

# **Diagnosis and Treatment of Osteoporosis in Chinese**

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UCSF

# OSTEOPOROSIS: SCOPE

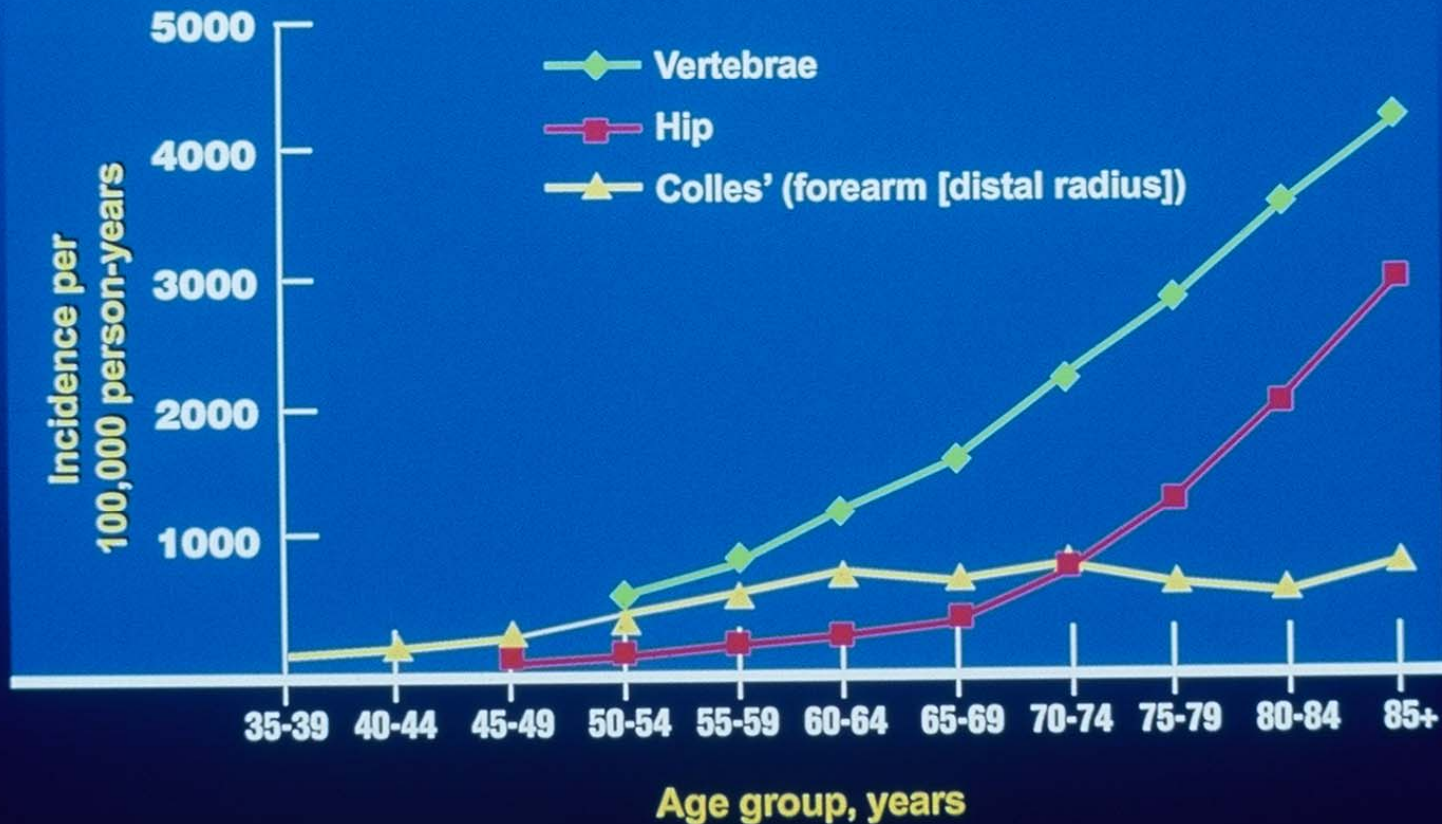
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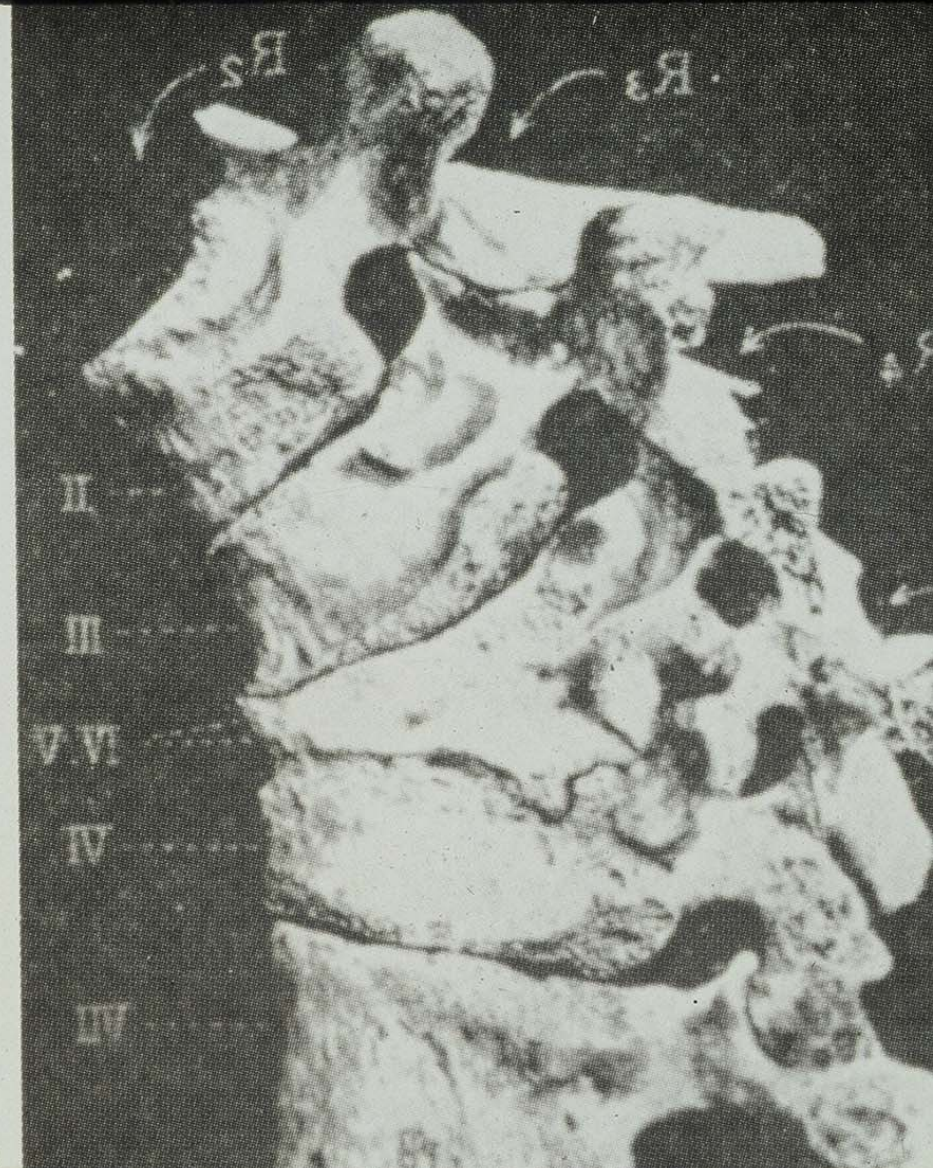
- **28 million Americans are affected or have low bone mass<sup>1</sup>**
- **4 out of 5 are women<sup>1</sup>**
- **Risk of developing a hip fracture is equal to a woman's combined risk of developing breast, uterine, and ovarian cancer<sup>1</sup>**
- **1.5 million fractures annually<sup>1</sup>**
- **Cost to society of \$14 billion per year<sup>2</sup>**

