

Osteoporosis: A Ticking Time Bomb

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What Is Osteoporosis and How Many People Are Affected?

Osteoporosis is a progressive skeletal disease characterized by low bone mass and micro-architectural deterioration, with a consequent increase in bone fragility and susceptibility to fracture.

The Numbers

- Currently affects >75 million people in Europe, Japan, and the U.S.
- The number of osteoporotic hip fractures has quadrupled in the past decade
 - Will continue to rise as older population doubles by 2040

Osteoporotic Fractures Caused By Falls Is Another Key Area That Needs Attention

Because of weaker bones, people with osteoporosis are at a greater risk of injury when they fall

- **By 2050, 6.3 million people will suffer hip fractures worldwide**
- **~1.5 million osteoporotic fractures in the U.S. each year**
 - 300,000 hip fractures – 700,000 vertebral fractures – 250,000 wrist fractures
- **Cost of care: \$17 billion/year or \$47 million/day**
- **15% of hip fracture patients walk unaided at 6 months**
- **25% require long-term care**
- **Multiple fractures are common**

Sources: Chan, KM, Anderson M, Lau EM. Exercise interventions: defusing the world's osteoporosis time bomb. *Bulletin of the World Health Organization* 2003;81:827-830.

Dreinhofer MD, Feron JM, Herrera A, et al. Orthopaedic surgeons and fragility fractures: a survey by the Bone and Joint Decade and the International Osteoporosis Foundation. *The Journal of Bone and Joint Surgery*. 2004;86:958-961.

National Osteoporosis Foundation: Fast Facts. Available at: www.nof.org/osteoporosis/disease_facts.htm. Accessed Oct. 7, 2004.

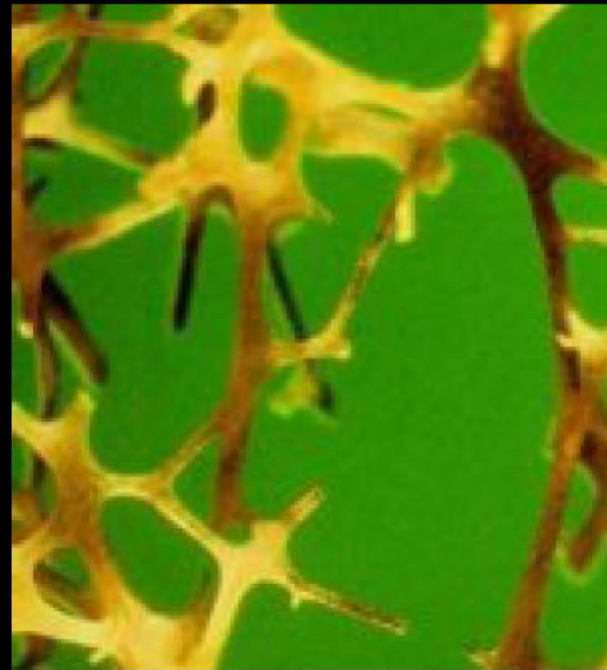
Fragility Fracture Patients Are Rarely Evaluated for Osteoporosis

90% - 95% of patients go home without a bone density test

“Orthopedic surgeons are missing a major opportunity to prevent future fractures by not providing appropriate investigation of fragility fracture patients themselves or initiating appropriate protocols of care to be provided by their colleagues.”

Osteoporosis – Definition

- Literally translates as “porous bones”
- Osteoporosis occurs when the holes between bone become bigger, making it fragile and liable to break easily



A progressive systematic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture

Composition of bone

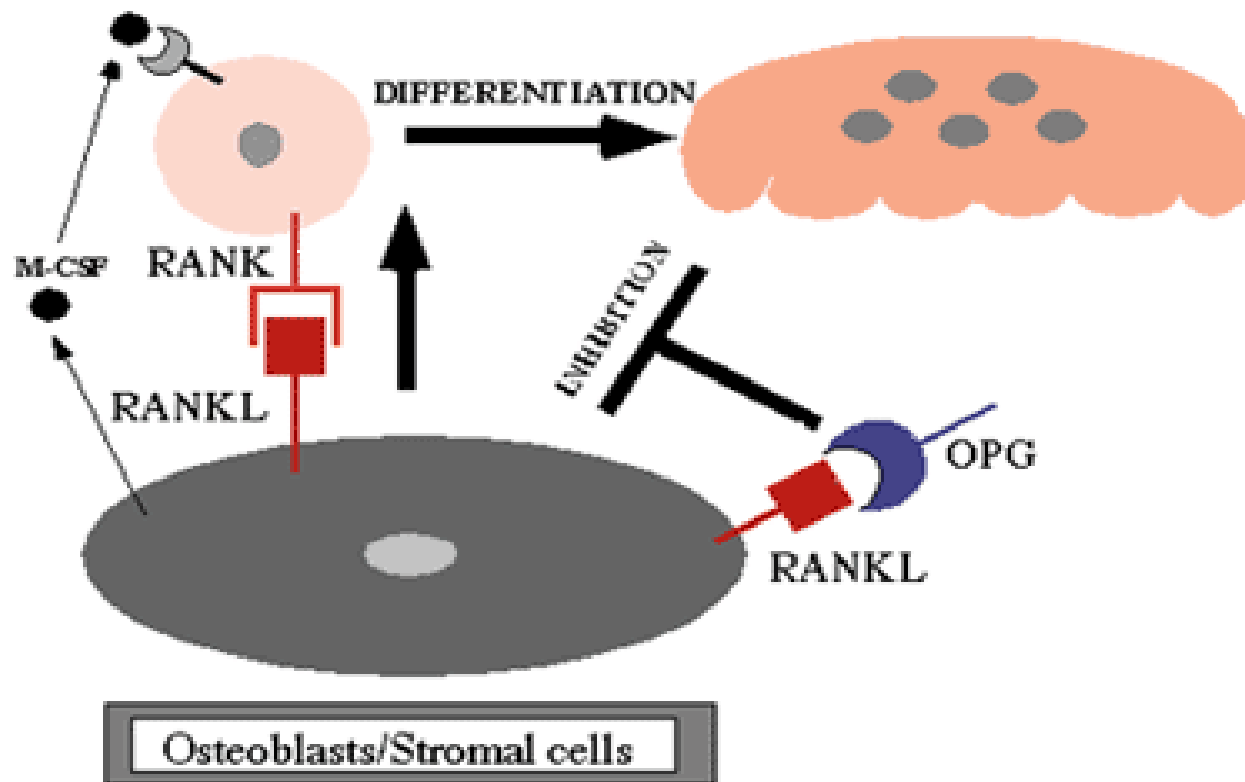
- Mineral -70%
- •Protein -22%
- •Water -8%

Pathogenesis

- Diminished bone mass can result from:
 - failure to reach an optimal peak bone mass in early adulthood
 - increased bone resorption
 - decreased bone formation after peak bone mass has been achieved
- All three of these factors probably play a role in most elderly persons. Low bone mass, rapid bone loss, and increased fracture risk correlate with high rates of bone turnover (ie, resorption and formation).
- In osteoporosis, the rate of formation is inadequate to offset the rate of resorption and maintain the structural integrity of the skeleton

