# Osteoporosis

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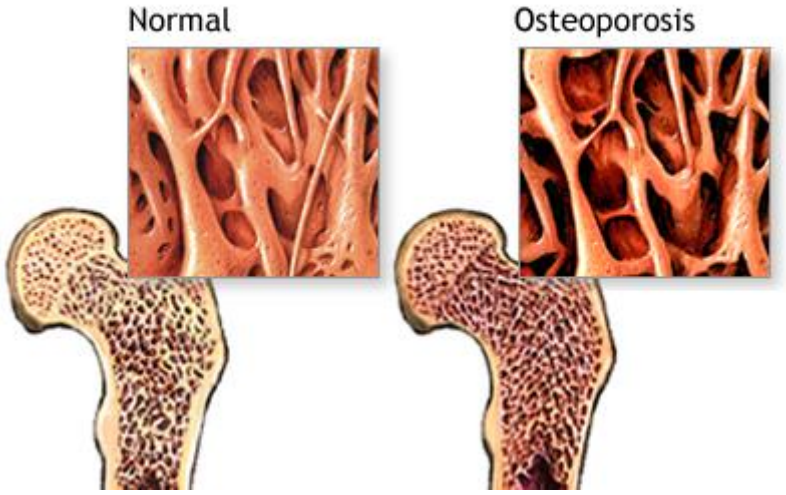
## What are the major components of the bone?

The main structural elements of bone are osteoid, which is a protein matrix, and hydroxyapatite (calcium phosphate) crystals, which are embedded in the osteoid. The major functional cells are osteoclasts, which resorb old bone and osteoblasts, which form new bone.

## What is osteoporosis?

Osteoporosis is a predisposition to skeletal fractures resulting from a reduction in total or regional bone mass. Both hydroxyapatite and osteoid are reduced proportionately in osteoporotic bone.




## What are the major risk factors for osteoporosis?

Non-modifiable: age, race (Caucasian, Asian), female gender, early menopause (<45years old), slender build (<57kgs), positive family history.

Modifiable: low calcium intake, low vitamin D intake, estrogen (female hormone) deficiency, sedentary lifestyle, cigarette smoking, alcohol excess (>2 drinks/day), caffeine excess (>2 servings/day), medications (glucocorticoids, excess thyroxine).

## What are the indications for bone mass measurement issued by National Osteoporosis Foundation?

- Women with age >65 years or older
- Postmenopausal women under age 65, with other risk factors
- Women considering therapy for osteoporosis
- Women on hormone replacement therapy for prolonged periods.

## How is bone density measured?

Standard radiographs are inadequate for accurate bone mass assessment. The most accurate and widely used methods in current practice are dual energy x-ray absorptiometry (DEXA), computed tomography (CT), ultrasound (US). In my openion, DEXA offers the best accuracy and precision with the least radiation exposure in most patients. Radiation exposure is 2 uSv per site (a chest X ray is 100uSv).

Spine and hip densitometry (central densitometry) measurements are the best predictors of fracture risk and have the best precision for longitudinal monitoring. Peripheral densitometry measurements (heel,radius, hands) are more widely available and less expensive.

## Should bone densitometry screening be done at central or peripheral sites?

Densitometry values can vary greatly in the same individual at different skeletal sites. Therefore, even when peripheral bone densitometry values are normal, follow up central densitometry must still be considered in the following circumstances:

- History of fragility fractures.
- Two or more risk factors for bone loss.
- Medical conditions associated with bone loss.
- Medications that cause bone loss
- Postmenopausal women not on HRTs, who would consider treatment if bone density is low.

## How do I interpret a bone densitometry report?

The most useful values on the bone densitometry report are the T- score, Z-score and the absolute bone densitometry (BMD).

T score: a comparison of patient's bone mass to that of young normal subjects (age 30). The T-score is the number of standard deviations (SDs) the patient's value is below or above the mean value for young normal subjects (peak bone mass). A T score of -2 indicates that the patient is 2 SDs below normal peak bone mass. The T score indicates whether or not the patient has osteoporosis.

