

Introduction to Osteoporosis



OBJECTIVES

- Understanding the definition of osteoporosis
- Causes of osteoporosis
- Impact of osteoporosis
- Diagnosis of osteoporosis
- Treatment of osteoporosis

Types of Bone

I. Cortical Bone:

The compact bone of Haversian systems such as in the shaft of long bones

II. Trabecular Bone:

The lattice – like network of bone found in the vertebrae and the ends of long bones.

The difference pattern of bone loss affecting trabecular and cortical bone results in two different fracture syndrome.

I. Osteoblasts:

The bone forming cells which are actively involved in the synthesis of the matrix component of bone (primarily collagen) and probably facilitate the movement of minerals ions between extracellular fluids and bone surfaces.

II. Osteocytes:

The are believed to act as a cellular syncytium that permits translocation of mineral in and out of regions of bone removed from surfaces.

III. Osteoclasts:

The bone resorption cells.

Bone has three major functions:

1. Provide rigid support to extremities and body cavities containing vital organs.
2. Provide efficient levers and sites of attachment of muscles which are all crucial to locomotion.
3. Provide a large reservoir of ions such as calcium, phosphorus, magnesium and sodium which are critical for life and can be mobilized when the external environment fails to provide them

Osteomalacia

Failure of organic matrix (osteoid) of bone to mineralize normally.

A number of factors are critical for normal bone mineralization. An absence or a defect in any one of them may lead to osteomalacia, the most common biochemical causes are a decrease in the product of concentrations of calcium and phosphate in the extra-cellular fluid so that the supply of minerals to bone forming surfaces is inadequate.

*Primary
Osteoporosis*

Type I Osteoporosis (Post Menopausal)

Fractures of bones composed mainly of Trabecular bone.

e.g., Distal Radius - Colle's fracture
Vertebra - Crush & Wedge fractures

Usually affects woman within 15 years of menopause.

Type II Osteoporosis (Senile)

Fractures of bones composed of both cortical & Trabecular bone.

e.g., Hip - Femure neck fracture

Usually affects individual over age of 70 years.

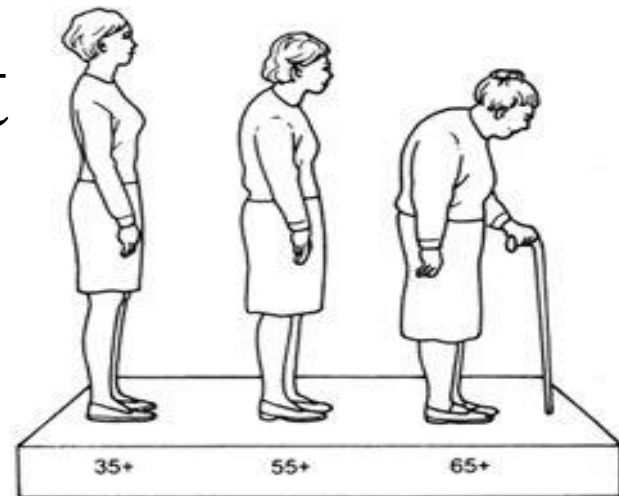
Difference in the two type of involutinal Osteoporosis

Type I

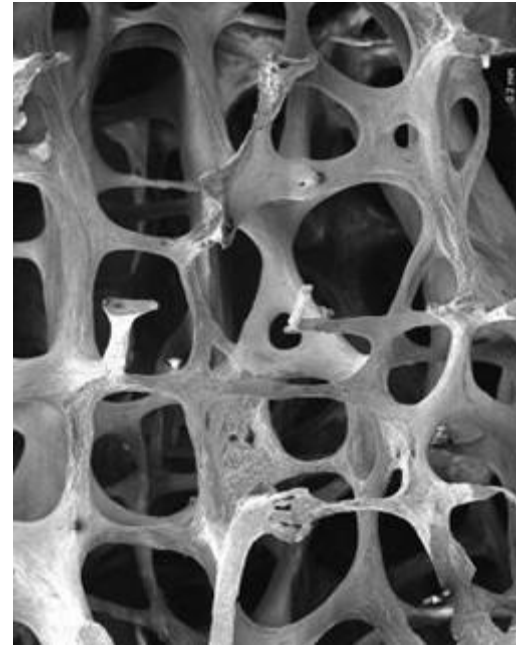
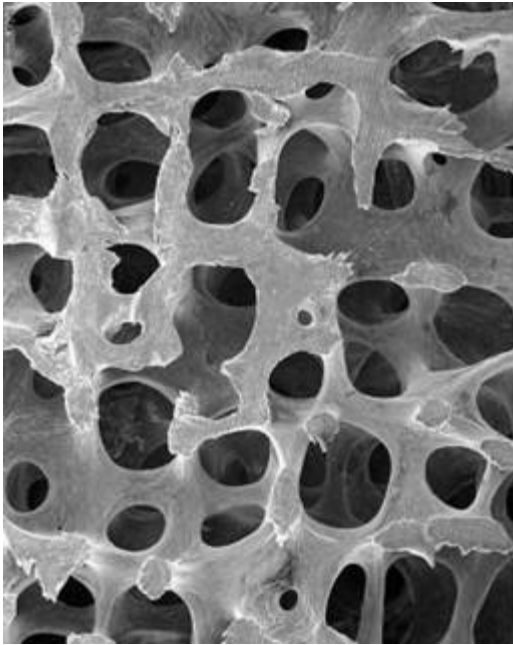
Type II

| | | |
|--|-----------------------------------|---|
| Age (Yr.) | 51 : 75 | >70 |
| Sex Ratio (F:M) | 6 : 1 | 2 : 1 |
| Type of bone loss | Mainly trabecular | Trabecular & Cortical |
| Rate of bone loss | Accelerated | Not accelerated |
| Fracture sites | Vertebrae (Crush) & distal radius | Vertebrae (Multiple wedge), hip, pelvis, proximal humerus |
| Parathyroid Hormone | Decreased | Increased |
| Calcium absorption | Decreased | Decreased |
| Metabolism of 25(OH) ₂ D to 1,25(OH) ₂ d | Secondary Decreased | Primary Decreased |
| Main causes | Factors related to menopause | Factors related to aging |

Skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Bone strength reflects the integration of bone density and bone quality



Normal vs. osteoporotic bone



Risk Factors: non-modifiable

- Age (increasing)
- Low BMI (small, low weight;< 58 kg)
- Ethnicity: Caucasian > Asian/Latino > African American
- Family History of Fracture

Risk Factors: Modifiable

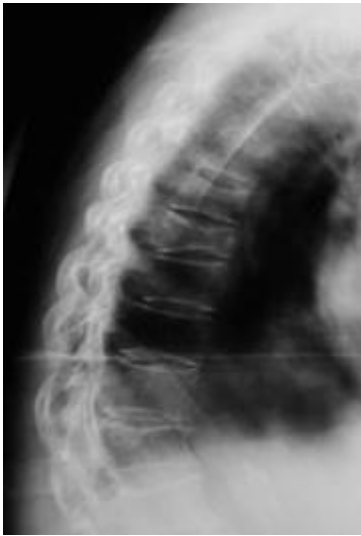
- Sex Hormones (low estrogen/testosterone)
- Low calcium and vitamin D
- Inactive lifestyle
- Excessive alcohol
- Cigarette smoking
- Rheumatoid arthritis
- Hyperparathyroidism (primary or secondary)
- Hyperthyroidism
- GI conditions which impair adequate nutrition
- Steroids or Cushing's
- Proton pump inhibitors

Clinical presentation of osteoporosis

- Generally patients are asymptomatic even with very low bone densities
- Hip Fractures
- Acute or chronic back pain secondary to vertebral fractures
- Atraumatic or low impact fractures

COMMON SITES OF FRACTURE :

SPINE , FOREARAM AND HIP



DIAGNOSIS OF OSTEOPOROSIS

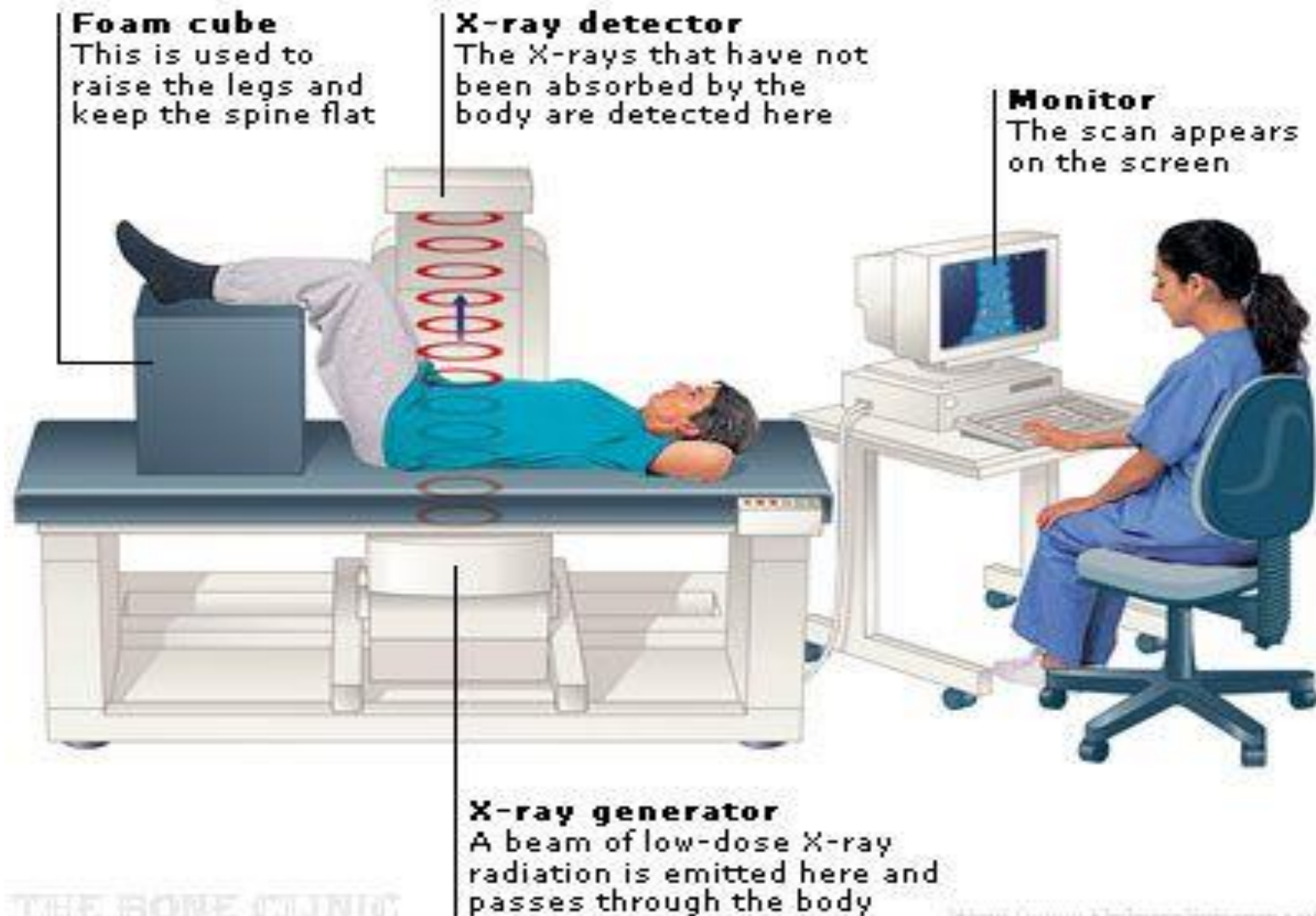
Assessment of bone mass available methods

