



Osteoporosis

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Osteoporosis

Osteopenia: Leads up to osteoporosis

Osteoporosis: severely low Bone Mass Density (BMD)

2 million men and 8 million women in the USA

1 in 2 women and 1 in 5 men after age 50 will have a fracture related to osteoporosis

Hip fractures affect 20% of women above age 50

50% of women above age 80

Most frequent fractures in hip, spine, and wrist

Incidence is increasing due to increased life expectancy

Osteomalacia/Rickets

Not the same as osteoporosis
“soft bones”
Improper mineralization due to vitamin D
deficiency



Bone Structure

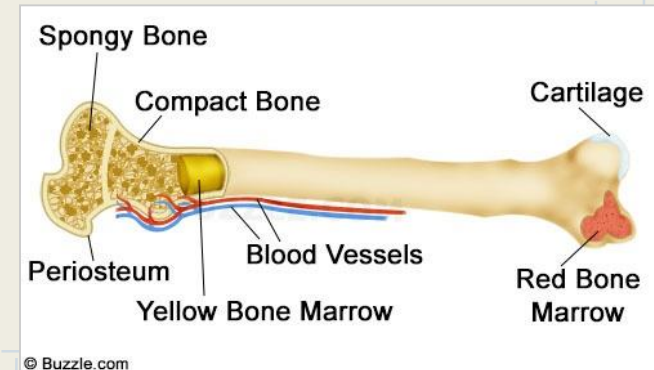
Functional unit is the osteoid made of proteins, calcium and phosphate crystals

Cortical bone → hard outer bone
arranged into osteons

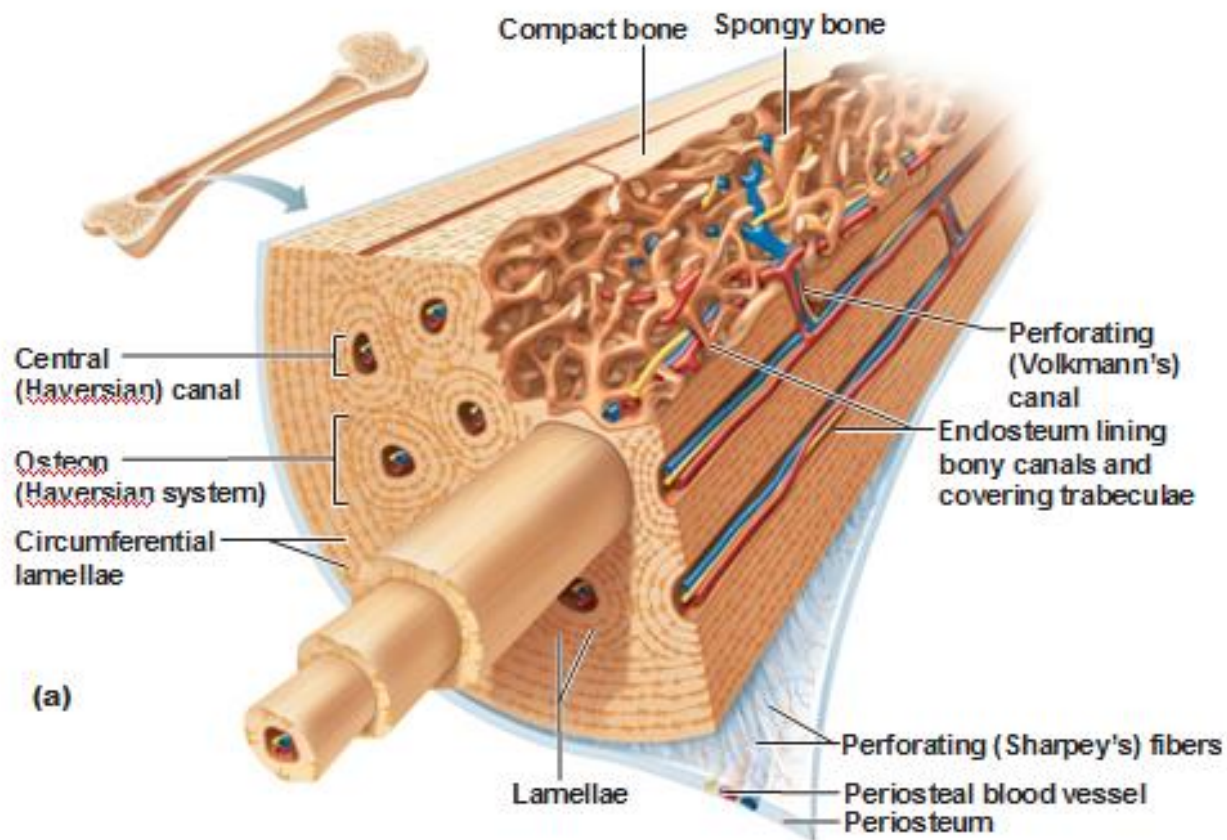
Trabecular bone → inner spongy bone

is more sensitive to estrogen stimulation, and its degradation is usually responsible for fractures

porous



Microscopic Structure of Compact Bone



Bone Cells

Osteoblasts:

- form bone tissue
- mineralization
- cytokine production

Osteocytes: Mature Osteoblasts

- trapped in the bone matrix in lacunae

Osteoclasts:

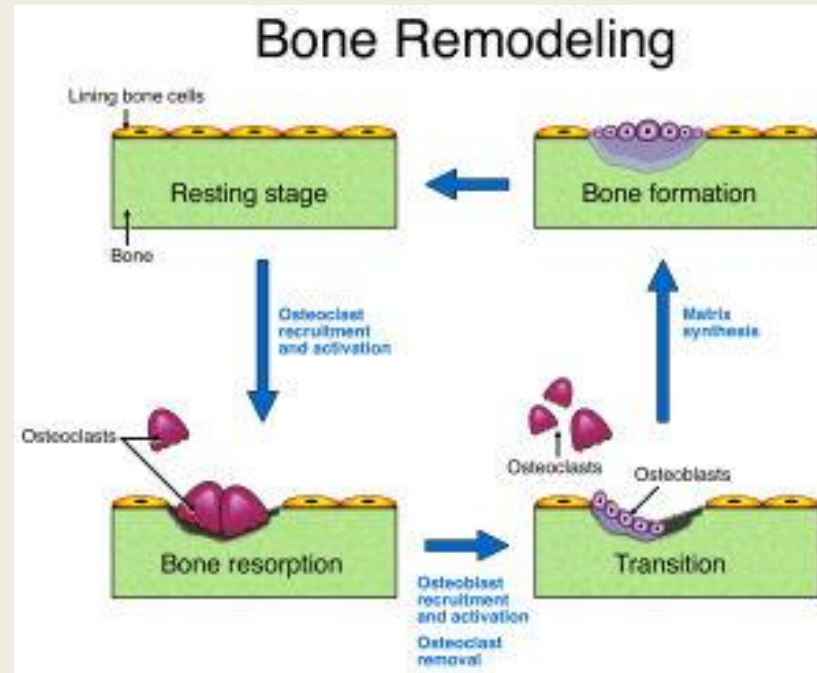
- break down bone tissue with acid and enzymes

Bone Modeling

growth of skeleton until maturity
length and height
at the epiphyseal plate
ends at about age 16-20

Bone Remodeling

After bone growth completes, it continues to be remodeled



Homeostasis

Usually this is balanced

When dietary Ca is low, bone mineralization is in negative balance

Osteoclast activity will be higher than osteoblast activity

This occurs for everyone with age

This makes bones weak and vulnerable to fracture

Calcium Homeostasis

99% body Ca in Bones; 1% in blood serum

Blood Serum Ca is essential for body functioning

Bones serve as a Ca store to maintain blood Ca homeostasis particularly when the diet is inadequate

Local Factors

Bone Breakdown	Bone Formation
NO (osteoclast autocrine stimulation)	Growth Factors
Arachnoid Acid Metabolites	Matrix molecules (osteopontin)
Inflammatory Cytokines (IL1, IL6, TNF)	
Prostaglandins	
RANK receptors	Osteoprotegerin Receptors

Convergence Theory

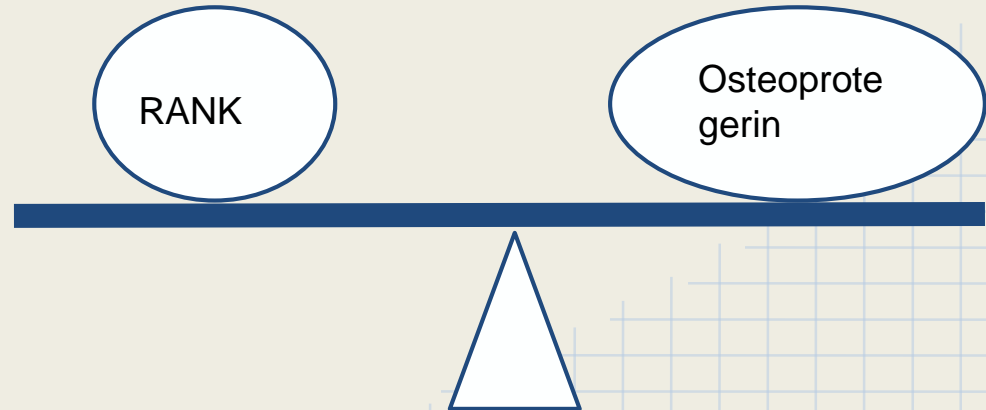
RANK Receptors= cytokine receptors on osteoclasts