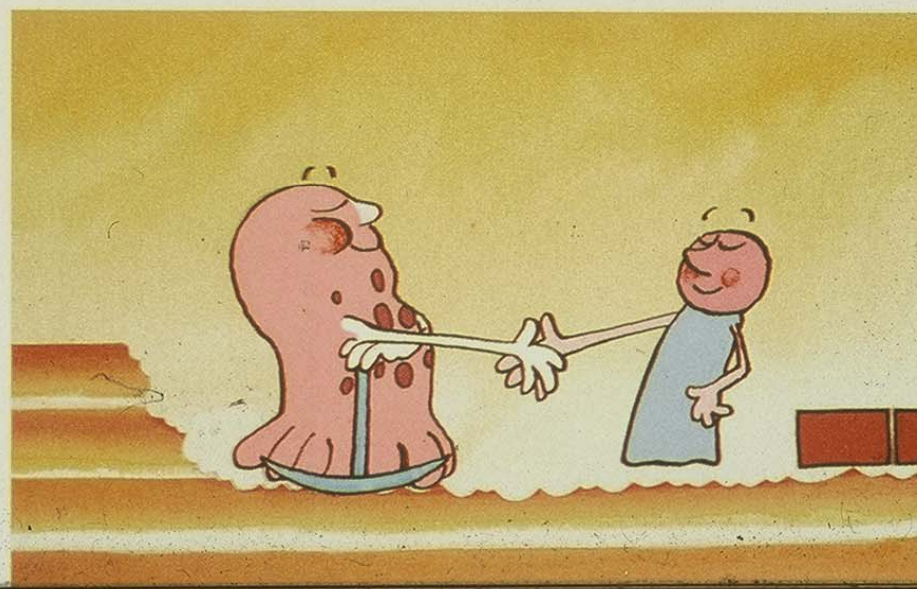
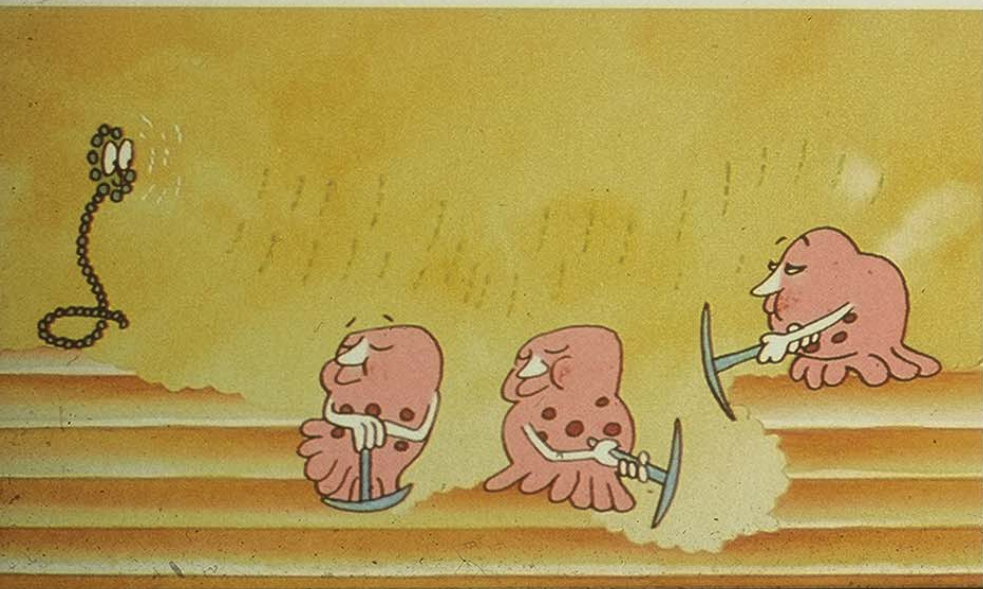
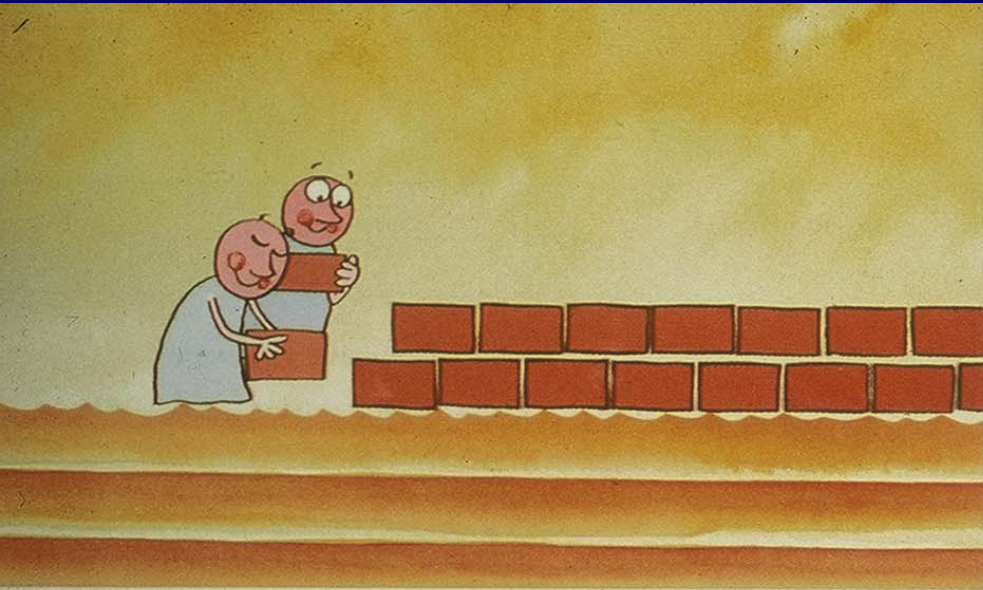
**1. Stand up to osteoporosis: your guide to staying healthy and independent through prevention and treatment. Washington, DC: National Osteoporosis Foundation;1997:10.**  
**2. J Bone Miner Res. 1997;12:24-35.**

# OSTEOPOROSIS: IMPACT ON WOMEN

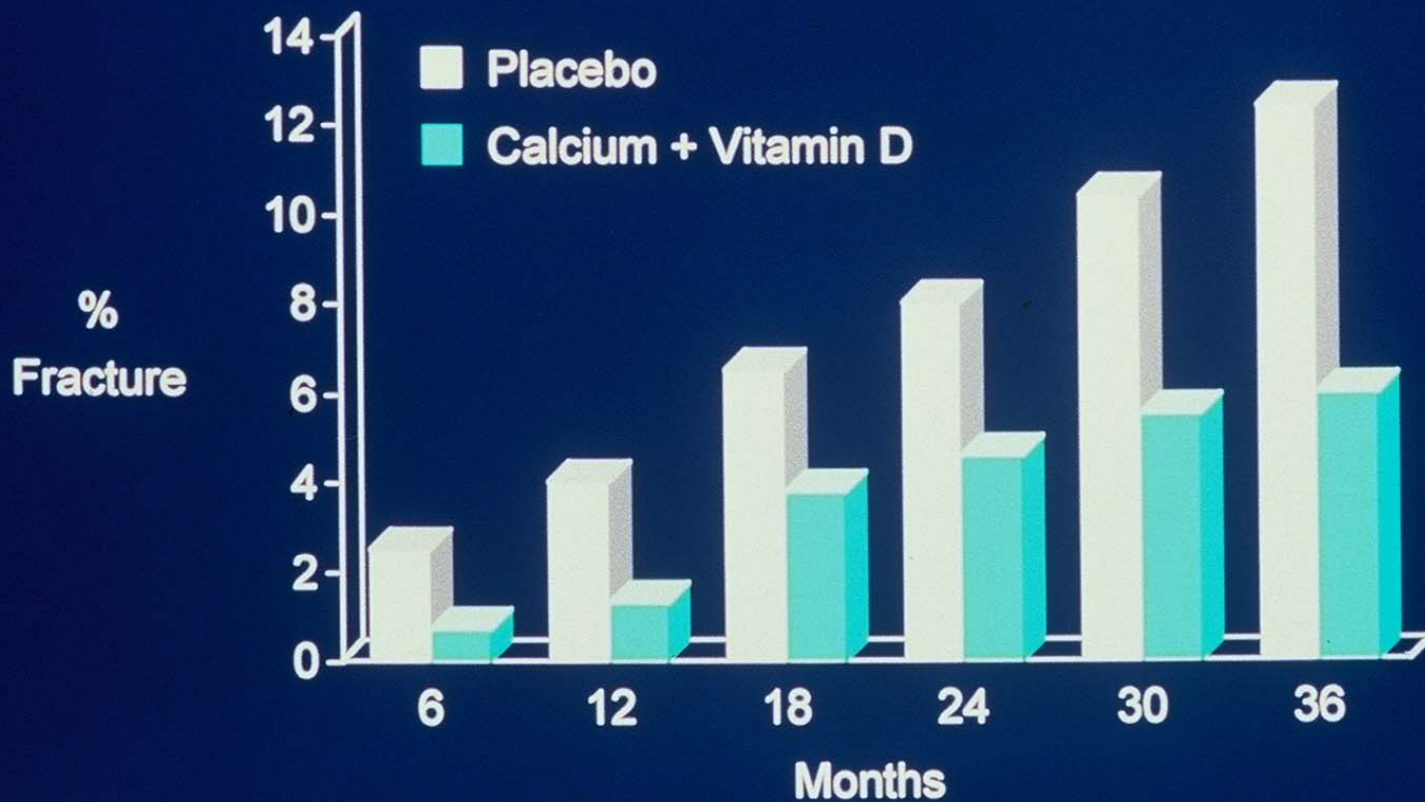
## Incidence of fracture among women







# Reduction of Nonvertebral Fracture with Calcium and Vitamin D



$p=0.02$

Dawson-Hughes B et al, *N Engl J Med* 1997;337:670.

