

Smjernice u liječenju osteoporoze

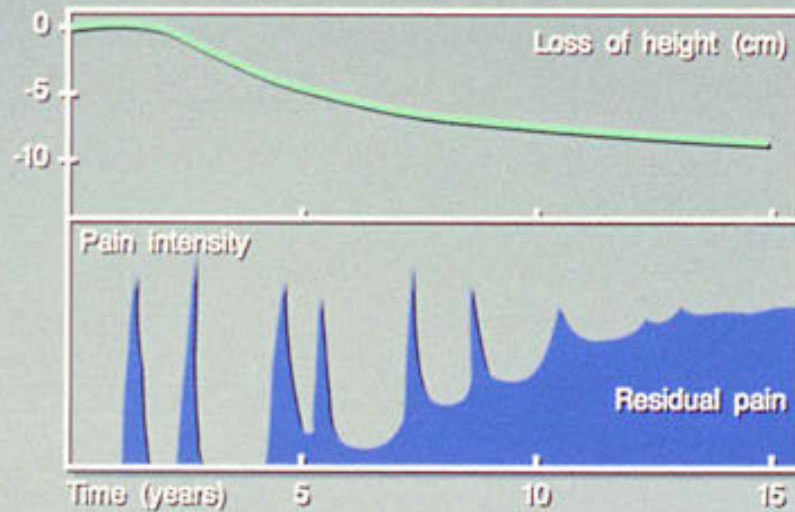
10. hrvatski kongres o ginekološkoj endokrinologiji , humanoj
reprodukciji i menopauzi

Prof dr Mirko Koršić FRCP

Hotel Neptun, Brijuni

10 – 13.09. 2015

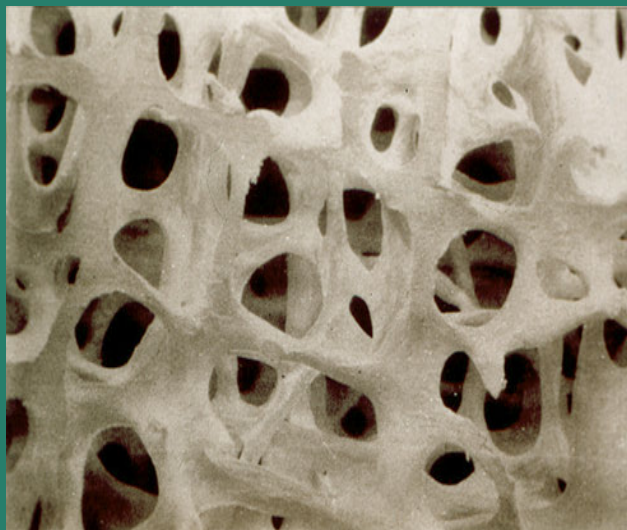
Osteoporosis clinical picture



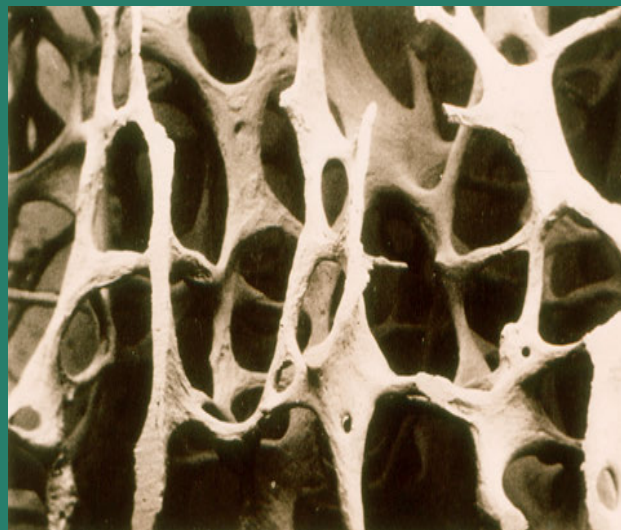
Definicija osteoporoze

Osteoporoza je bolest skeletnog sustava, koju karakterizira smanjena čvrstoća koštanog tkiva i povećana sklonost prijelomima. Čvrstoća kosti je rezultata skupnog djelovanja gustoće koštanog minerala i kakvoće koštanog tkiva.

NIH Consensus Conference 2001



Normalna kost



Osteoporoza

Evolicija dijagnoze osteoporozе

Pre-denzitometrijsko razdoblje (1940-1980 g.):

Fx i/ili rdg / stanjeni korteks, prozirnost kostiju

Denzitometrija (1980 do danas):

DEXA: ls kralješnica , vrat bedrene kosti

BMD T vrijednost >2,5

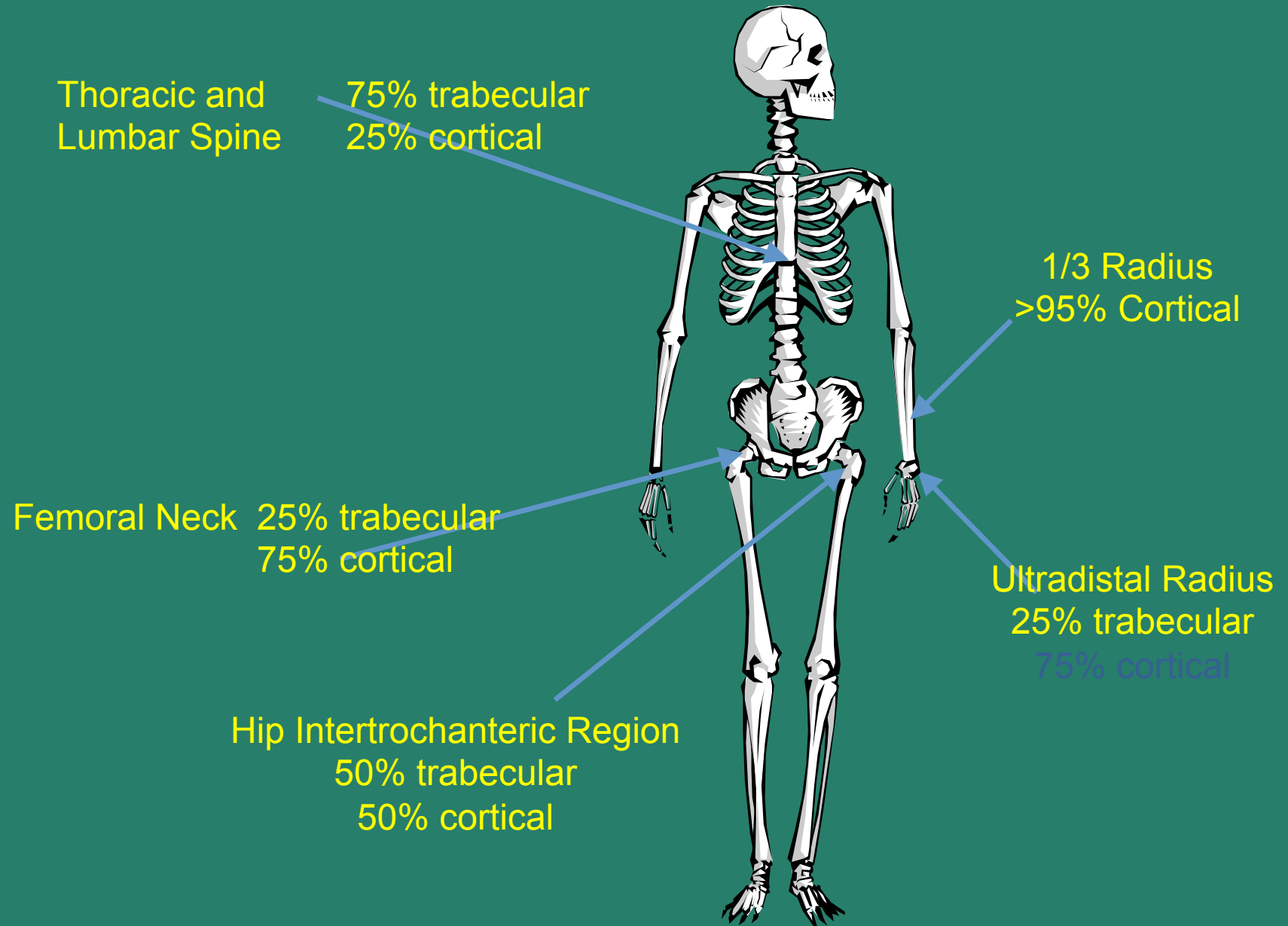
Predviđanje rizika (2000 do danas)

