

# Osteoporosis: An Overview of the Disease and Its Consequences

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Harbour View Breast Cancer Support Group  
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# Osteoporosis in the Clinic: 3 Cases



**Ms. P**

- ▶ 60 years of age
- ▶ No prevalent fx
- ▶ Family history of fx
- ▶ Menopause at 47 years
- ▶ Has never had a BMD test



**Ms. Q**

- ▶ 82 years of age
- ▶ History of hip fx
- ▶ Widow, lives independently
- ▶ Alcohol >2 drinks per day
- ▶ Depression

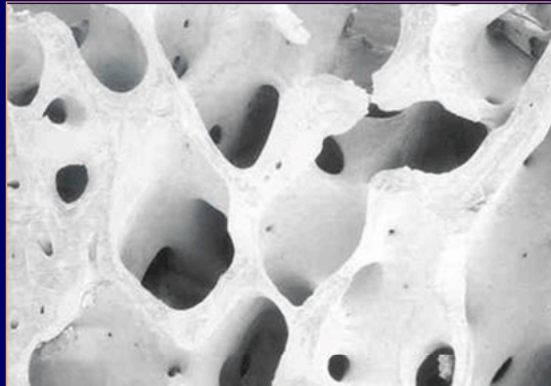


**Ms. R**

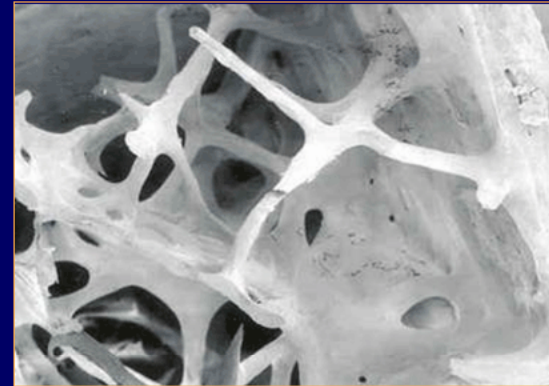
- ▶ 72 years of age
- ▶ No documented vertebral fractures
- ▶ Height loss
- ▶ Inadequate calcium and vitamin D
- ▶ Sedentary lifestyle

# Osteoporosis: Definition

**Normal Bone**



**Osteoporotic Bone**



©2005, David W. Dempster, PhD

## **NIH Definition:**

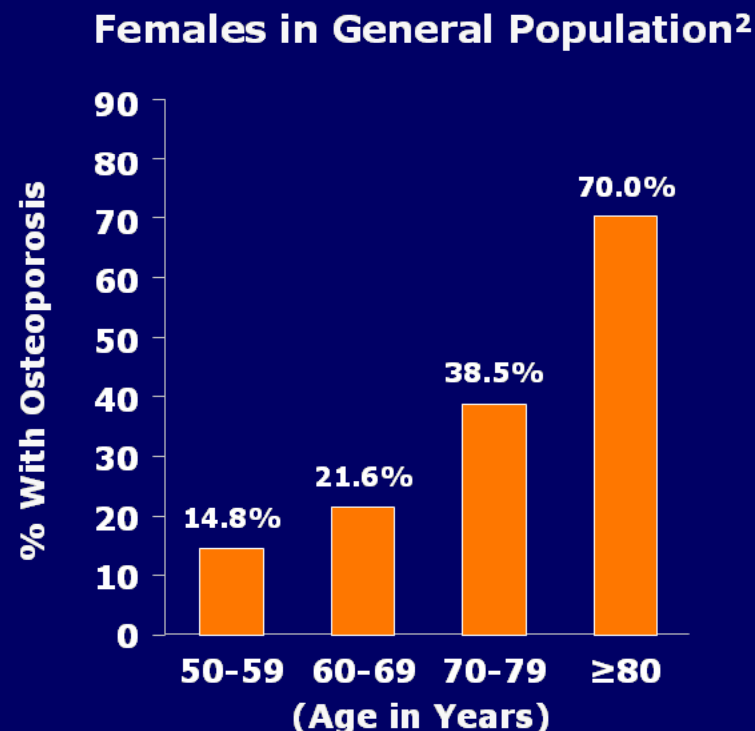
“Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture”

# Epidemiology of Osteoporosis in the US

- ▶ 44 million Americans, 80% of whom are women
  - 10 million have established osteoporosis
  - 34 million have osteopenia or low bone mass
  - 1.5 million fractures occur per year in US

# Osteoporosis is Common Among US Women

- ▶ 10 million Americans have established osteoporosis, 80% of whom are women<sup>1</sup>
- ▶ 1.5 million fractures occur per year in US



# Risk Factors for Osteoporotic Fractures

## Genetic/Nonmodifiable

- ▶ Age
- ▶ Female sex
- ▶ Asian or white ethnicity
- ▶ Previous fragility fracture
- ▶ Family history of hip fracture or osteoporosis
- ▶ Small frame

