Osteoporosis Educational Series:

Diagnosis and Management of Osteoporosis in Adults:

Egyptian Academy of Bone Health
and Metabolic Bone Diseases

Objectives:

- **At the end of this presentation, attendees will be able to:**
- **Characterize the pathophysiology of osteoporosis**
- **Identify the clinical diagnosis of osteoporosis**
- **Summarize treatment and prevention options**

Pre Quiz

Question 1 of 5

Who needs to be treated for osteoporosis? (Choose one)
T-score between -1.00 to -2.5 at femoral neck, total hip or spine **AND** a FRAX score showing 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20% (FRAX)

a) 10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 20%

b) 10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 10%

c) 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20%

d) 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 30%

Pre Quiz

Question 2 of 5

Which of the following may be interpreted as improved state of bone turnover after treatment for osteoporosis? (Choose one)

a) A T-score of -1.5 in the spine
b) Suppression of urine NTX
c) Improved DXA acquired BMD in both spine and femoral neck regions
d) Suppressed levels of bone formation and resorption markers

Pre Quiz

Question 3 of 5

Which of the following would indicate treatment failure, or need to consider alternate treatment for osteoporosis?

a) BMD improved 1% since last DXA done 2 years ago
b) Fracture of femoral shaft while being treated with bisphosphonate for 5 years
c) Increased levels of bone markers since last measure a year ago
d) Femoral neck BMD did not change since last DXA 2 years ago

Pre Quiz

Question 4 of 5

An 80 year old Caucasian woman with dementia, falls and right hip fracture (1 year ago) while being on bisphosphonate, was referred for evaluation and treatment of osteoporosis. She had a mastectomy, followed by chemotherapy for breast cancer at age 66 and has been cancer free since then. Which of the following would be the best treatment option for her at this time? (Choose one)

a) Ibandronate
b) Calcitonin
c) Teriparatide
d) Denosumab

Pre Quiz

Question 5 of 5

Selective Estrogen Receptor Modulator (SERM) is one of the first options for osteoporosis treatment.

a) True

b) False

Osteoporosis

- Definition
- Risk Factors
- Screening
- Treatment to prevent fractures
- Monitoring response to treatment
- Special circumstances
- Cases

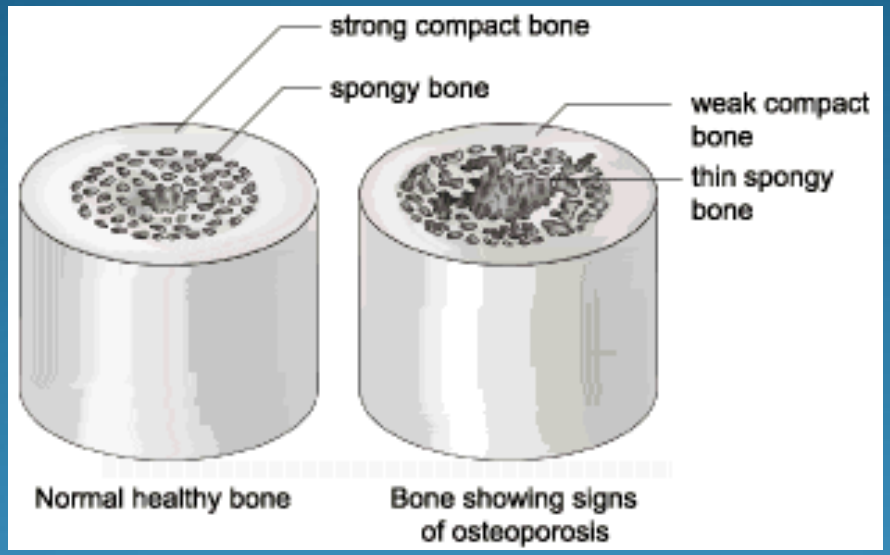
Osteoporosis: Definition

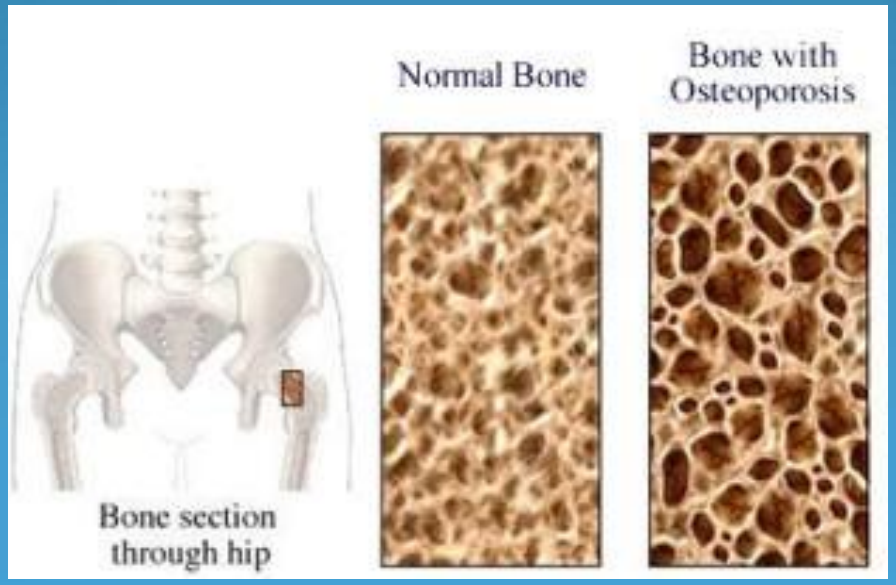
- Low bone mass and microarchitectural disruption causing weakening of bone which predisposes to fractures

Osteoporosis Organizations

- National Osteoporosis Foundations 2013
- American College of Rheumatology 2010
- US Preventive Services Task Force 2010
- American Association of Clinical Endocrinologists
- North American Menopause Society

Osteoporosis bone





Bone Remodeling

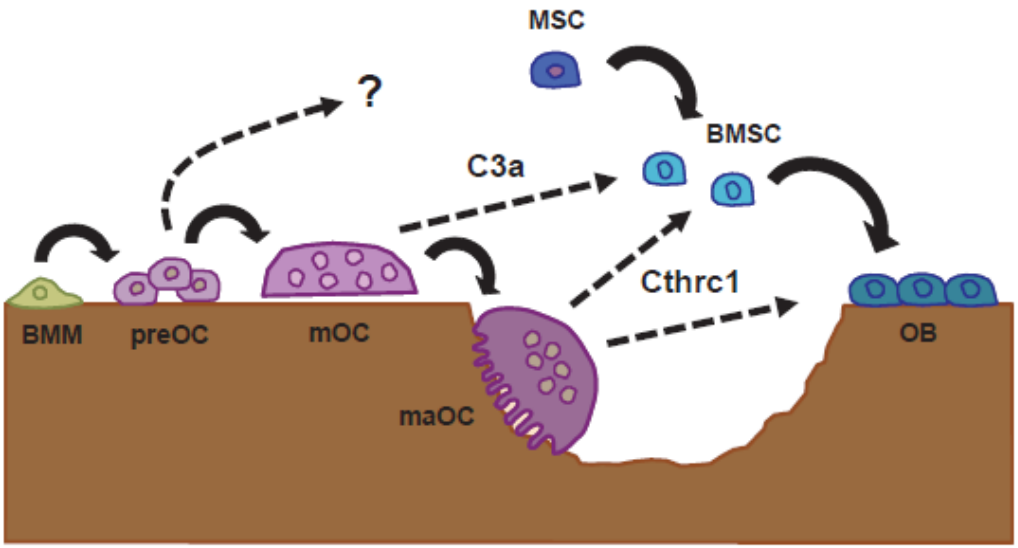
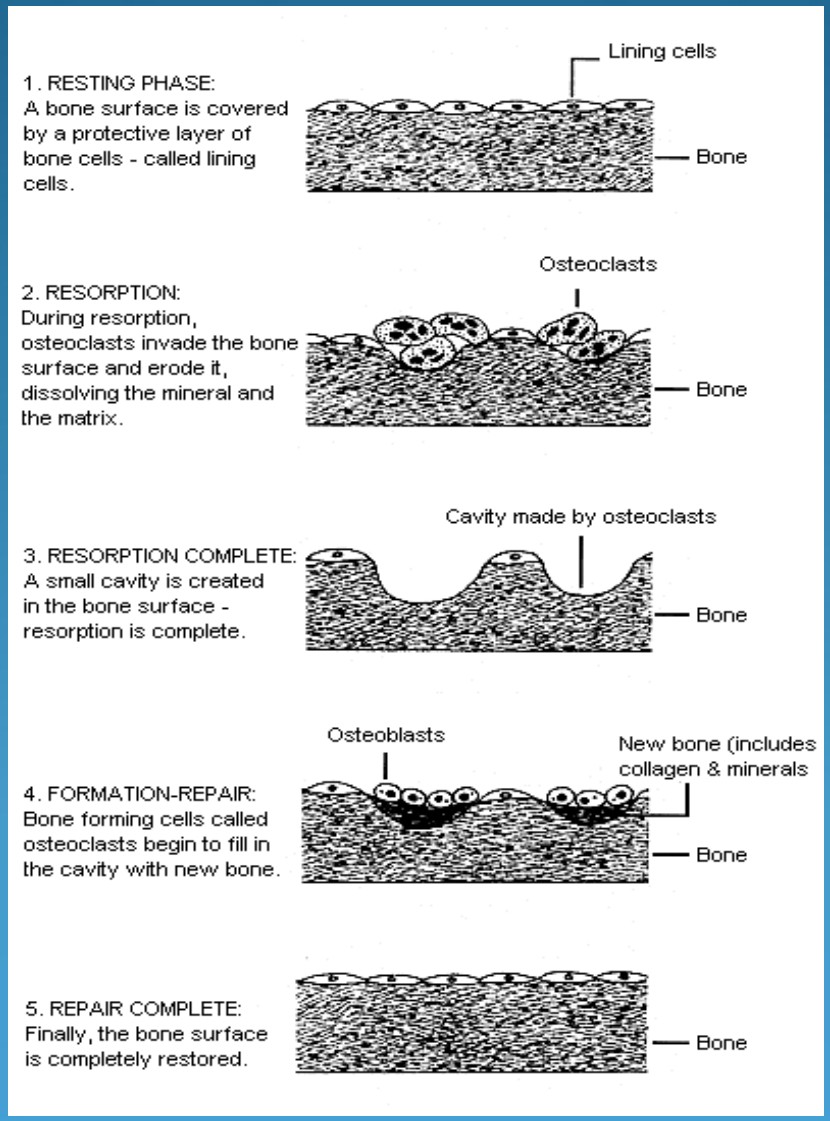


Fig.1. Complement component 3a (C3a) and collagen triple helix repeat containing 1 (Cthrc1) in the communication between osteoclasts (OC) and osteoblasts (OB). Bone marrow macrophages (BMM) become committed preOC and then mature, multinucleated OC (mOC). C3a is derived from mOC and acts on bone marrow stromal cells (BMSC) to stimulation osteoblastogenesis. Cthrc1 is secreted from mature active OC (maOC) in the middle of bone resorption and stimulates OB differentiation as well as recruitment of BMSC or mesenchymal stem cells (MSC) to resorption lacunae.

J Bone Metab 2014;21:163-167

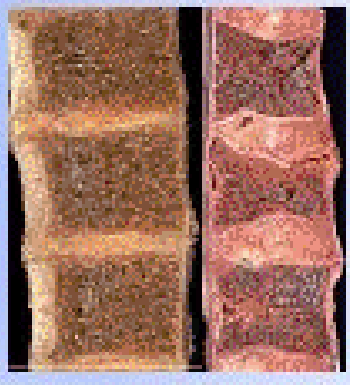
Bone Remodeling

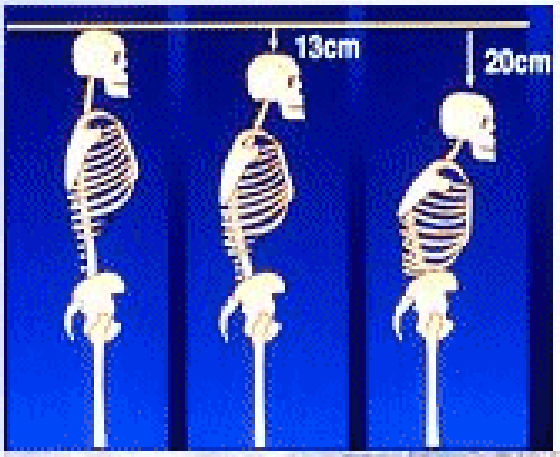


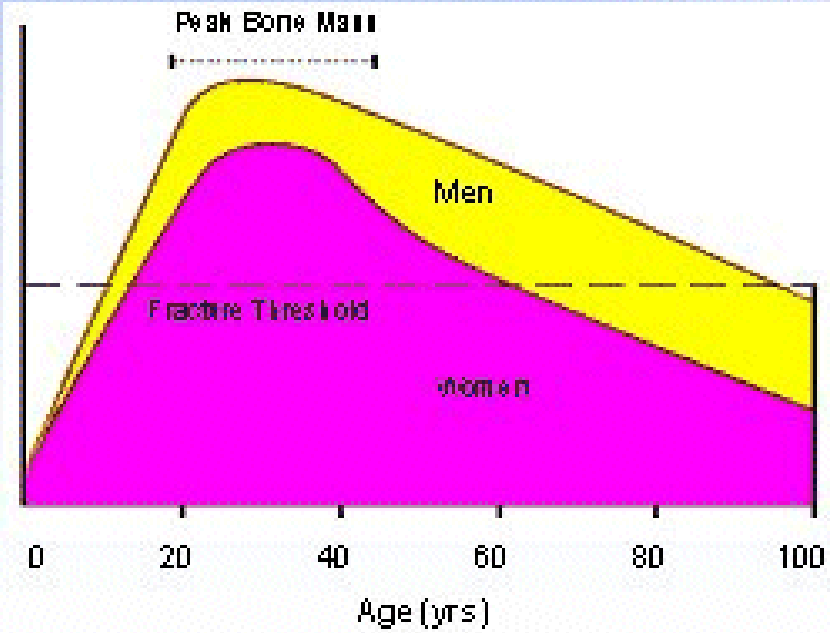
Osteoporosis Overview

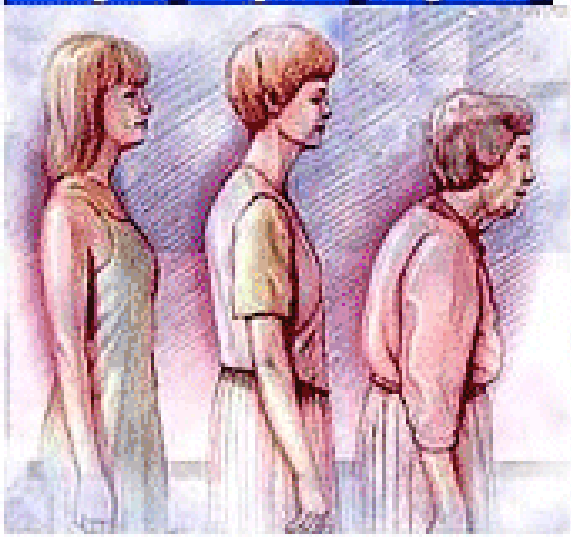
Osteoporosis

"the silent disease"