# WHI Study

## Hazard Ratio of Combination HRT

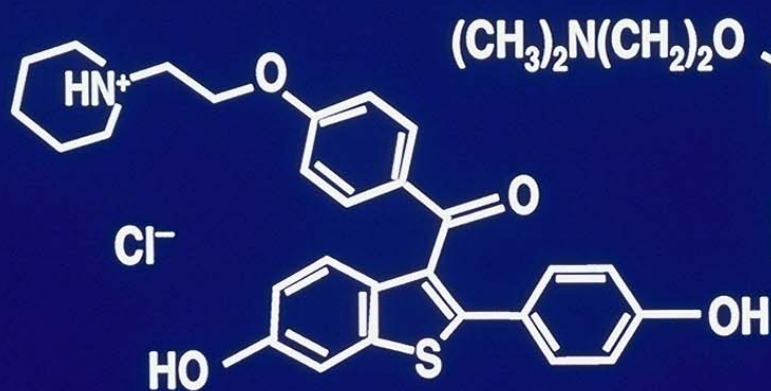
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<b>Outcome</b>	<b>HR Vs placebo</b>
<b>CHD</b>	<b>1.29</b>
<b>Stroke</b>	<b>1.41</b>
<b>VTE</b>	<b>2.11</b>
<b>Breast Cancer</b>	<b>1.26</b>
<b>Colorectal cancer</b>	<b>0.63</b>
<b>Hip fracture</b>	<b>0.66</b>

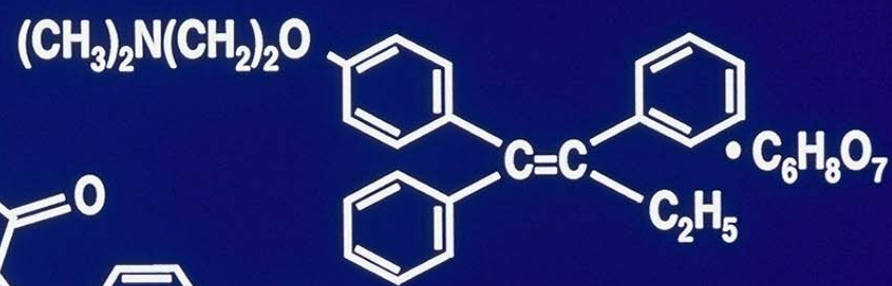
# Chemical Structure of Estradiol and Selected SERMs