Osteoclast precursors

Mature osteoclasts



RANKL — [red square] — RANK

DIFFERENTIATION

On osteoclast precursor

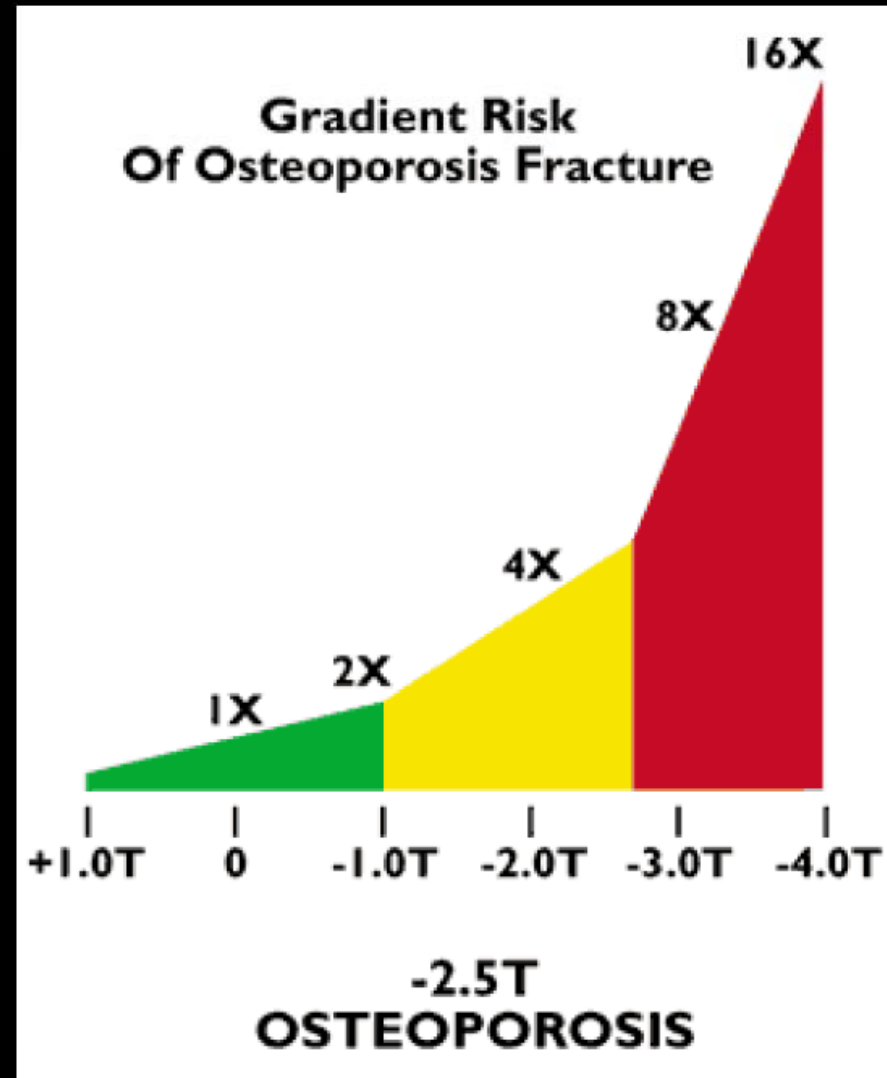
RANKL — [red square] — OPG
"decoy receptor"

INHIBITION

On Osteoblast

Increased risk of fracture

- Osteoporosis has been termed a silent disease because, until a fracture occurs, symptoms are absent.
- Chief clinical manifestations are vertebral and hip fractures
- Rate of fracture increases exponentially with increasing magnitude of T-scores



Osteoporosis

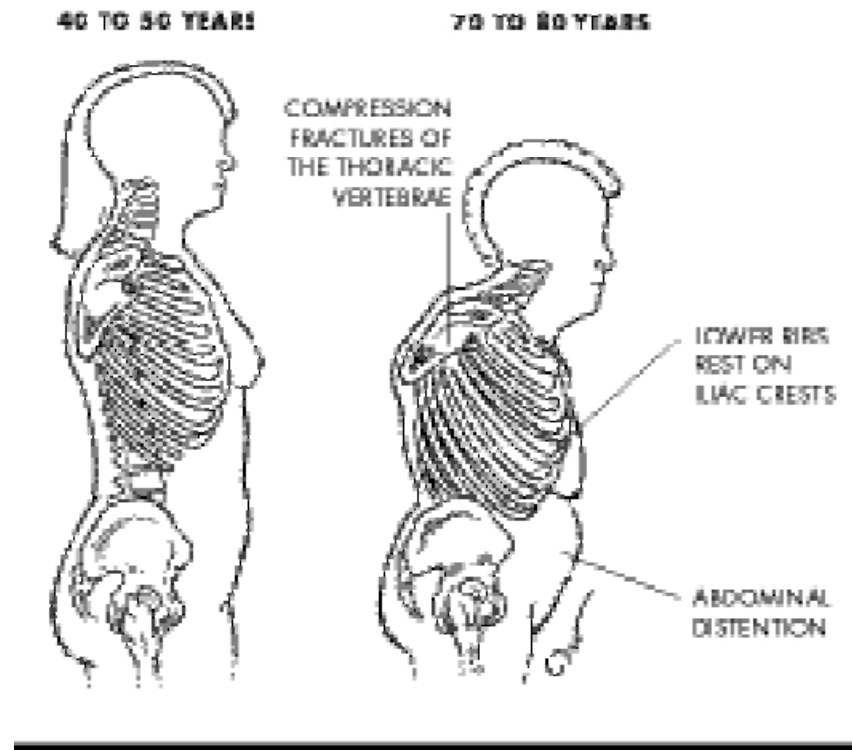
- Dx No clinical signs
- No blood tests
- Gold standard: Bone Mineral Density

- Importance
- Fragility fracture occurs from minimal trauma
- Risk: Once fracture within 5 yrs, 10% re-fracture
With next year 20%

- All fractures are important
- Mortality and morbidity is increased with fractures
- ☐ Fractures cause compromise COPD, UTI, Pressure sore

Dowager's Hump

- Women do not realize that the curvature of the spine means the intestines have nowhere to go except forwards.
- Many women think that they are getting fat, and they go on a diet trying to regain their youthful waistline.



Risk Factors

- Age
 - Low Body Mass Index [at 35 years: women have 30% less bone mass than men]
 - Steroid
 - Family history
 - Alcohol
 - Smoking
 - Inadequate sunlight
 - Decrease activity
- 60% of COPD patients have osteoporosis
- Low vitamin D and calcium intake

Race

- Caucasian and Asian women have lower bone density than blacks by as much as 5 to 10 percent.
- Until recently it was thought that Caucasian women were at greatest risk for osteoporosis, but a recent large-scale study has found that Hispanic, Asian, and Native American women are at least as likely to have low bone mass as Caucasians.
- Heredity. Having a mother, grandmother, or sister with a diagnosis of osteoporosis or its symptoms ("dowager's hump" or multiple fractures) increases your risk.

Osteoporosis Is Especially Common in White and Asian Women Over 50 Years Old

Women:

	White/Asian	Hispanic	Black
Early bone mass loss	52%	49%	35%
Osteoporosis	20%	10%	5%

Men:

	White/Asian	Hispanic	Black
Early bone mass loss	35%	23%	19%
Osteoporosis	7%	3%	4%

COPD

- Major cause of chronic morbidity and mortality
- Ill most frequent cause of death by 2020
- (Celli et al, 2004)
- COPD progresses [systemic consequences]
- osteoporosis

Normal Bone Loss

Bone mass peak: Middle of third decade

Men	0.3%/yr after 25 year [both cortical and cancellous]
Women	0.5%/yr after 25 year
Postmenopause	2-3%/yr for 6-10 yrs [more cancellous than cortical] then 0.5%/yr

Why Should We Screen for Osteoporosis?

- Osteoporosis is common
- Osteoporosis is serious - fractures cause increased morbidity and mortality
- Osteoporosis is easy to detect
- Effective treatments are available
 - Fracture risk can be reduced by about 50%
- Osteoporosis is preventable

X ray

- Screening X-ray findings are generally insufficient for the screening of primary osteoporosis
- A normal x-ray of bone cannot reliably measure bone density but is useful to identify spinal fractures, explains back pain, height loss or kyphosis.
- X-rays may detect osteopenia only when bone loss is $> 30\%$.
- X-ray findings can also suggest other causes of metabolic bone disease, such as the lytic lesions in multiple myeloma and the pseudofractures characteristic of osteomalacia.

Screening – DEXA



- Can be used to measure bone mineral density in the spine, hip, wrist, or total body.
- However, the standard apparatus is expensive and not portable. Small DEXA machines that can measure the forearm, finger, or heel are less expensive and are portable.

Osteoporosis

Low bone mineral density (BMD)

- 1-2.5 S.D Osteopenia
- $BMD \geq 2.5$ Osteoporosis
- Severe osteoporosis >2.5 SD + Pathological #

BMD & Fracture risk

1 S.D : 2.3 fold increase in hip # and 2.6 in Spine #

-

Why & What DXA Measures:

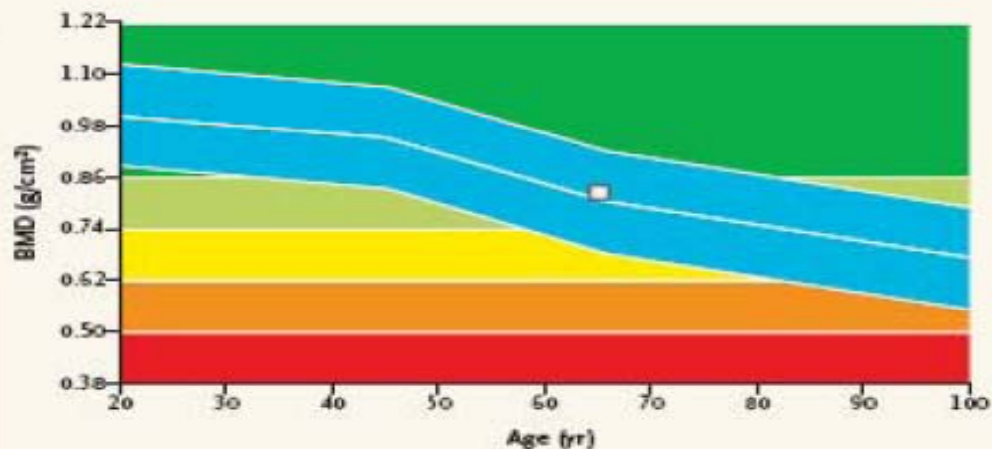
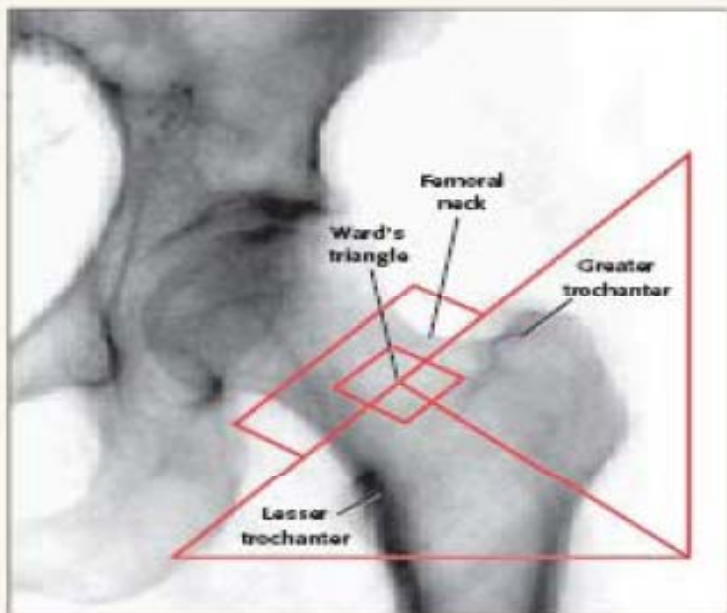
Why DEXA

- To diagnose osteoporosis
- To predict fracture risk [Fragility fracture, Hormonal problems, On steroids, Oophrectomy, COPD]
- To monitor therapy

What it measures

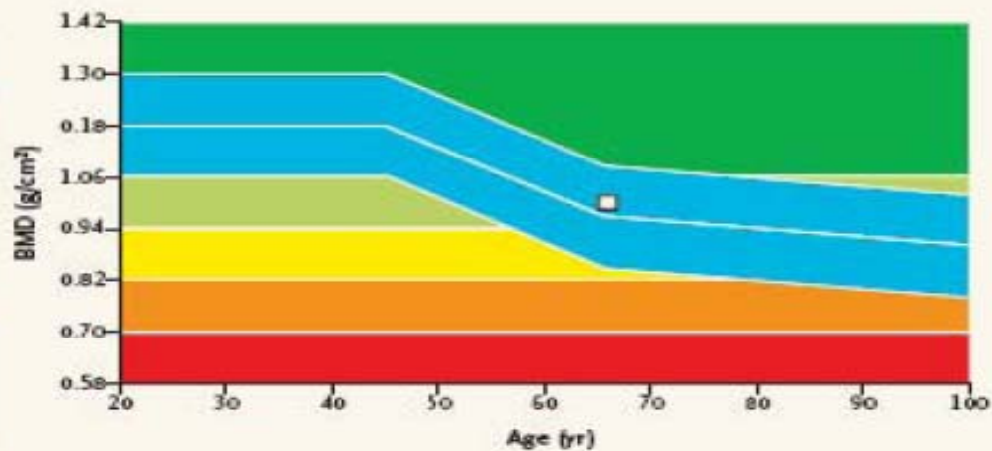
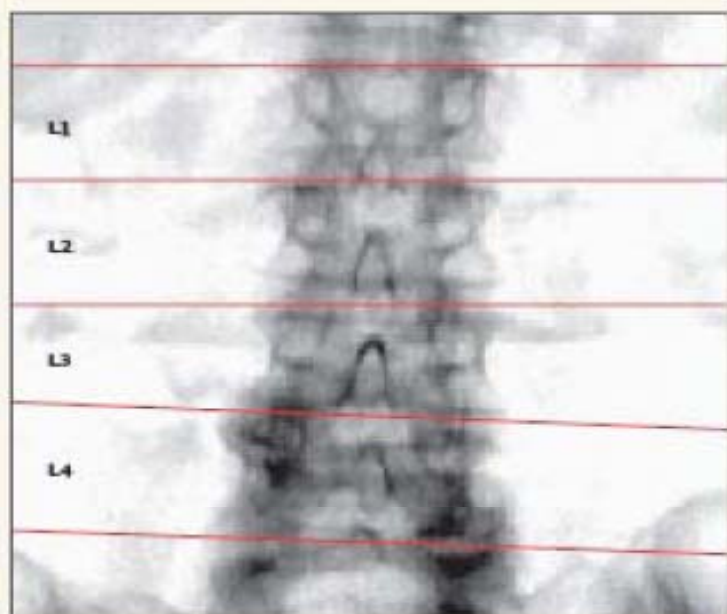
- Bone Mineral Content (BMC) : In Grams and Area In cm^2
- “T-score” compares the patient’s BMD with the young-normal mean BMD and expresses the difference as a standard deviation (SD) score

A



Region	BMD (g/cm ²)	Young adult		Age-matched	
		(%)	(T)	(%)	(Z)
Neck	0.829	85	-1.3	101	+0.1
Ward's triangle	0.670	74	-1.8	101	+0.1
Trochanter	0.769	97	-0.2	107	+0.5
Total	0.941	94	-0.5	106	+0.4

B

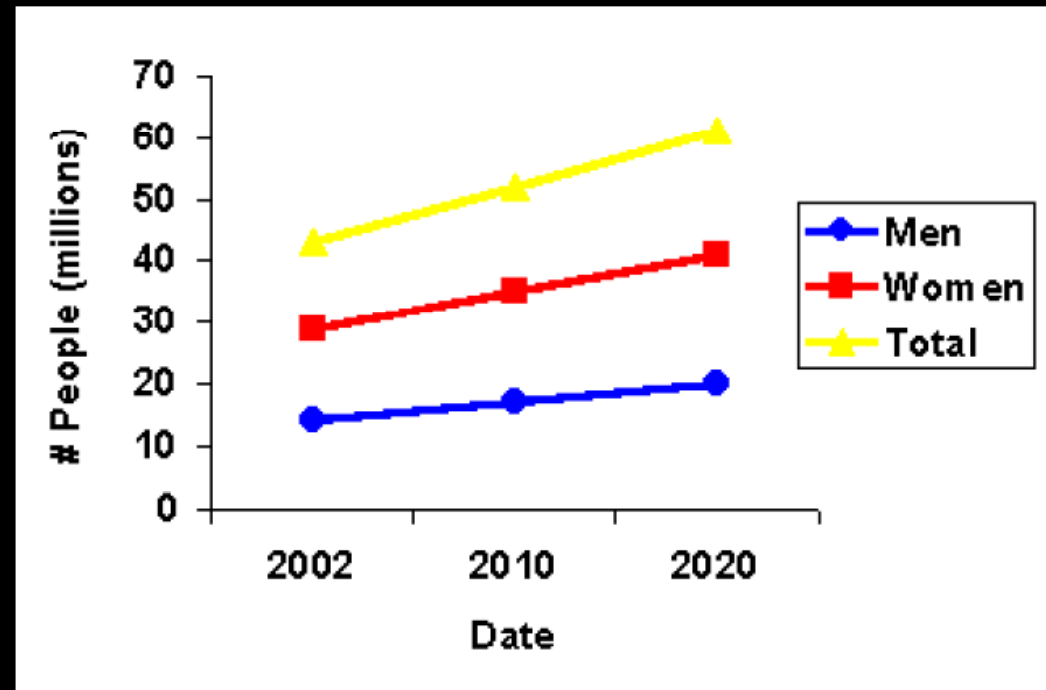


Region	BMD (g/cm ²)	Young adult		Age-matched	
		(%)	(T)	(%)	(Z)
L1	0.772	68	-3.0	84	-1.3
L2	0.975	81	-1.9	98	-0.2
L3	1.039	87	-1.3	104	+0.4
L4	1.203	100	0.0	121	+1.7
L2-L4	1.086	91	-0.9	109	+0.8

Figure 1. Dual-Energy X-Ray Absorptiometry of the Spine and Hip of a 66-Year-Old Postmenopausal Woman.