## Potentially Modifiable

- ▶ Menopause-related estrogen deficiency
- ▶ Low body weight
- ▶ Calcium/vitamin D deficiency
- ▶ Inadequate physical activity
- ▶ Excessive alcohol intake
- ▶ Cigarette smoking
- ▶ Long-term glucocorticoids

# Vertebral Fractures Have Significant Consequences for Patients, Including Dorsal Kyphosis



## Vertebral Fractures

- ▶ Associated with
  - Acute and chronic pain
  - Kyphosis and height loss
  - Impaired function
  - Increased morbidity and mortality
  - Increased fracture risk

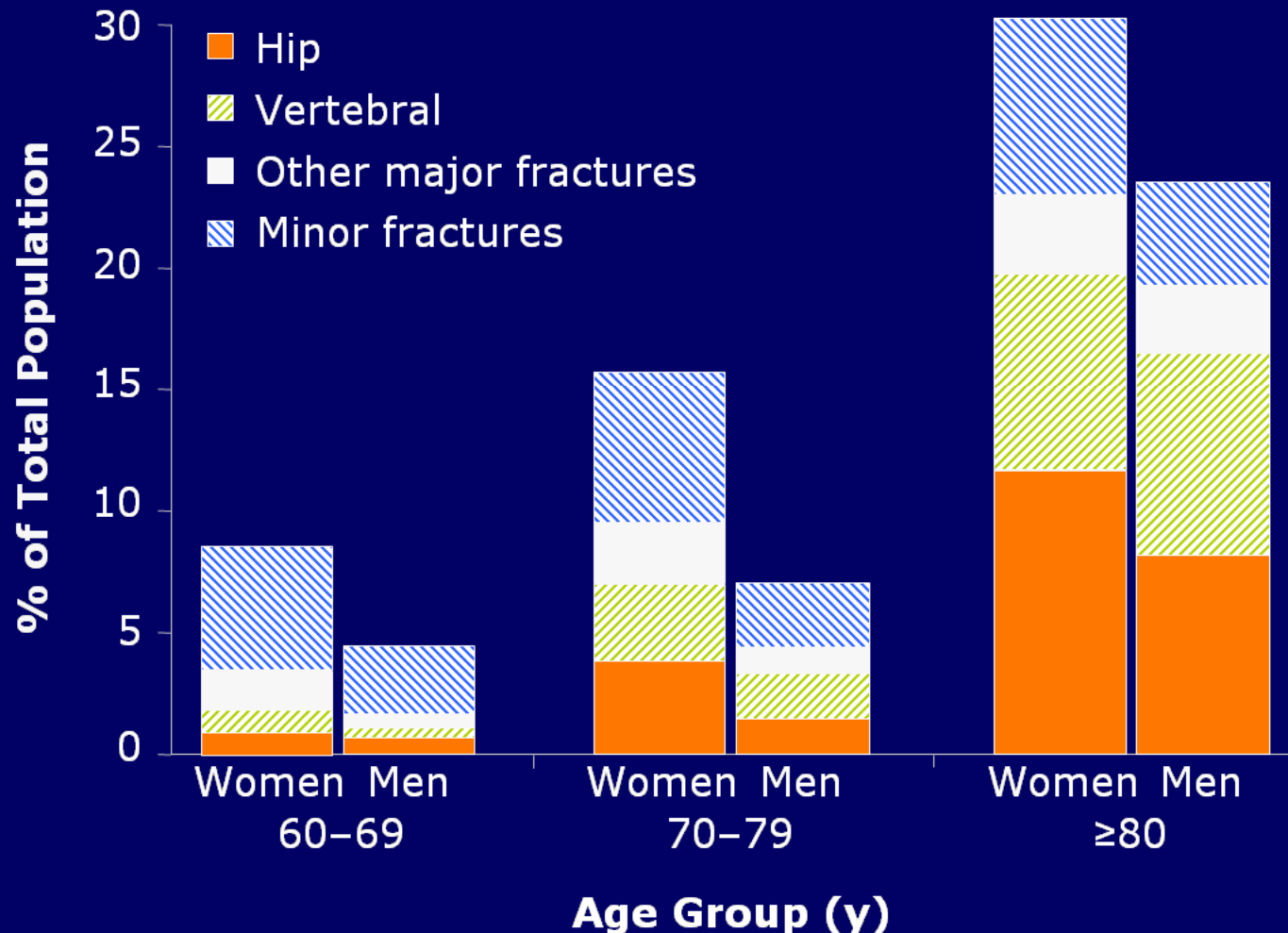
# Hip and Other Non-Vertebral Fractures Have Significant Consequences