Overview

- Prevalence: 10 million Americans with osteoporosis
- Affects 18-28% of women and 6-22% of men over the age of 50 years old
- Half of all postmenopausal women and a quarter of men over 50 years old will have an osteoporosis related fracture

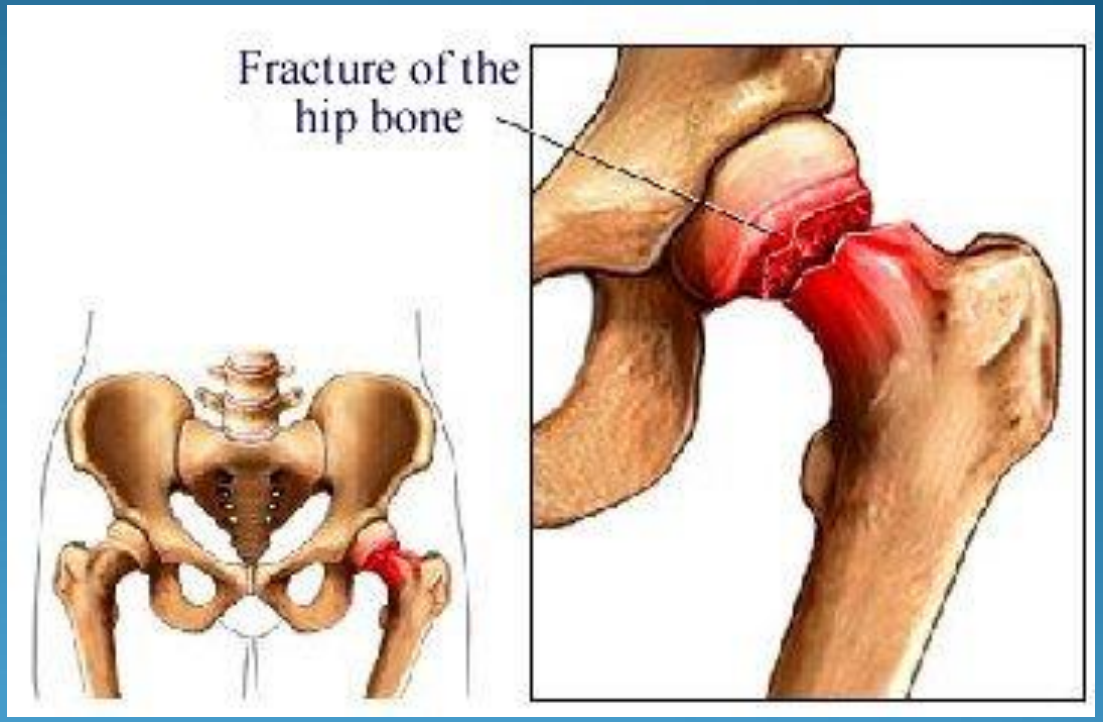
Clinical Findings

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

Fractures

- The main clinical consequence of osteoporosis
- There are more than 1.5 million osteoporosis related fractures per year
- Hip fractures: 300,000
- Vertebral fractures: 700,000
- Wrist fractures: 250,000
- Other sites: > 300,000

