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Original Link: http://www.uptodate.com/contents/osteoporosis-prevention-and-treatment-beyond-the-basics

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OSTEOPOROSIS OVERVIEW

Osteoporosis is a common problem that causes bones to become abnormally thin, weakened, and easily broken (fractured). Women are at a higher risk for osteoporosis after menopause due to lower levels of estrogen, a female hormone that helps to maintain bone mass.

Fortunately, preventive treatments are available that can help to maintain or increase bone density. For those already affected by osteoporosis, prompt diagnosis of bone loss and assessment of fracture risk are essential because therapies are available that can slow further loss of bone or increase bone density.

This topic review discusses the therapies available for the prevention and treatment of osteoporosis. A separate topic discusses bone density testing. (See <u>"Patient information: Bone density testing (Beyond the Basics)"</u>.)

OSTEOPOROSIS PREVENTION

Some of the most important treatments for preventing osteoporosis include diet, exercise, and not smoking. These recommendations apply to men and women. (See "Overview of the management of osteoporosis in postmenopausal women" and "Treatment of osteoporosis in men".)

Diet — An optimal diet for preventing or treating osteoporosis includes consuming an adequate number of protein and calories as well as optimal amounts of calcium and vitamin D, which are essential in helping to maintain proper bone formation and density.

Calcium intake — Experts recommend that premenopausal women and men consume at least 1000 mg of calcium per day; this includes calcium in foods and beverages plus calcium supplements. Postmenopausal women should consume 1200 mg of calcium per day (total of diet plus supplements). However, you should not take more than 2000 mg calcium per day due to the possibility of side effects. (See "Patient information: Calcium and vitamin D for bone health (Beyond the Basics)".)

The main dietary sources of calcium include milk and other dairy products, such as cottage cheese, yogurt, or hard cheese, and green vegetables, such as kale and broccoli (table 1). A rough

method of estimating dietary calcium intake is to multiply the number of dairy servings consumed each day by 300 mg. One serving is 8 oz of milk (236 mL) or yogurt (224 g), 1 oz (28 g) of hard cheese, or 16 oz (448 g) of cottage cheese.

Calcium supplements (calcium carbonate or calcium citrate) may be suggested for women who cannot get enough calcium in their diet (table 2). Calcium doses greater than 500 mg/day should be taken in divided doses (eg, once in morning and evening).

Vitamin D intake — Experts recommend that men over 70 years and postmenopausal women consume 800 international units of vitamin D each day. This dose appears to reduce bone loss and fracture rate in older women and men who have adequate calcium intake (described above). Although the optimal intake has not been clearly established in premenopausal women or in younger men with osteoporosis, 600 international units of vitamin D daily is generally suggested. (See "Calcium and vitamin D supplementation in osteoporosis".)

Milk supplemented with vitamin D is a primary dietary source of dietary vitamin D; it contains approximately 100 int. units per 8 oz (236 mL). Another good source is salmon, with approximately 600 int. units per 3.5 oz (98 g) serving. Experts recommend vitamin D supplementation for all patients with osteoporosis whose intake of vitamin D is below 400 int. units per day.

Protein supplements — Protein supplements may be recommended in some people to ensure sufficient protein intake. This may be particularly important for those who have already had an osteoporotic fracture.

Alcohol, caffeine, and salt intake — Drinking alcohol excessively (more than two drinks a day) can increase the risk of fracture due to an increased risk of falling, poor nutrition, etc., so it should be avoided.

Restricting caffeine or salt has not been proven to prevent bone loss in people who consume an adequate amount of calcium.

Exercise — Exercise may decrease fracture risk by improving bone mass in premenopausal women and helping to maintain bone density for women after menopause. Furthermore, exercise may decrease the tendency to fall due to weakness. Physical activity reduces the risk of hip fracture in older women as a result of increased muscle strength. Most experts recommend exercising for at least 30 minutes three times per week.

The benefits of exercise are quickly lost when a person stops exercising. A regular, weight-bearing exercise regimen that a person enjoys improves the chances that the person will continue it over the long term. (See "Patient information: Exercise (Beyond the Basics)".)

