

Osteoporosis: An Overview

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Definition of Postmenopausal Osteoporosis

- Postmenopausal osteoporosis is defined as a (silent) skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.

Osteoporosis is Silent Unless a Fracture Happens



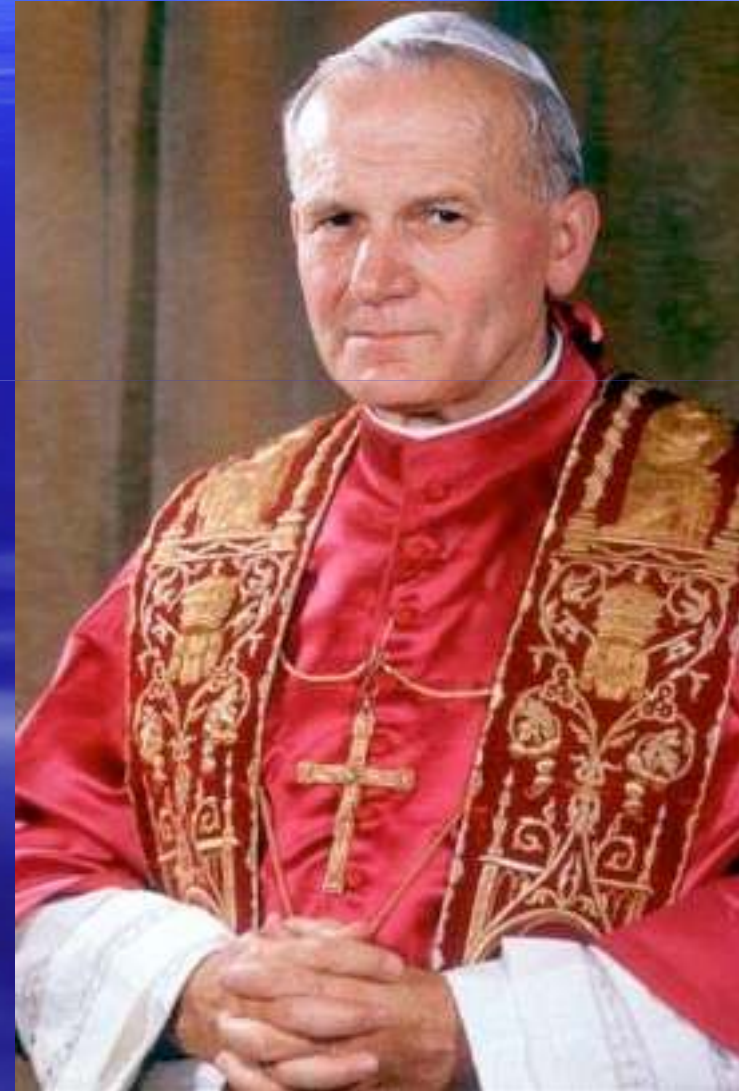
World Health Organization Criteria for Classification of Osteopenia and Osteoporosis

Category	T Score
Normal	Above -1
Low bone density (osteopenia)	Between -1 and -2.4
Osteoporosis	-2.5 or below

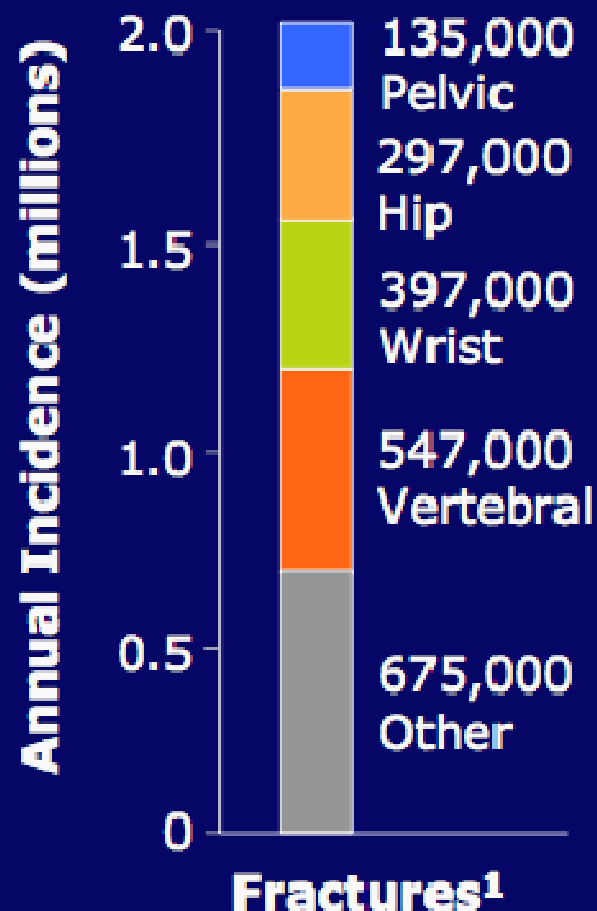
Osteoporosis is a Disease of both Women and Men