Hip Fracture



Hip Fracture – imaging

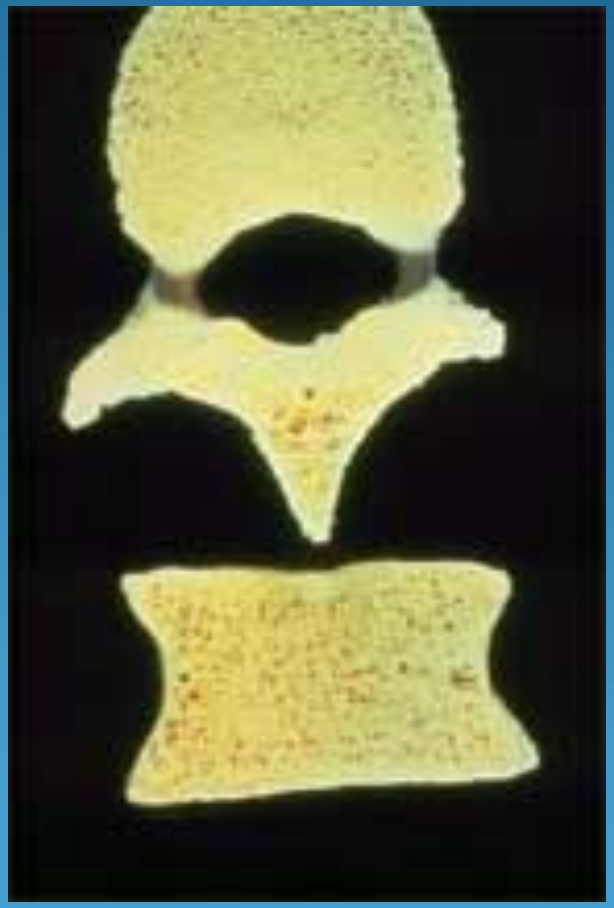
Hip Fracture

Hip Fracture – surgical repair c pin

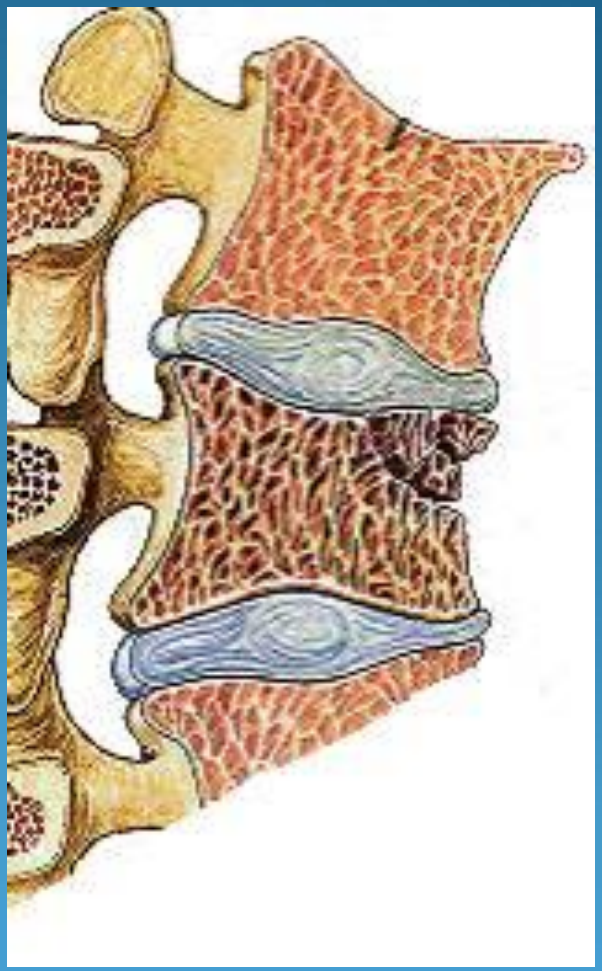
Bone with osteoporosis

Osteoporosis

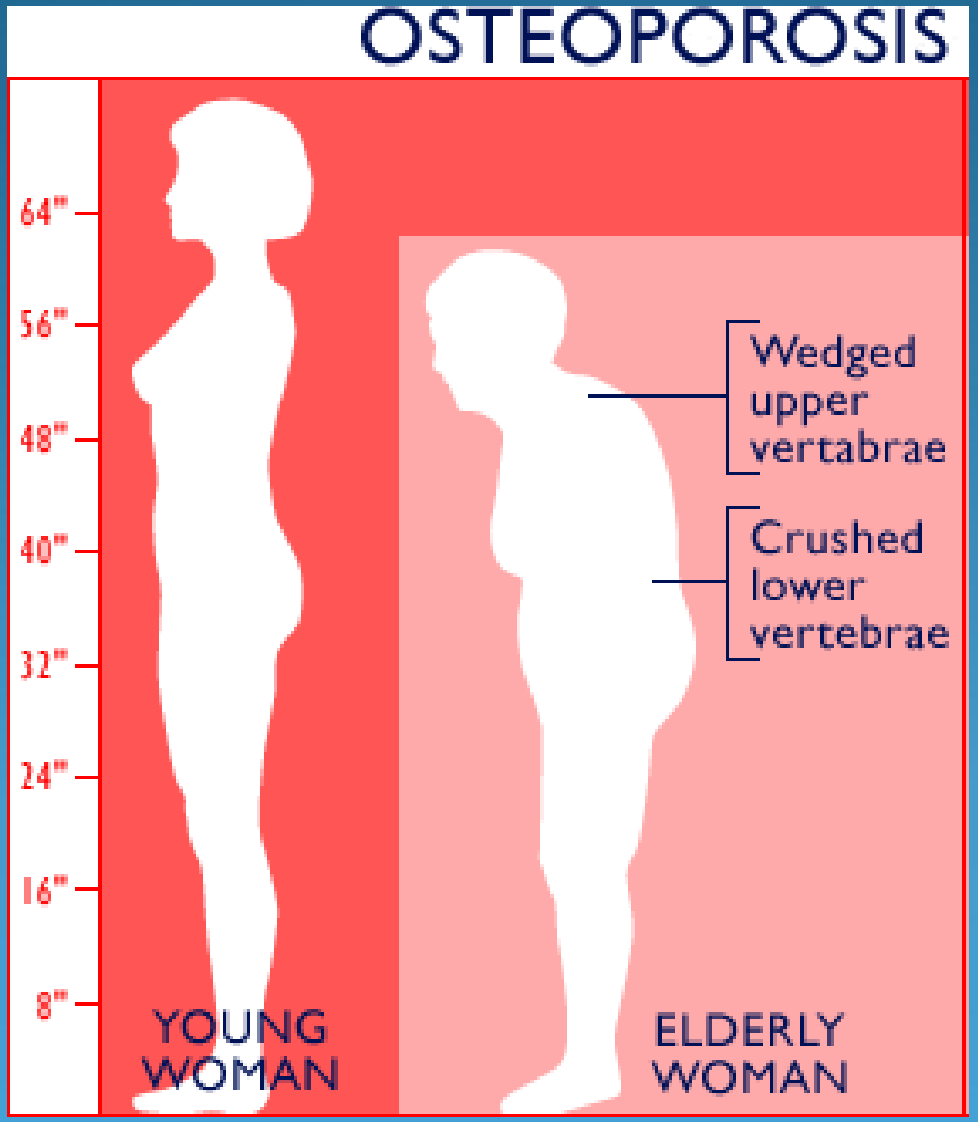
Normal



Vertebral Fracture- x-ray



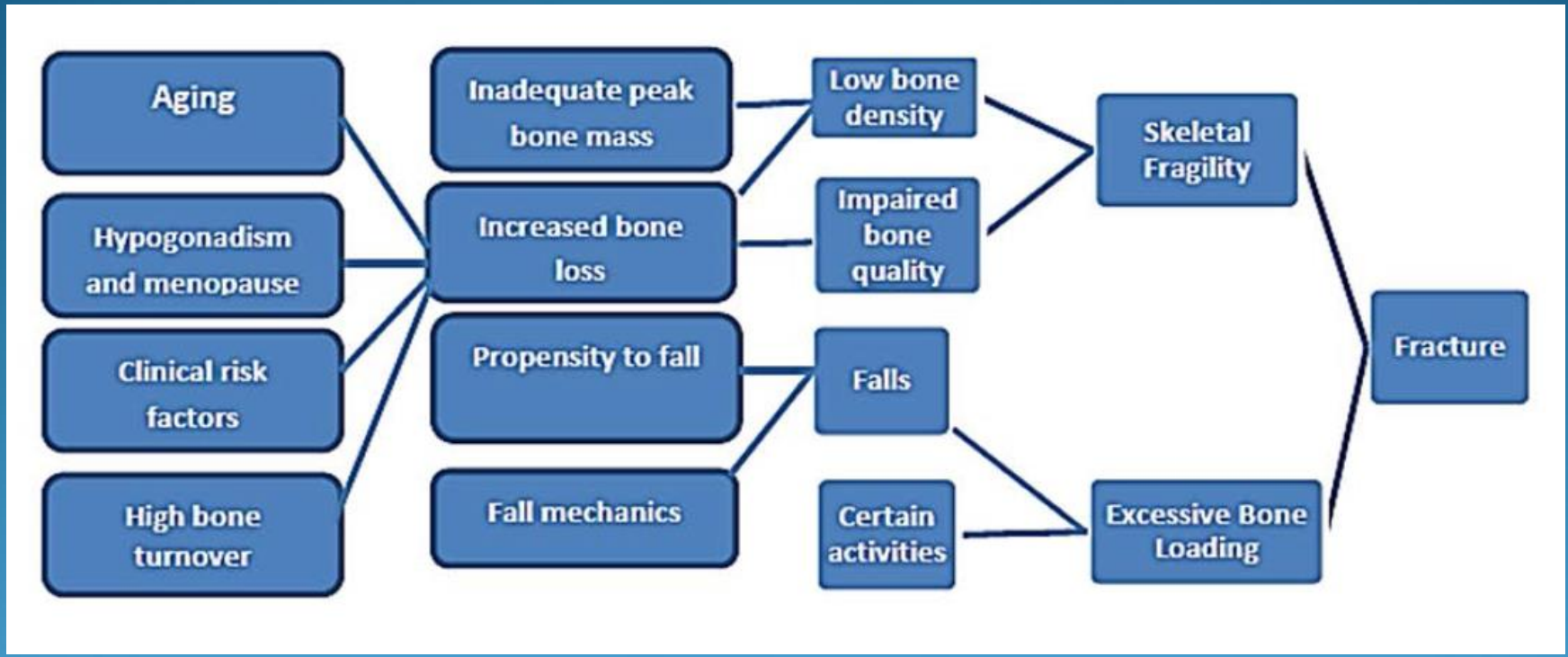
Osteoporosis and aging



Cost to Society

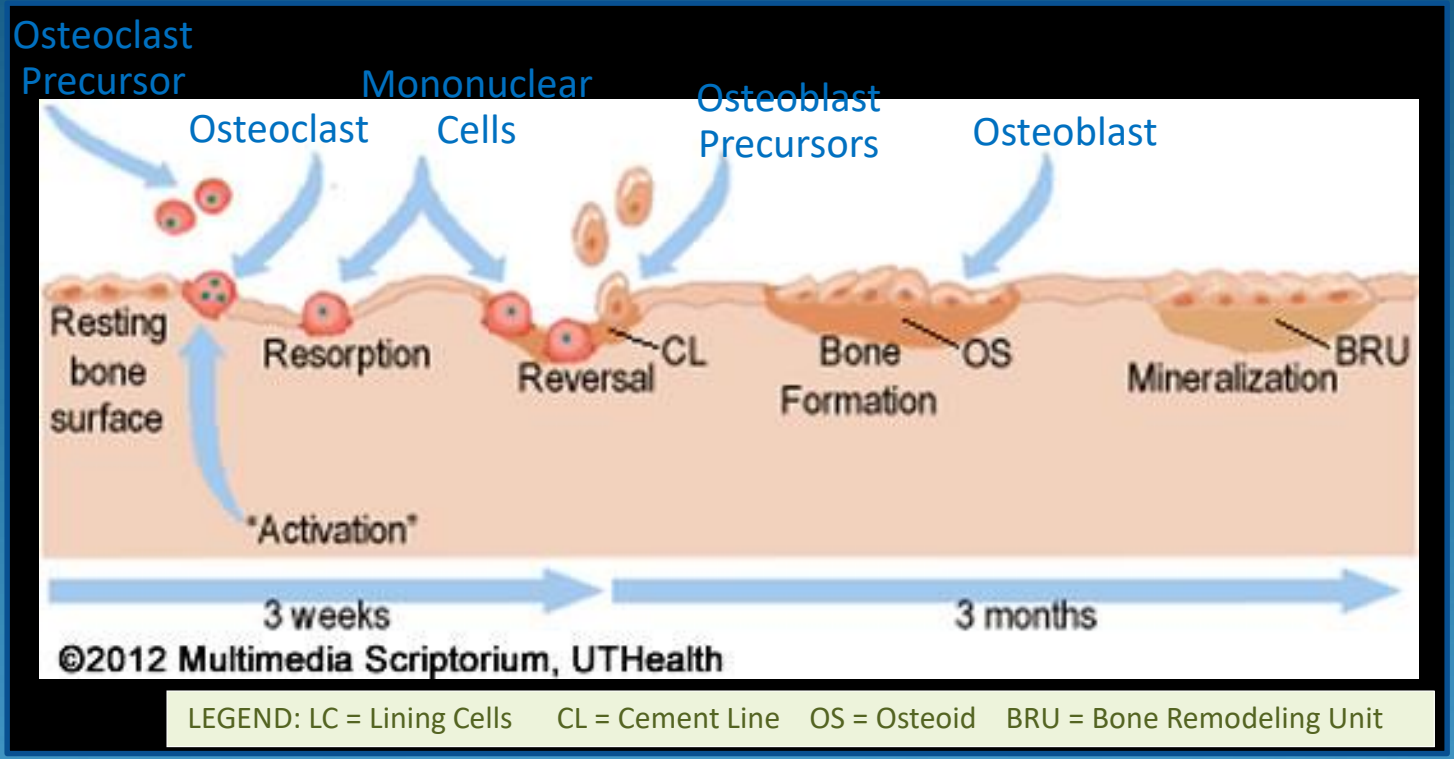
- 432,000 hospitalizations for fracture annually
- $14 billion dollars per year in US related to fractures – includes hospital and nursing home costs
- Estimated to increase to $25.3 billion in 2025

Pathogenesis for osteoporotic fracture



National Osteoporosis Foundation

Pathogenesis of Osteoporosis



Normal Bone Remodeling Sequence

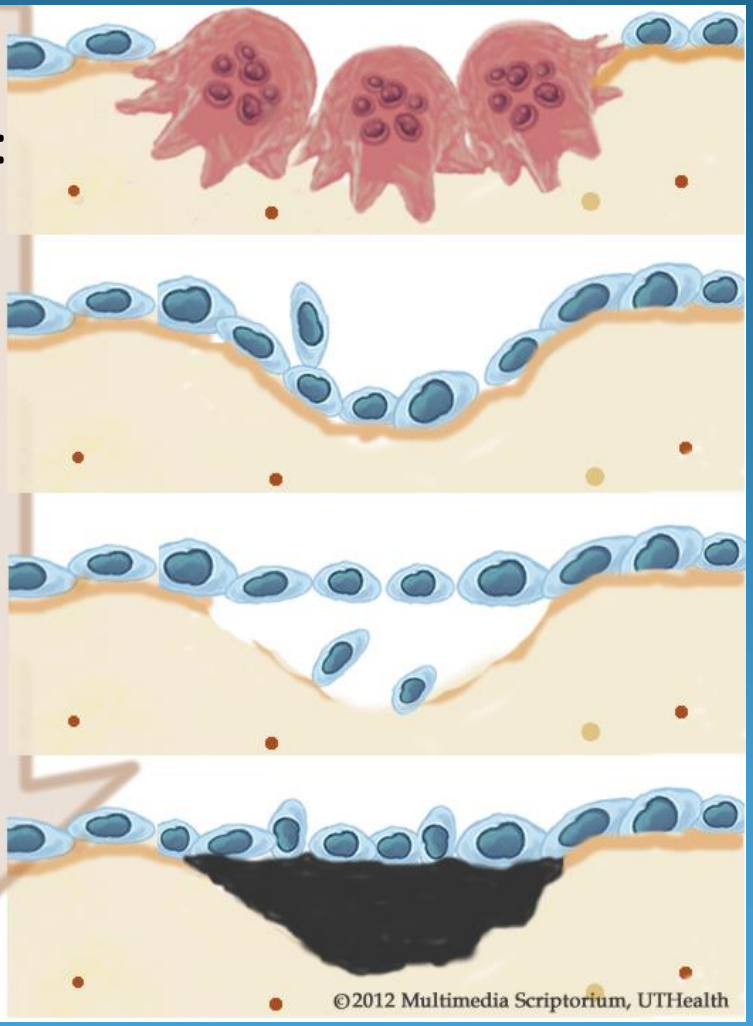
Resorption = Formation No change in bone mass

Unbalanced Remodeling and Osteoporosis

Resorption > Formation → Net bone loss

Influencers:

- Inadequate calcium or vitamin D
- Menopause
- Aging
- Medications or diseases



Basic Pathology

High Bone Turnover State

↓

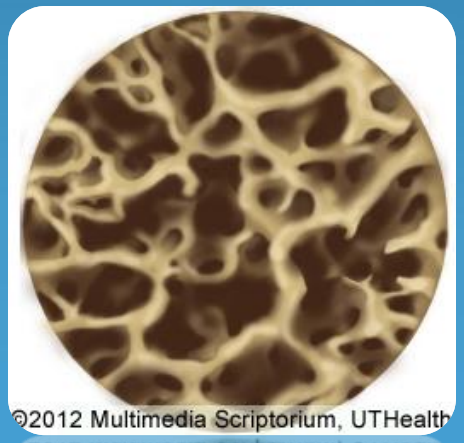
Unbalanced Remodeling

↓

Osteoporosis

Normal
Bone Structure

Osteoporotic
Bone Structure



Risk Factors: non-modifiable

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

Risk Factors: Modifiable

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

Risk Factors for Hip Fracture

- Bone Mineral density
- Fall on hip
- Neuromuscular impairment
- Ethnicity (Caucasians)
- Age
- Multiple falls in last year
- BMI (if lower)
- Vision impairment
- Physical inactivity

X-ray evidence of osteoporosis

May be present and can be clue for further evaluation

Screening

- DEXA scan is the most reliable method
- All women 65 years old and older be routinely screened for osteoporosis.
- Men > 70
- Younger patients (50-64) with equivalent risk of 65 year old woman
- Special populations: glucocorticoids, anti-estrogen, anti-testosterone

DEXA scan

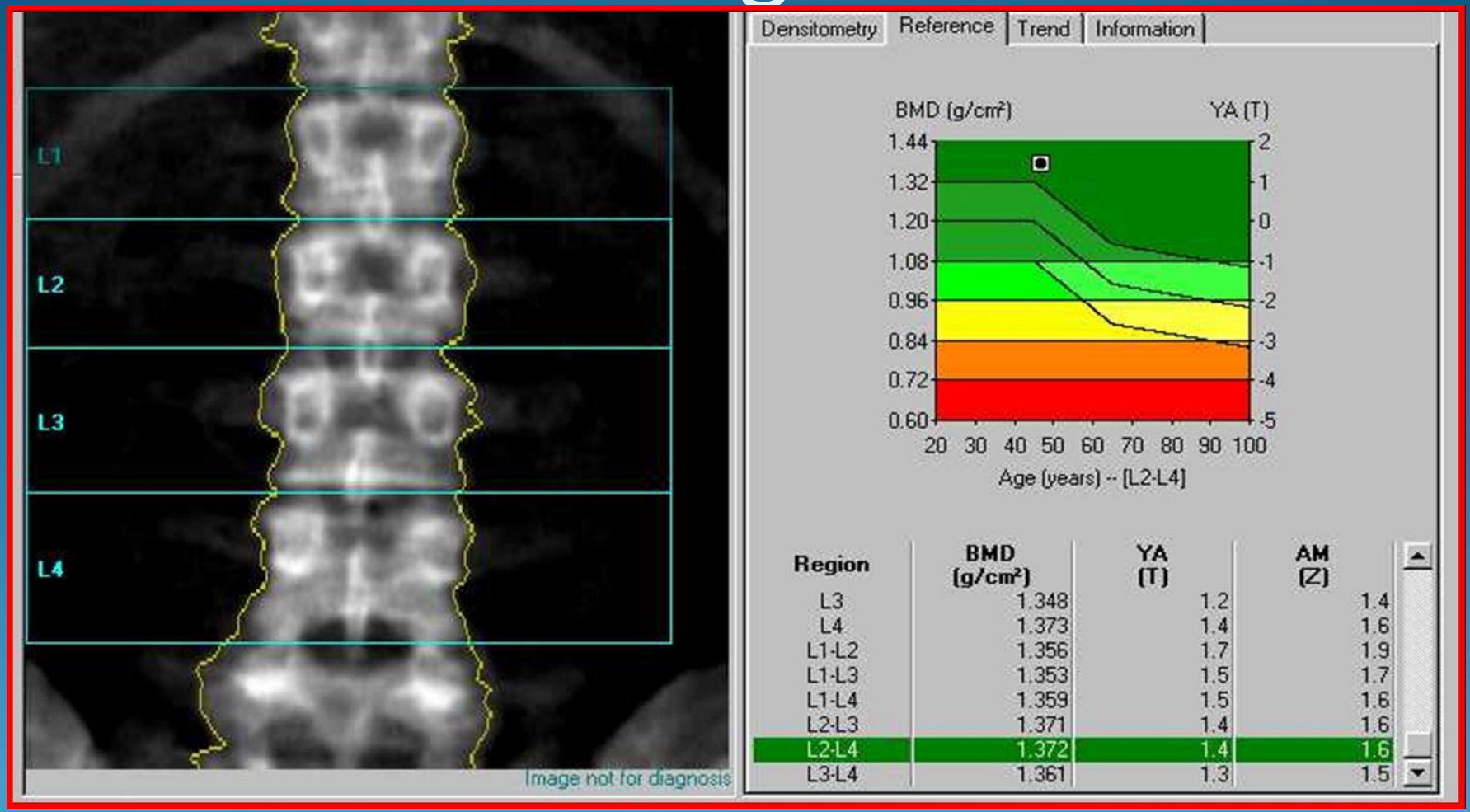
- Dual energy x-ray absorptiometry
- two photons are emitted from an x-ray tube, gives very precise measurements at clinically important sites with minimal radiation.
- Measures bone mineral density, approximation of bone mass and best predictor of fracture risk
- Measurement: standard deviation of normal young subjects (T-score) and age-matched (Z-score)

DEXA Scan

- Patients lie on exam table for approx 5 minutes while exam is performed.