Osteoporosis – Prevalence

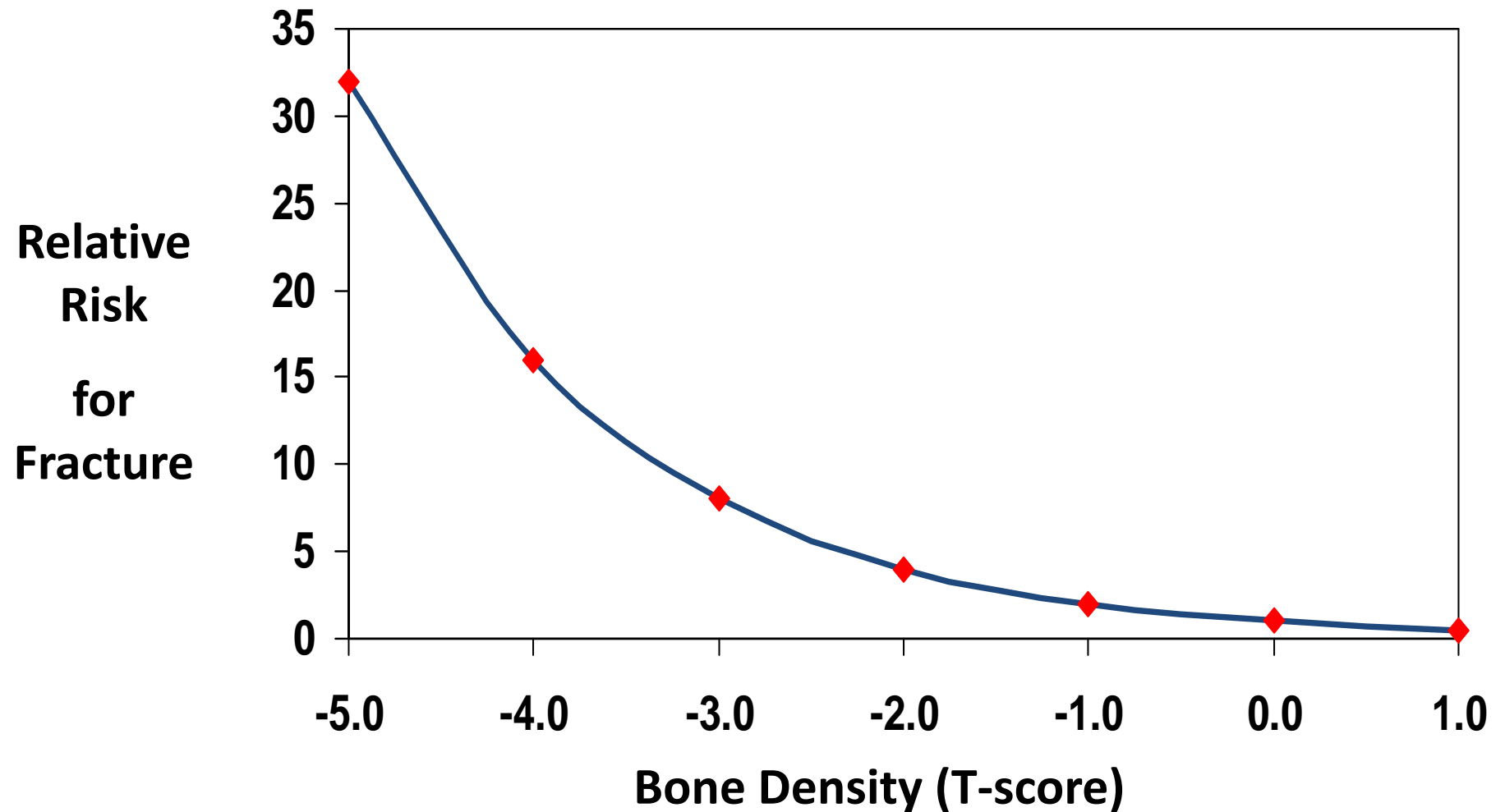
- In the USA, the estimated prevalence of osteopenia is 15 million in women and 3 million in men.
- The estimated prevalence of osteoporosis is 8 million in women and 2 million in men.
- Although, osteoporosis affects >10 million individuals in the United States, only 10 to 20% are diagnosed and treated



Estimated global prevalence

- Osteopenia and osteoporosis are major public health problems, resulting in substantial morbidity and estimated health costs of >\$14 billion annually.

Fracture Risk Doubles with Every SD decrease in BMD



Osteoporosis

Post Menopausal I Senile (type II)

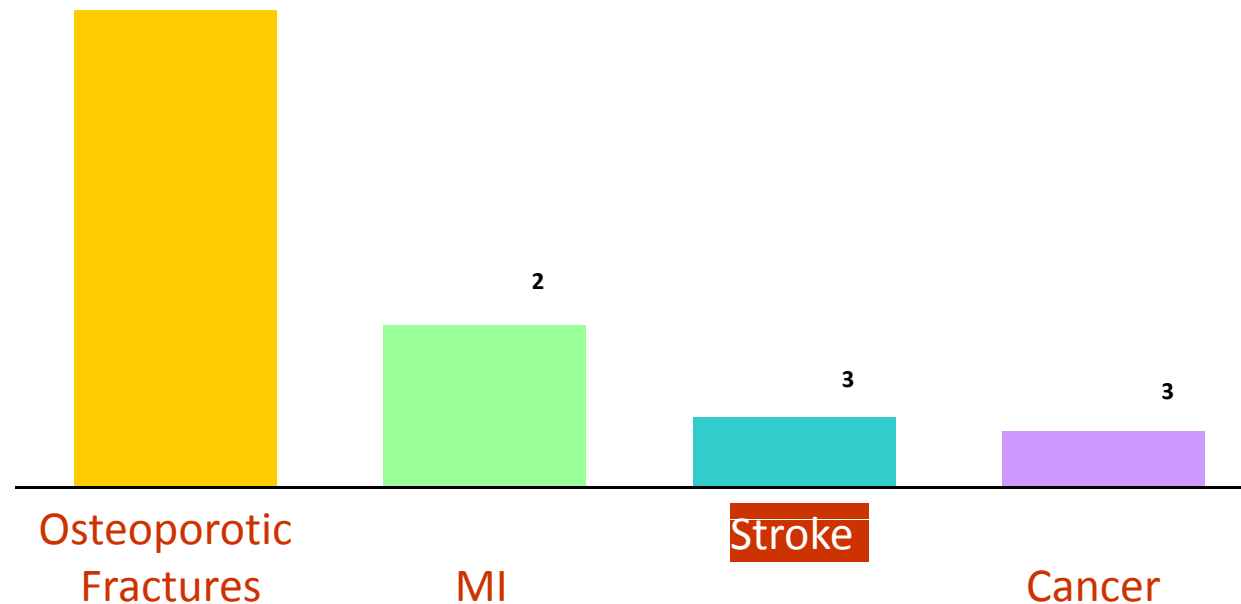
Age	55-75	>70
F:M	6:1	2:1
Pathogenesis	Increase osteoclastic	Decreased Osteoblastic
Bone loss	Mainly trabecular	Cortical + Trabecular
Ca & PO ₄ ; Alk PO ₄	N	-do-
Urine Ca	Increased	Normal
1 25 OH D	Decreased (PTH)	Decreased to rec response
PTH	<u>Decreased</u>	Increased

Causes of Secondary Osteoporosis

- Endocrine
 - Cushing's syndrome
 - Hyperthyroidism
 - Hyperparathyroidism
 - **Estrogen or testosterone deficiency**
- Renal
 - Renal failure or insufficiency
 - due Albright osteodystrophy
- Rheumatologic
 - Ankylosing spondylitis
 - Rheumatoid arthritis
- Gastrointestinal
 - Malabsorption

