# Osteoporosis Treatment and Diagnosis

Jan, 2016

**Shawn Baca, M.D., F.A.C.R.**

Rheumatology Associates of South Florida RASF
RASF Clinical Research

Osteoporosis Diagnosis and Treatment Center of South Florida

Voluntary Clinical Associate Professor, Schmidt
School of Medicine at Florida Atlantic University

President Elect Palm Beach County Medical Society

Boca Raton, Florida

# Disclosures

None regarding this talk

# OBJECTIVES

- Medical impact of osteoporosis
- Define Osteoporosis and the risk factors associated with it
- Treatment and prevention of osteoporosis
- Controversies in osteoporosis management

# Definition of Osteoporosis

"Osteoporosis is defined as a skeletal disorder characterized by compromised *bone strength* predisposing to an increased risk of fracture."

***Bone strength = bone density + bone quality***

***Bone density:*** grams of mineral/ volume

***Bone quality:*** architecture, turnover, damage accumulation, and mineralization

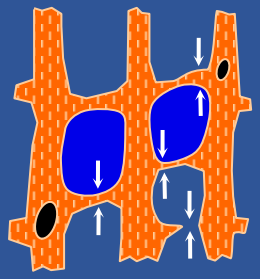
NIH Consensus Development Conference on Osteoporosis, 2000.

# Osteoporosis: Conceptual Definition

**20 years**

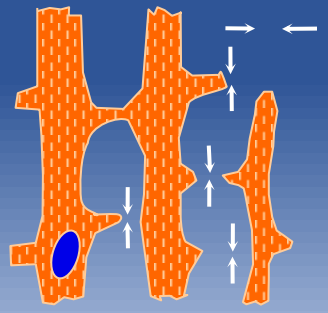
**Normal Bone**

**50 years**



**Decrease in connections and thickness of horizontal trabeculae.**

**80 years**



**Decrease in trabecular strength and increased susceptibility to fracture.**

Mosekilde L. *Calcif Tissue Int* 1993,53(Suppl 1): S121-S126.

# Structure

## Composition

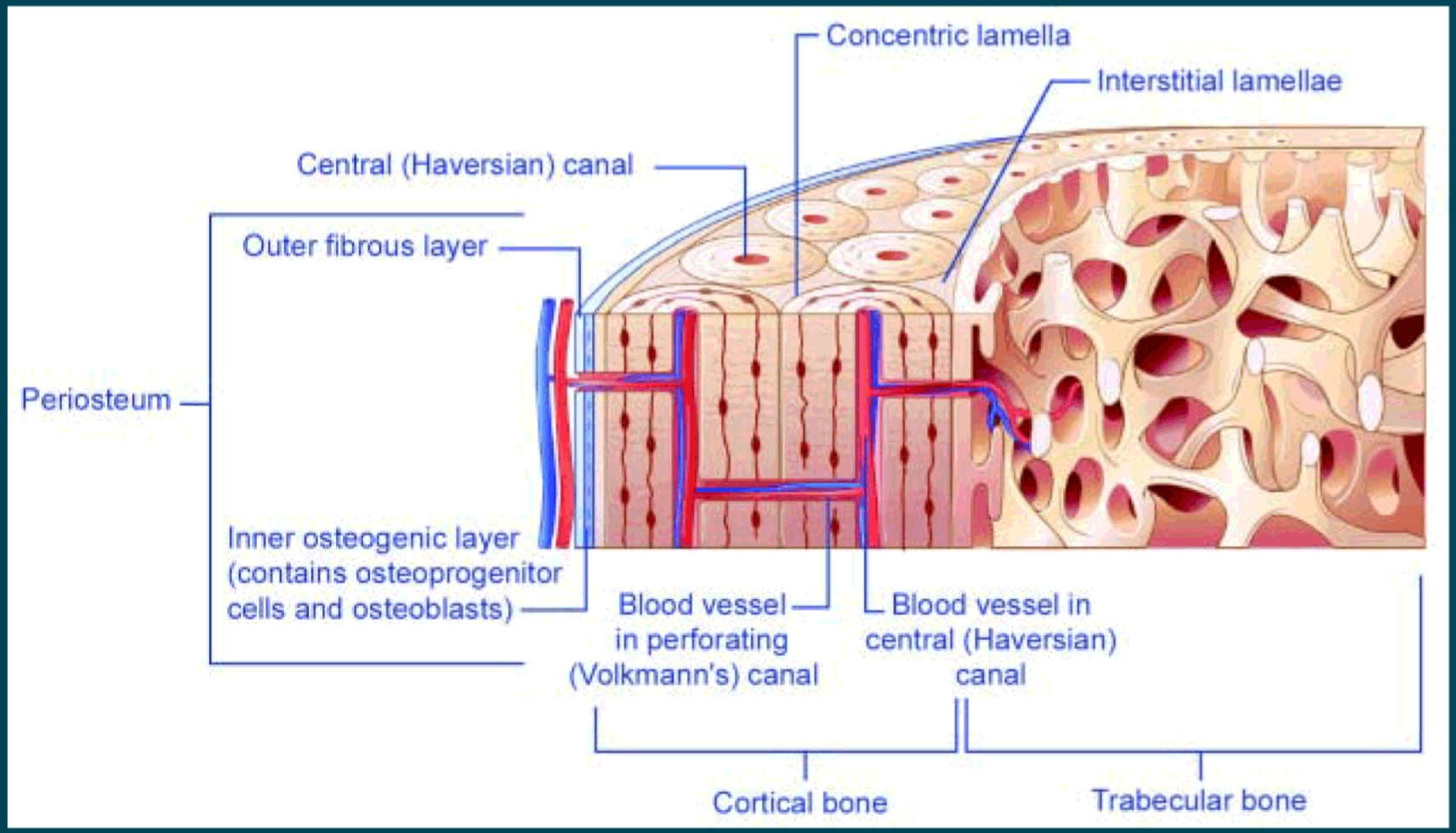
**Organic:** 90 % type 1 collagen and contains osteoclasts and osteoblasts.