Cost is $125-200 for this screening test

DEXA-image


L1
L2
L3
L4
Image not for diagnosis
Densitometry
Reference
Trend
Information
BMD (g/cm²)
YA (T)
1.44
1.32
1.20
1.08
0.96
0.84
0.72
0.60
2
1
0
-1
-2
-3
-4
-5
20 30 40 50 60 70 80 90 100
Age (years) -- [L2-L4]
Region
BMD (g/cm²)
YA (T)
AM (Z)
L3 1.348 1.2 1.4
L4 1.373 1.4 1.6
L1-L2 1.356 1.7 1.9
L1-L3 1.353 1.5 1.7
L1-L4 1.359 1.5 1.6
L2-L3 1.371 1.4 1.6
L2-L4 1.372 1.4 1.6
L3-L4 1.361 1.3 1.5

DEXA scan: interpretation

WHO Definition of Osteoporosis Based on BMD		
Classification	**BMD**	**T-score**
Normal	Within 1 SD of the mean level for a young-adult reference population	T-score at -1.0 and above
Low Bone Mass (Osteopenia)	Between 1.0 and 2.5 SD below that of the mean level for a young-adult reference population	T-score between -1.0 and -2.5
Osteoporosis	2.5 SD or more below that of the mean level for a young-adult reference population	T-score at or below -2.5
Severe or Established Osteoporosis	2.5 SD or more below that of the mean level for a young-adult reference population	T-score at or below -2.5 with one or more fractures

- Some experts use Z-score of < -2 to view for secondary causes of osteoporosis; also can be used in young patients to assess for peak bone density

DEXA scan: uses

- To detect those at risk for bone fracture (those with low bone density)
- To confirm diagnosis of osteoporosis in those with fracture
- To determine rate of bone loss
  - Compare on same machine if possible
    - GE (Bedford, Massachusetts)
    - Hologic (Madison, Wisconsin)
- To determine response to therapy

Hologic versus GE

Table 2 Means and standard deviation of Hologic Apex and GE-Lunar Prodigy BMD in g/cm^2

Variables	r^2 value	BMD results			sBMD results		
		Hologic	Prodigy	Difference	Hologic	Prodigy	Difference
L1-L4 spine	0.99	0.941±0.159	1.110±0.180	−0.169±0.063 (16.5%)**	1.011±0.168	1.053±0.174	−0.042±0.060 (4.1%)**
L2-L4 spine	0.98	0.970±0.160	1.132±0.190	−0.164±0.048 (15.6%)**	1.040±0.170	1.075±0.184	−0.035±0.050 (3.3%)**
Left total hip	0.95	0.841±0.124	0.912±0.131	−0.072±0.028 (8.2%)**	0.854±0.125	0.862±0.128	−0.009±0.027 (1.0%)*
Right total hip	0.96	0.837±0.124	0.905±0.132	−0.068±0.028 (7.8%)**	0.850±0.125	0.855±0.129	−0.005±0.027 (0.5%)
Left neck	0.84	0.706±0.108	0.870±0.119	−0.164±0.043 (21.0%)**	0.787±0.117	0.794±0.111	−0.007±0.043 (1.0%)
Right neck	0.87	0.711±0.108	0.867±0.118	−0.156±0.038 (20.0%)**	0.792±0.118	0.791±0.111	−0.0006±0.038 (0.6%)

*$P<0.05$

**$P<0.001$

GE machines measure higher bone density

Population database difference for T scores

GE: Madison, Wisconsin

Hologic: Bedford, Massachusetts

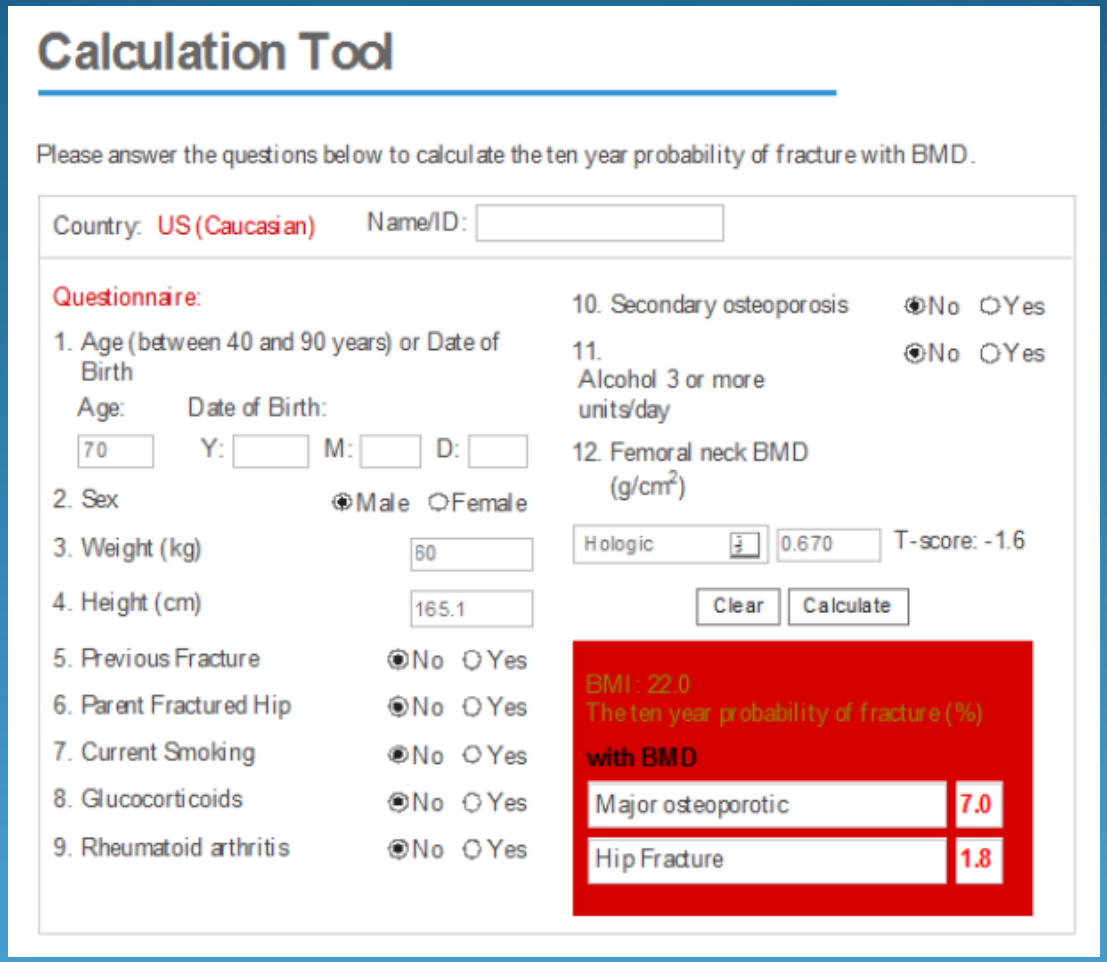
Osteoporos Int (2010) 21:1227–1236

FRAX Risk Factors

Clinical Risk Factors Included in the FRAX Tool	
Current age	Rheumatoid arthritis
Gender	Secondary causes of osteoporosis: Type1 (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition or malabsorption and chronic liver disease
A prior osteoporotic fracture (including clinical and asymptomatic vertebral fractures)	Parental history of hip fracture
Femoral neck BMD	Current smoking
Low body mass index (BMI, kg/m^2)	Alcohol intake (3 or more drinks/d)
Oral glucocorticoids $\geq$5 mg/d of prednisone for >3 months (ever)	

National Osteoporosis Foundation

FRAX Score



Calculation Tool

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

Country: US (Caucasian) Name/ID:

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: 70 Date of Birth: Y: M: D:
2. Sex ◉Male ○Female
3. Weight (kg) 60
4. Height (cm) 165.1
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/cm^2)
    Hologic 0.670 T-score: -1.6

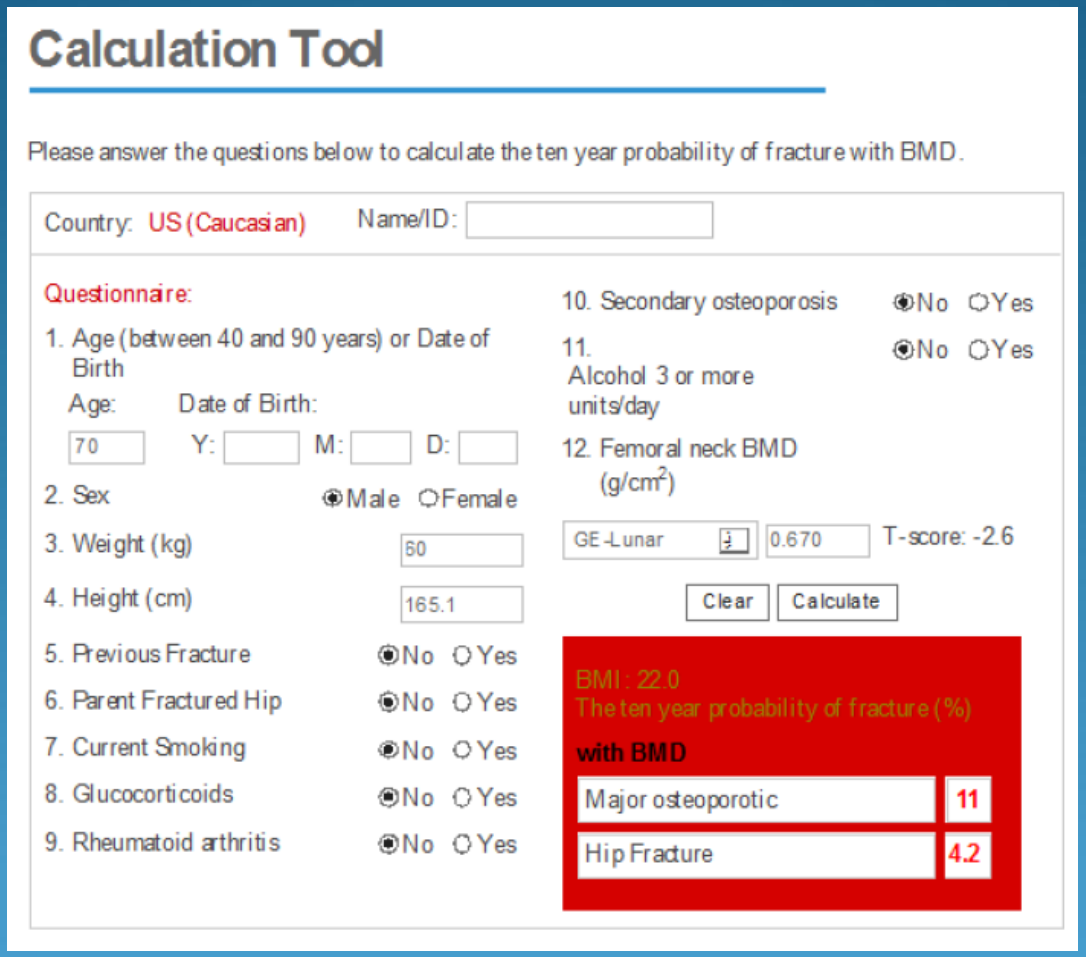
Clear Calculate

BMI: 22.0
The ten year probability of fracture (%)
with BMD

Major osteoporotic	7.0
Hip Fracture	1.8

- Threshold for treatment :
- **3% Hip Fracture, 20% Major osteoporotic FX** in the next 10 years

FRAX Score



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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/cm^2) GE-Lunar 0.670 T-score: -2.6

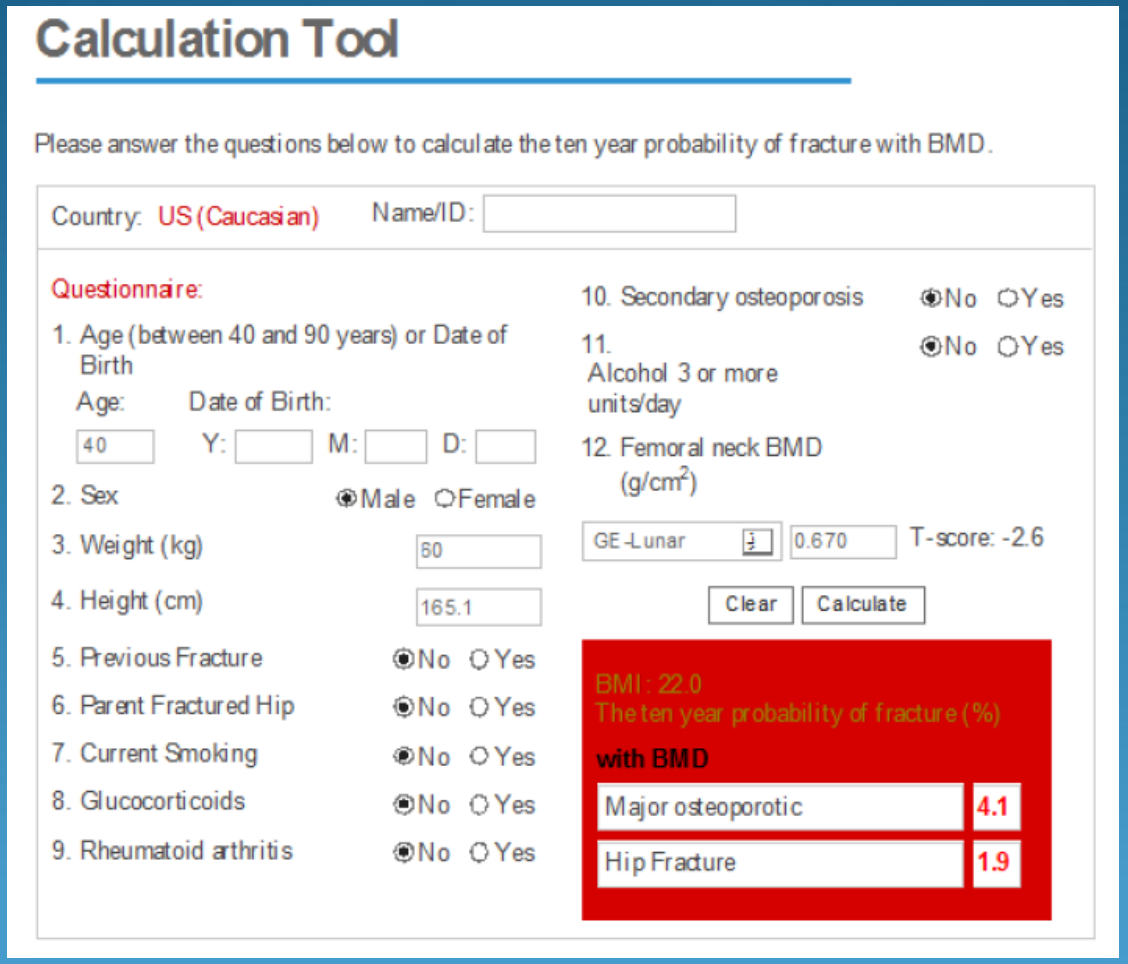
Clear Calculate

BMI: 22.0
The ten year probability of fracture (%)
with BMD

Major osteoporotic	11
Hip Fracture	4.2

- Everything is same except on GE-Lunar rather than Hologic
- On Hologic FRAX was 1.8% at hip and 7.0 Major Osteoporotic fx.

