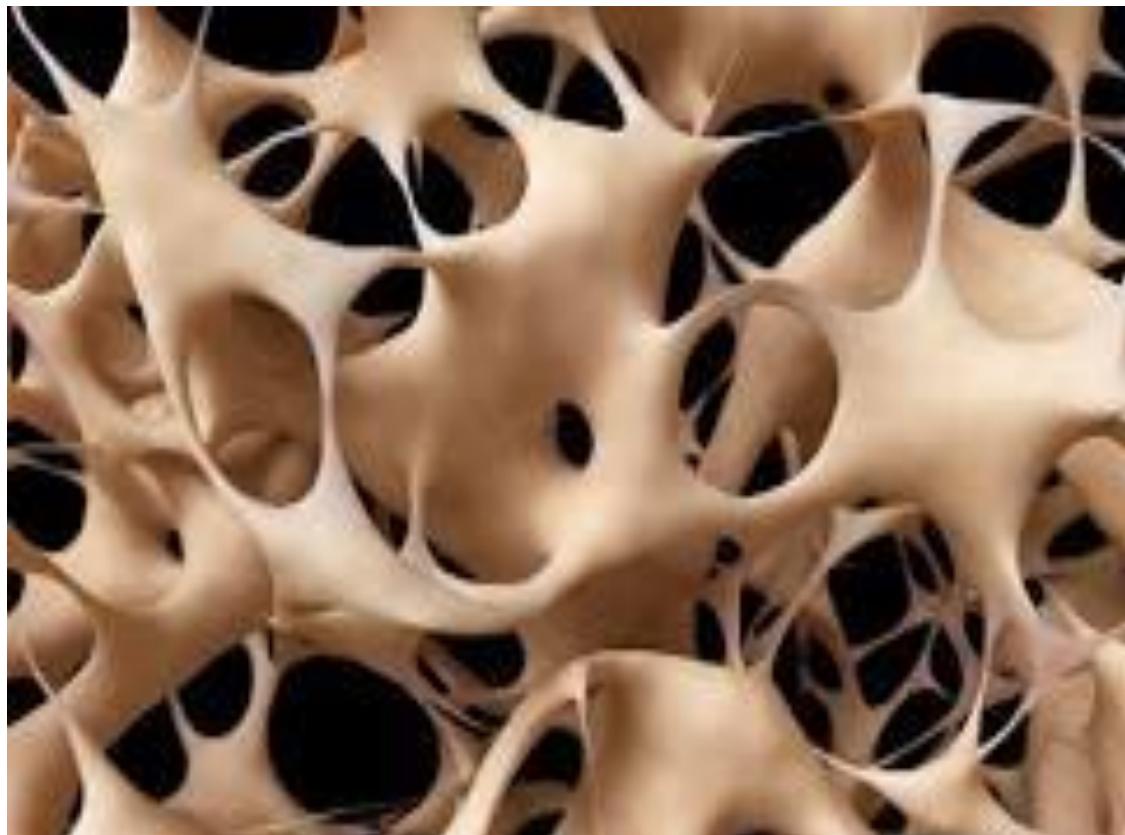


Osteoporosis- a health science research project



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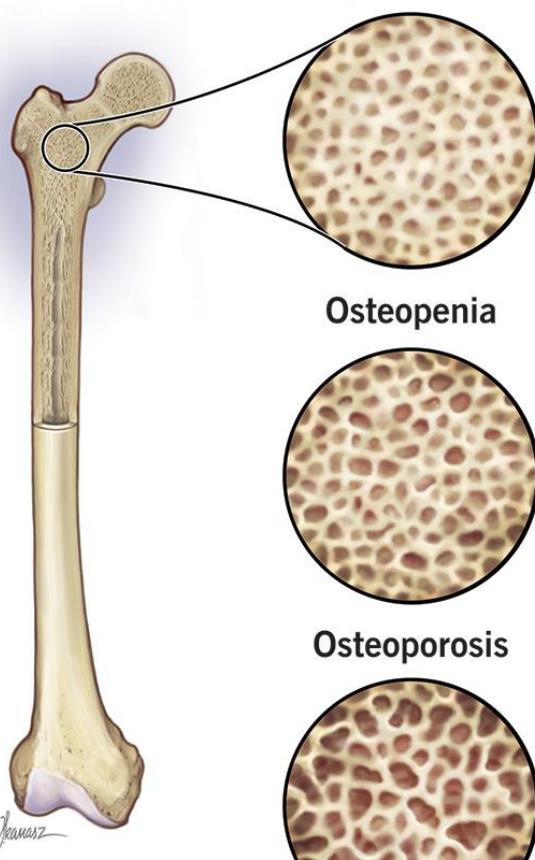
What is osteoporosis?

Osteoporosis causes bones to become weak and brittle. The bone mass is low and there is a deterioration of the bone tissue, which increase the risk of bone fractures. Osteoporosis-related breaks most commonly occur in the hip, wrist or spine.

Bone is living tissue that is constantly being broken down and replaced. Osteoporosis occurs when the creation of new bone doesn't keep up with the loss of old bone. Bones are in a constant state of renewal — new bone is made and old bone is broken down. When you're young, your body makes new bone faster than it breaks down old bone and your bone mass increases. After the early 20s this process slows, and most people reach their peak bone mass by age 30. As people age, bone mass is lost faster than it's created.

Osteopenia

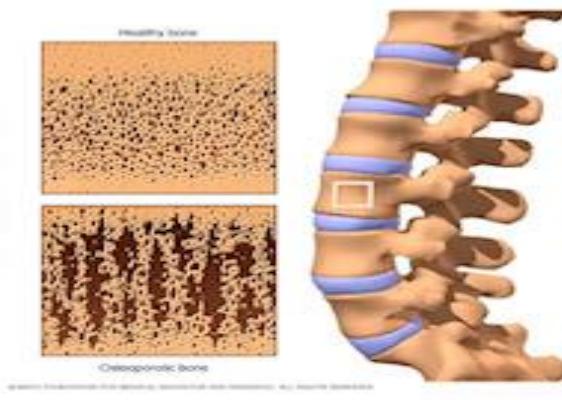
Healthy bone density



 Cleveland
Clinic
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Symptoms

How likely you are to develop osteoporosis depends partly on how much bone mass you attained in your youth. Peak bone mass is partly inherited and varies also by ethnic group. The higher your peak bone mass, the more bone you have "in the bank" and the less likely you are to develop osteoporosis as you age.



Osteoporosis weakens bone

Under a microscope, healthy bone has the appearance of a honeycomb matrix (top). Osteoporotic bone (bottom) is more porous.

Key Symptoms & Signs

Osteoporosis causes the bones to become porous, making them look and act like thin, hollow sponges. Osteoporosis affects men and women of all races. Postmenopausal women, especially those of Asian and Caucasian descent with slender frames, are at highest risk and face the most significant risk of developing the disease. Because osteoporosis lacks initial symptoms directly attributable to the condition, it is important to understand how it manifests in the earlier stages, to identify and slow the progression.

1. Hypotonia

While joints and connective tissue provide flexibility, muscles provide strength to move the body. In older adults with the condition, osteoporosis makes bones weaker and more prone to injury, which affects how the surrounding muscles work. Muscles can lose their ability to contract and become less toned. Low muscle tone or hypotonia leads to reduced strength, contributing to atrophy. Loss of muscle leads to lower lean body mass and less protection against external impacts, which leads to bones fracturing more easily.

