS OF OSTEOPOROSIS

**THERE ARE 3 WAYS THAT OSTEOPOROSIS CAN BE DIAGNOSED.**

<table>
<thead>
<tr>
<th>1</th>
<th>BONE MINERAL DENSITY (BMD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-score, a number output of DXA scan, indicates fragility of bone. Normal is zero (0). The more negative the number, the weaker the bones and the more likely they are to break. If the T-score is -2.5 or below (such as -3.0), then the patient has osteoporosis.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2</th>
<th>FRACTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>If a patient over the age of 50 years has had a fracture of the spine, hip, wrist, humerus (shoulder), rib, and/or pelvis, then they probably have osteoporosis (fractures of toes, fingers, nose and skull not included). A fracture of the spine or hip means osteoporosis regardless of the T-score. The occurrence of a fracture suggests that bones are weaker than they should be and that further evaluation may be needed. In older adults, even fractures with major trauma, such as an auto accident, may be a sign of osteoporosis.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3</th>
<th>FRAX&lt;sup&gt;®&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRAX&lt;sup&gt;®&lt;/sup&gt; is a country and ethnicity specific fracture risk calculator that is included in the software of most DXA systems and is accessible online for anyone at <a href="https://frax.shef.ac.uk/FRAX/index.aspx">https://frax.shef.ac.uk/FRAX/index.aspx</a></td>
<td></td>
</tr>
</tbody>
</table>

With input of bone density, age, sex, height, weight, and answers to 7 questions, FRAX<sup>®</sup> calculates the chances of having different types of fractures in the next 10 years. If the 10-year probability of major osteoporotic fracture (spine, hip, shoulder, or forearm) is 20% or more, or the 10-year probability of hip fracture is 3% or more, then a diagnosis of osteoporosis can be made. FRAX<sup>®</sup> can be used before age 65 if patient is at risk, to help you evaluate their fracture risk. The FRAX<sup>®</sup> model accepts ages between 40 and 90 years.
SECONDARY CAUSES OF OSTEOPOROSIS

PRIOR TO INITIATING PHARMACOLOGIC ANTIFRACTURE TREATMENT, PATIENTS SHOULD BE EVALUATED FOR SECONDARY CAUSES OF OSTEOPOROSIS.

<table>
<thead>
<tr>
<th>ENDOCRINE OR METABOLIC CAUSES</th>
<th>NUTRITIONAL/GI CONDITIONS</th>
<th>DRUGS</th>
<th>DISORDERS OF COLLAGEN METABOLISM</th>
<th>OTHER</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acromegaly</td>
<td>• Alcoholism</td>
<td>• Anti-epileptic drugs</td>
<td>• Ehlers-Danlos syndrome</td>
<td>• AIDS/HIV</td>
</tr>
<tr>
<td>• Diabetes mellitus</td>
<td>• Anorexia nervosa</td>
<td>• Aromatase inhibitors</td>
<td>• Homocystinuria due to cystathionine deficiency</td>
<td>• Ankylosing spondylitis</td>
</tr>
<tr>
<td>Type 1</td>
<td>• Calcium deficiency</td>
<td>• Chemotherapy/immunosuppressants</td>
<td>• Marfan syndrome</td>
<td>• Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>Type 2</td>
<td>• Chronic liver disease</td>
<td>• Medroxyprogesterone acetate</td>
<td>• Osteogenesis imperfecta</td>
<td>• Gaucher disease</td>
</tr>
<tr>
<td>• Growth hormone deficiency</td>
<td>• Malabsorption syndromes/ malnutrition (including celiac disease, cystic fibrosis, Crohn’s disease, and gastric resection or bypass)</td>
<td>• Glucocorticoids</td>
<td>• Hemophilia</td>
<td>• Hypercalciuria</td>
</tr>
<tr>
<td>• Hypercortisolism</td>
<td>• Total parenteral nutrition</td>
<td>• Gonadotropin-releasing hormone agents</td>
<td>• Immobilization</td>
<td>• Hypophosphatasia</td>
</tr>
<tr>
<td>• Hyperparathyroidism</td>
<td>• Vitamin D deficiency</td>
<td>Luteinizing hormone (LH)</td>
<td>• Major depression</td>
<td>• Myeloma and some cancers</td>
</tr>
<tr>
<td>• Hyperthyroidism</td>
<td></td>
<td>Follicle-stimulating hormone (FSH)</td>
<td>• Myeloma and some cancers</td>
<td>• Organ transplantation</td>
</tr>
<tr>
<td>• Hypogonadism</td>
<td></td>
<td>• Heparin</td>
<td>• Renal insufficiency/failure</td>
<td>• Renal tubular acidosis</td>
</tr>
<tr>
<td>• Hypophosphatasia</td>
<td></td>
<td>• Lithium</td>
<td>• Rheumatoid arthritis</td>
<td>• Systemic mastocytosis</td>
</tr>
<tr>
<td>• Porphyria</td>
<td></td>
<td>• Proton pump inhibitors</td>
<td></td>
<td>• Thalassemia</td>
</tr>
<tr>
<td>• Pregnancy</td>
<td></td>
<td>• Selective serotonin-reuptake inhibitors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other causes include:

- Alcoholism
- Anorexia nervosa
- Calcium deficiency
- Chronic liver disease
- Malabsorption syndromes/malnutrition (including celiac disease, cystic fibrosis, Crohn’s disease, and gastric resection or bypass)
- Total parenteral nutrition
- Vitamin D deficiency

- Anti-epileptic drugs
- Aromatase inhibitors
- Chemotherapy/immunosuppressants
- Medroxyprogesterone acetate
- Glucocorticoids
- Gonadotropin-releasing hormone agents
- Luteinizing hormone (LH)
- Follicle-stimulating hormone (FSH)
- Heparin
- Lithium
- Proton pump inhibitors
- Selective serotonin-reuptake inhibitors
- SGLT2-inhibitors
- Thiazolidinediones
- Thyroid hormone (in supraphysiologic doses)

- Ehlers-Danlos syndrome
- Homocystinuria due to cystathionine deficiency
- Marfan syndrome
- Osteogenesis imperfecta

Other causes include:

- Aids/HIV
- Ankylosing spondylitis
- Chronic obstructive pulmonary disease
- Gaucher disease
- Hemophilia
- Hypercalciuria
- Immobilization
- Major depression
- Myeloma and some cancers
- Organ transplantation
- Renal insufficiency/failure
- Renal tubular acidosis
- Rheumatoid arthritis
- Systemic mastocytosis
- Thalassemia
## Pretreatment Laboratory Tests

(Ass Appropriate or As Deemed Appropriate by HCP)

<table>
<thead>
<tr>
<th>BLOOD OR SERUM</th>
<th>URINE</th>
<th>MARKERS OF BONE TURNOVER*</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Alkaline phosphatase (ALP)</td>
<td>• 24-hour urinary calcium</td>
<td>• Biochemical markers of bone turnover</td>
</tr>
<tr>
<td>• Celiac screening</td>
<td></td>
<td>• Bone-specific Alkaline Phosphatase (BAP)</td>
</tr>
<tr>
<td>• Complete blood count (CBC)</td>
<td></td>
<td>• CTX or Urine NTX</td>
</tr>
<tr>
<td>• Chemistry levels (calcium, renal function, phosphorus, and magnesium)</td>
<td></td>
<td>• Osteocalcin</td>
</tr>
<tr>
<td>• Follicle-stimulating hormone (FSH) - women</td>
<td></td>
<td>• P1NP</td>
</tr>
<tr>
<td>• Liver function tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Parathyroid hormone (PTH) level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Protein electrophoresis (multiple myeloma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Testosterone and gonadotropin levels - men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Thyroid-stimulating hormone (TSH) level +/- free T4</td>
<td></td>
<td></td>
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<tr>
<td>• Vitamin D (25[OH]D level)</td>
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</tbody>
</table>

*Bone turnover markers may be needed prior to referring patient to a specialist

Given that falls are the leading cause of fracture in older adults, it is critical that all patients being considered for treatment receive comprehensive fall risk evaluation and referral for at-home safety assessment and adaptive modifications.
WHO TO TREAT? WHEN TO TREAT?
POSTMENOPAUSAL WOMEN AND MEN AGED 50 AND OLDER PRESENTING WITH THE FOLLOWING SHOULD BE CONSIDERED FOR TREATMENT.

**HIP OR VERTEBRAL FRACTURE**
- Risk triples after the first vertebral fracture and increases up to 23 times after the third.
- Fracture incidence declines in patients with spine or hip fractures who are treated with approved pharmacologic agents.
- This is true for patients with previous fractures, whether their T-score classification is osteopenia (low bone mass) or osteoporosis.

**WRIST OR FOREARM FRACTURE PLUS LOW T-SCORE ≤ -2.5 AND LOWER BMD**
- Treatment should be considered for any postmenopausal woman or a man aged ≥50 years with low BMD who fractures a wrist or forearm.
- T-score is less predictive of future fracture risk than the fracture itself.
- Pharmacotherapy prevents fracture in patients with osteoporosis by BMD-DXA at any clinically relevant site (femoral neck, total hip, or lumbar spine).

**LOW BONE MASS AND FRAX® SCORE ABOVE TREATMENT THRESHOLD**
- A BMD T-score between -1.0 and -2.5 at the femoral neck or lumbar spine
  
  **AND**

- A 10-year probability of a hip fracture ≥3% or a 10-year probability of a major osteoporosis related fracture ≥20% based on the US-adapted FRAX® algorithm are indicative of high fracture risk and need for pharmacologic intervention.

*FRAX® score should be calculated by provider to ensure accuracy*

All patients being considered for treatment of osteoporosis should also be counseled on risk reduction including adequate intake of calcium, vitamin D sufficiency, smoking cessation, avoidance of excessive alcohol intake, and optimization of physical activities that include weight-bearing, muscle-strengthening, and balance exercises.
## Osteoporosis Medication and Treatment

There are many safe and effective medications available to slow down the loss of bone and reduce the risk of breaking a bone.