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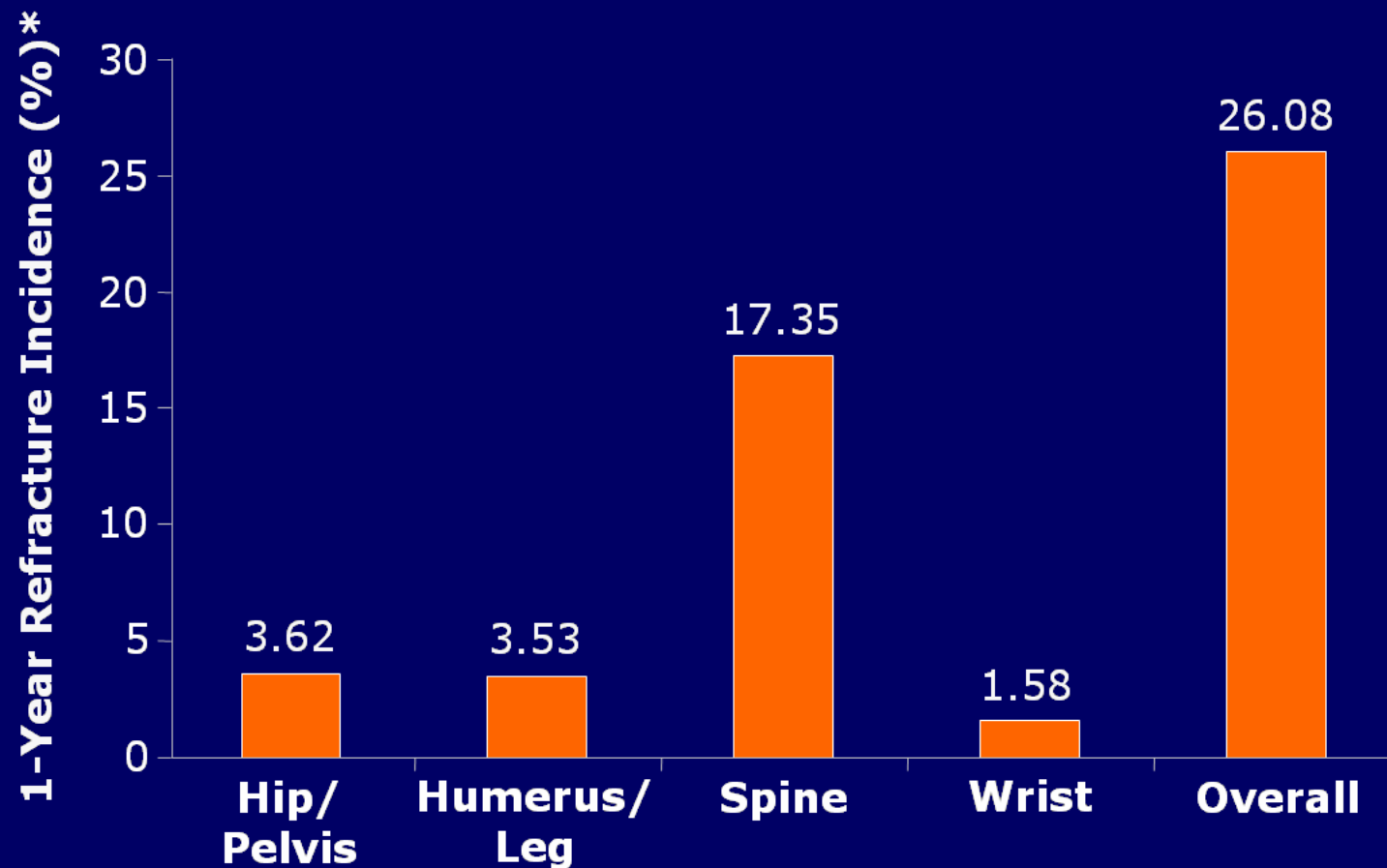
- ▶ Hip fracture associated with
  - Loss of ambulatory status in 30% of patients
  - Increased morbidity and mortality
  - Increased fracture risk
  - Major reason for admission to chronic care facilities
- ▶ Non-vertebral fractures
  - Pain
  - Increased risk of future fractures