**Inorganic:** 2/3 of mass and is composed of hydroxyapatite

**Cortical bone:** Outside portion that provides 80 percent of mass and responsible for strength and rigidity of bone. Contains Haversian Canals that carry blood and nutrients

**Trabecular bone:** Internal spongy bone that provides flexibility of bone and production of hematopoietic cells

# Microscopic Bone Structure: Cross Section of Bone

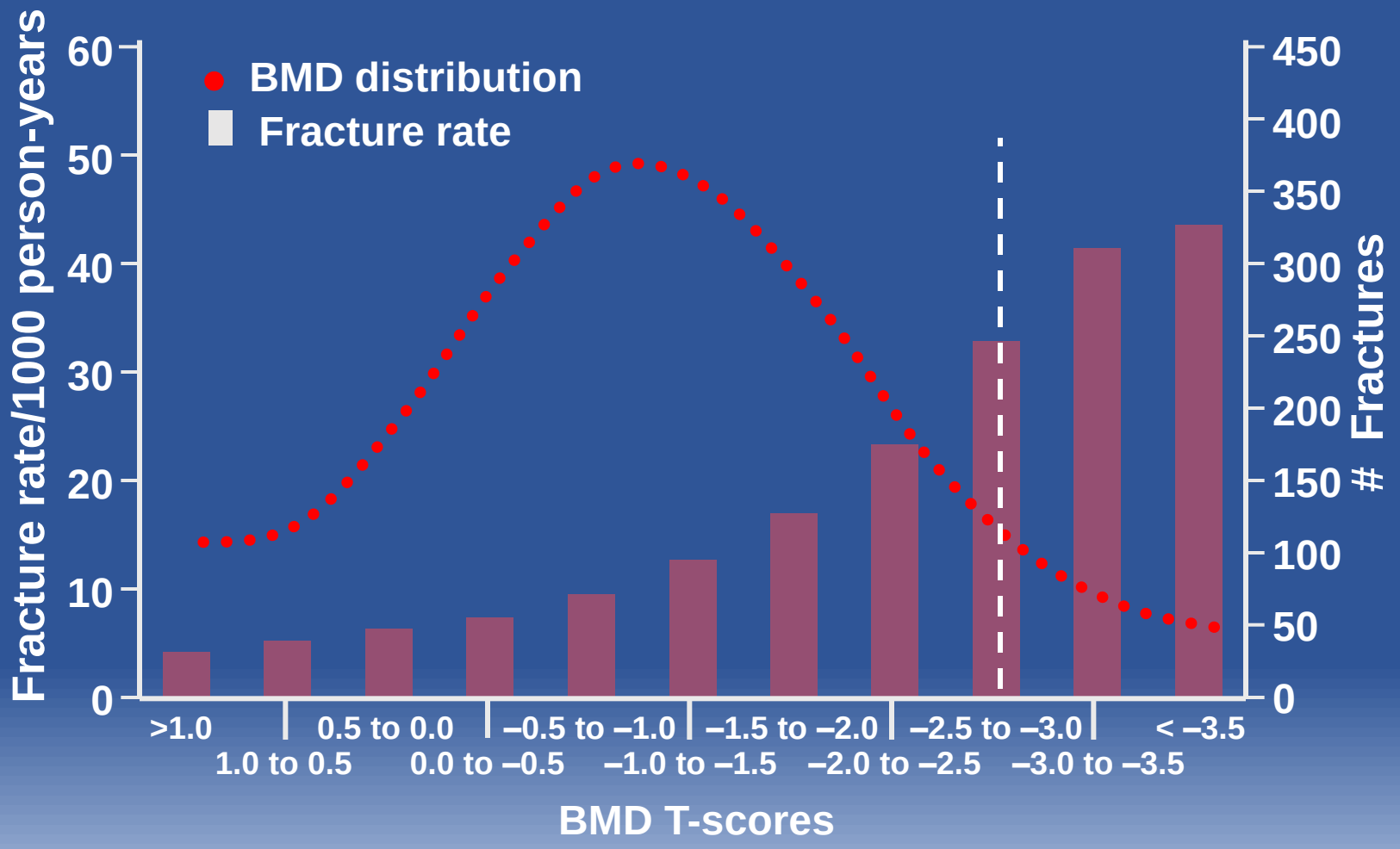


# NORA: Summary

- Lower BMD in the NORA population is associated with higher fracture rate but in addition
  - 50% of osteoporosis fractures occurred in women with T-scores above –2.5
  - Failure to evaluate these women for preventive treatment adds to the societal cost of osteoporosis

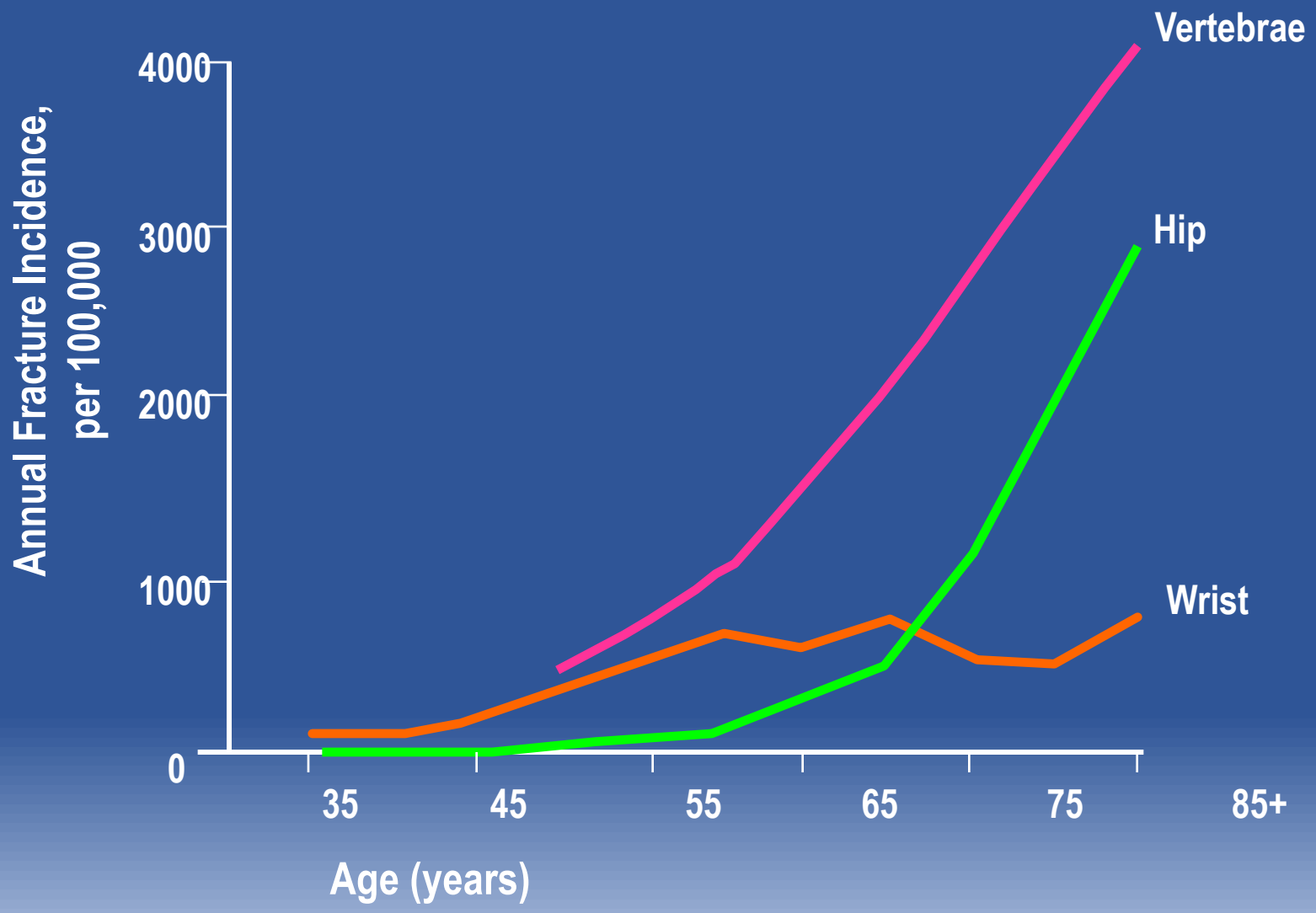
Siris ES, et al. *J Bone Miner Res*. 2001;16:S337.
Siris ES et al., JAMA 2001; 286:2815-22.

