“Osteoporosis - The Silent Killer”

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Definition of osteoporosis

"...a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk."

World Health Organization (WHO), 1994

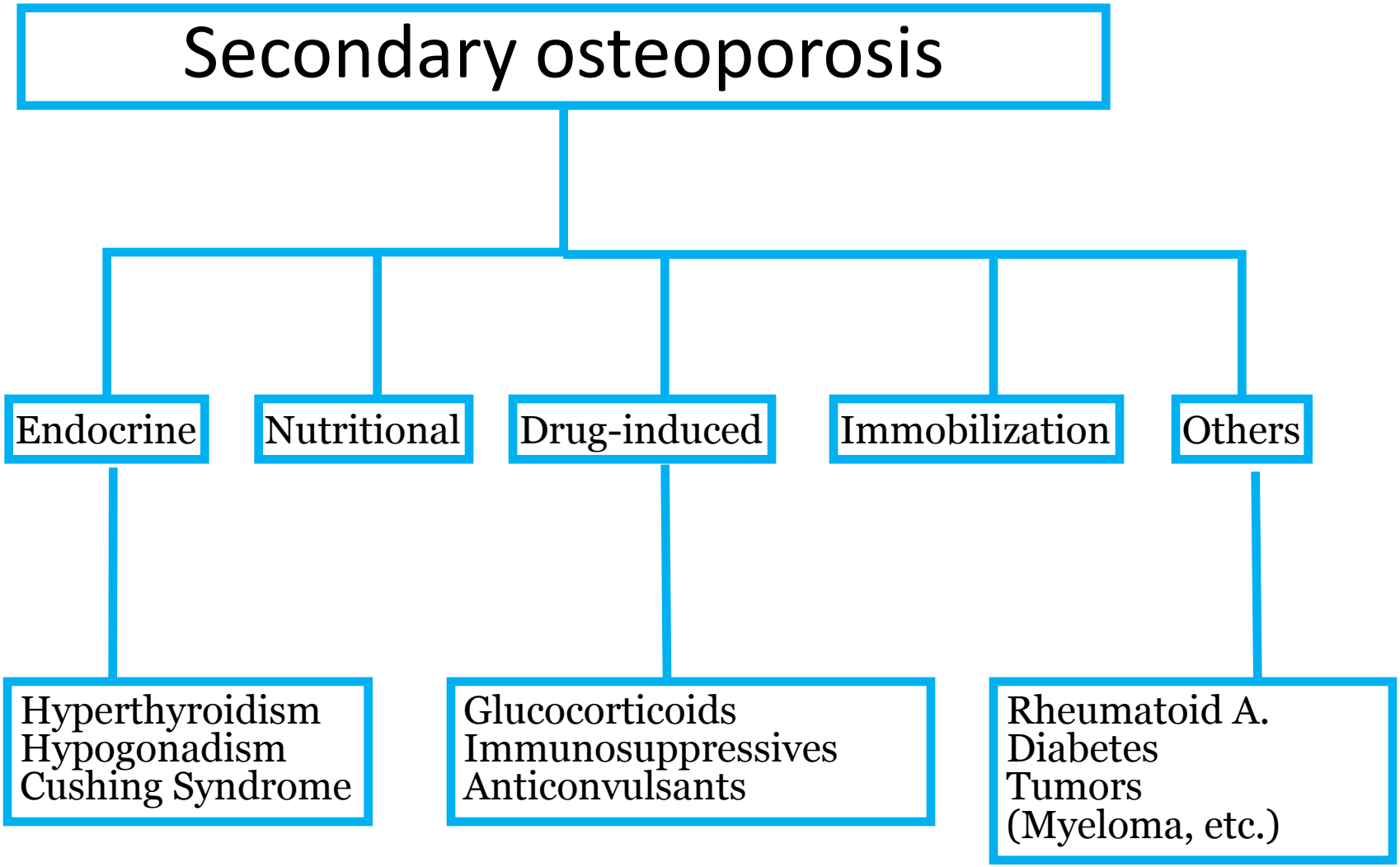
Primary osteoporosis

Postmenopausal

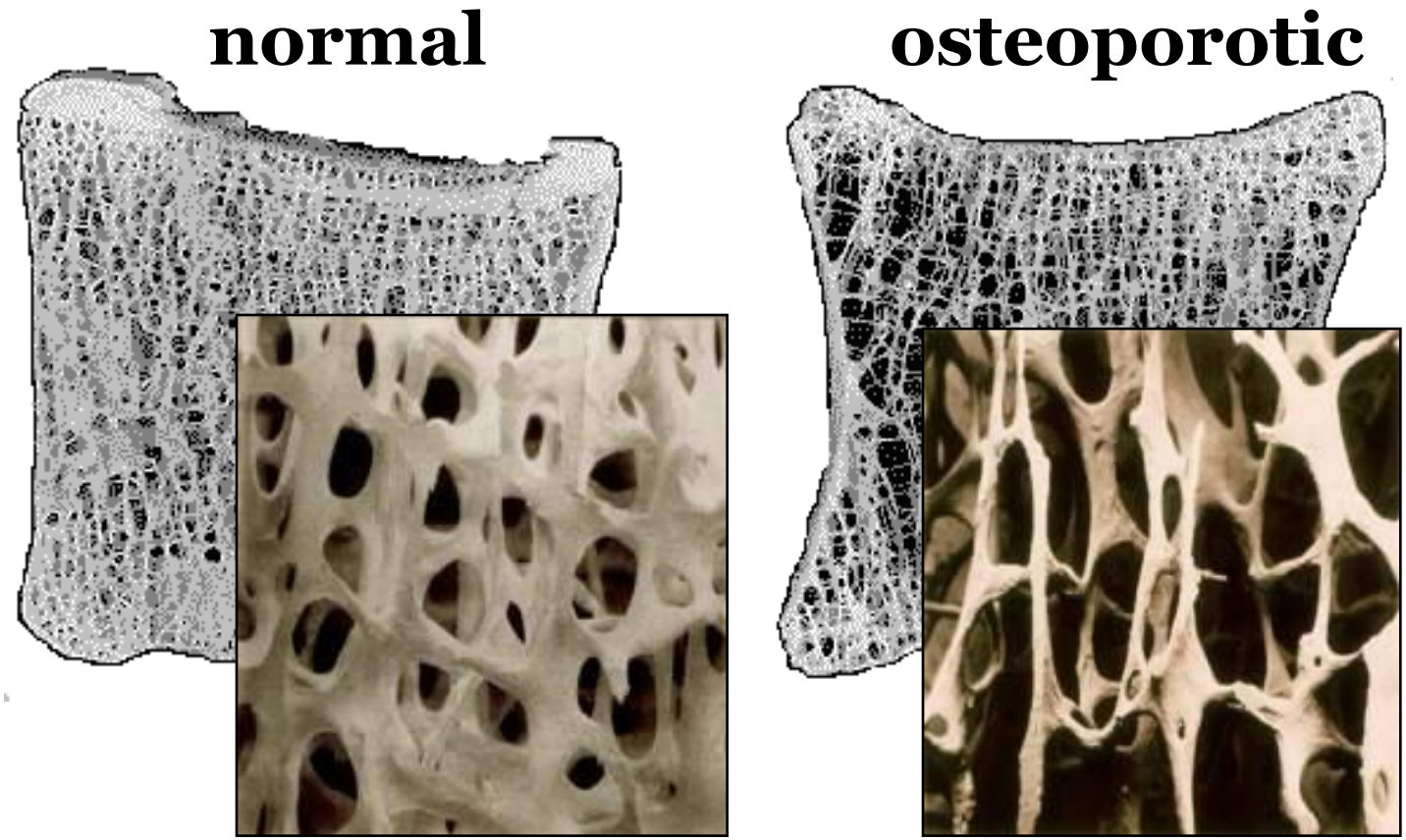
- Decreased estrogen results in increased osteoclastic activity without increased osteoblastic activity
- Bone loss – 2-3% per year of total bone mass
- Most common fx: vertebral, distal forearm

Age related

- Starts in 3rd decade of life, slow decline in bone mass at rate of 0.5-1% per year
- Most common types of fx: hip and radius
- F>M


Secondary osteoporosis
Endocrine
Nutritional
Drug-induced
Immobilization
Others
Hyperthyroidism
Hypogonadism
Cushing Syndrome
Glucocorticoids
Immunosuppressives
Anticonvulsants
Rheumatoid A.
Diabetes
Tumors
(Myeloma, etc.)

Vertebral body



Osteoporosis prevalence

- Affects 200 million women worldwide[1]
  - 1/3 of women aged 60 to 70
  - 2/3 of women aged 80 or older
- Approximately 30% of women over the age of 50 have one or more vertebral fractures[2]
- Approximately one in five men over the age of 50 will have an osteoporosis-related fracture in their remaining lifetime[1]

1. IOF, 2005 (www.osteofound.org)
2. Dennison E & Cooper C, Horm Res, 2000;54 suppl 1:58-63

Osteoporosis in India

- Based on 2001 census, approximately 163 million Indians are above the age of 50; this number is expected to increase to 230 million by 2015[1]

- Even conservative estimates suggest that of these, 20 per cent of women and about 10-15 per cent of men would be osteoporotic. The total affected population would, therefore, be around **25 million**. These figure can increase to **50 million**[2]

1. Nordin BEC. Clin Orthop 1966; 45 : 17-30.
2. Gupta AKIndian J Med Res 1967; 55 : 1341-8.

Osteoporosis in India

- 1 out of 8 males and 1 out of 3 females in India suffers from osteoporosis, making India one of the largest affected countries in the world[1]
- Two points worth noting about osteoporosis in India - the high incidence among men and the lower age of peak incidence compared to Western countries.
- The incidence of hip fracture is 1 woman to 1 man in India[2]
- In most Western countries, while the peak incidence of osteoporosis occurs at about 70-80 years of age, in India it may afflict those 10-20 years younger, at age 50-60.[2]

1. http://www.outlookindia.com 2004
2. Damodaran PSingapore Med J. 2000 Sep; 41(9): 431-5

Osteoporosis- fundamental pathological mechanisms

- Failure to achieve a skeleton of optimal strength during growth and development
- Excessive bone resorption resulting in loss of bone mass and disruption of architecture
- Failure to replace lost bone due to defects in bone formation

Risk Factors for Osteoporotic Fracture

(Major)

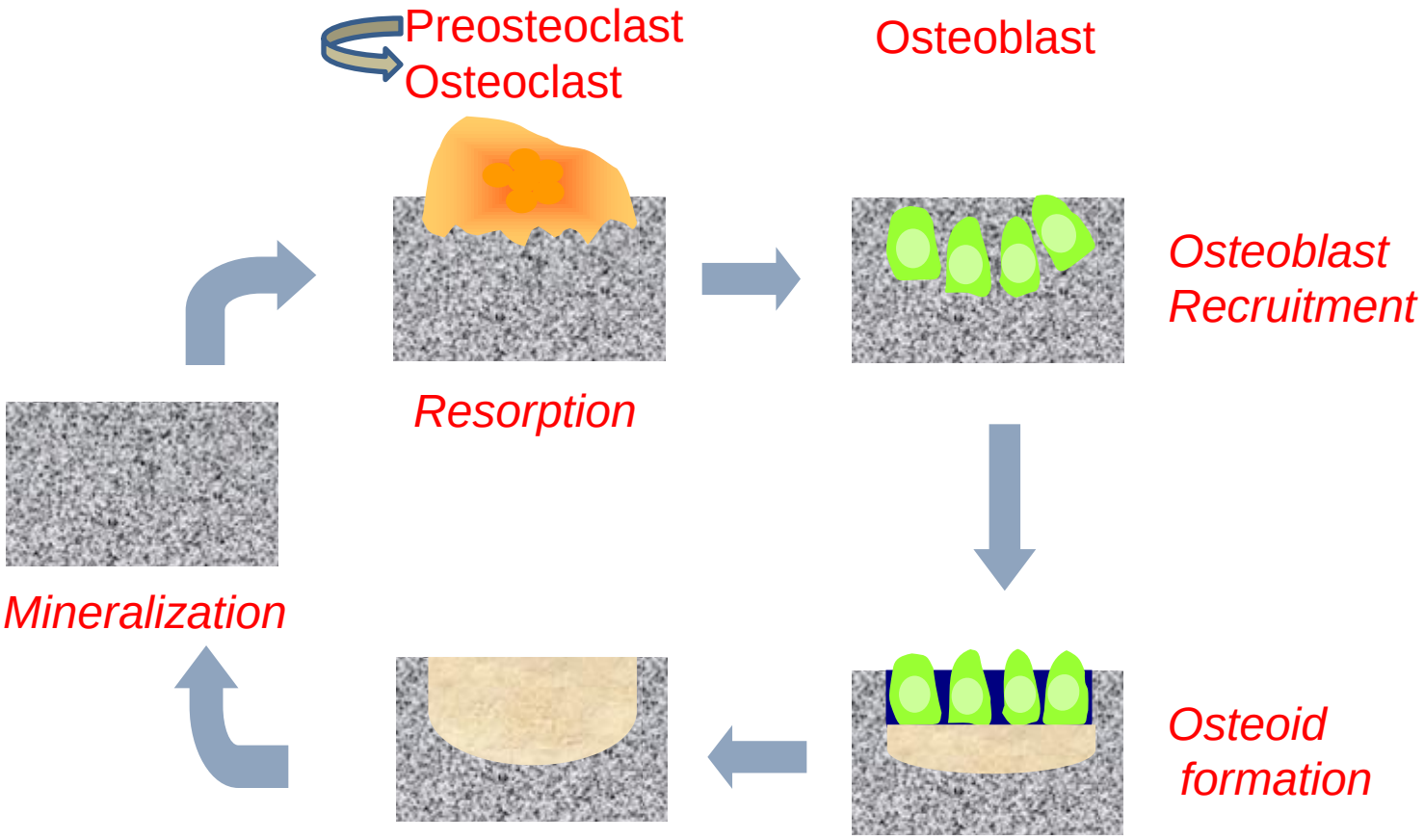
- Age > 70
- Menopause < 45
- Hypogonadism
- Hip Fracture in Parents
- Glucocorticoids
- Malabsorption
- High Bone Turnover
- Anorexia Nervosa
- BMI < 18
- Immobilisation
- Chronic Renal Failure
- Transplantation