Osteoprotegerin= RANK receptor blockers

Osteoprotegerin: RANK ratio signifies if bone is growing or being broken down

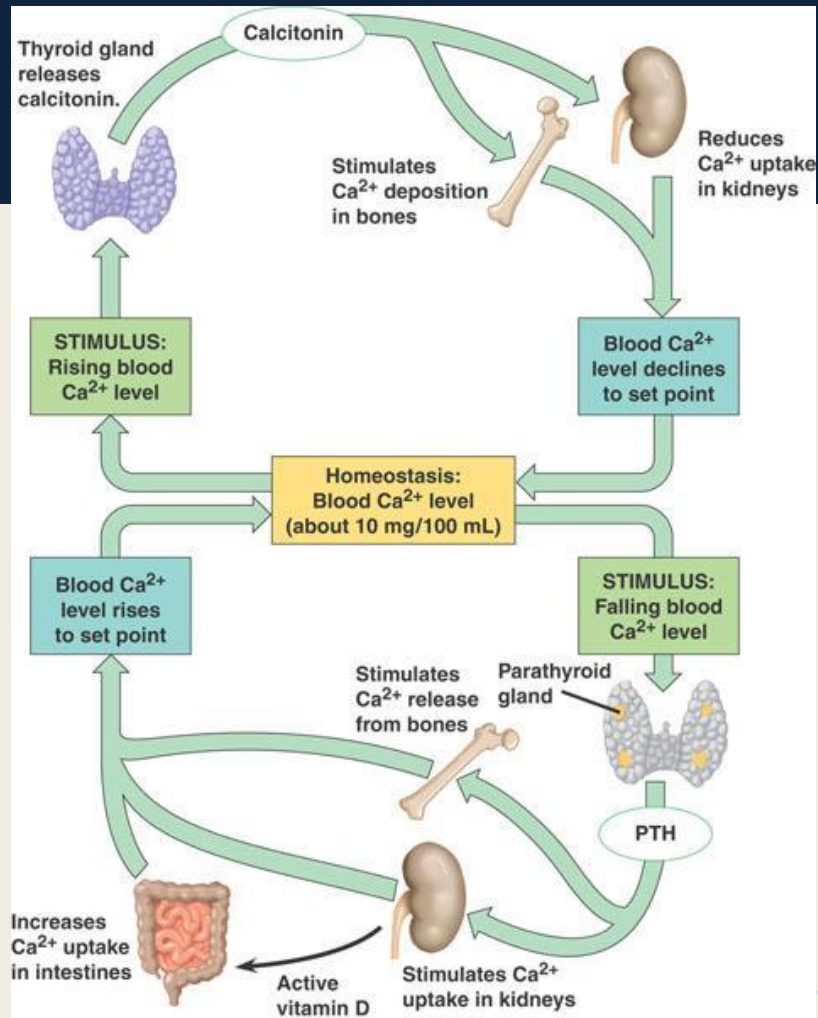
High ratio=bone formation

Low ratio= bone breakdown



Systemic Hormones

Bone Breakdown	Bone Formation
Parathyroid Hormone (PTH)	Estrogens and Androgens
Glucocorticoids	Calcitonin
Thyroid Hormone	Vitamin D/Calcitriol (inhibits PTH)
	Insulin like growth factor (IGF)
	Leptin





Causes of Osteoporosis

Primary Osteoporosis

Age

Hormones

Primary Osteoporosis

Age Related

Before age 18-24, bone growth is in positive balance
when you hit your Peak Bone Mass (PBM) your BMD will start to decrease

happens to all people

related to decreased osteoblast activity and bone matrix protein production

potential for osteoporosis depends on how high your PBM is

Factors Affecting PBM

Gender

Race

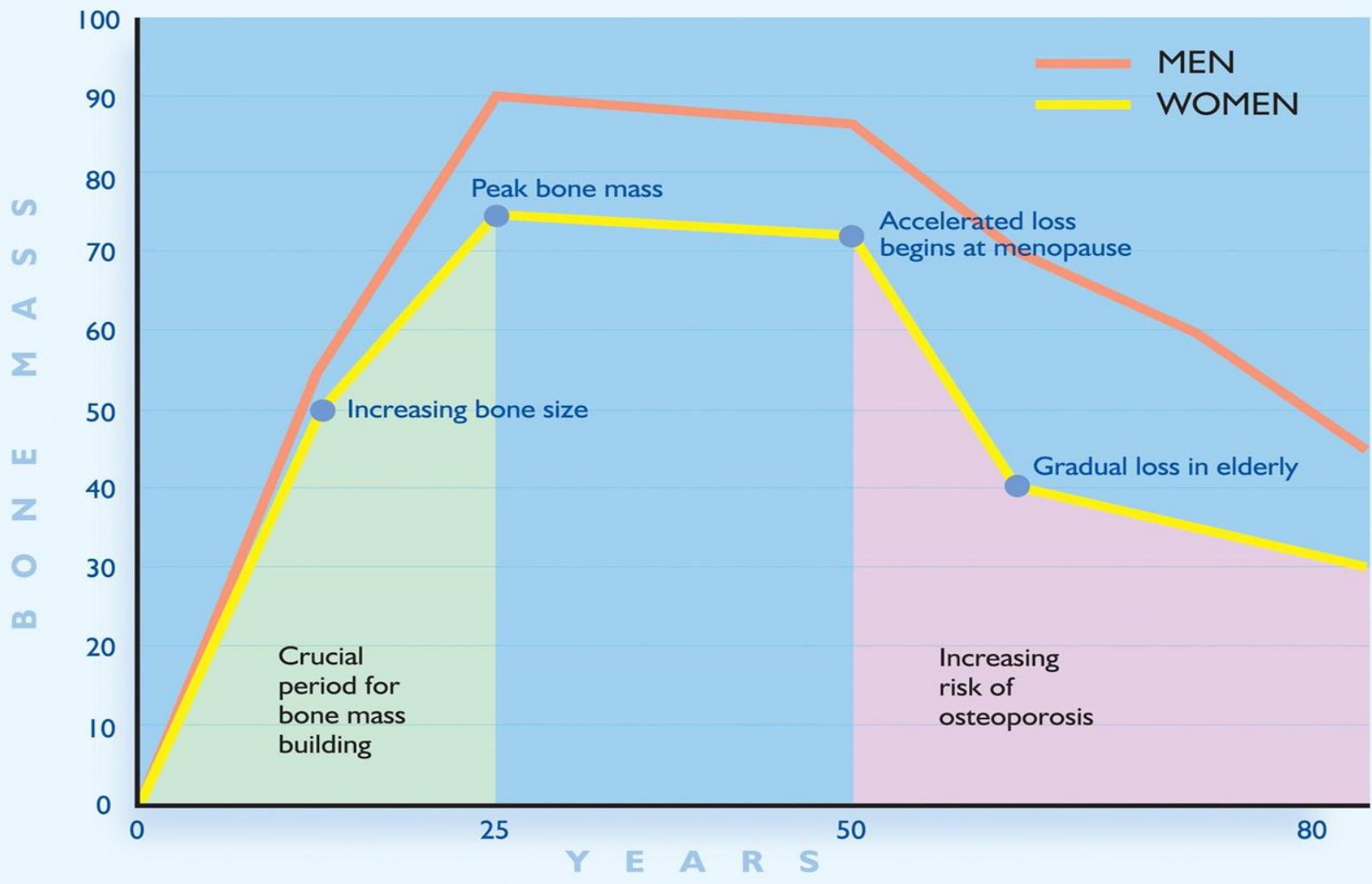
Physical Activity

Body Weight/Stature

Diet

Menopause

Hormones



Primary Osteoporosis

Hormone related

Decreased estrogen release at menopause

estrogen blocks inflammatory cytokines that stimulate osteoclasts

Also affects men with age, since androgen production decreases with age

Androgens are precursors to estrogen

Causes of Osteoporosis

Secondary Osteoporosis

Drugs

Disease

Secondary Osteoporosis

Drugs

Glucocorticoids → decrease osteoblast activity; increase osteoclast

Loop Diuretics → increase Ca excretion

Antacids → Al interferes with Ca absorption

Methotrexate (arthritis)

Tetracycline (antibiotic)

Cyclosporin (immunosuppressive)

Heparin (anticoagulant)

Secondary Osteoporosis

Diseases

Decrease Absorption of Ca: CF, SBS, Celiacs, chronic diarrhea,
Crohn's, cancer

Increased excretion of Ca: Chronic kidney failure

Inflammation

Secondary Osteoporosis

Oral Contraceptive use

effects on BMD are inconclusive

depends on duration, type, and dose

most concerning for women still building PBM

Pregnancy

probably does not have a huge effect on BMD

needs increase, but absorption of calcium in the GI increases as well

But, adolescents who are pregnant are at a higher risk

Lactation

Will decrease BMD

BMD is usually regained once child is weaned

Risk Factors/Prevention

1. Diet
2. Physical Activity
3. Alcohol
4. Smoking
5. Caffeine
6. Body Weight
7. Eating Disorders
8. Falls

Diet: Macronutrients

Adequate calories and protein are essential for the building bone and avoiding negative nitrogen balance

Calcium must be adequate for protein to have a positive effect on bone

If Ca intake is inadequate, too high or low protein will have a pronounced effect on bone

Very high protein may decrease BMD

- increased acidic load

- increased urinary Ca excretion

Diet: Micronutrients

Vitamin D

- inhibits PTH

- increases GI Ca absorption

- decreases kidney Ca excretion

- Stimulates bone uptake of Ca and Phosphate

Phosphate

- high levels increase PTH

- Proper Ca:PO₄ important for proper mineralization

Calcium: The primary prevention

- Adequate amounts keep serum levels normal and prevent bone breakdown

Physical Activity

adds stress to bone strengthening them
the bone adapt to the strain
frequency, duration, and intensity
must be impact exercise
immobility is a risk factor for osteoporosis

Caffeine

caffeinated beverages displace milk
diuretic effect may increase calcium excretion rate
impairs proper PTH function and secretion

Cigarettes/Tobacco

associated with increased fracture risk of 1.2-1.5 X

associated with earlier menopause

Cigarette toxins...