Comparative Incidence of Chronic Diseases

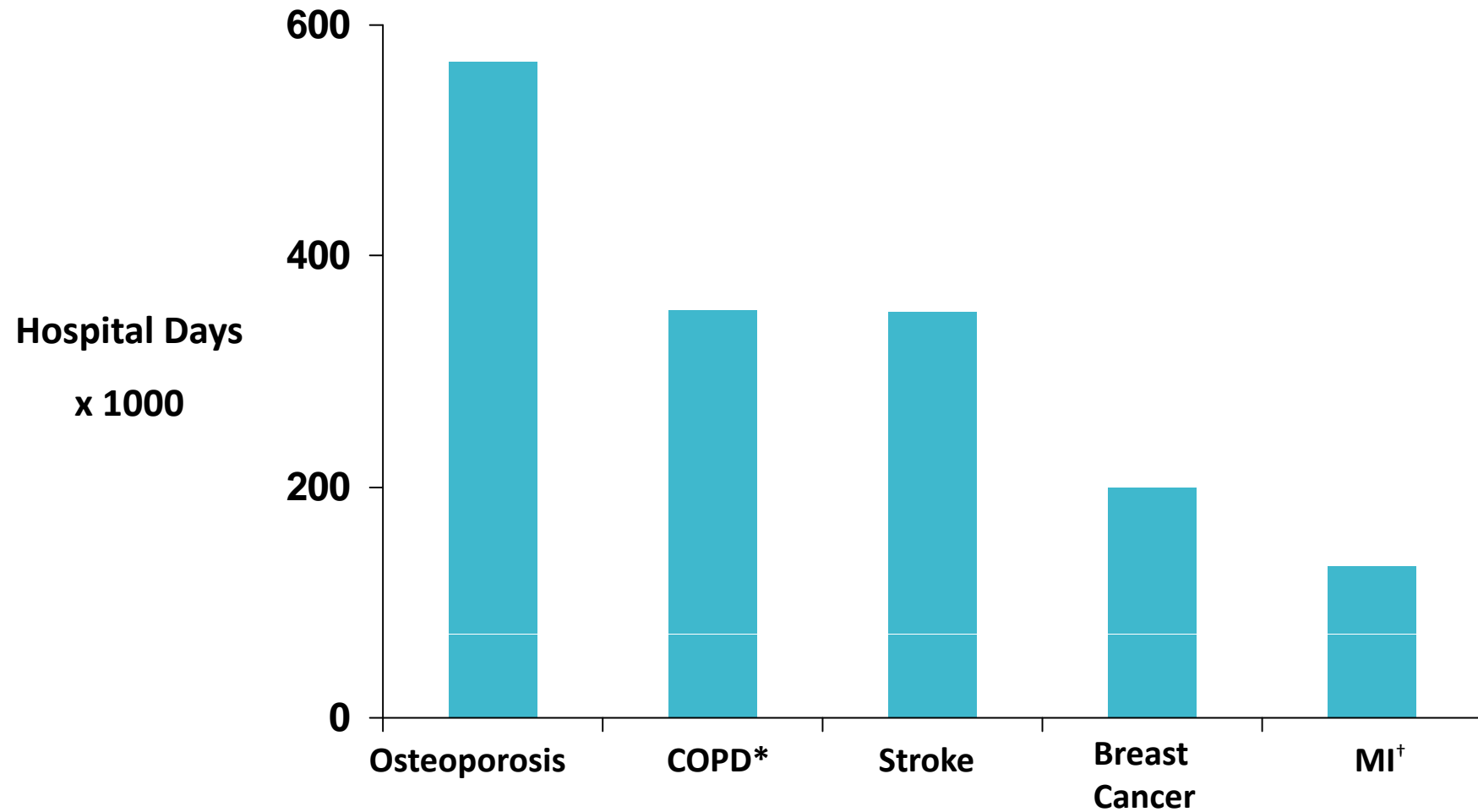
Annual
Incidence
in the
US x 1000



¹Osteoporosis Fast Facts. National Osteoporosis Foundation. 2000.

²National Institutes of Health. *Healthy Heart Handbook for Women*. 2000.

The Burden of Osteoporosis

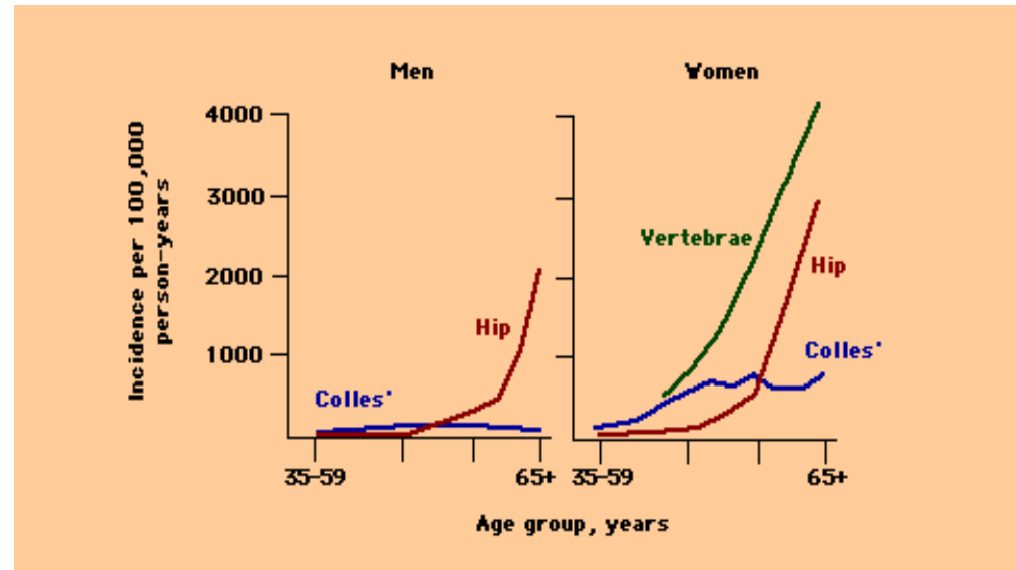


*Chronic obstructive pulmonary disease

†Myocardial infarction

Lippuner K, et al. *Osteoporos Int.* 1997.

Why Treat Osteoporosis?



- 30-50% of women and 15-30% of men will fracture in their lifetime
- Overall mortality after hip fracture is 20% in 12 months

Preventing Subsequent Fractures

- Calcium and vitamin D alone are not sufficient¹
-
- Bisphosphonates can^{2,3}:
 - Prevent fractures
 - Single vertebral – 50%
 - Multiple fracture 90%
 - Reduce days with limited activity from back pain

¹Lindsay R, et al. Presented at: World Congress on Osteoporosis; June 15-18, 2000, Chicago, Ill.

²Liberman UA, et al. *N Engl J Med.* 1995.

³Nevitt MC, et al. *Arch Intern Med.* 2000.

Exercise

- Exercise in young individuals increases the likelihood that they will attain the maximal genetically determined peak bone mass.
- Meta-analyses of studies performed in postmenopausal women indicate that weight-bearing exercise prevents bone loss but does not appear to result in substantial bone gain

Treatment Options

- Calcium + Vitamin D +Calcitriol
- Bisphosphonates
 - Disodium Etidronate (Etidrate)
 - Alendronate (Fosamax)
 - risedronate
- Raloxifene (SERM)
- Parathyroid hormone
- Strontium ranelate
- Hip protectors

Intake Recommendations for Men and Women

National Academy of Sciences

Age yrs	Calcium mg/d	Vitamin D UI/d
30-50	1000	200
51-70	1200	400
71+	1200	600

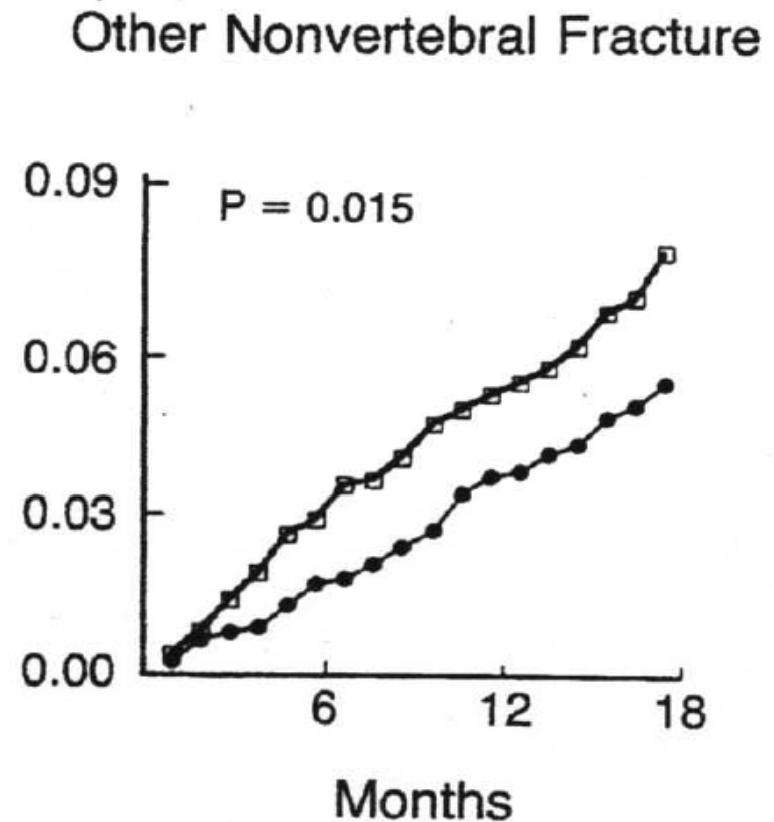
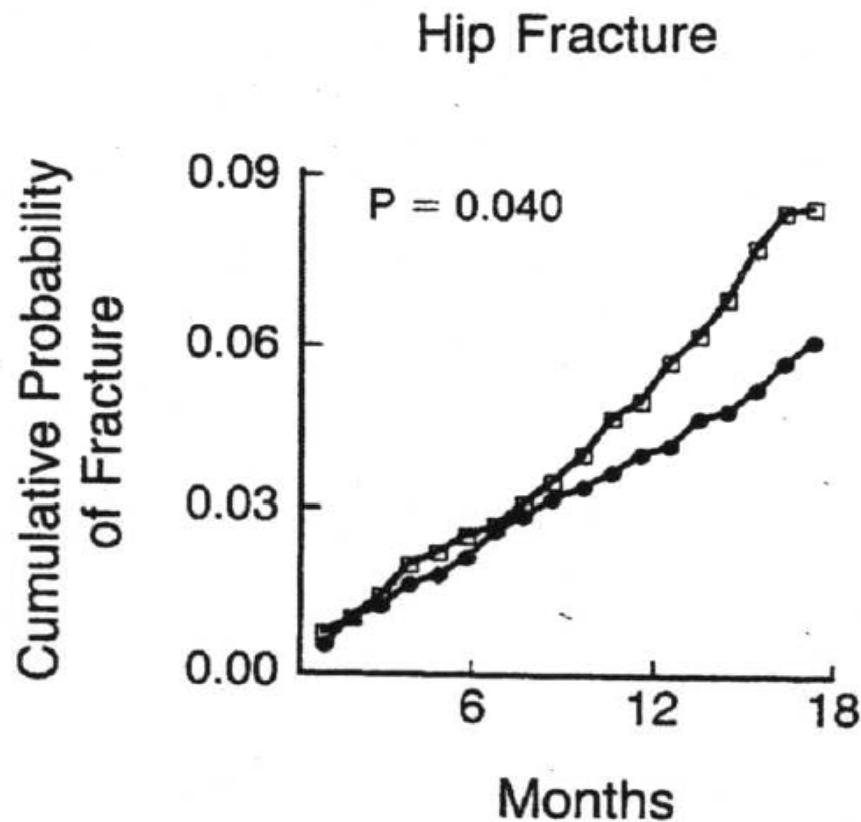
Calcium