2. Receding Gums

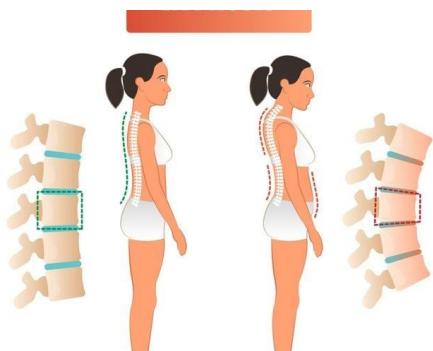
People usually think of osteoporosis affecting common fracture sites such as the hip and wrist, but the jawbone that anchors the teeth can also be impacted by this disease. Bone loss in the jaw leads to lose dentures, gums detaching from teeth, and periodontitis, an infection of the gum and bones. Studies show periodontitis has a stronger link to osteoporosis than previously thought. Some studies also suggest that low bone density increases the risk of periodontitis.

3. Weak Grip

Handgrip is one of the best ways to gauge muscle strength and can help doctors determine the impact of osteoporosis. A Korean study of postmenopausal women found a correlation between low bone mass density and handgrip strength. Specifically, doctors associate low grip strength in the dominant hand with reduced spine, neck, and hip bone mass densities.

4. Kyphosis

The abnormal convex curvature of the upper spine leading to hunched shoulders is kyphosis. In those with osteoporosis, kyphosis is the result of compression fractures of cervical and thoracic vertebrae; the symptom can cause sharp pain or none. Repeated breaks in this part of the spine cause the curve, resulting in height loss. If kyphosis becomes more severe, it can result in a significant bump at the base of the neck, called a dowager's hump.



5. Brittle Nails

Studies show that nails may indicate bone health, highlighting protein and mineral deficiencies that standard tests might miss. Bone and nails contain both the protein keratin and collagen type 1, which also forms the strong fibres found in ligaments and tendons. Tests done on nail samples from women with and without osteoporosis showed that nails from those with osteoporosis had 25 percent less keratin, making them weaker and less resilient.

6. Loss of Height

Most people expect to lose some height as they age. However, those who lose $\frac{3}{4}$ inch quite quickly, or a total of 2.5 inches since young adulthood may have osteoporosis. Fractures or breaks in the vertebrae can result in a decrease of up to 20% of vertical bone height. This process is called vertical compression, and it causes pain in addition to significant height loss.

7. Hearing Loss

The malleus, incus, and stapes are the three tiny bones in the middle ear that transmit sound. As people age, they become more susceptible to hearing loss, in part due to the degradation of these vital bones. Research suggests that those 50 years and older with osteoporosis are more at risk of acute sensorineural hearing loss. Doctors hypothesize that changes in the flow of calcium ions disturbs electrical balances in the ear, resulting in the loss of auditory cells.

8. Blindness

Osteoporosis-pseudoglioma is a rare genetic form of osteoporosis that leads to vision loss. A mutation in the LRP5 gene that assists with bone density and retinal development causes this symptom. Studies show that the mutation leaves eyes without a properly formed retina, resulting in children born with vision abnormalities and thinned bones.

9. Scoliosis

Scoliosis is the S-curve misshaping of the spine that results in a side-to-side shift or forward or backward bend. The condition is usually associated with children, but adult-onset scoliosis develops due to many factors, including weak bones. Adult-onset scoliosis is more likely to show up in women after menopause, as bone loss occurs. Scoliosis in adults can cause severe symptoms or no symptoms at all.

10. Fragility Fractures

Fragility fractures are the most common symptom of osteoporosis, occurring when weakened bones fracture from minimal trauma. These kinds of fractures happen during falls from standing height or lower. They can even happen from a bump, strain, or coughing; in some cases, this type of injury is the first indication of weakened bones. Data suggests that about 13 percent of men and 40 percent of women with osteoporosis will experience a fragility fracture in their lifetime. Men also have a higher rate of mortality from fragility fractures relative to women.

Risk factors

Several factors can increase the likelihood that you'll develop osteoporosis — including your age, race, lifestyle choices, and medical conditions and treatments.

Unchangeable risks

Some risk factors for osteoporosis are out of your control, including:

- **Your sex.** Women are much more likely to develop osteoporosis than are men.
- **Age.** The older you get, the greater your risk of osteoporosis.
- **Race.** You're at greatest risk of osteoporosis if you're white or of Asian descent.
- **Family history.** Having a parent or sibling with osteoporosis puts you at greater risk, especially if your mother or father fractured a hip.
- **Body frame size.** Men and women who have small body frames tend to have a higher risk because they might have less bone mass to draw from as they age

Other risk factors

Some health conditions can make you more likely to develop osteoporosis, including:

- Endocrine disorders — any condition that affects your parathyroid glands, thyroid gland and hormones (like thyroid disease and diabetes).
- Gastrointestinal diseases (like celiac disease and inflammatory bowel disease [IBD]).
- Autoimmune disorders that affect your bones (like rheumatoid arthritis or ankylosing spondylitis — arthritis that affects your spine).
- Blood disorders (or cancers that affect your blood like multiple myeloma).

Preventable risk factors

Medications

- **Diuretics** (medications that lower your blood pressure and clear extra fluid from your body). Thiazide diuretics are associated with increased bone mineral density and a reduced risk of certain fractures, particularly in individuals with acute clinical conditions such as new-onset stroke or spinal cord injury. They lower urinary calcium excretion, which may reduce bone resorption and slow bone loss. Long-term use has been linked to sustained improvements in bone mineral density at sites like the total body, legs, and forearm.
- **Corticosteroids** (medications that treat inflammation). Long-term use of oral or injected corticosteroid medicines, such as prednisone and cortisone, interferes with the bone-rebuilding process.
- **Medications used to treat seizures.** Anti-seizure medications (ASMs) are associated with an increased risk of osteoporosis and bone fractures in people with epilepsy, particularly with long-term use. Enzyme-inducing Antiseizure medications such as phenytoin (Dilantin), carbamazepine (Tegretol), primidone (Mysoline), and phenobarbital are most strongly linked to reduced bone mineral density. These

drugs accelerate the breakdown of vitamin D, impairing calcium absorption and weakening bones.

- **Hormone therapy for cancer** (including to treat breast cancer or prostate cancer). Hormone therapy for breast cancer significantly increases the risk of osteoporosis, particularly in postmenopausal women, due to oestrogen depletion. Aromatase inhibitors (AIs)—commonly used in postmenopausal women with oestrogen receptor-positive breast cancer—induce a hypoestrogenic state, leading to accelerated bone loss and a greater than twofold increased risk of osteopenia and osteoporosis. This risk is even higher with combined chemotherapy and Aromatase inhibitors therapy (up to threefold increased risk). In premenopausal women, tamoxifen can cause bone loss, especially when combined with chemotherapy, due to treatment-induced premature menopause. Ovarian suppression also causes a sudden drop in oestrogen, increasing fracture risk.
- **Blood thinners.** Warfarin and heparin, traditional blood thinners that interfere with vitamin K, are associated with an increased risk of osteoporosis and fractures, especially with prolonged use (over one year). This is because vitamin K is essential for activating proteins like osteocalcin that maintain bone strength. Warfarin's inhibition of vitamin K can lead to reduced bone mineral density and increased bone breakdown.
- **Proton pump inhibitors** (like those that treat acid reflux, which can affect your calcium absorption). Proton Pump Inhibitors (PPIs) like omeprazole are associated with an increased risk of osteoporosis and fractures, particularly with long-term use. While short-term use is unlikely to pose a significant risk, prolonged Proton Pump Inhibitors use—especially over several years—has been linked to lower bone mineral density, reduced bone quality, and higher rates of osteopenia and osteoporosis, especially in the femoral neck.

Surgical procedures that potentially can increase the risks of osteoporosis:

There are no surgical procedures that directly *cause* osteoporosis. However, certain surgeries can increase the risk of developing osteoporosis or worsen existing bone loss due to their impact on bone metabolism, mobility, or hormonal balance.