- decrease osteoblasts

- decrease estrogen production

- increase hepatic enzymes that breakdown estrogen

- stimulate osteoclasts

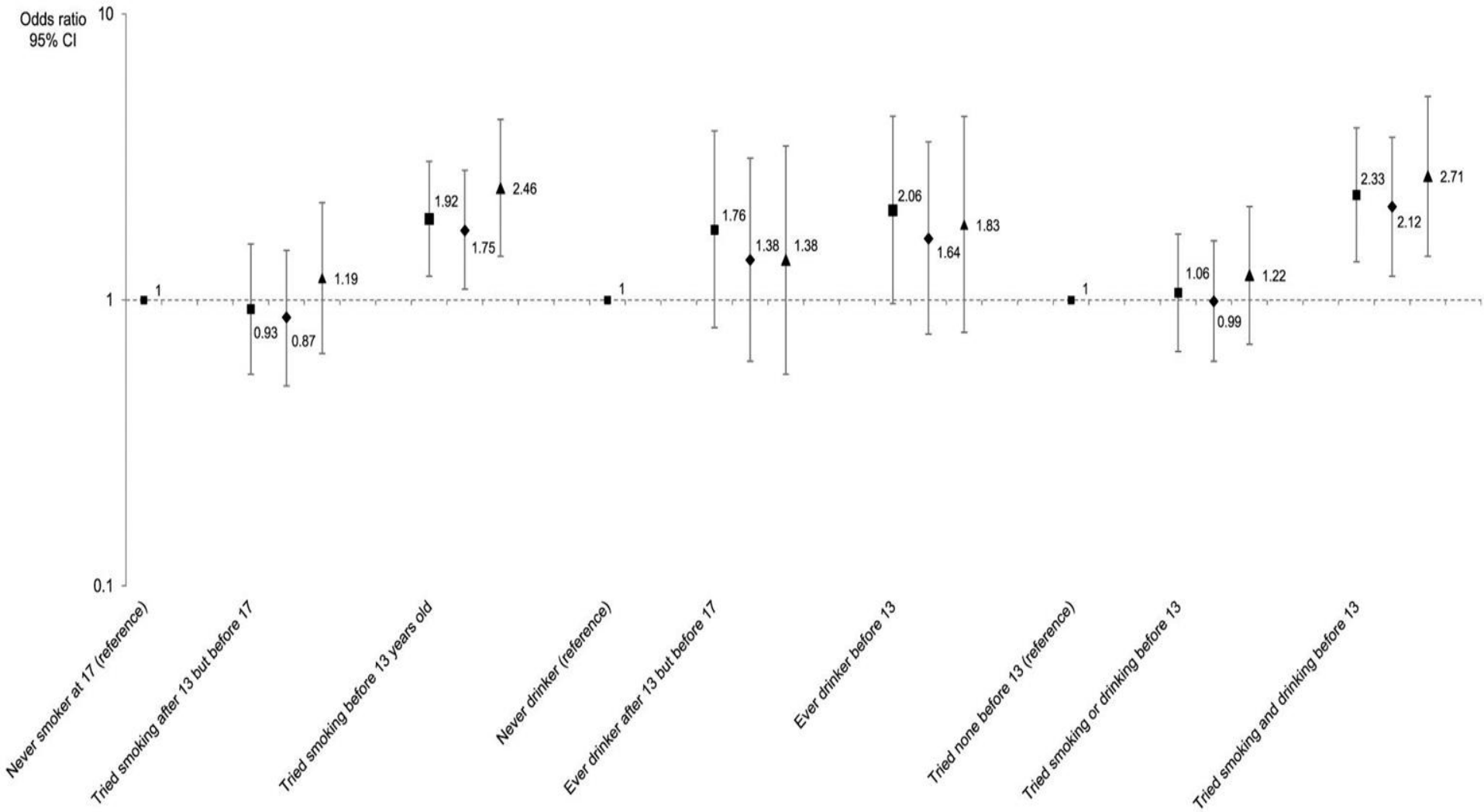
Alcohol

associated with other risk factors for osteoporosis

moderate intake is not associated with low BMD, possibly higher BMD

acetaldehyde from alcohol metabolism may be toxic to bone cells

may cause gonadal dysfunction, decreasing sex hormones



Body Weight

Body weight is positively associated with BMD
Attributable to adipose and lean mass

Risk factors:

- Underweight

- Low BMI

- Low body fatness

Eating Disorders

Peak bone mass (PBM)

→ diminished in cases of anorexia nervosa

Amenorrhea

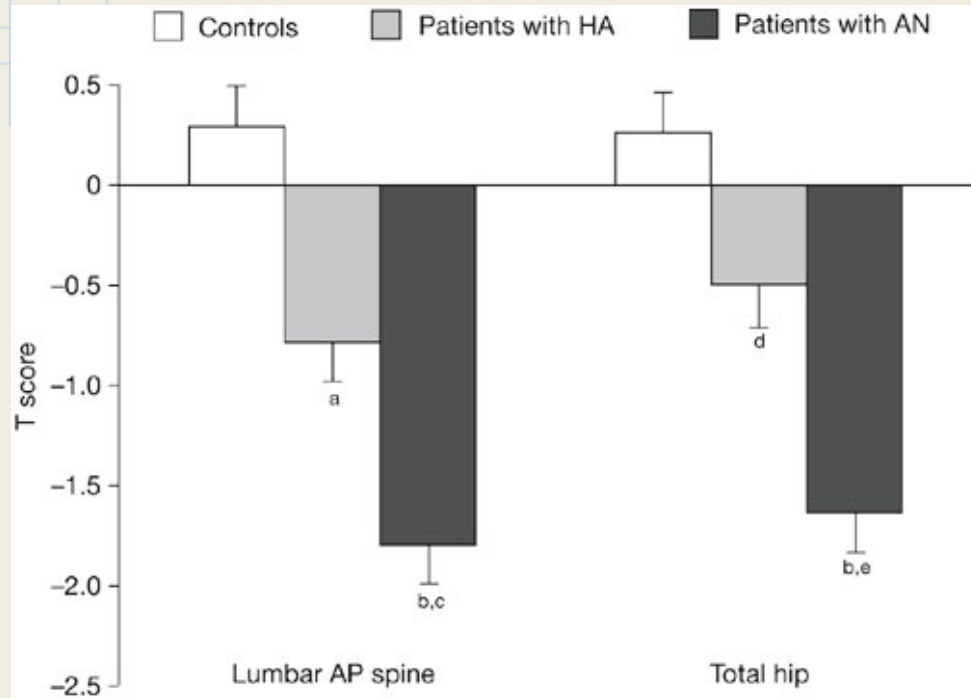
Low estrogen levels contribute to loss of bone density

Excessive cortisol

Malnutrition, including calcium deficiency

→ Increased risk of fracture

Anorexia & Bone Loss



Women with anorexia nervosa have more severe bone loss than normal weight women with hypothalamic amenorrhea
See Diagnosis section for explanation of T-scores

Clinical Assessment

Risk factors

Age

Older than age 60

Ethnicity

Blacks and Hispanics have a greater BMD than whites and Asians

Likely due to larger muscle mass, differences in body weight, lifestyle factors, and dietary intake

Female gender

Men also lose bone density with aging, but they begin with a high bone density

Men reach osteoporotic levels at an older age than women

All women over age 65 should get a bone density test

Clinical Assessment

Bone Deformity

- Most common manifestation

- Pain only occurs with a fragility fracture

- Bones lose volume, become weak, and may collapse or become misshapen

Vertebral Collapse

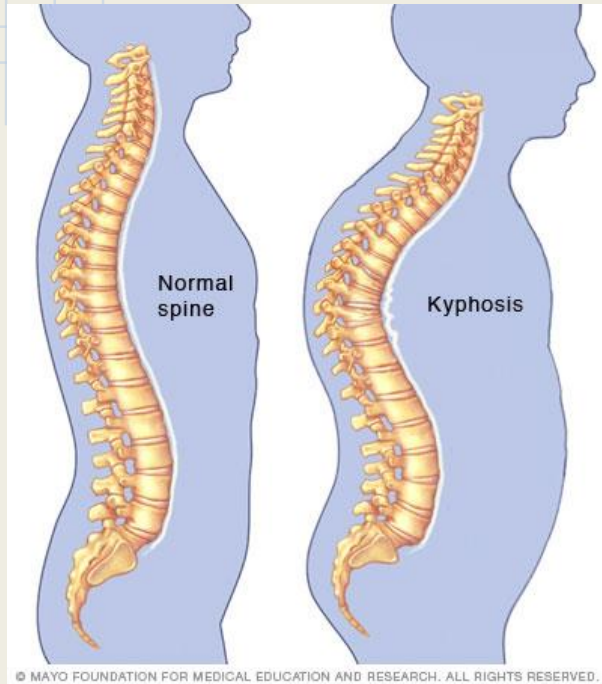
- Kyphosis (hunchback or “dowager’s hump”) & lordosis

