

BONE UP/date

OREGON OSTEOPOROSIS CENTER

Clinical Edition

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An Overview of Osteoporosis

What is Osteoporosis?

Osteoporosis is a disorder in which bone loss causes a gradual decrease in the strength of bone which becomes fragile and susceptible to fracture. During childhood and adolescence, calcium is deposited in bones as they grow. This process continues until peak bone mass is reached before age thirty. From then on, bone loss occurs gradually and progressively in both men and women for the remainder of our lives. In women, there is an acceleration of bone loss in the first few years after menopause. This period of more rapid bone loss is related to the deficiency of estrogen (female hormone) that occurs at that time, and is an important reason for the increased frequency of osteoporosis in women compared to men.

Osteoporosis can be due to an increased rate of bone loss which happens in adulthood, to a decrease in the amount of bone made during our growth years (low peak bone mass) or both. Peak bone mass is mainly determined by heredity. Individuals with a family history of osteoporosis frequently have lower than average bone mass as young adults. Peak bone mass may also be influenced by calcium intake and the amount of exercise during the growth years. Bone loss occurs when the amount of bone removed by bone dissolving cells (osteoclasts) exceeds the amount of bone formed by osteoblasts (cells that build new bone). After menopause in women and with aging in both men and women, the activity of osteoclasts increases; osteoblasts work harder but cannot keep up, and bone loss occurs. Many factors can influence the rate of bone loss. These include estrogen deficiency, calcium intake, level of physical activity, lifestyle factors such as the use of alcohol and tobacco, and a variety of medical problems which can interfere with bone health, including the use of prednisone and low male hormone levels in men. When we measure bone density, we determine the combined effects of peak bone mass and the amount of bone loss. Bone loss results in a decrease in bone density and destruction of the structure of bone. It is the loss of bone structure – not just the bone density value – that cause bone fragility and fractures.

Bone Density Testing

This is performed by a simple, painless procedure called DXA (dual energy x-ray absorptiometry). In this test, a low energy beam is passed through the bone in the spine, hip, or other skeletal site. The amount of x-ray that passes through is an accurate measurement of the calcium content of the bone. Bone density measurement can determine the presence and the severity of osteoporosis and can be used to predict the future risk of developing osteoporosis and fractures. Unfortunately, bone density testing does not give us information about the structure or quality of bone.

Bone density results are usually expressed as T-scores – a comparison to the average values in young adults aged 20-30. Healthy young women normally have T-scores between -2 and

+2. Postmenopausal women with values between -2 and -2.5 are said to have low bone density. Low bone density values do not necessarily mean that bone loss has occurred. They may be the result of lower than average peak bone density, perhaps as a consequence of inheritance. Values less than -2.5 are consistent with the diagnosis of osteoporosis. Before confirming the diagnosis of osteoporosis, other diseases that can cause low bone density (such as osteomalacia and multiple myeloma) must be excluded. The diagnosis of osteoporosis, when based on BMD, only applies to postmenopausal women – not to men, premenopausal women or persons with other types of bone diseases – because we do not know the relationship between BMD and fracture risk in these groups. Bone density testing can also be used to predict the likelihood (risk) that a person will experience a fracture related to osteoporosis. As BMD values decrease, fracture risk progressively increases (See Figure 1).

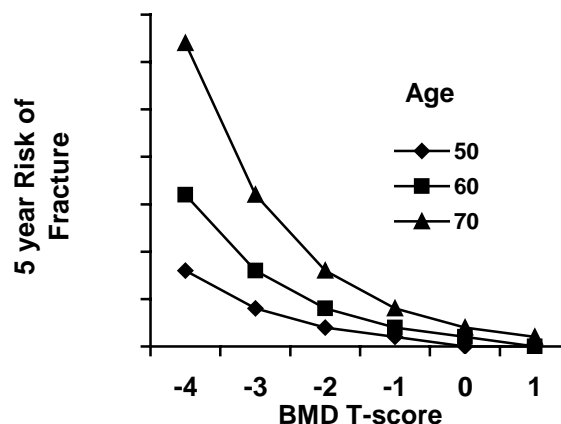


Figure 1. Relationship between bone density (BMD), age and fracture risk

Other risk factors such as age, body size and whether other fractures have occurred also influence fracture risk. If two women, ages 50 and 70, have exactly the same low BMD value, the older woman is more likely to have a fracture in the next 5 years. (Figure 1). Having a previous spine fracture increases the probability of fracture significantly. Thin women are at higher fracture risk than are heavier women.

