UNDERSTANDING
Osteoporosis

A comprehensive guide brought to you by

GARVAN
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Please discuss any questions or concerns about your health, specific medical conditions or treatment options with your doctor.

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Osteoporosis is a very common disease that causes bone to fracture more easily than normal. Fractures caused by osteoporosis can cause long-term disability and are associated with early death. There is limited public awareness of osteoporosis and it is often called a silent disease because there are no symptoms until a fracture occurs.

Elderly men and women are most commonly affected by osteoporotic fractures. However, younger people with certain illnesses (such as anorexia nervosa) or who are taking certain medications (such as prednisone) can also be affected.

Osteoporosis is often confused with osteoarthritis, which is a different disease. Osteoarthritis is an inflammation of the joints causing joint stiffness and pain while osteoporosis is a symptomless thinning of the bones.

From 50 years of age, one in three women and one in five men will suffer a bone fracture due to osteoporosis (an osteoporotic fracture) in their remaining lifetime. In the over 60s this rises to half of all women and one third of men.

There are effective treatments for osteoporosis that can prevent fractures; but only a small proportion of people (less than 20% of women and 10% of men) who could benefit from treatment receive it.

The consequences of an osteoporotic fracture are extremely serious. Because of this, and the high frequency at which they occur despite the availability of good treatments, it is crucial that we have a greater awareness and understanding of the disease.

The Garvan Institute of Medical Research is at the forefront of world-wide research into osteoporosis. Garvan has made significant contributions to global knowledge about the disease both at the molecular level in the laboratory and also at the clinical level by observing large populations over time. Researchers at Garvan are part of a world-wide effort to decrease osteoporotic fractures and the suffering they cause.
What is osteoporosis?

“Osteo” comes from the Greek word for bone and “porosis” from the Greek word for “passage” or “cavity”. Osteoporosis is the medical term that describes bone that is porous and full of holes, and therefore more likely to fracture.

Normal bone has a hard mineral scaffolding with very small holes. In osteoporosis, the edges of the matrix break up leaving larger holes that cause the bone to become weak and prone to fracture.

People who suffer from osteoporosis can fracture even after only minor falls or bumps. In the worst cases of osteoporosis even a sneeze can break a bone. We call these fractures caused by osteoporosis “minimal trauma fractures” or “fragility fractures.” They are defined as fractures that occur after a fall or bump from standing height or less – a fall that would not cause the bone of a healthy young adult to break. It is these fractures that can be prevented.

As well as supplying a strong scaffold for our bodies and protecting our organs, our bones have many other functions. They provide attachment sites for muscles and also contain bone marrow, which produces blood and immune cells. The bone matrix is made up of a structural protein called collagen and other proteins which together provide a scaffold for a mineral salt made up of calcium and phosphate, “hydroxyapatite”. This mixture of protein and mineral salts makes bone as strong as iron and as light as wood. The grid of hydroxyapatite salts within the bone matrix is incredibly strong and remains for a long time following death. A human skeleton found in Rome is thought to be 4,500 years old.
Calcium is a critical component of bone and overall health. Bone needs calcium to form its hard matrix, but calcium is also required for optimal muscle and nerve function. In a healthy person, the blood calcium level is kept within a narrow range. If blood calcium gets too high or too low, the muscles and nerves will not function.

Bone plays a critical role by providing the body with a reservoir for calcium. Bone stores 99% of the body’s calcium and in times of need calcium is removed from bone and enters the blood. This is why it is so important to get enough calcium from food sources because the body will take calcium from bone to keep blood levels within a normal range.

We often think of bone as a hard static tissue but at the cellular level, it is really very dynamic. It is constantly being broken down and built up again. Bone is made up of many different types of cells that have different functions, but work together to maintain the delicate balance between bone break-down and bone build-up.

The most common type of cell in bone is called an osteocyte. Osteocytes are star shaped cells that are integral to bone remodelling. Osteocytes help to control the activity of cells called “osteoclasts”, which break down bone and cells called “osteoblasts” which build bone up. Every five to ten years, half of all the bone in your body has been replaced by this constant process of bone remodelling. This remodelling continues as long as we are alive.

The balance between the breakdown of bone and the way it is built up again is greatly influenced by age. As we age, more bone is broken down and there is less building up of bone. This imbalance leads to osteoporosis. Increasing age is the most significant risk factor for osteoporosis but it does not mean that osteoporosis is an inevitable part of ageing and fractures can still be prevented.

Older people often miss out on treatment for osteoporosis even though their risk of getting the disease is higher and the chance that they will benefit from treatment is also higher.