- Diminished height

Common fractures

- Long bones (femur and humerus), distal radius, ribs, vertebrae

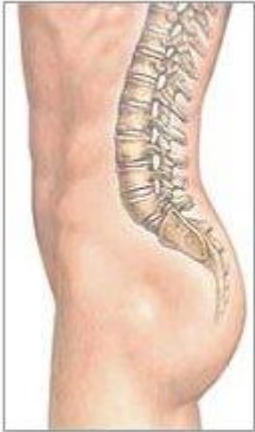
Kyphosis



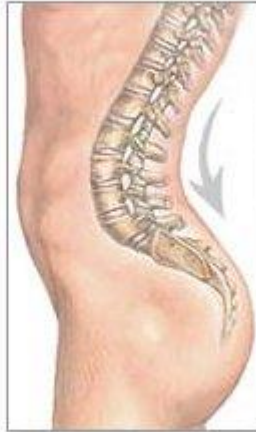
Lordosis

Inward curvature of the spine or “sway back”

Normal spine



Lordosis of the spine



Exaggerated
lumbar
curve



Biochemical Markers

Bone remodeling & turnover

Resorption markers (osteoclasts):

Serum C-telopeptide (CTX)

Urinary N-telopeptide (NTX)

Plasma tartrate-resistant acid phosphatase

Formation markers (osteoblasts):

Serum bone specific alkaline phosphatase (BSAP)

Total plasma alkaline phosphatase also used

Osteocalcin (OC)

Aminoterminal propeptide of type 1 procollagen (P1NP)]

Biochemical Markers

Bone Turnover

Elevated levels of markers of bone turnover may predict bone loss

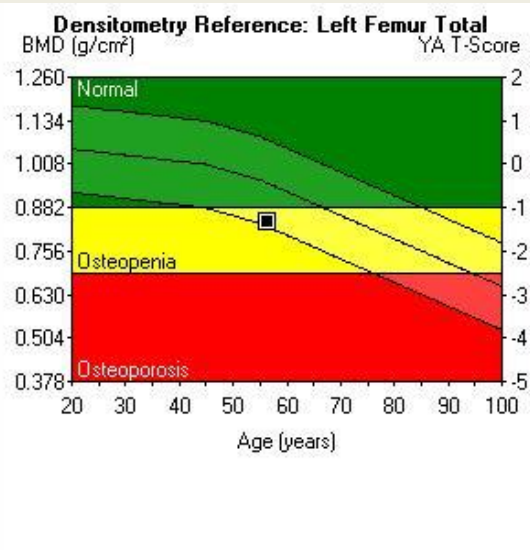
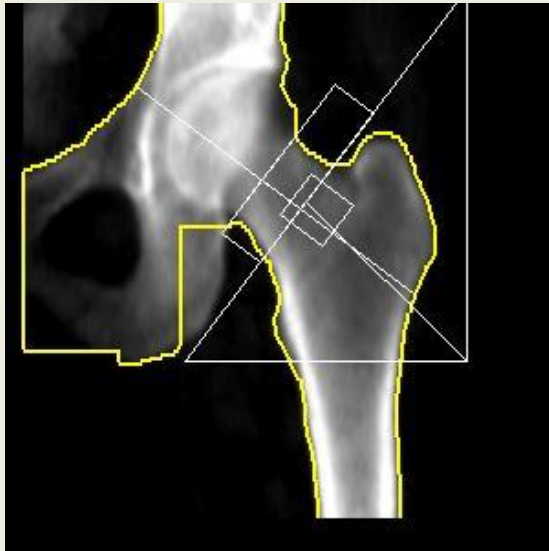
Bone markers are used to monitor effectiveness of medication on bone turnover

Declines in the levels of markers after 3-6 months of treatment may be predictive of fracture risk reduction

Diagnosis

Bone Mineral Density (BMD)

X-ray to measure calcium and other bone minerals packed into a segment of bone



Bone Density

Medical term	Measures:	Significance:
Bone mineral content (BMC)	Bone mass	May be a more accurate measure of growth
Bone mineral density (BMD)	Ratio of BMC to bone size	Indirectly measured via densitometry
Bone area	Total size of bone	Larger bone size= smaller BMD

Diagnosis: Central DXA

DXA: Dual-energy x-ray absorptiometry

The “gold standard” for diagnosis

Measures bone density at lumbar spine, total hip, and femoral neck

Does not provide information about bone strength or fracture risk

Helpful piece of information in the total fracture risk assessment

Bone quality relates not just to bone mass→ also bone microarchitecture

Crystal size/shape, brittleness, protein structure, water volume, etc.

pDXA

Peripheral DXA (pDXA)

Scan other parts of the body than the hip and spine

Forearm, heel, wrist, fingers

Can be used as a screening tool

Need to scan hip or spine with a central DXA scan in order to diagnose osteoporosis

Other scans

CT scans

Computerised tomography

Uses x-rays and a computer to take pictures of bone

Can be used to measure bone density

CT scans use higher levels of radiation than a DXA scan, thus a DXA is preferable

MRI

Used for soft tissues, not for bones

Heel ultrasounds, other ultrasounds and x-rays

Can be used for screening, but a central DXA is ultimately used for dx

Diagnosis: T-score

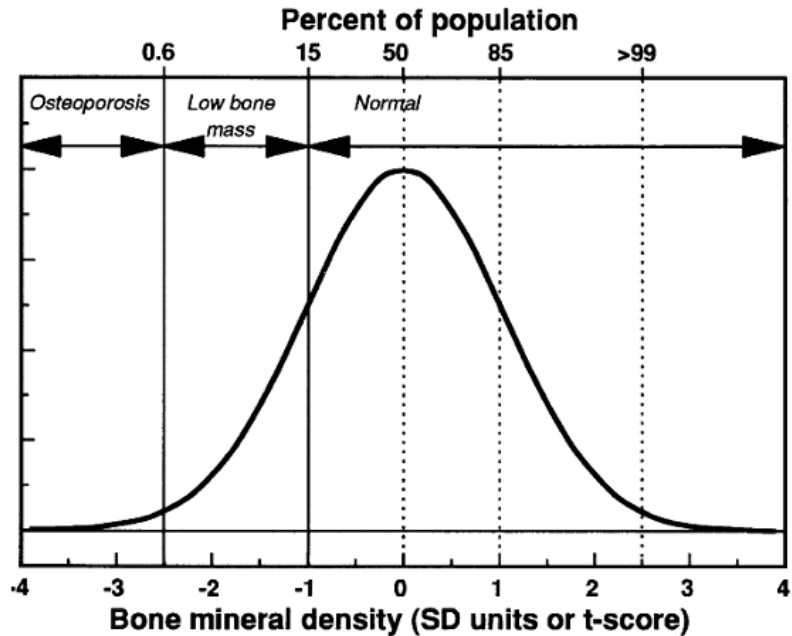


Fig. 1. Diagnostic thresholds for women based on the distribution of bone mineral density in the young healthy female population.

T-score shows the amount of bone you have compared to the ideal or peak BMD of a healthy 30-year-old of your same gender
Differences are measured in standard deviations (SDs)
More SDs below 0, the lower your BMD

T-score Definitions

WHO Definitions Based on Bone Density Levels

Level	Definition
Normal	BD within 1 SD (+1 or -1) of the young adult mean
Low bone mass	BD between 1 and 2.5 SD below the young adult mean (-1 to -2.5 SD or lower)
Osteoporosis	BD is 2.5 SD or more below the young adult mean (-2.5 SD or lower)
Severe (established) osteoporosis	BD is more than 2.5 SD below the young adult mean, and there have been one or more osteoporotic fractures

T-score vs Z-score

T-score

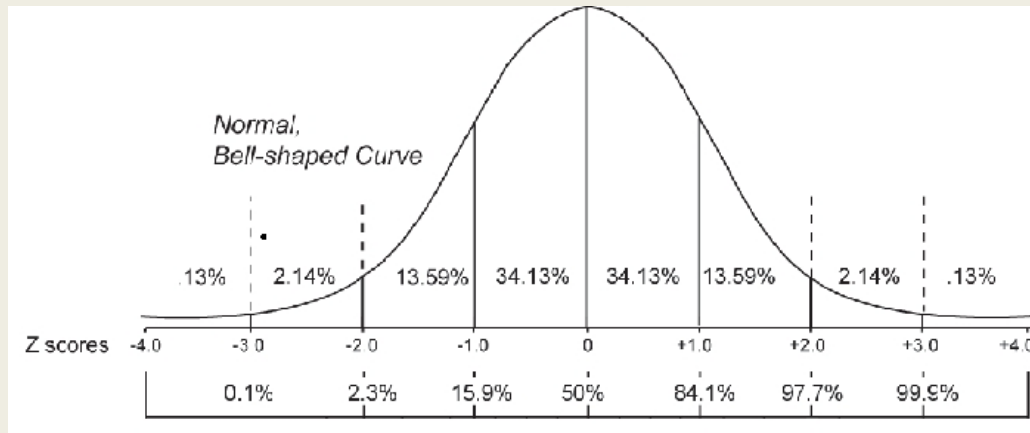
Used only for postmenopausal women and in men over age 50
Compares to healthy adult