- **Gastrointestinal surgeries**, such as bariatric surgery (e.g., gastric bypass), can impair nutrient absorption, particularly calcium and vitamin D, which are essential for bone health. This can lead to secondary osteoporosis over time. Surgery to reduce the size of your stomach or to remove part of the intestine limits the amount of surface area available to absorb nutrients, including calcium. These surgeries include those to help you lose weight and for other gastrointestinal disorders.
- **Hysterectomy**, especially when performed before natural menopause, can lead to a sudden drop in oestrogen levels, accelerating bone loss and increasing osteoporosis risk.
- **Prostate cancer surgery (e.g., radical prostatectomy) or testosterone-lowering therapies** for prostate cancer can reduce testosterone levels, which play a role in maintaining bone density, thereby increasing fracture risk.

- **Long-term immobilization** following any surgery—especially spinal or joint surgeries—can lead to rapid bone loss due to disuse atrophy, increasing the risk of osteoporosis.
- **Transplant rejection drugs Glucocorticoids** and **calcineurin inhibitors** (such as cyclosporine and tacrolimus), which are essential for preventing organ transplant rejection, are major contributors to osteoporosis in transplant recipients.

More information regarding transplant rejection drugs:

- **Glucocorticoids** (e.g., prednisone) are strongly associated with rapid bone loss, particularly in trabecular bone (e.g., spine), and increase fracture risk even at low doses (as low as 2.5 mg/day prednisolone). They impair bone formation, promote osteoblast and osteocyte apoptosis, and reduce bone mineral density, with the most significant loss occurring within the first 6 months post-transplant.
- **Calcineurin inhibitors** (cyclosporine, tacrolimus) also contribute to bone loss through complex mechanisms, including indirect effects on vitamin D metabolism, secondary hyperparathyroidism, and dose- and duration-dependent bone resorption, despite their in vitro inhibition of osteoclast activity.

The risk of osteoporosis is higher in heart and liver transplant recipients compared to kidney transplant recipients, due to higher immunosuppressive doses and longer exposure. Post-transplant osteoporosis is a common complication, with fracture rates ranging from 8% to 65% in the first year. Prevention and management strategies include calcium and vitamin D supplementation, early steroid tapering, and use of bone-targeted therapies like denosumab, which has shown effectiveness in improving bone mineral density and reducing fracture risk in kidney transplant recipients, though it requires careful monitoring for complications like hypocalcaemia (abnormal low levels of calcium in the blood) and urinary tract infections.

It's important to note that while these surgeries may increase osteoporosis risk, osteoporosis itself is not a direct outcome of surgery, but rather a potential complication due to physiological changes or reduced activity post-surgery. Preoperative and postoperative bone health management is crucial to mitigate these risks.

Dietary factors

Diets that are high in processed foods, red and processed meats, excessive sodium, caffeine, and sugary beverages—particularly colas—can increase the risk of osteoporosis. These dietary patterns are associated with lower bone mineral density and a higher risk of fractures.

Key Dietary Factors Linked to Increased Osteoporosis Risk:

- **High sodium intake:** Promotes calcium loss through urine, contributing to bone weakening.

- **Excessive caffeine:** Consuming more than three cups of coffee daily may interfere with calcium absorption.
- **Cola consumption:** The phosphoric acid in colas may contribute to bone loss, especially when they replace calcium-rich beverages like milk.
- **Unbalanced Western diet:** High in refined grains, fried foods, sweets, and processed meats, this pattern is inversely linked to bone mineral density and increases fracture risk.
- **Low protein intake:** Inadequate protein can impair bone tissue maintenance, increasing fracture risk.
- **Low intake of bone-protective nutrients:** Diets lacking in **calcium, vitamin D, vitamin K, magnesium, and vitamin C** fail to support bone health. A lifelong lack of calcium plays a role in the development of osteoporosis. Low calcium intake contributes to diminished bone density, early bone loss and an increased risk of fractures.
- **Eating disorders:** Severely restricting food intake and being underweight weakens bone in both men and women.

Evidence from research:

- The **Western dietary pattern** has been consistently linked to lower bone mineral density and higher hip fracture risk in multiple studies, including the Framingham Offspring Study and Co-twin controlled studies.
- Diets high in **inorganic phosphorus** (common in processed food additives) disrupt calcium-phosphorus balance and harm bone health.
- A **low intake of fruits, vegetables, and dairy** reduces the intake of key nutrients like potassium, magnesium, and vitamin K, all of which are vital for bone strength.

Adopting a balanced diet rich in fruits, vegetables, low-fat dairy, fish, nuts, legumes, and whole grains—such as the Mediterranean or Asian dietary patterns—is protective against osteoporosis.

Lifestyle choices

Some bad habits can increase your risk of osteoporosis. Examples include:

- **Sedentary lifestyle.** People who spend a lot of time sitting have a higher risk of osteoporosis than do those who are more active. Any weight-bearing exercise and activities that promote balance and good posture are good for your bones, but walking, running, jumping, dancing and weightlifting seem particularly helpful.
- **Excessive alcohol consumption.** Regular consumption of more than two alcoholic drinks a day increases the risk of osteoporosis.
- **Tobacco use.** The exact role tobacco plays in osteoporosis isn't clear, but it has been shown that tobacco use contributes to weak bones.
- **Not spending enough time outdoors.** Not getting enough vitamin D, Vitamin D enhances intestinal calcium absorption (from 10-15% to 30-40% and helps regulate

parathyroid hormone, preventing secondary hyperparathyroidism. Deficiency leads to increased bone turnover, reduced bone mineral density, and higher fracture risk.

Hormone levels

Osteoporosis is more common in people who have too much or too little of certain hormones in their bodies. Examples include:

- **Sex hormones.** Lowered sex hormone levels tend to weaken bone. The fall in oestrogen levels in women at menopause is one of the strongest risk factors for developing osteoporosis. Treatments for prostate cancer that reduce testosterone levels in men and treatments for breast cancer that reduce oestrogen levels in women are likely to accelerate bone loss.
- **Thyroid problems.** Too much thyroid hormone can cause bone loss. This can occur if your thyroid is overactive or if you take too much thyroid hormone medicine to treat an underactive thyroid.
- **Other glands.** Osteoporosis has also been associated with overactive parathyroid and adrenal glands.

Medical problems

The risk of osteoporosis is higher in people who have certain medical problems, including:

- Celiac disease.
- Inflammatory bowel disease.
- Kidney or liver disease.
- Cancer.
- Multiple myeloma.
- Rheumatoid arthritis.

Complications

Bone breaks, particularly in the spine or hip, are the most serious complications of osteoporosis. Hip fractures often are caused by a fall and can result in disability and even an increased risk of death within the first year after the injury.

In some cases, broken bones in the spine can occur even if you haven't fallen. The bones that make up your spine, called vertebrae, can weaken to the point of collapsing, which can result in back pain, lost height and a hunched-forward posture.

How is osteoporosis diagnosed?

The outward signs of osteoporosis (height loss, easily broken bones, dowager's hump) combined with a patient's gender and age are strong signs that the patient has osteoporosis. A technology called dual X-ray absorptiometry (DXA) is the state-of-the-art technique for measuring bone mineral density (how much calcium is in the bones) and to diagnose osteoporosis.

The DEXA scan will return two different scores- a T and a Z score, which gives you information about the density of your bones.

T and Z scores explained

Both the T-score and the Z-score are comparisons of the bone density, with the average bone densities of different populations.

T-Score

A T-score compares your bone density to that of a healthy 30-year-old adult—the age when bone mass is typically at its peak. It is the primary measure used to diagnose osteopenia (low bone mass) and osteoporosis.

- **T-score ≥ -1.0 :** Normal bone density
- **T-score between -1.0 and -2.5 :** Osteopenia (low bone mass, increased fracture risk)
- **T-score ≤ -2.5 :** Osteoporosis (significantly reduced bone density, high fracture risk)

Each one-point decrease below 0 represents a 10–12% loss in bone density. **A T-score of -2.5 or lower indicates osteoporosis**, and the risk of fracture doubles with each standard deviation below normal.