Z-score: a comparison of patient's bone mass to that of age matched subjects. The Z-score indicates whether or not the patient's bone mass is appropriate for age or whether other factors are likely to account for excessively low bone mass. The Z-score is the number of SDs the patient's value is below or above the mean value for age-matched normal subjects.

Absolute BMD: The actual bone density value expressed in g/cm2 . This is the best parameter to use for calculation of percent changes in BMD during longitudinal follow up.

## How is the diagnosis of osteoporosis made?

It is made when a patient has a characteristic osteoporotic fracture or when the T-score on the bone densitometry is sufficiently low. The World Health Organization criteria for T-score interpretation are as follows.

T -score >-1: Normal.

T-score between -1 and -2.5: Osteopenia.

T-score <-2.5: Osteoporosis.

T-score of less than -2.5 makes a diagnosis of osteoporosis even in the absence of a fracture. Before concluding that reduced bone mass or a fracture is due to osteoporosis, one must first rule out other causes of low bone mass.

## What estimates of bone loss and fracture risk can be made from a patient's bone mineral density measurement by DEXA?

| T-score | % Bone Loss* | Fracture risk† |
|---|---|---|
| -1 | 12% | 2 times increased |
| -2 | 24% | 4 times |
| -3 | 36% | 8 times |
| -4 | 48% | 16 times |

*note that one has to lose 30% of bone mineral density to see osteopenia on routine radiographs.

†if a person has had a previous fragility fracture, the risk of subsequent fracture doubles again, i.e., if T-score was -3, fracture risk is 2 X 8=16.

## What are the limitations of BMD measurements?

The WHO diagnostic criteria apply only to postmenopausal white women.

Disparities exist among bone density values at different sites and with different methods.

Low bone mass does not necessarily indicate on-going bone loss.

Low bone mass is not always osteoporosis.

Bone densitometry cannot distinguish among the causes of low bone mass.

## *What other conditions must be considered as causes of low bone mass?*

Osteomalacia

Osteogenesis imperfect

Hyperparathyroidism

Hypogonadism

Cushing's syndrome

Liver disease

Multiple myeloma

Rheumatoid arthritis

Renal failure

Idiopathic hypercalciuria.

Celiac disease

Mastocytosis

Alcoholism

Chronic obstructive lung disease

Inflammatory bowel disease

Medications : corticosteroids, cyclosporine, dilantin, antiseizure medications, heparin.

**What would be a cost effective evaluation to rule out these possibilities?**

A complete history and physical examination should always be performed. Apart from this complete blood count with erythrocyte sedimentation rate, serum calcium, phosphorus, alkaline phosphatise, creatinine, CO2, chloride, serum TSH, serum testosterone (men), 24 hr urine calcium and creatinine.

**Apart from drugs what other measures are useful for preventing and treating osteoporosis?**

Adequate calcium intake: 1000mg/day, premenopausal women and men. 1500mg/day, postmenopausal women and men >65 years of age.

Adequate Vitamin D intake: 400-800 units/day.

Adequate exercise: aerobic and resistance.

Smoking cessation.

Limitation of alcohol consumption to 2 drinks/day or less.

Limitation of caffeine consumption to 2 servings/day or less.

Fall prevention.

## How do I assess my dietary calcium intake?

The major bioavailable sources of calcium are dietary products and calcium fortified drinks. Their calcium content approximately are given below:

Milk- 300mg/cup (8oz).

Cheese- 300mg/oz.

Yogurt-300mg/cup (8oz).

Fruit juice with calcium- 300mg/cup (8oz).

Total these amounts plus 300mg for the general non dairy diet and you have a reasonable estimate of your daily dietary calcium intake.