FRAX Score



Calculation Tool

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

Country: US (Caucasian) Name/ID:

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: 40 Date of Birth: Y: M: D:
2. Sex ◉ Male ○ Female
3. Weight (kg) 60
4. Height (cm) 165.1
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/cm^2)

GE-Lunar 0.670 T-score: -2.6

Clear Calculate

BMI: 22.0
The ten year probability of fracture (%)
with BMD

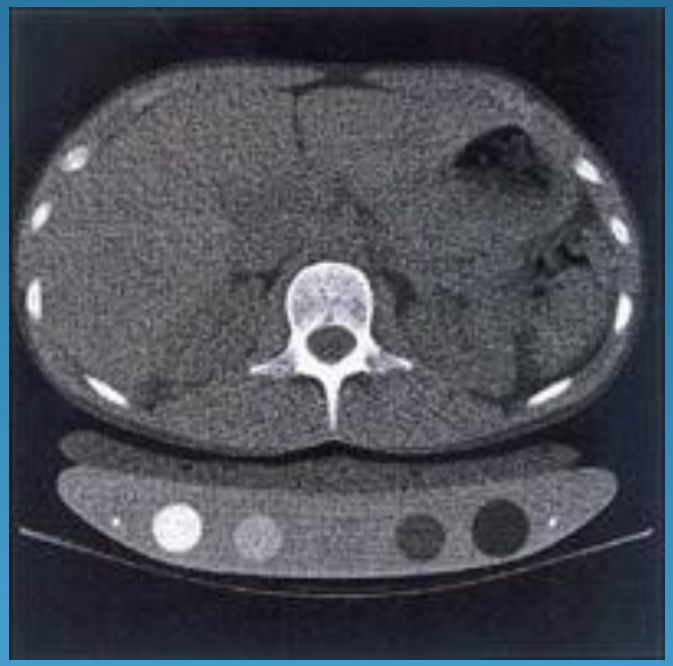
Major osteoporotic	4.1
Hip Fracture	1.9

- Impact of Age on fracture risk: 40 year old instead of 70 year old
- 70 year old had FRAX of 4.2% hip and 11% major osteoporotic

T-score and Z-score

- T-score
  - Postmenopausal women and men
  - Used to determine if patient has osteoporosis and whether treatment is required
- Z-score
  - Premenopausal women
  - Used to determine bone mineral density relative to healthy young controls.
  - For same score, risk of fracture is much lower due to age.
  - When considering treatment in patient's with spontaneous fractures (clinical picture as well), it is important to consider effect of medication on future pregnancy (fetal bone health)

Quantitative CT scan



Vertebral Imaging

Consider vertebral imaging tests for the following individuals:***
• All women age 70 and older and all men age 80 and older if BMD T-score at the spine, total hip or femoral neck is ≤ -1.0.
• Women age 65 to 69 and men age 70 to 79 if BMD T-score at the spine, total hip or femoral neck is ≤ -1.5
• Postmenopausal women and men age 50 and older with specific risk factors: ▪ Low trauma fracture during adulthood (age 50) ▪ Historical height loss of 1.5 inches or more (4 cm)* ▪ Prospective height loss of 0.8 inches or more (2 cm)** ▪ Recent or ongoing long term glucocorticoid treatment

* Current height compared to peak height during young adulthood
** Cumulative height loss measured during interval medical assessment
*** If bone density testing is not available, vertebral imaging may be considered based on age alone

National Osteoporosis Foundation

Standard Laboratory Tests

- CMP (creatinine, calcium, alkaline phosphatase)
  - Creatinine: assess for renal function for choice of treatment
  - Calcium:
    - if too low consider cause and replete
    - If too high consider hyperparathyroidism
  - Alkaline phosphatase: osteomalacia or Paget's disease
- 25-OH Vitamin D
  - Important to replete if low (low vit D can lead to elevated PTH)
- 24-hour Urine calcium
  - Hypercalciuria: if elevated
  - Malabsorption: if low

Additional Laboratory Tests

- PTH (with calcium)
  - If calcium is elevated
  - If considering using teriperatide (Forteo)
  - Patients with ESRD
- SPEP/UPEP with immunofixation
  - In patients with fragility fracture
  - Consider in patients to be placed on teriperatide (Forteo)
- Testosterone
  - In men with osteoporosis
- 24 hour urine cortisol
  - In patients with cushingoid features and unexpected osteoporosis

Bone Markers

Formation

- Serum osteocalcin
- Serum bone specific alkaline phosphatase (BAP)
- Serum pro-collagen type 1 amino-terminal propeptide (P1NP)

Resorption

- Serum C-terminal cross-linking telopeptide of type I collages (CTX)
- Urine N-terminal cross-linking telopeptide of type I collagen (NTX)
  - 2nd void sample in the AM

Monitoring Treatment Success

DXA Acquired BMD

- Stable or improved BMD
  - Loss of BMD <%CV showing no significant change over mechanical drift from QA report for DXA machine

Bone Markers

- Suppression of Bone markers
  - Both formation and resorption markers

Prevention

- Adequate nutrition, particularly calcium and vitamin D
  - Calcium: 1000 – 1200 mg daily (diet plus supplementation)
  - Vitamin D: goal level of around 30-50 (most 1000 units daily)
- Weight bearing exercise
- Discourage smoking
- Discourage alcohol abuse
- 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.

Who Needs to be Treated?

- Hx of hip fracture
- Other prior fractures and T-score between -1.0 to -2.5 at femoral neck, total hip or spine
- T-score ≤-2.5 at femoral neck, total hip or spine
- T-score between -1.0 to -2.5 at femoral neck, total hip or spine AND secondary cause ↑ risk of fracture
  - Steroid use, total immobilization
- T-score between -1.0 to -2.5 at femoral neck, total hip or spine AND 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20% (FRAX)

Treatment with medications

- Osteoporosis:
  - Based on DEXA scan (T score < -2.5 in PM Women)
  - Based of FRAX score

    10 yr risk for fracture >3% Hip, >20% Major
  - Based on **Atraumatic** or **Low Trauma Fractures**
- osteopenia or osteoporosis plus steroid treatments or anti-estrogen/testosterone therapy.
- osteopenia and high risk for fracture: on individual basis to decide whether treatment should be given

Treatment Options

- Bisphosphonates
  - Oral
  - Alendronate 10 mg daily or 70 mg weekly
  - Risedronate 5 mg daily or 35 mg weekly or 150 mg/mo
  - Ibandronate 150 mg/mo
  - Intravenous
  - Zoledronic acid 5 mg/yr
- Calcitonin
- (no longer used)
- Teriparatide
  - 20 mcg sq daily
  - Recombinant human PTH (not >2 yrs)
  - Contra-indicated in cancer patients
- Denosumab
  - 60 mcg sc/q 6
  - Humanized monoclonal antibody
  - Usually as a 2nd agent
- Calcium (1200-1500 mg) + vitamin D (800-1000 IU daily)

Hormones as Treatment Options

SERM

(Selective estrogen receptor modulators) – decreased risk for breast cancer)

- Raloxifene – not commonly used because it increases risk of DVT

Estrogen/Progestin

- Not encouraged due to increased risk of breast cancer, stroke, DVT and coronary diseases

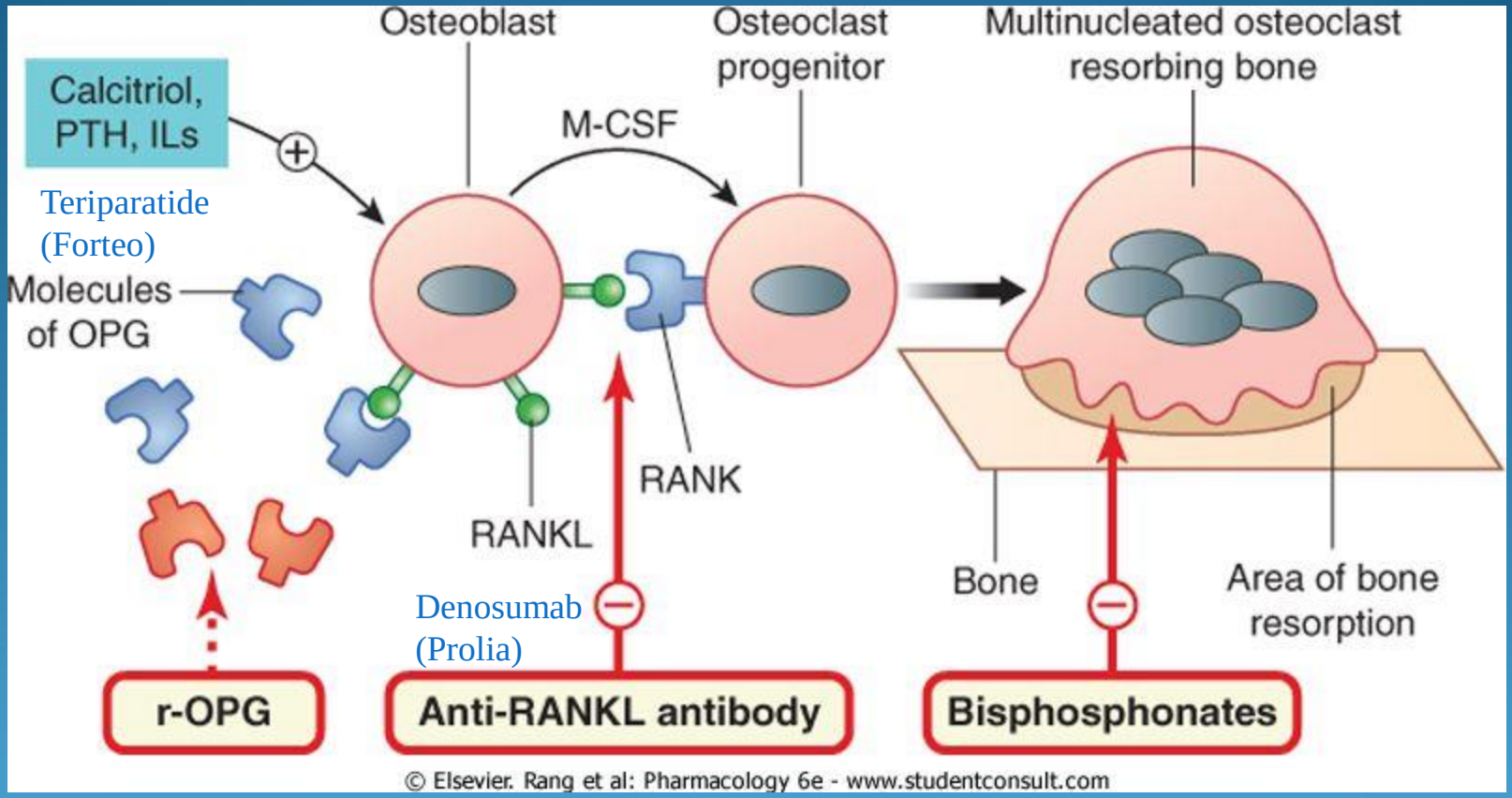
Testosterone

- If hypogonadism is the cause of osteoporosis

Treatment Options

- 1. Bisphosphonates
- 2. Denosumab (Prolia)
- 3. Teriperatide (Forteo)
- 4. SERMs (Selective estrogen receptor modulators) – decreased risk for breast cancer (raloxifene)
- 5. Hormone replacement therapy
- 6. Calcitonin : no longer used

Treatment


Osteoblast
Osteoclast progenitor
Multinucleated osteoclast resorbing bone
Calcitriol, PTH, ILs
M-CSF
Teriparatide (Forteo)
Molecules of OPG
RANK
RANKL
Denosumab (Prolia)
Bone
Area of bone resorption
r-OPG
Anti-RANKL antibody
Bisphosphonates
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Bisphosphonates

- generally 1st line
- Medications: alendronate, risendronate, zolendronic acid, ibandronate.
- Suppress resorption by preventing osteoclast attachment to bone matrix
- Cannot be used with eGFR < 30-35%
- Decrease vertebral and nonvertebral in most
  - Reduction in fracture risk by approximately 50%
  - Nonvertebral fx prevention not proven for ibandronate
  - Zolendronic acid: 70% vertebral, 41% hip
- Side effects:
  - Esophagitis (not in IV forms)
  - AVN of Jaw
  - Atypical fragility fractures, delayed fracture healing

Bisphosphonates

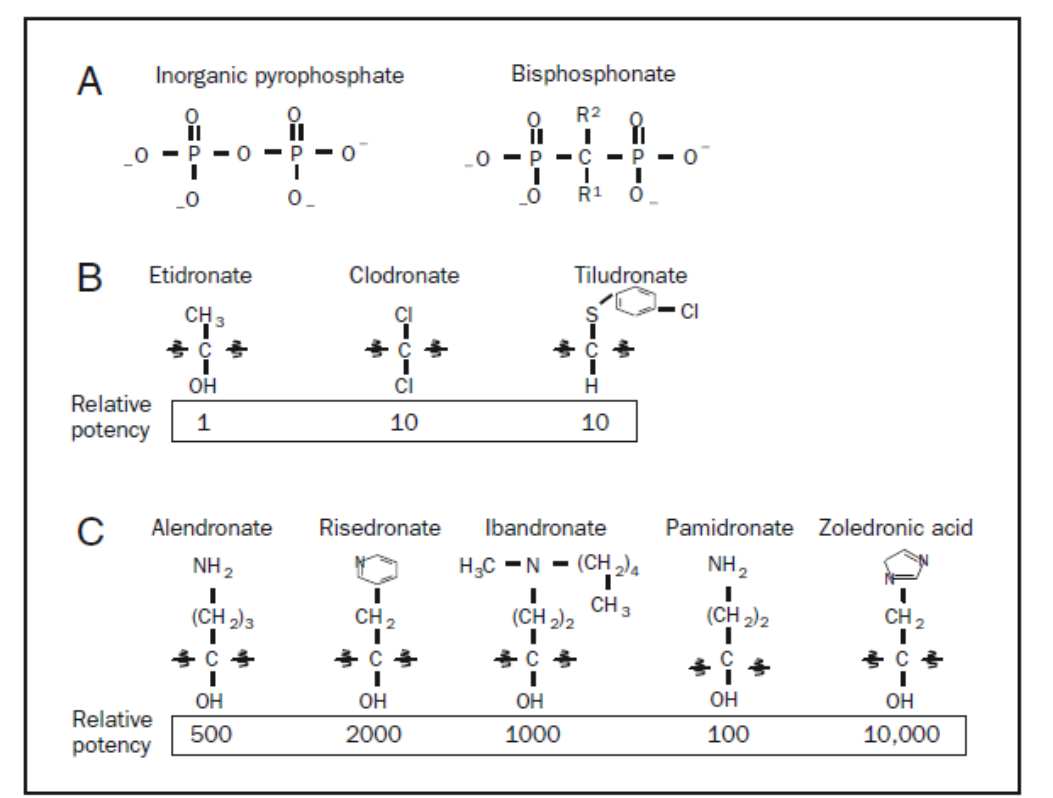


FIGURE 1. Bisphosphonate structures and approximate relative potencies[6] for osteoclast inhibition.