# NORA: Fracture Rates




Adapted from Siris ES et al., JAMA 2001;286:2815-22.

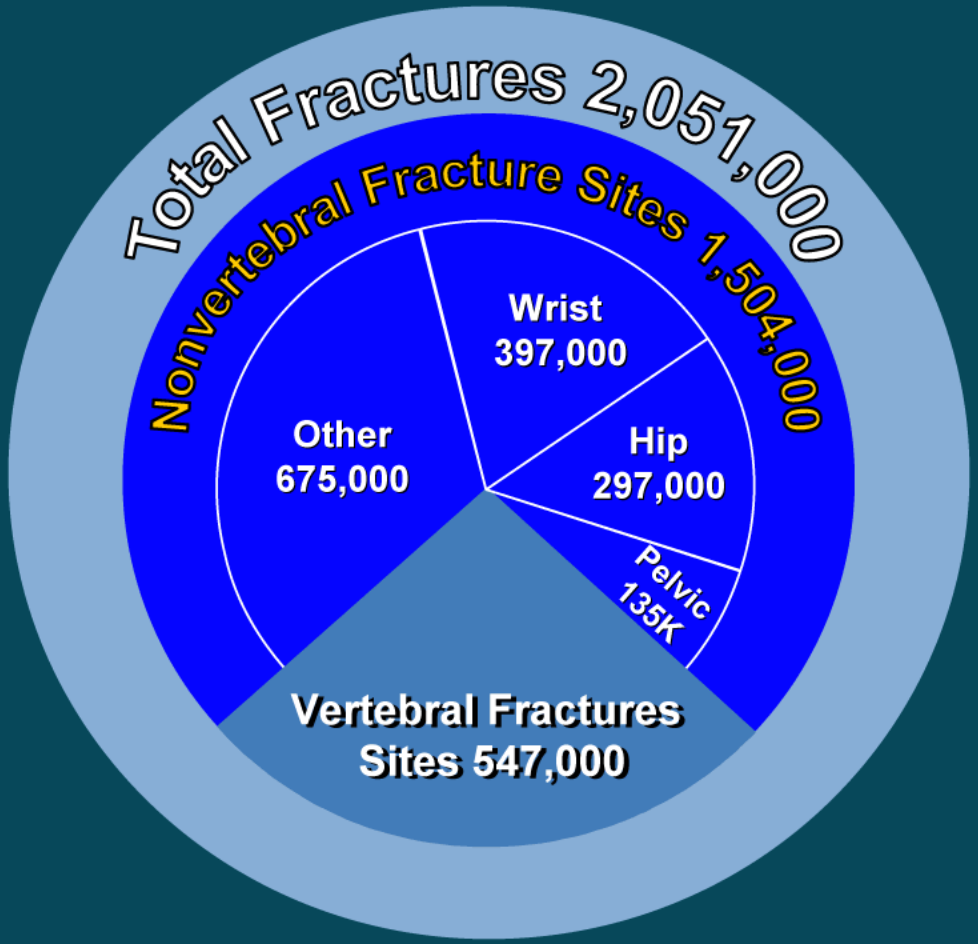
# Age and Fracture Rates




Riggs B. N Engl J Med 1986;314:1676

# Medical and Societal Impact of Osteoporosis

# Estimated Annual Incidence of Osteoporosis-Related Fractures in Women and Men




Values are from 2005 estimates.

Fast Facts on Osteoporosis. NOF Website. At: www.nof.org/osteoporosis/diseasefacts.htm.

# Incidence

- NOF has estimated that more than 10 million Americans have osteoporosis and
- an additional 33.6 million have low bone density of the hip.
- About one out of every two Caucasian women will experience an osteoporosis-related fracture at some point in her lifetime
- Approximately one in five men

US Department of Health and Human Services. *Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville, MD: US* Department of Health and Human Services, Office of the Surgeon General; 2004.

# Economic Toll of Osteoporosis-related fractures

- 432,000 hospital admissions
- 2.5 million medical office visits
- 180,000 nursing home admissions annually in the US
- The cost osteoporosis-related fractures has been estimated at $17 billion for 2005 and 25.3 billion in 2025. [1]