Smoking — Stopping smoking is strongly recommended for bone health because smoking cigarettes is known to speed bone loss. One study suggested that women who smoke one pack per day throughout adulthood have a 5 to 10 percent reduction in bone density by menopause, resulting in an increased risk of fracture. (See <u>"Patient information: Quitting smoking (Beyond the Basics)"</u>.)

Falls — Falling significantly increases the risk of osteoporotic fractures in older adults. Taking measures to prevent falls can decrease the risk of fractures. Such measures may include the following:

- Removing loose rugs and electrical cords or any other loose items in the home that could lead to tripping, slipping, and falling.
- Providing adequate lighting in all areas inside and around the home, including stairwells and entrance ways.
- Avoiding walking on slippery surfaces, such as ice or wet or polished floors.
- Avoiding walking in unfamiliar areas outside.
- Reviewing drug regimens to replace medications that may increase the risk of falls with those that are less likely to do so.
- Visiting an ophthalmologist or optometrist regularly to get the optimal eye glasses.

Medications — Prolonged therapy with and/or high doses of certain medications can increase bone loss. The use of these medications should be monitored by a healthcare provider and decreased or discontinued when possible. Such medications include the following:

- Glucocorticoid medications (eg, prednisone)
- Heparin, a medication used to prevent and treat abnormal blood clotting (ie, anticoagulant)
- Certain antiepileptic drugs (eg, phenytoin, carbamazepine, primidone, phenobarbital, and valproate)

OSTEOPOROSIS MEDICATIONS

The non-drug measures discussed above can help to reduce bone loss. A medication or hormonal therapy may also be recommended for certain men and women who have or who are at risk for osteoporosis.

Who needs treatment with a medication? — People with the highest risk of fracture are the ones most likely to benefit from drug therapy. In the United States, the National Osteoporosis Foundation (NOF) recommends use of a medication to treat postmenopausal women (and men \geq 50 years) with a history of hip or vertebral fracture or with osteoporosis (T-score \leq -2.5). An explanation of T-scores is provided in the table (table 3).

In addition, the NOF recommends drug therapy for people who have osteopenia (T-score between -1.0 and -2.5) and an estimated 10-year risk of hip or osteoporosis-related fracture ≥3 or ≥20 percent, respectively. The absolute risk of fracture can be calculated using the World Health Organization FRAX calculator (www.shef.ac.uk/FRAX/), click on Calculation Tool, and select country.

However, some people who do not meet these criteria will benefit from a medication to treat osteoporosis or osteopenia. The final decision about use of a medication should be shared between the patient and healthcare provider.

Treatment in premenopausal women — The relationship between bone density and fracture risk in **premenopausal** women is not well defined. A premenopausal woman with low bone density may have little increased risk of fracture. Thus, bone density alone should not be used to diagnose osteoporosis in a premenopausal woman; further evaluation is generally recommended. (See "Evaluation and treatment of premenopausal osteoporosis".)

Bisphosphonates — Bisphosphonates are medications that slow the breakdown and removal of bone (ie, resorption). They are widely used for the prevention and treatment of osteoporosis in postmenopausal women. (See <u>"The use of bisphosphonates in postmenopausal women with osteoporosis"</u>.)

These drugs need to be taken first thing in the morning on an empty stomach with a full 8 oz glass of plain (not sparkling) water. The person must then wait:

- At least half an hour (with alendronate [Fosamax®] and risedronate [Actonel®]) before eating or taking any other medications.
- At least one hour (with ibandronate [Boniva®]) before eating or taking any other medications.

These dosing instructions help ensure that the drugs will be absorbed, and also reduce the risk of side effects and potential complications.

An enteric coated delayed-release formulation of risedronate is also available. Unlike immediate-release risedronate and other oral bisphosphonates, delayed-release risedronate is taken immediately after breakfast and with at least four ounces of water.

Patients should remain upright (sitting or standing) for at least 30 minutes after taking any oral bisphosphonate to minimize the risk of reflux.

Side effects of bisphosphonates — Most people who take bisphosphonates do not have any serious side effects related to the medication. However, it is important to closely follow the instructions for taking the medication; lying down or eating sooner than the recommended time after a dose increases the risk of stomach upset.