Z-Score

A Z-score compares your bone density to the average of people your age, sex, and ethnicity. It is used to identify secondary causes of low bone density—such as underlying medical conditions or medications—especially in younger adults, premenopausal women, and men under 50.

- **Z-score ≤ -2.0 :** May indicate an abnormality requiring further investigation for secondary osteoporosis
- **Z-score between -1.0 and -2.0 :** Low bone density for age, but not necessarily pathological
- **Z-score > -2.0 :** Bone density is within the expected range for age

Z-scores are less useful for diagnosing osteoporosis in older adults, where T-scores are the standard. However, they help assess whether bone loss is more severe than expected for age and guide further testing.

What do T-score and Z-score results indicate?

A score 0 means that you have a bone density average relative to the group you are being compared against. A negative score represents your level of bone loss. A positive score would mean that you have a greater than average bone density.

What is a DEXA scan?

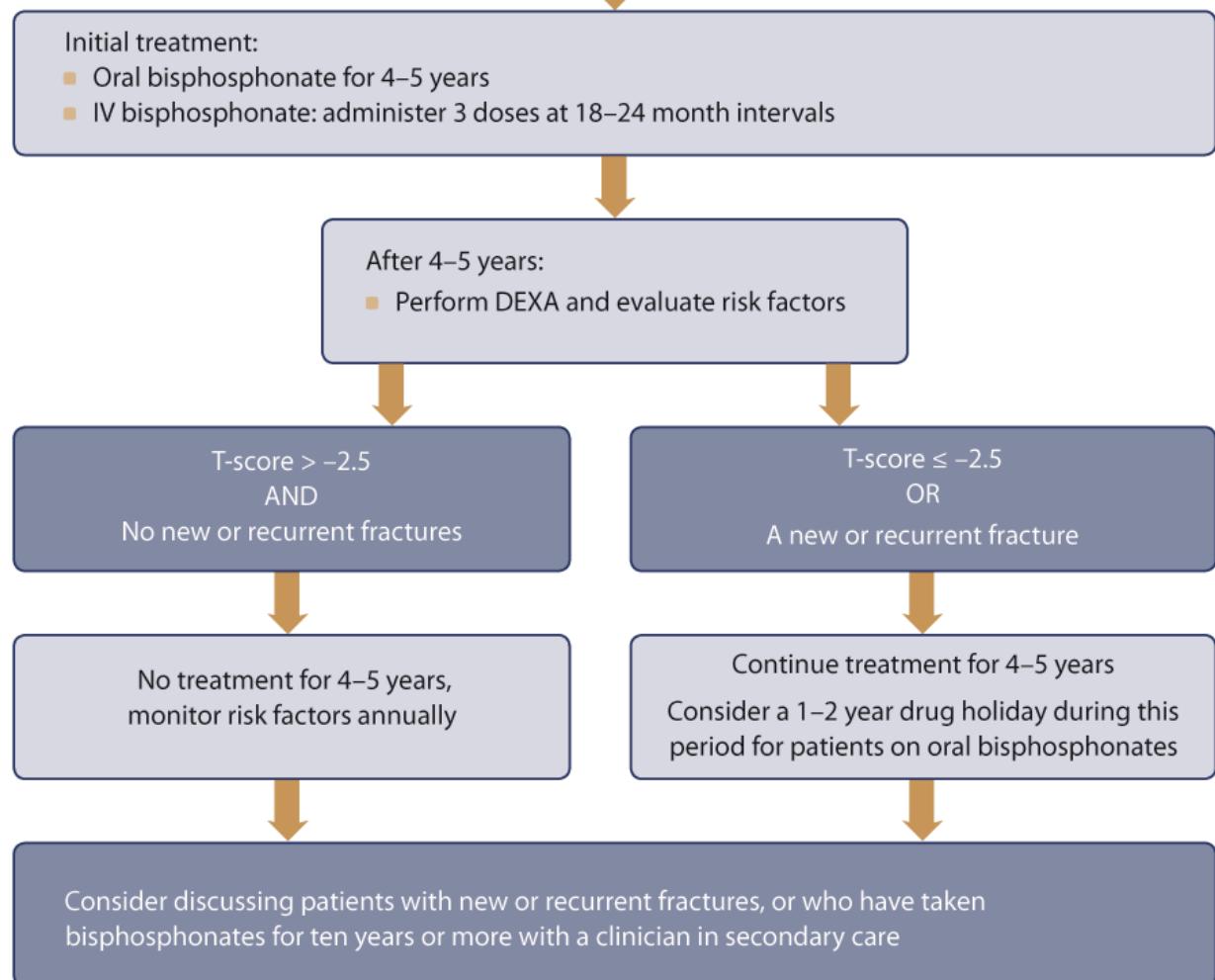
A DEXA (Dual-Energy X-ray Absorptiometry) bone density scan is a fast, painless, low-dose X-ray test that measures bone mineral density in your spine, hips, and sometimes wrist, to diagnose osteoporosis or osteopenia, assess fracture risk, and monitor bone health over time, comparing your results to healthy young adults (T-score) and age-matched peers (Z-score). It's the gold standard for early detection, helping doctors plan treatments to prevent fragile bones and serious fractures.



DEXA- scan

Bisphosphonate recommended based on:

- DEXA: T-score ≤ -2.5
- OR
- Fracture risk tool: hip fracture risk $\geq 3\%$ over ten years



Mainstream treatment

Bisphosphonates

Bisphosphonates help to treat osteoporosis and other conditions that affect the density and strength of the bones and for some conditions that cause very high blood calcium (hypercalcemia).

Bisphosphonates work by slowing down bone resorption. They help strengthen bones and prevent future bone fractures. They accumulate within bone tissue where they help

rebalance the remodelling cycle to increase bone mineral density. There is clear evidence that bisphosphonates reduce the incidence of fractures in people with osteoporosis.

Oral bisphosphonates:

Alendronate (Fosamax®), Risedronate (Actonel®), Ibandronate (Boniva®).

IV bisphosphonates:

Pamidronate (Aredia), Zoledronic acid (Reclast), Zometa.

What conditions do bisphosphonates treat?

- Osteoporosis in postmenopausal women or people assigned female at birth (AFAB).
- Osteoporosis in men or people assigned male at birth (AMAB).
- Osteoporosis prevention.
- Glucocorticoid-induced osteoporosis
- Cancer-related hypercalcemia.
- Paget's disease of the bone.
- Multiple myeloma.
- Cancer that has metastasized to your bones.

Other conditions.

- The treatment of osteogenesis imperfecta in children and adults.
- The prevention of glucocorticoid-induced osteoporosis.
- Fracture prevention in children and adults — due to having multiple risk factors for fracture such as chronic illnesses — and organ transplant candidates

New Zealand guidelines recommend that bisphosphonates should initially be taken for:

- Four to five years of alendronic acid or risedronate
- Three doses of zoledronic acid, at 18–24-month intervals

Key practice points:

- Ageing, genetics, menopause, nutrition, body fat, physical activity, co-morbidities and medicine use, e.g. oral or high dose inhaled corticosteroids can all influence bone health
- Clinical risk factors combined with a DEXA scan to assess bone mineral density, or a risk calculation tool can be used to assess a patient's risk of fractures.
- A ten-year risk of fracture of $\geq 3\%$ or T-score ≤ -2.5 at the hip is commonly used as a threshold for initiating treatment.
- Bisphosphonates are a first-line pharmacological treatment for people at high risk of fracture. The number needed to treat over three years to prevent one vertebral fracture is 14–20, and at least 91 to prevent one hip fracture.