- ↓ Calcium
- ↓ Ca intake → absorption ← ↓ VitD
- ↓ Circulating [Ca⁺⁺]
- ↑ PTH
- ↑ Bone remodeling
- ↑ Bone loss → ↑ Fracture risk

Vitamin D

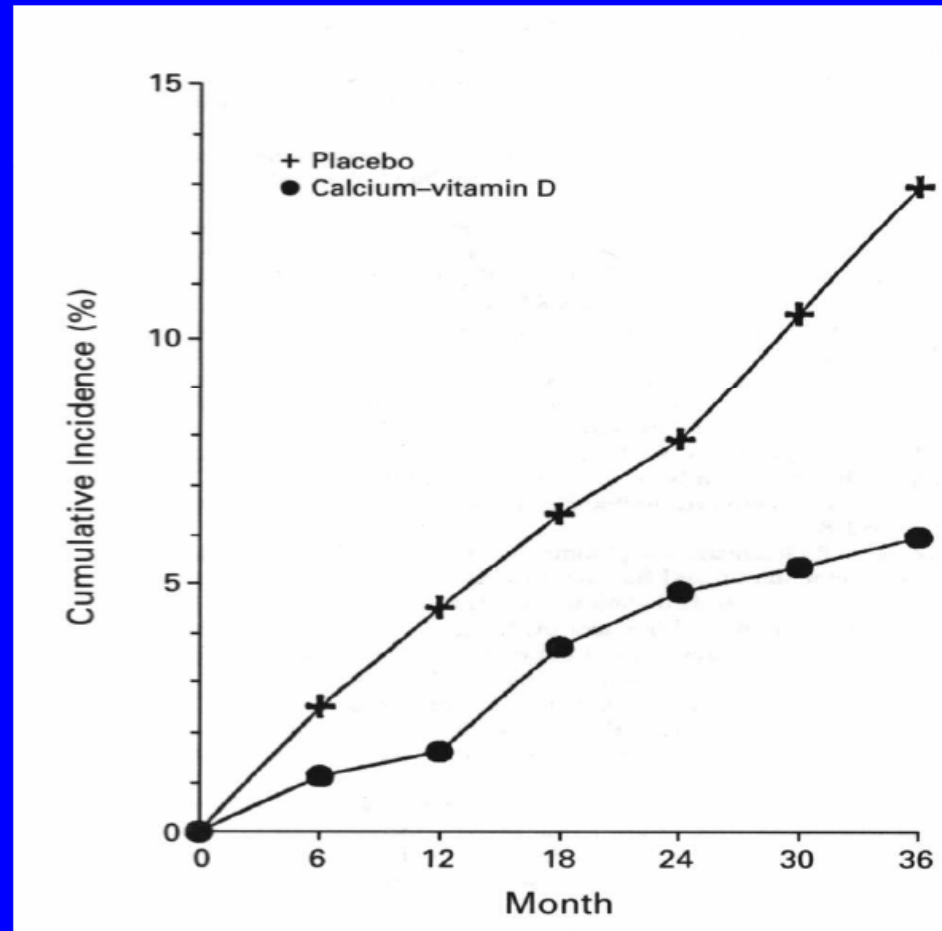
- Calciferol 1.25 mg
 - monthly for replacement
 - weekly for treatment (easier to remember)
- No advantage in using calcitriol if renal function is normal

Effect of Calcium and Vitamin D on Fracture Rates in Very Elderly French Nursing Home Residents



Chapuy MC. N Engl J Med 1992; 327: 1637-42.

Effect of Calcium and Vitamin D on Non-vertebral Fracture Rates in Healthy Men and Women



Dawson-Hughes B, et al. N Engl J Med 1997; 337:670-6.

Conclusions

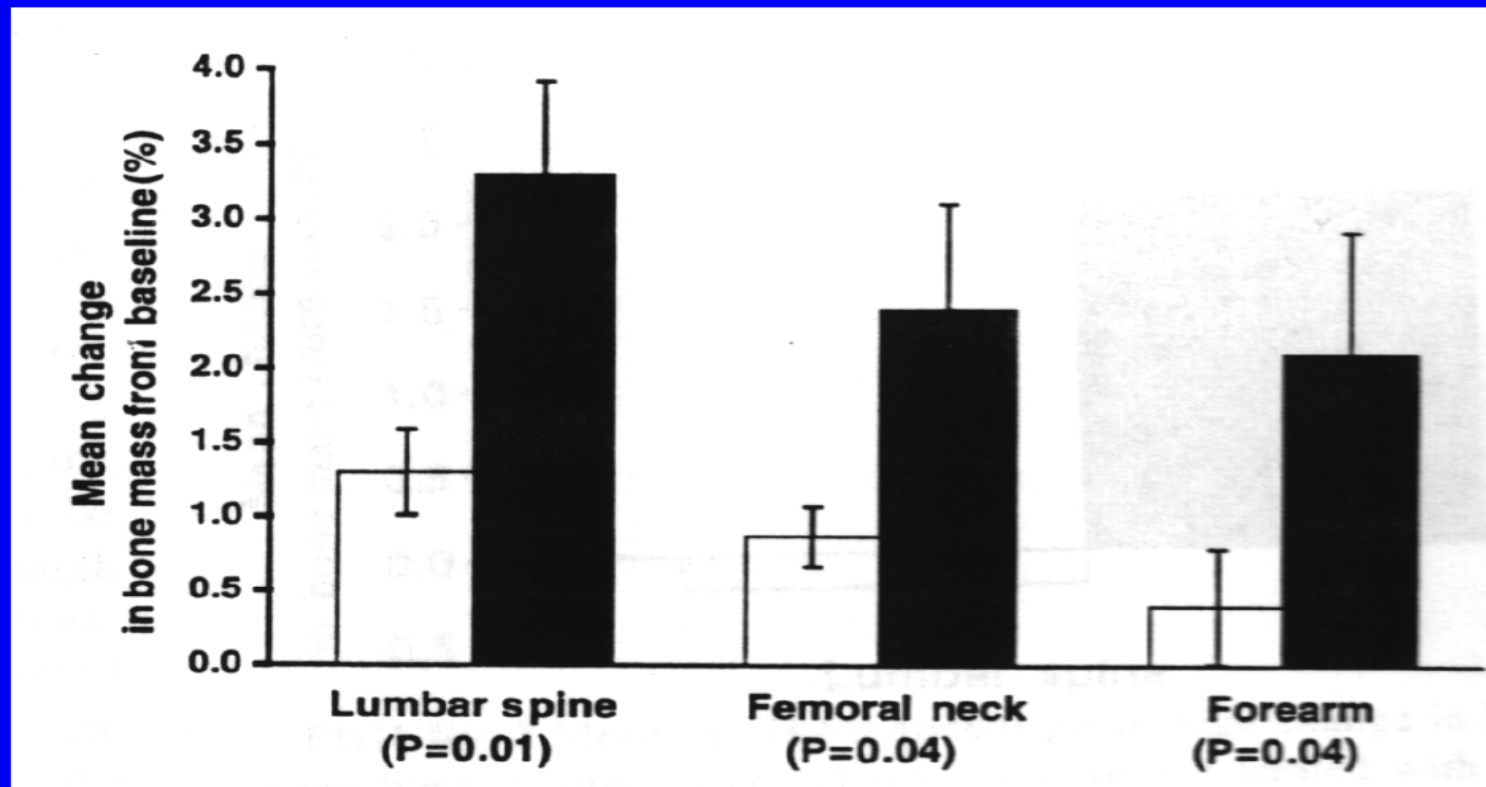
- Dietary protein and vitamin K
 - roles needs further definition
 - amounts > RDA may benefit bone
- Calcium and vitamin D
 - lower fracture rates in the elderly
 - dietary intakes are very low
 - supplements are needed

Estrogen

- Estrogen can prevent menopausal bone loss in most women. Estrogen replacement therapy (ERT) is the treatment of choice for postmenopausal women, particularly those who had an early menopause, and for women who have had a hysterectomy.
- ERT is particularly effective during the first few years after menopause when bone loss is most rapid.
- Epidemiologic studies and the few prospective clinical trials of estrogen suggest that ERT or HRT decreases the risk of osteoporotic fractures by 30 to 50%.
- Because other antiresorptive drugs may have an additive effect when given with estrogen, combination therapy should be considered in patients who have very low bone density, continue to lose bone, or incur a fracture while taking ERT or HRT.

