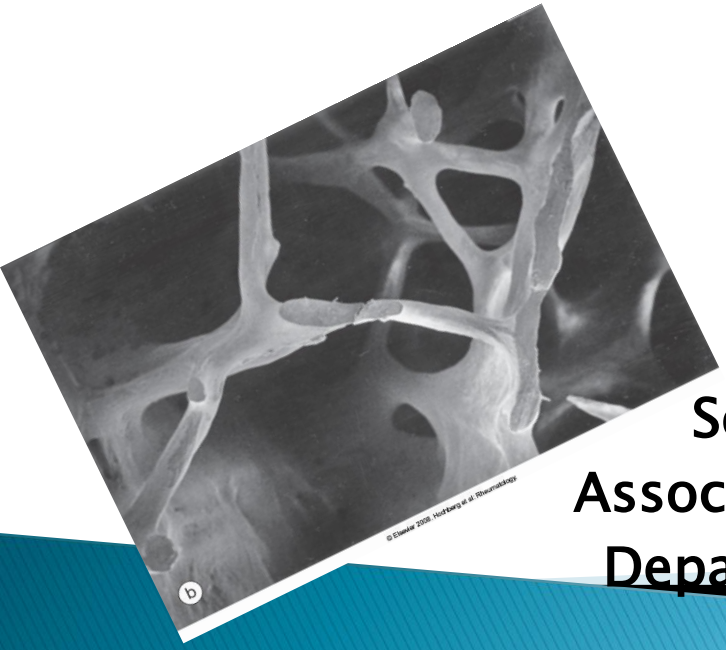
Osteoporosis



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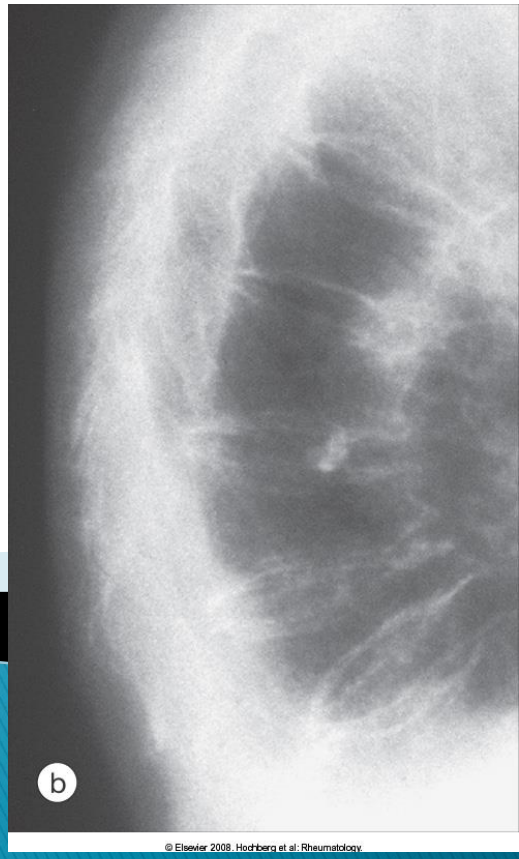


Introduction

- Osteoporosis is a chronic potentially debilitating condition which as our aging populations grows will become an increasing cause of mortality and morbidity

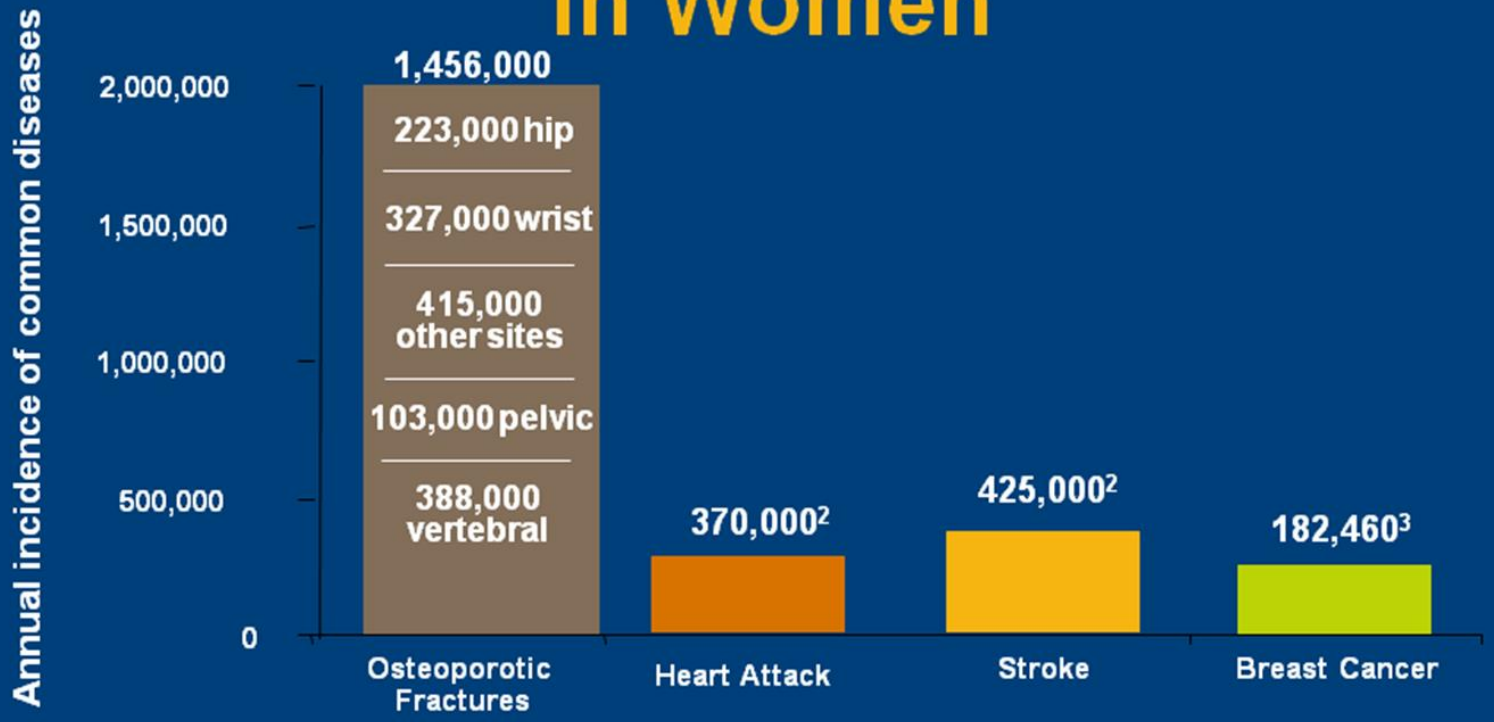
- Based on data from the National Health and Nutrition Examination Survey III (NHANES III), NOF has estimated that more than **10 million Americans have osteoporosis** and an additional **33.6 million have low bone density of the hip** [1]