- Initial treatment should be for four to five years with oral bisphosphonates (alendronic acid or risedronate) or a total of three infusions of zoledronic acid at intervals of 18–24 months
- Request a DEXA scan after this time to assess treatment efficacy and guide future management:
 - Patients at low risk of fractures could stop using bisphosphonates
 - Patients at high risk of fractures, such as with a T-score ≤ -2.5 or who have new or recurrent fractures, should continue treatment with bisphosphonates for another four to five years

Determining an appropriate duration of bisphosphonate use

There is sustained fracture prevention for three to five years of bisphosphonate treatment, however, the risks, albeit small of rare adverse effects increase with time. There is currently little evidence to guide prescribing decisions beyond five years of treatment with bisphosphonates, including the relative benefits and risks of re-initiating bisphosphonates after a "drug holiday", and no clinical trials have investigated use beyond ten years. The current state of evidence is likely to remain the case for some time.

Pros:

- All bisphosphonates have a high affinity for calcium and in the body, they concentrate in the skeleton at sites of active bone remodelling. Both classes of bisphosphonates become embedded in new bone during the anabolic phase of remodelling by binding to the hydroxyapatite (a naturally occurring mineral form of apatite) of bone, where they remain inert. When bone containing bisphosphonates that is resorbed, the bisphosphonates are released in the acidic lacuna created by the osteoclast and are taken up by these cells.
- Used for reduced bone density and inhibits bone resorption
- Good for acute fracture management in upper and lower extremity
- Bisphosphonates work by slowing down bone resorption. They help strengthen bones and prevent future bone fractures. They accumulate within bone tissue where they help rebalance the remodelling cycle to increase bone mineral density. There is clear evidence that bisphosphonates reduce the incidence of fractures in people with osteoporosis.
- Blocking the activity of osteoclast cells and thus decreases the breakdown of bone. As a nitrogenous bisphosphonate, zoledronic acid is a potent inhibitor of bone resorption, allowing the bone-forming cells time to rebuild normal bone and allowing bone remodelling.
- It works to prevent bone loss by blocking a certain receptor in the body to decrease bone breakdown. It works to treat Giant Cell tumour of bone by blocking a certain receptor in the tumour cells which slows the tumour growth. It works to treat high calcium levels by decreasing bone breakdown as the breakdown of bones releases calcium.
- It has an oestrogen-agonistic effect on bone, increasing bone mineral density and mass by decreasing bone resorption.

- Zoledronic acid has been found to have a direct anti-tumor effect and to synergistically augment the effects of other antitumor agents in osteosarcoma cells.
- Zoledronic acid has shown significant benefits versus placebo over three years, with a reduced number of vertebral fractures and improved markers of bone density. An annual dose of zoledronic acid may also prevent recurring fractures in patients with a previous hip fracture.
- Risedronate reduces the risk of vertebral and nonvertebral fractures by about 40%.
- Zoledronic acid reduces vertebral fracture risk by about 70%. It reduces the risk of hip fractures and other nonvertebral fractures by about 35%.
- Ibandronate reduces the risk of vertebral fractures by about 50%.

Cons:

- Long term use may develop atypical fractures and delay healing in fracture healing; evidence suggest that bisphosphates negatively influence healing.
- Common side effects include gastrointestinal issues, like reflux and oesophagus inflammation.
- Hives, rash, itching, difficulty breathing or swallowing, swelling of the face, eyes, throat, tongue or lips,
- Fever or chills
- Redness, tenderness, swelling or warmth of area of skin
- Fever, cough, shortness of breath
- Ear drainage or severe ear pain
- Frequent or urgent need to urinate, burning sensations when urinating
- Severe abdominal pain
- Painful or swollen gums, loosening of the teeth, numbness or heavy feeling in the jaw, poor healing of the jaw.
- Unusual bleeding or bruising
- Nausea, vomiting, headache, and decreased alertness after stopping denosumab and for up to 1 year afterwards.
- New or unusual thigh, hip, or groin pain
- There is currently little evidence to guide prescribing decisions beyond five years of treatment with bisphosphonates, including the relative benefits and risks of re-initiating bisphosphonates after a "drug holiday", and no clinical trials have investigated use beyond ten years. The current state of evidence is likely to remain the case for some time.
- Common side effects include fever, joint pain, high blood pressure, diarrhoea, and feeling tired.
- Serious side effects may include kidney problems, low blood calcium, osteonecrosis (death of the bone cells due to disrupted blood supply) of the jaw. Use during pregnancy may result in harm to the baby.
- Denosumab injection products may increase the risk: fractures of the thigh bone(s). Pain in your hips, groin, or thighs for several weeks or months before the bone(s) break, or you may find that one or both of your thigh bones have broken even though you have not fallen or experienced other trauma. May also cause broken bones to heal slowly. May impair bone growth and prevent teeth from coming in

properly in children. May also increase the risk of spinal fractures months to years after your treatment is discontinued. May cause other side effects.

- Raloxifene Adverse Effects: hot flashes, flu-like symptoms, muscle spasms, arthralgia, and infection. Less common effects are insomnia, vomiting, sinusitis, deep venous thrombosis (DVT), bronchitis, pharyngitis, breast pain. Raloxifene-treated women reported peripheral oedema

Although bisphosphonates can prevent further bone loss, they cannot reverse bone loss. Existing anti-osteoporotic drugs typically act by inhibiting bone resorption, promoting bone formation, and exerting a dual effect. Yet, most of these pharmaceuticals have fundamental limitations, such as targeting only one specific site and a tendency to cause side effects.

Percentage of people getting side effects from bisphosphonate use

The percentage of people experiencing side effects varies by type:

- **Gastrointestinal (GI) side effects:** These are the most common, including heartburn, nausea, and esophagitis. A meta-analysis found no significant increase in severe GI side effects with oral bisphosphonates compared to placebo (risk ratio = 1.01). However, non-severe GI events occurred in up to **54.9%** of patients in some studies, with once-weekly alendronate showing a higher risk (RR = 1.16) for non-severe events.
- **Acute-phase reactions:** These occur mainly with intravenous zoledronic acid or high-dose oral regimens, including flu-like symptoms (fever, fatigue, myalgia). Incidence ranges from **5% to 7.6%** depending on the drug and dosing.
- **Atypical femoral fractures (AFFs):** These are rare, occurring in approximately **1 in 10,000 to 1 in 100,000 patient-years**, with risk increasing slightly after prolonged use (>5 years).
- **Osteonecrosis of the jaw (ONJ):** Very rare in osteoporosis patients, estimated at **1 in 10,000 to 1 in 100,000 patient-years**, significantly lower than in cancer patients receiving high-dose IV bisphosphonates.

Overall, while side effects are reported, serious adverse events are uncommon, and the benefits of fracture prevention typically outweigh the risks for most patients.

Prevention of osteoporosis

- Focus on a healthy lifestyle with weight-bearing exercise,
- A diet rich in calcium and Vitamin D,
- Avoiding smoking and excessive alcohol.
- Maintain a healthy weight,

- Manage falls risk,
- Ensure adequate protein intake, with supplements considered if diet falls short, especially for older adults.

Diet & Supplements

Calcium: Aim for 1000mg/day (men 50-70) and 1200mg/day (women 51+, men 71+) through dairy, leafy greens, fortified foods, or supplements. The best way to get enough calcium every day is to eat a variety of healthy foods from all the different food groups. Getting enough vitamin D every day from foods like enriched milk or from natural sunlight is important to help the body absorb and use calcium from food. Essential for bone structure.

Calcium citrate is generally considered for osteoporosis, due to its superior absorption, especially in older adults or those with low stomach acid. It is also preferred over calcium carbonate if people take proton pump inhibitors or H2 blockers. Best to take this along with other supplements.