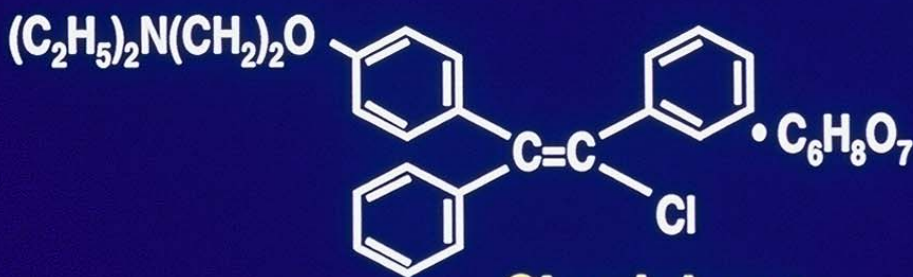
**Estradiol**



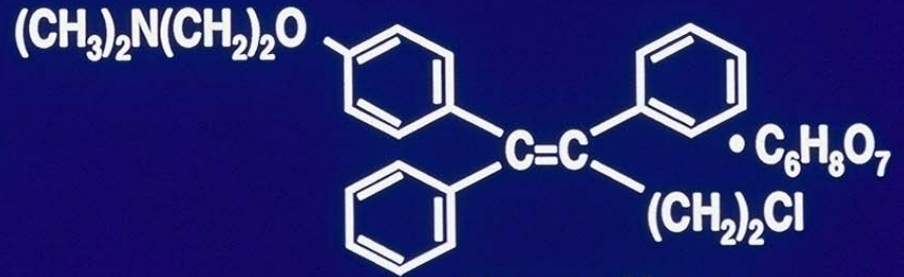
**Raloxifene**



**Tamoxifen**



**Clomiphene**

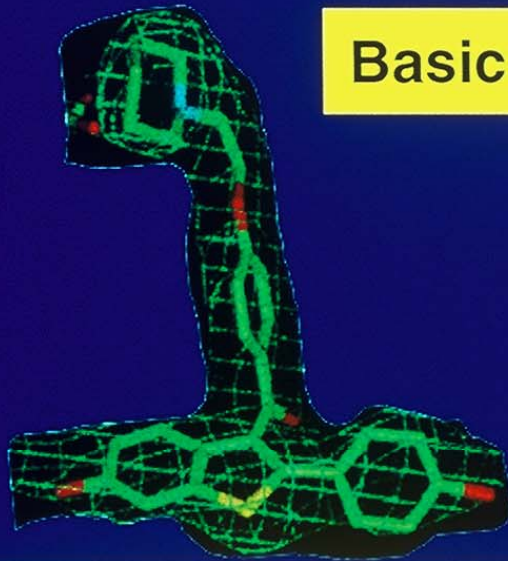


**Toremifene**



# EVISTA<sup>®</sup> (raloxifene HCl) as a SERM

## 3-Dimensional Model of EVISTA



Basic side chain



**Estrogen antagonist**

- Uterus
- Breast

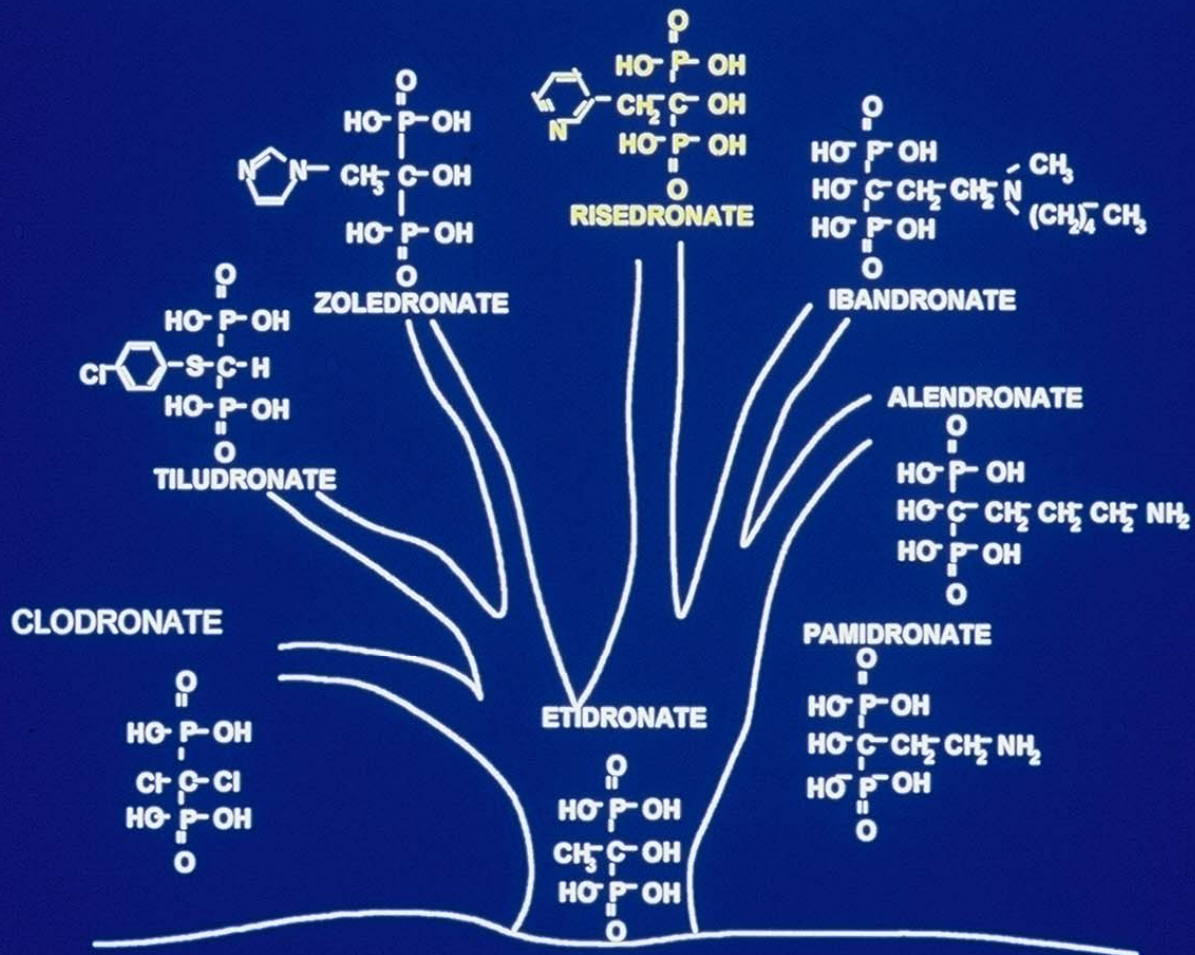
Benzothiophene moiety



**Estrogen agonist**

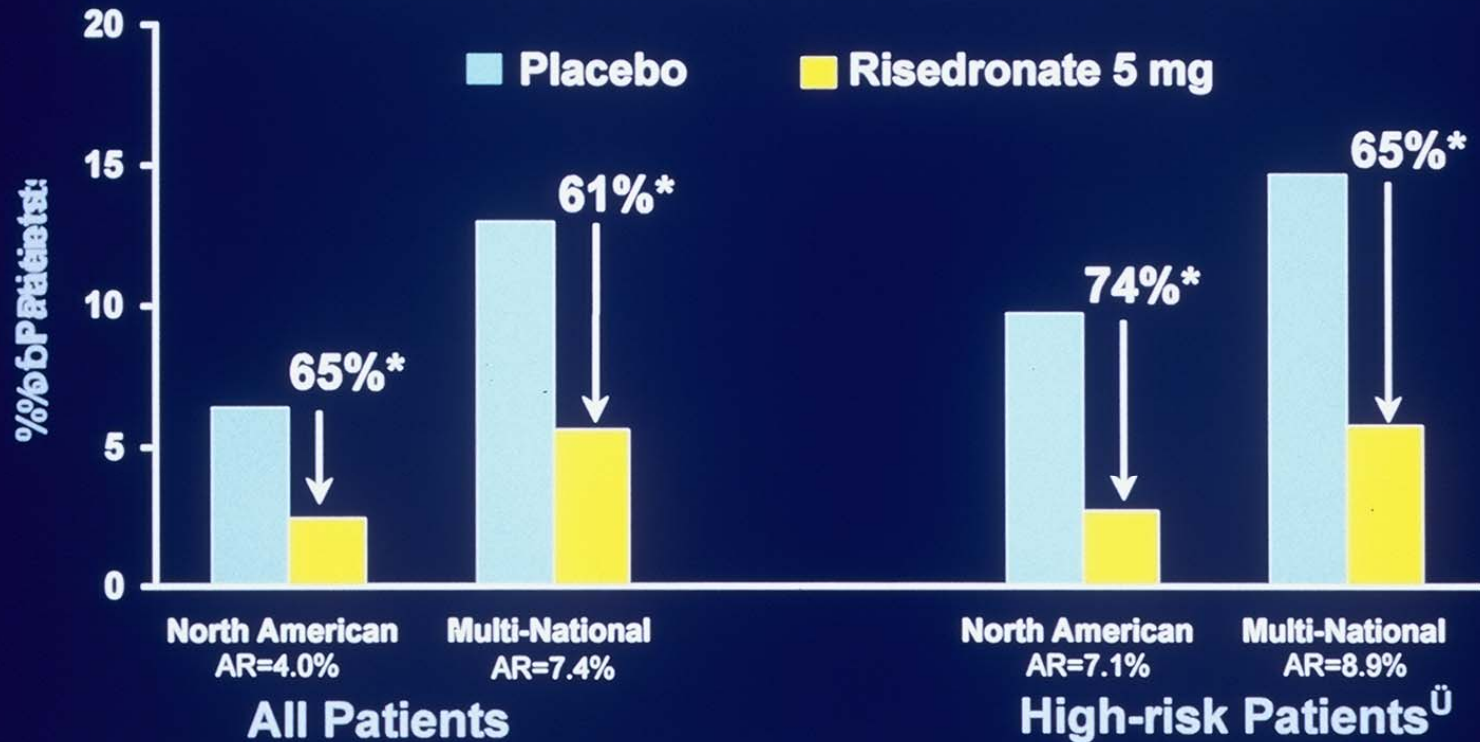
- Bone
- Serum lipids

# Bisphosphonates



# Risedronate Reduces Vertebral Fracture Risk in the First Year of Treatment

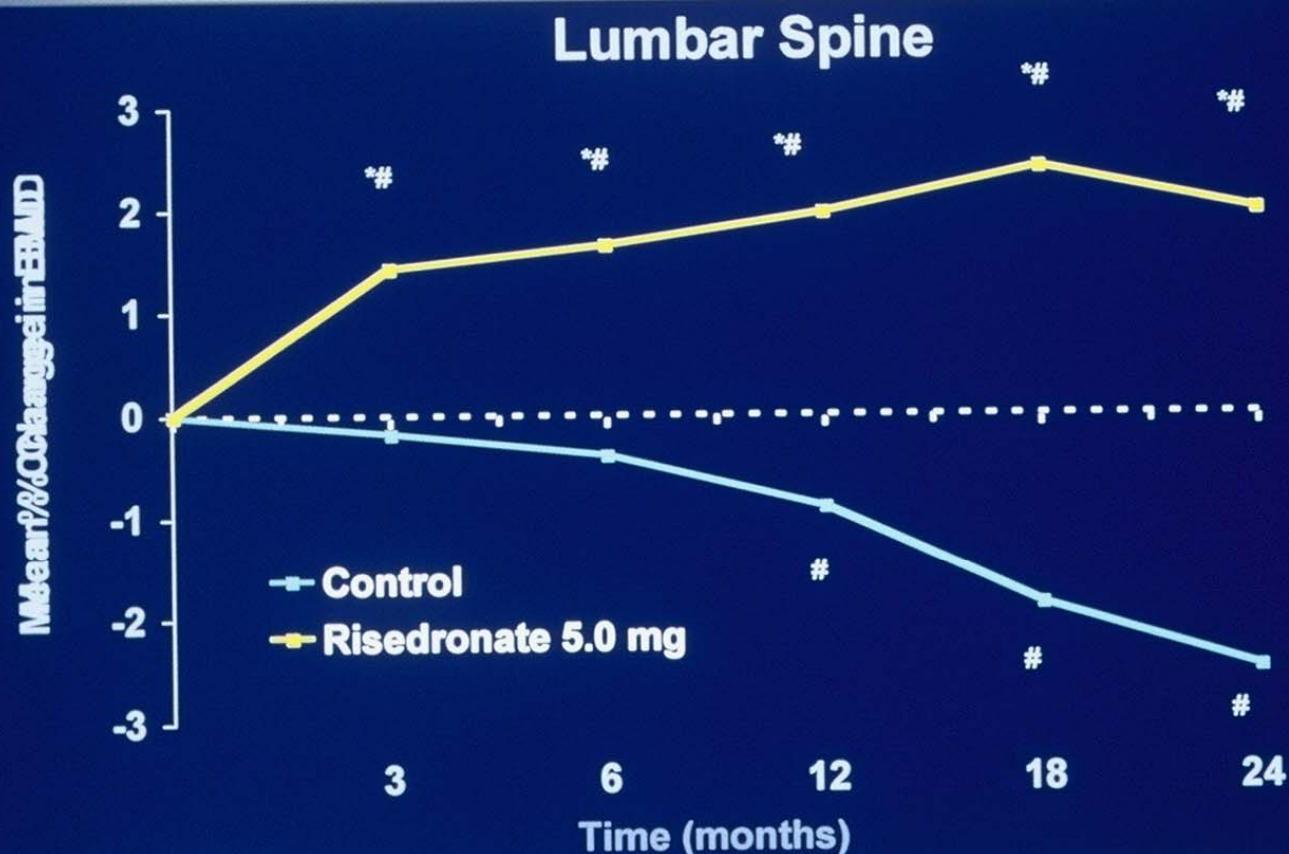
One-Year Vertebral Fracture Reduction Regardless of Disease Severity



AR=Absolute Risk Reduction; \* p<0.001; <sup>ü</sup> ≥2 prevalent vertebral fractures  
 Harris et al, JAMA 1999; 282: 1344-52. Reginster et al, OI, 2000; 11:83-91. <sup>ü</sup> Watts et al, JBMR 1999;14(suppl. 1): S136.

Please see Actonel package insert for full prescribing information

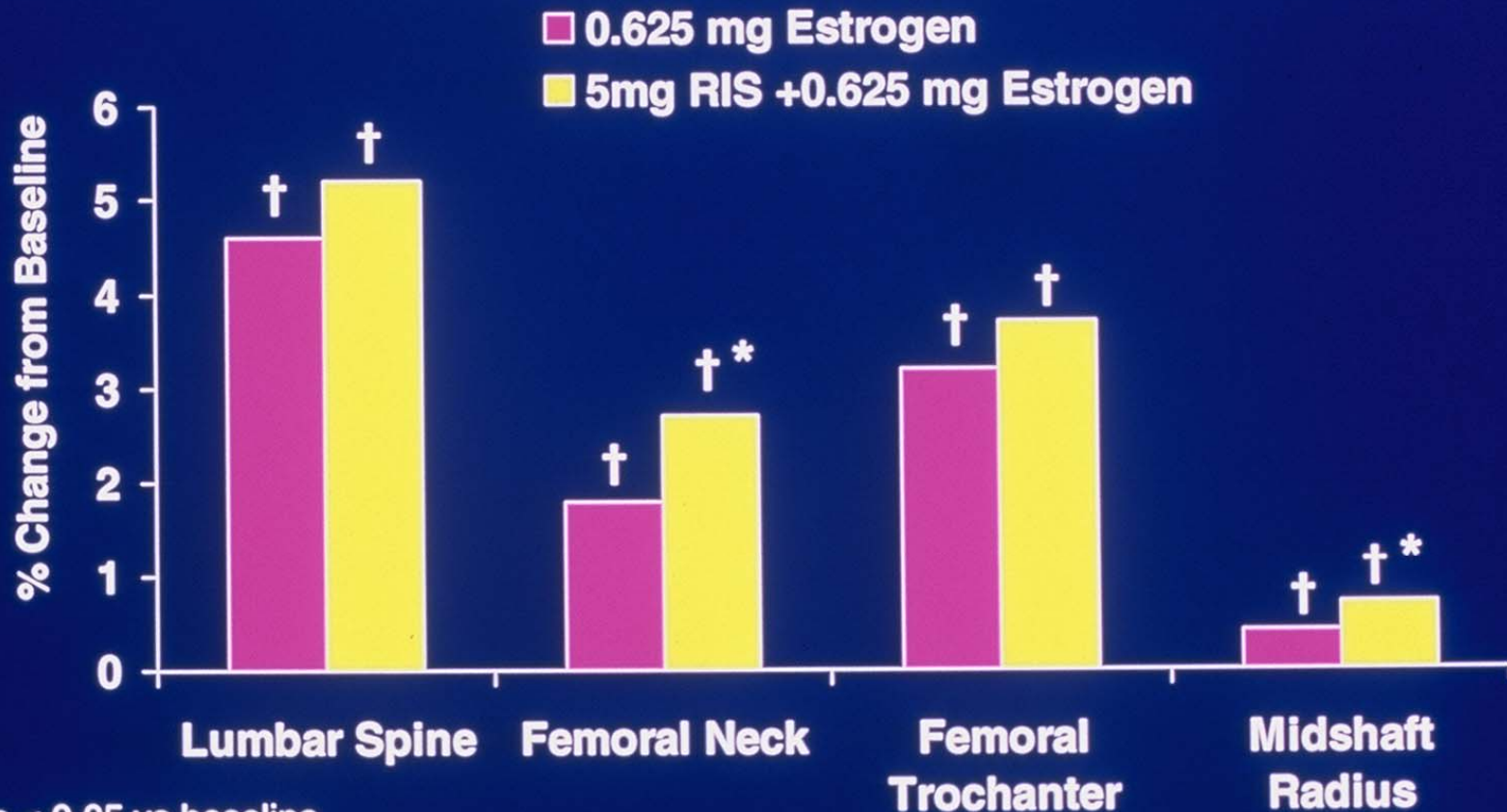
# Risedronate Increases BMD by 3 Months in Early Postmenopausal Women



\*p<0.05 vs. control; #p<0.05 vs. baseline. Hooper et al., *Calcified Tissues*, 1999; 64 (supplement 1): S69.