Z-score

Used for females prior to menopause and in males younger than age 50
The number of SDs above or below what's expected for someone of your age, sex, weight, and ethnic or racial origin
Indicates something other than aging is causing abnormal bone loss
Not used for osteoporosis dx
Important in children and adolescents

Z-scores: Adults

Z-Score	Definition
Above -2.0	“Within expected range for age”
-2.0 or lower	“Below expected range for age”



Z-scores: Children

Children & adolescents

Preferred term: “*Low bone mineral content or bone mineral density for chronologic age*”

When BMC or BMD Z-scores are less than or equal to -2.0

Things that should not appear in a pediatric report:

T-scores

The terms “osteopenia” or “osteoporosis”

Osteoporosis assumes poor bone quality, which cannot be assumed in premenopausal women or men under 50 yrs

Need knowledge of clinically significant fracture history

Sometimes osteoporotic bone can be seen in young people with eating disorders

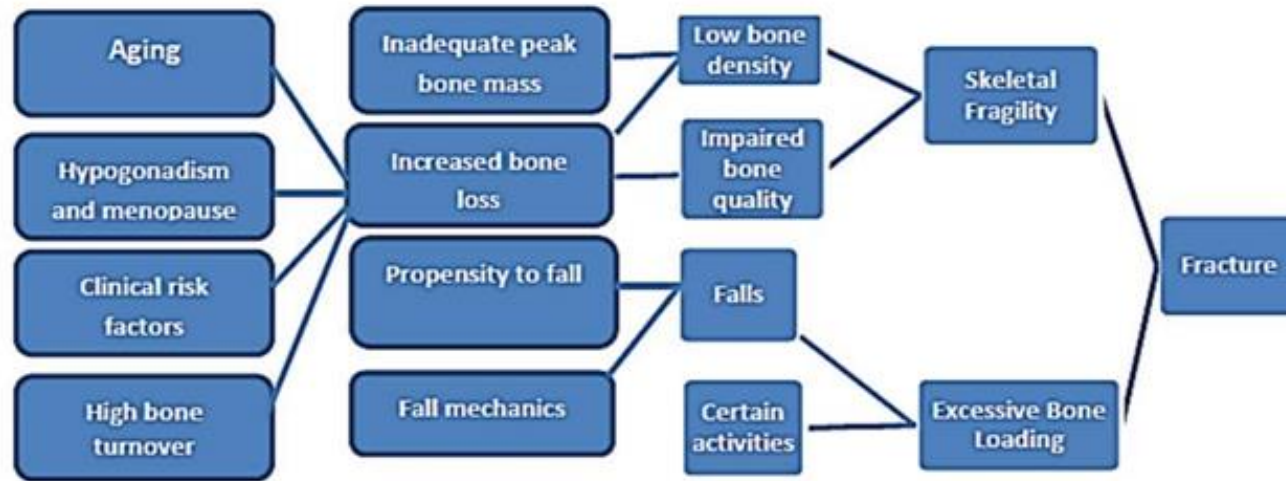
Age Span of Diagnosis

	Women	Men
Prevalence of osteoporosis:	Increases after age 50	Does not increase until 60-79 years according to Krause, some studies say 80
Osteoporotic fractures:	1 in 2 women over age 50	1 in 5 men over age 50

Looker AC et al. Osteoporosis or low bone mass at the femur neck or lumbar spine in older adults: United States, 2005-2008. Washington DC, National Center for Health Statistics; 2012.

Fracture Risk

FIGURE 2. Pathogenesis of Osteoporosis-Related Fractures



National Osteoporosis Foundation. *Clinician's Guide to Prevention and Treatment of Osteoporosis*. Washington, DC: National Osteoporosis Foundation; 2010.

Fracture Risk

Hip fractures

Chronic pain

Disability

Diminished quality of life

Premature death

Fatal complications

Pulmonary embolism

Hemorrhage

Shock

Surgical complications

FRAX

FRAX: WHO's Fracture Risk Assessment

A downloadable computer-driven questionnaire

Integrates risks associated with clinical risk factors and BMD


Algorithms predict two outputs

- 10-year probability of a hip fracture

- 10-year probability of a major osteoporotic fracture (spine, forearm, hip, or shoulder)

www.shef.ac.uk/FRAX

FRAX

Country : **UK** Name / ID : [About the risk factors](#) 

Questionnaire:

1. Age (between 40-90 years) or Date of birth
Age: Date of birth:
Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

5. Previous fracture No Yes

6. Parent fractured hip No Yes

7. Current smoking No Yes


8. Glucocorticoids No Yes

9. Rheumatoid arthritis No Yes

10. Secondary osteoporosis No Yes

11. Alcohol 3 more units per day No Yes

12. Femoral neck BMD

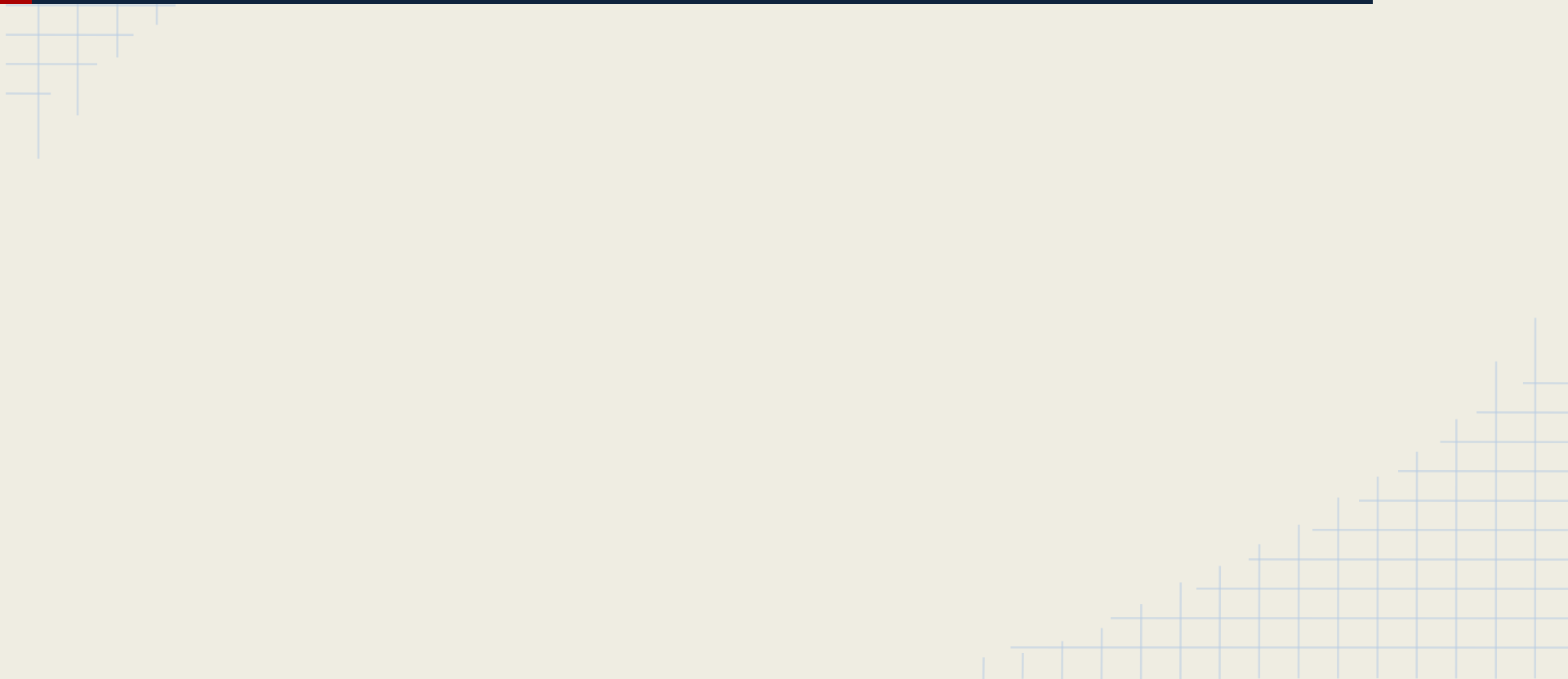
BMI 

The ten year probability of fracture (%)

without BMD

<input type="checkbox"/> Major osteoporotic	<input type="text"/>
<input type="checkbox"/> Hip fracture	<input type="text"/>

Medical Therapy



Medications

Estrogen Replacement Therapy (ERT)

Estrogen blocks the release of cytokines that promote osteoclasts from osteoblasts.

Prevention of osteoporosis

Increase bone density

Risks:

may increase risk of breast cancer, MI, stroke, pulmonary emboli, deep vein thrombosis

less risk if used within the first few years of menopause

Medications

Bisphosphonates

Block osteoclastic bone resorption

Prevents future fractures

Contraindicated:

Glomerular Filtration Rate (GFR) <30-35ml/min

Side Effects:

Dysphagia

Gastritis

Esophagitis

Jaw necrosis with long term use

Alendronate, Risedronate, Ibandronate, Zoledronic Acid

Medications

Selective Estrogen Receptor Modulators (SERMs)

Estrogen Agonists/Antagonists

Stimulate estrogen receptors in bone without stimulating receptors in the breast.