- Nitrogen containing bisphosphonates

Mayo Clin Proc. 2008;83(9):1032-1045

Bisphosphonates

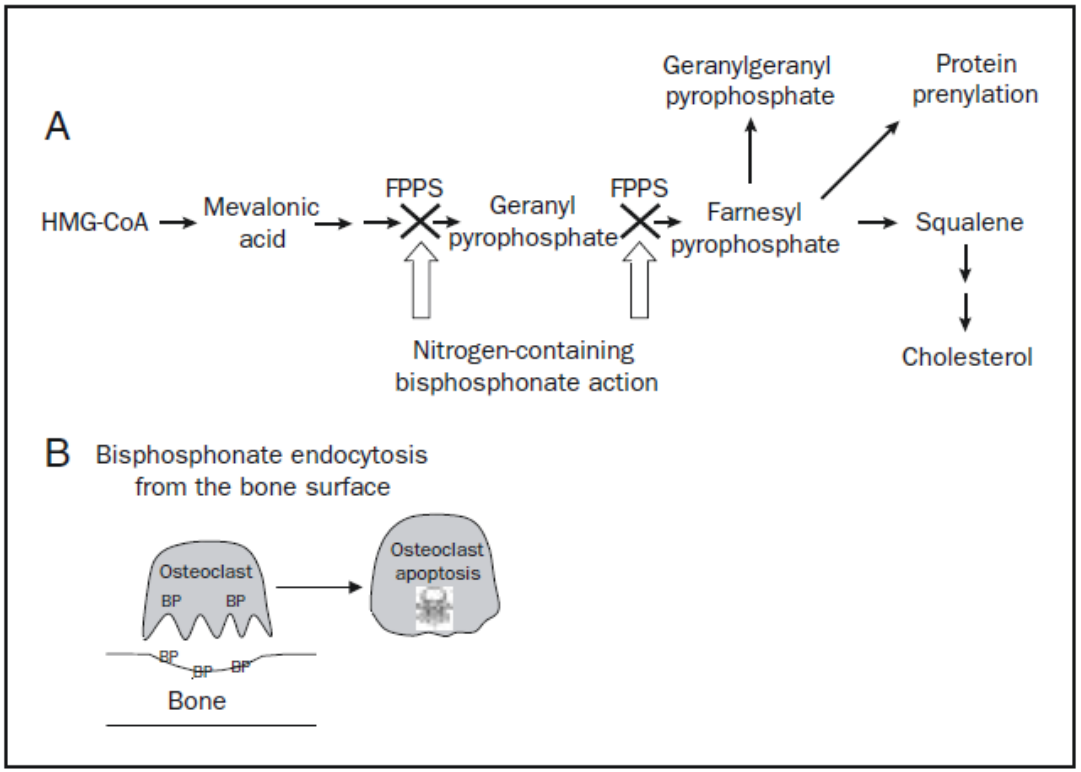


FIGURE 2. A, Nitrogen-containing bisphosphonates selectively inhibit farnesyl pyrophosphate synthase (FPPS) within osteoclasts. B, Osteoclast endocytosis of bisphosphonate from the bone surface leads to FPPS inhibition and osteoclast apoptosis. BP = nitrogen-containing bisphosphonate; HMG-CoA = 3-hydroxy-3-methylglutaryl coenzyme A.

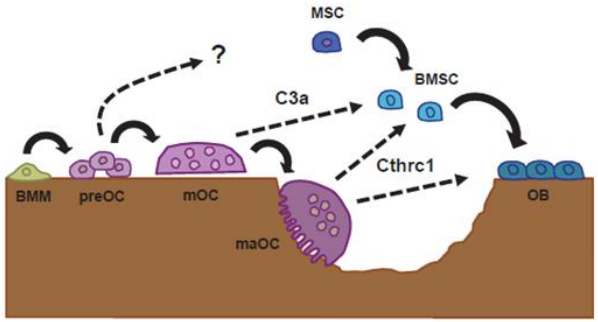
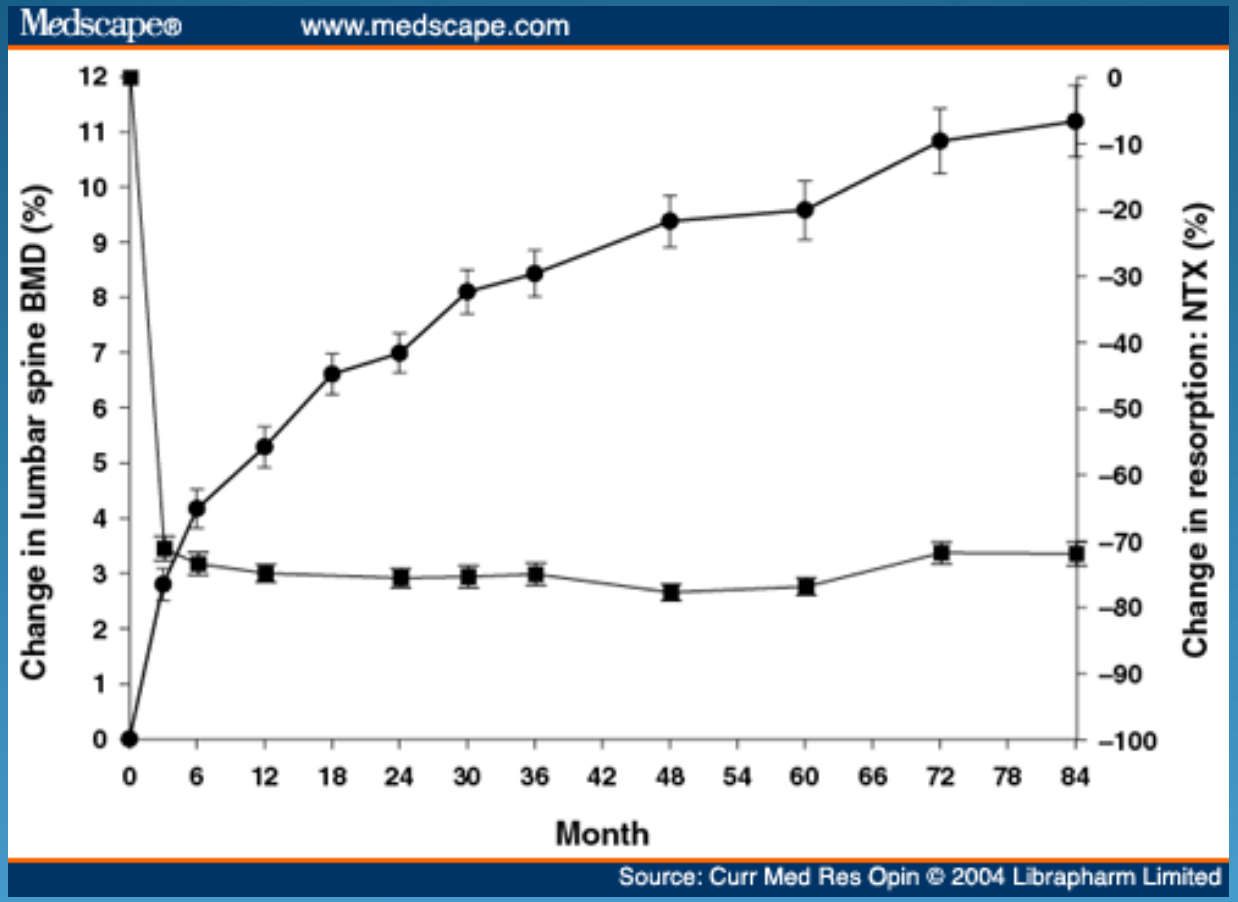


Fig.1. Complement component 3a (C3a) and collagen triple helix repeat containing 1 (Cthrc1) in the communication between osteoclasts (OC) and osteoblasts (OB). Bone marrow macrophages (BMM) become committed preOC and then mature, multinucleated OC (mOC). C3a is derived from mOC and acts on bone marrow stromal cells (BMSC) to stimulation osteoblastogenesis. Cthrc1 is secreted from mature active OC (maOC) in the middle of bone resorption and stimulates OB differentiation as well as recruitment of BMSC or mesenchymal stem cells (MSC) to resorption lacunae.

Mayo Clin Proc. 2008;83(9):1032-1045

Bisphosphonates



Alendronate

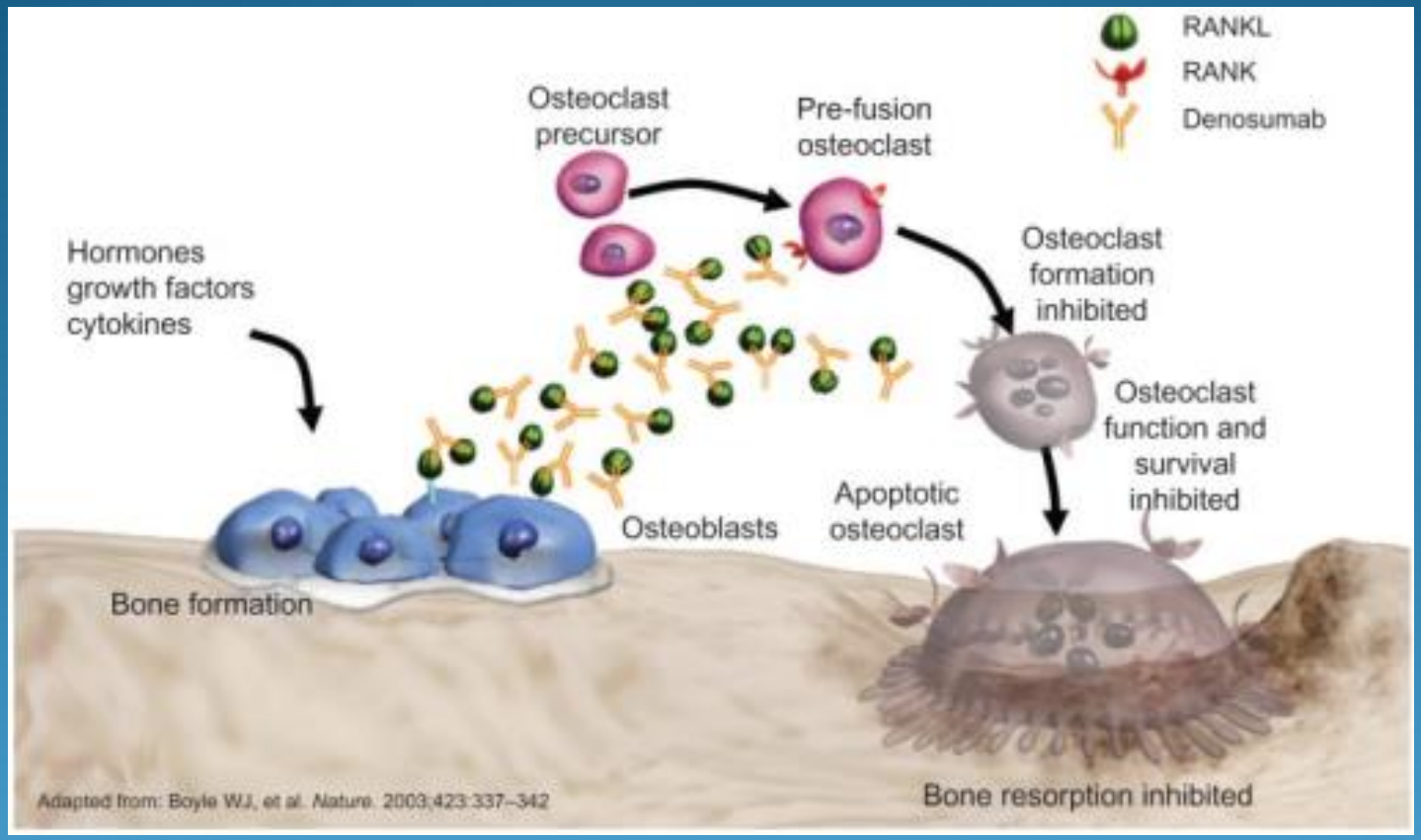
Increase in bone mineral density (circles)

Decrease in urinary N-telopeptides (squares)

Are All Bisphosphonates The Same?