# Fracture Incidence Increases With Age: 5-Year Fracture Rates in Women and Men



# 1-Year Risk of Refracture in Patients With Incident Vertebral Fracture

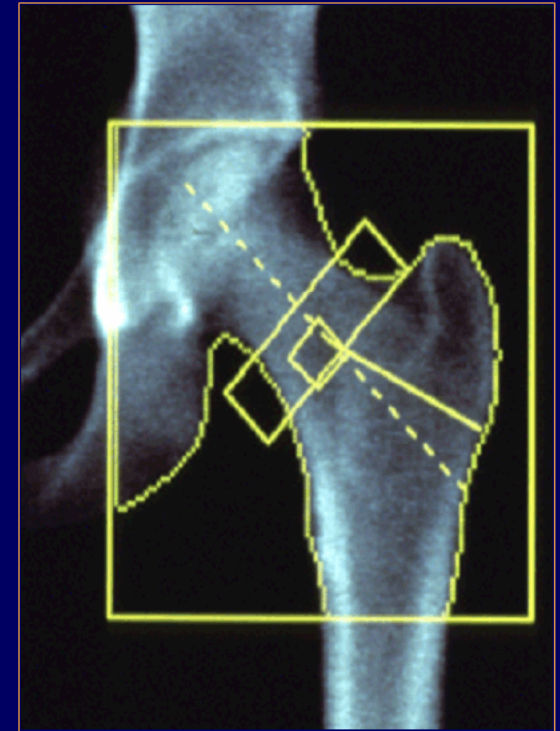


\*Based on Kaplan-Meier analyses.

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

# Clinical Presentation of Osteoporosis

- ▶ Usually asymptomatic and undiagnosed
- ▶ Signs and symptoms
  - Low-trauma fractures of spine, wrist, or hip
  - Loss of height
  - Kyphosis (rounded back)
  - Acute or chronic back pain
- ▶ Diagnostic tests
  - Bone mineral density measurement
  - Spine x-ray or morphometry



# WHO Bone Density Criteria for Diagnosing Osteoporosis

Diagnosis	BMD T-Score: Number of SD Below Mean in Healthy Young Women*
Normal	–1 or above
Low bone mass [osteopenia]	Between –1 and –2.5
Osteoporosis	–2.5 or less
Severe osteoporosis	–2.5 or less with fragility fractures

- ▶ Reduction by 1 SD equals a 10% to 12% decrease in BMD
  - 1 SD change increases fracture risk by 1.5- to 2.0-fold

# National Osteoporosis Foundation Guidelines

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- ▶ Recommend BMD testing for
  - All women 65 years of age and older
  - Younger postmenopausal women with one or more risk factors (other than being white, postmenopausal, and female)
  - Postmenopausal women who present with fractures (to confirm the diagnosis and determine disease severity)

# Nonpharmacologic Interventions

- ▶ Goal of nonpharmacologic interventions is to prevent future fractures through lifestyle change
  - Diet and dietary supplements
    - Calcium
    - Vitamin D
  - Exercise
  - Fall prevention
  - Smoking cessation

# Decision to Treat Is Affected by Several Factors

- ▶ Current AACE position on treatment intervention
  - Women with postmenopausal osteoporosis
    - Women with low-trauma fractures and low BMD
    - Women with BMD T-scores of  $-2.5$  and below
  - If risk factors are present, women with borderline-low BMD (T-scores of  $-1.5$  and below)
  - Women in whom nonpharmacologic preventive measures are ineffective (bone loss continues or low trauma fractures occur)
- ▶ Individual clinician judgment is important
- ▶ Forthcoming guidelines are likely to be based on absolute fracture risk probability over 10 years rather than on BMD alone

# Classes of Pharmacologic Agents Currently Approved for the Treatment of Osteoporosis

## ▶ **Antiresorptive agents**

- Bisphosphonates
  - Weekly oral alendronate
  - Weekly or monthly risedronate
  - Monthly oral or quarterly IV ibandronate
- Calcitonin
- Selective estrogen receptor modulators (SERMs)

## ▶ **Anabolic agents**

- Parathyroid hormone

## ▶ **Estrogen therapy and hormone therapy**

- (Indicated for prevention only)