Photo courtesy of David Kennerly



Each Year, Americans Experience Over 2 Million Osteoporosis-Related Fractures



- ▶ 50% of women, and 25% of men >50 years old will experience OP-related fracture in their remaining lifetime¹
- ▶ In the year following vertebral fracture, 26% of patients will fracture hip, pelvis, vertebrae, wrist, humerus, or leg²
- ▶ Hip fractures associated with¹:
 - Increased risk of mortality in year following fracture, due to complications
 - Loss of ambulatory status in 15% of patients; 20% of previously ambulatory patients require long-term care
- ▶ Women with hip fracture are at four-fold greater risk of a second hip fracture¹

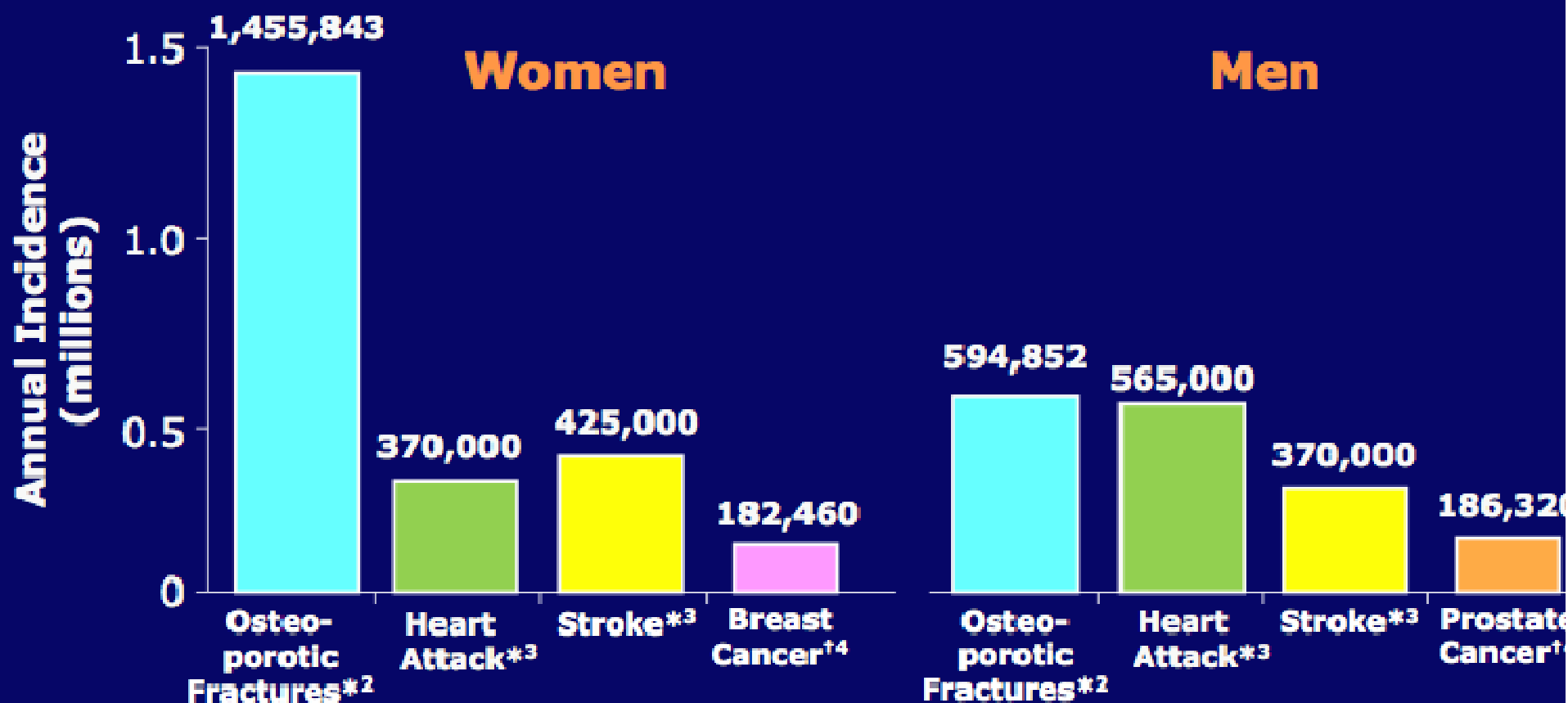
OP = osteoporosis.