- Dairy (milk, yogurt, cheese)
- Leafy greens (kale, broccoli, collards, turnip greens, okra)
- Canned fish with bones (sardines, salmon)
- Fortified plant milks (soy, almond, oat) & juices
- Tofu, almonds, beans, sesame seeds

Vitamin D: Get adequate sun exposure; consider 800-1000 IU/day via fortified foods or supplements, especially after age 50. Getting about 5–10 minutes of exposure to sunlight 4–6 times per week can prevent vitamin D deficiency and therefore avoid the need for supplements. Vitamin D supplements such as colecalciferol, is usually reserved for frail older adults.

Vitamin D helps your body absorb to calcium. It can be found in:

- Fatty fish (salmon, mackerel, tuna)
- Egg yolks
- Fortified milk & cereals
- Sunlight exposure

Protein: Include meat, fish, beans, nuts, eggs, or dairy in meals.

It provides strength and flexibility (collagen). It can be found in:

- Meat, chicken, fish, eggs, dairy
- Legumes (lentils, chickpeas)
- Nuts, seeds, tofu

Other Key Minerals: Magnesium, Vitamin K, and Potassium (found in fruits, veggies, nuts) also support bone health.

Thomas Batram recommends:

Daily Vitamin A, B12 (50mcg), Vitamin C (500mg), Vitamin D, Vitamin E, Folic acid 200 (mcg), Vitamin B6 (50mg), calcium citrate 1g, Magnesium citrate (500mg), Boron, Zinc (15mg)

What to Limit or Avoid

- Excess Salt & Sugar: Diets high in these can negatively impact bone health.
- Processed Foods: Ultra-processed items can increase osteoporosis risk.
- Excess Alcohol: Heavy drinking harms bones.

A Bone-Healthy Diet Pattern

- Focus on Whole Foods: Emphasize fruits, vegetables, whole grains, lean proteins, and healthy fats.
- Mediterranean Style: Studies suggest this diet pattern can improve bone mineral density.
- Hydration: Drink plenty of water and calcium-fortified beverages



Key Components of an Osteoporosis Exercise Programme

A multi-component program is considered the gold standard for managing osteoporosis.

- **Weight-bearing/Impact-loading Exercises:** These activities work against gravity and stimulate bone formation in the hips, legs, and spine. Examples include brisk

walking, dancing, stair climbing, and low-impact aerobics. High-impact activities like jumping may be suitable for some low-risk individuals but require professional guidance.

- **Resistance Training:** This involves using weights, resistance bands, or body weight to build muscle strength and put beneficial stress on the bones. Targeting major muscle groups 2-3 times per week is recommended.
- **Balance Training:** Crucial for fall prevention, which is a major concern with osteoporosis. Exercises include single-leg stands, heel-to-toe walking, and Tai Chi.
- **Postural and Back Extensor Training:** Specific exercises to strengthen back muscles help improve posture and reduce the load on the spine, decreasing fracture risk.
- **Flexibility Exercises:** Gentle stretching can improve range of motion, but exercises involving forward bending of the spine or forceful twisting must be avoided.



Tai chi exercises

Specific programmes in New Zealand

Several evidence-based programmes are available in NZ under the supervision of qualified professionals:

Onero™ Programme: This is an evidence-based, high-intensity resistance and impact training programme specifically designed to prevent osteoporotic fractures by stimulating bone development and preventing falls. It is delivered in supervised small group sessions by licensed practitioners and generally requires two sessions per week.

Key Features of ONERO:

- **Evidence-Based:** Developed from research like the LIFTMOR study, demonstrating significant bone mineral density and functional improvements.

- **High-Intensity Loading:** Uses resistance and impact to create a stimulus that encourages bone growth, derived from the Latin word for "load" (Onero).
- **Supervised & Safe:** Requires initial assessment and small group classes (capped at 4 people) to ensure proper technique and safety, minimizing injury risk.
- **Focus Areas:** Targets bone density, muscle strength, balance, coordination, and reducing fall risk.
- **Structured Program:** Typically involves 1-2 sessions per week for long-term commitment, with online options also available.

Otago Exercise Programme (OEP): Developed in NZ, this program consists of 17 strength and balance exercises and a walking plan to be performed at home three times a week. It is highly effective for reducing falls in frail older adults.

- **What it is:** A structured, individualized program of 17 leg muscle strengthening and balance exercises, often using ankle weights, designed to be done at home.
- **How it works:** Prescribed and monitored by a trained physiotherapist, with progression as you get stronger.
- **Key Exercises:** Knee bends, calf raises, sit-to-stands, leg lifts, single-leg stands, heel-to-toe walking, and walking backwards/sideways.
- **Frequency:** Aim for 3 times a week for 30 minutes, plus walking on alternate days.

"Live Stronger for Longer" Classes: This is a New Zealand initiative that helps older adults find local, approved community strength and balance classes. You can search for a class using the Live Stronger for Longer website.

Core Principles

- **Strength & Balance:** Regular focus on leg and core strength and stability.
- **Fall Prevention:** The primary goal is to reduce the risk and impact of falls.
- **Consistency:** Aim for activity most days, even if short, and reduce sedentary time.
- **Adaptability:** Exercises should be suitable for your fitness level, with modifications for beginners.

PhysioFITT: A targeted activity program offered by various physiotherapy clinics in NZ to support people who are inactive due to health conditions like osteoporosis to begin exercising safely.

PhysioFITT is a personalized exercise program designed to help people overcome barriers to physical activity. It involves a structured approach to ensure exercises are appropriate for specific health conditions like osteoporosis and aims to:

- **Assess** individual needs and current fitness levels in an initial session.
- **Develop** a safe, progressive, and modified exercise plan over three follow-up sessions across 3-4 months.
- **Provide support** via email and phone throughout the program.

Recommended Exercises for Osteoporosis in NZ

Physiotherapists recommend a combination of exercise types to strengthen bones, improve muscle mass, and reduce the risk of falls and fractures:

- **Weight-Bearing Exercises:** These activities force you to work against gravity and are crucial for stimulating bone growth.
 - Brisk walking
 - Dancing
 - Stair climbing
 - Light jogging (if safe and approved by your healthcare provider)
- **Resistance Training:** This involves using weights or bands to build muscle strength, which puts tension on the bone, promoting strength.
 - Sit-to-stands from a sturdy chair
 - Wall push-ups
 - Band rows (squeezing shoulder blades)
 - Using free weights (bicep curls, shoulder presses) with proper form and supervision
- **Balance and Flexibility Exercises:** These are vital for fall prevention by improving coordination and stability.
 - Tai chi
 - Yoga
 - Single leg stands (near a counter for support)
 - Heel-toe walking

Buff Bones®: An internationally recognised medically endorsed system that blends Pilates, functional movement, and therapeutic strength training to support bone health.

- **What it is:** A medically endorsed movement system blending Pilates, functional movement, and strength training for bone and joint health.
- **Benefits:** Improves posture, alignment, balance, reduces pain, and builds muscle safely for osteoporosis.
- **Where to find it:** Offered at specialized clinics in NZ, such as BodyWorks Physio.

Lifestyle Factors

- **Quit Smoking:** Smoking accelerates bone loss.
- **Healthy Weight:** Avoid being too thin (BMI <19).
- **Fall Prevention:** Remove home hazards, use non-slip mats, get vision checked. Fall prevention exercises with a physio through ACC



Yoga stretches

Herbal science studies

The soybean (*Glycine max* L.) Epidemiological studies have shown that the consumption of food that contains soy may reduce the risk of fracture in postmenopausal women, particularly among those in the early years following menopause. Authors of several observational studies have noticed that populations with a high intake of soy are characterized with a lower incidence of osteoporotic fractures than Western populations.

To date, many clinical trials, systematic reviews, and meta-analyses have been carried out on this topic. Their results suggest that soy phytoestrogens exert significant effects on bone metabolism, and that they inhibit, to some degree, osteoporosis in postmenopausal women.