There has been concern about use of bisphosphonates in people who require invasive dental work. A problem known as avascular necrosis or osteonecrosis of the jaw has developed in people who used bisphosphonates. The risk of this problem is very small in people who take bisphosphonates for osteoporosis prevention and treatment. However, there is a slightly higher risk of this problem when higher doses of bisphosphonates are given into a vein during cancer treatment.

Experts do not think that it is necessary for most people to stop bisphosphonates before invasive dental work (eg, tooth extraction or implant). However, people who take a bisphosphonate as part of a treatment for cancer should consult their doctor before having invasive dental work.

Alendronate — Alendronate (Fosamax®) reduces vertebral and nonvertebral fractures, and decreases the loss of height associated with vertebral fractures. It is available as a pill that is taken once per day or once per week.

Risedronate — Risedronate (Actonel®) is approved for both prevention and treatment of osteoporosis. It can be taken once per day, once per week, or once per month. Risedronate reduces the risk of both vertebral and hip fractures.

Ibandronate — Ibandronate (Boniva®) can be used for prevention and treatment of osteoporosis. It is available as a pill that is taken once per day or once per month. It is also available as an injection that is given into a vein once every three months. Although ibandronate reduces the risk of bone loss and spine fractures, there is no proof that it reduces the risk of hip fractures.

Zoledronic acid — A once yearly intravenous dose of zoledronic acid (Reclast®) is also available for the treatment of osteoporosis. This medication is given into a vein over 15 minutes and is usually well tolerated. Yearly intravenous zoledronic acid can improve bone density, decrease the risk of spine and hip fractures, and decrease the risk of recurrent fractures in high-risk patients with recent hip fracture [1].

Side effects of zoledronic acid can include flu-like symptoms within 24 to 72 hours of the first dose. This may include a low grade fever, muscle and joint pain. Treatment with a fever-reducing medication (acetaminophen) generally improves the symptoms. Subsequent doses typically cause milder symptoms.

Intravenous zoledronic acid is an appealing alternative for people who cannot tolerate oral bisphosphonates or who prefer a once yearly to a monthly, weekly, or daily regimen. However, the ideal duration of therapy and long-term safety (>3 years) have not been established.

"Estrogen-like" medications — Certain medications, known as selective estrogen receptor modulators (SERMs), produce some estrogen-like effects in the bone. These medications provide protection against postmenopausal bone loss. In addition, SERMs decrease the risk of breast cancer in women who are at high risk. Currently available SERMs include raloxifene (Evista®) and tamoxifen. Raloxifene can be used for the prevention and treatment of osteoporosis in postmenopausal women, although it may be less effective in preventing bone loss than bisphosphonates or estrogen. (See "Patient information: Medications for the prevention of breast cancer (Beyond the Basics)".)

SERMs are not recommended for premenopausal women.

Estrogen/progestin therapy — In the past, estrogen or estrogen-progestin therapy was considered the best way to prevent postmenopausal osteoporosis and was often used for treatment. Data from the Women's Health Initiative (WHI), a large clinical trial, found that combined estrogen-progestin treatment reduced hip and vertebral fracture risk by 34 percent. A similar reduction in fracture risk was seen in women who took estrogen alone.

Estrogen had the additional advantage of controlling menopausal symptoms. However, the WHI found that estrogen plus progestin does not reduce the risk of coronary artery disease, and slightly increases the risk of breast cancer, stroke, and blood clots. The details of the WHI are discussed elsewhere. (See "Patient information: Postmenopausal hormone therapy (Beyond the Basics)".)

Thus, estrogen is not recommended for the treatment or prevention of osteoporosis in postmenopausal women. However, some postmenopausal women continue to use estrogen, including women with persistent menopausal symptoms and those who cannot tolerate other types of osteoporosis treatment, and those women are usually protected against bone loss and so do not need to consider additional drugs to prevent bone loss.

Estrogen may be an appropriate treatment for prevention of osteoporosis in young women whose ovaries do not make estrogen. This treatment may be given as a skin patch or orally, such as a birth control pill. (See "Patient information: Absent or irregular periods (Beyond the Basics)".)

Calcitonin — Calcitonin is a hormone produced by the thyroid gland that, together with parathyroid hormone, helps to regulate calcium concentrations in the body. Synthetic calcitonin

is sometimes recommended as a treatment for osteoporosis. Calcitonin may be administered via nasal spray or injection (subcutaneous salmon calcitonin). Nasal administration is typically preferred due to ease of use and because the injections tend to cause more nausea and flushing. (See "Calcitonin in the prevention and treatment of osteoporosis".)

