The goal of this guide is to provide physicians with clear clinical pathways to prevent, diagnose, and treat osteoporosis.

The recommendations presented herein are designed to provide women with optimal and personalized care. They are based on a comprehensive assessment of research on osteoporosis and the 1998 recommendations of the National Osteoporosis Foundation (NOF). This guide is not intended to convey rigid standards, but instead, should be tailored to the needs of each individual woman.

Medical Impact of Osteoporosis

Osteoporosis is a "silent" disease process, governed by a gradual shift in the biologic balance between bone loss and bone replacement. Physicians who recognize that over time, all patients are increasingly at risk for bone loss--and take measures to prevent or reverse this process--can play a key role in the prevention, early detection, and treatment of osteoporosis.

The stakes are high, both medically and economically. Research studies show that osteoporosis is a major public health problem:

- More than 28 million Americans are at risk for developing or have osteoporosis, yet only about 25% are diagnosed with the disorder.
- Nearly half of all women will experience an osteoporotic fracture at some point in their lifetime.
- A woman's risk of hip fracture is equal to her combined risk of breast, ovarian, and uterine cancer.
Clinical Strategy

Assessing Women's Risk

With advancing age and the postmenopausal decline of estrogen, women are at increased risk for osteoporosis (defined as low bone mass that leads to skeletal fragility and fracture).

The decision to use hormone replacement therapy (HRT), however, must be made within the context of many complex factors—the individual woman's risk of cancer, her desire to relieve menopausal symptoms, and the potential benefits of reducing the risk of osteoporosis. Once the decision about HRT is made for the individual patient, there are different clinical pathways for preventing, detecting, and treating osteoporosis.

Major Risk Factors

Bone mineral density testing should be considered for all postmenopausal patients with one or more of the following major risk factors, particularly women not on hormone replacement therapy (HRT):

- Family history of osteoporosis (first-degree relative)
- Body mass index (BMI) is below the 25th percentile, i.e., '22 kg/m^2 (e.g., <127 lb at 5'4")
- History of bone fracture as an adult
- Current cigarette smoking

Other Risk Factors

Physicians should use clinical discretion to assess the impact of the following risk factors (in addition to female sex) on bone health and the need for BMD testing:

- Lifelong low calcium intake
- Caucasian race
- Inadequate physical activity
- Recurrent Falls
- Estrogen deficiency
  - Menopause at age <45
  - Premenopausal amenorrhea >1 year
- Advanced Age
- Excessive alcohol
- Dementia
- Poor health/frailty

Clinical Pathways

Lifelong Evaluation

As supported by research studies, the clinical pathways for preventing and treating osteoporosis are differentiated into three distinct groups:

Childhood to Menopause
Discuss Universal Prevention Strategies
Beginning with young women, discuss the nutritional and lifestyle factors that promote bone health and help prevent osteoporosis: calcium, vitamin D, weight-bearing exercise, and avoidance of smoking and excessive alcohol (see "Bone Health: Universal Recommendations"). A strategy begun in early adulthood will have a major impact on bone density later in life.

Menopause to 64
Assess Risk Factors
In guiding clinical decisions for postmenopausal women, physicians should assess each patient's risk factors, which...
determine the need to obtain a baseline BMD. Universal strategies to prevent osteoporosis should be encouraged.

**Age 65 and Older**  
**Perform BMD Testing**  
For this age group, women are at increased risk for fracture. A baseline BMD is recommended for all patients, regardless of hormone therapy. Universal strategies should be encouraged.

### Evaluation and Treatment of Osteoporosis

- **Women of All Ages**  
  Counsel on nutritional and lifestyle strategies to prevent bone loss.

- **Women with Potential Secondary Causes of Osteoporosis**  
  Do BMD Refer to Specialist as appropriate  
  (See "Secondary Causes")

### Childhood to Menopause

- **Menopause to Age 64**

### Age > 65

- **No Major Risk Factors for Osteoporosis**
  - BMD discretionary
  - +HRT BMD Discretionary
  - -HRT Do BMD

- **History of Fractures**
  - Do BMD
  - +/- HRT Do hip BMD

### Diagnosis and Treatment Strategies

BMD is reported in two values: Z-score and T-score. For a Z-score below -1.5, consider secondary causes of osteoporosis. These recommendations use the T-score to determine treatment strategy.

- **T-score**
  - **Above -1** Normal—continue with prevention strategies
  - **-1 to -2.5** Osteopenia—see "Management Recommendations,"
  - **Below -2.5** Osteoporosis—see "Management Recommendations,"
Secondary Causes

Low bone mass may result from secondary causes. A thorough history and physical should be performed to identify potential secondary causes. As appropriate, care of such patients should be done in consultation with specialists in skeletal health. Secondary causes of osteoporosis include a broad range of disease states and drugs, as partially listed below.