Estrogen

Effect of Estrogen \pm Calcium on Change in BMD



Nieves JW. Am J Clin Nutr 1998; 67: 18-24.

■ HERS; HERS II:

- **Hormone Rx**
 - 1. Increased risk of coronary heart disease
 - 2. Stroke
 - 3. Invasive breast Ca
 - 4. Increased Pulmonary emb
 - Decreases:
 - Colon Ca
 - # NOF
- 10,000 women taking HRT/yr**
- 8 more will develop invasive breast ca
 - Additional 7 will develop a heart attack
 - 8 will have a stroke
 - 18 will have blood clots
 - *6 fewer colorectal ca*
 - *5 fewer hip fractures*

- Bisphosphonates are potent antiresorptive drugs that directly inhibit osteoclast activity.
- For women who cannot tolerate estrogen or have contraindications (eg, preexisting breast cancer, risk factors for breast cancer), bisphosphonates are considered the next choice; these drugs increase bone mass and decrease the risk of fractures, particularly in patients taking glucocorticoids.
- Bisphosphonates, particularly alendronate, have also decreased the incidence of vertebral and nonvertebral fractures by $\geq 50\%$ in large cohorts of postmenopausal women.

Bisphosphonates - Etidronate

- Increases BMD and reduces vertebral fractures
- 400mg/day for 14 days, 77 days of calcium supplement (1000mg), cycles repeated.
- Or Daily alandronate
-
- Must be taken on an empty stomach
- Useful for steroid osteoporosis where no fracture
- Vitamin D supplement

Alendronate [Fosamax]

- Increases BMD and reduces hip, vertebral and non-vertebral fractures
- Special Authority (any doctor)
 - Severe Osteoporosis
 - History of significant osteoporotic fracture
 - Radiographic vertebral fractures are defined
 - T score < -3.0 on BMD
- No problem with mineralisation
- For prevention, alendronate is taken daily as a 5 mg tablet or weekly as a 35 mg tablet. For treatment, it is taken daily as a 10 mg tablet or weekly as a 70 mg tablet with or without vitamin D₃.

The tablet needs to be taken first thing in the morning after waking up and on an empty stomach.

How long to treat

- Past experience with bisphosphonates (Actonel[®], Boniva[®] and Fosamax[®]) suggests that upon discontinuation of any of these drugs, the benefits may continue for several years or longer. This is because the drugs remain in the bone for a long time. Eventually, however, the beneficial effect begins to lessen, bone remodeling rates increase and bone loss may occur.

One study found that alendronate (Fosamax[®]) continued to have a beneficial effect on bone mineral density for up to 10 years in postmenopausal women taking the medication. Biopsies of bone tissue in women on alendronate for 10 years show that bone tissue looks healthy and normal. Other studies show that treating with alendronate for more than five years improves bone strength and reduces clinical fractures of the spine.

Another study suggested that women who discontinued taking alendronate after five years of treatment did not significantly increase their fracture risk for up to an additional five years.

Vertebral compression fracture

- Is the most common clinical manifestation of osteoporosis
- Pain modification, activity modification, bracing
- Newer therapy: Vertebroplasty and Kyphoplasty may help in some cases
- Fusion with Pedicle screw fixation

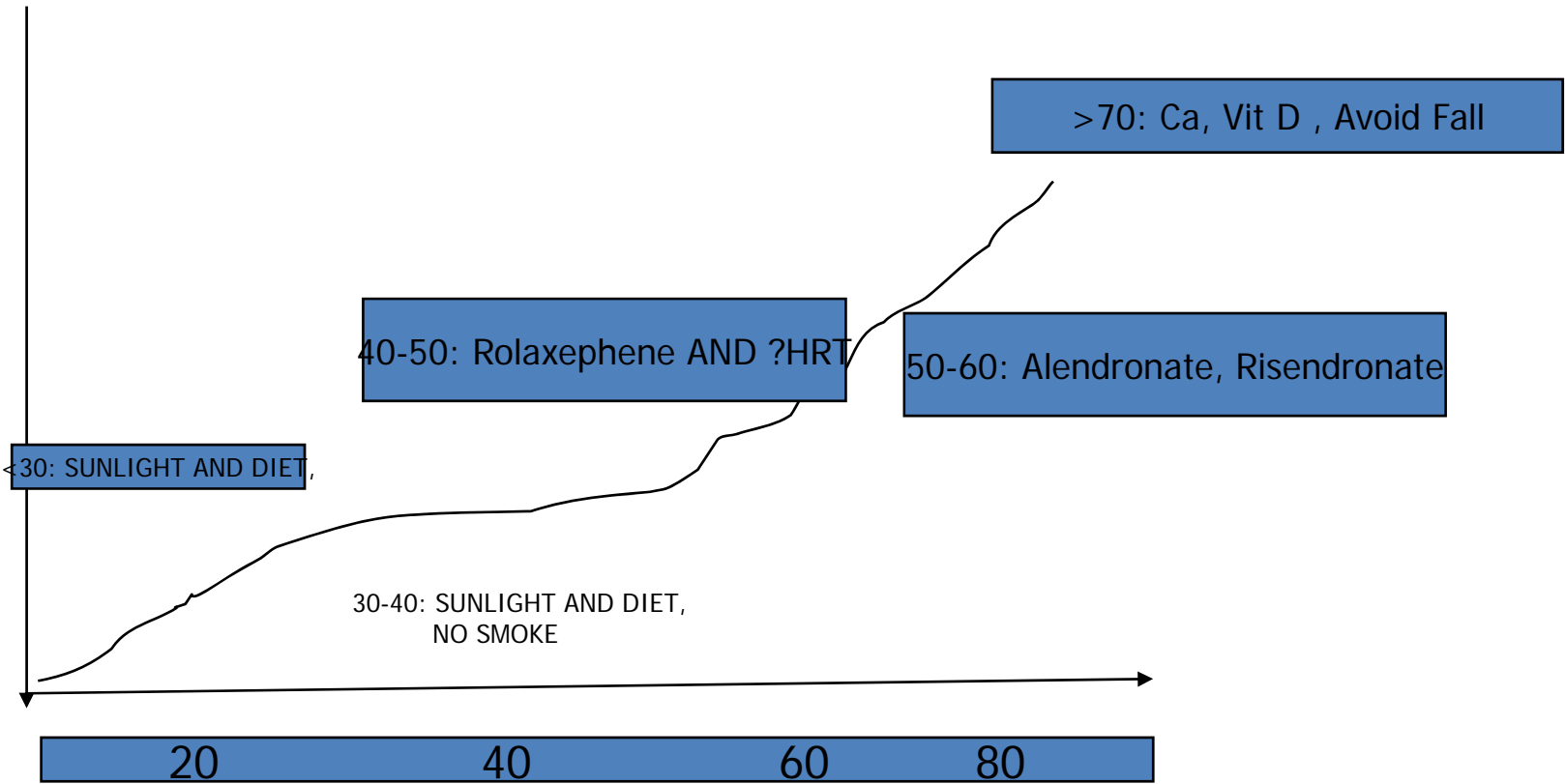
SERMS (Tamoxifen and raloxifene)

- **Postmenopausal**
- 1. Tamoxifen: The existing data suggest that tamoxifen decreases BMD in women before menopause but increases it after menopause
- 2. Raloxifene: A modest increase in BMD (about 2.5% at the spine) and a reduction of about 35% (with the 60-mg dose) in vertebral fractures throughout 3 years

- Calcitonin:
 - Prevention of bone loss is dose dependent
 - Effects better documented at the spine & forearm than at the hip
 - Has analgesic properties; pain relief occurs when it is given for up to 3 months to patients with acute pain following crush #

- Fluoride salts:
 - Marked anabolic effects on cancellous bone mass
 - at spine (level Ib)
 - Effects of vertebral # variable
 - No protective effects on hip # (level Ib)
 - Insufficient data