1. National Osteoporosis Foundation. *Fast Facts on Osteoporosis*. National Osteoporosis Foundation, Washington, DC. Feb 2008.

2. Lindsay R, et al. *Osteoporos Int*. 2005;16:78-85.

Annual Incidence of Osteoporosis-Related Fractures Higher Than Other Common Diseases

- ▶ 44 million Americans have low bone mass, including 10 million with established osteoporosis. Of these, 80% are women.¹



*New and recurrent cases. †New cases only.

1. National Osteoporosis Foundation. *Fast Facts on Osteoporosis*. National Osteoporosis Foundation, Washington, DC. Feb 2008.

2. Burge R, et al. *J Bone Miner Res*. 2007;22:465-475. 3. Lloyd-Jones D, et al. *Circulation*. 2009;119:e1-e161. 4. American Cancer Society. *Cancer Facts & Figures 2008*. American Cancer Society, Atlanta, Ga. 2008.

Who Needs to Be Screened for Osteoporosis?

- Women 65 years old or older
- men ≥ 70 years
- Younger postmenopausal women or men 50-70 years with risk factors (family history, steroid use, smoking, heavy ETOH use, ...)
- Women or men who have experienced a fracture
- Starting or taking long-term systemic glucocorticoid therapy (3 months or longer)

How Is Osteoporosis Diagnosed?

- Use a central dual-energy x-ray absorptiometry (DXA) measurement
- In the absence of fracture, osteoporosis is defined as a T-score of -2.5 or below in the spine (anteroposterior), **femoral neck**, or total hip
- Osteoporosis is defined as the presence of a fracture of the hip or spine (in the absence of other bone conditions)

Pearls

- Maintain adequate vitamin D intake; supplement vitamin D, if needed, to maintain serum levels of 25-hydroxyvitamin D [25(OH)D] between 30 and 60 ng/mL
- Limit alcohol intake to no more than 2 servings per day
- Limit caffeine intake
- Avoid or stop smoking

What Non-pharmacologic Measures Can Be Recommended for Treatment of Osteoporosis?

- All the foregoing measures plus the following:
- Maintain adequate protein intake
- Consider the use of hip protectors in individuals with a high risk of falling
- Take measures to reduce the risk of falling
- Consider referral for physical therapy and occupational therapy

Who Needs Pharmacologic Therapy?

- Those patients with a history of a fracture of the hip or spine
- Patients without a history of fractures but with a T-score of -2.5 or lower
- Patients with a T-score between -1.0 and -2.5 if **FRAX** major osteoporotic fracture probability is $\geq 20\%$ or hip fracture probability is $\geq 3\%$

Using the FRAX® Tool to Help Determine Fracture Risk in Treatment-Naïve Patients With Low Bone Mass

<http://www.shef.ac.uk/FRAX/>

- ▶ FRAX is a tool to help determine 10-year fracture risk in treatment-naïve patients with low bone mass
- ▶ Takes into account BMD and specific risk factors
- ▶ Identifies the high-risk patients who could benefit from treatment
- ▶ NOF recommends intervention based on 10-year fracture risk¹:
 - Major osteoporotic fracture: $\geq 20\%$
 - Hip fracture: $\geq 3\%$
- ▶ Clinical judgment remains the critical element

