

## Osteoporosis in Women — Epidemiology and Treatment

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**Osteoporosis is common in postmenopausal women due to the lack of endogenous estrogen. The condition is characterized by the loss of bone mass density. The most serious complication of osteoporosis in postmenopausal women is hip fracture. Screening with dual-energy X-ray absorptiometry (DEXA) is essential for the early recognition of osteoporosis in women, and for the prediction of the risk of hip fractures.**



### Overview

Osteoporosis is a common condition in postmenopausal women that is **characterized by the loss of bone mass due to structural deterioration and the formation of porous bone**. These changes are believed to be caused by the lack of estrogen and other hormonal changes that happen during menopause. Such abnormal changes in the bone composition and density are associated with an increased risk of fractures.

# Epidemiology of Osteoporosis in Women

Osteoporotic changes in bones are more common in postmenopausal women compared to premenopausal women, most likely **due to the low levels of circulating estrogens in the postmenopausal population**. The most serious complication of osteoporosis in men and women is osteoporotic fractures.

Osteoporotic fractures occur in approximately 40–50% of women during their lifetime and in about 13% of men. Up to 1 in 5 women will experience a hip fracture in their lifetime; therefore, the impact of osteoporotic fractures on health-related costs and the quality of life of those who sustain them is quite huge on the population level. Approximately, 2.5 million visits to the clinic occur per year for the evaluation of an osteoporotic fracture or osteoporosis.

The **most important complication of an osteoporotic fracture is an osteoporotic fracture-related chronic pain**. Chronic pain has a hugely adverse effect on the quality of life of the patient.

The most important risk factors for osteoporosis and osteoporotic-related fractures can be grouped into:

- Lifestyle factors
- Genetic factors
- Endocrinopathies
- Other chronic conditions

The **main lifestyle factors associated with an increased risk of fractures** in postmenopausal women are:

- Consumption of more than three alcoholic drinks per day
- Use of aluminum antacids
- High caffeine intake
- History of prolonged immobilization
- Low body mass index
- Low calcium or vitamin D deficiency

**Women with a history of the following illnesses are at an increased risk of osteoporosis premenopausally and postmenopausally:**

- Cystic fibrosis
- Hemochromatosis
- Homocystinuria
- Hypophosphatasia
- Marfan syndrome
- Porphyria

Additionally, women with a history of anorexia nervosa, panhypopituitarism, androgen insensitivity or other causes of premature ovarian failure are at an exquisitely increased risk of osteoporotic fractures.

**Diabetes, hyperparathyroidism, hyperthyroidism and adrenal gland diseases can also put the woman at an increased risk** of osteoporotic bone changes, especially during the perimenopausal period.

Absorption disorders, such as celiac disease, gastric bypass, inflammatory bowel disease, or pancreatic disease are associated with impaired vitamin D absorption and possibly a

higher risk of osteoporosis.

**Women presenting with an osteoporotic fracture, especially if young, should not use certain medications**, such as:

- Heparin
- Antiepileptics
- Aromatase inhibitors
- Chemotherapy
- Steroids
- Lithium

## Screening for Osteoporosis in Women

**Dual-energy X-ray absorptiometry (DEXA) is the method of choice for assessing the bone mass density in postmenopausal women** and in the prediction of the risk of osteoporotic-related fractures.

The result of DEXA is usually reported as a T-score that represents the difference between the patient's bone density from the mean of the population's normal bone mass density in standard deviations.

- Normal bone mass density should have a T-score less than 1 SD below the mean.
- Bone mass density between 1 to 2.5 SD indicates osteopenia.
- Osteoporosis is defined as a bone mass density below 2.5 SD below the mean.

More recently, it was suggested that **a Z-score might be more appropriate for the interpretation of a DEXA study result** than a T-score. Z-scores consider the patient's age. A Z-score that is below -2.0 is indicative of clinically significant osteoporosis.

### Overview of screening

<b>T Score</b>	<b>Z Score</b>
Standard deviations between patient and average peak young adult bone mass	Standard deviations between the patient and average bone mass for the same sex, age, and weight
The more negative the greater risk of fracture	'Z' score lower than -2.0 □ requires evaluation for secondary osteoporosis

**Note:** The measurement of hip bone mass density using DEXA has the strongest correlation and predictive power of osteoporotic fractures.

**Postmenopausal women should receive their first DEXA scan by the age of 65 years.** Younger postmenopausal women with multiple risk factors for osteoporosis should receive screening earlier than this cut-off.