<table>
<thead>
<tr>
<th>Class and Drug</th>
<th>Brand Name</th>
<th>Form</th>
<th>Frequency</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiresorptive Agents</strong></td>
<td></td>
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<tr>
<td><em>Bisphosphonates</em></td>
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</tr>
<tr>
<td>Alendronate</td>
<td>Fosamax®, Fosamax Plus D™</td>
<td>Oral (tablet, solution)</td>
<td>Daily/Weekly</td>
<td>Women &amp; Men</td>
</tr>
<tr>
<td>Alendronate</td>
<td>Binosto®</td>
<td>Oral (effervescent tablet)</td>
<td>Weekly</td>
<td>Women &amp; Men</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>Boniva®</td>
<td>Oral (tablet)</td>
<td>Monthly</td>
<td>Women</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>Boniva®</td>
<td>Intravenous (IV) injection</td>
<td>Every 3 months</td>
<td>Women</td>
</tr>
<tr>
<td>Risedronate</td>
<td>Atelvia®</td>
<td>Oral (tablet)</td>
<td>Weekly</td>
<td>Women</td>
</tr>
<tr>
<td>Zoledronic Acid</td>
<td>Reclast®</td>
<td>Intravenous (IV) infusion</td>
<td>One time per year/Once every two years</td>
<td>Women &amp; Men</td>
</tr>
<tr>
<td><strong>Rank Ligand (RANKL) Inhibitor</strong></td>
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<tr>
<td>Denosumab</td>
<td>Prolia®</td>
<td>Injection</td>
<td>Every 6 Months</td>
<td>Women &amp; Men</td>
</tr>
<tr>
<td><strong>Anabolic Agents</strong></td>
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<tr>
<td><em>Sclerostin Inhibitor</em></td>
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<tr>
<td>Romosozumab-AQOO</td>
<td>Evenity®</td>
<td>Injection</td>
<td>2 injections once monthly for 12 months</td>
<td>Women</td>
</tr>
<tr>
<td><strong>Parathyroid Hormone (PTH) Analog</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teriparatide</td>
<td>Forteo®</td>
<td>Injection</td>
<td>Daily</td>
<td>Women &amp; Men</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>Bonsity®</td>
<td>Injection</td>
<td>Daily</td>
<td>Women &amp; Men</td>
</tr>
<tr>
<td><strong>Parathyroid Hormone-Related Protein (PTHrP) Analog</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Abaloparatide</td>
<td>Tymlos®</td>
<td>Injection</td>
<td>Daily</td>
<td>Women &amp; Men</td>
</tr>
<tr>
<td><strong>Estrogen</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><em>Estrogen</em> (Hormone Therapy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen</td>
<td>Multiple Brands</td>
<td>Oral (tablet)</td>
<td>Daily</td>
<td>Women</td>
</tr>
<tr>
<td>Estrogen</td>
<td>Multiple Brands</td>
<td>Transdermal (skin patch)</td>
<td>Twice Weekly/Weekly</td>
<td>Women</td>
</tr>
<tr>
<td>Estrogen Agonists/Antagonists - also called Selective Estrogen Receptor Modulators (SERMs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raloxifene</td>
<td>Evista®</td>
<td>Oral (tablet)</td>
<td>Daily</td>
<td>Women</td>
</tr>
<tr>
<td><strong>Tissue Specific Estrogen Complex (TSEC)</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen/Bazedoxifene</td>
<td>Duavee®</td>
<td>Transdermal (skin patch)</td>
<td>Twice Weekly/Weekly</td>
<td>Women</td>
</tr>
</tbody>
</table>

*Estrogen is also available in other preparations including a vaginal ring, cream, by injection and as an oral tablet taken sublingually (under the tongue). The vaginal preparations do not provide significant bone protection.*
BONE REMODELING

BONE REMODELING IS A PROCESS IN WHICH NEW BONE TISSUE GRADUALLY REPLACES OLD BONE TISSUE. THIS RELATIONSHIP IS VITAL TO MAINTAIN NORMAL CALCIUM LEVELS IN OUR BLOOD.

THE BONE REMODELING PROCESS

IN PATIENTS RECEIVING OSTEOPOROSIS PHARMACOLOGIC TREATMENT:

- Routinely reassess risk for fracture, patient satisfaction and adherence with therapy, and need for continued or modified treatment.

- Reassess patient and BMD status for consideration of a drug holiday after 5 years of oral and 3 years of intravenous bisphosphonate in patients who are no longer at high risk of fracture (T-score ≥ −2.5, no new fractures).

- At each healthcare encounter, ask open-ended questions about treatment to elicit patient feedback on possible side effects and concerns.

- For geriatric patients, provider should ask about falls and fall risks.

ADDITIONAL RESOURCES

- BHOF’s Clinician’s Guide to Prevention and Treatment of Osteoporosis

- American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis—2020 Update

- BHOF Dental Risk Response Letter

- Osteoporosis management: Use a goal-oriented, individualized approach