We can also compare a bone density result with the values we expect in other women of the same age. Because of the bone loss seen with growing older, women over age 75 often have osteoporosis (T-score less than -2.5) despite the fact that their values are in the middle of the range expected for their age.

Who Should Be Tested?

BMD testing is important when the result will influence how the person is to be treated. Testing is most important in

those who are likely to have osteoporosis. This includes women who over age 65 and younger postmenopausal women who are thin (less than 127 pounds). Testing is also recommended in men and women over age 50 who have had a previous fracture, have a family history of spine or hip fracture, or have diseases known to have harmful effects on the skeleton. Because osteoporosis occurs very infrequently in healthy premenopausal women, and since they are not usually candidates for any of our current treatments even if BMD is low, testing is not recommended. Routine bone density screening is not recommended in healthy men younger than age 70

General Measures to Maintain Healthy Bones

The main objective of treating osteoporosis is to reduce the possibility of new fractures. This can be accomplished by preserving the strength of the skeleton and by reducing the frequency and effects of falls and other injuries.

1. *Adequate calcium and vitamin D intake:* Calcium is an important nutrient for preventing bone loss in adults. The older we become, the more important having enough calcium becomes. Vitamin D is necessary for the optimal assimilation of calcium. The recommended intake of calcium for adults is 1000-1500 mg per day, including both dietary calcium and supplements. For men and women over age 50, the recommended daily intake of vitamin D is 400 units (the amount in a multivitamin tablet) and is 600 units in women over age 70.
2. *Regular exercise:* Physical activity is an important component of a bone health program. Weight-bearing exercise may build larger, stronger bones in children. In older adults, regular exercise such as walking or dancing for 20-30 minutes a day will preserve muscle strength, improve balance and decrease the risk of falls that could result in fracture. It may also slow the rate of bone loss. Exercises that strengthen the muscles of the back are especially important for women with osteoporosis of the spine or with previous spinal fractures. These exercises can reduce pain and decrease the risk of another fracture. It is important to avoid activities that involve lifting with your back because injuries from this activity can result in new spine fractures. Instead of bending at the waist to lift, squat to pick up the object, and use your legs and bottom muscles to stand up.
3. *Avoid or stop smoking:* Smoking increases the rate of bone loss, especially in postmenopausal women, and is associated with an increased rate of fracture. The risk may go down when smoking is stopped.
4. *Correcting medical problems that promote bone loss:* These include over-treatment with thyroid hormone, use of prednisone, poor absorption of calcium or vitamin D, hyperparathyroidism, etc.
5. *Injury prevention:* Exercises to improve strength and balance, use of walking shoes with good gripping soles; using ambulatory aids when needed, using proper body mechanics and avoidance of falls.

Estrogen and Bone Health

The deficiency of estrogen at the time of menopause results in an increased rate of bone loss. Treatment with estrogen prevents bone loss in postmenopausal women, including older women with osteoporosis. Treatment for 5 years reduces the risk of spine and hip fracture. Studies evaluating the effective of estrogen treatment on fracture risk in women with osteoporosis have not been performed. For this reason, estrogen

is approved for the prevention of bone loss but not for treating women known to have osteoporosis.

In both younger and older postmenopausal women, lower dose estrogen is effective in preserving bone density. This is good news for women that are unable to tolerate the standard doses. Estrogen can be given in tablet form or through a patch placed on the skin. There are no differences in the bone effects among various forms of estrogen.

The main beneficial effect of estrogen is to control symptoms of menopause (hot flashes, night sweats, vaginal dryness). The previous hopes that estrogen therapy might decrease the incidence of heart disease, the risk of colon cancer and Alzheimer's disease have not yet been supported or proven in appropriate clinical studies. Some women experience mild side effects with estrogen therapy such as breast tenderness or menstrual bleeding. These symptoms can usually be controlled with proper adjustment of the dose. Estrogen also increases the risk of a form of cancer of the uterus, but this risk can be prevented by taking progesterone in addition to estrogen. There seems to be a slight increase in the risk of breast cancer in women who take estrogen for many years. Because of these risks and because we have other medicines to prevent bone loss, long-term use of estrogen is not recommended to prevent bone loss in women who do not have menopausal symptoms

Phytoestrogens (natural plant-derived estrogens) may have weak estrogen-like effects in the bone. While they may slow bone loss slightly in women beyond menopause, they are not strong enough to be considered as effective or attractive treatments for women with osteoporosis.