(Moderate)

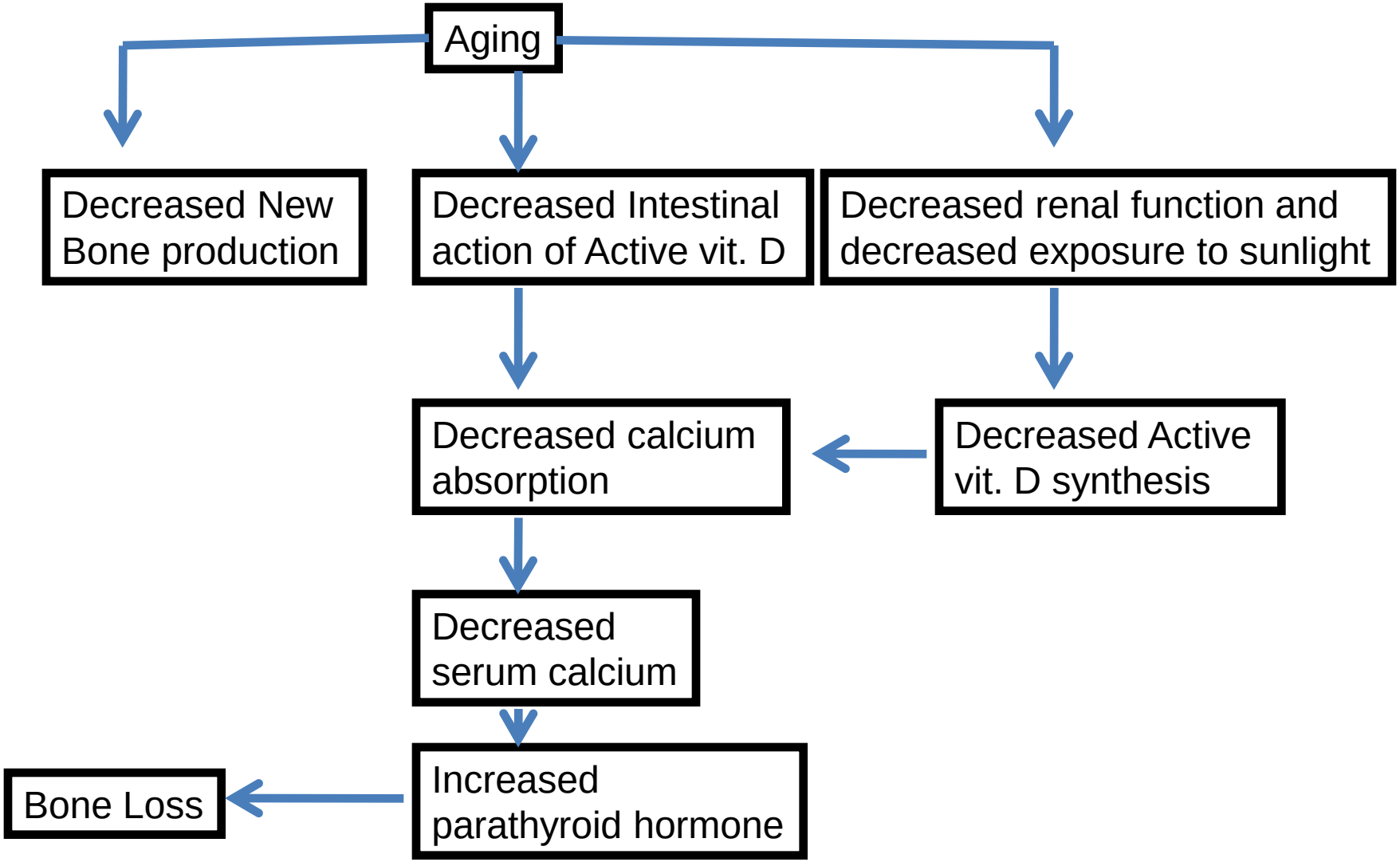
- Estrogen Deficiency
- Calcium Intake < 500 mg/d
- Primary Hyperparathyroidism
- Rheumatoid Arthritis
- Anticonvulsants
- Hyperthyroidism
- Diabetes Mellitus
- Smoking
- Alcohol Excess