*1. J Bone Min Res. 2007;22(3):465-475.*

# Medical Impact of Osteoporosis

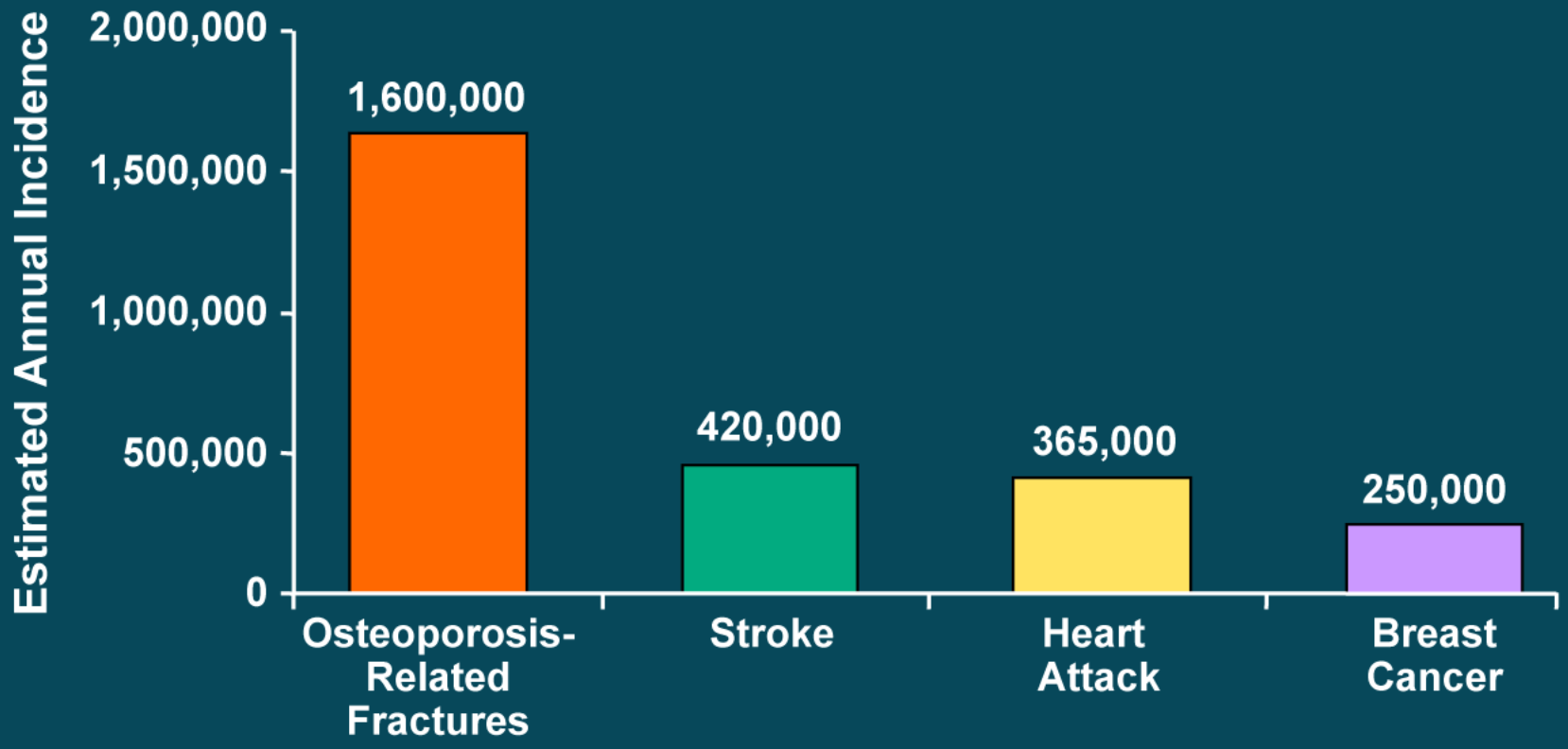
- Hip fractures result in 8 to 36 percent excess mortality within one year.
- Approximately 20 percent of hip fracture patients require long-term nursing home care, and only 40 percent fully regain their pre-fracture level of independence.
- Mortality is also increased following vertebral fractures

*Osteoporos Int. 2003;(14):879-883.*

# Medical Impact of Osteoporosis
continued

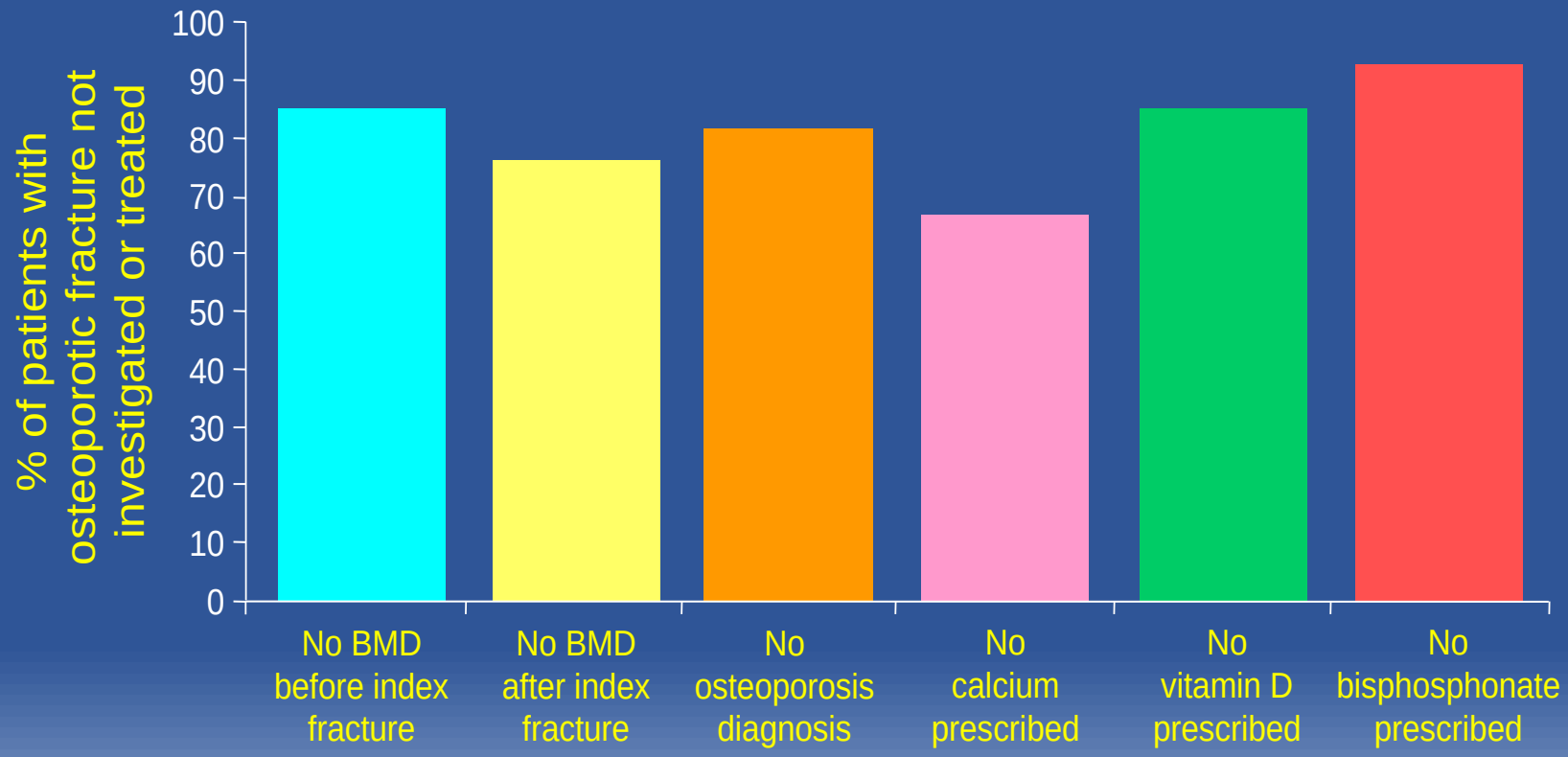
- Vertebral fractures can cause significant chronic complications including back pain, height loss and kyphosis, restrictive lung disease
- Lumbar fractures may alter abdominal anatomy, leading to constipation, abdominal pain, distention, reduced appetite and premature satiety.
- Wrist fractures can interfere with specific activities of daily living

# Osteoporosis-Related Fractures in Women Versus Other Diseases




Information from American Heart Association, American Cancer Society, and National Osteoporosis Foundation, 2008.