- About one **out of every two Caucasian women** will experience an osteoporosis-related fracture at some point in her lifetime, as will approximately **one in five men** [2]

Introduction

- According to the World Health Organization, the prevalence of osteoporosis among U.S. white women past menopause is estimated to be:
  - 14% in those 50-59 years of age,
  - 22% in those 60-69 years of age
  - 39% in those 70-79 years of age
  - 70% in those 80 years of age and older [3]
- Significant risk has been reported in people of all ethnic backgrounds. White and Asian racial groups, however, are at greatest risk.

Significance of Osteoporosis in Women



1 Annual fracture incidence in women all ages
2 Annual estimate new & recurrent MI ages 35+
2 Annual estimate new & recurrent stroke in women all ages
3 2008 new cases in situ & invasive breast cancer all ages

1 Burge, et al. *JBMR*. 2007. 465-75.
2 American Heart Association. Heart Disease and Stroke Statistics – 2009 Update. 2009.
3 American Cancer Society. Surveillance Research. 2008.

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Introduction: Economic Burden

- Osteoporosis-related fractures create a heavy **economic burden**:
  - 432,000 hospital admissions/year
  - 2.5 million medical office visits/year
  - 180,000 nursing home admissions /year [2]

- The cost to the healthcare system associated with osteoporosis-related fractures has been estimated at $17 billion

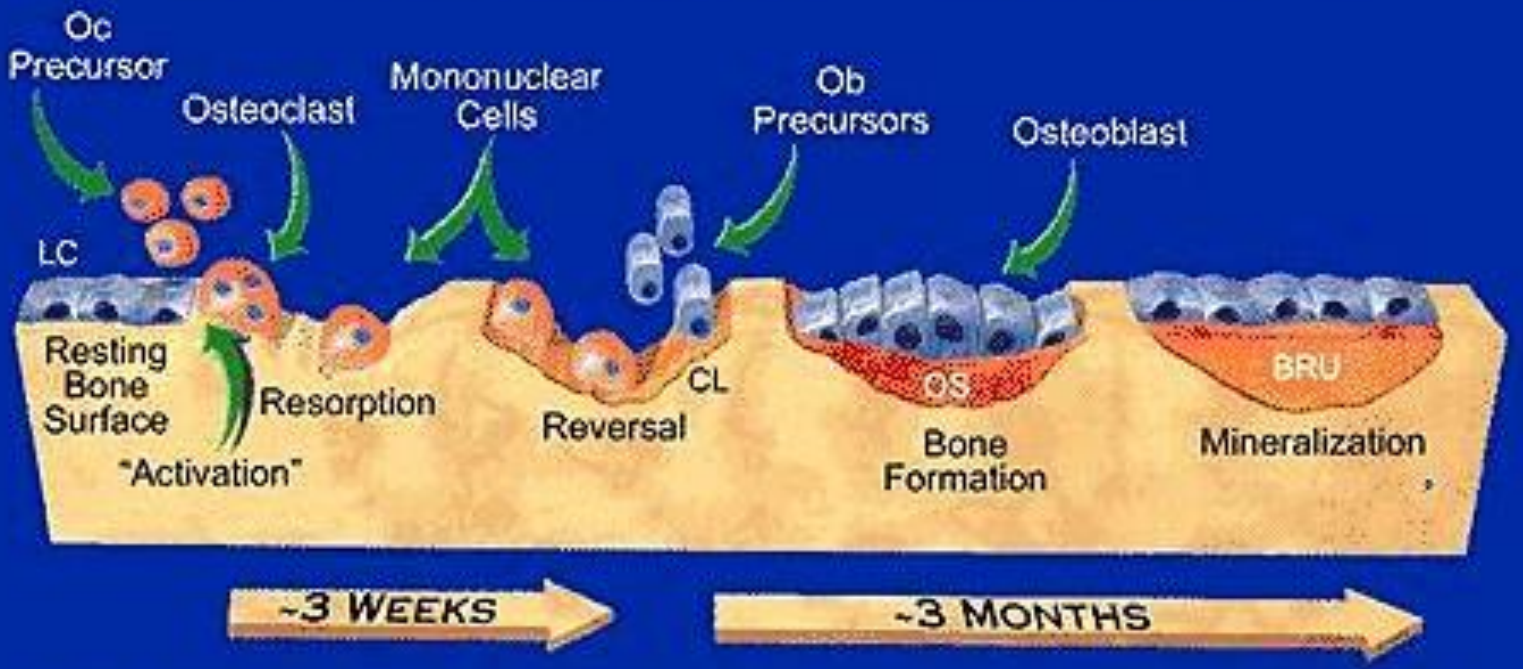
- Due to the aging population, the Surgeon General estimates that the number of hip fractures and their associated costs could double or triple by the year 2040