Pure progesterone has no effect on the skeleton and is certainly not an effective option for the treatment of women known to have osteoporosis.

Prescription Medications for Treating Osteoporosis

Six medications are currently approved by the FDA for the treatment of osteoporosis including alendronate, risedronate, ibandronate, raloxifene, calcitonin and teriparatide. The first five of these prescription medications work by turning down the activity of osteoclasts, the cells that dissolve old bone. Although bone density may increase with treatment, none of these drugs are true bone-building drugs. In contrast, teriparatide directly stimulates new bone growth. Each medicine is effective in reducing the risk of spine fractures and each has its own set of potential side effects and contraindications. Consequently, no single treatment is ideal for all patients.

Alendronate (Fosamax® {Merck})

This non-hormonal medication is a potent inhibitor of osteoclast activity and is the most extensively studied osteoporosis drug. It has been available for treating postmenopausal osteoporosis since 1995. It is also approved for treating men with low bone density. Treatment for three years increases spine bone density by 6-8% and hip bone density by about 5%. A significant reduction in both spine fractures (50%) and non-spine fractures (30-50%), including hip fracture, has been observed in women with osteoporosis. Treatment for up to ten years continues to be effective and has not been associated with significant safety concerns.

Risedronate (Actonel® {Procter & Gamble, Aventis})

This drug is in the same class of agents as alendronate and has been available since May 2000. Treatment for 3 years increases spine BMD by about 5% and reduces the risk of spine and hip fractures by 40-50% in women with osteoporosis. Fracture risk is reduced within the first year of treatment, and the effectiveness continues for at least five years. No safety concerns were seen with treatment for 7 years.

Ibandronate (Boniva® {Roche, GlaxoSmith Kline})

This bisphosphonate was approved in early 2005. Treatment for three years increased spine BMD by about 5% and reduce the risk of spine fractures by 53% in women with osteoporosis. No effect was observed on other fractures, although the study was not specifically designed to evaluate the effects of treatment on other fractures. Three years is the longest experience with the drug at this time. More recently, monthly oral dosing and an intravenous form of ibandronate became available. Three mg is administered by injection into the vein every 3 months. Flu-like symptoms (fever, muscle aches) that are usually mild happen infrequently with the oral monthly or intravenous doses.

The original studies with each of these drugs evaluated the effects of daily dosing. Both alendronate and risedronate can now be taken just once each week. Ibandronate is approved for use once each month. Weekly and monthly dosing appears to be as effective, equally or better tolerated but more convenient than is daily dosing.

Because bisphosphonates bind (stick) to food and even beverages such as coffee and juice, the drugs must be taken first thing in the morning with plain water at least 30 minutes before any food, beverage or other medications.

A possible side effect of both drugs is irritation of the esophagus resulting in heartburn or chest pain. This side effect occurs infrequently and is minimized by taking the drugs with a full glass (6-8 ounces) of water and not lying down for at least 30 minutes after the pill is taken.

Who should not take Actonel®, Fosamax® or Boniva®?

- Those with low blood calcium levels or significant deficiencies of calcium or vitamin D intake
- Patients with esophageal stricture or difficulty swallowing
- Individuals unable to remain upright after dosing
- Pregnant women (only rarely are these medications indicated for treating women before they reach menopause)
- Patients with seriously impaired kidney function.

Both alendronate and risedronate are approved for the treatment of men with osteoporosis, and both of these drugs are used to treat men and women with osteoporosis caused by glucocorticoid medicines like prednisone.