Brown JP & Josse RG, CMAJ, 2002;167(10 suppl):S1-S34

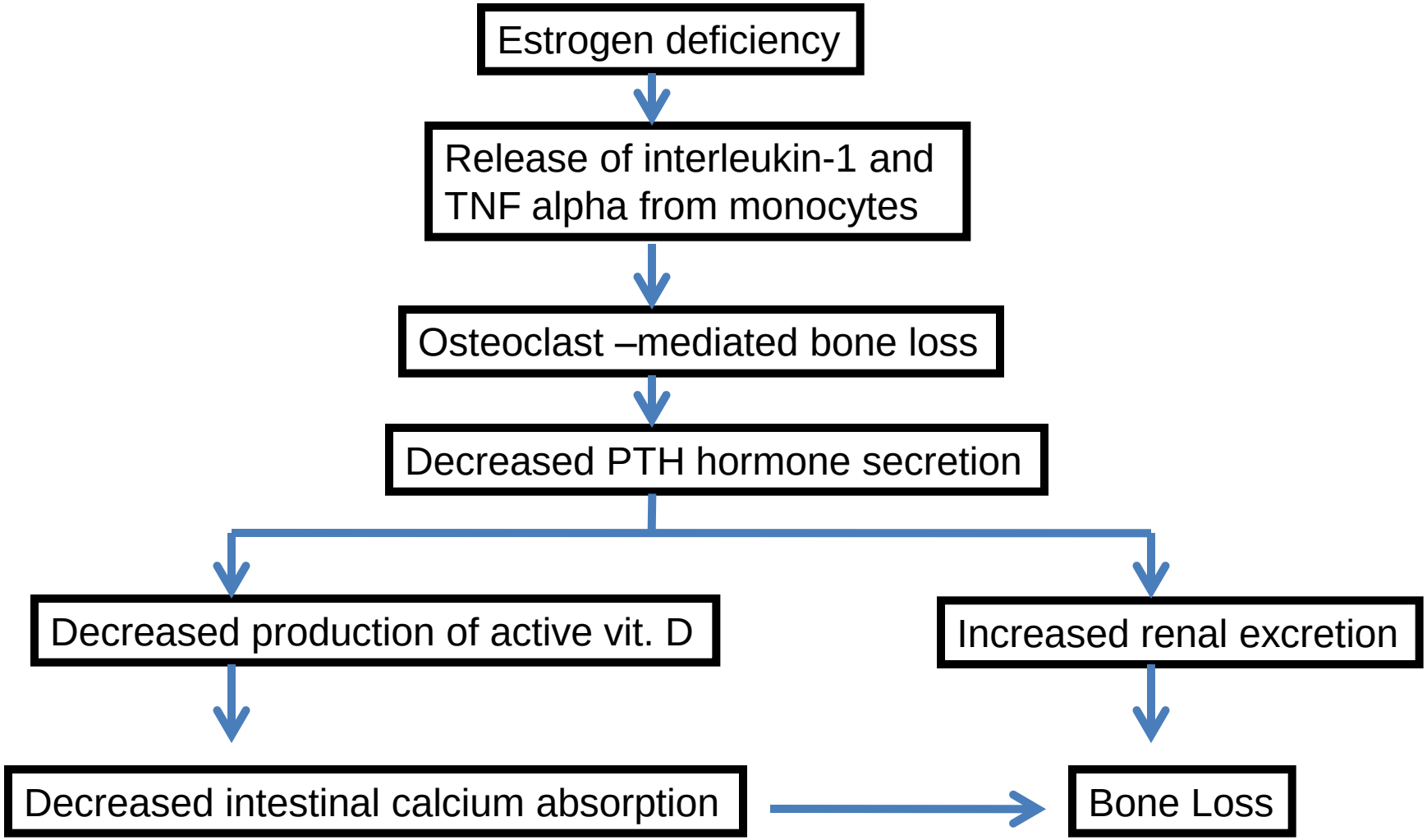
The Bone Remodeling Cycle



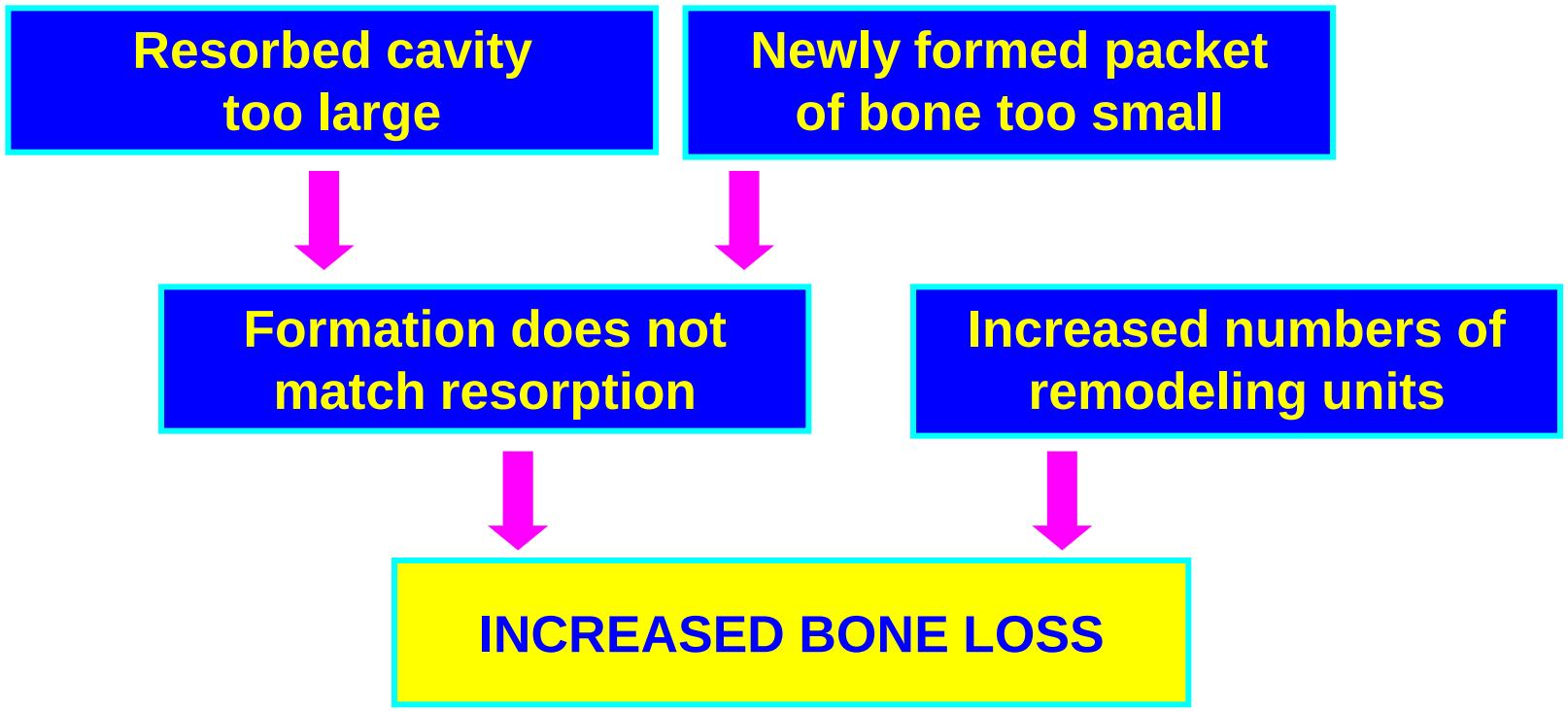
Senile Osteoporosis- Pathophysiology



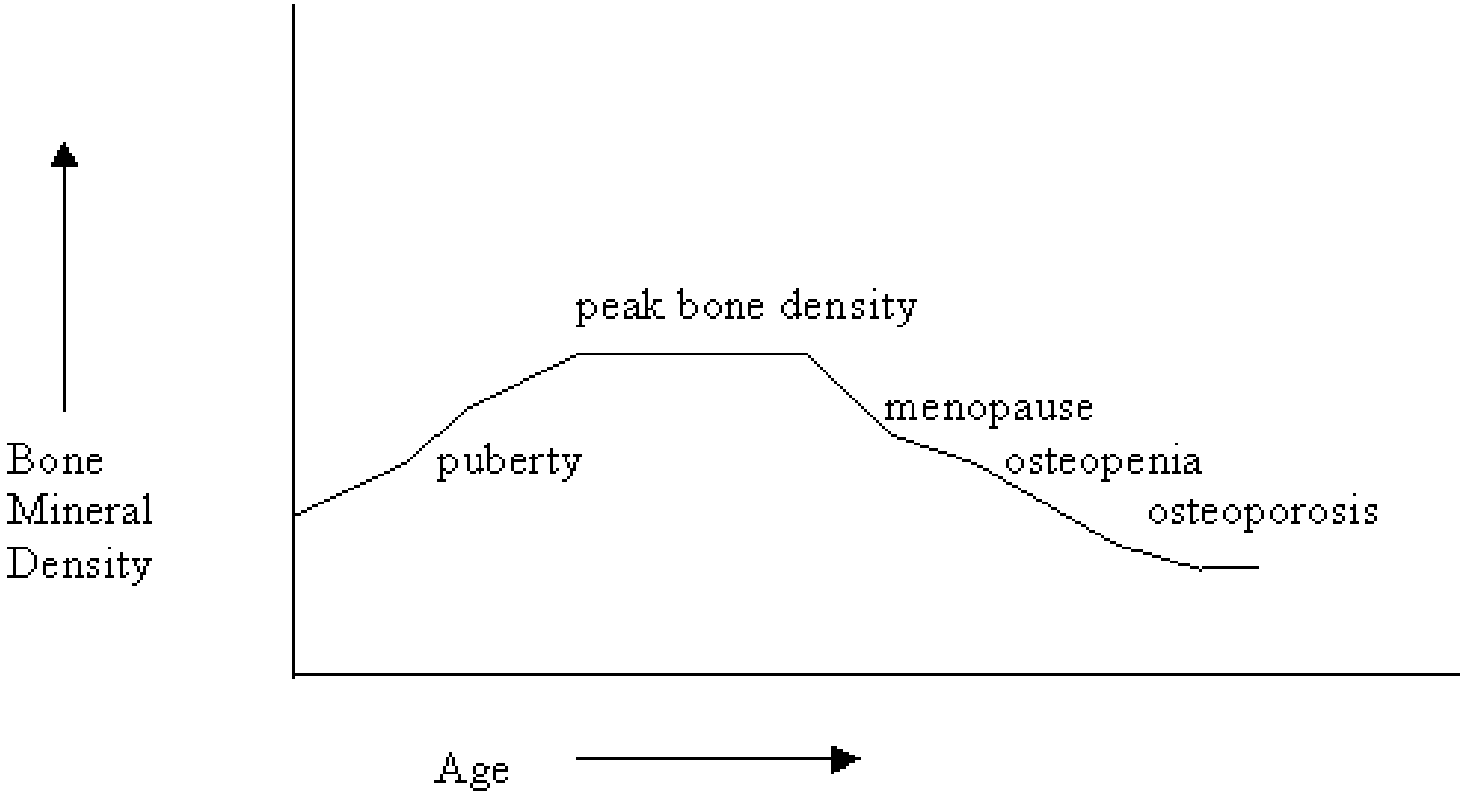
Post menopausal Osteoporosis- Pathophysiology



Pathogenesis of osteoporosis

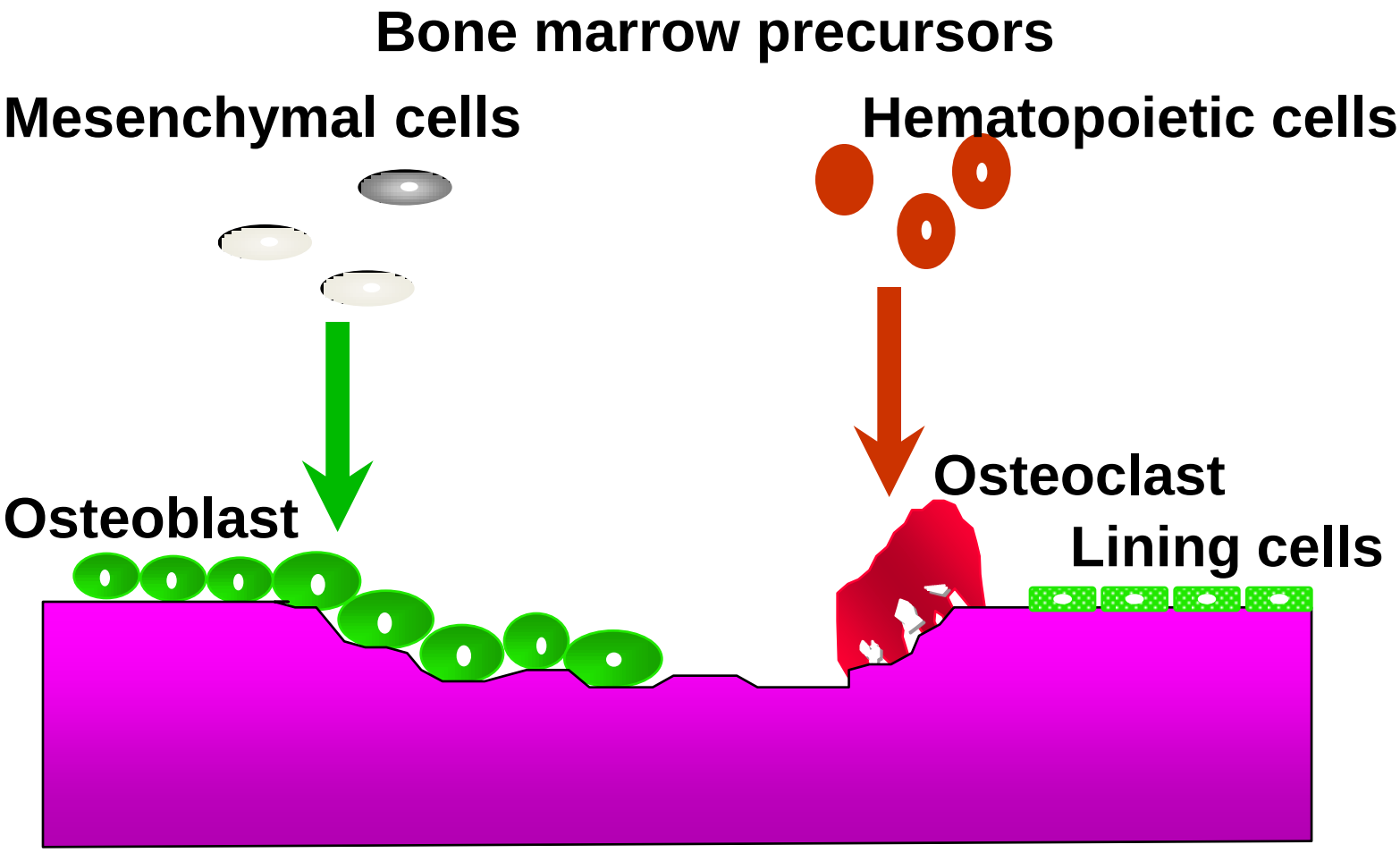


Bone mineral density increases until around age 35yrs and then levels off until menopause.

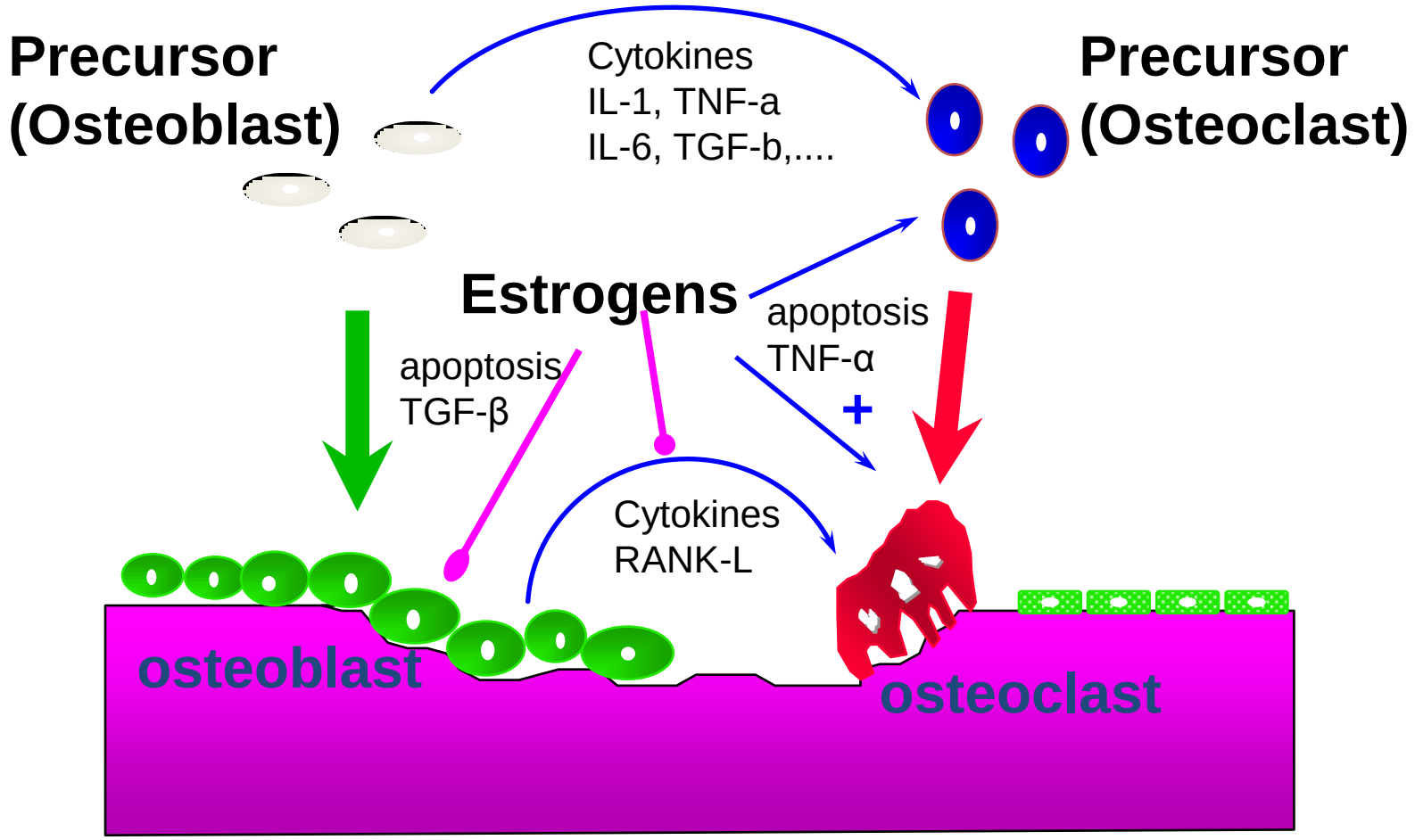


During the first six to eight years of menopause, there is a sharp decline in bone mineral density. It is estimated that between 1% and 5% of bone density is lost at this time.