- Single-Photon absorptiometry SPA
- Dual-Photon absorptiometry DPA
- Computed Tomography CT
- Dual-Energy X-ray Absorptiometry DEXA/DXA

They measure **bone mass** by the ability of the tissue to absorb the photons emitted from the radionuclide source or the X-ray tube.

Age related bone loss particularly trabecular bone in the spine begins in women before menopause.





WHO 1994

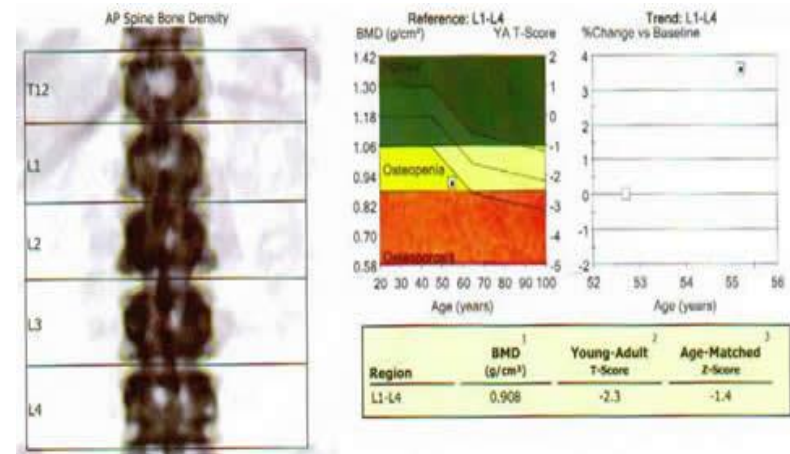
Definition based on BMD :

Normal : greater than or equal
to -1 SD

Osteopenia: BMD which lies
between - 1 and -2.5 SD

Osteoporosis : less than or
equal to - 2.5 SD

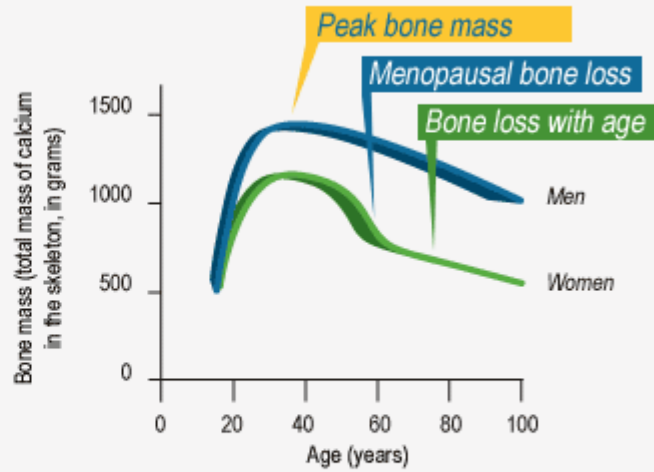
Severe osteoporosis :
osteoporosis with 1 or more
fragility fractures