The process whereby bone is broken down by osteoclasts is called “resorption”. Some of the medications prescribed by your doctor to treat osteoporosis slow down the way osteoclasts break down bone. That is why these medications are called “anti-resorptive”; they stop the osteoclasts breaking down bone. The balance between the breakdown of bone and the building up of bone then favours the building of bone. Four of the most common forms of these drugs are alendronate, risedronate, zoledronic acid and denosumab.
Why is osteoporosis important

More than 1.3 million Australians over 60 could be living with osteoporosis, many without knowing it. It costs the Australian economy billions a year in direct and indirect costs, making it a common and costly disease.

Fractures in older people are serious and can change lives forever. They undermine independence by making tasks of everyday living difficult. Twelve months after a hip fracture 80% of elderly people are unable to do normal every-day tasks such as shopping and climbing stairs. This is one of the reasons why fractures, especially hip fractures, often lead to the need for nursing home care.

All osteoporotic fractures are associated with early death. This association is one of the findings of the large epidemiology study conducted by the Garvan Institute with the people of the NSW town of Dubbo since 1989.

Once you have had a fracture your risk of another one doubles if you are a woman and quadruples if you are a man. This means it is crucial that people who have a fracture are tested for osteoporosis and have the option of treatment. Currently only about 20% of those people who have had an osteoporotic fracture and who could benefit from treatment receive effective anti-osteoporosis therapy.

One in five men over 50 will have a fracture due to osteoporosis.
Any condition that makes it difficult to absorb calcium or vitamin D, like coeliac disease, can also affect young people.

Both men and women achieve their lifetime peak bone density, their best bones, by the time they are 30 and after that bone loss starts.

**Which bones can fracture with osteoporosis?**

Any bone can break with osteoporosis but the most common fractures occur in the hip, spine and wrist.

Hip fractures are one of the most serious fractures associated with osteoporosis. Almost every hip fracture is associated with a fall. Up to 40% of hip fracture patients over 60 are dead one year following the fracture and one third need long-term care such as in a nursing home.

Vertebral (spine) fractures do not heal the same way other bones heal and therefore can cause lingering pain. They can be the cause of loss of height, and a disfiguring curvature of the spine that is historically known as the “Dowager’s hump.” Only about a third of vertebral fractures are associated with a fall and many seem to happen with normal bending and lifting or are not noticed. If you have lost more than 3cm in height since your peak young adult height, you may have an undiagnosed vertebral fracture.

Wrist fractures heal, but sometimes ongoing pain and loss of function can make it difficult to carry out normal tasks.

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**How common is osteoporosis?**

Osteoporosis is extremely common. Half of all women over the age of 60 will have a fracture related to osteoporosis. Though osteoporosis is more common in women, it is still a very common condition in men. One in five men over 50 will have a fracture due to osteoporosis. The consequences of a fracture for men are often much more serious than for women. Men suffer more disability after fracture and there is a greater association with early death for men after a fracture than there is for women. Because osteoporosis is so often considered as a disease of elderly women, men are rarely investigated and only treated in very small numbers.

**Why is osteoporosis important for young people?**

Osteoporosis can also affect younger people, especially in association with certain illnesses and medications. Young women who are very underweight can have thin bones.
A bone mineral density test is needed for the diagnosis of osteoporosis. This test is painless and very much like an X-ray. It is a specific test that measures the amount of mineral within your bones, and is one of the best ways of working out your risk of fracture.

A bone mineral density test will give you a density score that will tell you if your bone density falls within the range of normal, low bone mass (osteopenia) or osteoporosis. A T score of -1.0 or above is normal, between -1.0 and -2.5 is considered osteopenia (lower than normal density but not yet osteoporosis) and a score of -2.5 or below is diagnosed as osteoporosis.

How do I get an osteoporosis test?

- Everyone over 70, men and women, can get a free bone mineral density test ordered by their doctor to see if they have osteoporosis.
- Anyone who has had a minimal trauma fracture, that is a fracture after a fall from standing height or less, is also eligible for a free bone mineral density test.
- You are also eligible for a bone mineral density test if you are taking certain medications such as prednisone and have diseases such as coeliac disease or overactive thyroid or parathyroid glands.
What are the risk factors for osteoporosis?

Age
The older you are, the higher the risk. If you are over 70 years of age a bone mineral density test to help diagnose the disease is covered by medical benefits. However, while osteoporosis is common in older people, it does not affect everyone.

Family history
Genes play a large part in osteoporosis so if your father or mother or a close relative had a low trauma fracture or osteoporosis your risk is higher.