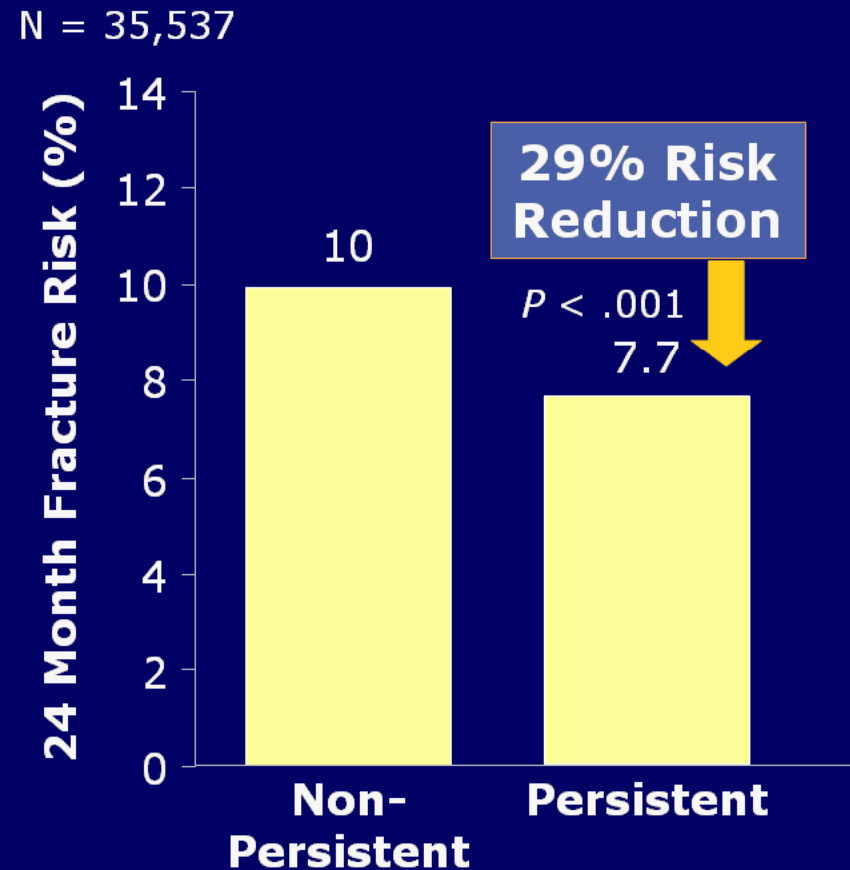
# Effects of Bisphosphonates

- ▶ ↓ Bone turnover
- ▶ ↑ BMD at lumbar spine and hip
- ▶ ↓ Risk of vertebral and hip fractures
- ▶ Sustained effects with continued treatment
- ▶ Best-studied class of agents used in osteoporosis
- ▶ Long-term safety record

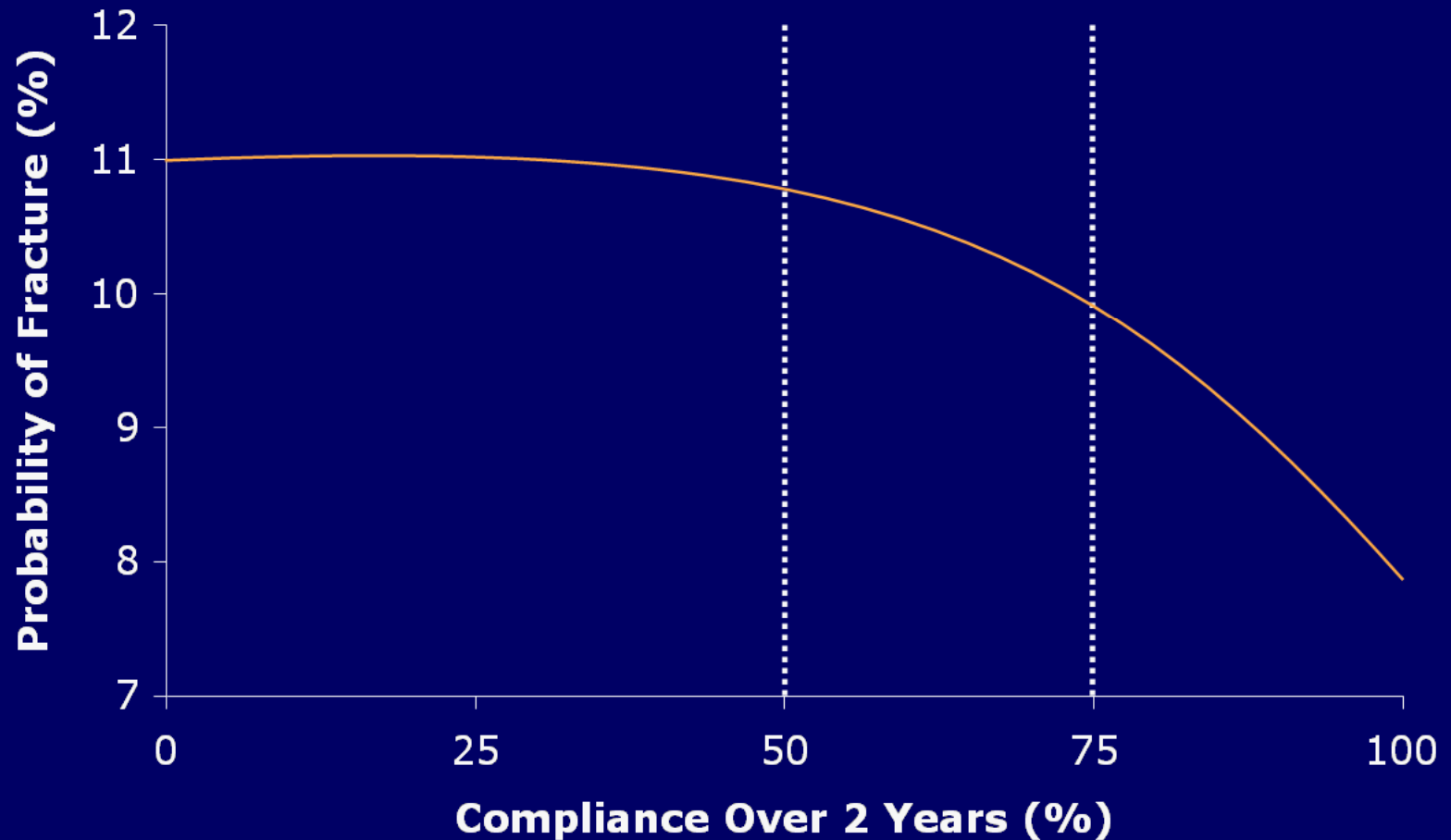
# Real-World Obstacles in the Management of Osteoporosis