Please see Actonel package insert for full prescribing information

# Percent Change from Baseline in BMD at 12 Months

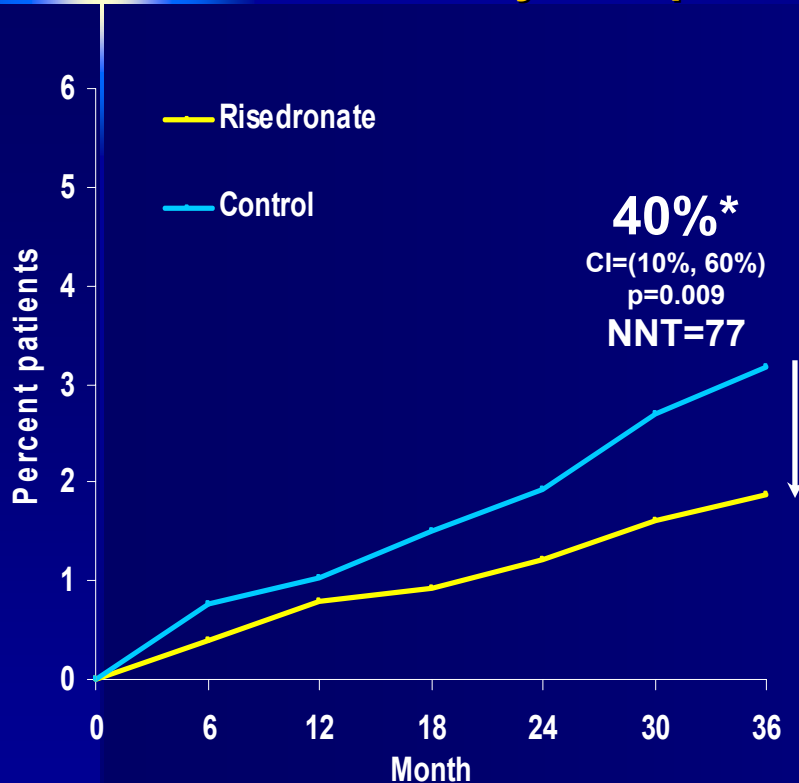


† p < 0.05 vs baseline

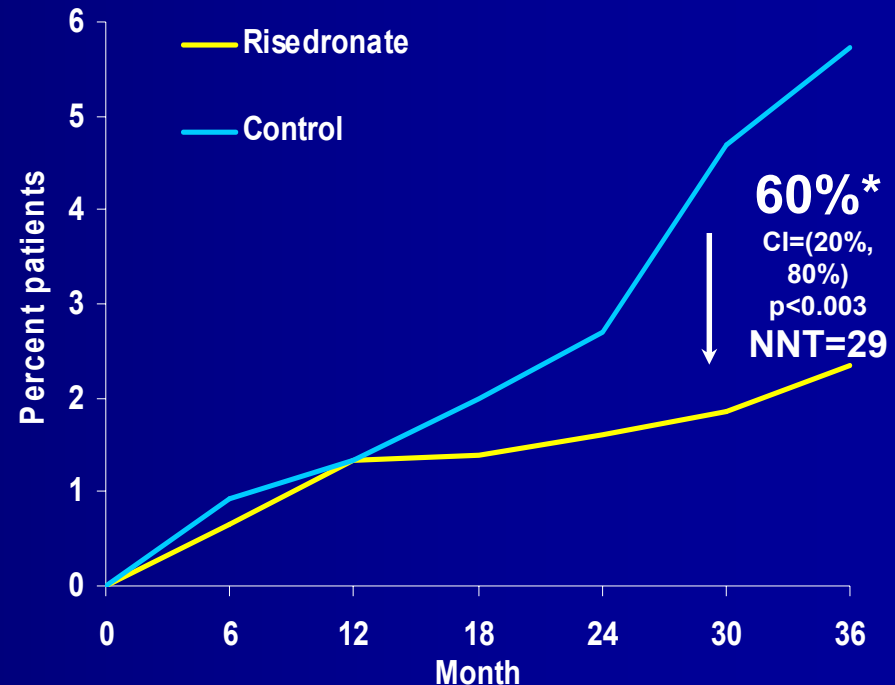
\* p < 0.05 vs estrogen

# Risedronate Effect on Hip Fracture in Low Bone Density Group

## Low Bone Density Group Total



## Low Bone Density with Prevalent Vertebral Fracture



\* Relative risk reduction, and 95% Confidence Intervals.

McClung, et. al., New England Journal of Medicine 2001; 344(5):333-340.

# Placebo-Treated Postmenopausal Women Rapidly Lose Microarchitectural Elements

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**Baseline**



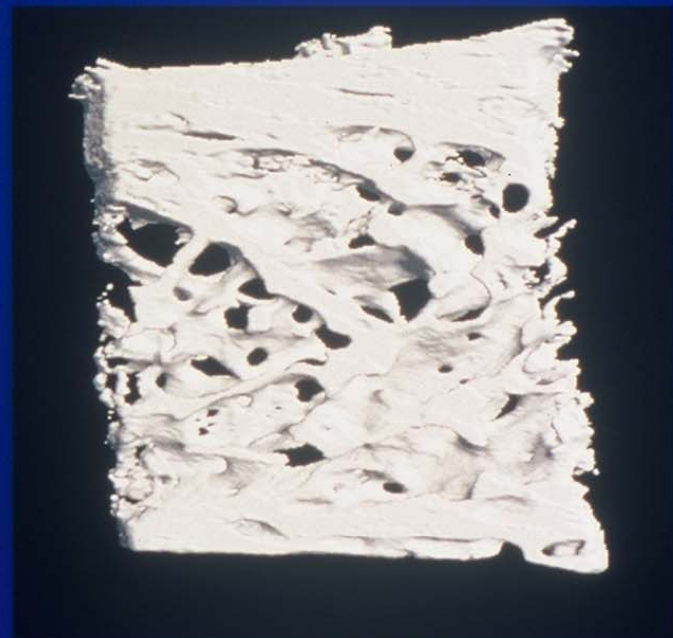
**1 Year**

## Risedronate-Treated Postmenopausal Women Maintain Microarchitectural Integrity

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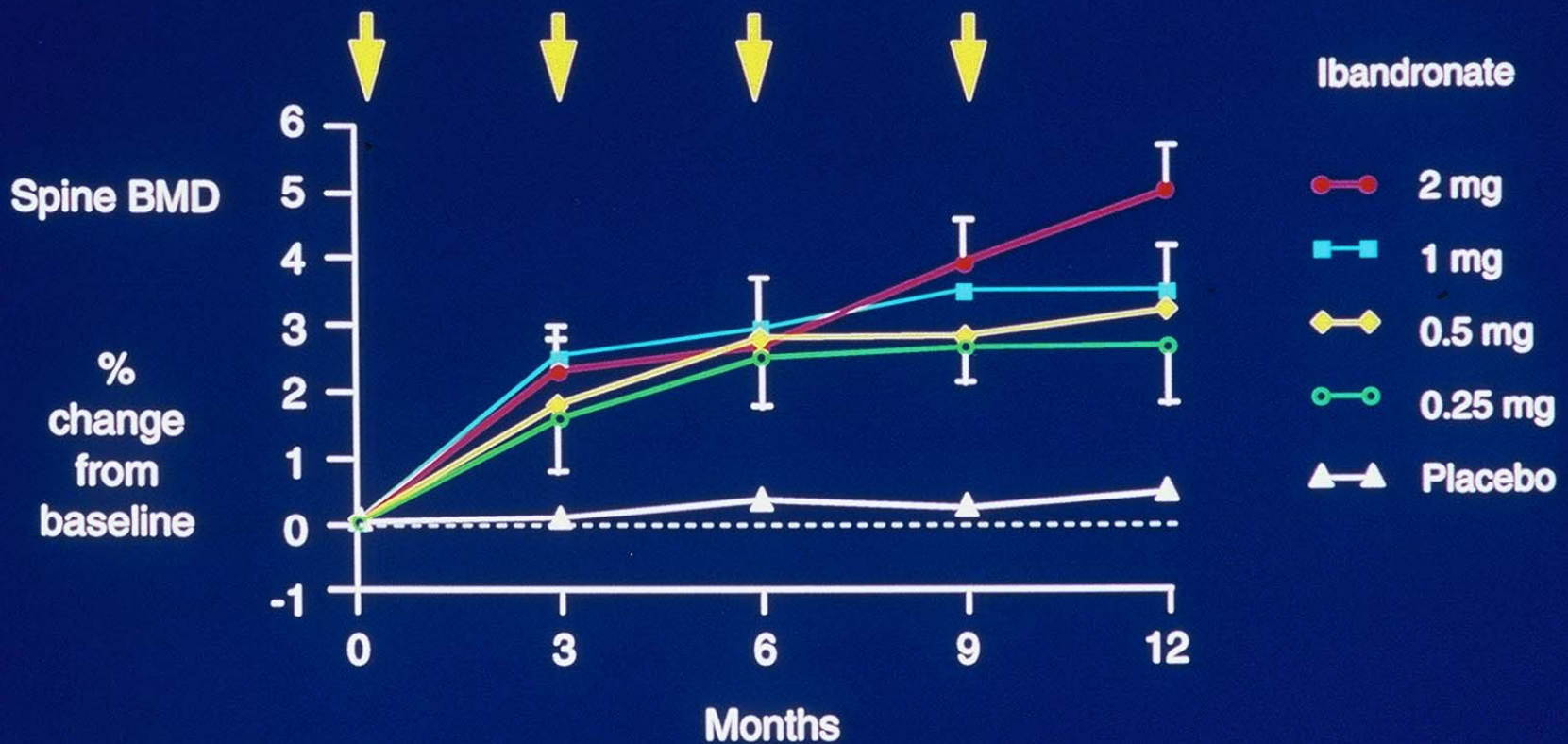
**Baseline**