Procjena apsolutnog rizika glavnih osteoporotičkih Fx

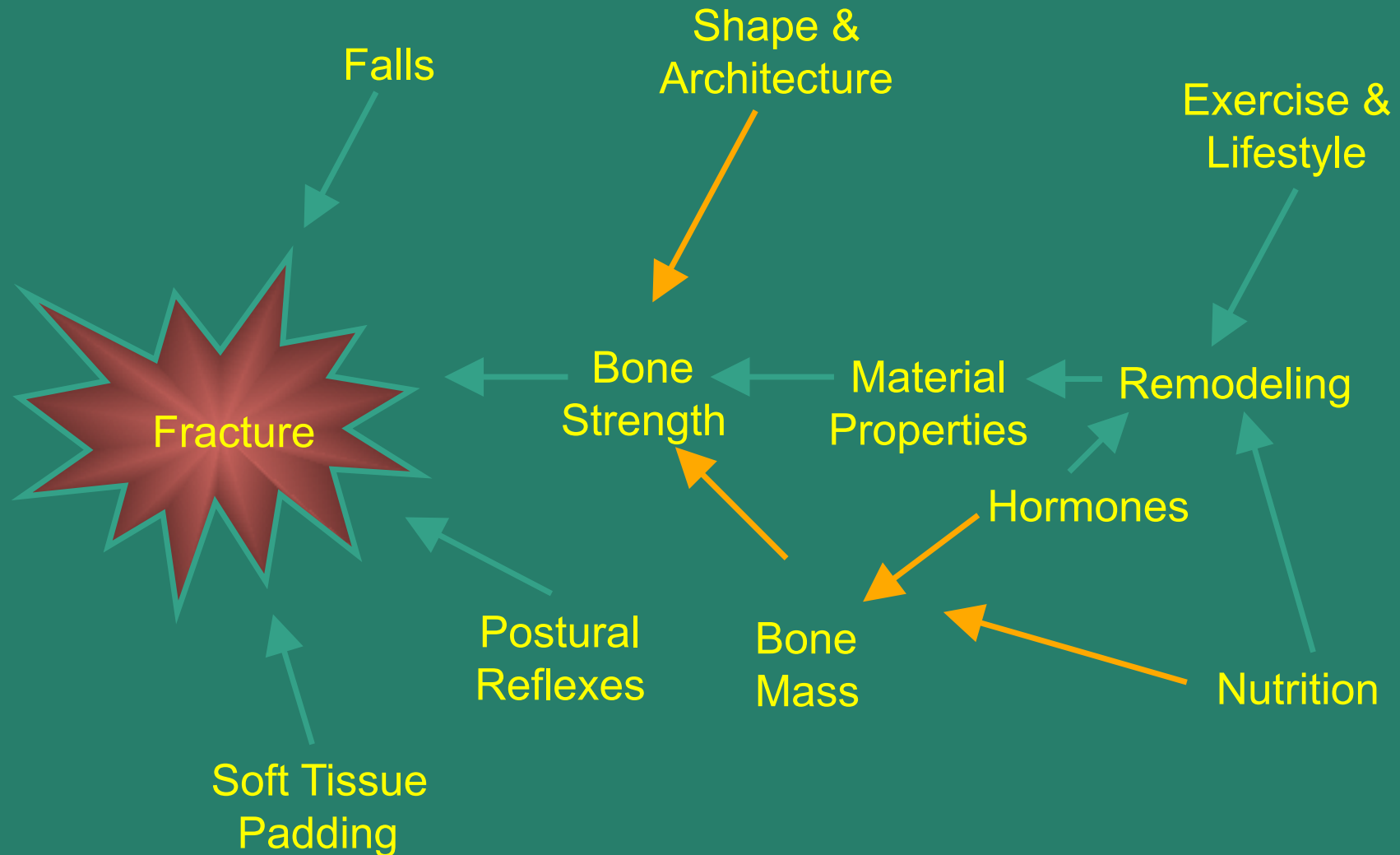
Upotreba Fracture Assessment Tool FRAX

Upotreba ostalih modela npr. Garvan i Q Fracture

Distribution of Cortical and Trabecular Bone



Factors Leading to Osteoporotic Fracture: Role of Bone Remodeling



Osteoporozna: Veličina problema

Visoka prevalencija – pogađa 200 milijuna žena širom svijeta¹

1/3 žena starosne dobi od 60 –70 godina

2/3 žena starosne dobi od 80 ili više godina

Oko 20-25% žena iznad 50 godina ima jedan ili više prijeloma kralježaka²

SAD: 25%³

Australija: 20%⁴

Zapadna Europa: 19%⁵

Danska: 21%⁶

Skandinavija: 26%⁵

1. International Osteoporosis Foundation

2. Melton LJ 3rd et al. *Spine* 1997;22:2S-11

3. Ettinger B et al., *J Bone Miner Res* 1992;7:449-56

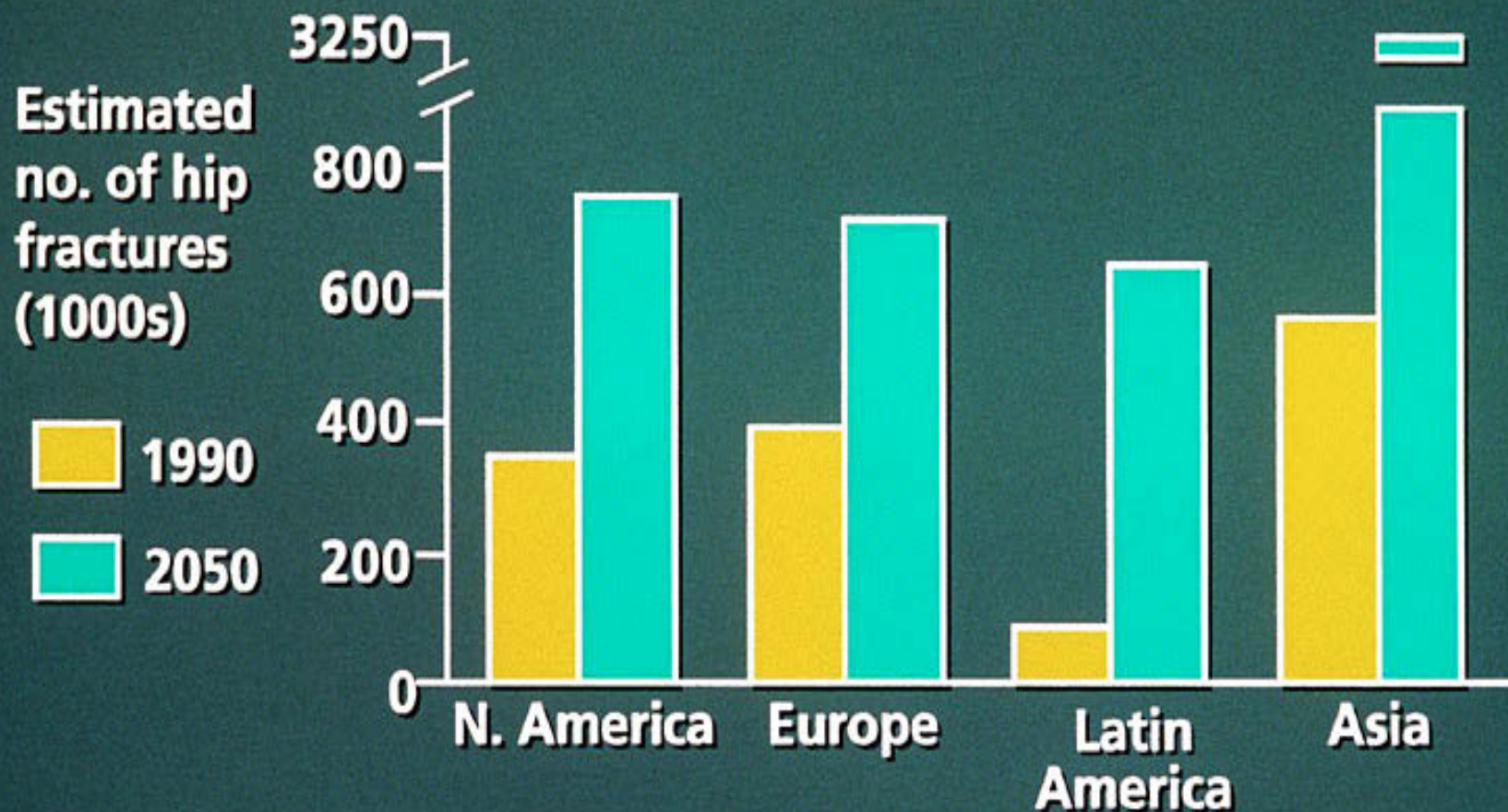
4. Jones G et al., *Osteoporos Int* 1996;6:233-9