Risks:

Deep Vein Thrombosis

Hot flashes

Raloxifene

Medications

Calcitonin

Blocks PTH stimulation of osteoclasts

Decreases risk of vertebral fractures

Recommended:

Women at least 5 years postmenopausal

When alternatives are not appropriate

Side effects:

Epistaxis

Rhinitis

Allergic reactions

Small increase in risk of cancer

Medications

Teriparatide

Increases number and function of osteoblasts

Often used before bisphosphonates

Recommended:

- men and postmenopausal women

- patients with high risk of fracture from glucocorticoid therapy

Contraindicated:

- patients with high risk of skeletal malignancy

Side Effects:

- Leg cramps

- nausea

- dizziness

Medications that Increase Bone Loss

BOX 25-4

Medications That Increase Calcium Loss and Promote Risk of Osteoporosis

Aluminum-containing antacids
Corticosteroids
Cyclosporine
Heparin
Lasix and thiazide diuretics
Lithium
Methotrexate
Phenobarbital
Phenothiazine derivatives
Phenytoin (Dilantin)
Thyroid hormone
Tetracycline

Krause pg 543

Hip Fractures

Environmental Risk Factors for falls
low level lighting
obstacles on the ground
loose rugs/slippery floors
no assistance devices

Within 1 year of fracture:

~24% of patients die

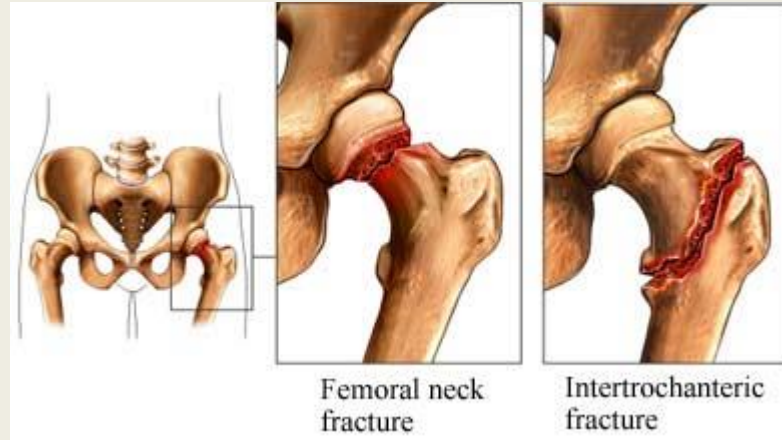
Length of Stay in hospital:

~6.2 days

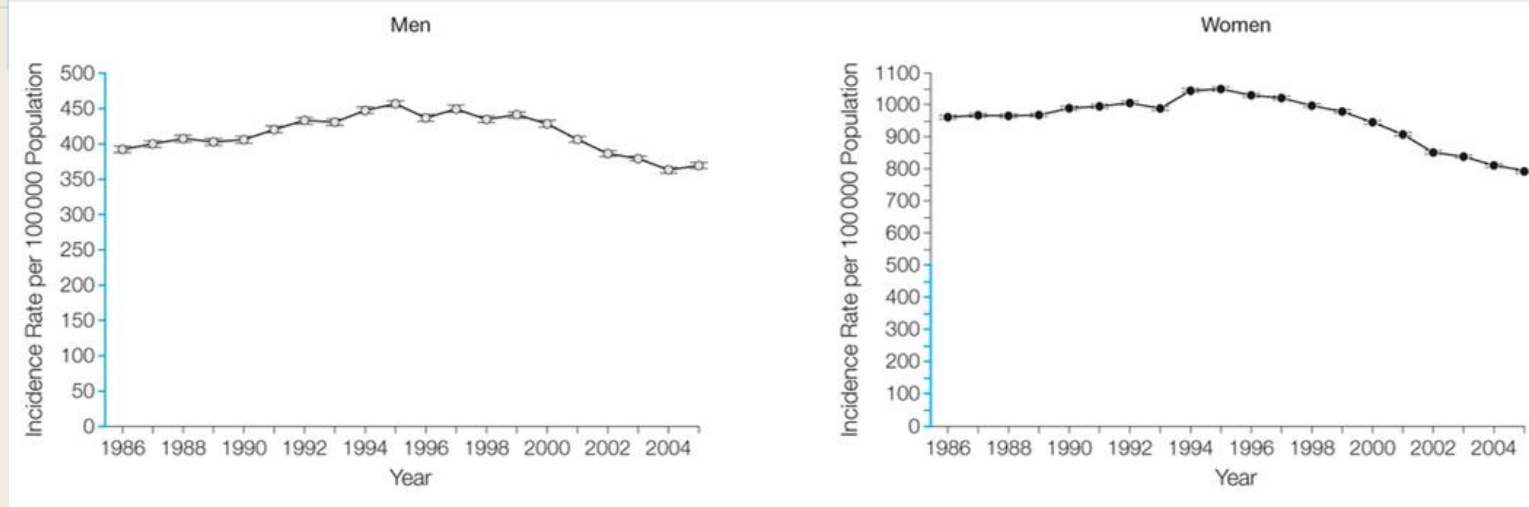
Destination of Discharge (2003-2005):

5.3% Home

52.8% Nursing facility

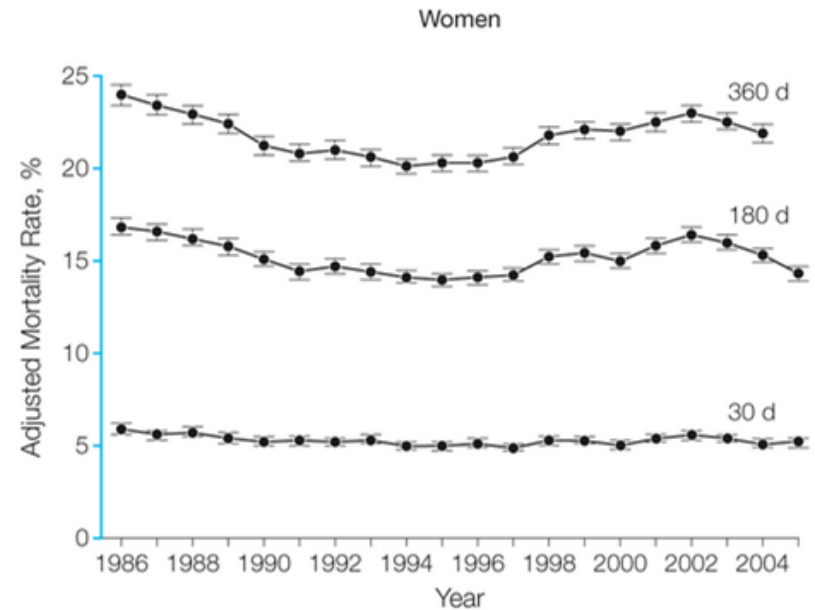
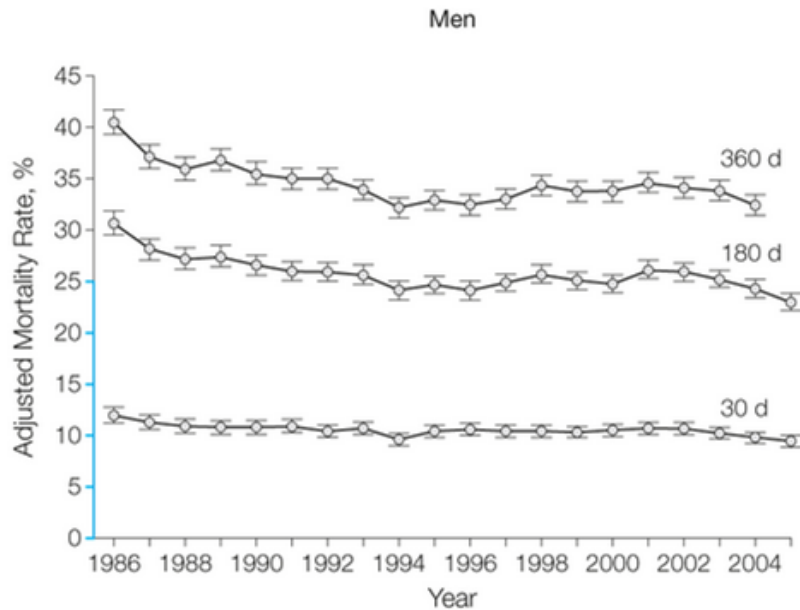


Trend in Age-Adjusted Hip Fracture Incidence for Men and Women



Brauer C, Coca-Perraillon M, Cutler DM, Rosen AB. Incidence and mortality of hip fractures in the united states. *JAMA*. 2009;302:1573-1579.

Trends in Risk-Adjusted Mortality at 30, 180, and 360 Days after Fracture



Brauer C, Coca-Perrillon M, Cutler DM, Rosen AB. Incidence and mortality of hip fractures in the united states. *JAMA*. 2009;302:1573-1579.

