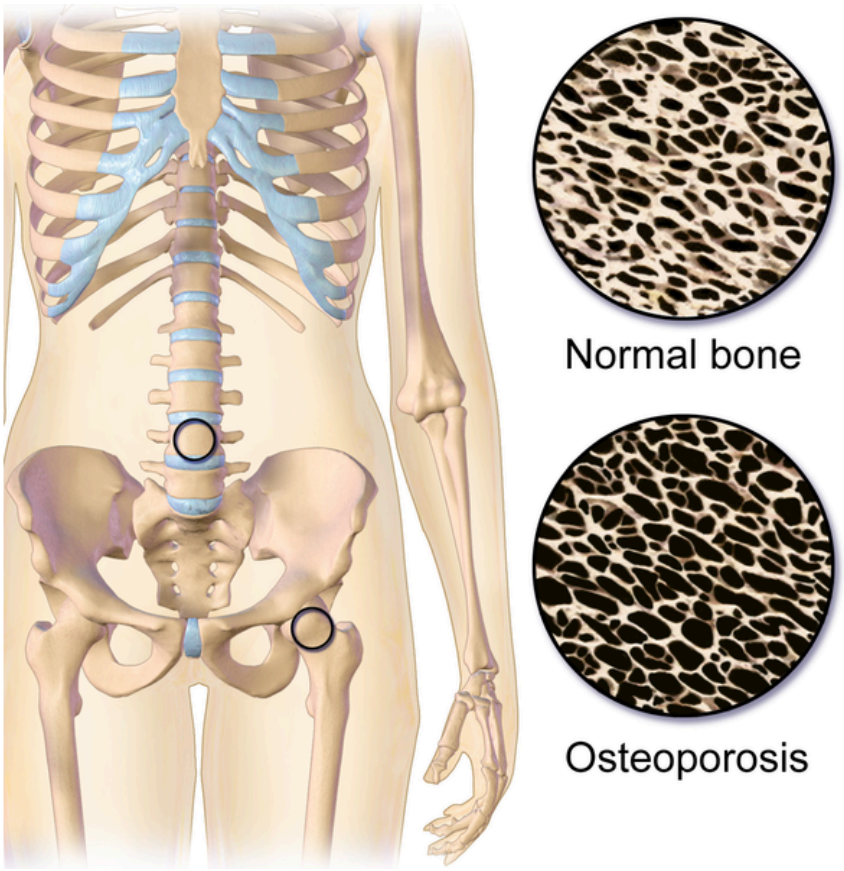
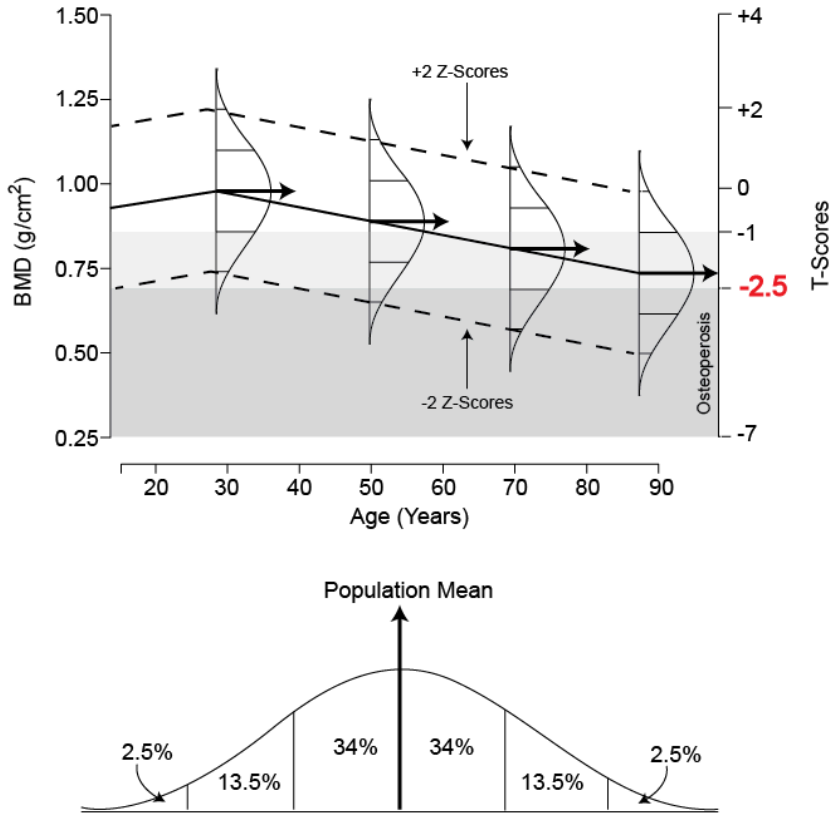
10.1.2

Osteopenia and Osteoporosis

Osteoporosis is defined as a **bone mineral density (BMD)** greater than 2.5 standard deviations below the mean of an adult 30 year old reference population. Osteoporosis occurs when there is a loss of both bone mineral and bone matrix material. This loss increases the porosity of the bone and decreases density. **Osteopenia** is defined as a BMD between 1 and 2.5 standard deviations below the mean for an adult 30 year old reference population. Osteopenia is less common and is a precursor for osteoporosis.