Objectives

- Discuss Pathophysiology of osteoporosis
- Understand the current evidence based recommendations for diagnosis, treatment and follow up management for osteoporosis
- Understanding what a bone density test is and how it determines your risk of fracture
- Understanding lifestyle and medication treatment options

OSTEOPOROSIS

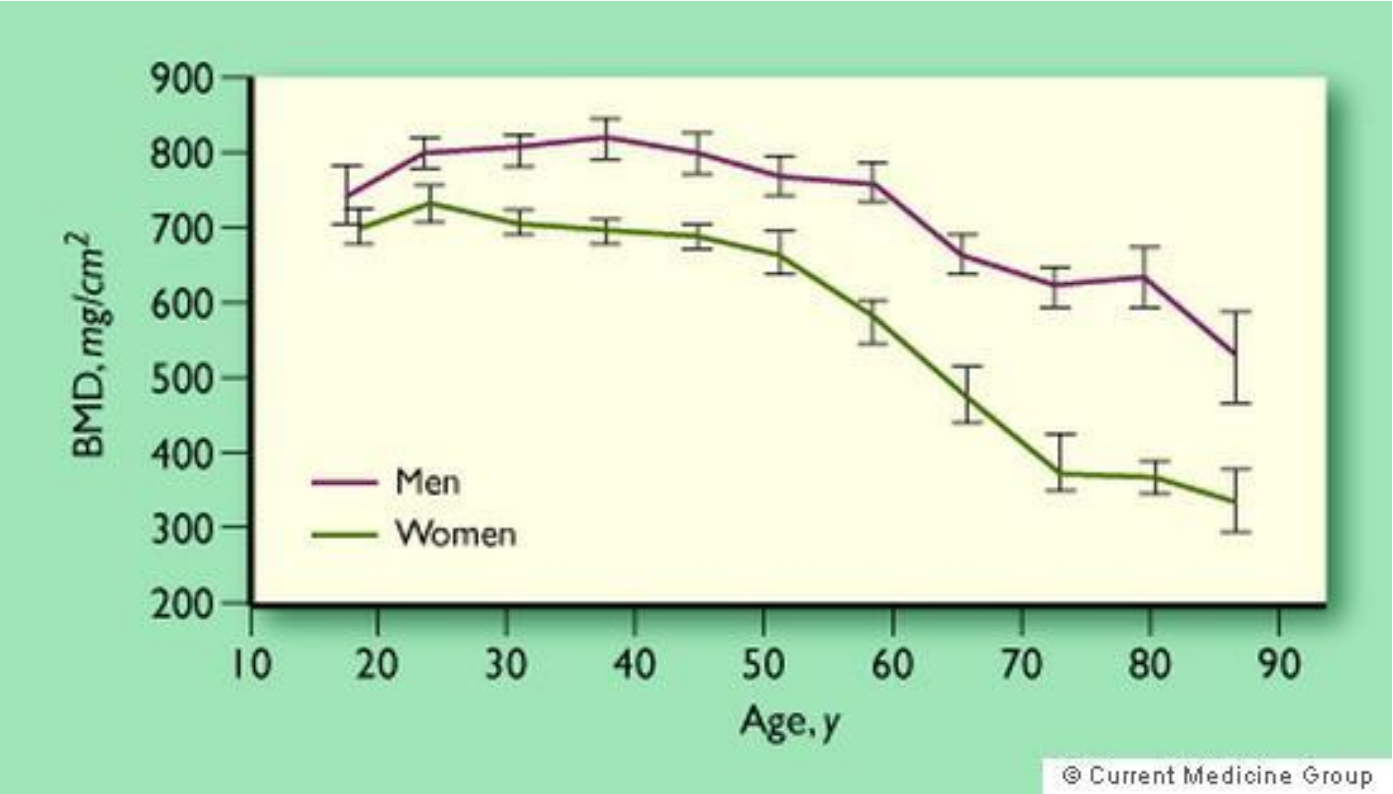
Bone destruction>formation



LC = Lining Cells CL = Cement Line OS = Osteoid BRU = Bone Remodeling Unit

Pathophysiology: Postmenopausal Osteoporosis

- For Women once menopause is reached there is an abrupt acceleration in the rate of bone loss which persists for 5 to 10 years