Younger individuals

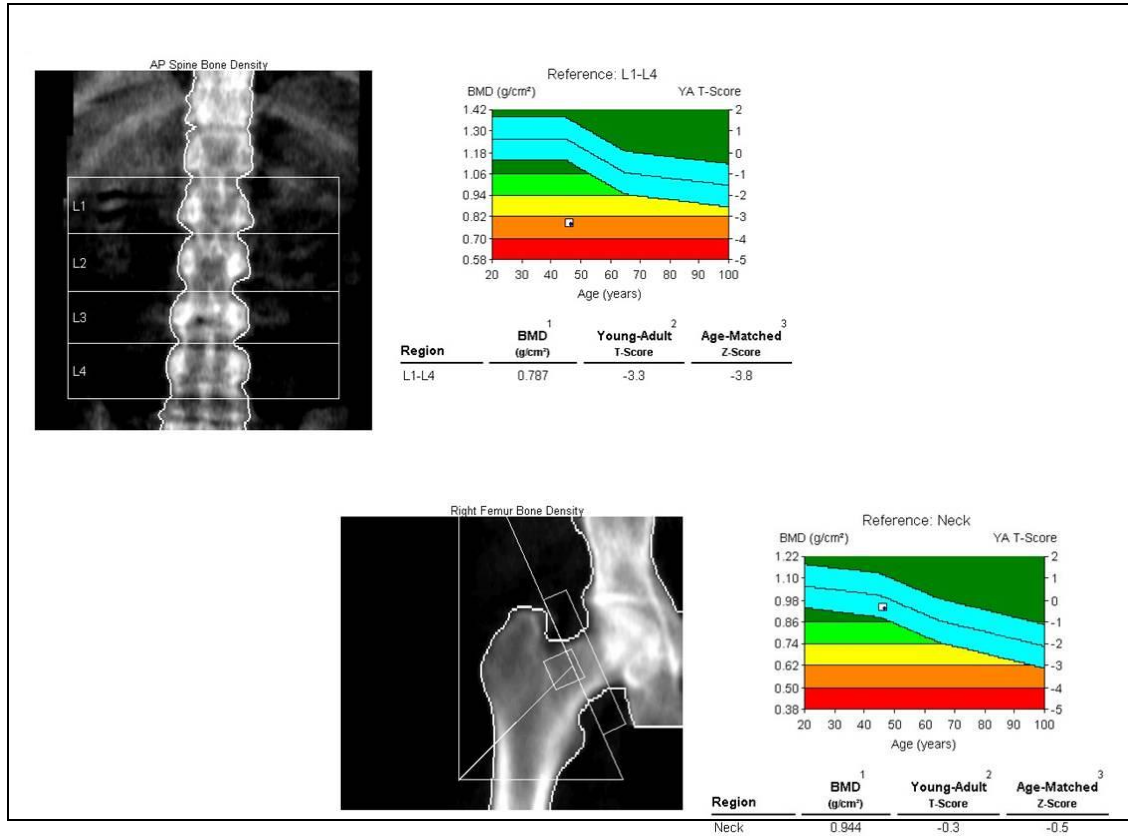
- USE Z SCORE (comparison to age-matched norms)
- If ≤ 2 (below expected range for age)

Osteoporose process

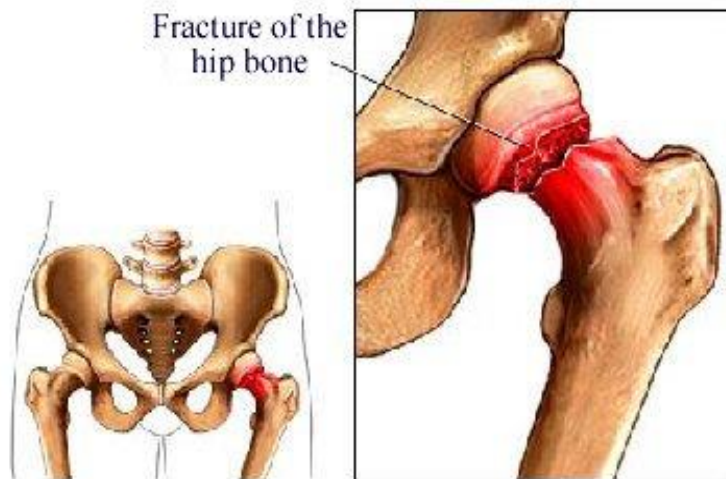


“ Osteoporosis is one of the most prevalent diseases in the western world, mainly among postmenopausal women but also among elderly men. ”

DXA RESULT

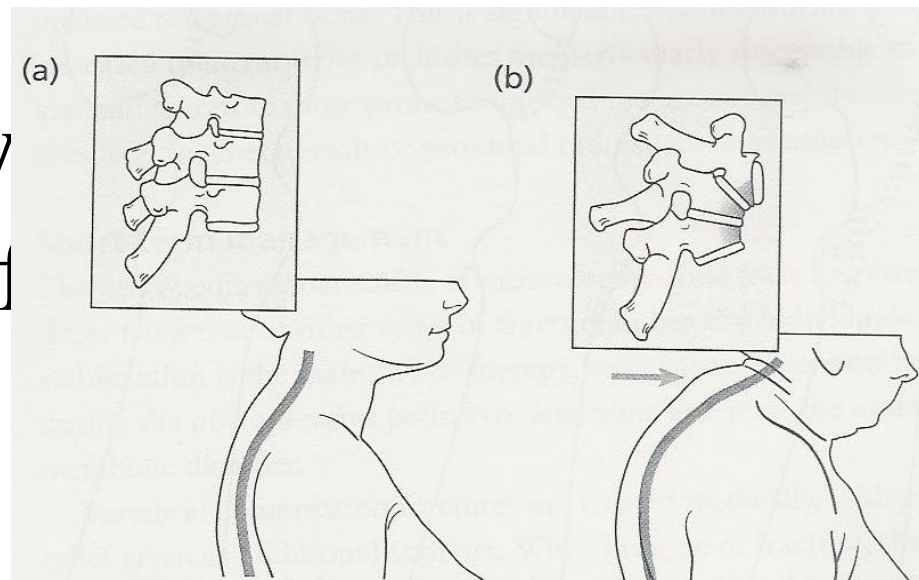


Hip fractures



- Hip fractures are bad
 - 20% patients with hip fracture die within the year
 - 25-30% need placement in skilled nursing facility

Affected Vertebral fractures : rarely reported by physicians
10 % of vertebral fractures result in hospitalizations
Prevalence increases with age
Male to female ratio 1: 1
Mid thoracolumbar region are most commonly affected.
Cause lower energy,poor sleep,pain,immobility and social isolation especially in men.
Back deoformities :loss of height and kyphosis.



Hip fractures

Cause serious disability and excess mortality

Highest incidence in Scandinavian and N American countries.

Women who have sustained fracture have a 10-20 % higher mortality than would be expected for their age.