The screenshot shows the FRAX questionnaire interface. At the top, there are fields for 'Country : UK' and 'Name / ID :'. A link 'About the risk factors' with an information icon is on the right. The main section is titled 'Questionnaire:' and contains 12 numbered questions. Questions 1-4 are demographic: 1. Age (between 40-90 years) or Date of birth (with sub-fields for Age, Y, M, D); 2. Sex (Male/Female); 3. Weight (kg); 4. Height (cm). Questions 5-12 are clinical: 5. Previous fracture; 6. Parent fractured hip; 7. Current smoking; 8. Glucocorticoids; 9. Rheumatoid arthritis; 10. Secondary osteoporosis; 11. Alcohol 3 or more units per day; 12. Femoral neck BMD (g/cm²). A dropdown menu for 'Select DXA' is open, showing options: 'Select DXA', 'GE-Lunar', 'Hologic', 'Norland', and 'T-Score'. A 'Calculate' button is visible at the bottom right.

What Drugs Can Be Used to Treat Osteoporosis?



What Drugs Can Be Used to Treat Osteoporosis?

- Use drugs with proven antifracture efficacy: Use alendronate (Fosomax) , risedronate (Actonel), zoledronic acid (Reclast), and denosumab (Prolia) as the first line of therapy
- Use ibandronate (Boniva) as a second-line agent
- Use raloxifene (Evista) as a second- or third-line agent
- Use calcitonin as the last line of therapy (Or in case of Painful spine Fracture)
- Use teriparatide (Forteo) for patients with very high fracture risk or patients in whom bisphosphonate therapy has failed
- Advise against the use of combination therapy

How Is Treatment Monitored?

- Obtain a baseline DXA, and repeat DXA ever 1 to 2 years until findings are stable. Continue with follow-up DXA every 2 years or at a less frequent interval
- Follow-up of patients should be in the same facility, with the same machine, and, if possible, with the same technologist
- Bone turnover markers may be used at baseline to identify patients with high bone turnover and can be used to follow the response to therapy

What Is Successful Treatment of Osteoporosis?

- BMD is stable or increasing, and no fractures are present
- For patients taking antiresorptive agents, bone turnover markers at or below the median value for premenopausal women are achieved
- *One fracture is not necessarily evidence of failure*
- Consider alternative therapy or reassessment for secondary causes of bone loss for patients who have recurrent fractures while receiving therapy

How Long Should Patients Be Treated?

- For treatment with bisphosphonates, if osteoporosis is mild, consider a “drug holiday” after 4 to 5 years of stability.
- If fracture risk is high, consider a drug holiday of 1 to 2 years after 10 years of treatment.
- Follow BMD and bone turnover markers during a drug holiday period, and reinstitute therapy if bone density declines substantially, bone turnover markers increase, or a fracture occurs

When Should Patients Be Referred? Endocrinologists?

- When a patient with normal BMD sustains a fracture without major trauma
- When recurrent fractures or continued bone loss occurs in a patient receiving therapy without obvious treatable causes of bone loss
- When a patient has a condition that complicates management (for example, renal failure, hyperparathyroidism, or malabsorption)

Some Measures for Prevention of Falls

- Anchor rugs
- Remove loose wires
- Use nonskid mats
- Install handrails
- Light hallways, stairways, and entrances
- Low heel shoes
- Hip protectors for patients who are predisposed to falling

Laboratory Tests to Consider in Screening for Secondary Osteoporosis

- Complete blood cell count
- COMP
- 24 hour urine collection for calcium
- Serum 25-hydroxyvitamin D
- ?cortisol

Some Causes of Secondary Osteoporosis

- **Endocrine disorders:** acromegaly, diabetes, PHPT, *Hypogonadism*.
- **Nutritional:** *alcoholism*, anorexia nervosa, chronic liver disease, Vitamin D deficiency, Malabsorption
- **Medicines:** glucocorticoids, antiepileptics, chemotherapy
- **Rare Disorders** (of the collagen metabolism): osteogenesis imperfecta, Marfan, Ehlers-Danlos
- HIV