Osteoporosis Locations.png; BruceBlaus; https://commons.wikimedia.org/wiki/File:Osteoporosis_Locations.png; This file is licensed under the Creative Commons Attribution-Share Alike 4.0 International license.



T-Scores for Osteoporosis *Image by BYU-I JS F16*

The image above explains how a "T-score" is assessed for bone density. The normal bell curve at the bottom shows how the percentages of a population are distributed around the population mean. Notice that the top graph shows normal bell curves of the population and how bone mass density falls at various ages. Adults at the age of 30 are generally very near their lifetime peak bone density. The other normal curves to the right of the one for age 30 adults show how bone mass density is distributed for ages 50, 70 and 85. The T-score in this case is the number of standard deviations that a value falls relative to the normal curve for a 30 year old. A T-score of -1 for a 30 year old reference population marks the point at which we would use the term osteopenia to describe a person's bone mass. A T-score of -2.5 for a 30 year old reference population classifies osteoporosis. For example: A 50 year old that has a bone mass density around .70 g/cm2 would find that this value is about 1.5 standard deviations below the average for a 50 year old, but it is 2.5 standard deviations below the average for a 30 year old reference population. Because we use the 30 year old reference population as our benchmark, this 50 year old would be considered to have osteoporosis. Again, these T- scores are always given for how many standard deviations a person's bone mass density falls in relation to the 30 year old reference population. Here is another example: A 70 years old who has a bone mass density close to .80 g/cm2 would be about a half standard deviation above the average for that age group, but would be -1 standard deviation below the average for the reference group of 30 years old. This person would therefore have a T-score of -1 and would be considered to have osteopenia. So, yes, you can see that close to 84% of the population of those 85 years old would be considered to have osteopenia or worse. Overall, make sure that you remember the T-scores that correspond with osteopenia (-1) and osteoporosis (-2.5) and that these scores are taken from a 30 year old reference population.

Now that you have a better understanding of how bone density is distributed among populations and how we measure it statistically, let's discuss some risk factors for the development of osteoporosis:

- **Genetics:** White or Asian individuals have a higher risk of developing osteoporosis while Hispanics and African Americans typically have a higher BMD and therefore have decreased risk. Those who have a family history of the disease are also at increased risk.
- **Hormone levels:** Because testosterone and estrogen favor bone retention, people with lower sex hormone levels are at a higher risk for developing osteoporosis. Hyperthyroidism increases risk because it causes an acceleration of bone turnover. Hyperparathyroidism causes a direct effect on the BMU to promote bone breakdown. Cushing's syndrome causes excess cortisol which can affect the BMU to cause decreased bone density. Diabetes appears to affect bone matrix through increased glycosylation (secondary to high blood glucose levels). This affects the activity of the cells involved in bone turnover and also increases risk.
- **Exercise levels:** Weight bearing exercise can decrease one's risk for developing osteoporosis because the weightbearing stimulates more osteoblast activity.
- **Low calcium intake/absorption issues:** Gastrectomy, celiac disease, and anorexia nervosa all affect nutrient absorption and can lead to decreased bone matrix production as well as decreased mineralization of bones.
- **Weight:** People who are heavier are actually less likely to develop the disease because their bones must adapt to support them. Lightweight individuals with small bone structure are at increased risk.
- **Gender:** Women are at increased risk due to the drop in female hormones that occur with menopause. With less estrogen inhibiting bone breakdown, women's BMD can drop significantly as osteoclasts greatly increase their activity.
- **Age:** Senile (associated with aging) osteoporosis occurs and is mostly due to decreased osteoblast activity.
- **Lifestyle risks:** A sedentary lifestyle, calcium/vitamin D deficiency, high-protein diet (cannot absorb calcium as well), excessive alcohol intake (directly inhibits osteoblasts and decreases calcium absorption), excessive caffeine intake (diuretic effect that can cause more loss of calcium) and smoking (there are actually nicotine receptors on osteoblasts that can result in decreased bone formation) all increase the risk for osteoporosis.
- **Drug-related factors:** Taking aluminum containing antacids long term can increase risk because aluminum binds up phosphorus which has an indirect effect on calcium balance because phosphorus and calcium are linked in their regulation. Some anticonvulsants cause a decrease in vitamin D production which can increase risk as well.