Fall Prevention

Adequate Vit D levels

Physical Activity

muscle strengthening

balance

Tai Chi

Home safety assessment

Decrease psychotropic medication

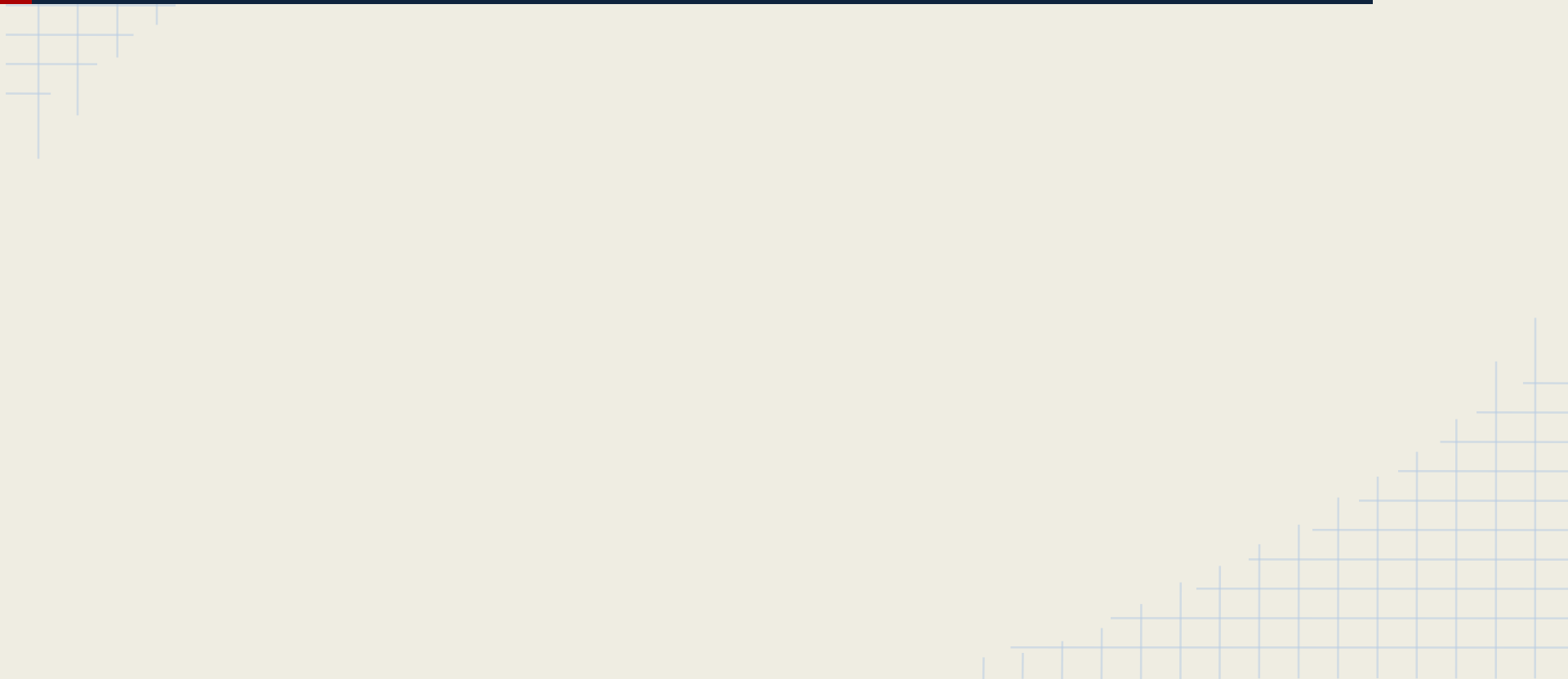


Hip Protectors

Probably reduce risk of fracture
Poor acceptance

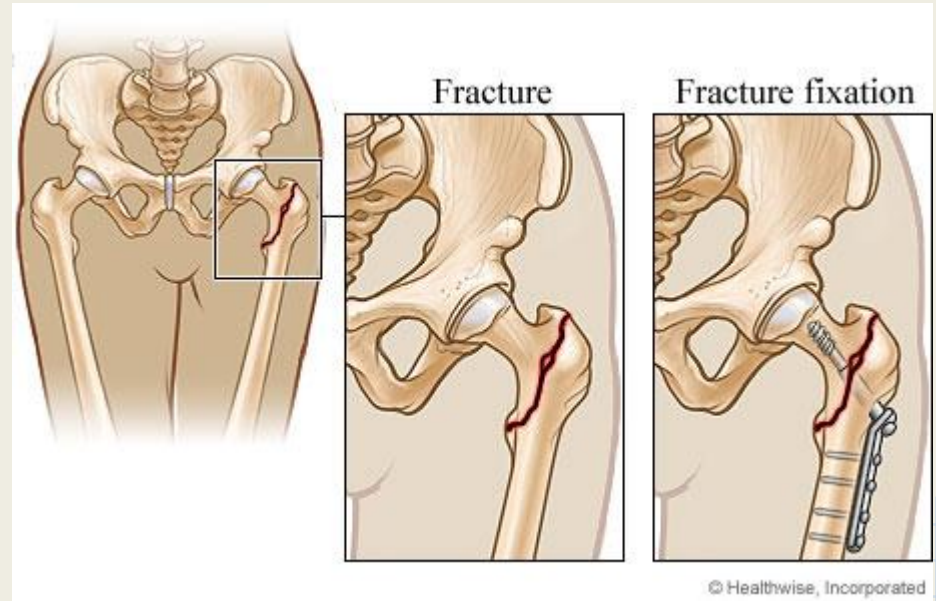


Surgery



Hip Repair (Pinning)

1. Properly align bones
2. Use screws, nails, pin, and rods to pin bone together



Hip Repair vs. Total Hip Replacement

Chammout G. Total hip replacement versus open reduction and internal fixation of displaced femoral neck fractures: A randomized long-term follow-up study. *J Bone Joint Surg.* 2012;94:1921-1928

Secondary End Points

Mortality

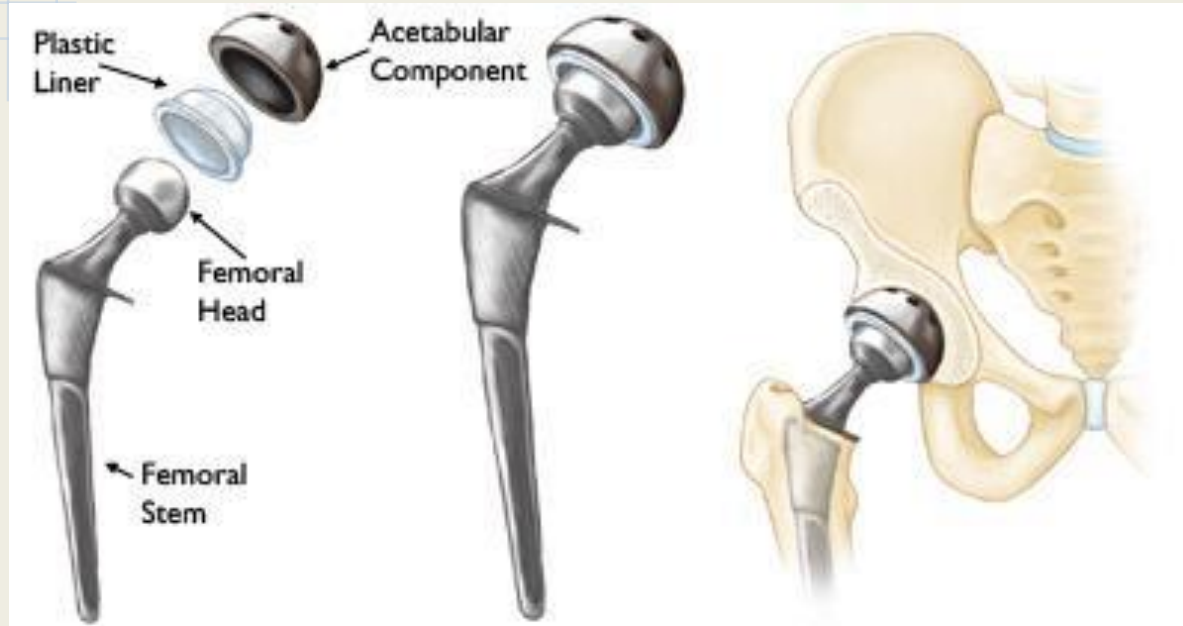
The mortality was high, regardless of treatment. At eleven and seventeen years, 25% and 13% of the patients, respectively, were still living. The mortality rate did not differ between the groups during the study period.

TABLE II Hip Complications and Reoperations up to Seventeen Years According to Allocated Treatment*

	Total Hip Replacement (N = 43)	Internal Fixation (N = 57)
Hip complications		
Dislocation†	9	1
Nonunion/mechanical failure	0	14
Osteonecrosis	0	17
Deep infection	0	2
Lateral pain	1	12
Aseptic loosening	2	1
Periprosthetic fracture	2	0
Total number of hip complications	14	47
Number of hips with any complication‡	11 (26%)	37 (65%)
Hip reoperations		
Closed reduction†	9	1
Screw removal	0	14
Excision arthroplasty (Girdlestone)	0	2
Hip arthroplasty as a secondary or tertiary procedure	0	20
Open reduction and internal fixation of periprosthetic fracture	2	0
Revision of total hip replacement due to aseptic loosening	2	1
Surgical debridement due to deep infection	0	2
Total number of hip reoperations	13	40
Number of hips with any major reoperation§	4 (9%)	22 (39%)
Number of hips with any reoperation#	10 (23%)	30 (53%)

*All complications and reoperations are counted, so more than one event may apply for each hip. The values are given as the number of hips. †In the total hip replacement group, one hip dislocated four times and five hips dislocated once. ‡RR = 0.39 (95% CI, 0.23 to 0.68; p < 0.001). §RR = 0.24 (95% CI, 0.09 to 0.64; p = 0.001). #RR = 0.44 (95% CI, 0.24 to 0.80; p = 0.003).