Raloxifene (Evista® {Lilly})

This drug is quite different from the previous two. It has estrogen-like effects in the bone while acting as an inhibitor of estrogen in the breast and uterus. It has been used for treating osteoporosis since 1999. Raloxifene treatment in women with osteoporosis for three years resulted in small increases (2-3%) in bone density of the hip and spine. The risk of vertebral (spine) fractures is reduced by 30-50%, but no effect on non-spine fractures has yet been observed with raloxifene treatment. This drug is usually used to treat women at increased risk for spine fracture but whose risk for hip fracture is quite low. Raloxifene is given as one tablet (60 mg) each day. The drug can be taken any time of day, even with meals. Therapy for up to four years has been well tolerated. Side effects include a worsening of hot flashes in some women, an increase in the frequency of leg cramps and a small but important increase in the risk of blood clots in the leg, lung or eye. (This is similar to the risk associated with estrogen therapy). Raloxifene treatment results in a moderate improvement in blood cholesterol levels, but whether the drug has an effect on reducing heart disease is not known. In older women with osteoporosis, the risk of breast cancer may be decreased as much as 60% with raloxifene treatment for four years. The effect of raloxifene on breast

cancer risk in younger women has not been adequately evaluated, and there is very little experience with the use of raloxifene in women who have previously had breast cancer. Raloxifene is not currently approved for the prevention of heart disease or of breast cancer.

Who should not take Evista®?

- Pregnant women (there is not a role for treatment of premenopausal women with raloxifene)
- Women with a previous history of blood clots should probably not take raloxifene

Calcitonin (Miacalcin® {Novartis})

Calcitonin is a naturally occurring non-estrogen hormone that regulates calcium metabolism. It has been used for treating osteoporosis since 1986. It was originally given as a daily injection. Since 1995, calcitonin has been available as a nasal spray, given as one spray (200 units) each day. It can be taken any time of day, including after meals. Treatment with calcitonin results in a very small (1-2%) improvement in bone density of the spine. No effect on hip density occurs. In the largest study with this drug, nasal calcitonin was shown to reduce the risk of spine fractures in women with severe osteoporosis. No effect of calcitonin therapy on the risk of other fractures has been observed. Our confidence in nasal calcitonin as an effective treatment for osteoporosis is less strong than it is with the other three drugs. Patients have been treated up to five years without significant side effects. Irritation or stuffiness of the nose sometimes occurs.

Who should not take Miacalcin®?

- Patients with low calcium levels
- Individuals known to be allergic to calcitonin

Teriparatide (Forteo® {Lilly})

Parathyroid hormone is a non-estrogen hormone that has an important role in calcium and bone metabolism. Teriparatide or TPT is an active form of parathyroid hormone. In November, 2002, the FDA approved TPT for the treatment of men and women with osteoporosis and high fracture risk. Unlike the other drugs, TPT stimulates the formation and growth of new bone tissue. In postmenopausal women with osteoporosis, treatment with TPT for 21 months increased bone density in the spine by 9%. The risk of spine fractures was reduced by 65%, and 53% fewer women had non-spine fractures. The study was too small to evaluate the effect of treatment on hip fracture risk. TPT is given once a day as an injection into the skin, like insulin treatment, at a dose of 20 mcg per day. Treatment will be given for up to 2 years. Whether PTH should be used in combination with other treatments has not yet been evaluated. Side effects (leg cramps, temporary small increase in blood calcium levels) are mild and infrequent. In rats, life-long treatment with high doses of TPT caused a form of bone cancer. No bone cancer has been seen in adults receiving TPT.

Who should not take Forteo®?

- Young adults or children
- Patients with other bone diseases like Paget's disease
- Individuals with have received high-dose radiation to the skeleton
- Patients with high blood calcium

Who Should Be Treated for Osteoporosis?

All older adults should receive adequate intake of calcium and vitamin D, exercise regularly and avoid habits harmful to bone (especially smoking). The goal of treatment with prescription medications is to reduce the risk of fracture,

although no treatment will prevent all fractures. Recent guidelines suggest treating patients at high to moderate risk for fracture. This includes adults with diseases that affect bone density, men and women with previous spine fractures and those with bone density values consistent with osteoporosis. Treatment may be considered in women with BMD values between -1.5 and -2.5 who have other risk factors for fracture (over age 70, previous non-spine fracture, thinness or a family history of hip or spine fracture). Prescribing osteoporosis drugs to treat women whose risk is low is not usually recommended.