Premature osteopenia or osteoporosis is being seen in increasing numbers among young athletic women. This problem appears to be related to what is being called the **female athlete triad**. The triad is:

1. Patterns of disordered eating and extreme exercise
2. Nutritional deficits that lead to menstrual dysfunction
3. Lowered sex hormones that lead to decreased bone density (remember that estrogen favors bone retention)

Prevention and early detection of decreased bone density is important for successful treatment of osteoporosis. Two methods are used for the diagnosis of osteoporosis. The first is a BMD assessment which uses dual energy x-ray absorptiometry (called a DEXA scan) and is frequently done for women over the age of 65 and men over the age of 70. Another diagnostic test is checking the patient's height to see if it has changed. This test is done because the vertebral bodies often experience compression fractures in patients with osteoporosis. This compression leads to a decrease in height and a dowager hump, which is an abnormal curvature of the spine that is caused by compression of the anterior vertebral bodies (otherwise known as kyphosis). The vertebrae collapsing in this way causes the head to move forward and the upper back to protrude more prominently in a posterior direction. While the dowager hump is often used for diagnosis, be aware that the most common location of fractures associated with osteoporosis occur in the humerus, distal radius, and the neck of the femur.

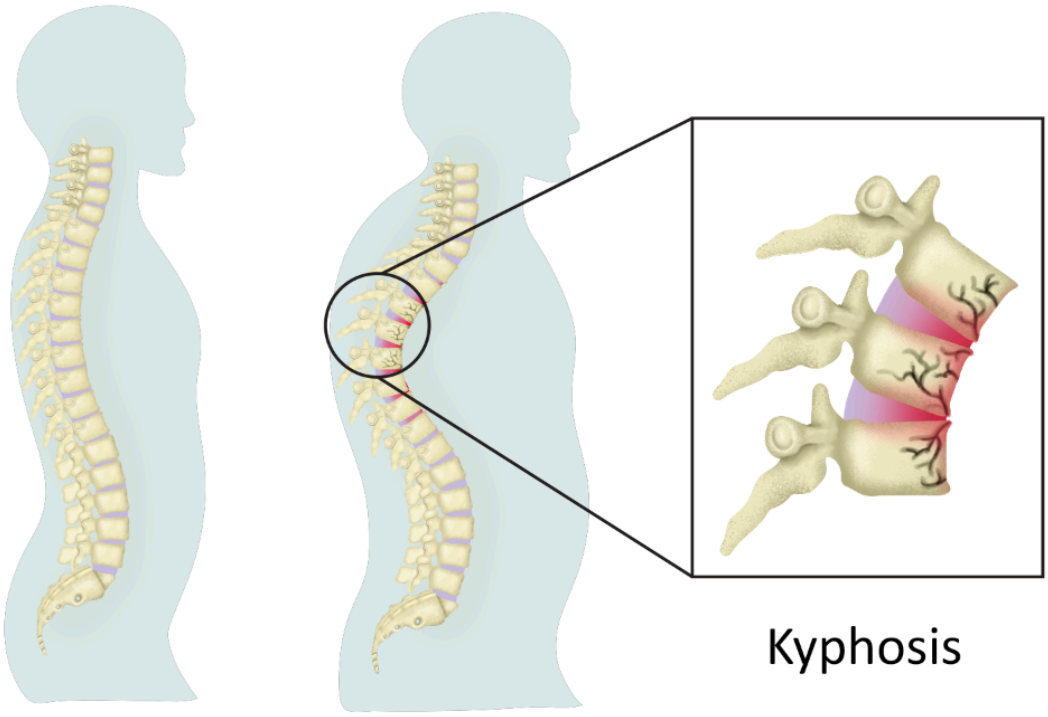


Image by Becky T. W20

Pharmaceutical Treatments for Osteoporosis

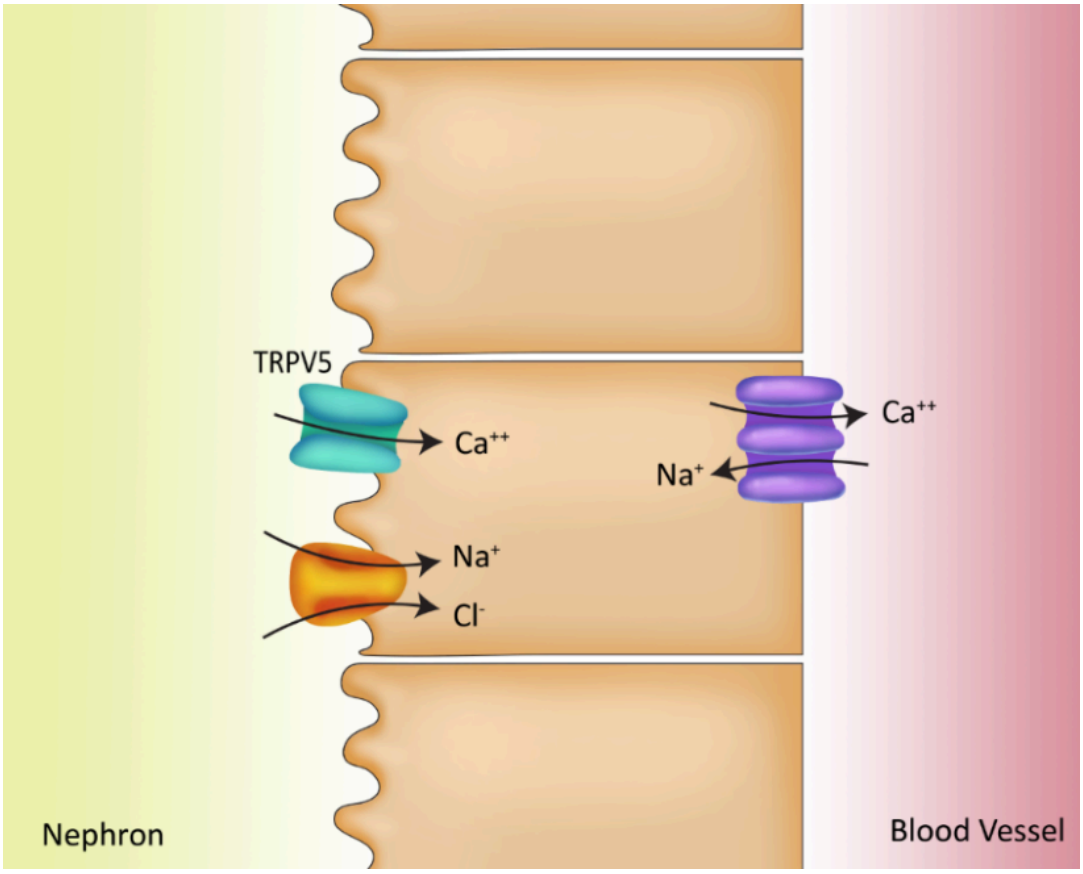
Watch the video Osteoclast and Osteoblast Regulation - Part 2

There are five main drug classes used in the treatment of osteoporosis:

1. A **RANKL inhibitor** like denosumab (Prolia) is a monoclonal antibody that acts as synthetic OPG to prevent RANK/RANKL interactions. This decreases the differentiation and activation of osteoclasts and therefore favors bone retention.
2. **Recombinant PTH** like teriparatide (Forteo) used intermittently activates osteoblasts more than osteoclasts. This is the opposite of how we previously discussed that PTH favors bone breakdown. It is not fully understood why low intermittent levels of PTH and high constant levels of PTH have the opposite effect. However, we do know that low doses of PTH increases the numbers of osteoblasts and prevents apoptosis.