5. O'Neill et al., *J Bone Miner Res* 1996;11:1010-8

6. Jensen GF et al., *Clin Orthop* 1982;166:75-81



Projected burden of osteoporotic hip fractures worldwide

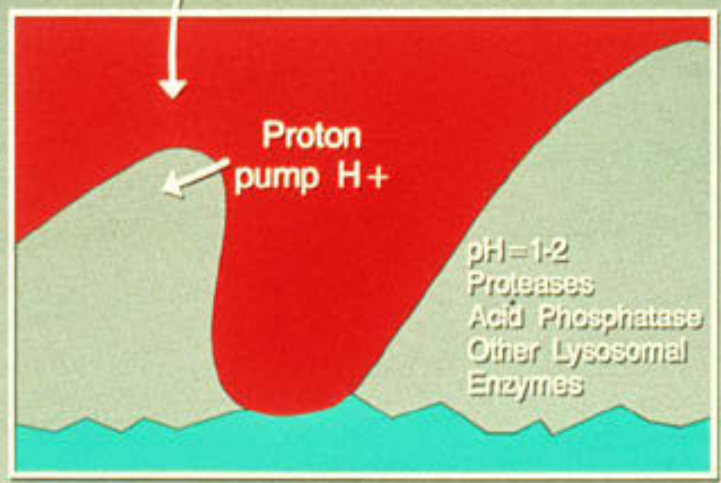
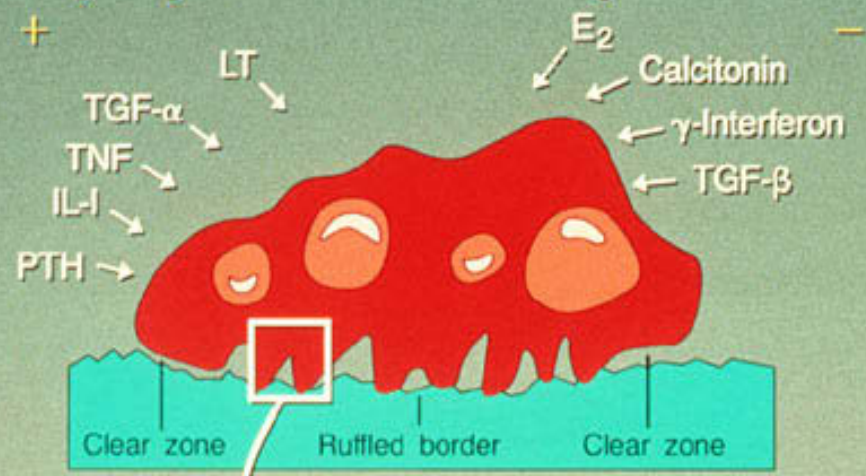


Total no. of hip fractures: 1990 = 1.66 million; 2050 = 6.26 million

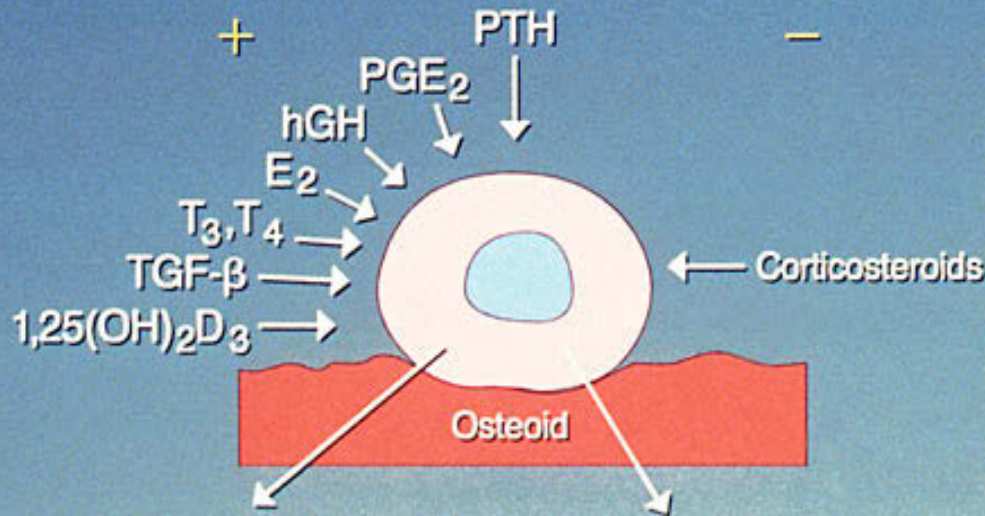
Adapted from Cooper C, Campion G, Melton LJ *Osteoporos Int* 2:285-289, 1992

The osteoclast

Syncytium with multiple nuclei



The osteoblast

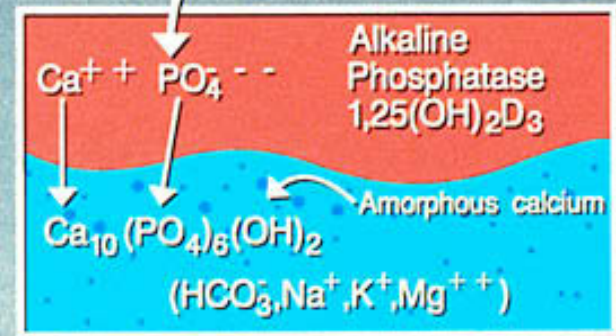
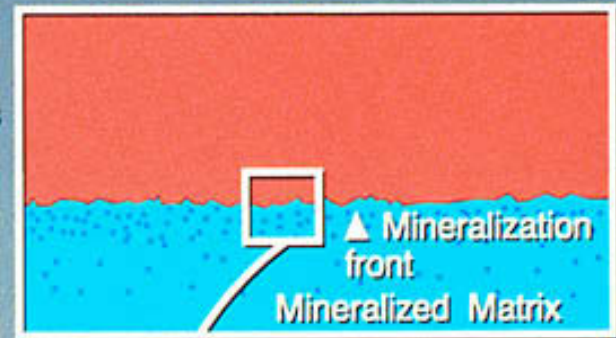