Phytoestrogen genistein given in the dose 54 mg daily for 1–3 years had positive effects on bone formation and osteopenia in postmenopausal women in several clinical trials. According to a randomized, placebo-controlled, double-blind study reported by Lappe et al., a lower dose of genistein administered for a shorter time (30 mg daily for 6 months) also prevented osteoporosis development and reduced fracture risk in postmenopausal women.

Red clover (*Trifolium pratense* L.) is often used to relieve symptoms of menopause, high cholesterol, and osteoporosis. Isoflavones: biochanin A, formononetin, and sissotrin, are responsible for its estrogenic activity. In intestines, biochanin A and formononetin are demethylated and metabolized to genistein and daidzein. The bone-preserving effects of red clover have also been examined, but not as extensively as those of soy.



Red clover

In a randomized, placebo-controlled study, an isoflavone preparation (Rimostil[®]) containing genistein, daidzein, formononetin and biochanin A was administered to 46 postmenopausal women in a double-blind protocol after a single-blind placebo phase and followed by a single-blind washout phase. A 6-month-long administration of an isoflavone combination extracted from red clover (57 mg/day or 85.5 mg/day) to postmenopausal females increased the bone mineral density of radius and ulna. In another clinical trial ($n = 205$), the red clover extract containing 41 mg isoflavone per tablet (Promensil[®]) ameliorated the decrease of bone mineral content and bone mineral density in lumbar spine in pre-, peri-, and postmenopausal women taking the supplement for 12 months. Authors also reported the elevation of bone formation markers.

In another 12-month, double-blind, parallel design randomised control trial, 78 postmenopausal osteopenic women were supplemented with calcium (1200 mg/day), magnesium (550 mg/day), calcitriol (25 mg/day) and given either red clover extracts rich in isoflavone aglycones and probiotics (Red clover extracts, 60 mg isoflavone aglycones/day and probiotics) or a masked placebo. Red clover extracts intake combined with supplementation (calcium, magnesium, and calcitriol) was more effective than supplementation alone. Twice daily red clover extracts intake over one year prevented a menopause-associated decrease of bone mineral density normalizing bone turnover, promoting a favourable oestrogen metabolite profile (2-OH:16 α -OH), and stimulating equal production in postmenopausal women with osteopenia.

Thorup et al. found that the intake of 150 mL red clover extract containing 37.1mg isoflavones for 12 weeks improved bone health in menopausal women ($n = 60$). The conclusions were based on bone mineral density and T-score at the lumbar spine and plasma CTX (C-terminal telopeptide of type I collagen. – this measures bone reabsorption). levels. However, a review of the potential skeletal benefit of red clover concluded that there was limited evidence of efficacy. For example, in a placebo-controlled 3-year trial in 401 women with a family history of breast cancer, 40 mg of red clover produced no effect on the bone mineral density.

In another study with perimenopausal women ($n = 250$), when taking two tablets per day containing red clover extract (28.6 mg or 41 mg isoflavones) for 12 weeks, no significant differences in bone turnover markers were observed compared to placebo.

Although the evidence is limited, it appears that red clover isoflavones may have a beneficial effect on bone mineral density in peri- and postmenopausal women.

Alfalfa (*Medicago sativa* L.) Alfalfa, is a known source of phytoestrogens, including spinasterol, coumestrol, coumestan, and ipriflavone. As mentioned above, the meta-analysis of 63 controlled trials investigating 6427 postmenopausal women revealed that ipriflavone (600 mg/day) is a promising molecule for the prevention and treatment of postmenopausal osteoporosis. Ipriflavone has been reported to induce osteoblast proliferation and prevent menopause-related bone loss.



Alfalfa

Epimedium (*Epimedium grandiflorum*) The traditional Chinese medicinal herb Epimedii has been utilized for centuries to treat bone fractures, bone loss, and menopause-associated disorders. The results of recent clinical trials have reported suggest that compounds or extracts of Epimedium may prevent or delay the onset of osteoporosis and reduce the risk of hip fractures. Icariin is a prenylated flavonol glycoside isolated from Epimedium herbs and has been shown to be the main bioactive component. In clinics, Epimedium is used to treat osteoporosis, climacteric period syndrome, breast lumps, hypertension, and coronary heart disease.



Epimedium

Hops (*Humulus lupulus L.*), hops extract is known for containing phytoestrogen components and exerting oestrogenic effects. In general, compounds of the oestrogenically active fraction of lupulin gland secretion belong in the following prenylflavonoids: xanthohumol, being the most abundant prenylflavonoid in hops, izoxanthohumol, 6-prenylnaringenin and 8-prenylnaringenin. Moreover, 8-prenylnaringenin has stronger oestrogenic properties than soy phytoestrogens. Ban et al. reported that hop extract Lifenol® prevented osteoporosis development in ovariectomized rats. Hop extract ameliorated the ovariectomy-induced decreased of bone mineral density, femur weight, and bone mineral content. Additionally, it restored the trabecular structure of calcaneus bone and inhibited ovariectomy-induced osteoclast activation. A mild osteoprotective effect of hop extract was also reported by other authors.



Hops

Horsetail (*Equisetum arvense L.*) It contains abundant constituents that may exert beneficial effects on bone health, e.g., silica, flavonoids, and triterpenoids.



Horsetail

The only clinical study evaluating the effectiveness of horsetail in the treatment of perimenopausal osteoporosis recruited 122 women in menopause for at least two years, who had not undergone oestrogen replacement therapy or drug therapy for recalcification: 30 patients were administered with titrated dry horsetail extract for 80 days; 31 patients were administered with placebo for 40 days and titrated horsetail extract for a further 40 days; 29 patients received no treatment whatsoever; 32 patients were treated with Osteosil Calcium for 80 days. All patients received two tablets per day according to procedures for randomized double-blind studies. Patients who received treatment with titrated horsetail extract after the period of placebo administration showed the same changes observed in patients treated with the active ingredient; treatment with titrated horsetail extract and with Osteosil Calcium improved bone metabolism and bone mineral density.

Additional herbal options

Withania: can help convalescence after illness or prolonged stress and enhance the immune function and for low white blood cell counts, amongst lots of other things.

They have adaptogenic and tonic effects, which are best suited to people who are debilitated or exhausted while agitated or under stress. It is used for nervous exhaustion, stress-induced health conditions, anaemia with emaciation, impotence with aging or due to stress, chronic inflammation depressed white blood cell count due to cytotoxic drugs and cognitive function deficits including those with aging and hypertension' (Sharon Tilgner)

Panax ginseng is used in this regard to restore strength when people have become physically exhausted or weakened. It is widely used by the elderly of the East. There is a deep appreciation of the herb's ability revitalise the life force and offset some of the tiredness and decline of getting old.

Thomas Batram recommends: Alteratives, Alfalfa, Black cohosh, Chamomile, Clivers- also known as Cleavers, Fennel, Dong quai, Fenugreek, Licorice, Meadowsweet, Mullein, Pimpernel, Helonias, Plantain, Rest Harrow, Shepherd's purse, Silverweed, Toadflax, Unicorn root.

Osteoporosis prescription David Hoffmann

- Vitex-agnus- castus 2 parts
- Equisetum arvense 1 part
- Avena sativa 1 part
- Urtica dioica 1 part

Dosage up to 5ml 3 times a day.

Herbal medicine findings on improvement on bone health

Chinese herbal medicine has demonstrated significant improvements in bone health, particularly in increasing bone mineral density. A 6-month clinical trial showed that XLGB, a multi-herb formula, improved lumbar spine bone mineral density by 2.11% in postmenopausal women, outperforming the control group.

Soy isoflavones have shown modest but notable benefits: a one-year study in postmenopausal Chinese women found that 80 mg/day of soy isoflavones provided mild protective effects on hip bone mass. In another study, 54 mg/day of genistein over 2 years significantly improved bone mineral density in the lumbar spine and femoral neck, matching the effects of hormone replacement therapy without adverse uterine or breast effects.