Stratified treatment of Osteoporosis



Studies:

- Aledronate: no osteomalacia [cf etidronate]
- 50% reduction in fractures at one year

- Risedronate: 60% decrease

- Zolendronate: once a year [efficacy is yet to be established]

Steroids and osteoporosis

- Dose & duration dependent [AVN = Idiosyncratic]
- Cumulative dose
- Threshold dose 7.5mg/d x 6 months
- Bone loss rapid in the 1st 6-12 months, thereafter loss of 2-3 x normal
- Trabecular bone > Cortical bone
- Alt-day Rx not protective
- Bisphosphonates reduce risk of fractures

Role of Vitamin K

- Vitamin K is required for the formation of osteocalcin
- •Osteocalcin is the most abundant noncollagenous protein in bone matrix
- •Osteocalcin acts as a regulator of bone mineralization
- •In vitamin K deficiency, undercarboxylated osteocalcin is produced
- •Undercarboxylated osteocalcin may not function normally

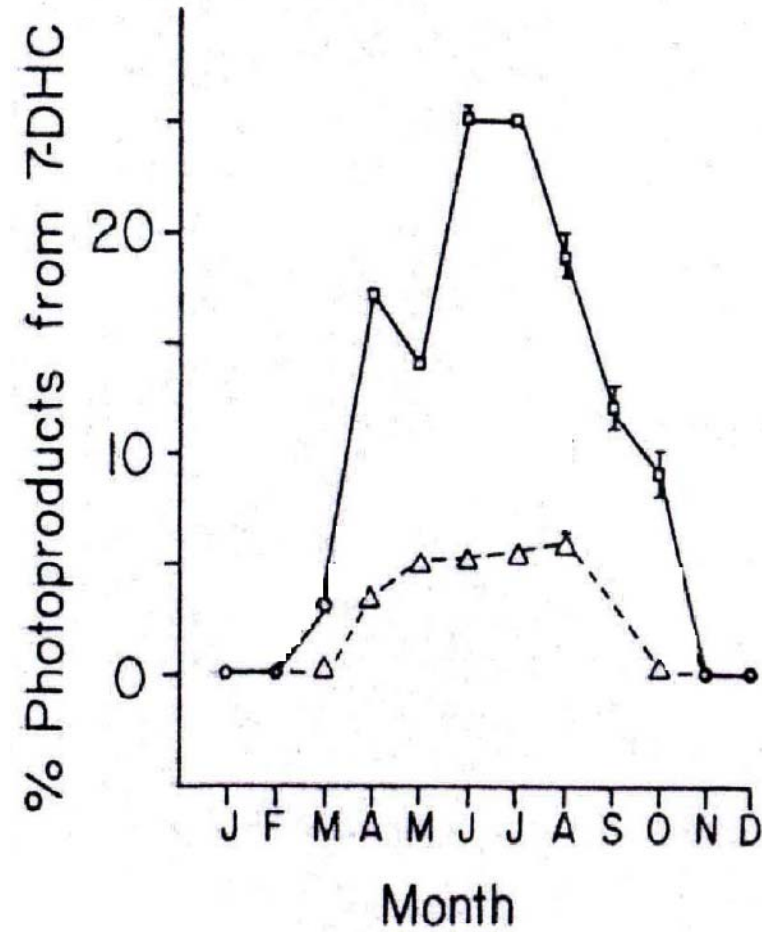
Vit K Vs Hip fracture

- Vitamin K Intake and Hip Fractures
- Framingham Study 1988-1995
- (888 subjects, 44 hip fractures)

- P for trend = 0.047
- Booth SL, et al. Am J Clin Nutr 2000; 71: 1201-8.
- Q Median vit K intake mcg/d RR hip fracture CI
- 1 56 1.0
- 2 105 0.53 0.22, 1.28
- 3 156 0.59 0.25, 1.39
- 4 254 0.35 0.13, 0.94

Vitamin D Synthesis By Season

Webb AR. JCEM 1988; 67: 373-8.

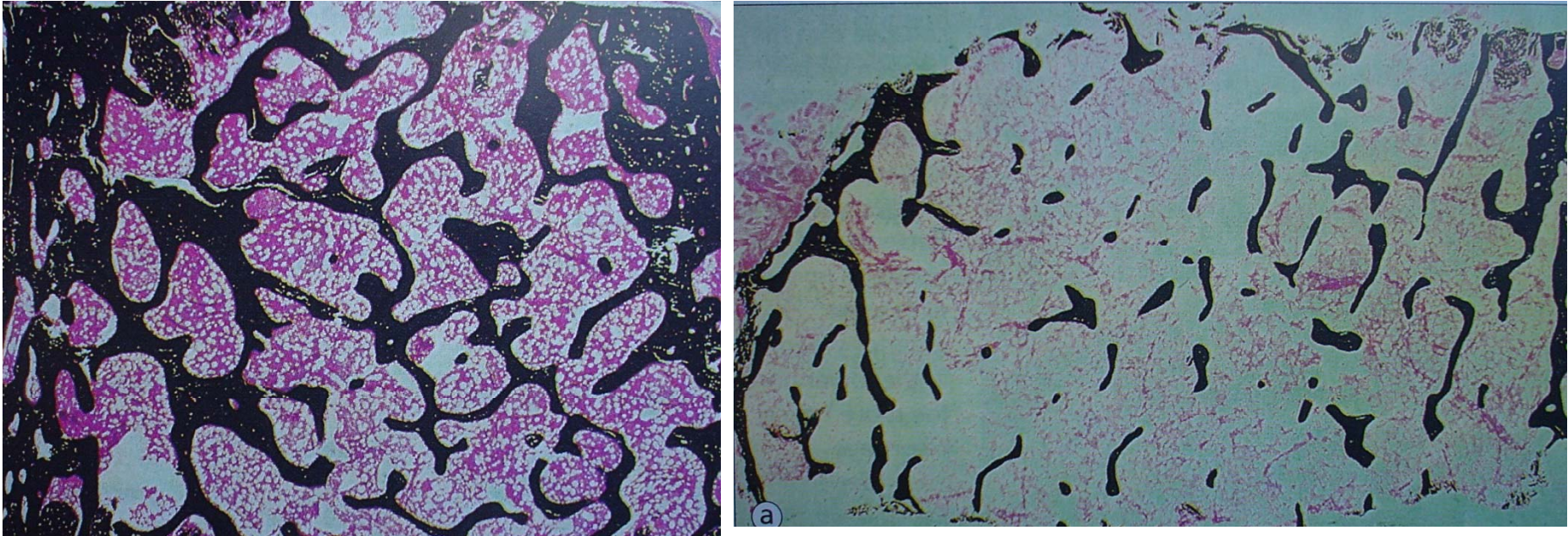


Effective Osteoporosis Education in the Outpatient Orthopaedic Setting 89A:301-306. Jeff E. Schulman

- The purpose of the present study was to investigate whether patients could be effectively educated with regard to osteoporosis and lifestyle modification during their outpatient visits to an orthopaedic surgeon's office.
- 11-question quiz that included items regarding their knowledge of osteoporosis, calcium intake, menopausal status, exercise, smoking, and whether or not they had had a bone mineral density scan.
- The quiz was completed during a visit to an outpatient sports medicine/general orthopaedic clinic.
In response to the educational intervention, significant improvements were seen in terms of the patients' ability to define osteoporosis ($p = 0.004$), the ability to identify being female as a major risk factor ($p < 0.001$), and the understanding that females should begin adequate calcium intake at a young age ($p < 0.001$).
- Significant increases in daily calcium intake ($p < 0.001$) and exercise level also occurred ($p < 0.003$). The postmenopausal group demonstrated a less robust response to the educational intervention.

- Recommendations were for "prevention and lifestyle changes, including physical activity and nutrition."
- Orthopaedic surgeons can be an integral part of osteoporosis prevention, diagnosis, and treatment by distributing a simple educational handout to their outpatient population.

Bone Biopsy



- a. Normal Iliac bone: 20% cortical and 37% trabecular bone
- b. Senile osteoporosis: 7% cortical and 13% trabecular bone
- c. Biopsy is rarely used
- d. Dexa scan is commonly used

Quantitative CT

- Vertebra is the usual site; Midvertebral level of L2-5; Single energy QCT
- Can measure: Cortical bone area, cancellous bone or an integrated sum
- Only method: Allows the direct measurement : True density
- D/A: - Higher radiation,
- Difficult assessment of hip
-

Quantitative Ultrasound

- No radiation; Portable and inexpensive
- Accessible sites: Cancellous: Calcaneus, Patella, phalanges
- Cortical: radius, tibia,
- Based: velocity and attenuation of an ultrasound wave
- Because of high correlation: recommended by FDA for clinical use.
- D/A: Limited to peripheral sites