- Different pharmacokinetics
  - Alendronate: long biologic half-life
  - Zolendronic Acid: intermediate biologic half-life
  - Risendronate: short biologic half-life
- Suggested drug holiday
  - Alendronate: 3-5 years
  - Zolendronate: 3 years
  - Risendronate :1 year

Denosumab (Prolia):



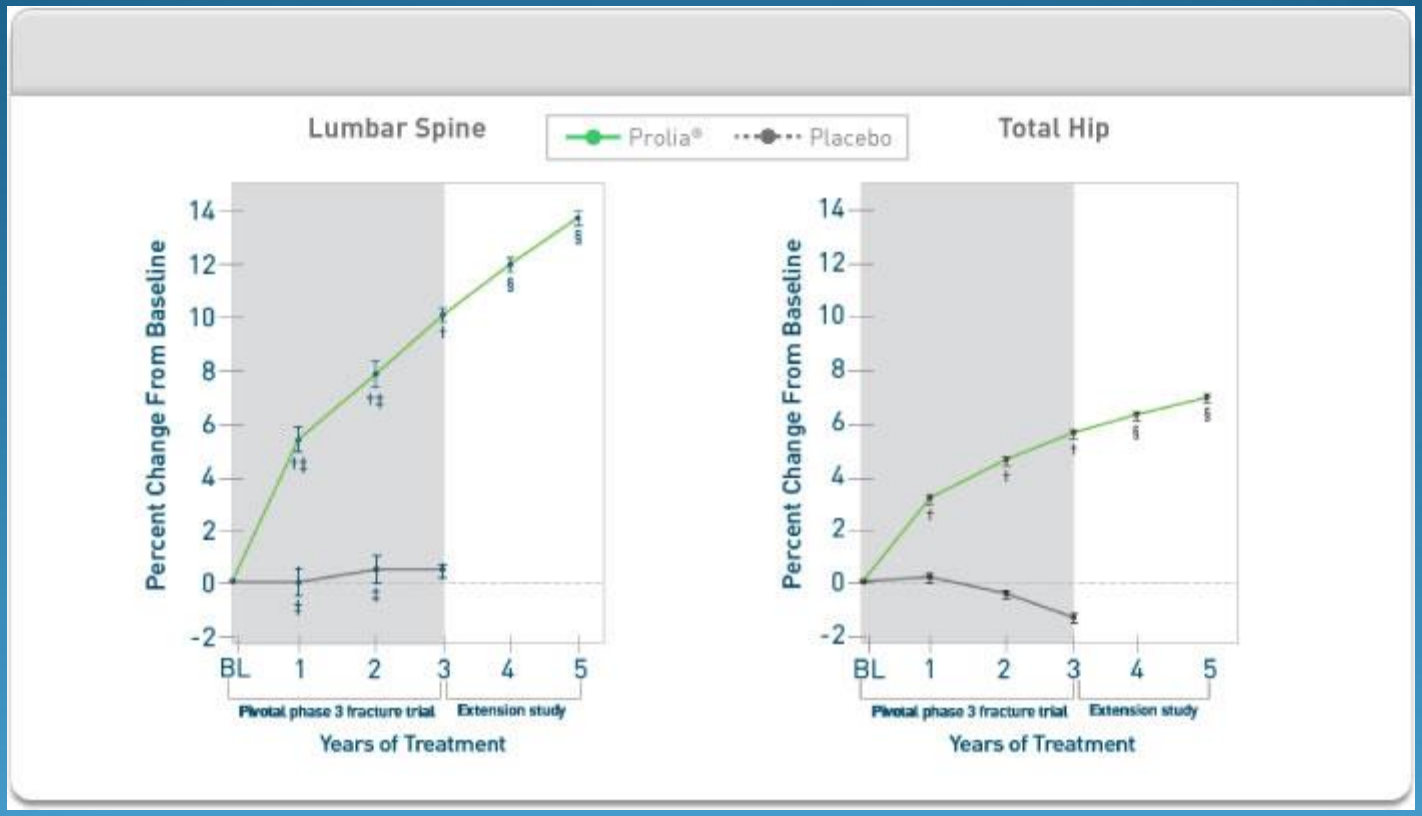
- Humanized monoclonal antibody to RANK Ligand
- Prevents formation of active osteoclasts
- Inhibits bone resorption

Lipton A, Smith MR, Ellis GK, Goessl C - Clin Med Insights Oncol (2012)

Denosumab (Prolia):

- Shorter biologic half-life than bisphosphonates
- Reduces Fractures
  - vertebral by 68%
  - Hip by 40%
- Approved for women receiving aromatase inhibitors and men receiving gonadotropin reducing treatment
- Contraindications:
  - current hypocalcemia
  - Pregnancy
  - hypersensitivity
- Potential Adverse Effects
  - Atypical fragility fractures
  - AVN of Jaw
  - Possible increased risk of infections (cellulitis, endocarditis)
  - Suppression of bone turnover (delayed fracture healing)

Denosumab (Prolia):



- Change in bone density over time

SERM

- Selective Estrogen Receptor Molecules: mixed agonists and antagonists of specific estrogen receptores.
- **Raloxifene**:
  - Decrease vertebral fracture by 55% (only 30% in those with history of vertebral fracture)
  - no effect on non-vertebral fractures
- Decreases risk for breast cancer
- Adverse effects:
  - ? Risk for CAD
  - Venous thromosis – increased risk
  - Hot flashes and leg cramps

Hormone Replacement Therapy:

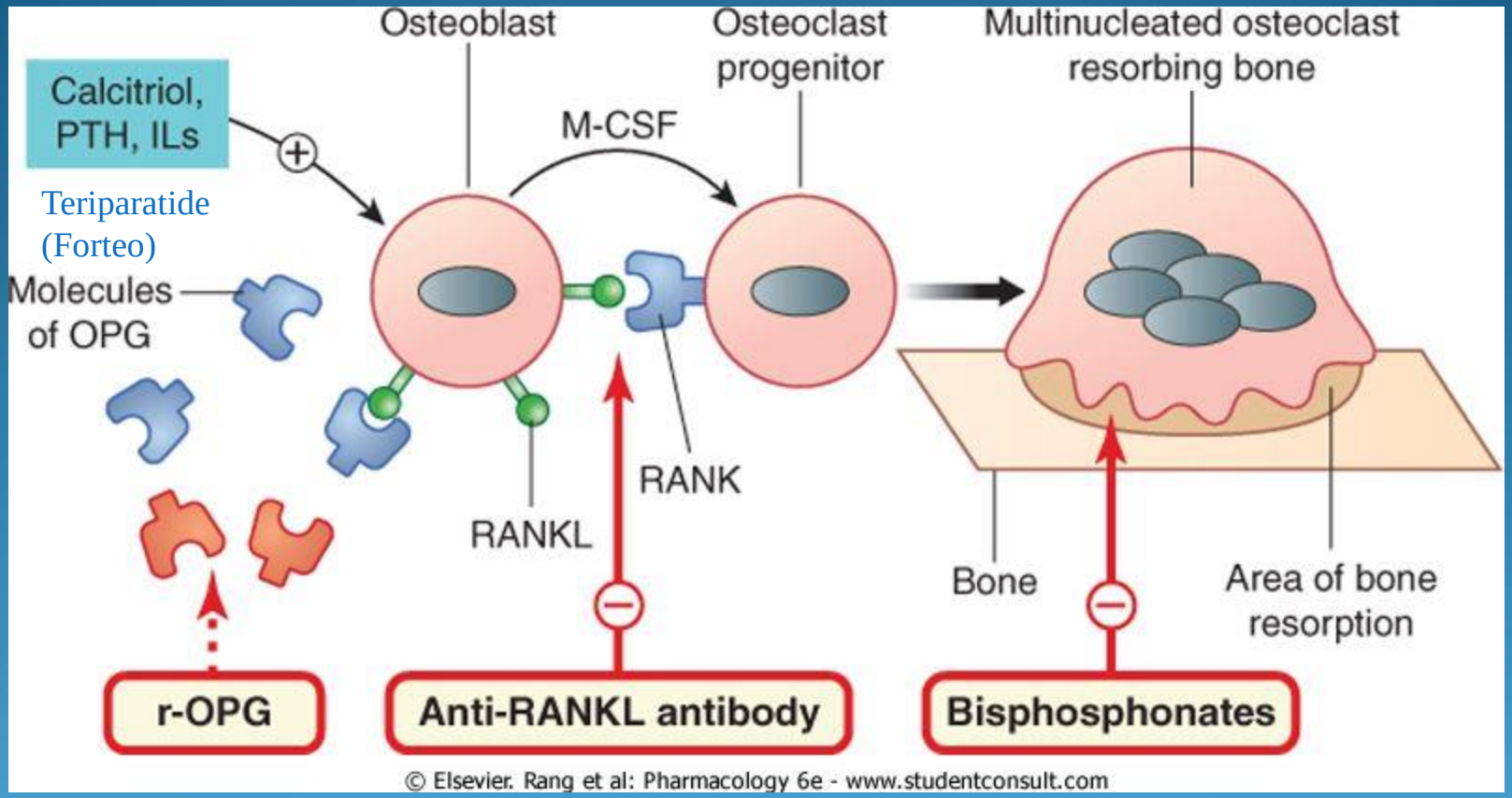
rise and fall

- Estrogens +/- progesterones
- HRT was once considered to be the primary therapy of osteoporosis prevention/treatment
- Blocks cytokine signaling to the osteoclast
- Women's Health Initiative trial: **34% reduction of hip fracture and vertebral fractures**, but increased risk for breast cancer, cardiovascular disease, thrombosis…
- Currently, HRT is not used to treat or prevent osteoporosis alone (often used for other indications such as severe postmenopausal symptoms.

Teriparitide (Forteo)

- Stimulates bone remodeling by increasing bone formation
- Moderate to severe osteoporosis:
- Reduction of fractures:
  - Vertebral : 65%
  - Nonvertebral 53%
- High doses in rats caused osteosarcoma but no cases of osteosarcoma seen in >200,000 patients who received the drug
- Should not be given for more than 2 years
- Side effects: mild hypercalcemia (10.5-11)
- Expensive and subcutaneous administration.
- Should not be given to patients with:
  - Hypercalcemia
  - Multiple Myeloma, bone mets, skeletal tumor
  - Children/teenagers with growing bones

Teriparatide (Forteo)



Response to therapy

- There are no definite guidelines as to when or if to repeat DEXA scans with treatment.
- Generally DEXA scans should not be performed before 2 years of treatment on same machine.

Osteoporosis in Men

- Later onset: approximately 10 years later.
- Often overlooked
- Worse prognosis with fracture

Osteoporosis in Men

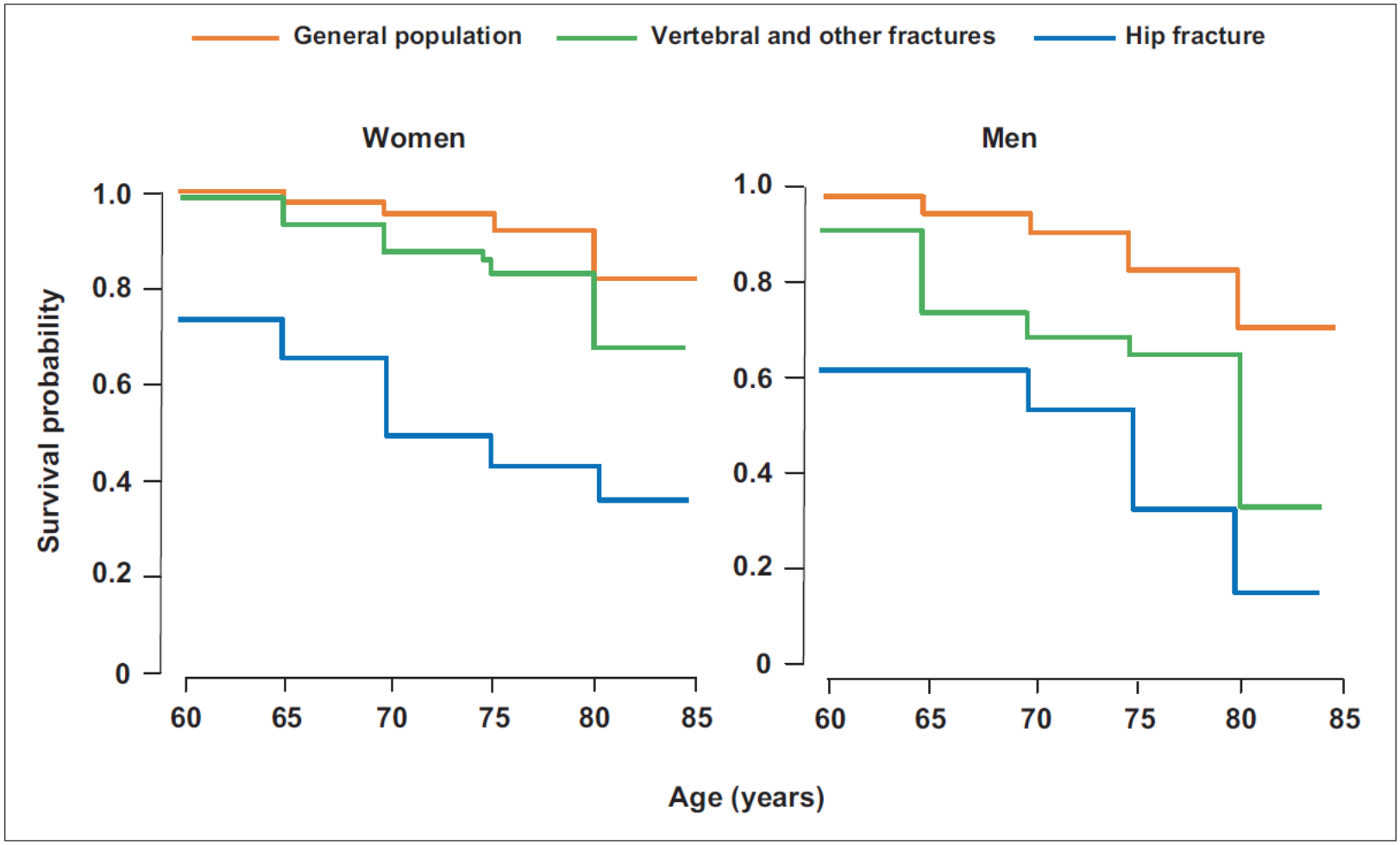


Fig. 1. Mortality following fracture in men and women.[4] Reprinted from Center JR, Nguyen TV, Schneider D, Sambrook PN, Eisman JA. Mortality after all major types of osteoporotic fracture in men and women: An observational study. *Lancet* 1999;353:878-82. Copyright ©1999 with permission from Elsevier.