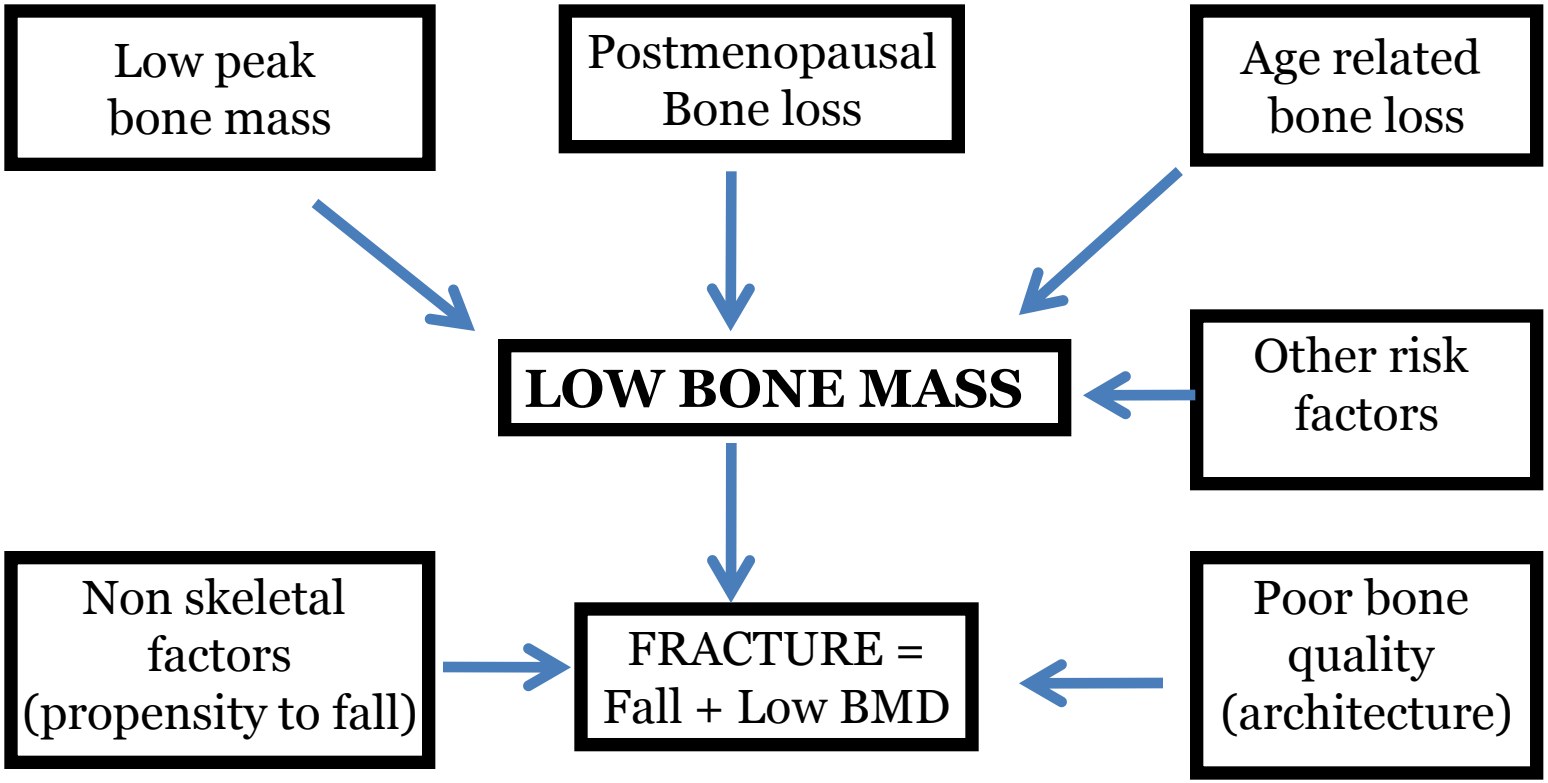
Bone remodeling



Estrogens: mechanism of action in bone

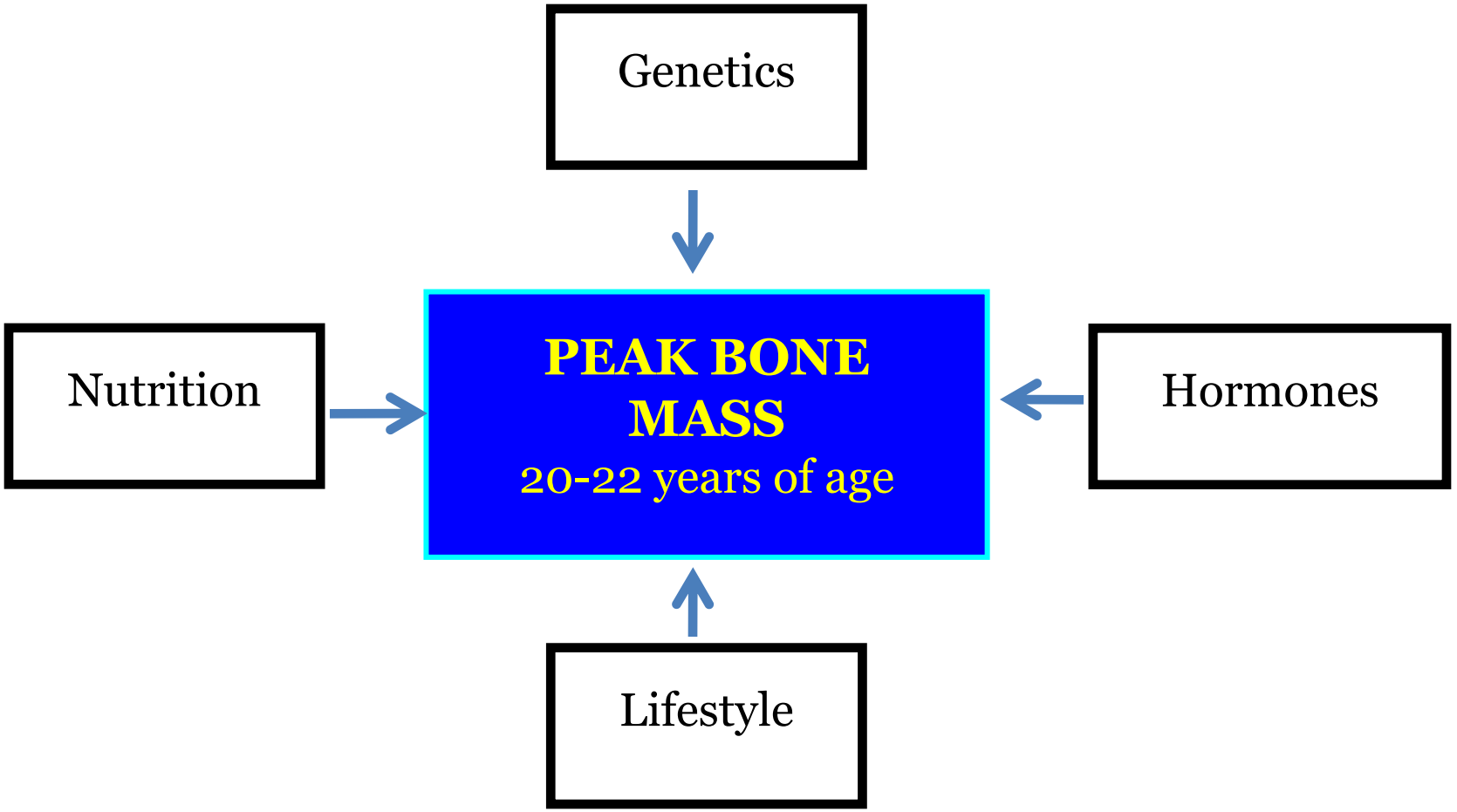


Pathogenesis of osteoporotic fracture

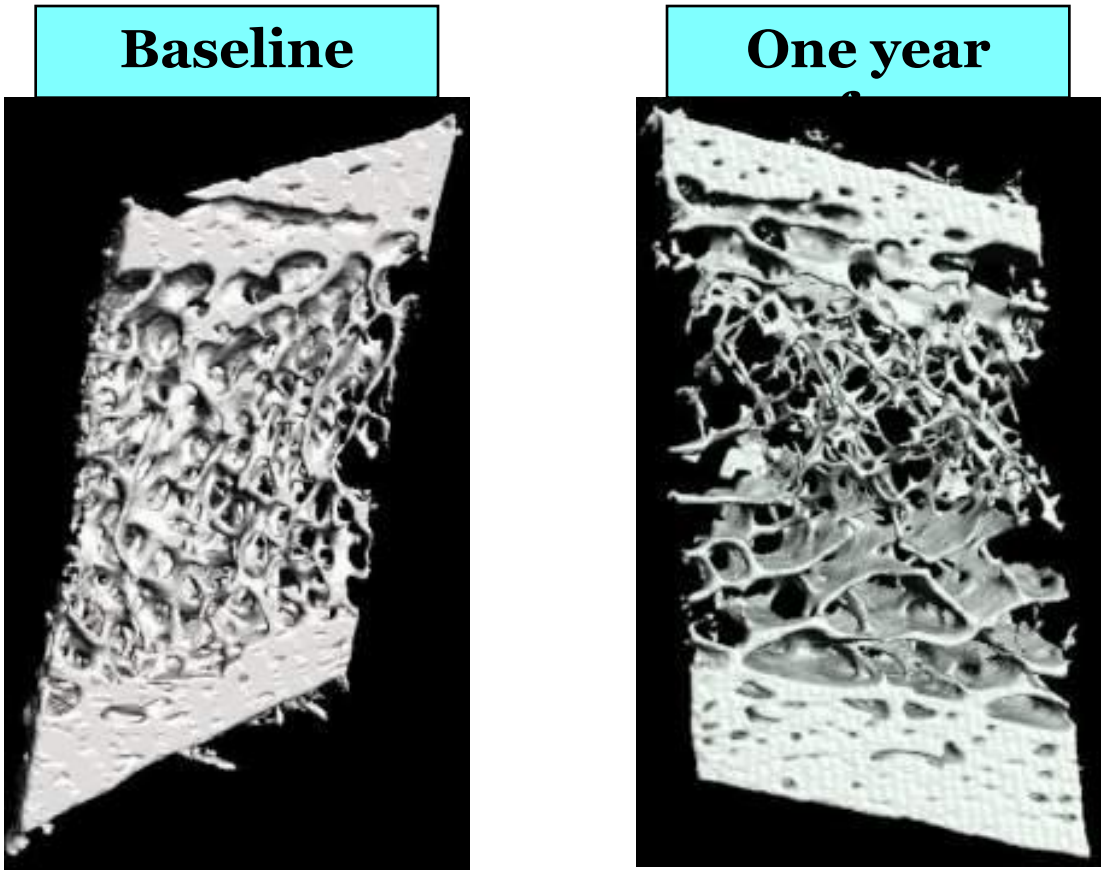


Adapted from Melton LJ & Riggs BL. Osteoporosis: Etiology, Diagnosis and Management Raven Press, 1988, pp155-179

Determinants of Peak Bone Mass



Alteration in bone structure in untreated postmenopausal women



Dufresne TE et al, Calcif Tissue Int, 2003;73:423-432

Osteoporosis Symptoms

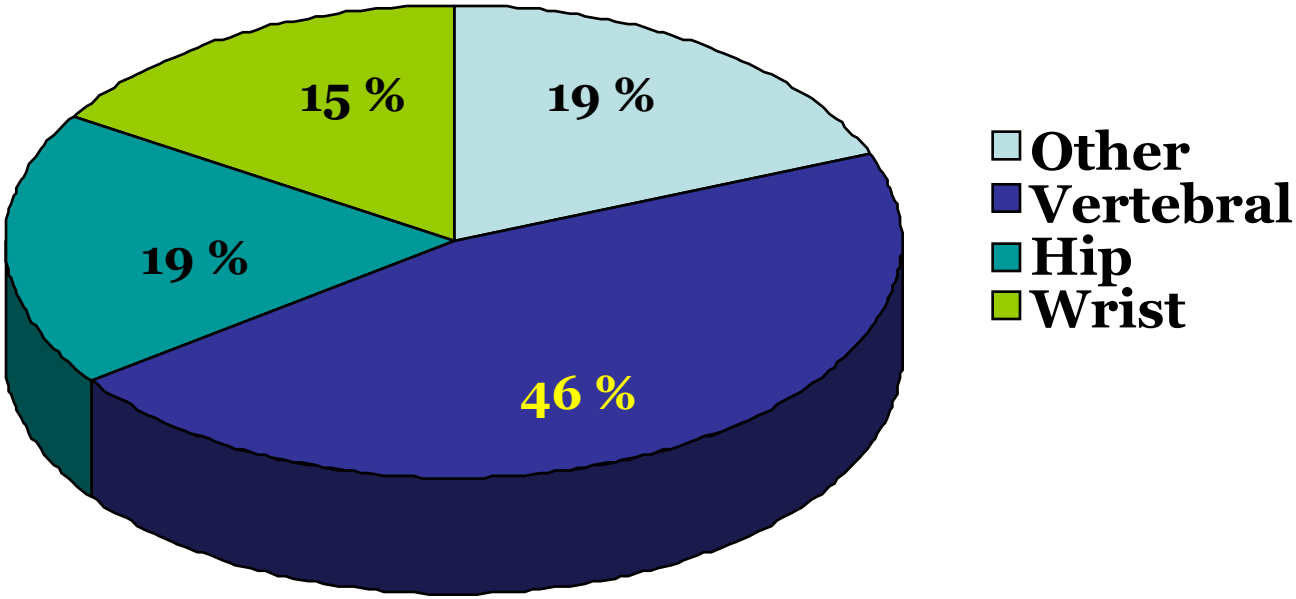
- Mostly asymptomatic until fracture- A person with osteoporosis can fracture a bone from a minor fall, or in serious cases, from a simple action such as a sneeze or even spontaneously.

- Vertebral (spinal) fractures may initially be felt or seen in the form of severe back pain, loss of height, or spinal deformities such as kyphosis or stooped posture. In many cases, a vertebral fracture can even occur with no pain.

- Women can lose up to 20 percent of their bone mass in the five to seven years after menopause, making them more susceptible to osteoporosis.