**1 Year**



# Intravenous Bolus Ibandronate for Treatment of Osteoporosis



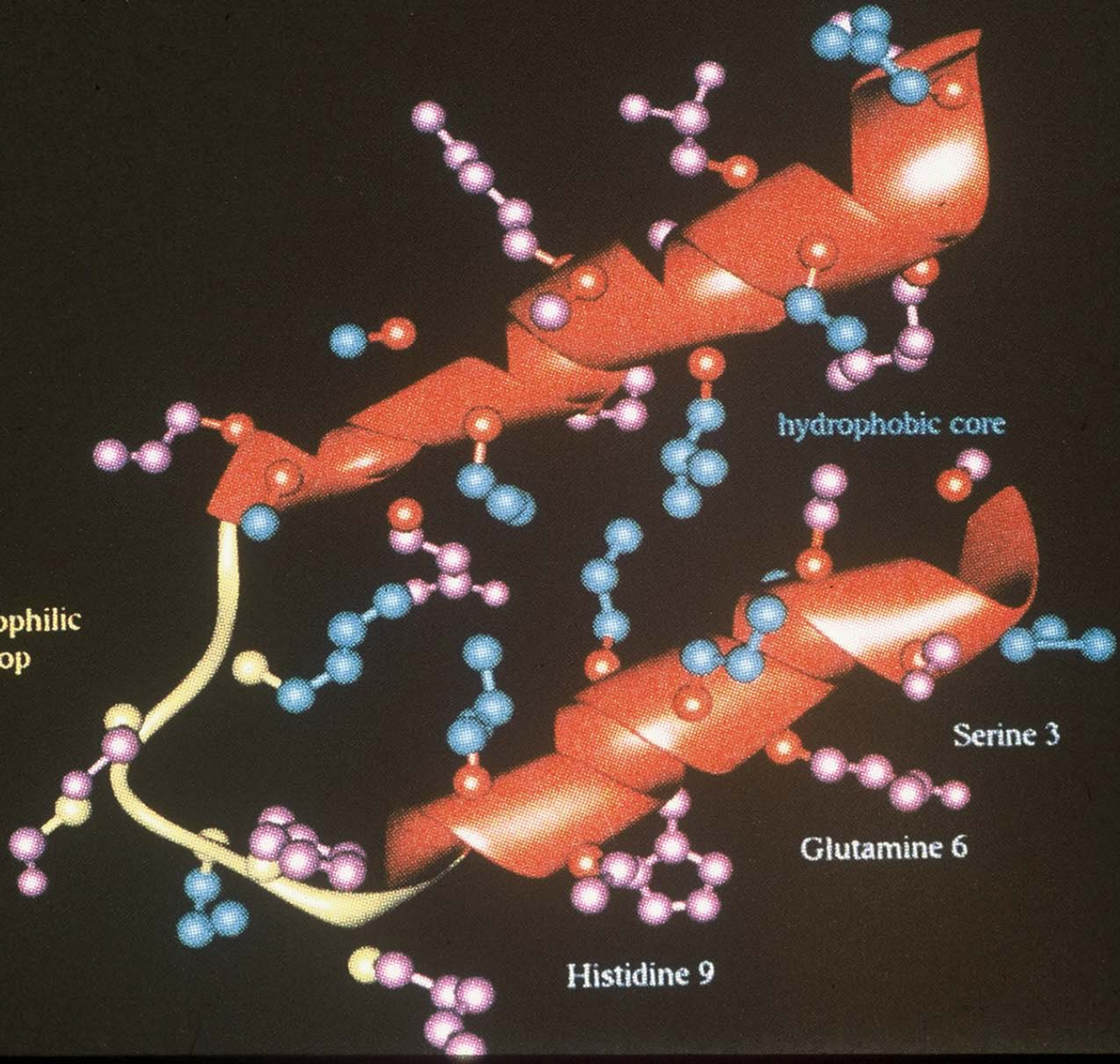
Hydrophilic  
loop

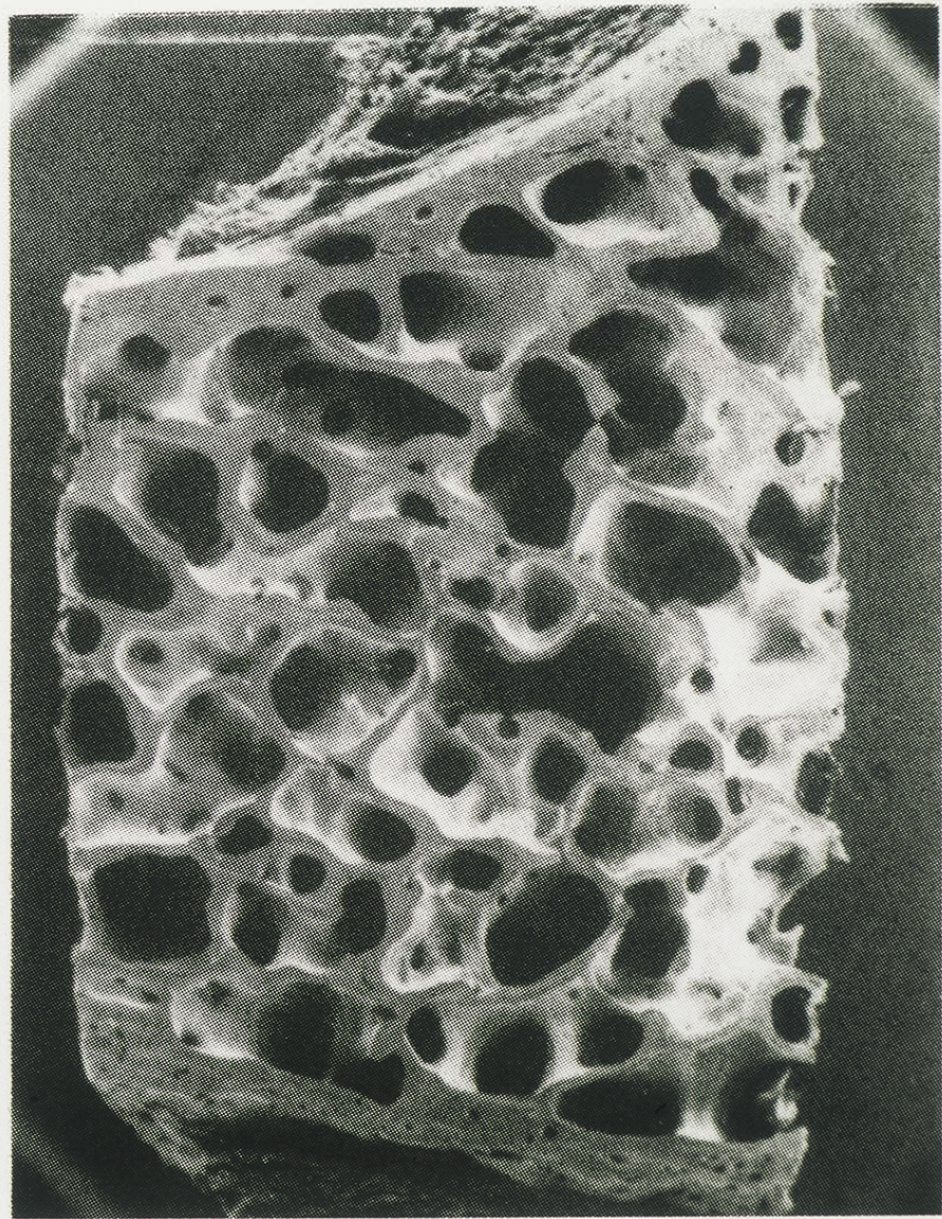
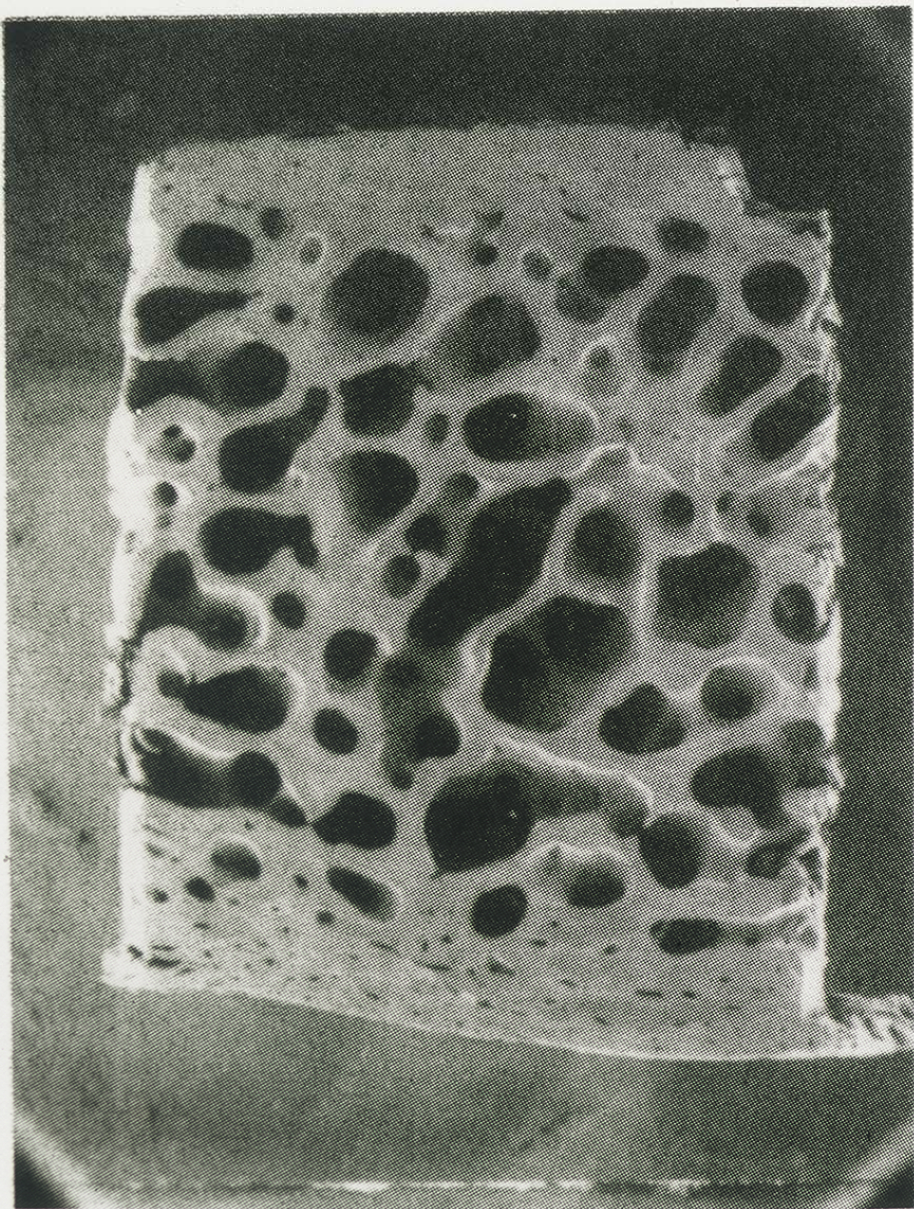
hydrophobic core