Enzymes

Alkaline phosphatase
 Collagenase
 Plasminogen activator

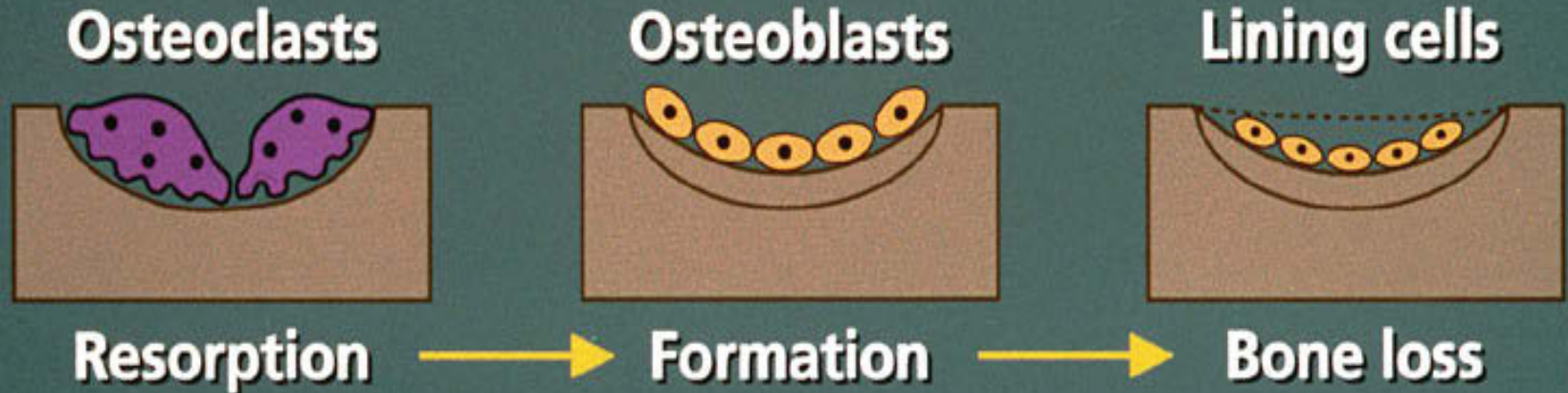
Matrix Constituents

Matrix proteins
 BGP, Osteonectin
 Collagen
 Glyco-proteins





Bone turnover in a remodeling unit in adults



Trabecular bone **20% of the skeletal mass**
80% of the turnover

Cortical bone **80% of the skeletal mass**
20% of the turnover



Abnormalities in osteoporosis

**Resorbed cavity
too large**

**Newly formed packet
of bone too small**

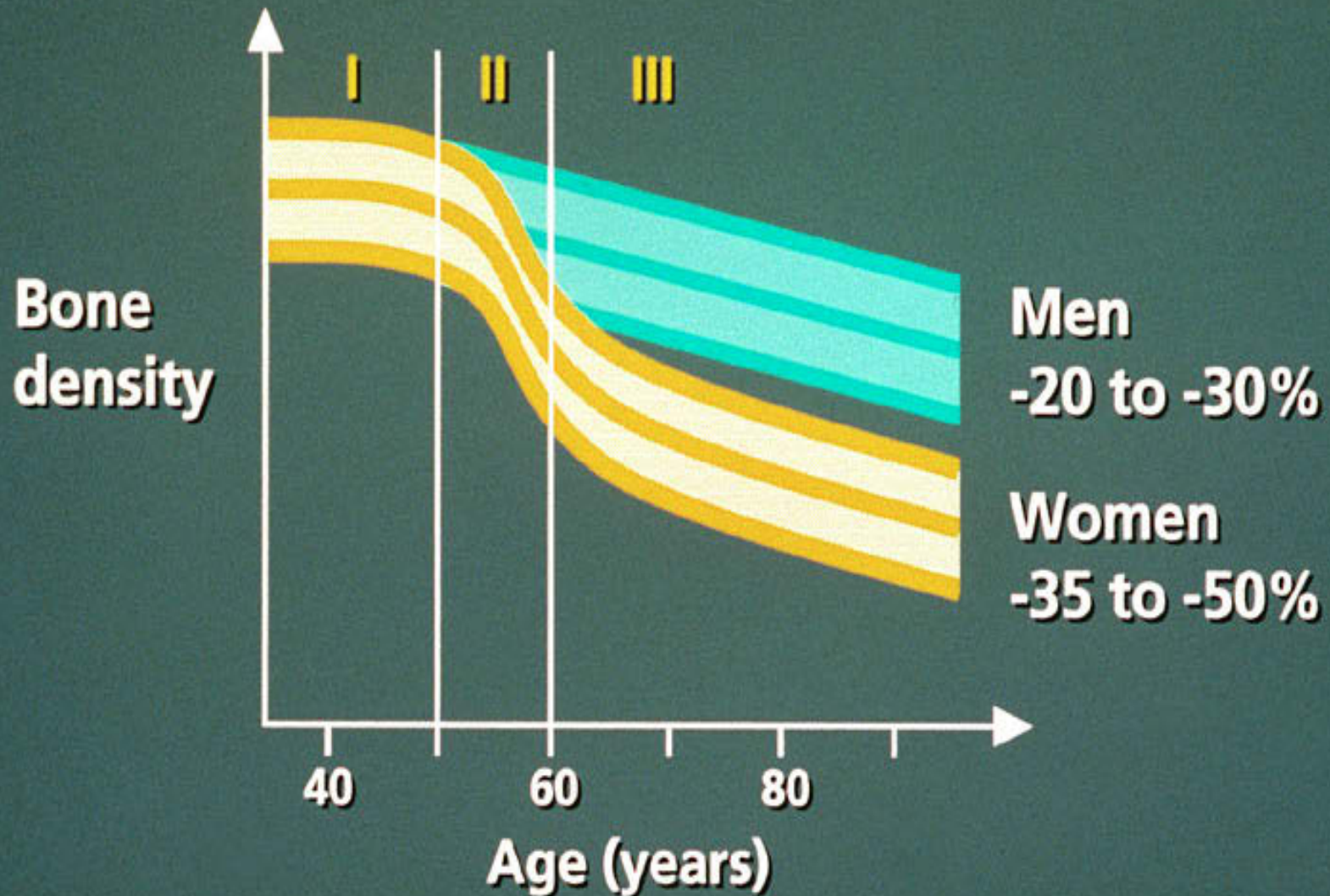
**FORMATION DOES NOT
MATCH RESORPTION**

**INCREASED NUMBER OF
REMODELING UNITS**

INCREASED BONE LOSS

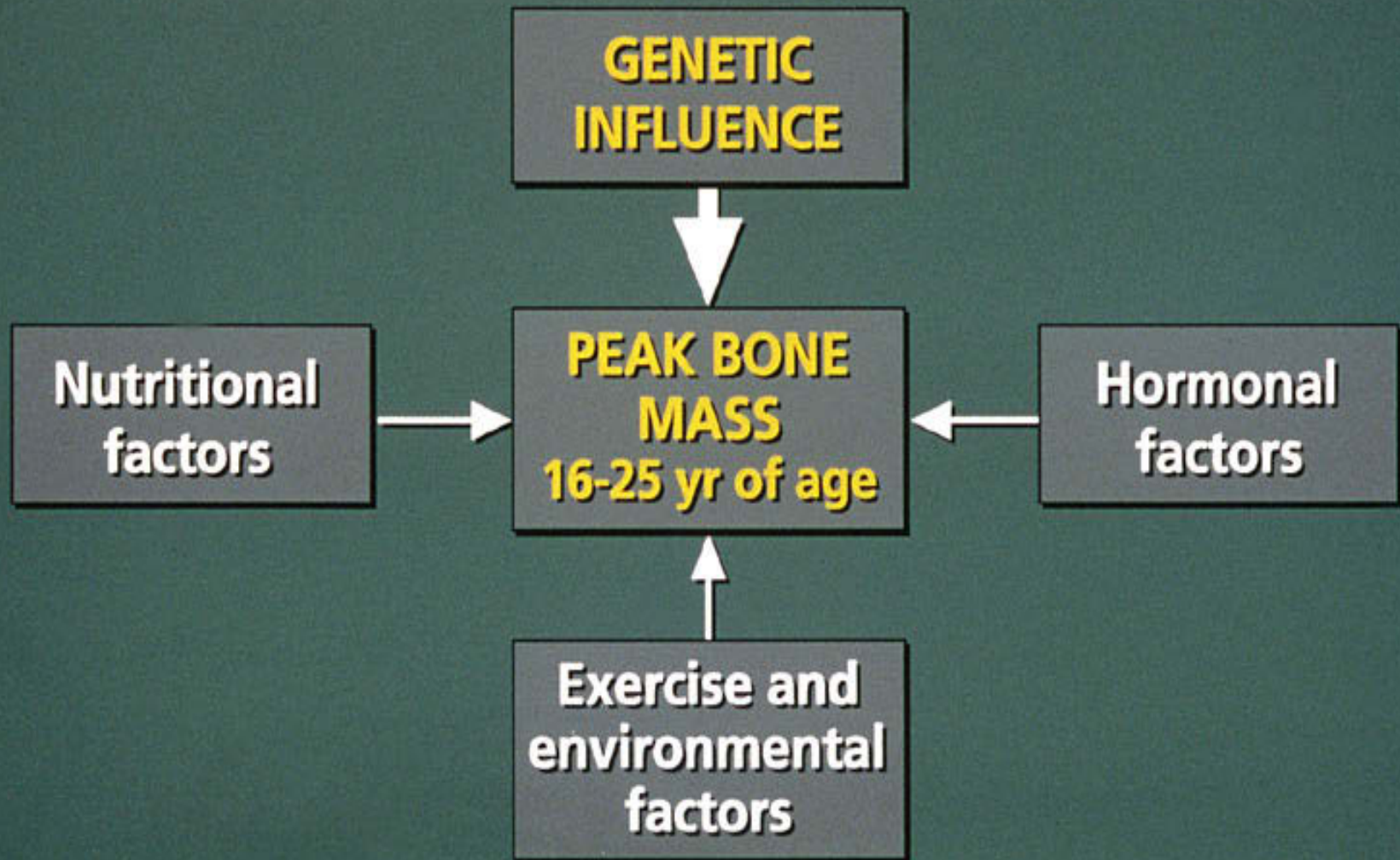


Bone loss during adult life



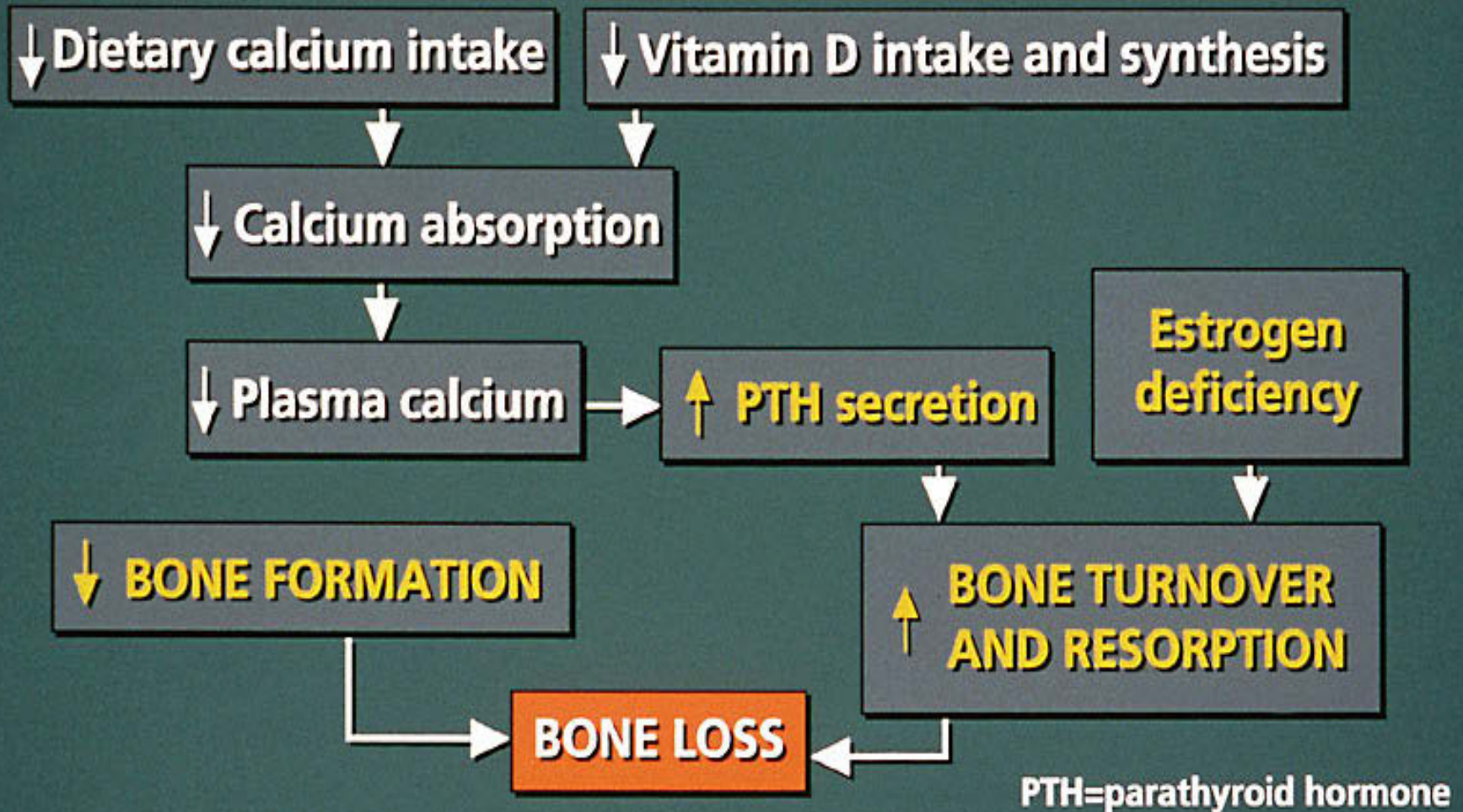


Determinants of peak bone mass



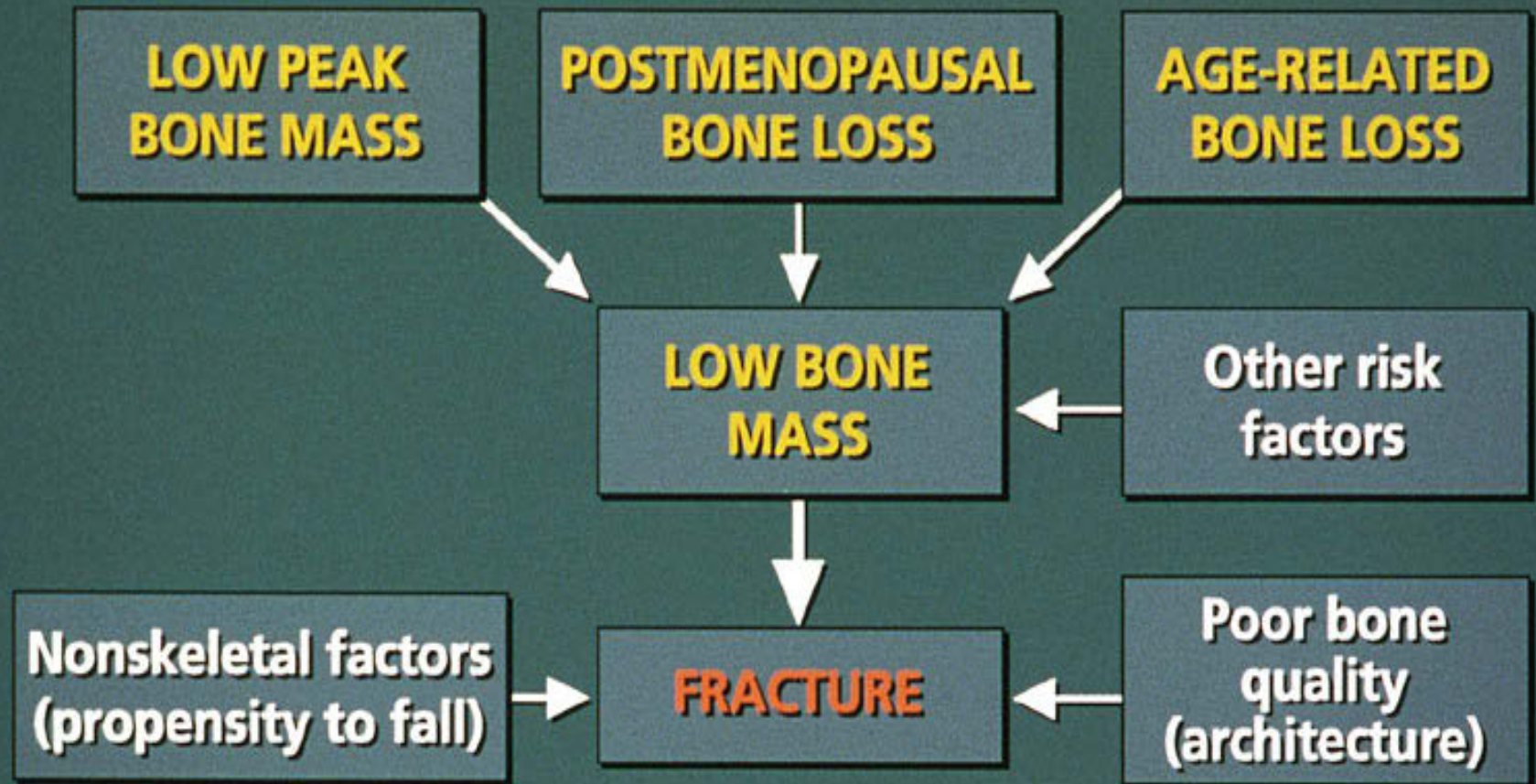


Age-related bone loss





Pathogenesis of osteoporotic fracture



Osteoporozna - dif. dijagnoza

Uobičajene pretrage:

- Krvna slika
- Jetreni testovi
- Ca, P (krv)
- T3 ,T4, TSH

Ponekad potrebne pretrage :

- Lat. snimka torakalne i lumbalne kralježnice
- Bence-Jones protein -Elektroforeza proteina
- 25OHD , Paratireoidni hormon ,
- Endomizijska/transglutamiza protutijela

Muškarci:

- Testosteron, Gonadotropini ,Prolaktin ,Kortizol/24h urin, Dex test.

Ciljevi prevencije/liječenj op