Diagnosis of Osteoporosis

- All **postmenopausal women and men age 50 and older should be evaluated clinically for osteoporosis risk** in order to determine the need for BMD (DEXA) testing.
- The more risk factors that are present, the greater the risk of fracture.
- In at risk individuals review of medical history, medications and lifestyle habits including diet is important

Why having Lupus places you at risk for bone loss?

- Female Gender
- Chronic inflammation
- Periods of decreased activity/hospitalizations
- Risk for falls
- Medications: Medication induced menopause, Steroids

TABLE 1: Conditions, Diseases and Medications That Cause or Contribute to Osteoporosis and Fractures

Lifestyle factors		
Low calcium intake	Vitamin D insufficiency	Excess vitamin A
High caffeine intake	High salt intake	Aluminum (in antacids)
Alcohol (3 or more drinks/d)	Inadequate physical activity	Immobilization
Smoking (active or passive)	Falling	Thinness
Genetic factors		
Cystic fibrosis	Homocystinuria	Osteogenesis imperfecta
Ehlers-Danlos	Hypophosphatasia	Parental history of hip fracture
Gaucher's disease	Idiopathic hypercalciuria	Porphyria
Glycogen storage diseases	Marfan syndrome	Riley-Day syndrome
Hemochromatosis	Menkes steely hair syndrome	
Hypogonadal states		
Androgen insensitivity	Hyperprolactinemia	Turner's & Klinefelter's syndromes
Anorexia nervosa and bulimia	Panhypopituitarism	
Athletic amenorrhea	Premature ovarian failure	
Endocrine disorders		
Adrenal insufficiency	Diabetes mellitus	Thyrotoxicosis
Cushing's syndrome	Hyperparathyroidism	

Gastrointestinal disorders		
Celiac disease	Inflammatory bowel disease	Primary biliary cirrhosis
Gastric bypass	Malabsorption	
GI surgery	Pancreatic disease	
Hematologic disorders		
Hemophilia	Multiple myeloma	Systemic mastocytosis
Leukemia and lymphomas	Sickle cell disease	Thalassemia
Rheumatic and autoimmune diseases		
Ankylosing spondylitis	Lupus	Rheumatoid arthritis
Miscellaneous conditions and diseases		
Alcoholism	Emphysema	Muscular dystrophy
Amyloidosis	End stage renal disease	Parenteral nutrition
Chronic metabolic acidosis	Epilepsy	Post-transplant bone disease
Congestive heart failure	Idiopathic scoliosis	Prior fracture as an adult
Depression	Multiple sclerosis	Sarcoidosis
Medications		
Anticoagulants (heparin)	Cancer chemotherapeutic drugs	Gonadotropin releasing hormone agonists
Anticonvulsants	Cyclosporine A and tacrolimus	Lithium
Aromatase inhibitors	Depo-medroxyprogesterone	
Barbiturates	Glucocorticoids (≥ 5 mg/d of prednisone or equivalent for ≥ 3 mo)	

TABLE 2: Risk Factors for Falls

Environmental risk factors
Lack of assistive devices in bathrooms
Loose throw rugs
Low level lighting
Obstacles in the walking path
Slippery outdoor conditions
Medical risk factors
Age
Anxiety and agitation
Arrhythmias
Dehydration
Depression
Female gender
Impaired transfer and mobility
Malnutrition
Medications causing oversedation (narcotic analgesics, anticonvulsants, psychotropics)
Orthostatic hypotension
Poor vision and use of bifocals
Previous fall
Reduced problem solving or mental acuity and diminished cognitive skills
Urgent urinary incontinence
Vitamin D insufficiency [serum 25-hydroxyvitamin D (25(OH)D) < 30 ng/ml (75 nmol/L)]
Neuro and musculoskeletal risk factors
Kyphosis
Poor balance
Reduced proprioception
Weak muscles
Other risk factors
Fear of Falling

From: NOF Rehabilitation Guide.[12]

Diagnosis

Table 3 Diagnostic tests in the work-up of secondary osteoporosis.