What About Treating Osteopenia?

Osteopenia is a diagnostic category defined by the World Health Organization (WHO) as postmenopausal women with T-score values between -1 and -2.5. It was designed so that the distribution of BMD values could be compared among countries and races, but it was never intended to be a true clinical diagnosis that implied a state of poor bone health or that required treatment. Note that since T-scores from -2 to +2 are considered normal, osteopenia includes many people with normal BMD values. Since it is not a disease state and, except in elderly adults, is not associated with high fracture risk, most patients with osteopenia do not need to be treated with a prescription drug. General measures to prevent bone loss are indicated, and repeating the bone density test in 2-5 years can be helpful to monitor skeletal health.

Non-Drug Treatments

Hip protectors

Hip fracture almost always occurs when someone falls to the side and lands on their hip bone. Hip protectors are undergarments that include a protective pad sewn into the hip region. If a fall occurs, the energy of the fall is defused away from the hip, reduces the force of the fall on the hip and prevents an injury or fracture. Studies have shown that with regular and consistent wearing of the hip protectors, hip fractures are largely preventable.

Vertebroplasty and Kyphoplasty

A compression fracture of the spine results in deformity and loss of height of a vertebral body. This may cause severe back pain, height loss and forward curvature of the back (kyphosis). After several weeks, these fractures heal, but the deformity persists. Vertebroplasty is a procedure involving the injection of bone cement through a needle inserted into a recently fractured vertebra. The objective of treatment is to relieve the pain due to the fracture. Kyphoplasty involves inserting a small balloon into the middle of the fractured vertebra through a needle. The balloon is then inflated with fluid which restores the height of the fractured bone. The balloon is then deflated and removed, and bone cement is injected into the space left by the balloon.

Improvement of pain has been reported with both of these procedures, but the long-term outcome of these new treatments awaits more experience and follow-up of patients who have undergone the procedures. The most important unanswered question about either of these treatments is whether they effect the risk of having another spine fracture.

These procedures are most successful when performed by an experienced radiologist or surgeon. Neither vertebroplasty nor kyphoplasty is for everyone with a fracture. Patients with a recent vertebral fracture (within a few months), and who experience pain that is not responsive to standard treatment are the best candidates for these procedures.

Summary

We now have a very attractive menu of drugs that are able to prevent bone loss and to reduce fracture risk in men and postmenopausal women with osteoporosis. General measures

are appropriate for all postmenopausal women. Drug treatment should be strongly considered in all postmenopausal women and men with previous spine fractures since age 50 or who have osteoporosis by bone density testing. The specific indications for drug therapy to prevent osteoporosis are less clear. Having more drugs now available for the treatment of osteoporosis means that fewer patients will be excluded from therapy because of the side effects of any one medication. We encourage you to speak with your health care provider about which option is the best for you.

OREGON OSTEOPOROSIS SUPPORT GROUP

The Oregon Osteoporosis Support Group meets the 3rd Wednesday of each month. The objective of the program is to provide up to date and complete information and education about osteoporosis. Topics discussed include new treatments, the roles of nutrition and exercise, and strategies for improvement in symptoms and function. Call (503) 215-6151 for information and directions.

Interested in Clinical Research? To obtain information about our clinical research activities or to discuss participation in one of our clinical trials, please call our research recruitment coordinator at (503) 215-1731.

NOTE: The opinions expressed here are those of Dr. Michael McClung, the founding director of the Oregon Osteoporosis Center where consultation, diagnostic testing and clinical research activities are conducted. Dr. McClung is a board certified endocrinologist who has



been interested in bone and calcium metabolism for more than 25 years. During that time, he has published many articles and book chapters and has become a national expert in the fields of osteoporosis and bone density testing. Dr. McClung is a well-known speaker and educator, and is an active member of multiple international societies focusing on bone diseases and their treatment. He is an Associate Professor of Medicine at Oregon Health & Sciences University and an Assistant Director of the Department of Medical Education at Providence Portland Medical Center.