3. **Man made calcitonin** like Fortical and Miacalcin are helpful in treating osteoporosis because like normal calcitonin, they favor calcium retention in the bone by increasing osteoblast activity.
4. **Selective estrogen receptor modifiers (SERMs)** like raloxifene (Evista) act like estrogen in the bone and favor bone retention. They are selective specifically for bone and don't increase the risk for breast or uterine cancer.
5. **Bisphosphonates** such as alendronate (Fosamax) bind to minerals on the bones that osteoclasts will then "eat" as they perform bone resorption. Osteoclasts that take in the bisphosphonates end up dying, which shifts the osteoblast/osteoclast activity in favor of the osteoblasts.

Another possible drug that may be used to treat osteoporosis is a thiazide diuretic like hydrochlorothiazide. As mentioned, this drug is a diuretic and may be used for purposes other than osteoporosis. However, its mechanism of action results in increased blood calcium levels. Thiazides block Na^+/Cl^- symporters on the apical surface of distal convoluted tubule (DCT) cells in the kidney. This blockage ends up lowering the intracellular Na^+ levels in renal tubular

cells. Lower intracellular levels of Na^+ in turn affect the activity Na^+/Ca_2^+ antiporter on the basolateral membrane of these cells by increasing the driving force for Na^+ to come into the cell. This results in more Ca_2^+ crossing the basolateral membrane through the Na^+/Ca_2^+ exchange protein and then entering the blood. Subsequently more Ca_2^+ is reabsorbed and results in less Ca_2^+ being lost in the urine so it can be used in bone. Thiazides therefore improve bone density and are also useful to reduce the risk of forming calcium-containing kidney stones.



Channels Influenced by Thiazides *Image by Becky T. BYU-I S20*

While these drugs can be wonderfully helpful, regular exercise and adequate supplementation are commonly the first steps in the prevention/treatment of osteoporosis. Studies have shown that many women don't receive enough calcium or vitamin D in their diet. A careful evaluation by a healthcare provider can help determine if a person should take supplements to help protect bone health.