Diagnostic test	*Purpose*
History and physical exam	To identify risk factors for fractures, the underlying disease, and potential drugs
Dual-energy X-ray absorptiometry (lumbar spine and hip)	To quantify bone mineral density
Spinal X-rays	To detect prevalent vertebral fractures To exclude osteolytic lesions or tumors
Diagnostic test	*To detect or exclude*
Complete blood count	Anemia as in myeloma/celiac disease Leukocytosis in leukemia
Renal and liver function test	Renal or liver failure, alcohol abuse
Serum calcium and phosphate levels	Primary hyperparathyroidism, myeloma
Serum C-reactive protein	Chronic infection/inflammation
Serum bone-specific or total AP activity	Paget's disease; osteomalacia
Serum 25-hydroxyvitamin D	Vitamin D deficiency, osteomalacia
Serum levels of basal TSH	Hyperthyroidism
Serum free testosterone levels (in men)	Male hypogonadism
Fasting glucose levels	Diabetes mellitus
Intact parathyroid hormone	Primary hyperparathyroidism
Serum protein electrophoresis, immunofixation	MGUS, myeloma
24-h urinary calcium excretion (with creatinine and sodium control)	Hypercalciuria
Anti-tissue transglutaminase antibodies	Celiac disease
Anti-HIV antibodies	HIV disease, AIDS
Morning fasting serum cortisol after dexamethasone suppression	Cushing's syndrome
Serum tryptase levels, urinary histamine excretion	Systemic mastocytosis
COL1A genetic testing	Osteogenesis imperfecta
Iliac crest bone biopsy	Systemic mastocytosis, MGUS/myeloma, osteomalacia, lymphoma/leukemia

Diagnosis: Assessing BMD

- **Dual-energy x-ray absorptiometry (DEXA)** measurement of the **hip and spine** is the technology now used to establish or confirm a diagnosis of osteoporosis, predict future fracture risk and monitor patients by performing serial assessments.

- The difference between the patient's score and the norm is expressed in **standard deviations (SD)** above or below the mean. Usually, 1 SD equals 10 to 15 percent of the BMD value in g/cm2.

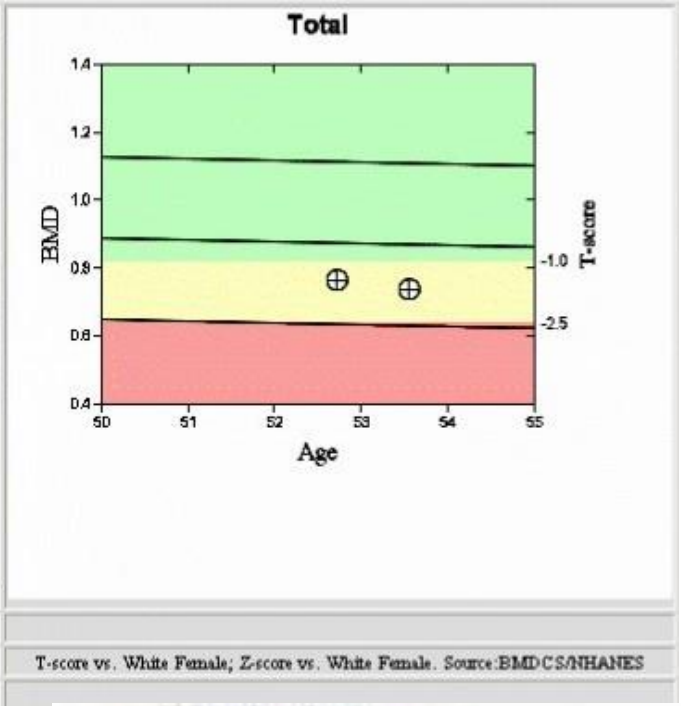
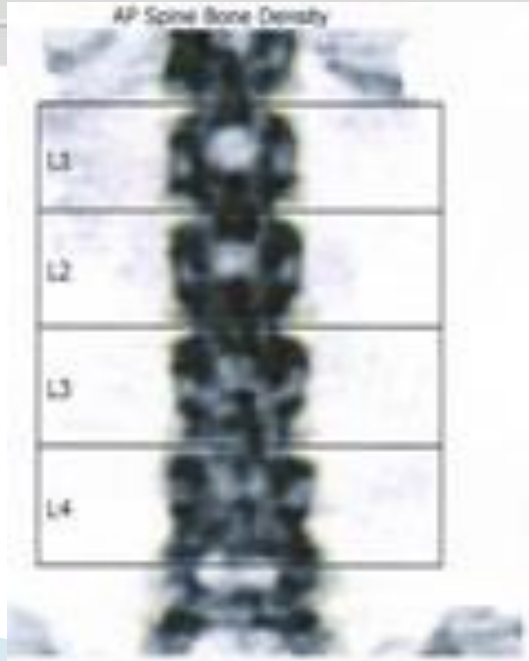
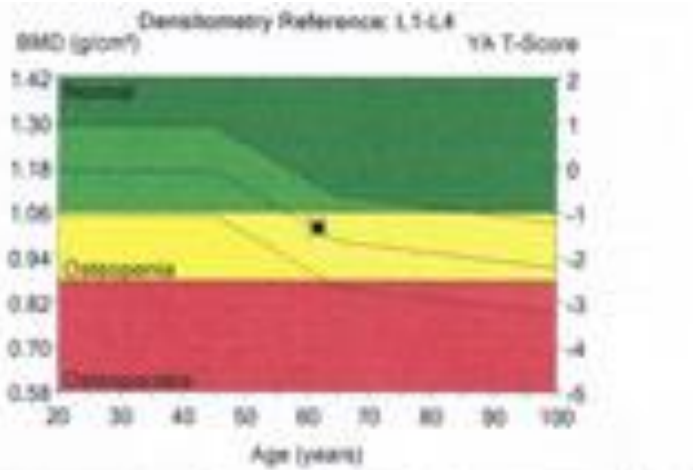