Previous low trauma fracture
One fracture indicates the start of a cascade effect: once you have had one fracture, the likelihood of another fracture doubles in women and is three to four times more likely in men, especially in the first 5-10 years after fracture. This means it is particularly important to receive treatment for osteoporosis soon after a first fracture.

Gender
Being female increases your risk of osteoporosis. This is mainly due to the loss of oestrogen after menopause. Oestrogen is one of the hormones that help bones stay dense and strong. This risk for osteoporosis increases further in women who have an early menopause (when periods stop before the age of 45).

Osteoporosis is also a very common condition in men. The hormone testosterone keeps bone strong in men, but levels lessen with age. It decreases at a more gradual rate than oestrogen, which means osteoporosis is less common in men than women. However, the consequences of an osteoporotic fracture can be more serious for men, so it’s crucial men are also checked for osteoporosis.

Falls
If you have previous history of a fall, it is more likely that you will have a fall that results in a fracture. Unfortunately, some people become so afraid of breaking another bone that they become more sedentary, contributing to further loss of bone and muscle. Exercise such as walking or gentle weights, aimed at improving muscle strength and balance, are good exercises to prevent falls in the elderly.

Medications
Prolonged use of certain drugs such as prednisone or too much thyroid hormone replacement can increase your risk of osteoporosis. In these situations, your medical practitioner may recommend bone density tests.

Other diseases
Some diseases associated with greater risk of osteoporosis include: hyperthyroidism, hyperparathyroidism, intestinal malabsorption (i.e. coeliac disease or any disease that causes the intestine to absorb less calcium) as well as rheumatoid arthritis and autoimmune conditions where long term prednisone is required.
How can I check my risk for osteoporosis?

Know Your Bones is a free online tool developed by the Garvan Institute of Medical Research and Osteoporosis Australia that helps you to understand your own risk of bone fracture.

The Know Your Bones tool will take you approximately five minutes to complete. The tool collects information about your age, gender, weight or bone mineral density, history of fracture, history of recent falls, and lifestyle factors. You will receive a summary for further discussion with your GP, and if you are aged 50 and above the tool provides a personalised assessment of fracture risk over five and 10 years.

You can use this calculator at any time at knowyourbones.org.au

Arrange a test if there is osteoporosis in your family

As there is a strong genetic component to why certain people are at risk of getting osteoporosis, it is important that those who have a strong family history of osteoporosis have a bone mineral density test.

What can I do to help prevent osteoporosis?

Make sure you are getting enough calcium

Calcium is one of the building blocks of bone. If you don’t have enough calcium in your diet it can contribute to osteoporosis. As we get older we absorb less calcium and this is another reason why increasing age is related to an increasing risk of osteoporosis.

Unfortunately blood tests for calcium levels do not give us a good idea of whether you are getting enough calcium. The body keeps calcium blood levels at a very constant level because calcium is so important for many of the body’s organs. If calcium intake is low, the body will take extra calcium from bone to keep the blood levels within the normal range for optimal nerve and muscle function. Bone serves as a type of calcium bank for the body so if you don’t have enough calcium in your diet the “deposits” of calcium in your bone will become low.

Because calcium is so important for strong bone formation it is easy to see how anyone with gut diseases such as coeliac disease will have a higher risk of osteoporosis because they can’t absorb enough calcium from their diet to keep their bones strong. Also, a low vitamin D level will mean less absorption of calcium. Good amounts of calcium are found in dairy products, with...
three serves of dairy a day providing a healthy amount of calcium. Low fat versions of dairy products still contain the same amounts of calcium as the higher fat versions. Dairy products such as milk, cheese and yogurt, have the most calcium. Calcium in green leafy vegetables (such as watercress, okra, curly kale) is not so well absorbed as in other foods. Dried fruit (figs, apricots and currants), sardines and whitebait also contain useful amounts of calcium. Some foods such as sesame seeds and tahini contain calcium, however you would need to eat a great quantity to get a useful amount.

How much is a serve of milk*, yoghurt*, cheese* and/or alternatives?

A standard serve is (500–600kJ):

- 1 cup (250ml) fresh, UHT long life, reconstituted powdered milk or buttermilk
- ½ cup (120ml) evaporated milk
- 2 slices (40g) or 4 x 3 x 2cm cube (40g) of hard cheese, such as cheddar
- ½ cup (120g) ricotta cheese
- ¾ cup (200g) yoghurt
- 1 cup (250ml) soy, rice or other cereal drink with at least 100mg of added calcium per 100ml

The following foods contain about the same amount of calcium as a serve of milk, yoghurt or cheese:

- 100g almonds with skin
- 60g sardines, canned in water
- ½ cup (100g) canned pink salmon with bones
- 100g firm tofu (check the label as calcium levels vary)

* Choose mostly reduced fat

Have some sunlight exposure to get enough vitamin D
Direct sunlight provides us with 90% of our body’s vitamin D. While too much sun exposure increases the risk of skin cancers, some sun exposure, ideally outside the time when the sun is strongest (before 11:00am and after 2.00pm), is necessary for the body to manufacture enough vitamin D.