Other drugs are usually recommended in preference to calcitonin because it is not clear if calcitonin improves bone other than the spine. However, due to its pain-relieving (analgesic) effects, calcitonin may be suggested as a first-line therapy for those who have a sudden, intense (acute) onset of pain due to vertebral fractures. The treatment regimen is typically changed once the acute pain subsides or if the pain fails to subside over a prolonged period (eg, four weeks).

Parathyroid hormone (PTH) — PTH is produced by the parathyroid glands and stimulates both bone resorption and new bone formation. Intermittent administration stimulates formation more than resorption. Clinical trials suggest that PTH therapy is effective in both the prevention and treatment of osteoporosis in postmenopausal women and in men.

A PTH preparation called Forteo®, given by daily injection, is approved for the treatment of severe osteoporosis for two years. It is more effective at building spine bone density and reducing spine fracture risk than any other treatment. Because it requires a daily injection and is expensive, it is usually reserved for patients with severe hip or spine osteoporosis (T score <-2.5 and an osteoporosis-related fracture). It is not recommended for premenopausal women.

Denosumab — Denosumab (Prolia®) is an antibody directed against a factor (RANKL) involved in the formation of cells that break down bone. Denosumab improves bone mineral density and reduces fracture in postmenopausal women with osteoporosis. It is administered as an injection under the skin once every six months. Although denosumab is generally well tolerated, side effects can include skin infections (cellulitis) and eczema. A mild transient lowering of blood calcium levels has also been reported, but this is not usually a problem in patients with good kidney function, who are taking enough calcium and vitamin D.

Because it is a new drug and there are no long-term safety data, denosumab is usually reserved for patients who are intolerant of or unresponsive to oral and/or intravenous bisphosphonates. Denosumab should not be given to patients with low blood calcium until it is corrected.

MONITORING RESPONSE TO TREATMENT

Testing may be recommended to monitor a person's response to osteoporosis therapy. This may include measurement of bone mineral density (DXA scan) or laboratory tests that indicate bone turnover (ie, rate of new bone formation and breakdown). (See "Patient information: Bone density testing (Beyond the Basics)".)

SUMMARY

- Osteoporosis causes bones to become abnormally thin, weakened, and easily broken. This
 condition can be treated and prevented with diet, exercise, and not smoking.
- Calcium and vitamin D can prevent and treat thinning bones. The main dietary sources of
 calcium include milk and other dairy products, such as cottage cheese, yogurt, or hard cheese,
 and green vegetables, such as kale and broccoli (table 1). Milk is a primary source of dietary
 vitamin D, containing approximately 100 international units per 8 oz (236 mL).

- Calcium and vitamin D can also be taken as a supplement (eg, in a pill) (table 2). A total of at least 1000 mg of calcium per day (total diet plus supplement) is recommended for premenopausal women and men. Women after menopause should consume 1200 mg calcium per day (total diet plus supplement). Experts also recommend 800 international units (IU) of vitamin D each day for men over 70 years and postmenopausal women, and 600 international units daily for younger men and premenopausal women.
- Exercise can help to prevent and treat thinning bones. Exercise should be done for at least 30 minutes three times per week. Any weight-bearing exercise regimen is appropriate (eg, walking).
- Smoking cigarettes can cause bones to become thinner and weaker. Stopping smoking can reduce this risk.
- Falling can cause fractures in the elderly. Preventing falls can lower the risk of fractures.
- Some medications can cause bone thinning. Such medications include glucocorticoid
 medications (eg, prednisone), heparin, and certain antiepileptic drugs (eg, phenytoin,
 carbamazepine, primidone, phenobarbital, and valproate). Patients should ask their healthcare
 provider about the possibility that these medications should be replaced or the dose lowered.
 (See 'Medications' above.)
- There are several medications that help **prevent** osteoporosis in women after menopause. We think alendronate (Fosamax®), risedronate (Actonel®), or raloxifene (Evista®) are the best medications for prevention. (See 'Bisphosphonates' above.)
- Alendronate (Fosamax®) or risedronate (Actonel®) are recommended to treat women after menopause who have osteoporosis. (See <u>'Bisphosphonates'</u> above.) Zoledronic acid (Reclast®) or raloxifene (Evista®) may be suggested for patients who cannot tolerate oral bisphosphonates, or who have difficulty taking the medication, including an inability to sit upright for 30 to 60 minutes.
- Denosumab (Prolia®) improves bone density and reduces fracture in postmenopausal women with osteoporosis. It is another option for patients who are intolerant of or unresponsive to oral and/or intravenous bisphosphonates. (See 'Denosumab' above.)
- Parathyroid hormone (Forteo®) is another medication that can be used to treat osteoporosis.
 We recommend this medication for men or postmenopausal women with severe hip or spine osteoporosis. (See <u>'Parathyroid hormone (PTH)'</u> above.)
- Hormone replacement (eg, estrogen, progesterone) is not usually recommended to prevent osteoporosis in women after menopause. Hormone therapy is recommended for young women whose ovaries do not make estrogen normally. (See 'Estrogen/progestin therapy' above.)
- Testing may be recommended to monitor how the bones respond to osteoporosis treatment. This may include a bone density scan (DXA) or laboratory tests. (See <u>"Patient information: Bone density testing (Beyond the Basics)"</u>.)