# Women With Osteoporotic Fractures Often Go Undiagnosed and Untreated




Data from Hajcsar EE, et al. *CMAJ*. 2000;163:819-822.

# Risk Factors Associated with Osteoporosis

# NOF Guidelines: Risk Factors

Major:

- Personal history of fracture as adult
- History of fracture in first-degree relative
- Low body weight (<127 lbs)
- Current smoking
- Oral steroid > 3 months

Additional:

- Impaired vision, early estrogen deficiency, dementia, frailty, recent falls, lifelong low calcium intake, low physical activity, alcohol (>2 drinks/day)

National Osteoporosis Foundation, 2003.

# Secondary Causes of Osteoporosis

Endocrine: Hyperparathyroidism (primary and secondary) Hyperthyroid (primary and iatrogenic), Hypogondism, elevated cortisol levels, androgen insensitivity

Hematologic: myeloma, thalassemia, mastocytosis, hemophila

Nutritional: Poor dietary calcium intake, poor dietary Vit D intake, excessive Vit D intake, excessive alcohol, excessive caffeine, eating disorders

Renal: renal bone diease, hypophosphatemia, hypercalciuria

Genetic: Osteogenesis imperfecta, Vit D resistance, Turners, Cystic Fibrosis, Glycogen Storage disease, hemochromatosis

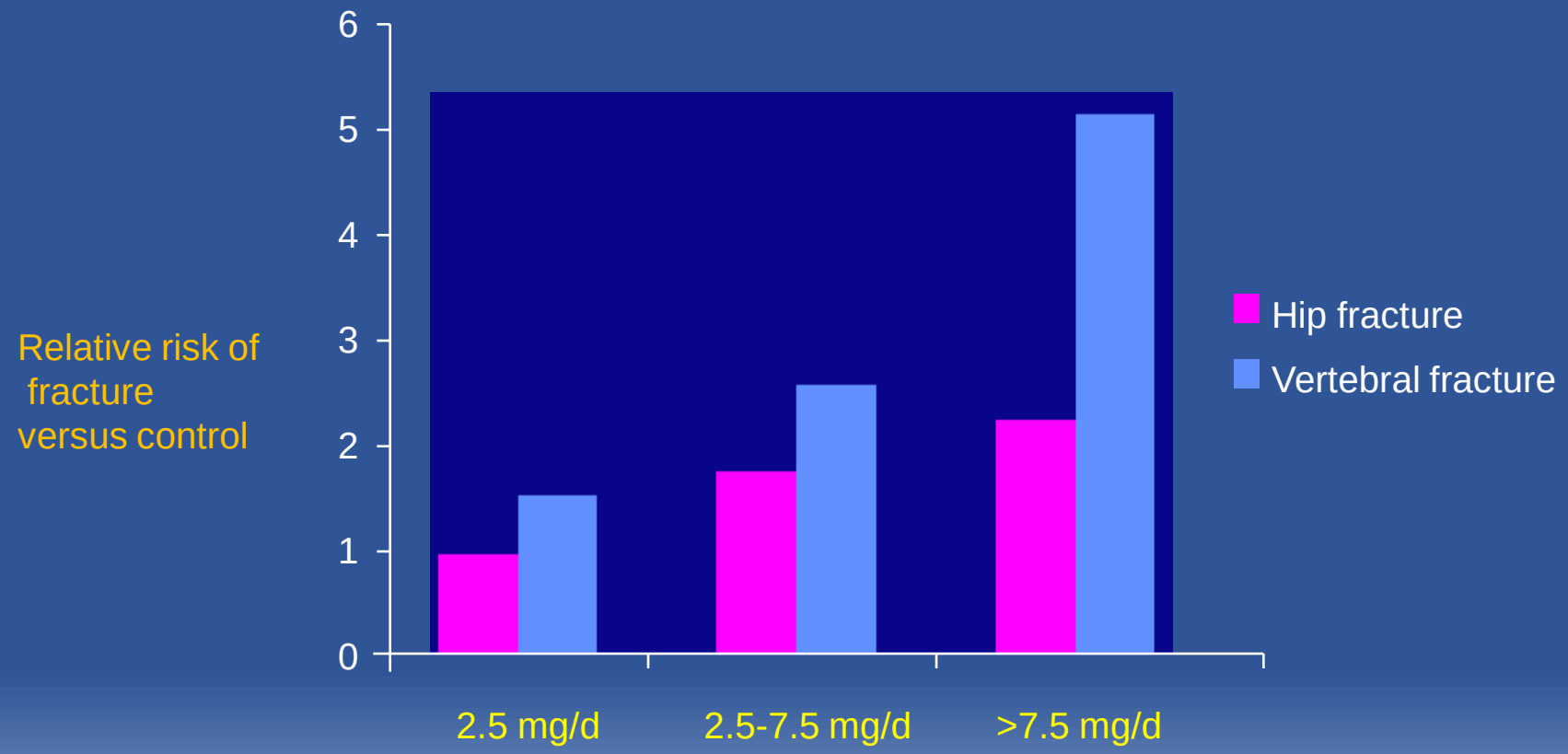
Rheumatic: poor weight bearing, chronic inflammation such as rheumatoid arthritis, spondylitis

Gastrointesinal: Celiac, Inflammatory bowel dis, PBC

# Medications Associated With Bone Loss

- Anticoagulants (heparin) and to less extent (coumadin)
- Cancer chemotherapeutic drugs
- Gonadotropin releasing hormone agonists
- Anticonvulsants
- Cyclosporine A and tacrolimus
- Lithium and Barbiturates
- Aromatase inhibitors
- Depo-medroxyprogesterone
- Glucocorticoids
- Excessive Thyroid Medication

# Fracture Risk and Dose of Glucocorticoids




Relative risk of fracture by dosages of glucocorticoids of prednisolone. van Staa TP, et al, 1998.