For most people, vitamin D deficiency can be prevented by 5–15 minutes exposure to direct sunlight on the face and upper limbs about six times per week. It does, however, depend on where you live: people in Queensland will need less exposure to direct sunlight than people in Tasmania in order to manufacture adequate vitamin D.

For some people and in some climates it is not possible to get out in the sun so taking vitamin D supplements is necessary. Adequate vitamin D is needed for the absorption of calcium and it is important to take both calcium and vitamin D supplements if either are low.

Stop smoking
There are many reasons to stop smoking, one of which is that it contributes to bone thinning. Heavy tobacco smoking, particularly current smoking, increases your risk of fragility fracture by 15-30%.

Avoid excessive alcohol
Excessive alcohol is also bad for bone and can also increase the likelihood of falls.

Prevent falls
Not all osteoporosis fractures occur because of a fall, but many do. The more falls you have, the more likely you are to have a fracture. Falls occur more frequently as we age because our reflexes slow down, making it harder to adjust to sudden changes.
in posture. Loss of muscle mass and strength as we get older also reduce our chances of managing a fall. Our sense of balance also deteriorates as we age. If you are less alert for any reason, including due to side effects of medications, this can increase your chance of falling. Other factors that increase the risk of falls are poor eyesight and unsafe objects in the home that people trip over.

To reduce the chance of a fall, you should stay active to maintain muscle strength, balance, and flexibility. You should have your vision and hearing checked regularly and corrected as needed and you should also discuss your medications with your doctor to see if any of them (or their combination) may increase the chance of a fall.

**Aim for a normal body weight**
Being too thin is bad for your health. Being underweight is a risk factor for osteoporosis for several reasons. Oestrogen is stored in fat, also fat can act as a shock absorber limiting the impact of falls. Thin people are more likely to fracture bones when they fall.

**Keep active with appropriate exercise**
For osteoporosis prevention, do exercises that strengthen your muscles. You can significantly reduce your risk of falling by activities that enhance your balance, flexibility, and strength. Walking and other weight bearing exercises are recommended. Any exercise that requires effort against gravity is good for your bones. While swimming may be a good exercise for your heart and lungs and muscles in general, it is not particularly good for osteoporosis because there is no effort against gravity. Having an active lifestyle throughout your entire life may help to maintain muscle and bone strength.

**Have your bones assessed by your doctor**
This is especially important if you have already had a low trauma fracture – a fall from standing height or a fracture that occurs without any fall at all. The chances of you having another fracture with minimal trauma are high, especially in the first few years after any fracture. This is the time when treatment may be particularly effective. If you have had a minimal trauma fracture you are entitled to a Medicare-reimbursed bone density scan to see if you have osteoporosis. You are also entitled to Medicare-reimbursed treatment. Your general practitioner is the best person to see for more information and a proper detailed assessment of what you might need.

**Ask your doctor about medications for osteoporosis**
Pharmacological treatments for osteoporosis have been shown in many studies to reduce the rate of fracture by 30 to 60%. Most osteoporosis medications work by slowing down the rate by which bone is broken down. All these medications are effective and your doctor will help you decide which is the best one for you depending on any other conditions or illnesses you may have.
BONE REMODELLING

Bone remodelling consists of a delicate balance of bone break-down and bone build-up that is orchestrated mainly by osteoclasts and osteoblasts. Osteoclasts are responsible for bone break-down and do this by pumping tiny charged particles called protons out into the osteoid matrix. The protons lower the pH, making it more acidic and dissolves minerals in the matrix and causes dents or pits on the bone surface. Osteoblasts then travel to these dents on the bone surface to lay down fresh bone. This process is beautifully coordinated because the osteoblast and osteoclast cells communicate with each other. They do this by way of "signalling molecules."

Bone has a much more flexible structure that contains many blood vessels. It is spongy and acts like a shock absorber. Cancellous bone is the type of bone that is affected earliest in most forms of osteoporosis.
Signalling molecules are substances secreted by one cell to affect or communicate with another cell. There are many different types of signalling molecules involved in bone remodelling – one important group is hormones. Hormones can be produced by cells within glands that exist a long way away from bone such as from the thyroid gland or the hypothalamus and pituitary gland in the brain. Also, hormones from the brain itself influence calcium metabolism and bone structure. One of the most powerful hormones that affects bone is oestrogen. Oestrogen actions on bone are complex but the major effect is to inhibit bone break-down. This action of oestrogen helps explain why the loss of oestrogen at menopause causes such a large decline in bone density.