Image not for diagnostic use	
92 x 116	T-score vs. White Female; Z-score vs. White Female. Source:BMDCS/NHANES
NECK: 47 x 10	
k = 1.144, d0 = 47.9	





Region	BMD [1] (g/cm²)	Young-Adult [2] (%)	Young-Adult [2] T-Score	Age-Matched [3] (%)	Age-Matched [3] Z-Score
L1	0.938	83	-1.6	98	-0.2
L2	1.080	91	-0.9	106	0.5
L3	1.028	86	-1.4	100	0.0
L4	1.008	84	-1.6	98	-0.2
L1-L4	1.018	86	-1.4	101	0.1

FIGURE 3. Z- and T-Scores

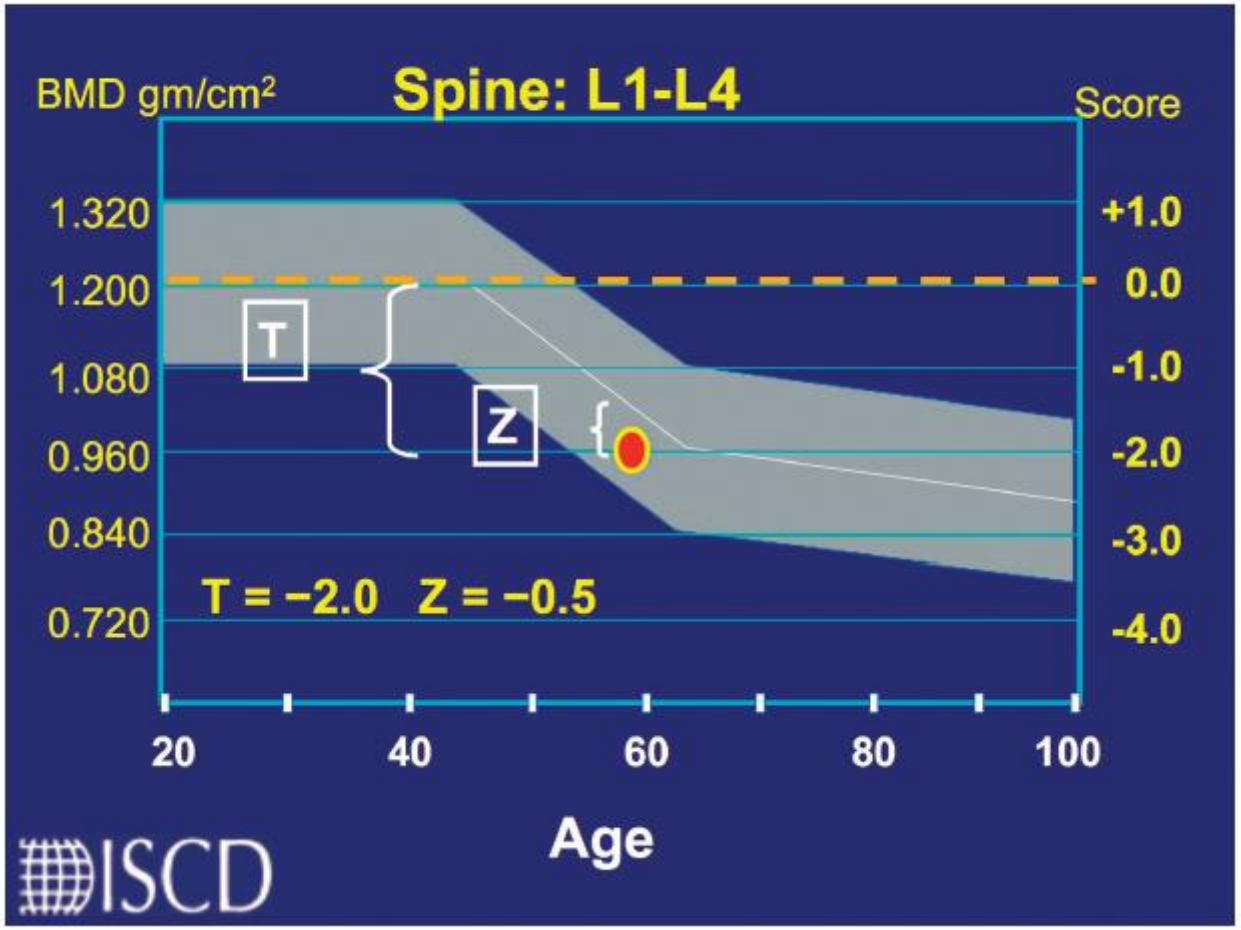


TABLE 4: Defining Osteoporosis by BMD

The World Health Organization has established the following definitions based on BMD measurement at the spine, hip or forearm by DXA devices:[13]
Normal: BMD is within 1 SD of a "young normal" adult (T-score at -1.0 and above).
Low bone mass ("osteopenia"): BMD is between 1.0 and 2.5 SD below that of a "young normal" adult (T-score between -1.0 and -2.5).
Osteoporosis: BMD is 2.5 SD or more below that of a "young normal" adult (T-score at or below -2.5). Patients in this group who have already experienced one or more fractures are deemed to have severe or "established" osteoporosis.
Note: Although these definitions are necessary to establish the presence of osteoporosis, they should not be used as the sole determinant of treatment decisions.