# Summary

- Quantifiable risk factors can be useful in identifying individual patient risk of vertebral and nonvertebral fracture

# DXA Testing: Who should we test?

NOF Clinicians Guide 2008

- Women age 65 and older and men age 70 and older

- In postmenopausal women and men age 50-69, recommend BMD testing if risk factors present

# Measurement of BMD

- T-score: the difference in standard deviation in a patient's BMD compared with peak bone mass in a young adult

**National Osteoporosis Foundation & World Health Organization* (T-score)**

| | |
|---|---|
| **Normal** | **-1.0 and above** |
| **Osteopenia** | **< -1.0 to > -2.5** |
| **Osteoporosis** | **-2.5 and below** |
| **Severe Osteoporosis** | **-2.5 and below w/fracture** |

* Physician's Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis Foundation, 1998

# T Score

- T score compares an individuals bone density to that of a normal young healthy adult population
- T score is  the measure used to describe an individuals diagnosis

# Z scores

- Z scores are used to compare a patients BMD within the same age group
- If a patient has a Z score that is substantially lower than 100 percent consider secondary causes of bone loss.

# Diagnosis

- If a patient has a site that is osteoporotic and a site that is osteopenic the diagnosis should be reported as osteoporosis.
- If a patient has had a fragility fracture and osteopenia they still are diagnosed w osteoporosis

# Hip Densities

- Femoral neck BMD is most predictive of fracture.
- Ward's triangle has the least clinical significance in determining fractures and should **not** be used in patient reports to determine fracture risk
- Total hip bmd should be used to compare between scans

# Lumbar spine densities

- Often have falsely higher results due to scoliosis, osteoarthritis or previous fractures.

# Follow up Scans

- Generally every two years but may need to be more frequent for certain clinical situations such as hyperparathyroidism or chronic glucocortiocosteriod treatment
- Can not directly compare scans of different manufactures
- Patients ***should be done on same machine*** for comparison even with same technology unless the same phantom is used for cross

  calibration

# NOF Guidelines

- Treat if patient had previous hip or vertebral fracture, clinical or morphometric
- Treat if t score <-2.5 total or femoral neck hip or spine DXA
- Treat in postmenopausal females or males with osteopenic t score total or femoral neck hip or spine DXA, and 10 year risk of fracture greater than 3 percent for hip and 20 percent for non vertebral fracture based on US adapted WHO absolute fracture risk model.

# FRAX Guidelines

- **PROs**
- **Takes other risk factors into consideration**
- **Addresses men**

- **CONS**
- **Devalues prevention and bases treatment on greater than 20 percent non vertebral, or 3 percent hip fracture rates over 10 years.**
- **Relies on use of the FRAX computer tool .**
- **Based on WHO cost containment**

**Country : US(Caucasian)** **Name / ID :** test patient About the risk factors

# Questionnaire:

1. Age (between 40-90 years) or Date of birth

   Age: 55 Date of birth: Y: M: D:

2. Sex ○ Male ◉ Female

3. Weight (kg) 65

4. Height (cm) 163

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

    T-score -2.1

Clear Calculate

BMI 24.5

**The ten year probability of fracture (%)**

**with BMD**

| | |
|---|---|
| Major osteoporotic | 18 |
| Hip fracture | 1.8 |

# Evaluating Patients With Low Bone Densities

# Tests used in Metabolic Evaluation of OP

- PTH intact
- 25, hydroxy vitamin D
- 24  hour urinary calcium
- SPEP
- Thyroid profile, Cortisol level
- Osteocalcin or BSAP, NTX or CTX
- Calcium, phosphorous, creatinine

# Discuss Lifestyle Issues

- Alcohol
- Smoking
- Exercise
- Diet
- Fall prevention

# Imaging

- Lateral x ray to see if patient had previous vertebral fracture or significant height loss
- DXA Morphometry

# Male Patients
# Special considerations

- Hormone therapy for prostate cancer produces rapid bone loss and all patients on androgen depravation therapy should be screened regularly
- Consider testosterone deficiency in all male patients with unexplained bone loss
- NOF recommends **all** males over age 70 should have a bone density test
- Problem: Medicare wont pay for males unless they have a positive test?!!!! So patients need to understand insurance and guidelines conflict