- Smanjiti rizik Fx
- Prepoznati osobe s povećanim rizikom za Fx
- Ukazati na važnost rizičnih čimbenika
- Savjet o prirodi bolesti
- Poticati zdrav stil života
- Primjena lijekova

Osteoporozna – rizični čimbenici

Neovisni o BMD	Ovisni o BMD
Dob	Neliječeni hipogonadizam
Raniji prijelom	Malapsorpcija
Prijelom kuka(majka)	Endokrine bolesti
Gukokortikoidi	Kronična bubrežna bolest
Alkohol > 3 jed/dan	Kronična jetrena bolest
Reumatoidni artritis	Kronična opstruktivna bolest pluća
Indeks tjelesne mase <19 kg/m ²	Neaktivnost
Pad: slabi vid, neuro-mišićna slabost kognitivne smetnje , sedativi, trankvilizatori Okoliš: tlo, tepisi , žice	Lijekovi : inhibitori aromataze , anti- androgena terapija, analozi Gn-RH, Inhibitori protonske pumpe, SSRI,

Osteporoza

prospektivne studije - FRAX

EVOS (European Vertebral Osteoporsis Study)

Dubbo osteoporosis study (Australia)

Canadian Multicentre Osteoporosis Study (Canada)

Rochester study (USA)

Rotterdam (Netherland)

Sheffield (UK)

Kuopio (Finland)

OFELY (L'os des femmes de Lyon)

Cohort Lyon multicentric EPIDOS (Epidemiologie de l'osteoporse)

Hiroshima (Japan)

Gothenburg 1 (Sweden)

Gotnenburg 2 (Sweden)

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **Croatia**

Name/ID:

[About the risk factors](#)

Questionnaire:

1. Age (between 40 and 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 or more units/day No Yes

12. Femoral neck BMD (g/cm²)

Select BMD



Weight Conversion

Pounds kg

Height Conversion

Inches cm

00000965

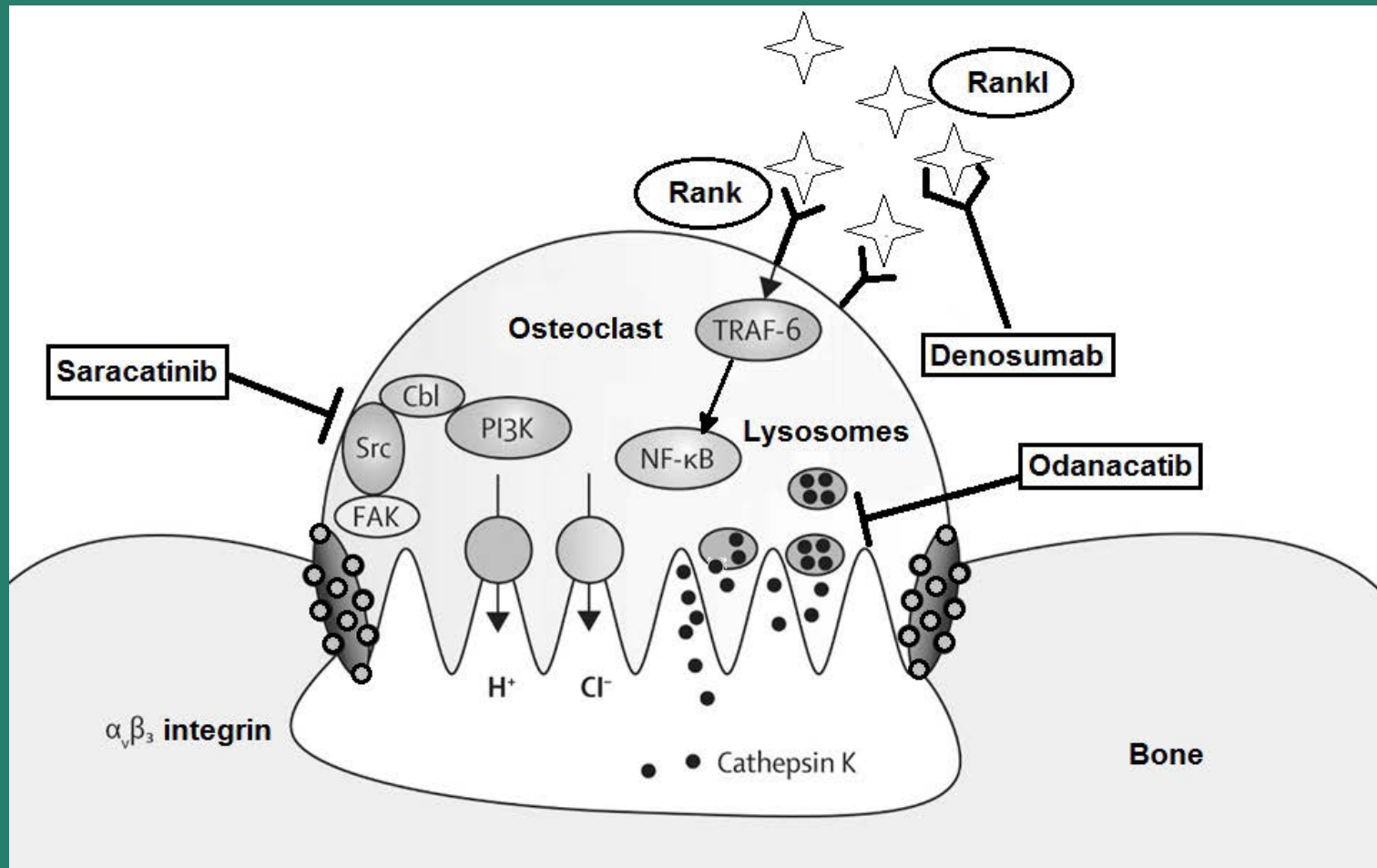
Individuals with fracture risk assessed since 1st June 2011

Osteoporozna – liječenje

- Vitamin D i kalcij
- Tjelesna aktivnost
- Prestanak pušenja, ne konzumirati alkohol
- Lijekovi

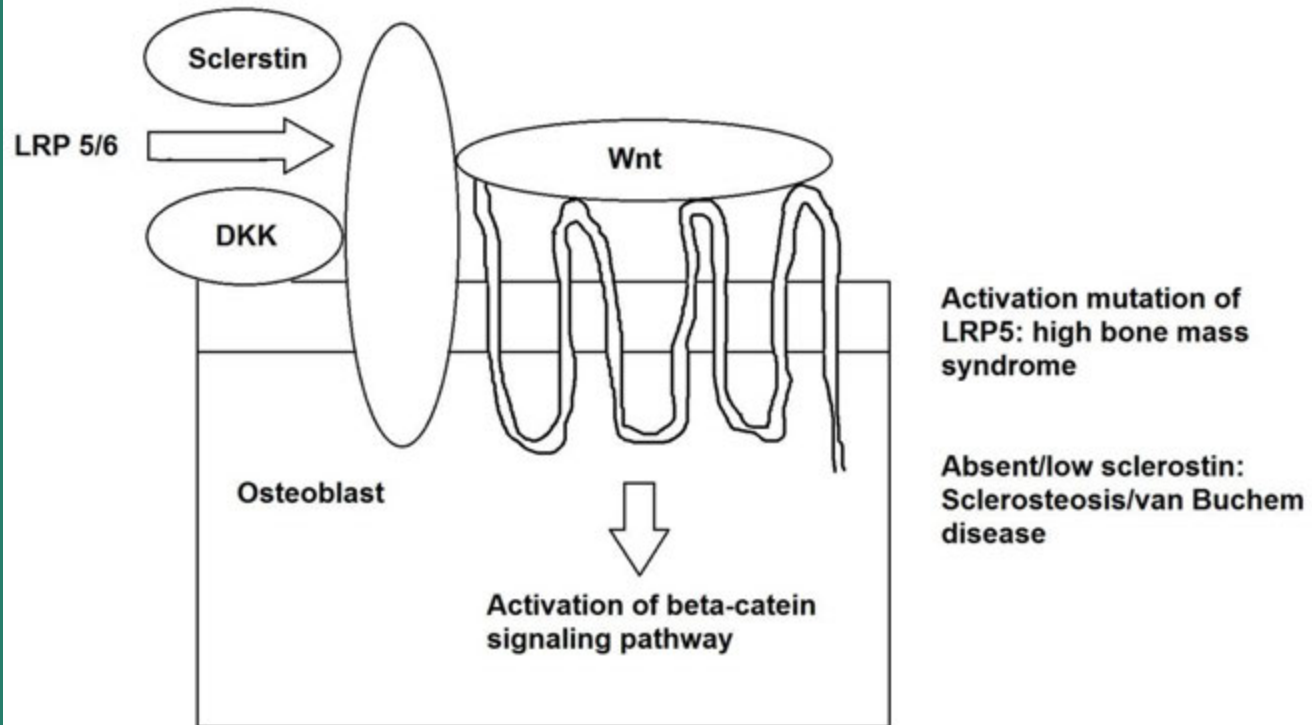
Rezultat: redukcija prijeloma kralješaka
30-70% nakon 3- 5 godine liječenja