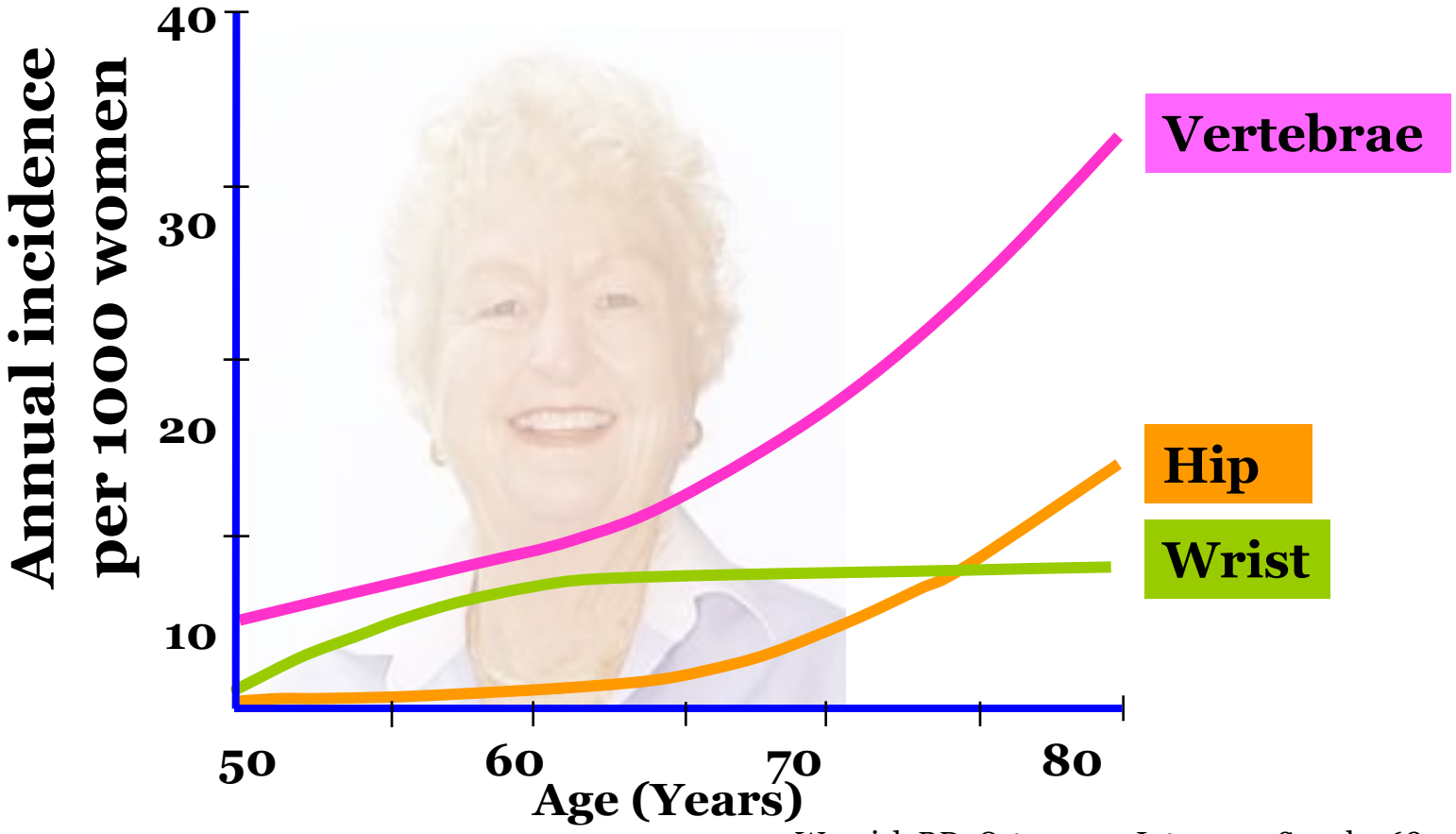
Osteoporosis affects the entire skeleton

- Osteoporosis is responsible for >1.5 million vertebral and non-vertebral fractures annually
- Spine, hip, and wrist fractures are most common



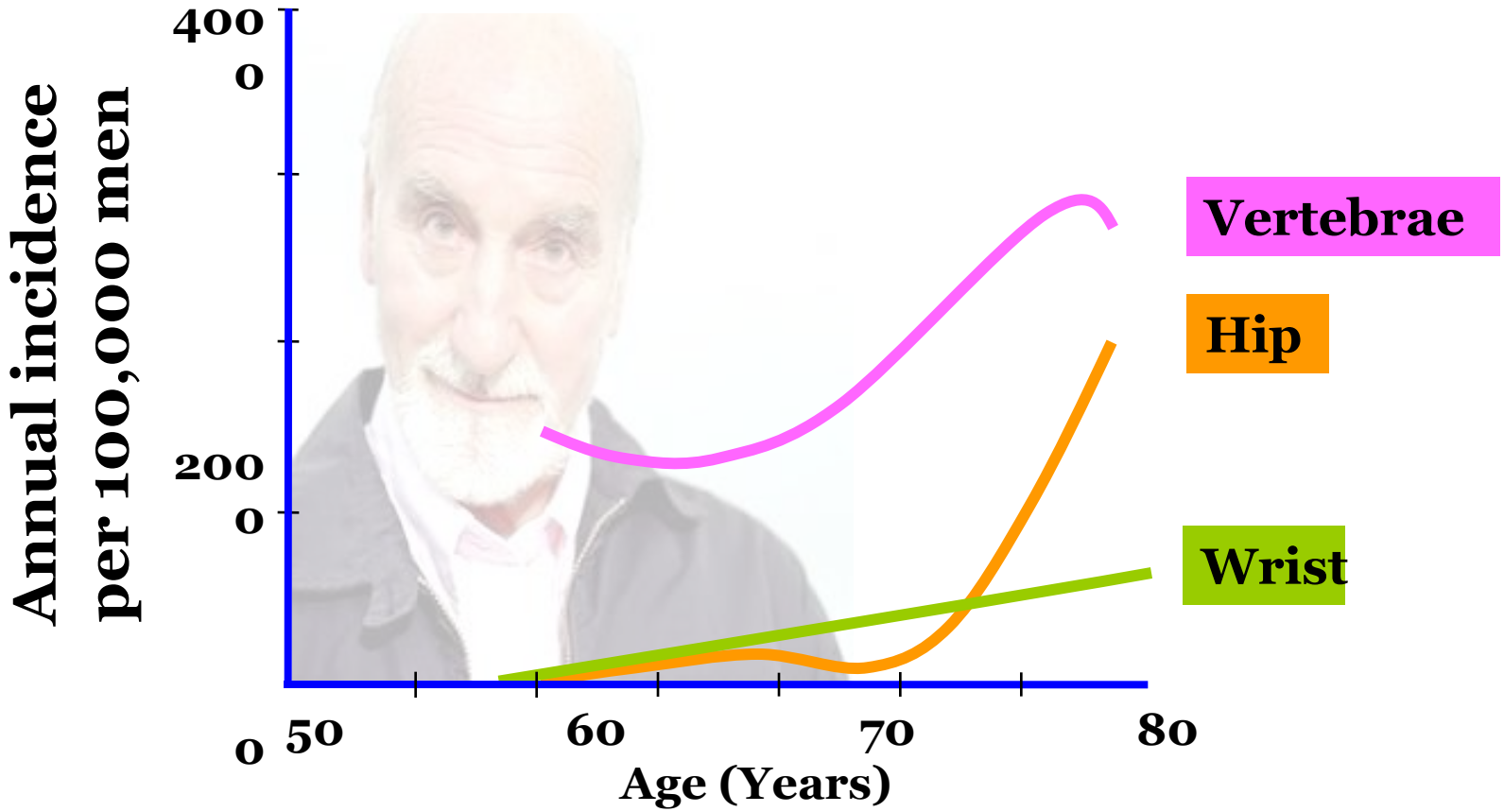
NIH/ORBD (www.osteo.org), 2000

Incidence of osteoporotic fractures in women



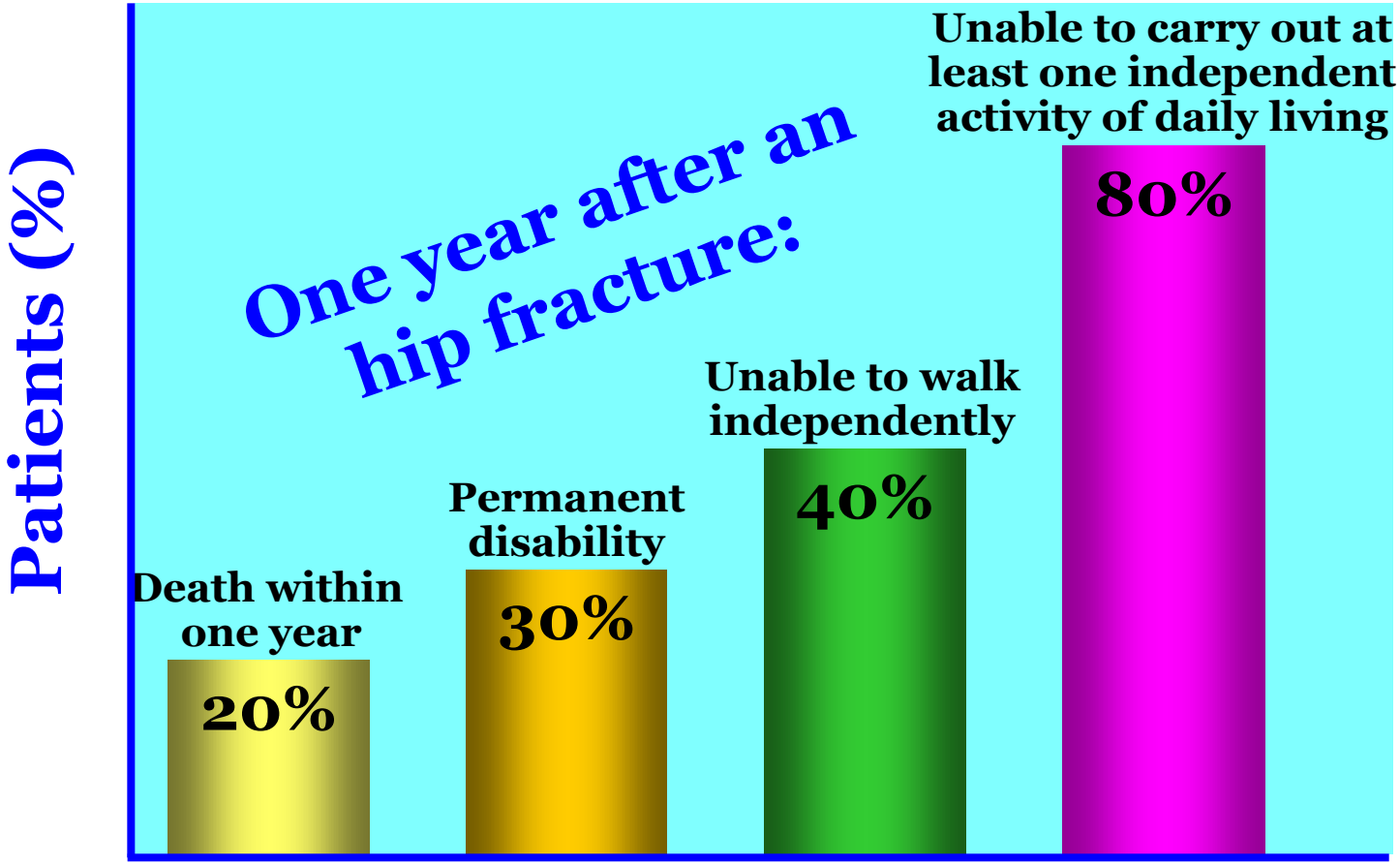
Wasnich RD, Osteoporos Int 1997;7 Suppl 3:68-72

Incidence of osteoporotic fractures in men



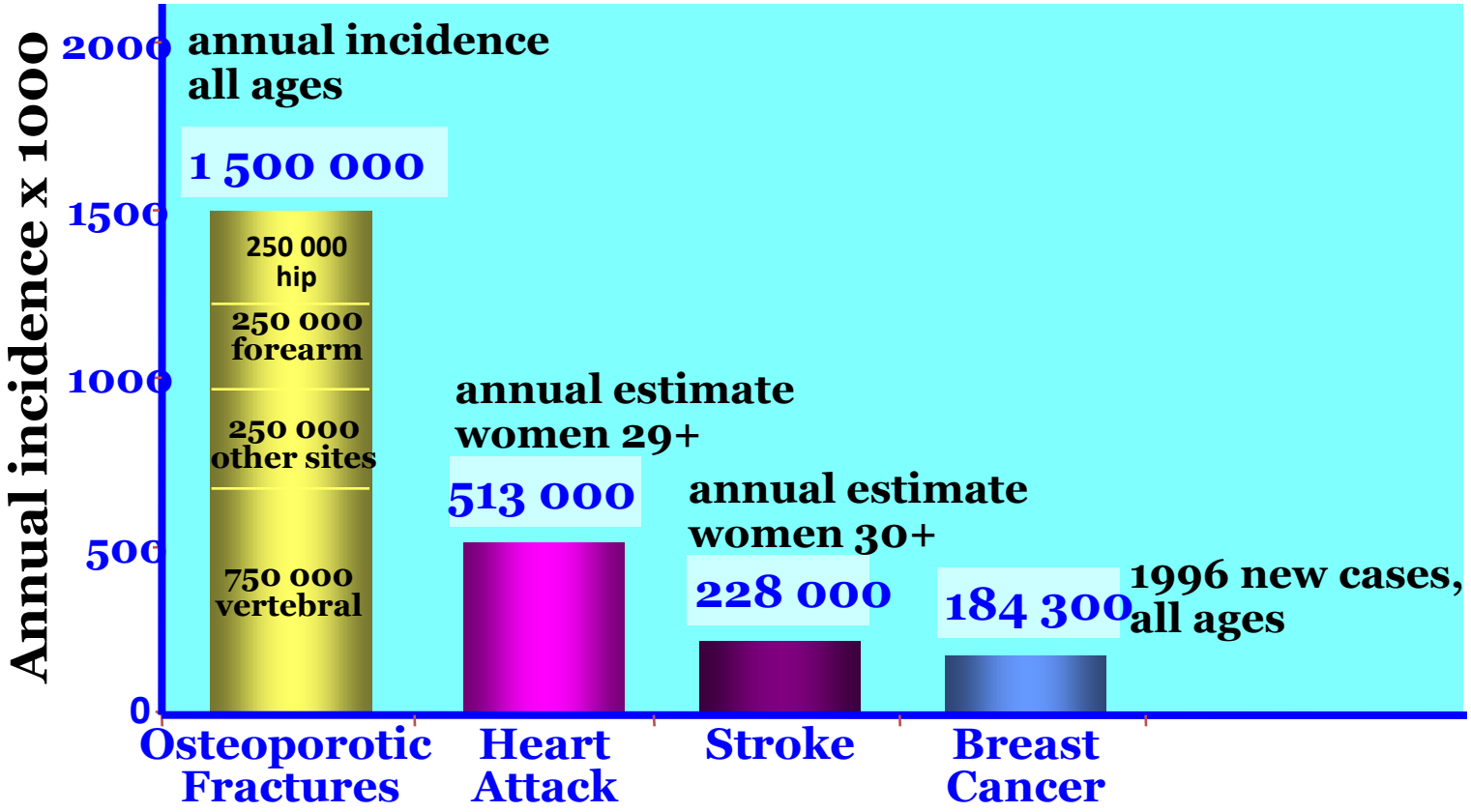
Wasnich RD, Osteoporos Int 1997;7 Suppl 3:68-72