# Osteoporosis Prevention and Treatment Options

# Overview of How Treatments Reduce Fracture Risk in Osteoporosis

## How Treatment Works to Prevent Fractures

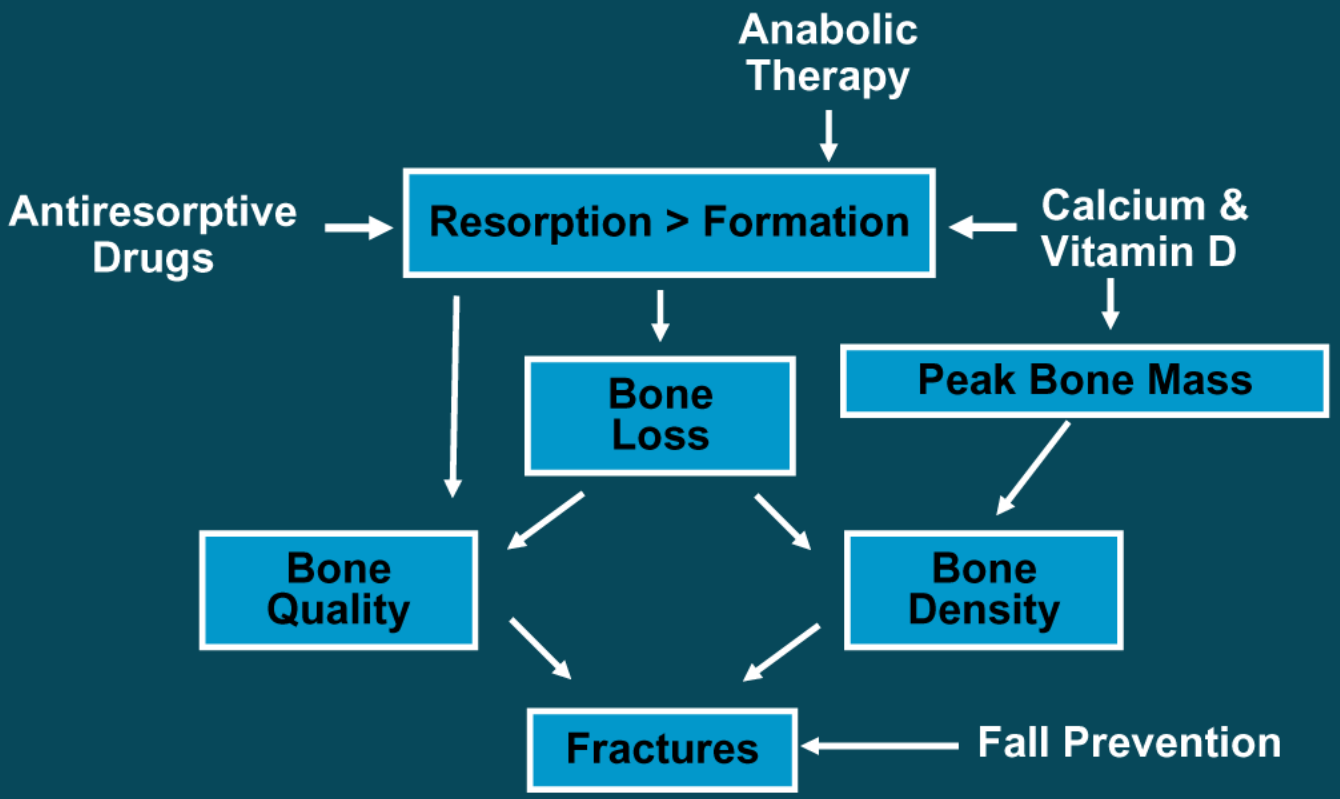



Figure courtesy of M.R. McClung.

# Non Pharmacologic Therapy

- Fall Prevention-assistive devices, walkers, canes, grab bars.
- Weight bearing exercise
- Balance and posture exercise
- Avoidance of sedative hypnotic medications
- Life style modification

# Calcium Recommendations

**Women**

| | |
|---|---|
| Age 50 & younger | 1,000 mg* daily |
| Age 51 & older | 1,200 mg* daily |

**Men**

| | |
|---|---|
| Age 70 & younger | 1,000 mg* daily |
| Age 71 & older | 1,200 mg* daily |

Clinician's Guide to Prevention and Treatment of Osteoporosis, Position Paper. Osteoporosis Int, 15 Aug 2014

# Estimating daily dietary calcium intake

Step 1: Estimate calcium intake from calcium-rich foods a

Product # of servings/day Estimated calcium/serving, in mg Calcium in mg

Milk (8 oz.) _____ ×300 = _____

Yogurt (6 oz.) _____ ×300 = _____

Cheese (1 oz. or 1 cubic in.) _____ ×200 = _____

Fortified foods or juices _____ ×80 to 1,000b = _____

Subtotal = _____

Step 2: Add 250 mg for nondairy sources to subtotal above +250

Total calcium, in mg = _____

# Prevention

- Non pharmacologic intervention, fall, lifestyle, and nutrition counseling
- Estrogen, Oral Bisphosphonates and SERMs all have FDA approval for prevention but are under prescribed
- Consider this for patients that you believe are high risk and look at the FRAX calculation.

# Pharmacologic options

## Antiresorptive therapy

Inhibit osteoclastic activity in excess of osteoblastic activity

HRT, SERMs, Calcitonin, Bisphosphonates, Biologic / currently Rank ligand inhibition

## Anabolic therapy

Increase osteoblastic activity in excess of osteoclastic activity

PTH analogs

# HRT and SERMs

Antiresorptive work via estrogen receptors on bone

Decrease bone turnover

Reduce the incidence of vertebral fractures HRT 34% , and up 30 to 50% Raloxifene

Estrogen approved for prevention but **NOT** treatment of osteoporosis

SERMs approved for both prevention and treatment

# Calcitonin

In the form of Salmon calcitonin

By injection and nasal spray

Advantages

No GERD issues, can help with pain of acute fractures, no renal issues

Disadvantages Not indicated for non vertebral fracture prevention

# Bisphosphonates

- Advantages
- Lower cost
- Available in many forms ie po and IV
- Daily, weekly, monthly dosing
- Do not have certain side effects of hormone medication such as dvt, hot flashes, or risk of maligancy