Postmenopausal women with a history of the following should receive their first DEXA scan when they are 50 years old:

- Tobacco smoking
- Rheumatoid arthritis
- Hip fracture in a parent
- Body mass index below 21 kg/m<sup>2</sup>
- Fracture after menopause

The screening interval is still under debate. Some **experts suggest repeating the DEXA scan every 2 years, whereas others recommended repeating the test**

**every 5 years.** We suggest using clinical judgment, the patient's own Z-scores or T-scores, and the patient's number of risk factors for osteoporotic fractures to guide the screening interval for that individual.

## Prevention of Osteoporotic Fractures in Women

The prevention of osteoporotic fractures in postmenopausal women might be primary or secondary. The administration of calcium or vitamin D is controversial. The National Osteoporosis Foundation, the National Academy of Sciences, and the Institute of Medicine **recommended daily calcium and vitamin D supplementation for the primary prevention of osteoporotic fractures.**

The US Preventive Services Task Force **recommends against the administration of calcium and vitamin D for the primary prevention of osteoporotic fractures.**

Because of the emergence of more randomized clinical trials that showed results in favor of calcium and vitamin D supplementation, we believe that they are helpful in decreasing the risk of osteoporotic fractures.

Low dose estradiol (0.14mg) as a skin patch that doesn't require progesterone for endometrial protection is the method of choice in hormonal replacement therapy for the prevention of osteoporotic fractures.

**Weight-bearing and non-weight-bearing exercises, especially of the lower limbs, definitely lower the risk of osteoporotic fractures** in postmenopausal women and are recommended. Postmenopausal women should be encouraged to limit their alcohol intake to less than 2 drinks per day and to quit cigarette smoking for women.

## Treatment of Osteoporosis in Women

**Treatment for osteoporosis should be started in any postmenopausal woman:**

- Who is older than 50 years.
- Who sustained a fragility fracture before or who has a DEXA t-score below 2.5.
- When loss of bone mass is associated with an elevated 10-year fracture risk using the FRAX online risk calculator.

This is especially true when the woman is at an increased risk of osteoporotic fractures due to the presence of multiple risk factors.

## Medical therapy for osteoporosis

**Bisphosphonates are the mainstay of the treatment of osteoporosis in postmenopausal women** and are very important in the secondary prevention of osteoporotic fractures. They decrease the risk of vertebral and non-vertebral fractures but do not have any effect on the bone mass density.

Unfortunately, **bisphosphonates are associated with a significantly increased risk of gastrointestinal tract side effects such as esophagitis.**

**Selective estrogen-receptor modulators are very effective in the prevention of vertebral and non-vertebral fractures** in osteoporotic women, but not in the prevention of hip fractures. They increase bone mass density which is another added advantage over bisphosphonates. Unfortunately, they are associated with an increased risk of venous thromboembolism disease.

**Hormone replacement therapy is known to lower the risk of osteoporosis, especially in women with premature ovarian failure** and the risk of osteoporotic-related fractures. They decrease the rate of bone mass density loss and are effective in lowering the rates of hip, vertebral and non-vertebral fractures in postmenopausal women.

They also ameliorate the vasomotor symptoms, urogenital symptoms and mood symptoms of menopause. **Hormone replacement therapy use after more than 10 years of menopause is not recommended** due to the increased risk of cardiovascular disease.

Parathyroid hormone and calcitonin can be also used for the secondary prevention of osteoporotic fractures in postmenopausal women. Their efficacy is inferior compared to the previous interventions, but they can be used as adjunctive therapy.

**Denosumab was recently approved by the FDA for the prevention of osteoporotic-related fractures** and the treatment of osteoporosis. It reduces the risk of vertebral and non-vertebral fractures in addition to lowering the risk of hip fractures. Denosumab also increases the bone mass density at the lumbar spine and hip.

The main side effects of denosumab are gastrointestinal irritation, dermatitis, limb and back pain, headache and hypercholesterolemia. Because bisphosphonates are very efficacious and considerably cheaper than this option, they **remain the first-line therapy for osteoporosis in postmenopausal women**. Denosumab has the advantage of being administered only once every six months, but the cost-effectiveness of the drug and the similar efficacy to bisphosphonates makes it a second-line therapy that should be used only in very high-risk patients.

#### US FDA Approved Options

Antiresorptives (bone-retaining)	Anabolics (bone-forming)
<ul style="list-style-type: none"> <li>• Bisphosphonates</li> <li>• Calcitonin</li> <li>• Estrogen agonists/antagonists, also called SERMS</li> <li>• Estrogen/hormone therapy</li> </ul>	<ul style="list-style-type: none"> <li>• Teriparatide (PTH (1-34))</li> <li>• Human monoclonal antibody to RANK-ligand.</li> </ul>

## References

Kling JM, Clarke BL, Sandhu NP. Osteoporosis Prevention, Screening, and Treatment: A Review. *Journal of Women's Health*. 2014;23(7):563-572. doi:10.1089/jwh.2013.4611.

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