Mehanizmi djelovanja lijekova

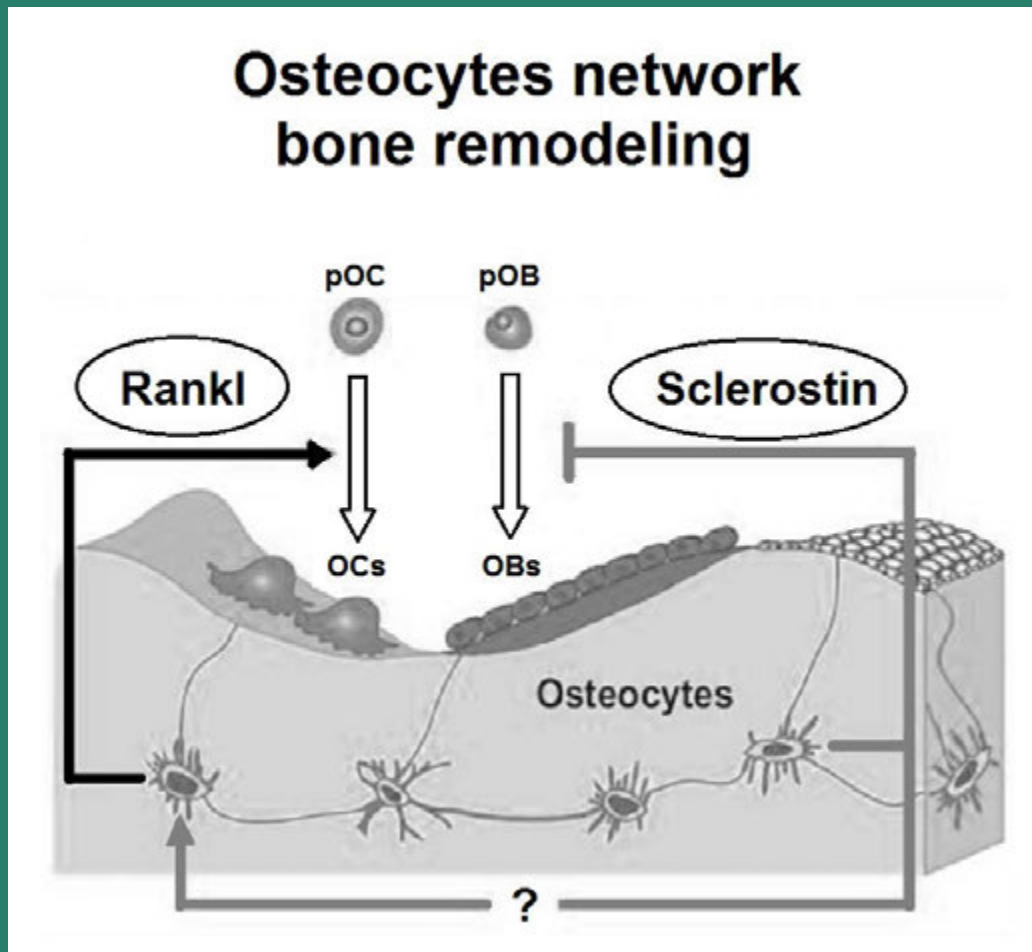


Wnt sig

The Wnt Signaling Pathway



Mreža osteocita koštana pregradnja



Osteoporoz

Redukcija rizika prijeloma – klinička istraživanja

lijek	vertebra	femur	non-vert.	doza/ put primjene
antiresorptivi				
bisfosfonati				
alendronat	+	+	+	oralno/ tjedno
risedronat	+	+	+	oralno/ tjedno ; mjesečno
ibandronat	+			oralno/mjesečno iv./ kvartalno
zoledronska kis	+	+	+	iv./ 1 x godišnje
raloxifen	+			oralno/dnevno
denozumab	+	+	+	sc./ 2 x godišnje
anabolici				
teriparatid	+		+	sc./ dnevno

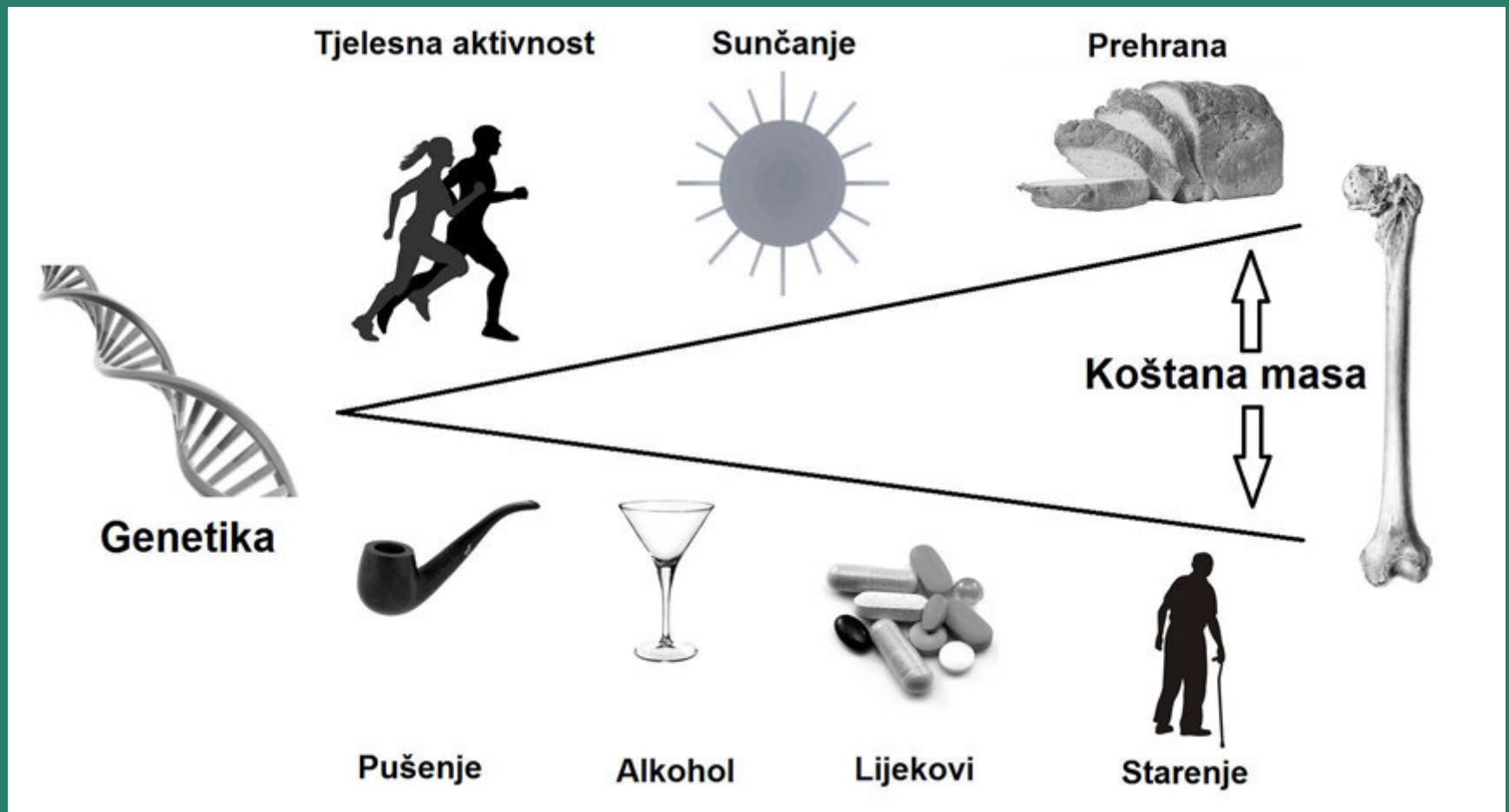
Cijani pristup liječenju osteoporozе

Klinički scenario	Izbor lijeka	Komentar
Primarna prevencija/ liječene PM	alendronat risendronat zoleidronska kis	klinički dokazi:prevencija Fx : vertebra., non-vert, vrat femura
Multiple kompresivne frakture krakalješnice (Vfx)	teriparatid bisfosfonati raloxifen denozumab	teriparatid signif smanjuje rizik nove Vfx (umjereni/jaki stupanj)
Osteoporozа (OP) i kronična bubrežna insuficijecija (KBZ) s eGFR 15-30 ml/min	denozumab	eliminacija nije ovisna o bubrežnom klirensu
OP i GI anomalije barijatriska kir. , nepodošenje bisfosfonata	zoledronska kis. denozumab teriparatid	zoledronska kis i denozumab/ parenteralno; teriparatid /nema GI nuspojava

Ciljani pristup liječenju osteoporoze

Klinički scenario	Izbor lijeka	Komentar
Postmenopauza/↑rizik Fx vrata femura	bisfosfonati ; denozumab	Dokazana prevencija Fx vrat femura
HNL godinama , ↑ rizik Fx	razmotriti prekid HNL-a; bisfosfonati, denoumab	WHI:↑ rizik - koronarna bolest, plućni embolizam, ca dojke
Kratko u postmenopauzi: ↓BMD ↑rizik ca dojke	raloxifen	raloxifen:↓ rizik VFx ;↓ rizik invazivnog ca dojke
Raloxifen godinama : stabilni BMD/ bez incidentne Fx na th	razmotriti prekid raloxifena; bisfosfonati, denozumab	Raloxifen ne prevenira Fx vrat femura; rizik embolije - stariji
Veći razmak primjene lijeka ?“compilance”, trajna skrb	bisfosfonati(ibandronat, zolnedr. kis.) denozuab	Različite doze i vramenski razmaci
Rizik glukokotikoidima izazvane osteoporoze	Bisfosfonati/ u obzir dolazi teriparatid	Preporuka : Am Coll of Rheumatology 2010