WHERE TO GET MORE INFORMATION

Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our web site (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient information: Osteoporosis (The Basics)

Patient information: Menopause (The Basics)

Patient information: Calcium and vitamin D for bone health (The Basics)

Patient information: Vitamin D deficiency (The Basics)
Patient information: Bone density testing (The Basics)

Patient information: Exercise (The Basics)

Patient information: Primary hyperparathyroidism (The Basics)
Patient information: Paraplegia and quadriplegia (The Basics)
Patient information: Aseptic necrosis of the hip (The Basics)

Patient information: Hip fracture (The Basics)

<u>Patient information: Vertebral compression fracture (The Basics)</u> Patient information: Medicines for osteoporosis (The Basics)

Patient information: Monoclonal gammopathy of undetermined significance (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient information: Bone density testing (Beyond the Basics)

Patient information: Calcium and vitamin D for bone health (Beyond the Basics)

Patient information: Postmenopausal hormone therapy (Beyond the Basics)

Patient information: Nonhormonal treatments for menopausal symptoms (Beyond the Basics)

Patient information: Exercise (Beyond the Basics)

Patient information: Quitting smoking (Beyond the Basics)

Patient information: Medications for the prevention of breast cancer (Beyond the Basics)

Patient information: Absent or irregular periods (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

The use of bisphosphonates in postmenopausal women with osteoporosis

Calcitonin in the prevention and treatment of osteoporosis

Calcium and vitamin D supplementation in osteoporosis

Clinical manifestations, diagnosis, and evaluation of osteoporosis in men

Clinical manifestations, diagnosis, and evaluation of osteoporosis in postmenopausal women

Evaluation and treatment of premenopausal osteoporosis

Metabolic bone disease in inflammatory bowel disease

Metabolic bone disease in primary biliary cirrhosis

Overview of the management of osteoporosis in postmenopausal women

Pathogenesis of osteoporosis

Postmenopausal hormone therapy in the prevention and treatment of osteoporosis

Screening for osteoporosis

Treatment of osteoporosis in men

Use of biochemical markers of bone turnover in osteoporosis

The following organizations also provide reliable health information.

National Library of Medicine

(www.nlm.nih.gov/medlineplus/healthtopics.html)

Osteoporosis and Related Bone Diseases National Resource Center

Toll-free: (800) 624-BONE (2663)

TTY: (202) 466-4315 (www.osteo.org)

National Osteoporosis Foundation

Phone: (202) 223-2226

(www.nof.org)

• National Women's Health Resource Center (NWHRC)

Toll-free: (877) 986-9472 (www.healthywomen.org)

• Osteoporosis Society of Canada

Phone: (416) 696-2663 x 294 (www.osteoporosis.ca/)

• The Hormone Foundation

(<u>www.hormone.org/public/osteoporosis.cfm</u>, available in English, Spanish, French, Italian, German, and Portuguese)

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Literature review current through: Oct 2013. | This topic last updated: Dec 17, 2012.

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