Icariin, a compound derived from *Epimedium* species, reduced bone loss in a 24-month trial, maintaining bone mineral density at 12 months and improving it in a time-dependent manner—though its effect was less potent than oestrogen or bisphosphonates.

Grape seed extract (GSE), rich in proanthocyanidins, enhanced osseointegration in ovariectomized rats, increasing bone-to-implant contact and improving implant stability, suggesting potential benefits in bone regeneration.

Overall, herbal interventions show measurable improvements in bone mineral density (1–2.11%) and bone turnover markers, with favourable safety profiles, particularly for genistein, icariin, and XLGB. However, results vary across studies, and larger, long-term trials are needed for definitive conclusions.

Herbal Medicine (HMs) Combined with Bisphosphonates (BPs)

A recent systematic review and meta-analysis of 35 randomized controlled trials involving 3,693 participants found that combining herbal medicines (HMs) with bisphosphonates (e.g., alendronate, ALE) led to greater improvements in bone mineral density (BMD) compared to bisphosphonates alone. Specifically, the combination therapy showed a 0.10 g/cm² increase in lumbar spine bone mineral density (95% CI: 0.07–0.12, $p < 0.001$) and 0.08 g/cm² at the femoral neck (95% CI: 0.05–0.12, $p < 0.001$), though evidence certainty was rated as very low due to high heterogeneity and risk of bias.

Key Findings by Subgroup

- Treatment Duration: In postmenopausal osteoporosis (PMOP), adding Herbal medicines to alendronate for ≤3 months resulted in significantly greater Bone mineral density gains at both the lumbar spine (0.13 g/cm²) and femoral neck (0.09 g/cm²) compared to alendronate alone. This benefit diminished at 6 months.

- Senile Osteoporosis: For older adults, combining Herbal medicines with alendronate for less than 3 months also improved Bone mineral density at the femoral neck (0.08 g/cm^2), with no added benefit seen at 6 months.
- Specific Herbal Formulations: The Xianlinggubao capsule (XLGB), one of the most studied herbal medicine showed a 0.08 g/cm^2 increase in lumbar spine bone mineral density (low certainty) and 0.11 g/cm^2 at the femoral neck (moderate certainty) when combined with alendronate. After excluding outlier studies, evidence quality improved to moderate certainty.

Biological Effects

The combination therapy was associated with favourable changes in bone markers:

- Increased bone formation
- Reduced bone resorption

Notably, in postmenopausal patients, both bone formation and resorption markers decreased, suggesting a balanced effect on bone remodelling.

Limitations

High heterogeneity across studies—due to variations in herbal medicine types, treatment duration, and osteoporosis subtypes—limited the strength of evidence. Sensitivity analyses reduced heterogeneity and improved certainty when outlier studies were excluded.

In summary, combining herbal medicine with bisphosphonates appears to enhance bone mineral density outcomes, particularly in the short term for post-menopausal osteoporosis, but results require cautious interpretation due to methodological limitations.

Constitutional medicine in osteoporosis

Osteoporosis isn't restricted to one particular constitution. But Christchurch medical herbalist Richard Whelan has found that over 90% of his patients with osteoporosis are of the EB (Elephant/ Butterfly- a cool/dry constitution). Although this group of patients often feel they need to cleanse, their biggest challenge in the healing cycle is nutrition and depletion. The signs compromised nail, skin and hair health. Their digestive fire can run too cool and dry; gentian can be a game changer in this case! Of course, their diet should not be overlooked, they need plenty of dairy (which this constitution can handle better than any other constitution), slow cooked meat, veggies, bone broth etc.

Liver support and gut health should not be overlooked whilst treating people with osteoporosis.

Legal challenges to osteoporosis medications (USA)



As of January 2026, litigation related to osteoporosis medications, particularly Fosamax (alendronate), remains active despite the closure of major multidistrict litigations. A U.S. appeals court revived over 500 Fosamax femur fracture lawsuits in September 2024, ruling that the FDA's rejection of a proposed label change did not pre-empt state law failure-to-warn claims, allowing these cases to proceed in New Jersey federal court.

As of October 2025, approximately 846 such lawsuits were awaiting legal processes, with the evidence-gathering phase currently paused.

- Fosamax Femur Fracture Lawsuits
- Osteonecrosis of the Jaw (ONJ) Lawsuits
- Legal Developments and Settlements
- Ongoing Risks and Medical Concerns: The FDA has issued warnings about the risks of atypical femur fractures and ONJ associated with bisphosphonates, including Fosamax, Actonel, Boniva, Reclast, and Atelvia. These drugs are now labelled with information about uncertain optimal treatment duration, reflecting ongoing medical debate about long-term use.

The Fosamax lawsuit raises questions about the drug's safety and potential side effects and seeks compensation for affected people.

Conclusion

The numbers don't lie; bisphosphonates can have a positive impact on bone mineral density. The positive effects of the bisphosphonates prescribed for osteoporosis outweigh the side effects.

When I started this research project, I was very biased in my opinion and thought that osteoporosis could be treated with just herbs and some exercise and that the pharmaceutical companies were the boogieman. Doing this project has opened my eyes and changed my opinion.

Until something better comes along, this condition needs treatment with allopathic medicine. We as herbalists can greatly support this process by supporting the digestive system, nutrition and protect the liver.

Since osteoporosis silently creeps in without too many symptoms, especially in the early stages, it is important for us as herbalists to be vigilant especially with our aging EB patients.

Of course, prevention is always better than cure when it comes to avoiding osteoporosis. But especially in Western society that is not an easy thing to achieve.

We need to eat well, but food also needs to be able to be digested- gut health is very important. We also need a healthy functioning liver, should do weightbearing exercises, and enjoy plenty of sunshine to our daily dose of vitamin D.

Resources

- Mayo clinic online
- Wikipedia online
- Merck manual of medical information, chapter 47, pages 218-220
- Fatty.com, Dianne Dixon, Reviewed By Kristie Leong, MD
- <https://www.medicalnewstoday.com/articles/what-is-the-safest-osteoporosis-drug#summary>
- Bisphosphonates (external link) New Zealand Formulary
- Bisphosphonates: addressing the duration conundrum (external link) BPAC, NZ, 2019
- Osteoporosis treatments and atypical femur fracture (external link) Medsafe, NZ, 2013
- Osteonecrosis: A Pain in the Jaw (external link) Medsafe Prescriber Update 33(2): 13-14 June 2012
- Osteonecrosis Of The Jaw And Bisphosphonates - Putting The Risk In Perspective (external link) Medsafe Publications, October 2007
- Reminder: Keeping an eye on bisphosphonates (external link) Medsafe Prescriber Update 32(3): 24 September 2011
- An update on bisphosphonates (external link) BPAC, NZ, 2014
- <https://versusarthritis.org/about-arthritis/treatments/drugs/bisphosphonates/>
- <https://my.clevelandclinic.org/health/treatments/24753-bisphosphonates>
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- <https://www.lezdotechmed.com/blog/fosamax-lawsuits/>
- Latest Osteoporosis News: Merck To Settle Fosamax Lawsuits, Bisphosphonates Deplete Antioxidants, Good News On Water Fluoridation, And More!
- <https://pmc.ncbi.nlm.nih.gov/articles/PMC8151026/>
- www.rjwhelan.co.nz
- Bartram's encyclopedia of Herbal medicine
- David Hoffmann – Medical Herbalism
- <https://search.brave.com/search?q=T+an+Z+scores+osteoporosis+meaning&source=web&summary=1&conversation=08a1708fb088003bb651c351156802563f90>
- <https://search.brave.com/search?q=surgical+procedures+that+can+increase+the+risk+of+osteoporosis&source=ios&summary=1&conversation=08a1caa54c31a04ea1430b7d188866945634>

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