Above 50 years of age , female to male ratio is 2: 1.

Mortality is higher in men , greater with co existent diseases

1-year mortality : 31 % in men and 17% in women

Risk of death is greatest immediately post fracture

Economic Impact

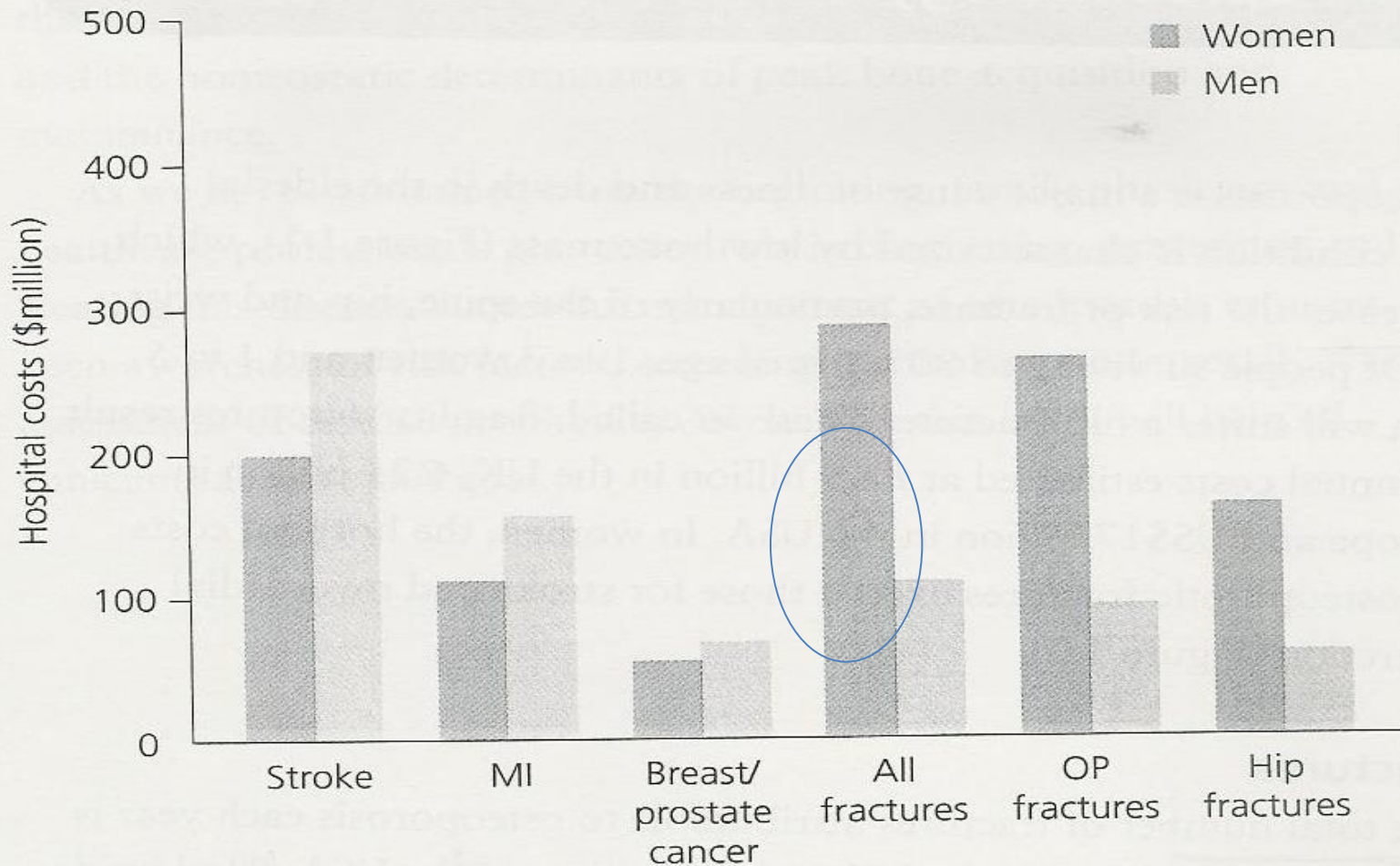
Huge

Osteoporotic fractures cost the US 17.9 billion per annum

UK : 1.7 billion

Cost is largely attributed to hip fractures

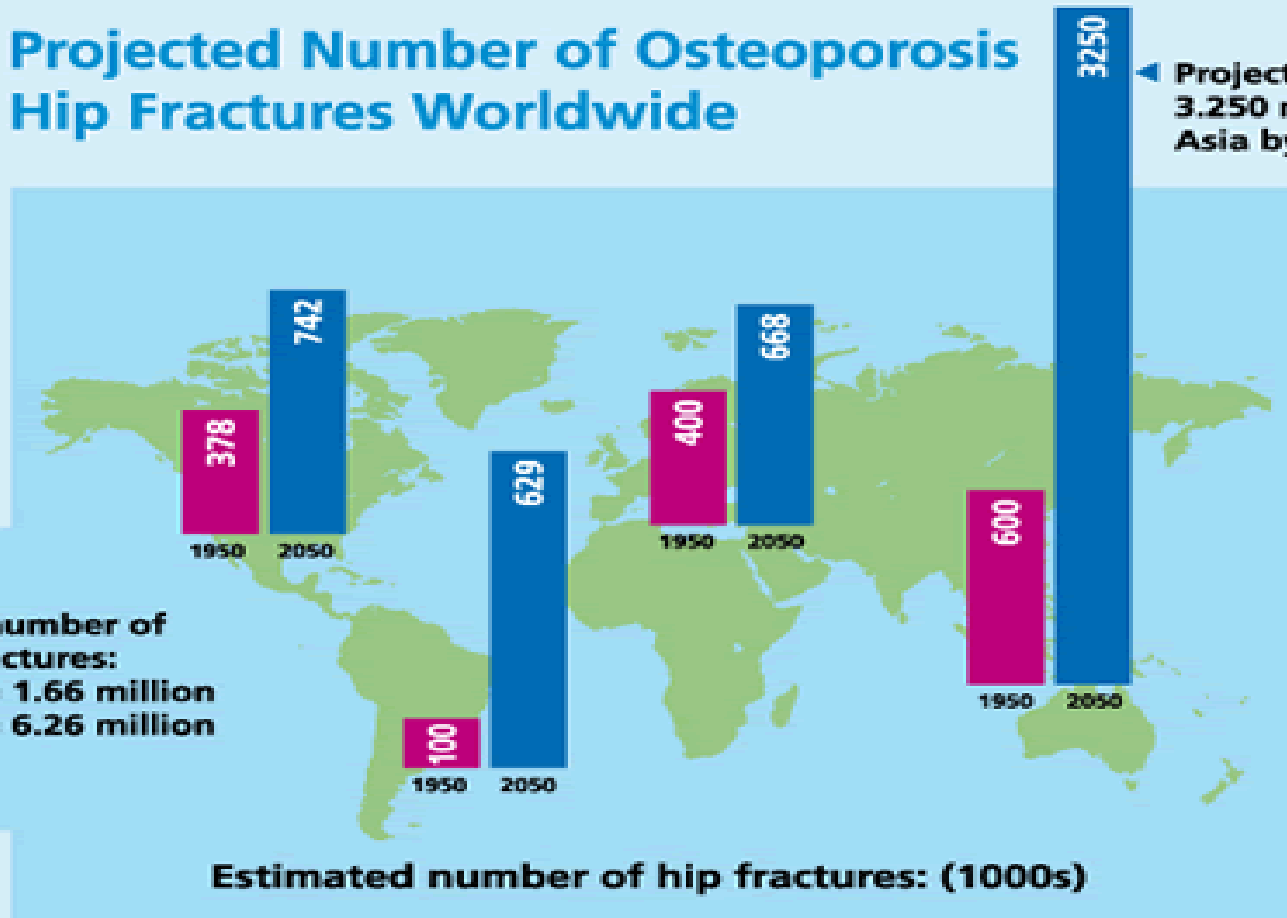
Impact of osteoporosis and cost

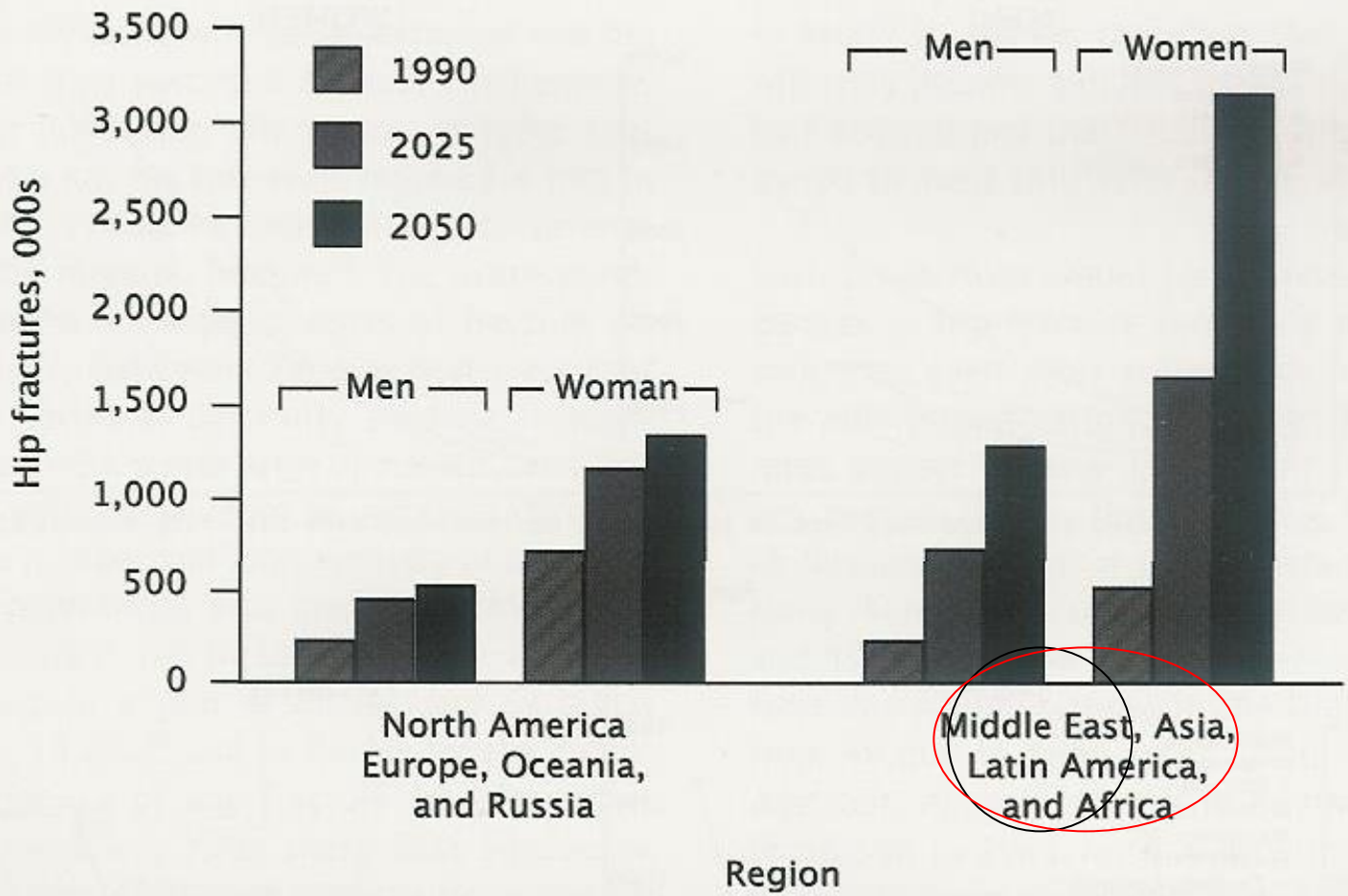


Projected Number of Osteoporosis Hip Fractures Worldwide

Projected to reach 3.250 million in Asia by 2050

Total number of hip fractures:
1950 = 1.66 million
2050 = 6.26 million





Identification of fracture risk

- **FRAX** (WHO fracture risk assessment tool) : 10 year probability of clinical fracture : hip & major osteoporotic fracture – hip, spine and forearm-
- Variables : age
 - BMI
 - previous fracture
 - current smoking
 - steroids
 - RA
 - secondary causes
 - alcohol
 - femoral neck BMD

WHEN TO SCREEN WITH DXA SCAN

- VERY CONTROVERSIAL
- IN US AND CANADA : WOMEN \geq 65 YEARS
- MEN \geq 70 YEARS
- SCREEN IN INDIVIDUALS WITH RISK FACTORS
EG. STEROIDS
- EUROPE : CASE FINDING IE IN PEOPLE WITH
RISK FACTORS

Exclude secondary causes especially in younger individuals and men