Can Urol Assoc J 2014;8(7-8):S156-8

Osteonecrosis of Jaw

- Can occur with bisphosphonates and denosumab
- Journal Article
  - J Oral Maxillofac Surg. 2012 Aug;70(8):1844-53
  - 30 patients with osteonecrosis of the jaw
    - Preceding: dental extraction 17, trauma 3, none 10
    - 83% healed by 3-52 months
    - Dental extraction average 18 mo, Trauma all by 12 mo
    - 57% with comorbidities: RA, steroids, DMARDs, diabetes
- Journal Article
  - Acta Otorrinolaringol Esp. 2014 Oct 9. pii: S0001-6519(14)00158-7. doi: 10.1016/j.otorri.2014.06.003. [Epub ahead of print
  - 70 patients with osteonecrosis of the Jaw
    - Mean time on bisphosphonates was 26.53 months
    - 25% with oral bisphosphonates, 75% IV bisphosphonate
    - 68% trigger identified, 48% dental extraction
    - Complete resolution in 58%, average time 16 months

Particular Circumstances

- Lack of response to bisphosphonates
- Drug Holiday
- After fracture – teriparatide (Forteo) favored
- Before surgery: spinal fusion, joint replacement: teriparatide favored
- Dental Extractions planned: favor teriparatide
- Monoclonal Gammopathy – avoid teriparatide (Forteo)
- Metastatic Cancer: avoid teriparatide
- Hyperparathyroidism: avoid teriparatide
- Chronic kidney disease: depends on eGFR
- End stage renal disease: favor denosumab (Prolia)

Particular Circumstances

- Atypical fracture: favor teriparatide (Forteo)
- AVN of Jaw: favor teriparatide (Forteo)

Review

- 1. 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. DEXA 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 mulitple risk factors, patients on steroids, anti-estrogen, and anti-testosterone therapy with abnormal bone densities (T score <-1).

Case 1

- 35 year old female with family history of mother with osteoporosis (mother just had hip fracture at age 70).
- She does not have prior steroid use, PPI use, rheumatoid arthritis, tobacco or alcohol.
- She had fracture of clavicle during high impact motor vehicle accident.
- DEXA scan was done after she requested it when her mother had recent fracture.
- Z score was -2.6
- What is the next step?

Case 1

- Check for causes of low bone density
  - Check routine labs including CMP and 25-OH Vit D.
  - Check urinary calcium excretion
    - Can use low dose hydrochlorthiazide if high
  - Check for problems with absorption
    - Such as IBD or Celiac Disease
  - Consider 24 hour urine cortisol if cushingoid

Case 2

- 39 year old premenopausal female with history of lupus who has been on long courses of steroids and has had hip fracture after fall from standing position a year ago. She has chronically been on PPI for GI prophylaxis.
- She does not have family history of fracture/osteoporosis, rheumatoid arthritis, tobacco or alcohol.
- Labs: creatinine 0.9, Calcium normal, 25-OH Vit D 15
- DEXA scan with Z score of -3.5 at spine and -3.3 at hip.
- What are the next steps?

Case 2

- Replace Vitamin D
  - 50,000 units weekly for 8-12 weeks, then 1000-2000 units/day
- Advise Calcium 1000-1400 mg daily (supplement + diet)
- Discuss plans regarding pregnancy in the next 5-10 years
  - If no plans for pregnancy consider bisphosphonate
  - If plan for pregancy consider teriparatide vs denosumab
- Teriparatide may be worth considering as initial treatment to increase bone density given several fractures

Case 3

- 75 year old female with multiple myeloma who has had multiple compression fractures and was on alendronate for 5 years, then off for 3 years; she had a hip fracture 10 months ago.
- She has family history of fracture and bone density shows decline in T score compared to prior 2 years ago.
- DEXA scan with T-score of -3.6 at lumbar spine and -2.9 at femoral neck.
- Creatinine 0.7, 25-Vit D 55, calcium normal, PTH normal
- What is the next step?

Case 3

- Restart osteoporosis treatment with denosumab (Prolia) since the patient is having ongoing fractures and has decreasing bone density.
- Avoid Teriparatide given diagnosis of multiple myeloma.

Case 4

- 80 year old male with end stage kidney disease with osteoporosis with T score of -3.1 at lumbar spine and -2.9 at femoral neck.
- He has kyphosis with vertebral compression fractures on x-ray of thoracic spine.
- Estimated GFR 20, 25-OH-Vit D 40, calcium normal, PTH mildly elevated.
- What is the treatment choice?

Case 4

- Denosumab (Prolia)
- Cannot use bisphosphonates given low eGFR.
- Avoid Teriparatide given elevated PTH
- For men, in general would be worth to check testosterone level and consider replacement therapy.

Case 5

- 70 year old female with osteoporosis with T score of -2.1 at lumbar spine and -2.6 at femoral neck.
- She has not had any fractures and does not have any other risk factors; no history of tumors.
- She does have frequent falls
- FRAX with 10 year hip fracture risk of 3.6%
- Labs with creatinine 0.9, vitamin D 8, normal calcium, elevated PTH
- What is the treatment?

Case 5

- Replete vitamin D since it is low
- Elevated PTH is likely secondary to low vitamin D level
- Bisphosphonates would generally be treatment of choice in this case.

References

- Up to Date
- Pelaz A, et al. Acta Otorrinolaringol Esp. 2014 Oct 9. pii: S0001-6519(14)00158-7. doi: 10.1016/j.otorri.2014.06.003. [Epub ahead of print]
- Oryan FS. J Oral Maxillofac Surg. 2012 Aug;70(8):1844-53
- Drake MT. Mayo Clin Proc. Bisphosphonates: Mechanism of Action and Role in Clinical Practice. 2008; 83(9): 1032-1045
- 2014 Clinician's Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis Foundation

Risk factors for Osteoporosis

Lifestyle factors		
Alcohol abuse	Excessive thinness	Excess Vitamin A
Frequent falling	High salt intake	Immobilization
Inadequate physical activity	Low calcium intake	Smoking (active or passive)
Vitamin D insufficiency		
Genetic diseases		
Cystic fibrosis	Ehlers-Danlos	Gaucher's disease
Glycogen storage diseases	Hemochromatosis	Homocystinuria
Hypophosphatasia	Marfan syndrome	Menkes steely hair syndrome
Osteogenesis imperfecta	Parental history of hip fracture	Porphyria
Riley-Day syndrome		

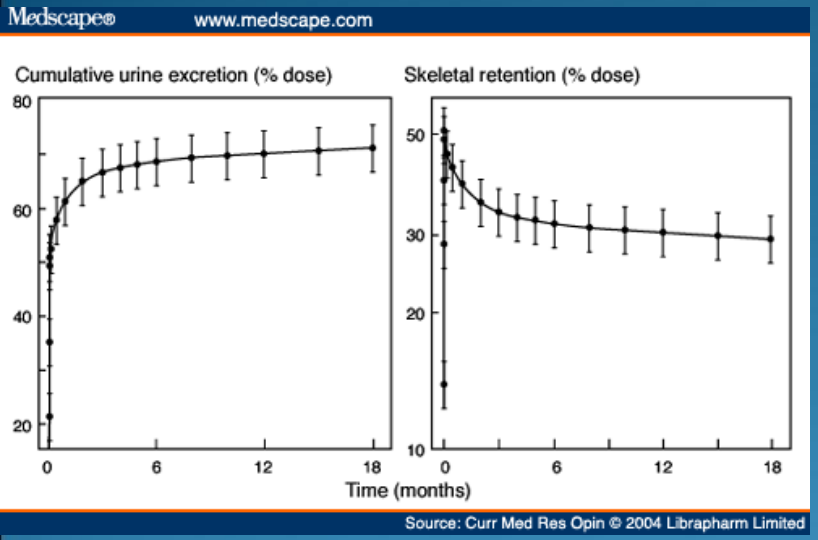
National Osteoporosis Foundation

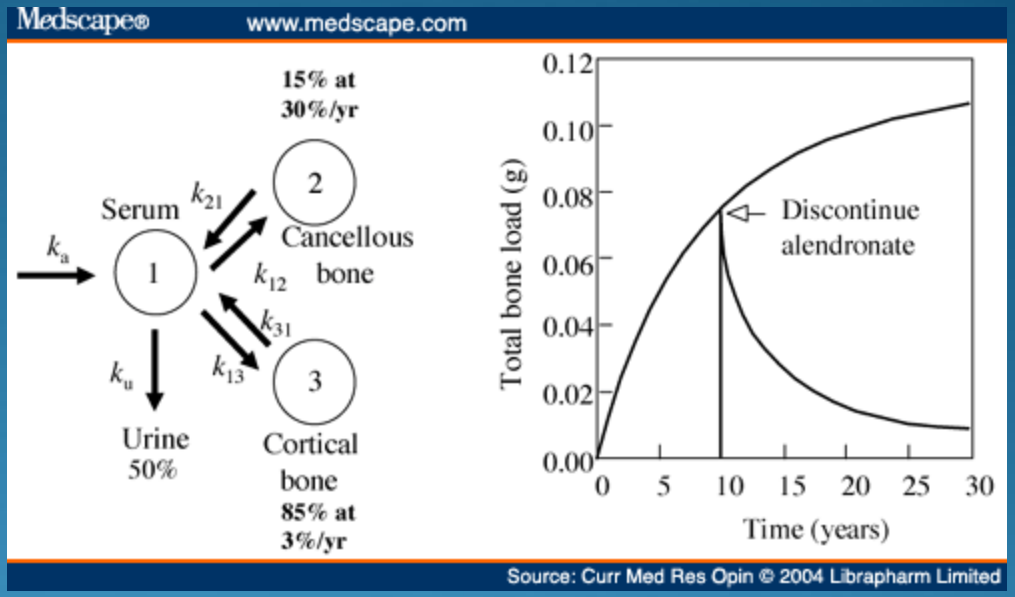
TABLE 1: Conditions, Diseases and Medications That Cause or Contribute to Osteoporosis and Fractures *(Continued)*

Hypogonadal states		
Androgen insensitivity	Anorexia nervosa	Athletic amenorrhea
Hyperprolactinemia	Panhypopituitarism	Premature menopause (<45 yrs)
Turner's & Klinefelter's syndromes		
Endocrine disorders		
Central obesity	Cushing's syndrome	Diabetes mellitus (Types 1 & 2)
Hyperparathyroidism	Thyrotoxicosis	
Gastrointestinal disorders		
Celiac disease	Gastric bypass	Gastrointestinal surgery
Inflammatory bowel disease	Malabsorption	Pancreatic disease
Primary biliary cirrhosis		
Hematologic disorders		
Hemophilia	Leukemia and lymphomas	Monoclonal gammopathies
Multiple myeloma	Sickle cell disease	Systemic mastocytosis
Thalassemia		
Rheumatologic and autoimmune diseases		
Ankylosing spondylitis	Other rheumatic and autoimmune diseases	
Rheumatoid arthritis	Systemic lupus	
Neurological and musculoskeletal risk factors		
Epilepsy	Multiple sclerosis	Muscular dystrophy
Parkinson's disease	Spinal cord injury	Stroke
Miscellaneous conditions and diseases		
AIDS/HIV	Alcoholism	Amyloidosis
Chronic metabolic acidosis	Chronic obstructive lung disease	Congestive heart failure
Depression	End stage renal disease	Hypercalciuria
Idiopathic scoliosis	Post-transplant bone disease	Sarcoidosis
Weight loss		
Medications		
Aluminum (in antacids)	Anticoagulants (heparin)	Anticonvulsants
Aromatase inhibitors	Barbiturates	Cancer chemotherapeutic drugs
Depo-medroxyprogesterone (premenopausal contraception)	Glucocorticoids (≥ 5 mg/d prednisone or equivalent for ≥ 3 months)	GnRH (Gonadotropin releasing hormone) agonists
Lithium Cyclosporine A and tacrolimus	Methotrexate	Parental nutrition
Proton pump inhibitors	Selective serotonin reuptake inhibitors	
Tamoxifen® (premenopausal use)	Thiazolidinediones (such as Actos® and Avandia®)	Thyroid hormones (in excess)

From: The Surgeon General's Report[1], with modification

Response to therapy





Alendronate

Bone 49 (2011) 42–49

- Medscape: Long Term Safety of bisphosphonates
- http://www.medscape.com/viewarticle/489616_print

Post Quiz

Question 1 of 5

Who needs to be treated for osteoporosis? (Choose one)
T-score between -1.00 to -2.5 at femoral neck, total hip or spine **AND** a FRAX score showing 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20% (FRAX)

a) 10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 20%

b) 10-yr probability of hip fracture ≥ 2% or any major osteoporosis-related fracture ≥ 10%

c) 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 20%

d) 10-yr probability of hip fracture ≥ 3% or any major osteoporosis-related fracture ≥ 30%

Post Quiz

Question 2 of 5

Which of the following may be interpreted as improved state of bone turnover after treatment for osteoporosis? (Choose one)

a) A T-score of -1.5 in the spine

b) Suppression of urine NTX

c) Improved DXA acquired BMD in both spine and femoral neck regions

d) Suppressed levels of bone formation and resorption markers

Post Quiz

Question 3 of 5

Which of the following would indicate treatment failure, or need to consider alternate treatment for osteoporosis?

a) BMD improved 1% since last DXA done 2 years ago
b) Fracture of femoral shaft while being treated with bisphosphonate for 5 years
c) Increased levels of bone markers since last measure a year ago
d) Femoral neck BMD did not change since last DXA 2 years ago

Post Quiz

Question 4 of 5

An 80 year old Caucasian woman with dementia, falls and right hip fracture (1 year ago) while being on bisphosphonate, was referred for evaluation and treatment of osteoporosis. She had a mastectomy, followed by chemotherapy for breast cancer at age 66 and has been cancer free since then. Which of the following would be the best treatment option for her at this time? (Choose one)

a) Ibandronate
b) Calcitonin
c) Teriparatide
d) Denosumab

Post Quiz

Question 5 of 5

Selective Estrogen Receptor Modulator (SERM) is one of the first options for osteoporosis treatment.

a) True

b) False

Osteoporosis Educational Series:

Diagnosis and Management of Osteoporosis in Adults:

Thank you

Egyptian Academy of Bone Health
and Metabolic Bone Diseases