Drugs Approved by the FDA for Prevention and Treatment of Osteoporosis

Drug	Postmenopausal osteoporosis		Glucocorticoid-induced osteoporosis		In men
	Prevention	Treatment	Prevention	Treatment	
Estrogen (multiple formulations)	Multiple regimens
Calcitonin (Miacalcin, Fortical)	...	200 IU intranasally once daily, or 100 IU SQ qod
Denosumab (Prolia)	...	60 mg SQ every 6 mo
Raloxifene (Evista)	60 mg PO daily	60 mg PO daily
Ibandronate (Boniva)	2.5 mg PO daily 150 mg PO monthly	2.5 mg PO daily 150 mg PO monthly 3 mg IV every 3 mo
Alendronate (Fosamax)	5 mg PO daily 35 mg PO weekly	10 mg PO daily 70 mg PO weekly ^b 70 mg + D ^c	...	5 mg PO daily ^d 10 mg PO daily ^e	10 mg PO daily 70 mg PO weekly
Risedronate (Actonel)	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily	5 mg PO daily	35 mg PO weekly 150 mg PO monthly
Zoledronic acid (Reclast)	5 mg IV every 2nd y	5 mg IV once yearly	5 mg IV once yearly	5 mg IV once yearly	5 mg IV once yearly
Teriparatide (Forteo)	...	20 µg SQ daily	...	20 µg SQ daily	20 µg SQ daily

Summary of Evidence for Fracture Risk Reduction

Drug	Fracture risk reduction		
	Vertebral	Nonvertebral	Hip
Calcitonin (Miacalcin, Fortical)	Yes	No effect demonstrated ^a	No effect demonstrated ^a
Raloxifene (Evista)	Yes	No effect demonstrated ^a	No effect demonstrated ^a
Ibandronate (Boniva)	Yes	No effect demonstrated ^a	No effect demonstrated ^a
Alendronate (Fosamax)	Yes	Yes	Yes
Risedronate (Actonel)	Yes	Yes	Yes
Zoledronic acid (Reclast)	Yes	Yes	Yes
Denosumab (Prolia)	Yes	Yes	Yes
Teriparatide (Forteo)	Yes	Yes	No effect demonstrated ^a

^a The lack of demonstrable effect at these sites should be considered in the context that the studies may not have been adequately powered.

Bisphosphonates

- Fosamax, Actonel, Boniva, or Reclast
- Oral intake or IV
- The most widely used drugs for treatment of osteoporosis
- Contraindicated in advanced renal disease
- Fosamax has been studied in trials up to 10 years
- Rare: ONJ, subtrochanteric fracture

Others

-
- ***Teriparatide (Forteo)*** for patients with very high fracture risk or patients in whom bisphosphonate therapy has failed
- Has a black box warning (osteosarcoma in rats)
- Treatment is only for 2 years
- Don't use if PHPT, history of Osteosarcoma, or H/O radiation tx
- ***Denosumab (Prolia)*** is considered first line tx by the AACE
- Serious infections may occur

Surgical Treatment of Osteoporotic Fractures

- Vertebroplasty and Kyphoplasty for vertebral fx for pain relief
- They involve percutaneous injection of bone cement under into a collapsed vertebra.
- Kyphoplasty also involves the introduction of inflatable bone tamps into the fractured vertebral body prior to fixation of the fracture with bone cement
- Kyphoplasty may help reversal of the vertebral deformity
- Both may increase the risk of vertebral fx in the adjacent vertebrae.

FDA Hearing on Bisphosphonates

- On September 9, 2011, the FDA reviewed the long term safety and efficacy of all approved bisphosphonates
- Safety concerns discussed included esophageal cancer, osteonecrosis of the jaw (ONJ) and atypical fractures of the femur.
- The panel voted 17 to 6 for a change in the label
- the FDA is not required to follow the advice of their advisory panels
- AACE therefore recommends to maintain current practice until the FDA publishes its final ruling