Box 2: Common secondary causes of bone loss

- Hyperparathyroidism (primary or secondary)
- Vitamin D inadequacy
- Malabsorption state (e.g., celiac disease, inflammatory bowel disease, short gut syndrome)
- Hypercalciuria
- Hyperthyroidism
- Chronic lung disease
- Malignancy (e.g., myeloma, bony metastasis)
- Rheumatoid arthritis
- Hepatic insufficiency

Secondary Factors causing Bone Loss

Factors Associated with Decreased Bone density

Medical Conditions

Premature menopause

Hypogonadism (in men)

Liver disease

Hyperthyroidism

Hyperparathyroidism

Hemiplegia

Chronic obstructive lung dis.

Drug Therapy

Glucocorticoids

Anticonvulsants (Phenytoin, Phenobarbitone)

Nutrition

? Low calcium & Vit. D intake

? High phosphorus, protein, sodium, caffeine intake

Behavioral factors

Smoking & Alcohol abuse

Laboratory & Radiological Findings

Bone profile ,ALP and PTH are within normal in patients with osteoporosis due to sex hormones deficiency and aging.

X-rays of skeleton do not show a decrease in osseous density until at least 30% of bone mass has been lost.

X-ray of spine show prominent trabeculae and prominent end plates of the vertebral bodies.

Cod fish appearance indicates protrusion of the disk into the body of the vertebrae secondary to mechanical failure.