- ▶ Insufficient rates of diagnosis
- ▶ Low awareness among physicians and patients of the imperative to treat
- ▶ Global challenge of adherence to therapy in chronic diseases, compromising effectiveness
- ▶ Poor adherence is two-fold problem
  - Low persistence: patient stops taking medication
  - Poor compliance: patient does not follow dosing instructions

# Poor Compliance and Persistence Lead to Compromised Fracture Risk Reduction



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



# Rationale for Less-Frequent and Easier-to-Follow Dosing Regimens

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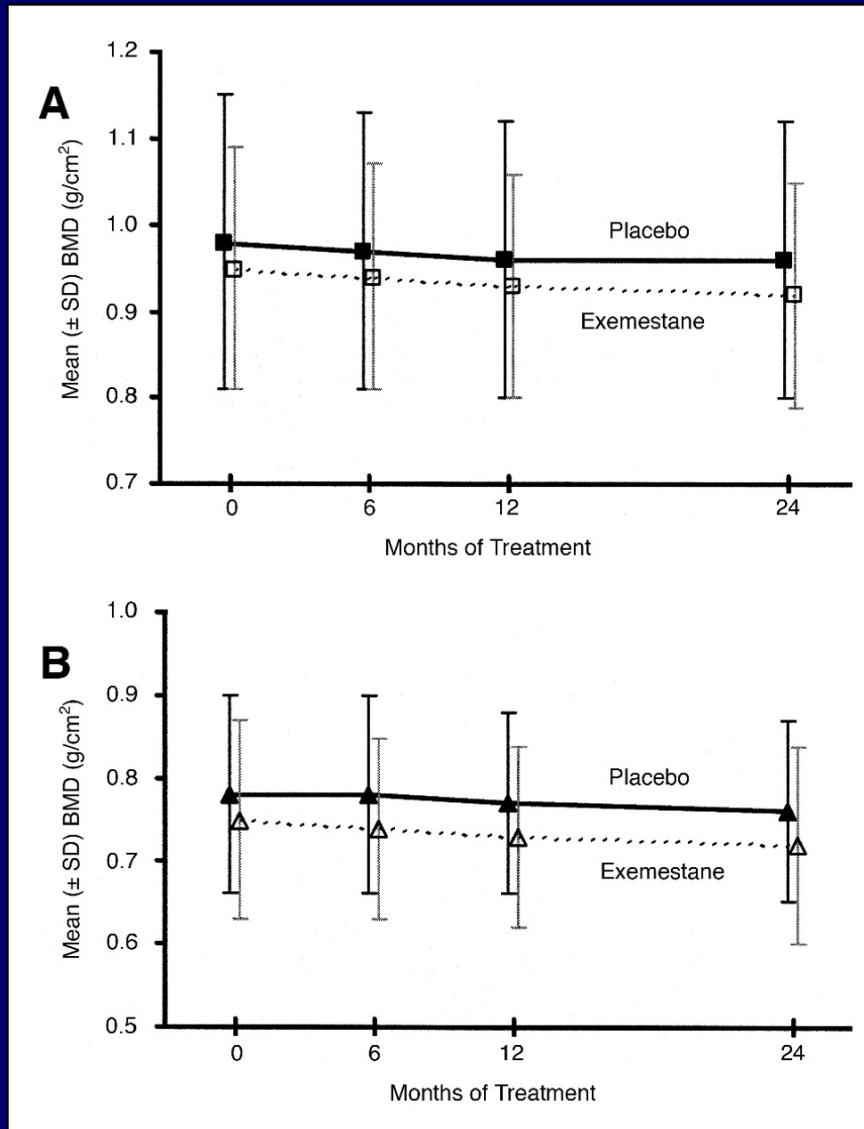
- ▶ For many clinicians, bisphosphonates are the standard of care in osteoporosis because of their rapid efficacy and long-term safety
- ▶ Poor adherence to daily, weekly, and monthly regimens of oral bisphosphonates results in compromised effectiveness
- ▶ A once-yearly IV bisphosphonate therapy can deliver real-world effectiveness by assuring adherence for the entire dosing interval