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CALCIUM AND VITAMIN D

Recommended Daily Calcium and Vitamin D Intake

	Calcium	Vitamin D
Adults ages 19-50	1000 mg	200 IU
Adults ages 51-70	1200 mg	400 IU
Adults over age 70	1200 mg	600 IU

Estimating Your Daily Calcium Intake

Daily Sources of Calcium Mg Intake

Daily dairy-free diet 300 mg

Dairy products** (300 mg x # of servings) ___ mg

Calcium fortified food ___ mg

Calcium supplements ___ mg

TOTAL DAILY CALCIUM INTAKE ___ mg

** Each dairy product serving (1 glass of milk, slice of cheese or cup of yogurt) contains about 300 mg

Frequently Asked Questions About Calcium

Which supplement is best absorbed? The main calcium supplements are the carbonate, citrate or phosphate salts of calcium. Calcium citrate is more predictably absorbed in older adults who lack stomach acid when the pills are taken on an empty stomach. All 3 calcium preparations are equally well absorbed when taken with food. We recommend that calcium carbonate be used first because it is less expensive and more efficient (fewer tablets have to be taken to get the same dose). If intestinal cramping or gas occurs, then switch to another form of calcium carbonate (Tums®, Viactiv® chewables), calcium citrate (Citrical®) or tricalcium phosphate (Posture®). Regardless of the supplement, no more than 600 mg of calcium should be taken at any one time. Patients taking Coumadin® (a blood thinner) should know that Viactiv® contains vitamin K that could interfere with the effect of Coumadin®.

How can I be sure that I am taking the right dose of calcium? Reading supplement labels can be confusing. Some products state plainly how many mg of calcium are in pill. Others state that taking 2 or 3 tablets daily will provide 1000 or 1200 mg of calcium. Other supplements describe the calcium intake in terms of the RDA (recommended daily allowance), and you must calculate the amount of calcium in each tablet. Here are some guidelines:

- Look for the % daily value or RDA
- Whatever the % is, add a "0" to find out how much actual calcium (elemental calcium) is in the serving. For example, if the nutrition facts on the label reads 50%, there is 500 mg of calcium per serving.

Do I need to take calcium tablets containing magnesium? While very severe magnesium deficiency interferes with

the control of blood levels of calcium, mild to moderate deficiency of Mg do not affect calcium absorption or assimilation. The results of the clinical studies showing the effectiveness of calcium have not included magnesium, and when Mg is added, there is no improvement in the outcome. Magnesium is available in a well-balanced diet or in a multivitamin with minerals.

Will taking calcium increase my risk of having kidney stones? No. In fact, adult men and women with intakes of calcium recommended for bone health have fewer kidney stones than do people on a low calcium diet. However, if you or a close relative have had a kidney stone in the past or a history of high blood calcium, discuss your calcium intake with your physician.

Do I have to take a calcium tablet that contains vitamin D? Although vitamin D is necessary for calcium assimilation, calcium and vitamin D do not have to be taken at the same time. The vitamin D has to be absorbed and activated before it stimulates calcium absorption. In other words, today's vitamin D supplement will absorb tomorrow's calcium. So, the two nutrients can be taken together or at different times of the day.

What interactions with other drugs does calcium have? Calcium can inhibit the absorption of both thyroid hormone and iron supplements. Simply take them at different times of the day to avoid the interaction. The cholesterol-lowering drugs like cholestyramine interfere with calcium and vitamin D absorption. Take the supplements at least 30 minutes before or 2 hours after the cholesterol resins. Calcium binds (sticks) tightly to some osteoporosis drugs like alendronate (Fosamax) or risedronate (Actonel) and inhibits the absorption and effectiveness of these drugs. Take Fosamax or Actonel in the morning, on an empty stomach and wait at least 30 minutes before breakfast or other food. Take your calcium supplements at the end of breakfast or at another meal.

Why do I need to consider estrogen or other drugs to prevent bone loss after menopause? Aren't I protected from losing bone if I eat enough calcium, exercise regularly and avoid habits like smoking? General measures like calcium, exercise and good habits are important for optimal bone health. However, the bone loss that occurs in the first 3-5 years after menopause in women is due to estrogen deficiency – not calcium deficiency. As a result, the general strategies do not completely prevent the bone loss that occurs in the first few years after menopause. For women with other risk factors for osteoporosis, and especially those who go through menopause early, bone density testing may be considered to determine whether treatment other than calcium, vitamin D and exercise is appropriate.

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