X-ray of the upper part of the femur may also be helpful in assessing reduced bone mass and calculating the risk for hip fracture.



PREVENTION AND TREATMENT

Prevention

- Adequate nutrition, particularly calcium and vitamin D
 - Calcium: 1000 – 1200 mg daily (diet plus supplementation)
 - Vitamin D: goal level above 50-75 nmol/l
- Weight bearing exercise
- Discourage smoking
- Reduction of risks for falling: consider OT evaluation for home hazards, minimize sedating medications.
- Hip protectors: can be useful if worn properly but often have low compliance

MANAGEMENT

- **Nonpharmacologic**
- Modification of life style measures
- Exercise
- Prevention of falls
- Adequate calcium and vitamin D intake
- Stopping smoking
- More sun exposure

Calcium and Vitamin D

- At least 1000 mg /day for men ≤ 65 or younger
- 1500 mg /day for older men. Ca citrate vs. Ca carbonate.
- Vitamin D : check 25 (OH) vit. D level . If very low you need to “replete” the stores first . Maintenance dose is 800 IU for men younger than 50 and 800-1000 IU for men older than 50
- 1000 IU for all patients with osteoporosis or reduced bone mass regardless of their age. Higher doses may need to be used especially in Saudi Arabia. Optimum level : at least 50nmol/l. Patients with high risk of fracture : 75 nmol/l.