Čuvanje koštane mase

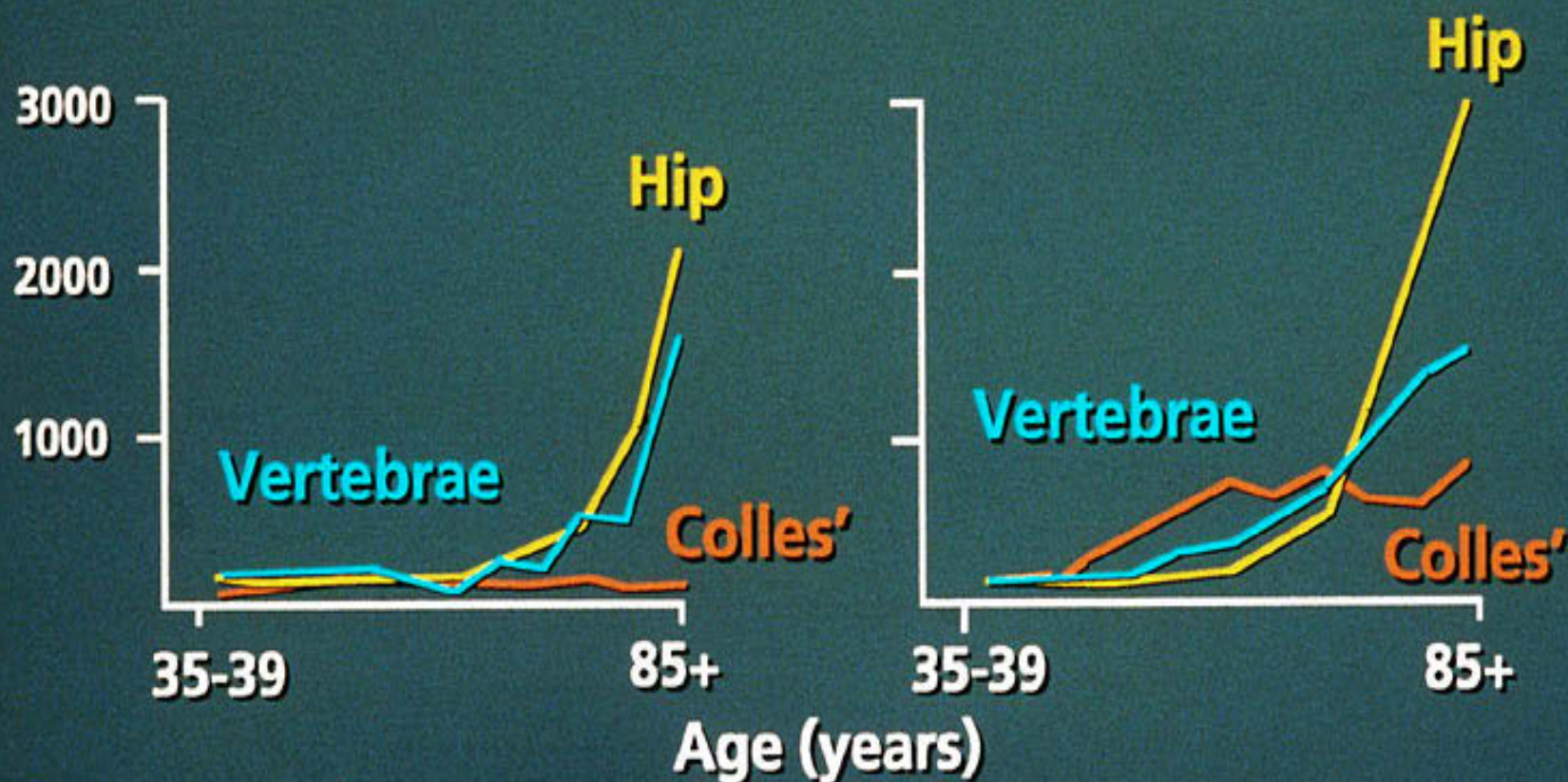




Incidence of fracture per 100,000 person-years

MEN

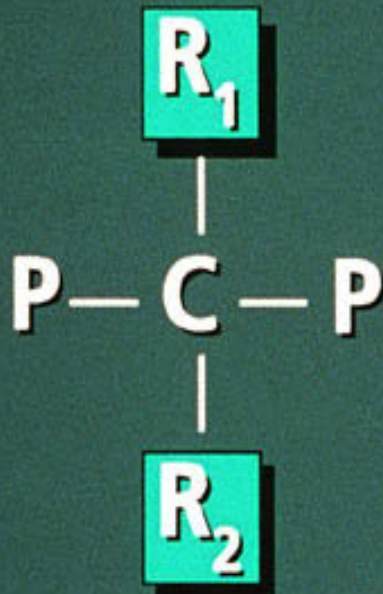
WOMEN



Adapted from Cooper C, Melton LJ III *Trends Endocrinol Metab* 3:224-229, 1992

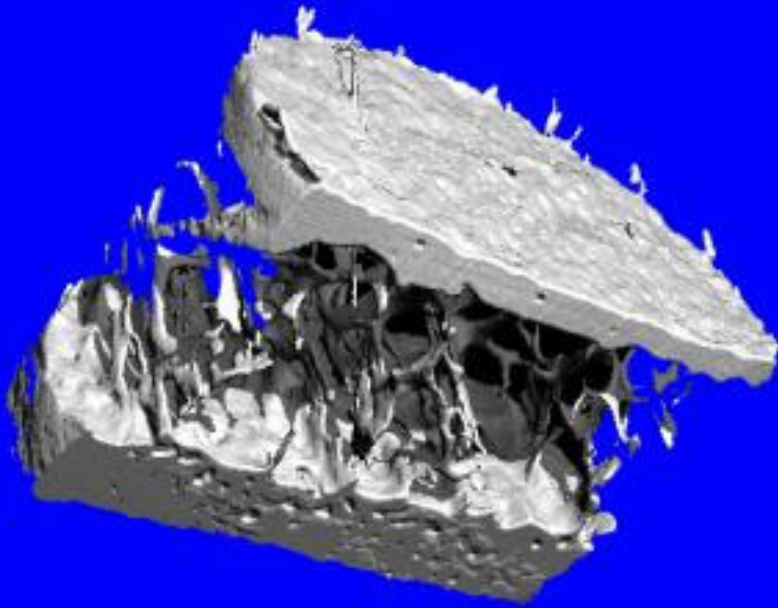


Bisphosphonates

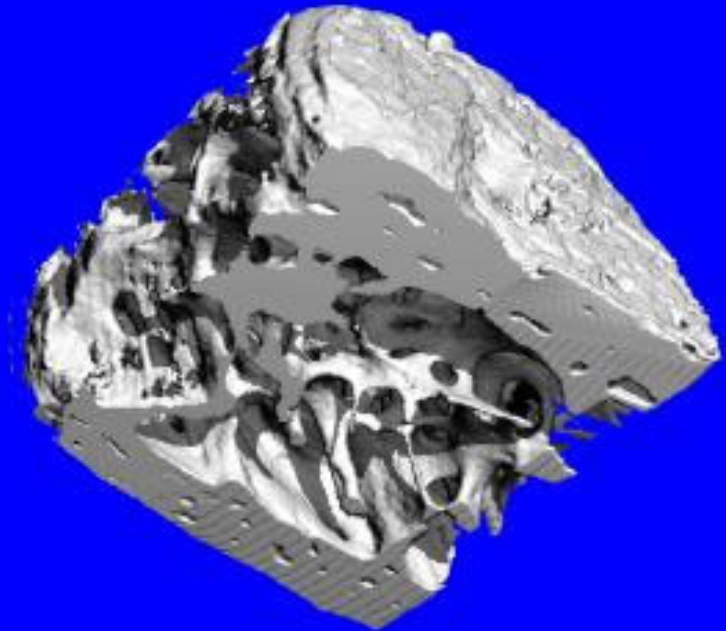


- Low intestinal absorption
- Bind to hydroxyapatite
- Long skeletal retention
- Inhibit bone resorption
- Potency depends on side chain

Teriparatide Improves Skeletal Architecture



Baseline



Follow up

Jiang UCSF

Patient treated
with teriparatide 20 μ g

Sourced from Jiang et al. *J Bone Miner Res* 18:1932-1941, 2003

Female, age 65

Duration of therapy: 637 days (approx 21 mos)

BMD Change:

⇒Lumbar Spine: +7.4% (group mean = $9.7 \pm 7.4\%$)

⇒Total Hip: +5.2% (group mean = $2.6 \pm 4.9\%$)

Osteoporozna – izbor

Izbor alendronat

Ostale mogućnosti: risedronat, ibandronat, zoledronična kiselina, denosumab, strocij ranelat, raloksifen

Posebnosti:

Bolesnik ne može uzimati lijek na usta: denosumab, zoledronična kiselina

Žene s teškom osteoporozom; ne podnose/ne reagiraju na terapiju: PTH

Mlađe postmenopauzalne žene s velikim rizikom prijeloma: HRT

Glukokortikoidna osteoporozna:

bisfosfonati/ prednizolon > 3 mjeseci; u dobi > 70 godina ili su već doživljeni prijelom;

prednizolon > 3 mjeseci; ostali – učiniti BMD / liječenje bolesnika s T -1,5 ili niže

Osteoclast - differentiation