All fractures are associated with morbidity



Cooper C, Am J Med, 1997;103(2A):12S-17S

Osteoporotic fractures: Comparison with other diseases

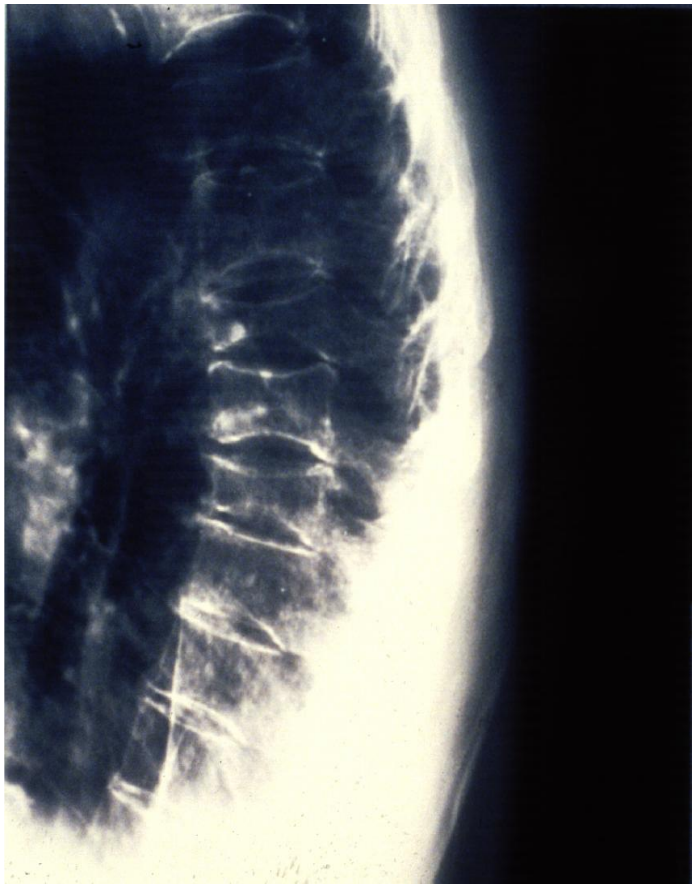


American Heart Association,1996
American Cancer Society,1996
Riggs BL & Melton LJ 3rd, Bone, 1995;17(5 suppl):505S-511S

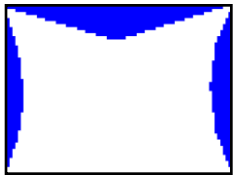
Vertebral fractures

- Most common fracture type
- Often silent
- Insidious, progressive nature
- Associated with
  - Deformity, height loss, back pain
  - Impaired breathing
  - Increased morbidity and mortality
- Predict future spine and hip fractures

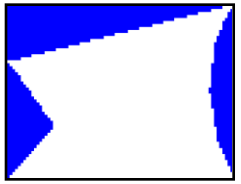
Types of vertebral fracture



Normal



Concave deformity (end-plate)



Wedge fracture

Compression fracture

Morbidity after vertebral fractures

- Back pain
- Loss of height
- Deformity (kyphosis, protuberant abdomen)
- Reduced pulmonary function
- Diminished quality of life: loss of self-esteem, distorted body image, dependence on narcotic analgesics, sleep disorder, depression, loss of independence

ONCE A WOMAN SUFFERS A FIRST VERTEBRAL FRACTURE, THERE IS A FIVE-FOLD INCREASE IN THE RISK OF DEVELOPING A NEW FRACTURE WITHIN ONE YEAR

Lindsay R et al, JAMA 2001;285:320-323

Useful diagnostic tests

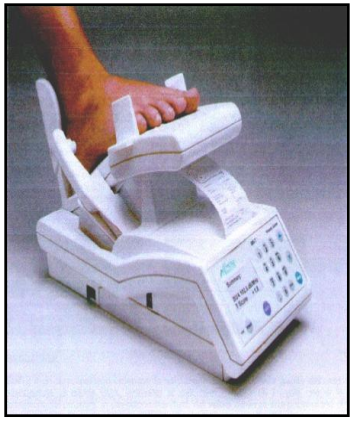
Disease	Mechanism	Tests	Complication
Cardiovascular Disease	Hypertension	Blood pressure	Stroke
Insulin-dependent Duabetes mellitus	Insulin deficiency	Blood glucose	Retinopathy
Osteoporosis	Skeletal bone loss	Bone mass	Fracture

Osteoporosis diagnosis

Bone mineral density(BMD) is a important predictor of fracture risk.

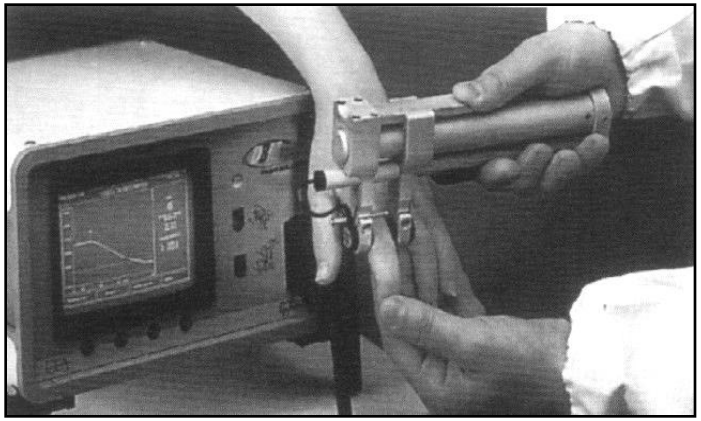
Spine/hip dual energy X-ray absorptiometry measurement (DXA) is the diagnostic standard

Quantitative ultrasound (QUS)



Advantages:

- **Lower cost than DXA**
- **Portability**
- **No radiation**



Role in detecting high risk patient:

Diagnosis and monitoring osteoporosis to be established

When to perform a bone density test?
National Osteoporosis Foundation (NOF) Guidelines

- All postmenopausal women under age 65 who have one or more additional risk factors for osteoporotic fracture (besides menopause)
- All woman aged 65 and older regardless of additional risk factors
- Postmenopausal women who present with fractures

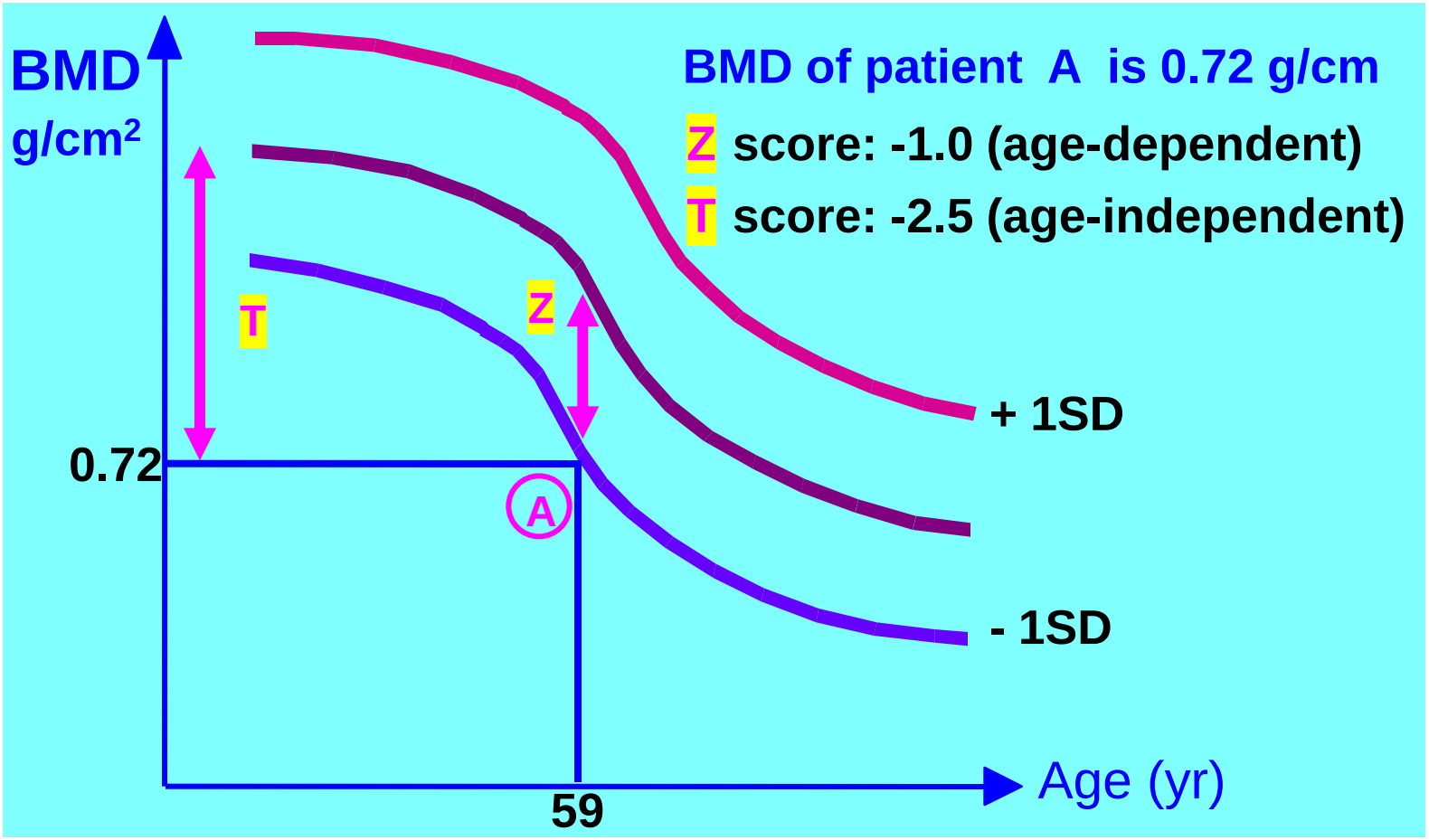
WHO criteria for osteoporosis in women

	T-Score
Normal	-1 and above
Low bone mass (osteopenia)	-1 to -2.5
Osteoporosis	< -2.5
Established osteoporosis	< -2.5 and one or more fractures

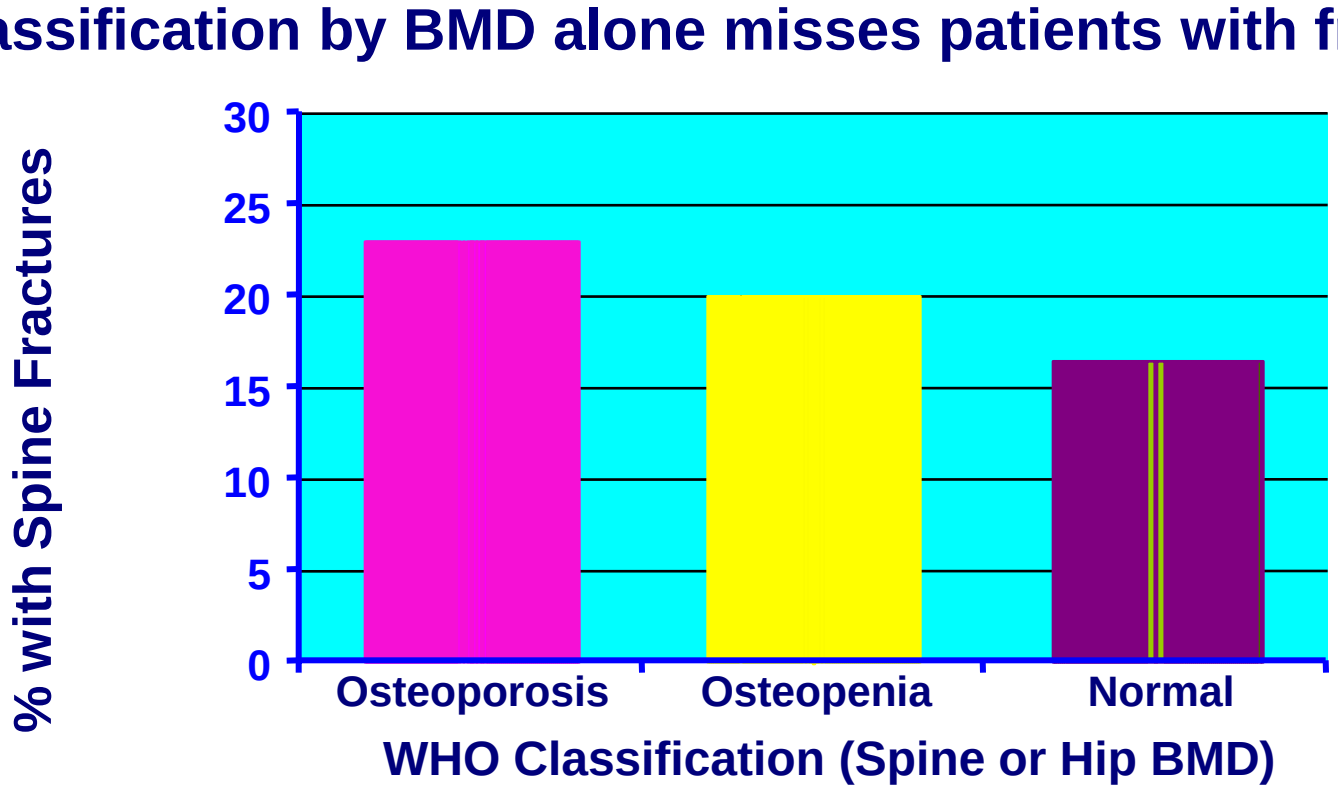
Kanis JA et al, J Bone Miner Res, 1994;9:1137-1141