Treatment: life style changes

Exercise:

- Increases bone strength by small gains in bone mass
- Weight bearing improves bone mass but in addition prevents falls

Weight-bearing aerobic activities:

- Walking
- Low impact aerobics
- Elliptical

Flexibility exercises

Stability and balance exercises

- Tai Chi
- Balancing

What type of exercises to avoid?

- **High-impact exercises, such as jumping, running or jogging.**
  - These activities increase compression in your spine and lower extremities and can lead to fractures in weakened bones.
  - Avoid jerky, rapid movements in general
  - Choose exercises with slow, controlled movements.
- **Exercises in which you bend forward and twist your waist, such as touching your toes or doing sit-ups.**
  - These movements put pressure on the bones in your spine, increasing your risk of compression fractures.

Other life style changes to avoid bone loss

- **Smoking:**
  - Direct toxic effect to bone by smoke
  - Population studies show that smokers have a lower hip BMD and higher prevalence of osteoporosis than nonsmokers
  - Nurses health study found that fracture risk fell but only after 10 years or more of abstinence from smoking**

Lifestyle Changes to prevent bone loss

- Alcohol
  - Greater than 3 drinks per day is associated increased fall propensity and fracture risk
- Caffeine intake
  - Caffeine decreases intestinal calcium absorption
  - Limit intake of coffee or soda to 6-8 ounce per day

Treatment

- Vitamin Supplementation
  - **Calcium and Vitamin D** have favorable effects on biochemical markers of bone turnover and reduce the risk of fracture
  - Calcium is a major constituent of the bone matrix and Vitamin D is necessary for intestinal absorption of calcium
  - Can too much calcium can be bad??

Treatment: supplements

- Supplements
  - Calcium 800-1200 mg/day (getting as much through diet)
  - Vitamin D 600-1000 IU per day
  - Studies have shown small gains or stability in BMD after initiation of Calcium/Vit D, physical activity over a period of 3 years

Woodis et al, 2014

8 oz. glass of milk
= 300 mg.

8 oz. plain yogurt
= 450 mg.

1 cup cottage cheese
= 1300 mg.

1 oz. cheddar cheese
= 200 mg.

1/2 cup vanilla ice cream
= 450 mg.

8 oz. orange juice
= 300 mg.

Choice of Calcium

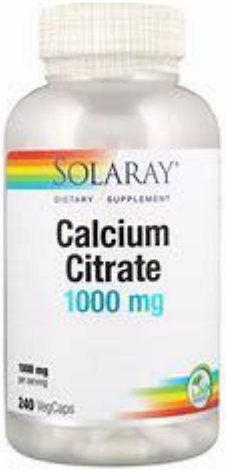
Calcium carbonate vs. citrate

Calcium carbonate

- Needs acid to dissolve and for absorption
- Less stomach acid as we age
- Often taken at meals when more stomach acid

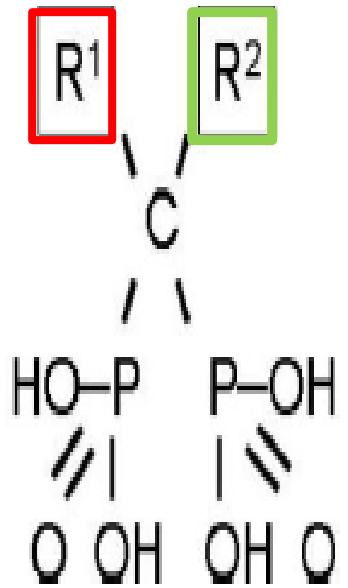
Calcium citrate

- Doesn't require stomach acid for absorption
- May be taken anytime—check with your healthcare provider
- May cost more



Treatment: Bisphosphonates

- Most common pharmacologic therapy for the treatment of osteopenia and osteoporosis
- Bind avidly to bone and inhibit osteoclast function
- The Relative potency of different bisphosphonates is a function of differences in side chain structure among the compounds



FDA Approved Bisphosphonates

TABLE 3. FDA-approved indications for nitrogen-containing bisphosphonates

	Postmenopausal osteoporosis		Glucocorticoid-induced osteoporosis		
Drug	Prevention	Treatment	Prevention	Treatment	Men
Alendronate (Fosamax)	√	√		√	√
Risedronate (Actonel)	√	√	√	√	√
Ibandronate (Boniva)	√	√			
Zoledronate (Reclast)	√	√	√	√	√

Bisphosphonate	Brand Name	Form	Frequency
Alendronate	Fosamax	Oral	Daily/weekly
Ibandronate	Boniva	Oral IV	Weekly/monthly Every 3 months
Risedronate	Actonel	Oral	Weekly
Zoledronic acid	Reclast	IV	Yearly