Serine 3

Glutamine 6

Histidine 9





## Risk for Osteoporotic Fracture

Low bone mass is the single most accurate predictor of increased fracture risk.

Compston, J.E., Cooper, C., and Kanis, J.A.: Bone densitometry in clinical practice, *Br. Med. J.* 310:1507-1510, June 10, 1995.

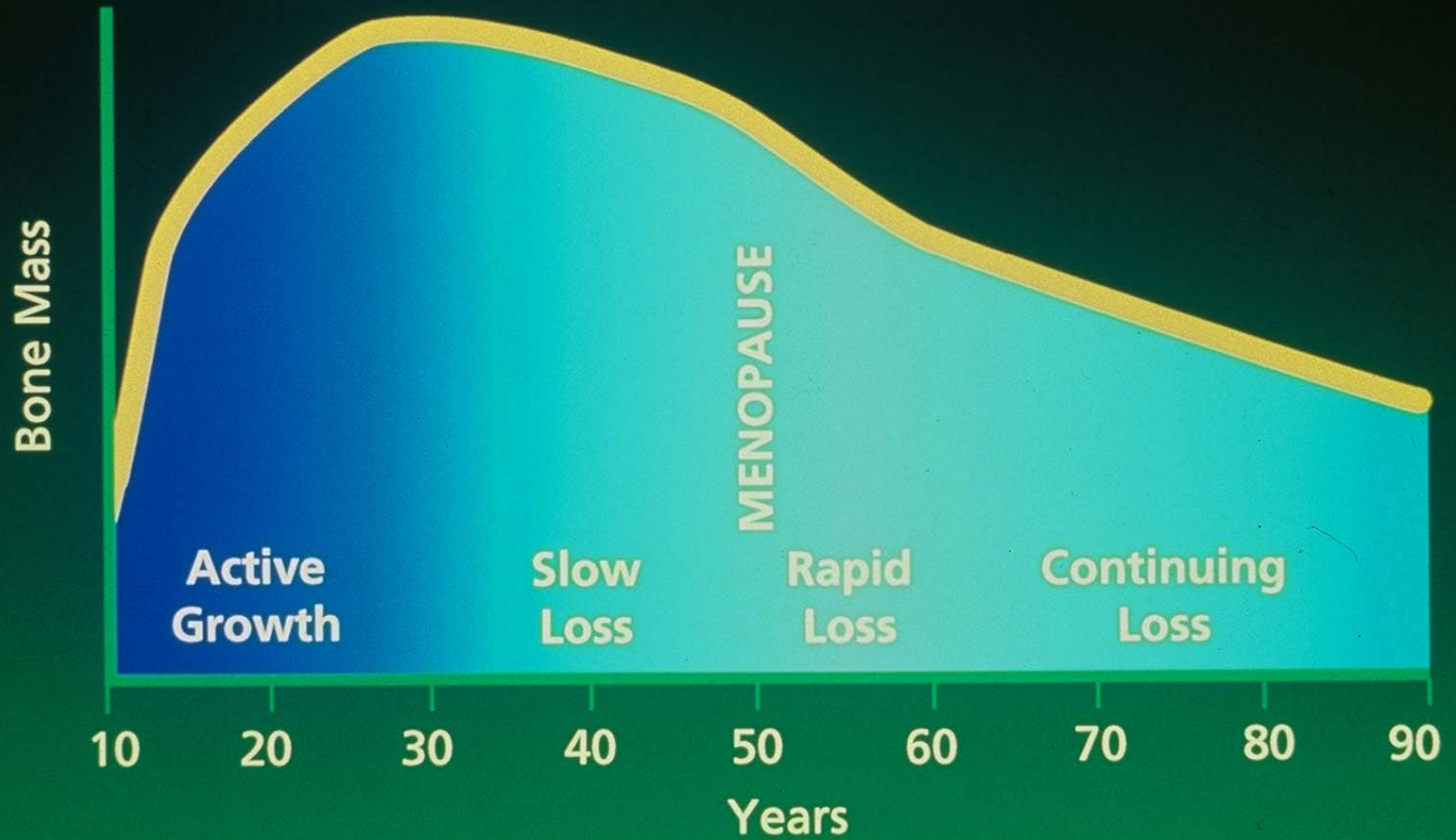
Consensus Development Conference: Diagnosis, prophylaxis, and treatment of osteoporosis, *Am. J. Med.* 94:646-650, June 1993.

Cummings, S.R. et al.: Bone density at various sites for prediction of hip fractures, *Lancet* 341:72-75, January 9, 1993.