Endocrine and Metabolic Abnormalities
Acromegaly, Cushing's syndrome, hypercalciuria, hyperparathyroidism, hyperthyroidism, hypogonadism including anorexia nervosa, prolactinoma, renal tubular acidosis, type 1 diabetes mellitus, vitamin D deficiency

Hematologic Disorders
Gaucher's disease, hemophilia, homocysteinuria, leukemia, lymphoma, multiple myeloma, pernicious anemia, thalassemia

Immobilization

Gastrointestinal Disease
Celiac disease, chronic liver disease, gastrectomy, hemochromatosis, inflammatory bowel disease, parenteral nutrition, primary biliary cirrhosis

Connective Tissue Abnormalities
Amyloidosis, Ehler-Danlos syndrome, Marfan's syndrome, osteogenesis imperfecta

Rheumatologic Disorders
Ankylosing spondylitis, rheumatoid arthritis

Drugs
Adrenocorticotropin, alcohol (excessive), anticonvulsants, cyclophosphamide, cyclosporine, glucocorticosteroids, heparin, lithium, methotrexate, tamoxifen (premenopausal), thyroxine (supraphysiologic doses)

Bone Mineral Density Testing
Bone mineral density (BMD) is a useful tool to assess bone health and guide clinical interventions to prevent low bone mass (osteopenia) from progressing to osteoporosis. BMD can be measured rapidly and reproducibly with little radiation exposure using dual X-ray absorptiometry of the spine, hip, or forearm. Result is reported as Z-score and T-score.

Whom to test

- Postmenopausal women to age 64
  - Not on HRT and having at least one major risk factor for osteoporosis
  - History of fracture (excluding major trauma, e.g. MVA) as an adult
  - Discretionary for others  (see flow chart)
- All women age 65 and older

Interpreting BMD Results

T-Score
Patient's BMD is compared with "young normal" adults of same sex; result is expressed as the number of standard deviations (SD) above or below the mean (example: T-score of -2.0 is 2 SDs below the mean).

Above -1: Normal- continue with prevention strategies.
Between -1 and -2.5: Osteopenia - see "Management Recommendations"
Z-Score
Patient’s BMD is compared with persons of same age and sex.

Below -1.5: Consider possible secondary cause of osteoporosis.
Reasonable secondary workup – CBC, serum Ca, 25 OH-vitamin D level, and TSH.

Insurance Coverage

Most private insurance carriers and Medicare* cover FDA-approved bone density technologies for the following conditions:

- Estrogen deficiency, at clinical risk for osteoporosis
- Vertebral abnormalities
- Long-term glucocorticoid (steroid) therapy
- Primary hyperparathyroidism
- Monitoring response to an approved osteoporosis drug therapy

* Medicare testing frequency is once every two years or once a year if on long-term (2–3 months) glucocorticoids. As of July 1, 1998, Boston practices are reimbursed $162.30 for BMD.

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Antiresorptive Therapy

Table 1
FDA-Approved Agents for Prevention of Osteoporosis

<table>
<thead>
<tr>
<th>Agent</th>
<th>Usual Dose</th>
<th>Expected Results</th>
<th>Average Wholesale Price (1 month supply)</th>
<th>Contraindications</th>
<th>Side Effects/Risks</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen (eg. Estrace, Premarin)</td>
<td>Premarin 0.625 mg po qd (patch is alternative). If uterus present, also take with Provera 2.5 mg qd (or 5 mg 14 days per month); or Prometrium 200 mg PO gd x 14 days/month; or use combination therapy, e.g.,</td>
<td>Increases bone density</td>
<td>Premarin $14.13</td>
<td>History of deep-vein thrombosis or pulmonary embolism; significant hypertri-glyceridemia; caution should be exercised for personal or family history of breast cancer</td>
<td>Endometrial hyperplasia or cancer (hence need to take with progestin if uterus present); vaginal bleeding; breast fullness/tenderness; DVT/PE; Increased risk for breast cancer with long term use.</td>
<td>Cardiac benefit uncertain. Observational studies suggest reduction in MI, but recent randomized trial showed no benefit. Improves symptoms of estrogen deficiency (e.g., hot flashes); observational studies suggest possibly reduces risk.</td>
</tr>
</tbody>
</table>
No reduction in clinical fractures in 4-year multicenter trial. Comparable fracture studies have not yet been done for estrogen and raloxifene in osteopenic women.