# The Problem of Bone Mineral Loss in Cancer Patients

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- ▶ Widespread use of hormonal manipulation in treatment of cancer greatly exacerbates problem
  - Aromatase inhibitors in the treatment of breast cancer
  - Weak LHRH agonists (Lupron) or orchiectomy in the treatment of prostate cancer

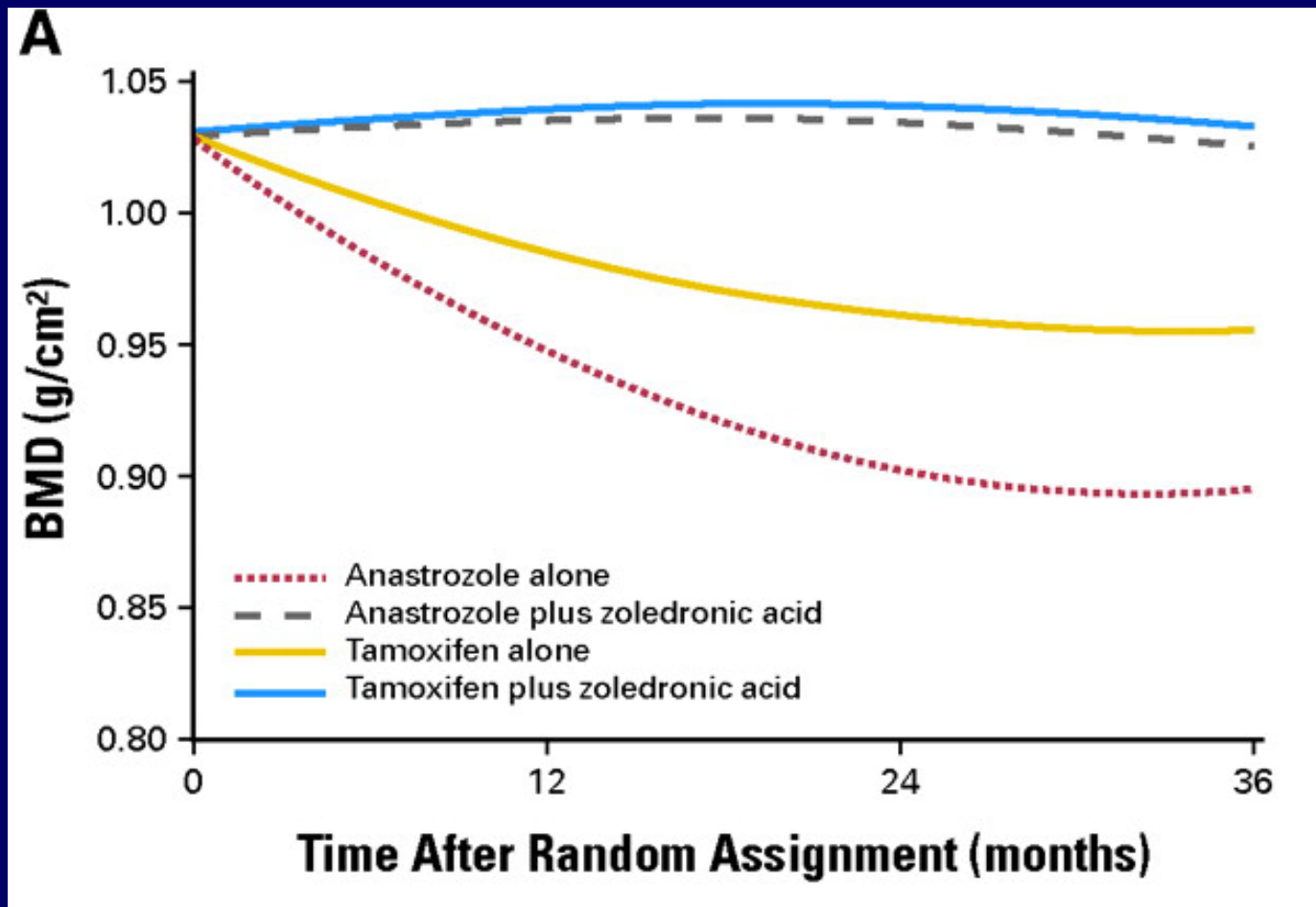
# Effect of 2-year treatment with placebo or exemestane on bone mineral density (BMD) of the lumbar spine (A) and femoral neck (B)