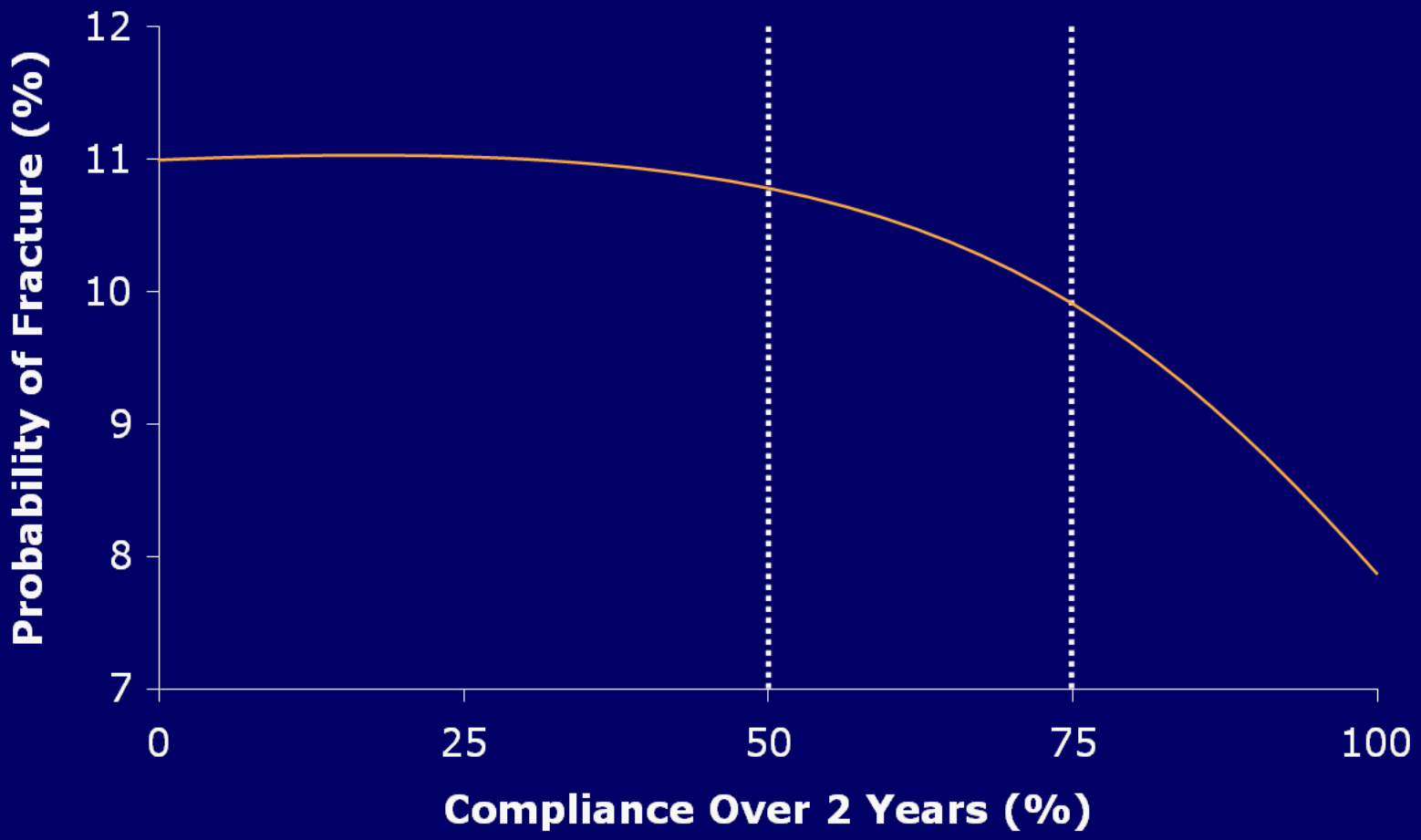
# Bisphosphonates

- Disadvantages
- GI upset, esophagitis
- Not recommended in  renal patients with GFR <30cc
- Potential risk??  Of ONJ, esophageal malignancies

# Bisphosphonates Special Considerations

- Ibandronate  not proven to reduce risk of hip and non vert fractures
- For patients wtih gastrointestinal upset delayed release risedronate  may be administered orally after breakfast
- Oral therapy reduces risk of vertebral fracture approx 50 percent for oral therapy and 70 percent for iv zoledronic acid
- Don’t use in patients with intolerance or Barrett’s Esophogus

# Refill Compliance and Fracture Protection Over 24 Months for Bisphosphonate-Treated Patients




Adapted from Siris E, et al. *Mayo Clin Proc.* 2006;81:1013-1022.

# Antiresorptive Biologics

- Denosumab a monoclonal antibody

  AMG 162 inhibition of rank ligand which prevents activation of osteoclasts

  Reduces risk of both vertebral and hip fracture

  Advantages: ease of administration and compliance and no GI or Renal toxicity

  Disadvantage: Higher cost

# Anabolic Therapy

Teraparatide: Biologic analog of PTH. Indications vertebral and non vertebral fractures prevention in patients with osteoporosis. Uses with more advanced disease.

Only current Anabolic agent

Advantage: Shows rapid onset of effect.

BMD and enzyme changes are seen in months

# Teraparatide cont

- Disadvantages
- Expensive, daily injections
- Limited to 2 years of treatment
- Patient needs to self inject daily (may be advantage if patient has gi issues with medications)
- Black box warning of osteosarcoma

# Future Therapies

- Sclerostin inhibitors
- Cathepsin K inhibitors

# Current Controversies With Therapy

# Duration of treatment

Effects of non bisphosphonates rapidly disappear after discontinuation.

Since bisphosphonates have a residual effect against fractures for a few years it may be possible to discontinue them for a period of time. However, patients at high risk of fracture continued therapy or different agent should be considered

Since there is no extensive evidence base to guide treatment, therapy should be individualized. Osteoporosis Int., 15 August 2014

# Osteonecrosis of the Jaw

Definition

- Exposed bone in maxillofacial region
- Unhealed for > 8wks
- No history of radiation to craniofacial region

Accepted by ASBMR, AAOMS and ESCEO, 2007

# ONJ

- Not a new diagnosis lst described in 1850 it was associated w heavy metals and infections.
- ONJ can also be seen w chemotherapy, radiation and steroids. Majority seen after tooth extraction.
- Mostly associated in cancer patients on IV bisphosphonates 97% of cases in German study
- There were no cases in any of the bisphosphonate osteoporosis drug studies with the exception of Reclast in the Horizon drug study in which there was 1 case in the placebo group and 1 case in the treated group. Therefore the incidence is extremely low at worst

# ONJ

- Rare in osteoporosis patients without cancer therapy
- Rate from 1 :100,000 to 1 : 263,000 to none depending on studies in patients without cancer associated therapy
- No evidence based guidelines only various expert opinions
- Risk felt to be higher in patients on IV bisphosphonates or Denosumab it is not seen w HRT or SERMs
- Prevention. Good oral hygiene regular dental care

  Hold drug with dental extractions and don't

  restart until bone completely healed.

# ONJ White Paper 2004

- Cessation or interruption of bisphosphonate  therapy may be considered in severe cases.
- However, close coordination between the dental specialist and the medical oncologist is recommended,
- Take into consideration the risk of skeletal complications (including hypercalcemia of malignancy) versus the risk of osteonecrosis. To date, cessation of bisphosphonate therapy appears to have no effect on established osteonecrosis. However, further study is needed

# FDA Statement November 12, 2008 for Atrial Fibrillation and Bisphosphonates

- After our review, based on the data available at this time, healthcare professionals should not alter their prescribing patterns for bisphosphonates and patients should not stop taking their bisphosphonate medication.
- However, across all studies, no clear association between overall bisphosphonate exposure and the rate of serious or non-serious atrial fibrillation was observed

# Esophageal Cancer and Alendronate

- NEJM Jan 1, 2009. Volume 360:89-90.
- Drug Administration (FDA) received reports of 23 patients in the United States receiving a diagnosis of esophageal cancer, with alendronate (Fosamax, Merck)
- Wysowski  of the FDA suggested, doctors should avoid prescribing the drug to people with Barrett's esophagus and further review is in progress.

# Impediments to Prevent and Treat Osteoporosis

- Poor reimbursement for DXA scanning threatens OP treatment
- The number of patients with Osteoporosis on treatment is staying flat at 15% due to poor reimbursement and patient fear ie overemphasis by media on potential drug side effects
- Drug reimbursement issues

**Osteoporosis care at risk in the United States** Osteoporos Int. 2008 Nov;19(11):1505-9. Epub 2008 Aug 29

# Conclusion

- Osteoporosis treatment has come a long way.  There are many available treatment options
- Don’t forget prevention and early treatment.  Clinical judgment should not be overruled by guidelines.
- Osteoporosis has significant morbidity and mortality in numbers that dwarf breast cancer and heart disease and we are not reaching the majority of patients who should be treated
- Every patient that leaves the hospital with an old or new fragility fracture should have their current osteoporosis treatment plan reviewed with a notation in the chart that follow up treatment is recommended

# Conclusion cont

- Lack of government and insurance support and public awareness of exaggerated negative publicity regarding treatment side effects vs benfits threatens to undermine the gains made in treating this serious disease
- Non compliance is a big issue in treating patients with osteoporosis and consistent follow up and support is needed