* No reduction in clinical fractures in 4-year multicenter trial. Comparable fracture studies have not yet been done for estrogen and raloxifene in osteopenic women.

### Table 2
**FDA-Approved Agents for Treatment of Osteoporosis**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Usual Dose</th>
<th>Expected Results</th>
<th>Average Wholesale Price</th>
<th>Contraindications</th>
<th>Side Effects</th>
<th>Other Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate* (Fosamax)</td>
<td>5 mg q AM on empty stomach; or 35mg q week. Take with 6-8 oz. water. Stay upright for 30 min after taking.</td>
<td>Increases bone density</td>
<td>$59.28</td>
<td>Active upper GI disease; history of esophageal abnormalities, achalasia; reflux esophagitis (relative contraindication); renal impairment</td>
<td>Espagitis/upper GI distress; myalgias/arthritis</td>
<td></td>
</tr>
<tr>
<td>Risedronate (Actonel)</td>
<td>5mg po q am on empty stomach. Take with 6-8 oz water. Stay upright for 30 min after taking.</td>
<td>Increases bone density</td>
<td>$54.80</td>
<td>History of esophageal abnormalities, achalasia, esophagitis (relative contraindication); renal impairment</td>
<td>Upper GI distress; myalgia; arthritis</td>
<td></td>
</tr>
<tr>
<td>Raloxifene* (Evista)</td>
<td>60 mg po qd</td>
<td>Increases bone density</td>
<td>$63.38</td>
<td>History of deep vein thrombosis or pulmonary embolism; hot flashes</td>
<td>May increase hot flashes</td>
<td>Early data suggest significant (&gt;50%) reduction in risk of breast cancer; no endometrial stimulation (do not need progestin)</td>
</tr>
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* Alendronate and Raloxifene are also approved for the prevention of colorectal cancer, Alzheimer's disease, but further study in randomized controlled trials are needed.
Bone Health
Universal Recommendations for All Women

Calcium

- **Menarche to age 18**: 1,300 mg/day
- **Age 19 to menopause**: 1,000 mg/day
- **Postmenopause**: 1,200 mg/day

**Dietary sources**

*Note:* Most Americans get 400-800 mg calcium from diet, primarily from dairy sources.

- **Yogurt (8 oz.)**: 300 mg (fruit), 400 (plain)
- **Milk (8 oz.)**: 300 mg
- **Cheese slice (1 oz.)**: 200 mg

**Calcium fortified cereals and juices are available**

Supplements

*To maximize efficacy, split daily intake (e.g., <500 mg twice per day)*

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**Calcitonin (Micalcin)**

- **200 IU/day in one nostril, alternate nostrils**
- **Vertebral fracture risk drop 33%; no significant reduction in hip or other non-vertebral fractures**
- **$42.54**
- **Allergy to Calcitonin**
- **Rhinorrhea**
- **May have beneficial analgesic effect**

**Raloxifene (Evista)**

- **60 mg po qd**
- **Vertebral (but not hip) fracture risk drop 30-50%**
- **$63.38**
- **History of deep vein thrombosis or pulmonary embolism; hot flashes**
- **May increase hot flashes**
- **Early data suggest significant (>50%) reduction in risk of breast cancer; no endometrial stimulation (do not need progestin)**

Note: Most Americans get 400-800 mg calcium from diet, primarily from dairy sources.

Calcium fortified cereals and juices are available.
Calcium carbonate

500-600 mg
(e.g. Oscal/Oscal D, Caltrate/Caltrate D, generic; Tums = 200-500 mg)
Requires acid stomach for absorption; take with meals to avoid gastric distress.

Calcium citrate

200-315 mg (e.g., Citrical/Citrical D) Better absorbed, fewer side effects, but more expensive.

Vitamin D

400-800 IU/day

400 IU is usual dose in multivitamins; for more, take vitamin D supplement or combined calcium-vitamin D supplement (e.g., Caltrate D, Citrical D, generic). Fortified milk (8 oz) contains 100 IU. For patients with no vitamin D deficiency, upper safety limit is 2,000 IU/day; patients with vitamin D deficiency require higher doses.

Exercise

Weight-bearing and strength-training (upper and lower body)

Includes walking, jogging, stair climbing, dancing, tennis, weight-lifting.

Continuous activity for 40 minutes at least two times per week

Smoking

Avoid cigarette smoking

Alcohol

Avoid excessive alcohol

Low bone density in alcohol-dependent women has been documented, but the daily amount of alcohol intake that increases osteoporosis risk is undetermined. Advice on alcohol should be balanced with research that suggests >1 drink/day increases risk of breast cancer; 2 drinks/day (upper limit) protects against cardiovascular disease.