Hormones travel through the blood stream and can reach the bone. However there are also local signalling molecules that are secreted by cells within the bone itself. Two of these local hormones, called RANK ligand and osteoprotegerin, are produced by osteoblasts to communicate with osteoclasts and they work together. In animal studies, increased production of osteoprotegerin leads to an increase in bone mass, while loss of osteoprotegerin leads to osteoporosis and increased fractures. The way in which hormones produced in bone communicate with the rest of the body is being studied at the Garvan Institute. This research has the potential to lead to new treatments.
Garvan is internationally recognised for its work in osteoporosis and has made significant breakthroughs in the understanding of this complex disease.

Garvan pioneered the discovery of the critical role of our genes in the development of osteoporosis. Our goal for the future is to build upon these key discoveries to develop new and more effective approaches to prevent and treat osteoporosis, as well as cancers that grow in bone and diseases of joints such as osteoarthritis.

Garvan is also committed to raising awareness of osteoporosis and evidence-based approaches to its prevention and treatment with the public and medical community.

**The Dubbo Osteoporosis Epidemiology Study**

Garvan’s Dubbo Osteoporosis Epidemiology Study is the longest running, large-scale epidemiological study of osteoporosis in men and women in the world. It focuses on identifying risk factors for fractures in both men and women as well as identifying new genes that are important to bone health.

Researchers at the Garvan Institute have been following what happens to people after they have a fracture in a large population in Dubbo since 1989.

From the results of this study there have been many significant findings that have shaped how we think about osteoporosis.

The Dubbo study found that the “cascade effect” (once you have one minimal trauma fracture you are much more likely to have more fractures) occurs after all types of fractures. The second fracture usually happens within five years after the first, which is another reason why it’s important to get treatment for osteoporosis as soon as possible.

Previously it was thought that only minimal trauma fractures of the hip and spine were associated with early death in the elderly. This long-term study has shown fractures of any bone are associated with increased mortality, even fractures of the wrist and, in fact, any fragility fracture.

The study has demonstrated that osteoporosis isn’t just a disease of elderly women. It occurs in men as well as women and a third of all fractures occur in men.

Researchers involved in the Dubbo study have tried to make it easier to find who is at highest risk of fracture and therefore in most need of treatment. The study has found other factors apart from bone mineral density contribute to your risk such as muscle strength and postural stability. So how strong you are and how steady you are on your feet matter in working out how likely you are to fracture and whether you require treatment.
Garvan’s contribution to osteoporosis and bone biology research in Australia and worldwide

1987 Demonstrated the strong heritability of bone density and osteoporosis risk

1989 Established the Dubbo Osteoporosis Epidemiology Study, now the world’s longest running large-scale epidemiological study of osteoporotic fractures in men and women

1992 Demonstrated that variation in the vitamin D receptor gene contributes to differences in bone density and susceptibility for osteoporosis

1993 Reported the first randomised control trial of prevention of bone loss in corticosteroid users

1999 Found that osteoporosis is not just a disease affecting elderly women – for every three fractures one occurs in men

1999 The first to demonstrate increased mortality risk following all major fractures and not just hip fractures

2002 Discovered that Neuropeptide Y (NPY) regulates bone synthesis

2008 Developed a web-based fracture risk calculator tool to predict an individual’s risk of bone fracture – now widely used by doctors and patients worldwide

2009 Identified Neuropeptide Y, acting within the brain and bone, as a mechanism matching bone mass to body weight

2011 Showed that the main effective treatment for osteoporosis extends survival by up to five years

2012 Identified nine new genes that contribute to bone strength

2016 Revealed that genetic profiling can help predict whether an individual will break a bone through osteoporosis

2017 Demonstrated a new therapeutic approach that can rebuild and strengthen bone, offering hope for individuals with the debilitating bone cancer, multiple myeloma.
Further reading

Osteoporosis Australia
osteoporosis.org.au

NPS National Prescriber Service
Osteoporosis how do I treat it?
nps.org.au/publications/consumer/medicinewise-living/2013/osteoporosis-how-do-i-treat-it

NHMRC National Health and Medical Research Centre
Preventing osteoporosis-related fractures from happening again.


Australian Institute for Health and Welfare
aihw.gov.au
Garvan's mission is to make significant contributions to medical research that will change the directions of science and medicine and have major impacts on human health.

Excellence
Innovation
Collaboration
Integrity
Respect
Passion

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