Interpretation of bone mineral density

(BMD)



Classification by T-score alone misses patients with fractures



- **50% of women with vertebral fracture are not osteoporotic by BMD**
- **1/3 of women needing Rx are missed using BMD alone**

Greenspan S et al, J Clin Densitom 2001;4:373-380

Biochemical markers of bone turnover

Formation markers

- **Osteocalcin**
- **Bone specific alkaline phosphatase**
- **Procollagen type-1 N-propeptide**
- **Procollagen type-1 C-propeptide**

Resorption markers

- **Hydroxyproline**
- **Hydroxylysine**
- **Pyridinoline**
- **Deoxypyridinoline**
- **Bone sialoprotein**
- **Acid phosphatase**
- **Tartrate-resistant acid phosphatase**
- **Type-1 collagen telopeptides (CTX, NTX)**

Potential role of biochemical markers of bone turnover in the management of osteoporosis

- **Prediction of bone loss**
- **Prediction of fracture**
- **Monitoring of therapy**
- **prediction of response and improving compliance**

Differential Diagnosis

Metastasis

Multiple Myeloma

Osteoporotic Fracture

Osteoporosis in men

Primary osteoporosis (50%)	Secondary osteoporosis (50%)
• Idiopathic	• Glucocorticoid excess (15%) • Hypogonadism (10%) • Alcoholism (7%) • Hypercalciuria (2%) • Smoking • Gastrointestinal disorders • Immobilization • Others…

Bilezikian JP, J Clin Endocrinol Metab, 1999;84:3431-3434

Non pharmacological approaches
to the prevention of
postmenopausal osteoporosis

- **Adequate intake of dietary calcium & protein**
- **Regular physical activity**
- **Minimize alcohol intake**
- **Minimize risk of fall**
- **Recommend hip protectors in those prone to falls**

Osteoporosis in men

Prevention and treatment of osteoporosis in men

In secondary osteoporosis, treat the cause

- **Androgens**
- **Limit corticosteroid therapy, alcoholism or smoking**
- **Use thiazides for hypercalciuria**

In "IDIOPATHIC" osteoporosis

- **Exercise and prevention of falls**
- **Calcium and vitamin D supplements**
- **Bisphosphonates (alendronate)**
- **PTH (teriparatide)**

Nguyen TV et al, Am J Epidemiol, 1996;144:255-263.
Legrand E et al, Osteoporos Int, 1999;10:265-270.

Non pharmacological approaches to the prevention of osteoporosis

Table 4. General Preventive and Lifestyle Measures.*

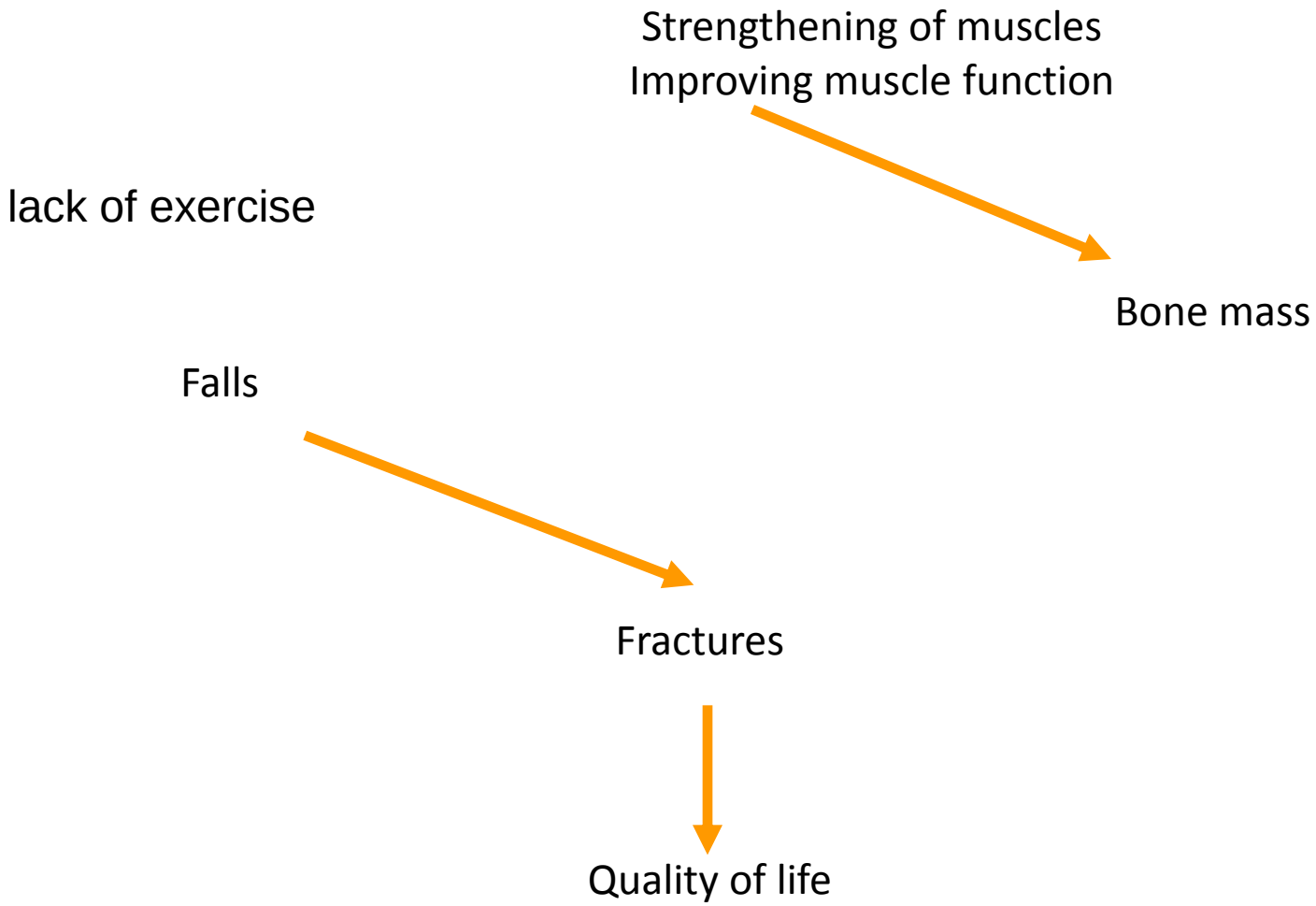
Weight-bearing exercise, including resistance training to improve muscle mass, strength, and balance, performed at least 3 times per week
Adequate calcium intake (1200–1500 mg per day) through diet, supplements, or both
Adequate vitamin D intake (800–2000 IU of vitamin D per day, especially for men >65 years of age; target serum level of 25-hydroxyvitamin D, ≥30 ng/ml [75 nmol/liter])
Smoking cessation
Avoidance of excessive alcohol use†
Use of fall-prevention programs, including home-based interventions, visual assessment, balance exercises, and tai chi

* Appropriate intake of calcium and vitamin D should be encouraged from childhood.

† Excessive use is defined as 18 oz (533 ml) or more of full-strength beer, 7 oz (207 ml) or more of wine, or 2 oz (59 ml) or more of spirits per day.

Ebeling P. N Engl J Med 2008;358:1474-1482

Exercise


Strengthening of muscles
Improving muscle function
lack of exercise
Bone mass
Falls
Fractures
Quality of life

Risk factors for falling

- **Age**
- **Impaired gait or balance; lower body muscle weakness**
- **Poor vision; cataracts**
- **Malnutrition; excessive alcohol intake**
- **Certain medical conditions, e.g. arthritis, diabetes, postural hypotension, cognitive impairment, peripheral neuropathy**
- **Polypharmacy; certain medications, e.g. psychoactive medications, antihypertensives**
- **Footwear with slippery soles, high heels**
- **Factors in the home, e.g. poor lighting, loose rugs, loose cabling, uneven or wet surfaces, bathtubs without handrails or bath mat, clutter at floor level, stepping over pets**
- **Environmental factors, e.g. wet or cracked paving or steps, ice or snow**

Prevention of postmenopausal bone loss by low-magnitude, high-frequency mechanical stimuli.

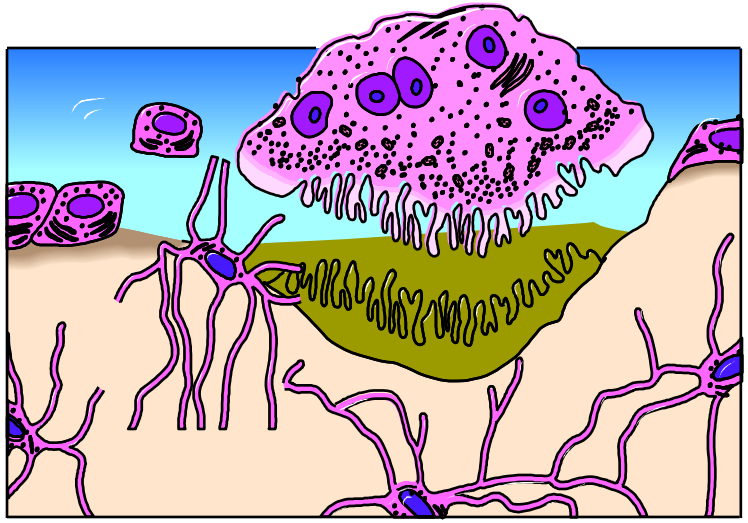
One-year prospective, randomized, double-blind, and placebo-controlled trial of 70 postmenopausal women:

Brief periods (<20 minutes) of a low-level (0.2*g*, 30 Hz) vibration applied during quiet standing can effectively inhibit bone loss in the spine

Rubin et al: J Bone Miner Res. 2004; 19:343-351

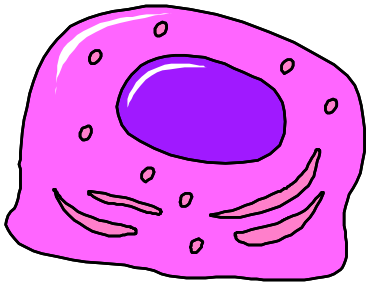
Treatment objectives

Osteoclast



Inhibition of resorption

Osteoblast



Stimulation of formation

Osteoporosis treatment

Anti-Resorptive pharmacological Agents

- **HRT**
- **SERM/Raloxifene**
- **Calcitonin**
- **Bisphosphonates**
  - Alendronate
  - Risedronate
  - Ibandronate

Anabolic Agents

- **Parathyroid hormone (PTH)**
- **Strontium ranelate**

Anti-fracture efficacy of the most frequently used treatments for postmenopausal osteoporosis

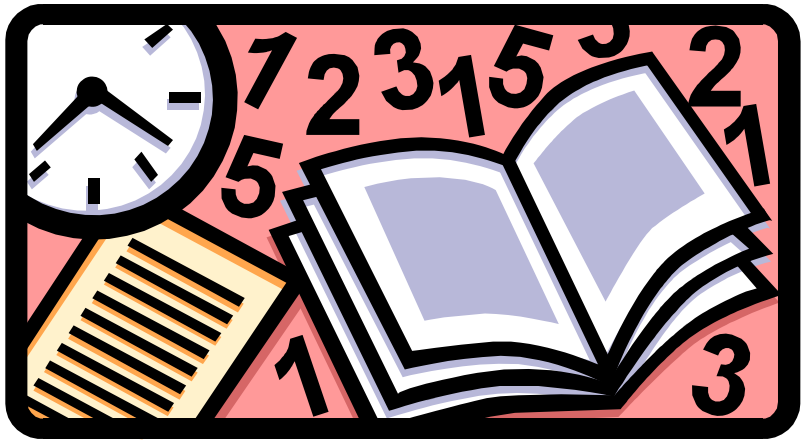
As derived from placebo controlled randomized trials

Drug	Vertebral fractures	Non-vertebral fractures (hip)
Alendronate	+ + +	+ +
Calcitonin (nasal)	+	o
Etidronate	+	o
HRT	+ +	+
PTH	+ + +	+ +
Raloxifene	+ + +	o
Risedronate	+ + +	+ +
Strontium ranelate	+ + +	+

Adapted from Delmas PD. Lancet. 2002;359:2018-2026.

Calcium: How much to give?