Management Recommendations

Prevention of Osteoporosis

T-score between -1 and -2.5

- Review daily intake of calcium (1,200 mg) and vitamin D (400-800 IUs)
- Review weight-bearing exercise, avoiding smoking and excessive alcohol
- Consider preventive therapy with antiresorptive agent (Table 1); for patients already on HRT, consider alternative therapy or possible combination

Treatment of Osteoporosis

T-score below -2.5

Review daily intake of calcium (1,200 mg) and vitamin D (400-800 IUs)
Review weight-bearing exercise, avoiding smoking and excessive alcohol

Initiate osteoporosis therapy (Table 2);

Follow-up for Osteopenia and Osteoporosis

Annual visit; review nutritional and lifestyle guidelines

Confirm compliance with therapy (50% or more discontinue HRT within 1 yr)

Repeat BMD in 12-24 months; subsequently at physician's discretion

If BMD is falling and antiresorptive therapy was not initiated in osteopenia setting, reconsider antiresorptive therapy

Indications for Referral to Specialist

Secondary causes of osteoporosis

Contraindications to standard osteoporosis therapy

Bone loss on osteoporosis therapy

Fracture on osteoporosis therapy

Complex medical history

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### Brigham and Women’s Hospital Osteoporosis Guideline Authors

<table>
<thead>
<tr>
<th>Meryl S. LeBoff, MD</th>
<th>Soheyla Gharib, MD</th>
<th>Caren G. Solomon, MD, MPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Director, Skeletal Health and Osteoporosis Program; Director, Bone Density Unit, Endocrine-Hypertension Division, Department of Medicine</td>
<td>Associate Director of Academic Affairs, Division of Women's Health, Department of Medicine</td>
<td>Division of Women's Health, Division of General Internal Medicine</td>
</tr>
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<thead>
<tr>
<th>Bonnie Bermas, MD</th>
<th>David G. Fairchild, MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associate Director for Clinical Affairs, Division of Women's Health; Division of Rheumatology, Department of Medicine</td>
<td>Medical Director, Brigham and Women's Physician Hospital Organization</td>
</tr>
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</table>

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<thead>
<tr>
<th>Elizabeth Ginsburg, MD</th>
<th>Paula A. Johnson, MD, MPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Director of In Vitro Fertilization Department of Obstetrics and Gynecology</td>
<td>Medical Director, Department of Quality Management Services; Cardiovascular Division and Division of General Internal Medicine, Department of Medicine</td>
</tr>
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### Brigham and Women’s Hospital Osteoporosis Review Board

<table>
<thead>
<tr>
<th>Thomas S. Thornhill, MD</th>
<th>Michael E. Weinblatt, MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chairman, Department of Orthopedic Surgery</td>
<td>Director of Clinical Rheumatology, Division of Rheumatology, Department of Medicine</td>
</tr>
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<thead>
<tr>
<th>Troyen A. Brennan, MD</th>
<th>Barbara Weissman, MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>President, BWH Physicians Organization</td>
<td>Vice Chair for Ambulatory Services; Chief, Musculoskeletal Radiology, Department of Radiology</td>
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<tr>
<th>JoAnn E. Manson, MD, DrPH</th>
<th>Gordon H. Williams, MD</th>
</tr>
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<tbody>
<tr>
<td>Chief, Division of Preventive Medicine</td>
<td>Chief, Endocrine-Hypertension Division, Department of Medicine</td>
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<th>Robert L. Barbieri, MD</th>
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<tr>
<td>Chairman, Department of Obstetrics and Gynecology</td>
</tr>
</tbody>
</table>
Editorial Board

Soheyla D. Gharib, MD
Editor In Chief
Associate Director for Academic Affairs, Division of Women’s Health, Department of Medicine

Judy Ann Bigby, MD
Medical Director, Community Health Programs
Director, HMS Center for Excellence in Women’s Health

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Director, Primary Care Services
Brigham and Women’s Hospital

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Director, Center for Cardiovascular Disease in Women
Director, Department of Quality Management Services
Cardiovascular Division and Division of General Internal Medicine

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Department of Medicine

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Director, Clinical Immunology Laboratory at the Center for Neurologic Diseases, Department of Neurology

Rosemarie Maddi, MD
Department of Anesthesiology, Perioperative and Pain Medicine

Tamara Martin, MD
Orthopedic Surgeon, Department of Orthopedic Surgery

Jack Meyer, MD, FACR
Director of Breast Imaging, Department of Radiology

Jo Shapiro, MD
Chief, Division of Otolaryngology
Department of Surgery

Mary D. Chapin, RN
Director, Women’s Health Guidelines