Total Hip Replacement



Cemented vs Uncemented

- Cemented is usually used for patients with osteoporosis.
- Uncemented requires a longer recovery time.

<https://www.youtube.com/watch?v=kXPc8qtJzcoC>

Minimally Invasive THR

Faster recovery
Shorter hospital stay



Minimally Invasive
Incision

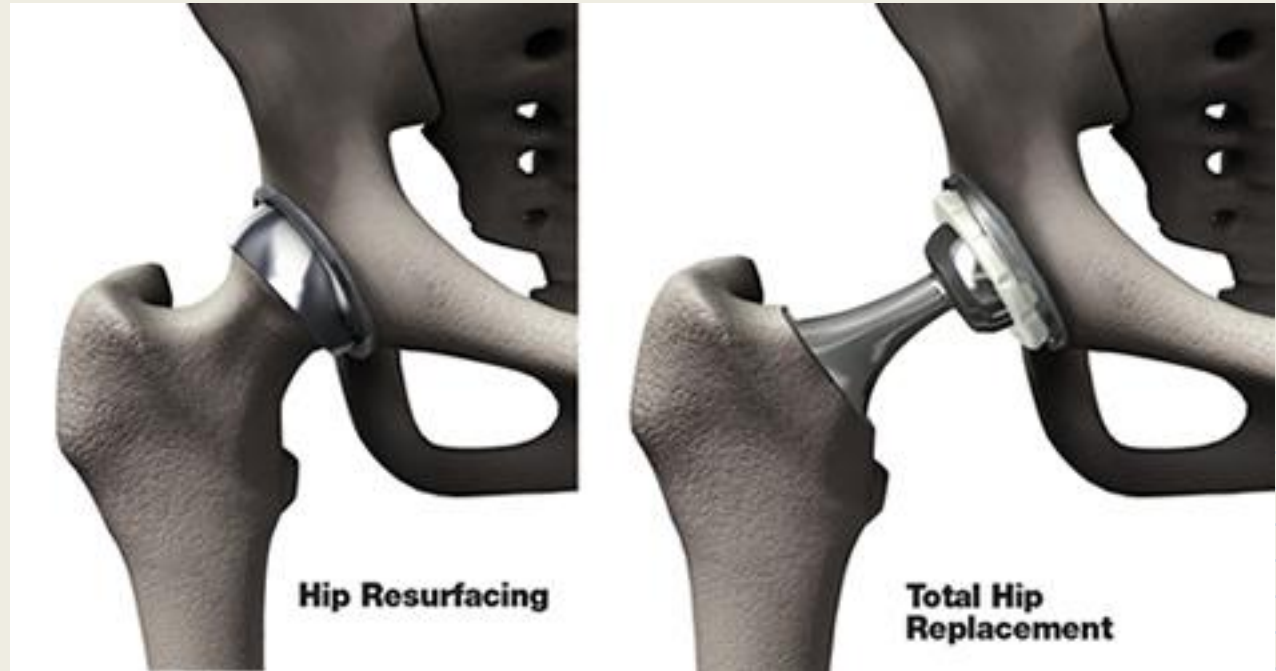


Traditional Incision

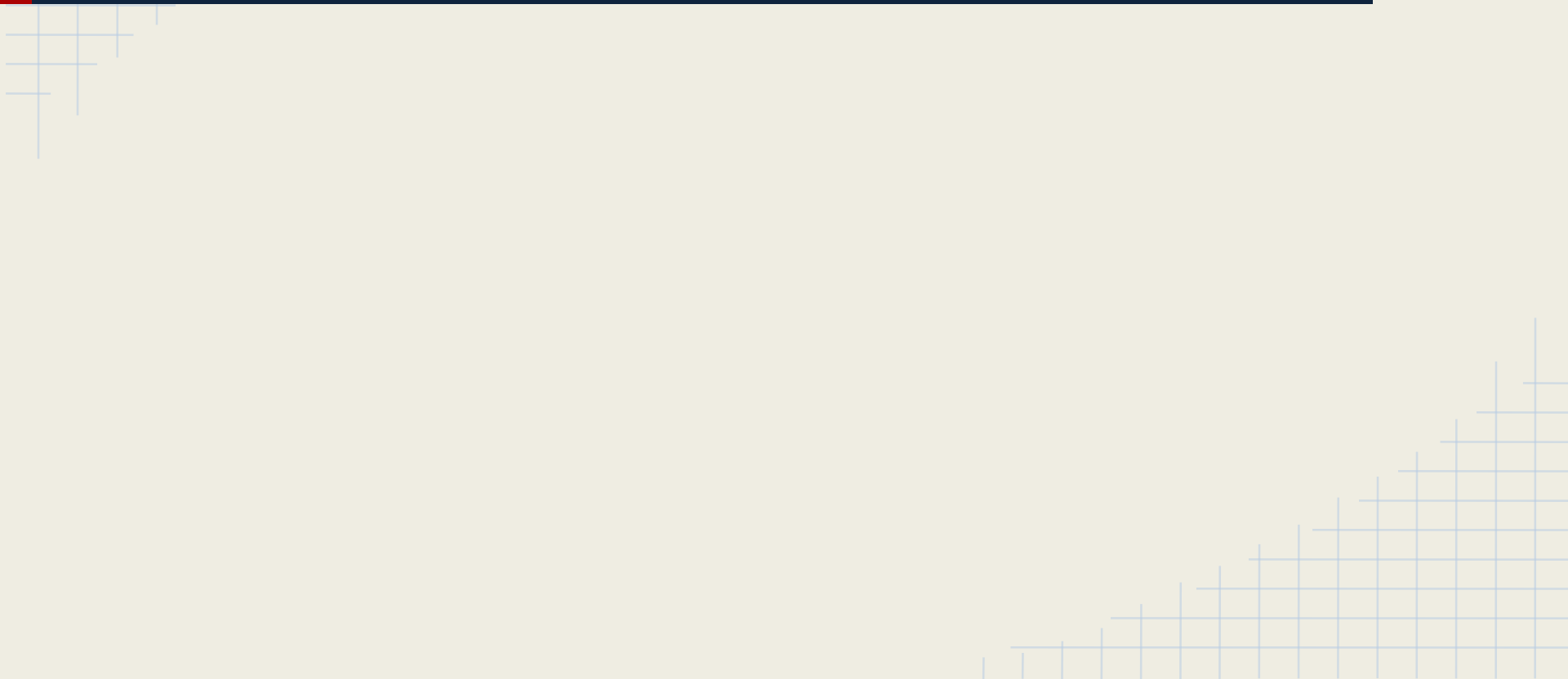
Hip Resurfacing

Cap in socket
Metal cap over ball

Not recommended for
patients with poor
bone quality (e.g.
osteoporosis)



MNT



Nutritional Assessment

Anthropometrics

Age, gender, height, weight, BMI

Biochemical markers

Clinical

Fractures

Appearance of spine

DXA

FRAX

Medications

Dietary

24 hour recall

Food frequency
questionnaire

Smoking

Alcohol

History

Family members

Nutritional Diagnosis

P: Inadequate calcium intake

E: related to inadequate nutrition knowledge

S: As evidenced by reported food intake and osteoporotic fracture.

P: Increased protein-energy needs

E: Related to hypermetabolism

S: As evidenced by hip fracture and total hip replacement surgery

Nutritional Intervention

Adequate calcium and vitamin D

Adequate calories, protein, and energy

Avoid smoking

Moderate or no alcohol intake

Calcium & Vit D

IOM Recommendations	Calcium	Vitamin D
Women 51+ yrs	1200 mg/day	800-1000 IU/day
Men 50-70yrs	1000 mg/day	800-1000 IU/day
Men 71+ yrs	1200 mg/day	800-1000 IU/day
Supplement if: <ul style="list-style-type: none">• Diet is inadequate.• Blood serum 25-hydroxy vit D <30 ng/dL		

Vitamin K

Increases bone mineral density

Decreases risk of fractures

Osteocalcin carboxylation

Vit k from diet alone may not be enough

Elderly consume less green leafy vegetables

High Calcium Foods

Dairy:

yogurt
milk
cheese



Fish:

canned sardines
canned salmon (with bones)



Fortified Foods:

orange juice
cereal



Sources of Vit D

Sunlight

Decreased ability of skin to make vit D with:

Age

Darker skin tone

Northern latitudes

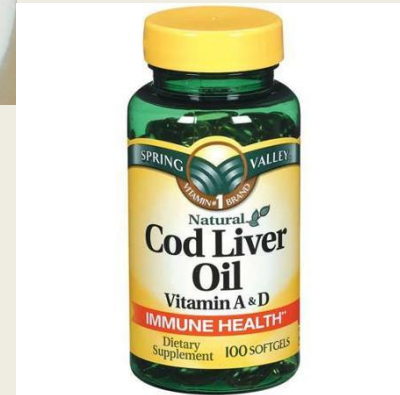
Foods:

Egg yolks

Fatty fish

Cod liver oil

Mushrooms



Prognosis

Future fractures can be prevented with medication.
Fractures, especially of the hip, can be disabling.

References

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