Other drugs for Osteoporosis

- Denosumab (Prolia)
  - Every 6 month injection
  - Is a monoclonoal antibody that prevents bone break down by blocking osteoclasts
- Paratyroid Hormone (Forteo)
  - Daily injection
  - The only FDA approved anabolic agent – bone forming agent
- Estrogen
  - Not considered first line therapy for osteoporosis since WIH studies of risk for blood clots and cancer

Treatment: Side Effects

Treatment : Side effects

- Side effects of Bisphosphonates
  - Oral Bisphosphonates
    - GI irritation
      - Proper administration
      - Individuals with aphasia, severe dysmotility or strictures should not be treated with oral bisphosphonates
  - IV Bisphosphonates (Ibandronate, Zolendronic Acid)
    - Flu like symptoms after first dose
    - Acute phase reactions (fever, lymphopenia)
    - Hypocalcemia
    - Renal toxicity

Treatment Side effects

- **Osteonecrosis of the Jaw (ONJ)**
  - Definition: necrotic bone in the maxillofacial region not healing after 6-8 weeks; often follows dental extraction or other invasive dental procedures
  - Clinical S/S: pain swelling, soft tissue ulceration, loosening of teeth
  - First report linking bisphosphonate with ONJ appeared in 2003: All 36 patients were being treated for skeletal complications of malignancy with 10x higher the dose of bisphosphonate than that used to treat osteoporosis
  - Subsequent reports, case studies reported incidence of ONJ at lower doses however about 90% of cases were in cancer patients

Side Effects: ONJ

- **Conclusion**:
  - Though not established yet there may be a causal link between ONJ and bisphosphonate use
  - Current guidelines suggest to inform patients of this potential but low risk
  - Regular **dental visits and maintenance of good oral hygiene should be reinforced**
  - **Patients who plan future invasive dental surgery if circumstance permits: start bisphosphonate therapy after completion of procedure and healing**
  - Patients already on therapy should avoid major dental work unless necessary; time off therapy is advised if procedure is needed but no evidence on outcomes for this

Treatment Side Effects

- **Subtrochanteric Fractures**
  - Definition: Unusual low energy subtrochanteric (5 cm distal to lesser trochanter) fractures and pelvic insufficiency fractures in patients on long term bisphosphonates
  - Thought to be due to over suppression of burn turnover leading to impaired bone remodeling, accumulation of micro damage in bone and increased skeletal fragility
  - Clinical S/S: prodromal pain in region of fracture; Radiographic: cortical hypertrophy, transverse fracture pattern and medical cortical spiking
  - Several case reports and retrospective studies have suggested this association [15]

Side effects: Subtrochanteric Fractures

- **Conclusion:**
  - Data itself is insufficient proof that long term bisphosphonate use is the only cause of atypical low trauma subtrochanteric fractures
  - Recent studies demonstrate that the risk-benefit ratio favors drug therapy in those at risk of osteoporosis related fracture
  - Randomized control trials with appropriate definition and radiographic description is needed

Can osteoporosis be prevented?

- Genetics, medical conditions, medication use will determine your likelihood of developing osteoporosis.
- When you have osteopenia- it can be to some degree prevented going to osteoporosis with lifestyle modifications and vitamin supplementation
- **Screening** is very important if you have had fractures already or are postmenopausal

RUSH OSTEOPOROSIS CENTER

The services we offer include:

- Dexa scan of the spine and hip
  - To assess the patient's bone mineral density
- Lateral Vertebral Assessment
  - Dexa scan to rule out compression fractures
- Dexa scan of the radius
  - Site of measurement for patients with hyperparathyroidism, or who've had hip or spine surgery.
- FRAX calculation
  - To estimate the patient's fracture risk
- Dexa scanning for research purposes in clinical trials
- All exams are read by a Rheumatologist.

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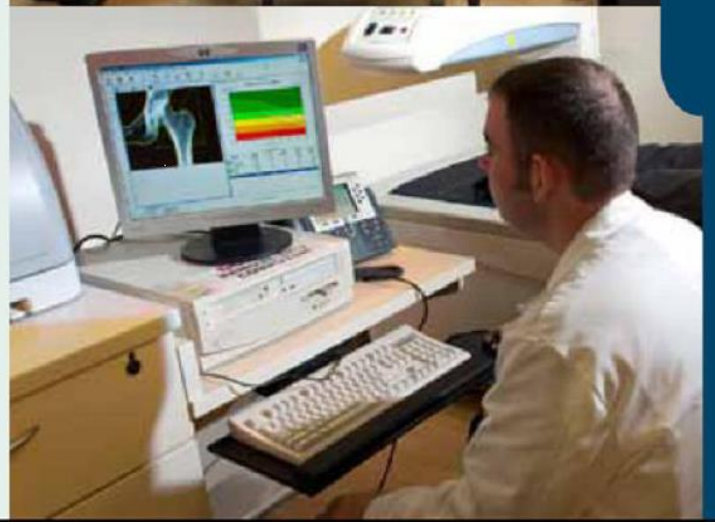

Thank you

- https://www.nof.org/
- https://www.rush.edu/services/osteoporosis-care