## How can I ensure an adequate intake of calcium and vitamin D? What is the best calcium supplement?

A person absorbs only one third of the calcium he or she ingests. Low-fat dairy products are the safest way to increase calcium intake without increasing the risk of kidney stones. You should judge your calcium intake as per the contents of calcium in various dairy products which is mentioned above. Any shot falls in dietary calcium intake should be supplemented with calcium tablets, elixirs, or multivitamins. Multivitamins contain 400 units of vitamin D per tablet; one or two tablets per day are sufficient for most patients.

Patients who require calcium supplements above their diet to reach adequate daily calcium intake should take either calcium carbonate or calcium citrate. Calcium carbonate is less expensive but needs acidification for best absorption. Because of the acid buffering capacity of the calcium carbonate, it should be taken with meals and in split dose of no more than 500-1000mg per dose (e.g.500mg thrice daily). Calcium citrate may be better alternative in patient with achlorohydria or on medications to limit acid in the stomach.

It is important to make sure how much elemental calcium is in each pill. To determine whether a particular calcium supplement will be absorbed, put one pill in a glass of vinegar and see if it is dissolved in 30 minutes. If not, it isn't being absorbed.

Patients who develop constipation due to calcium, should take a calcium/magnesium preparation since the magnesium may stimulate gut motility.

## What are the most affective pharmacologic approaches currently available for the prevention and treatment of osteoporosis?

Bone- resorption inhibiting agents: oestrogen, bisphosphonates, raloxifene, calcitonin.

Bone-formation stimulating agnets: fluoride, androgens, growth hormone, parathyroid hormone.

## When should medical therapy be initiated for the prevention and treatment of osteoporosis?

The non pharmacologic measures are appropriate for all individuals who want to reduce the risk of developing osteoporosis. The national osteoporotic foundation further recommends that pharmacologic therapy be initiated in any patient who has T-score of -2.0 or less and in patients with a T-score of -1.5 or less in the presence of other osteoporotic risk fractures.

## When is urinary N telopeptide useful?

Measurement of the level of N-telopeptides (NTX) in the urine provides an estimate of activity of bone turnover. NTX is a breakdown product of type 1 collagen in the bone. A 24hr urine or second voided morning spot urine can be used. There is a 15% average difference between the value obtained between these methods of urine collection. A normal urine NTX is a 20-65 BCE/mmol Cr. However, a value greater 50 predicts loss of BMD over the next year while a value between 2.0 and 35 represents good control on present therapy.

## What is considered a significant change in BMD on DEXA scan?

Because of the precision error of a central DEXA scan, a change of ≥ 3% in the spine and ≥ 6% in the femur is considered significant. Ostephytes, vertebral fractures, and aortic calcification can falsely increase values in the spine. Hip malposition and including the ischium in the field of measurement can affect femur position.

## How does glucocorticoid (GC) therapy cause osteoporosis?

GC therapy in supraphysiologic doses (prednisolone >7mg/dl) have several detrimental effect on the bone. First, they directly inhibit the osteoblastic bone formation. Second, they impair intestinal calcium absorption and promote renal calcium excretion, thereby lowering serum calcium levels sufficiently to increase the secretion of parathyroid hormone (PTH), which then stimulates bone resorption. They also impair secretion of gonadal steroids, which further increase bone resorption.

## When should osteoporosis prevention and treatment measures be instituted in patients taking GC therapy?

Non-pharmacologic measures are indicated in all patients taking GCs. Pharmacological interventions should be considered for patients who will be on 7.5 mg/day of prednisone (or an equivalent dose of another GC) for at least 3months, particularly in postmenopausal women and in any individuals who have T-scores of -1 or less or who have fragility fractures.

## What is the treatment for GC induced osteoporosis (GIOP)?

Patients on GC therapy should take calcium (1500mg/day) and vitamin D (800 units/day). If urinary calcium excretion exceeds 300mg/day, a thiazide diuretic may be added. Most of the bisphosphonates are useful in GIOP. Calcitonin can be used, but its effects are less than that of bisphosphonates. Patients with decreased function of gonads should receive gonad steroid replacements.

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