- Indian RDA = 400 mg
- US RDA = 800 – 1200 mg in males
- In osteoporosis: 1500 to 2000 mg/d
- Premenopausal women: 1000 mg/d
- Postmenopausal women: 1500 mg/d



Nutrition: Reference intake for calcium

Age (years)	Calcium intake (mg/day)
1-3	500
4-8	800
9-18	1300
19-50	1000
>51	1200

National Institutes of Health, 1994

Dietary Calcium

FOOD	Ca in mg/ 100 g
Ragi	344
Rice	10
Whole wheat flour	48
Whole Bengal gram	202
Rajmah	260
Sesame seeds	1450

Dietary Calcium

FOOD	Ca in mg/100 g
Egg	60
Mutton	150
Buffalo milk	210
Cow milk	120
Cheese	790
Shrimp	4384
most fish	good

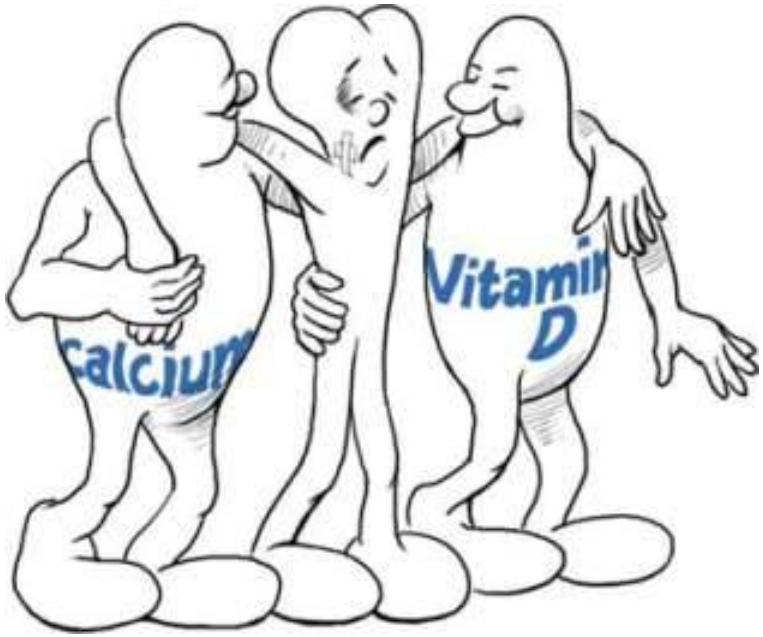
The challenge

Calcium is a comparatively difficult element for the body to absorb

Factors affecting Calcium absorption

- **Chemistry of the salt:**
  - **Each Ca source has unique physical, structural, and chemical properties that are largely determined by the anions associated with the Ca**
- **Physiological function**
  - **Gastric acid secretion – required for ionization of Ca before absorption**
  - **Endogenous solubility of the Ca salt (esp. aqueous solubility)**
- **Age (absorption of calcium decreases with increasing age)**
- **The composition of meals – plant foods (containing phytates, oxalates)**
- **The timing of meals**
- **Lifestyle factors (e.g., physical activity)**
- **Use of concomitant medications like PPIs for acid suppression therapy**

Calcium + Vitamin D helps reduce bone loss and fractures* in elderly



Surgical management of Osteoporotic fractures

- Orthopaedic goals of fracture management
  - Re-establish length Alignment and stability

Challenges in Surgical management of Osteoporotic fractures

- **Achieving fixation and stability**
  - In osteoporotic patients with deficient bone, stability is the true challenge.
  - Standard fracture devices (pins, intramedulary rods, plates and screws) often fail, since the bone is inadequate to support them, and develops cavities where the devices are secured.

Arthroplasties in osteoporotic fractures

Arthroplasty as an alternative to fixation- Knee

- Technically demanding
- Revision component often needed
- Complications common

Arthroplasty as an alternative to fixation- Hip

- Hemiarthroplasy established and widely preferred to ORIF in displaced subcapital fractures
    - But still controversial
- Total arthroplasty acceptance increasing

Arthroplasty as an alternative to fixation- Shoulder

- Useful particularly for 3- part and 4 part fractures and fracture dislocations
- Early treatment best
- Good pain relief, but poor movement and function
- Soft tissues influence outcome

Osteoporotic Hip- Intertrochanteric fractures

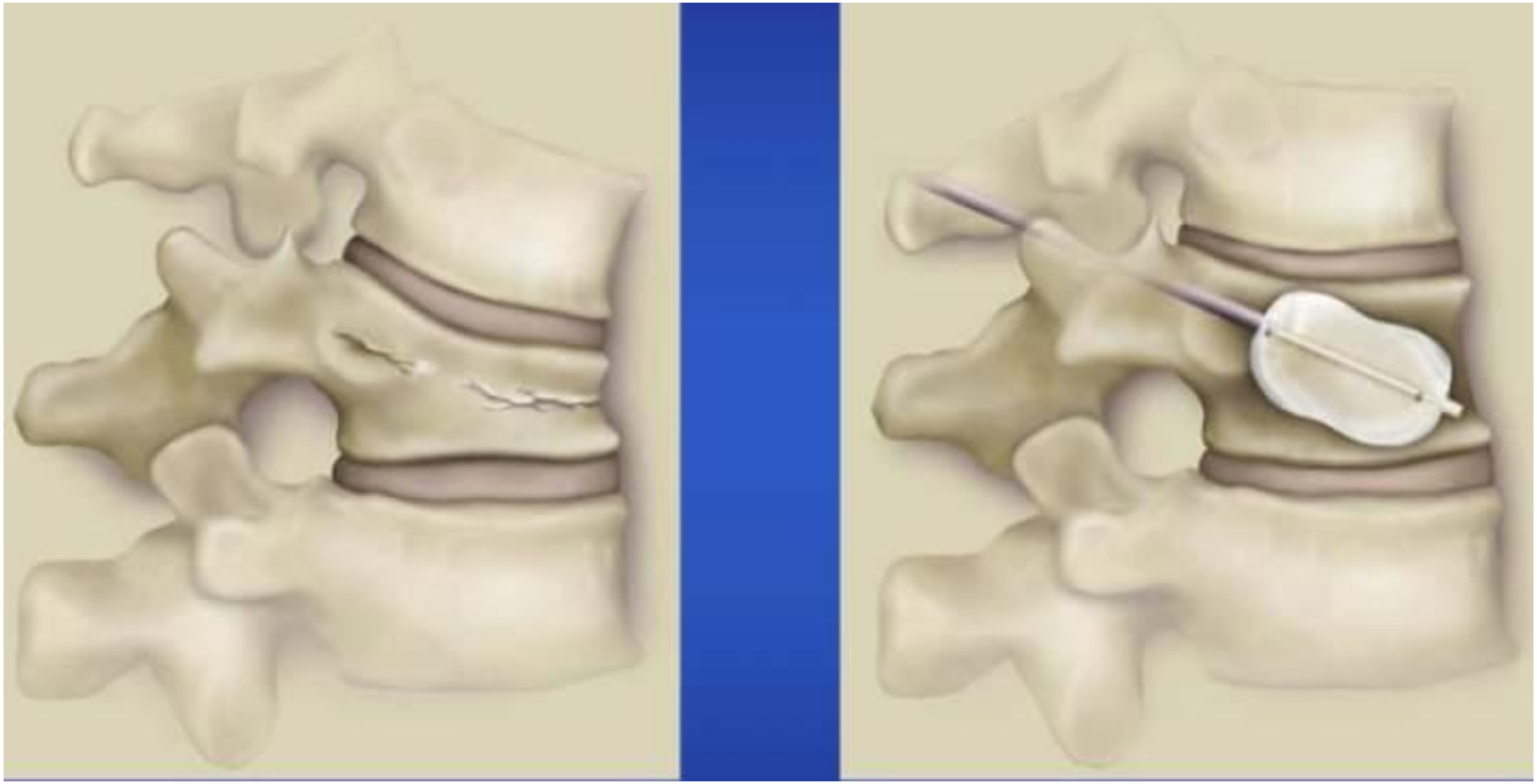
- ORIF
- Sliding hip compression screw (with or without cement supplementation has been the gold standard
- Intramedullary nail devices with an intersecting blade-plate have grown in popularity

Intramedullary devices can provide excellent fixation for unstable peritrochanteric fractures

Osteoporotic vertebral fractures
Vertebroplasty and Kyphoplasty

- Filling void in crushed vertebral body with PMMA (Polymethylmethacrylate)Bone Cement
- Patient in prone position- transpedicular injection of cement
- Vertebroplasty – high pressure injection – good pain relief
- Kyphoplasty – pre-insertion of balloon to create a void for low pressure injection- aiming for height restoration

Balloon Kyphoplasty



Bone grafts

- Wrist and hip fractures present biomechanical challenges that must be addressed with specialized implants and judicious use of bone grafts and/or graft substitutes

- Bone graft contains
  - actual cortical and/or cancellous hard bone (osteoconductive)
  - bone cells and protein factors that induce the formation of new bone (osteoinductive).

Bone grafts

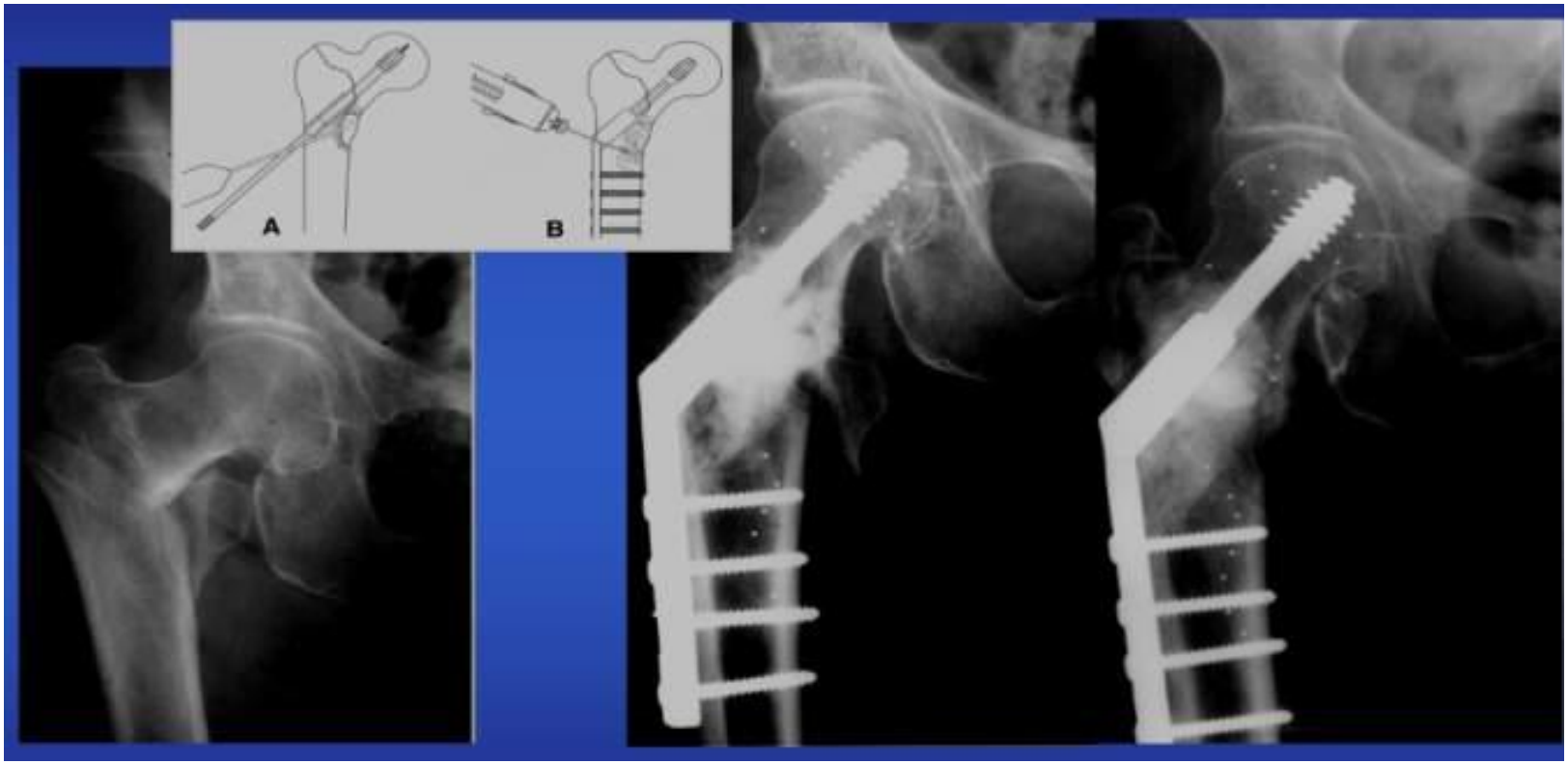
- Autogenous grafts from the iliac crest provide both components
- Allogeneic donor bone, which carries the risks of transmissible agents and a host versus-graft response.
- Various bone graft products are available commercially

Other types of bone fillers

- Polymethylmethacrylate (PMMA) bone cement
  - Inert two-part polymer
  - Used in selected total joint replacements, especially in the elderly
  - Helpful in hip and spinal compression fractures.

Other types of bone fillers

- Biocompatible calcium-phosphate compounds



The surgeon's responsibilities

- Identify the orthopaedic patient with risk factors and fragility fractures
- Inform the patient about the need for an osteoporosis evaluation
- Investigate whether osteoporosis is an underlying cause of the fracture
- Ensure that appropriate intervention is initiated
- Educate the patient and their family