## The Problem with Aromatase Inhibitors

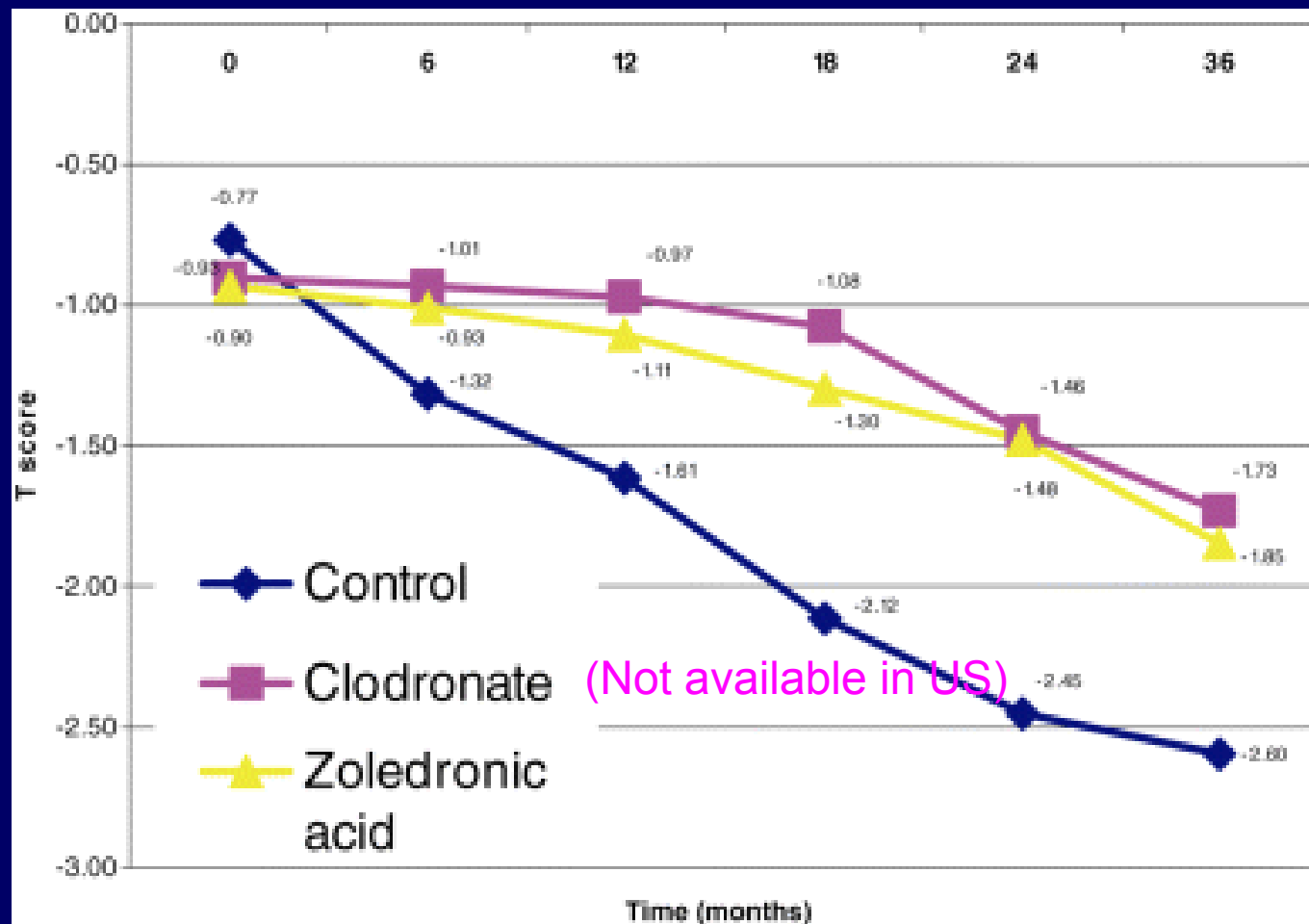
Lonning, P. E. et al. *J Clin Oncol*; 23:5126-5137 2005

Changes from baseline bone mineral density (BMD) over time in the lumbar spine over time in patients treated for 36 months with anastrozole or tamoxifen { +/- } zoledronic acid





# Use of Bisphosphonates with Androgen Deprivation



Rodrigues, *Int. J. Urol.*  
14(4): 317-20, 2007

# Intravenous Reclast for Osteoporosis

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- ▶ Most aggressive approach currently available
- ▶ Avoids side effects of oral bisphosphonates
- ▶ Cost competitive
- ▶ Once-a-year dosing very convenient
- ▶ Insurance reimbursement in a state of flux
  
- ▶ Available at Harbour View Women's Center by special arrangement
- ▶ Requires prescreening for medical issues (dental health, adequacy of kidney function and vitamin D stores) by physician

# Conclusions

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- ▶ Osteoporosis is a major public health issue with significant morbidity, mortality, and health care costs
- ▶ Prevalence increasing as population ages
- ▶ Effective therapies are available, but treatment and adherence patterns are suboptimal in the real-world setting
- ▶ Better diagnosis and longer-acting therapies with few adverse events that address obstacles to adherence may improve real-world outcomes

## For more information....

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- ▶ Contact Laurie Jesz at 673-5861 or me...
- ▶ James J. Stark, MD, FACP at 397-4200...just across the street...



Or visit me on the web:  
[www.StarkOncology.com](http://www.StarkOncology.com)