Treatment Options

- 1. Bisphosphonates (anti resorptive)
- 2. Denosumab (anti resorptive)
- 3. Teriperatide (anabolic)
- 4. SERMs (Selective estrogen receptor modulators) –
- 5. Hormone replacement therapy
- 6. Romosozumab (anabolic)

Table

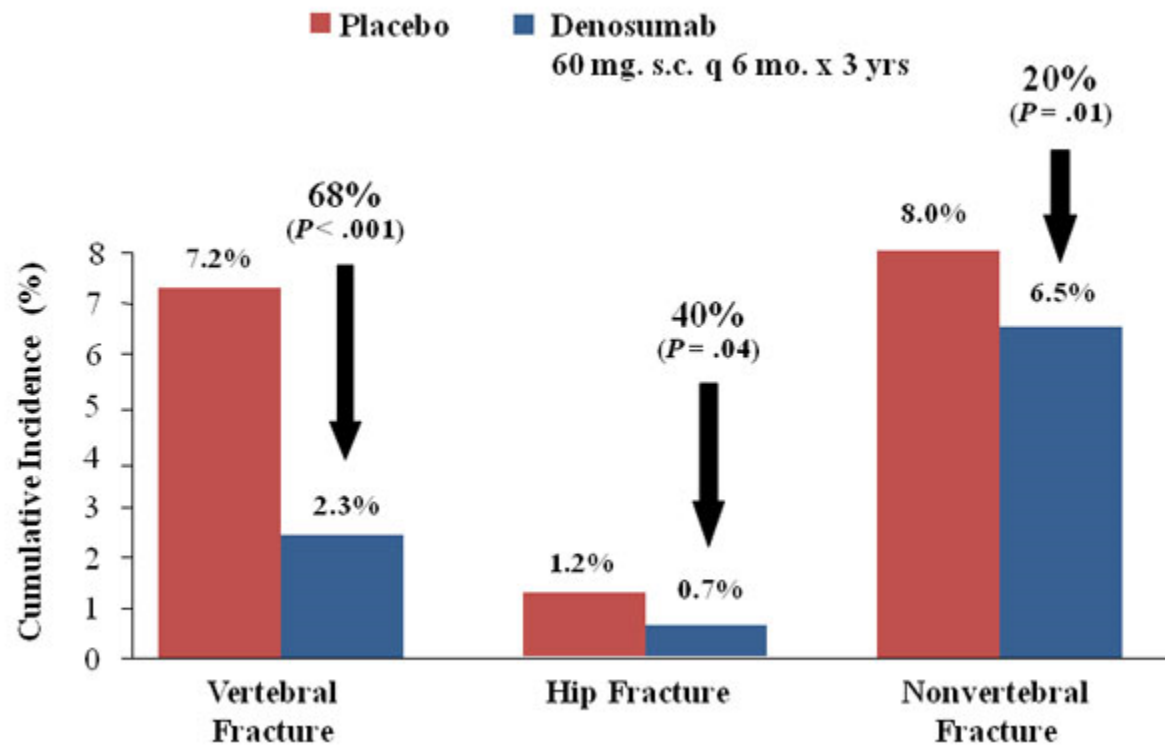
Prescription Agents for Osteoporosis

| Medication | Prevention Dose | Treatment Dose |
|---|--|-----------------------------------|
| Bisphosphonates | | |
| Alendronate sodium (Fosamax)—Merck | 5 mg po daily 35 mg po weekly | 10 mg po daily 70 mg po weekly |
| Risedronate sodium (Actonel)—Procter & Gamble/Aventis | 5 mg po daily 35 mg po weekly | 5 mg po daily 35 mg po weekly |
| Estrogens (various) | Equivalent to 0.3-0.625 mg conjugated equine estrogen daily | Not indicated |
| SERMs | | |
| Raloxifene (Evista) —Lilly | 60 mg po daily | 60 mg po daily |
| Calcitonin-Salmon | | |
| (Miacalcin)—Novartis | Not indicated | 200 IUs intranasally daily |
| Parathyroid Hormone | | |
| Teriparatide (Forteo) —Lilly | Not indicated | 20 mcg sq daily |

Po = by mouth; SERMs = selective estrogen receptor modulators; IUs = international units; sq = subcutaneously.

| | Indications | Dosage | Notes |
|--------------------------|---|---|---|
| Raloxifene | Prevention and treatment of postmenopausal osteoporosis | 60 mg/day | <ul style="list-style-type: none"> • May reduce risk of breast cancer; improves lipids • Associated with increased risk of deep vein thrombosis and pulmonary embolism |
| Teriparatide* | Treatment of osteoporosis in postmenopausal women at high risk for fracture | 20 µg/day (subcutaneous injection) | <ul style="list-style-type: none"> • Teriparatide given to rats for most of their lifetime caused some rats to develop a form of bone cancer • Use of the drug for > 2 years not recommended |
| Calcitonin | Treatment of postmenopausal osteoporosis in women who have been menopausal for ≥ 5 yr | 200 IU/day intranasally; alternate nostrils daily | <ul style="list-style-type: none"> • Generally safe; patients may experience rhinitis or epistaxis |
| Certain estrogens | Prevention of postmenopausal osteoporosis | Various doses and regimens | <ul style="list-style-type: none"> • Increased risk of thrombosis and stroke |

Denosumab : monoclonal Ab to the receptor activator(RANKL)



summary

- **Screening**
 - All women > 65 years
 - Men > 70
 - Women 50-64 with risk factors
 - Patients on steroids or anti-estrogen/anti-testosterone treatment
- **2. Prevention with adequate calcium/vitamin D, weight bearing exercise should be advised for all.**
- **3. DXA scan is the primary screening tool**
- **4. Aggressive therapy should be offered to patients with atraumatic/low-impact fractures and those with osteoporosis, osteopenia with multiple risk factors, patients on steroids, anti-estrogen, and anti-testosterone therapy with abnormal bone densities (T score <-1).**