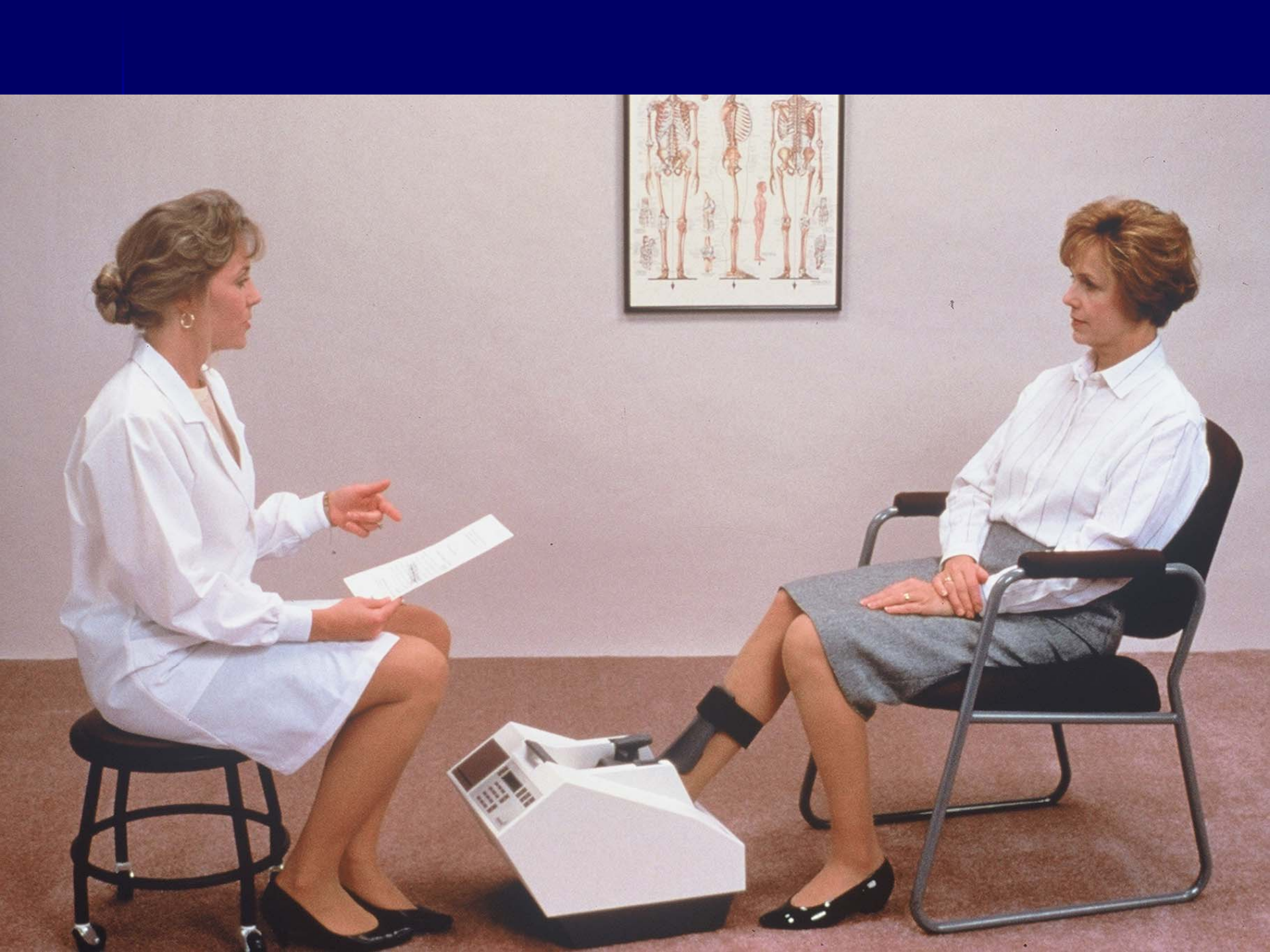
Kanis, J.A.: Osteoporosis and its consequences, in *Osteoporosis*, Cambridge, MA, Blackwell Science, Inc., 1994 pp 1-20.

WHO Study Group: Assessment of fracture risk and its application to screening for postmenopausal osteoporosis, World Health Organization, WHO Technical Report Series, No. 843, 1994, pp 1-18.

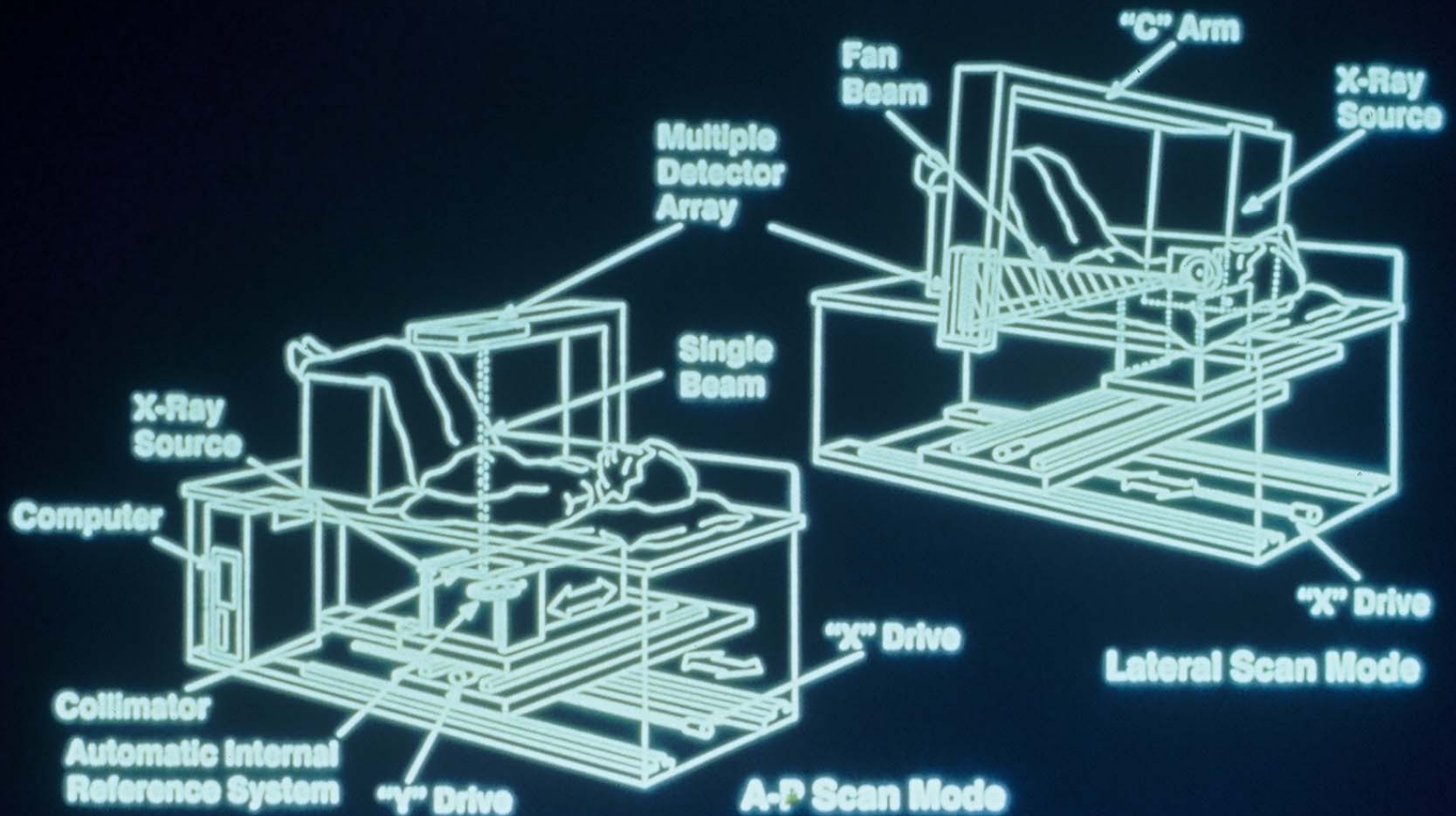
# Bone Mass in Women



Adapted from Wasnich, R.D. et al.: *Osteoporosis: Critique and Practicum*, Honolulu, Banyan Press, 1989, pp. 179-213.

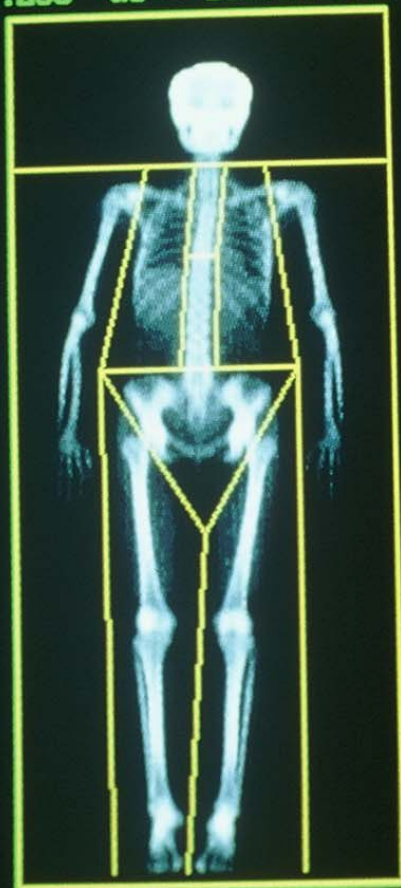


# QDR-2000™ Principle of Operation



# Hologic, Inc.

k = 1.255 d0 = 139.5(1.000)[0]



321 x 170

Hologic QDR 1000 (S/N WB001)  
Whole Body Version 5.00

A05188906 Thu May 18 15:33 1989  
Name: LILLIAN WHOLE BODY  
Comment:  
I.D.: Sex: F  
S.S.#: - - Ethnic: 0  
ZIPCode: Height: 162.56 cm  
Scan Code: MDS Weight: 59.02 kg  
BirthDate: 05/26/47 Age: 42  
Physician:

Region	Area (cm <sup>2</sup> )	BMC (grams)	BMD (gms/cm <sup>2</sup> )
Head	244.9	392.3	1.602
Left Arm	178.4	138.3	0.775
Right Arm	182.5	145.0	0.795
Left Ribs	205.0	113.6	0.554
Right Ribs	233.2	130.0	0.557
Thoracic	92.2	84.2	0.914
Lumbar	122.6	110.6	0.902
Pelvis	316.7	269.7	0.852
Left Leg	350.7	328.6	0.937
Right Leg	364.9	344.9	0.945
TOTAL	2291.2	2057.2	0.898



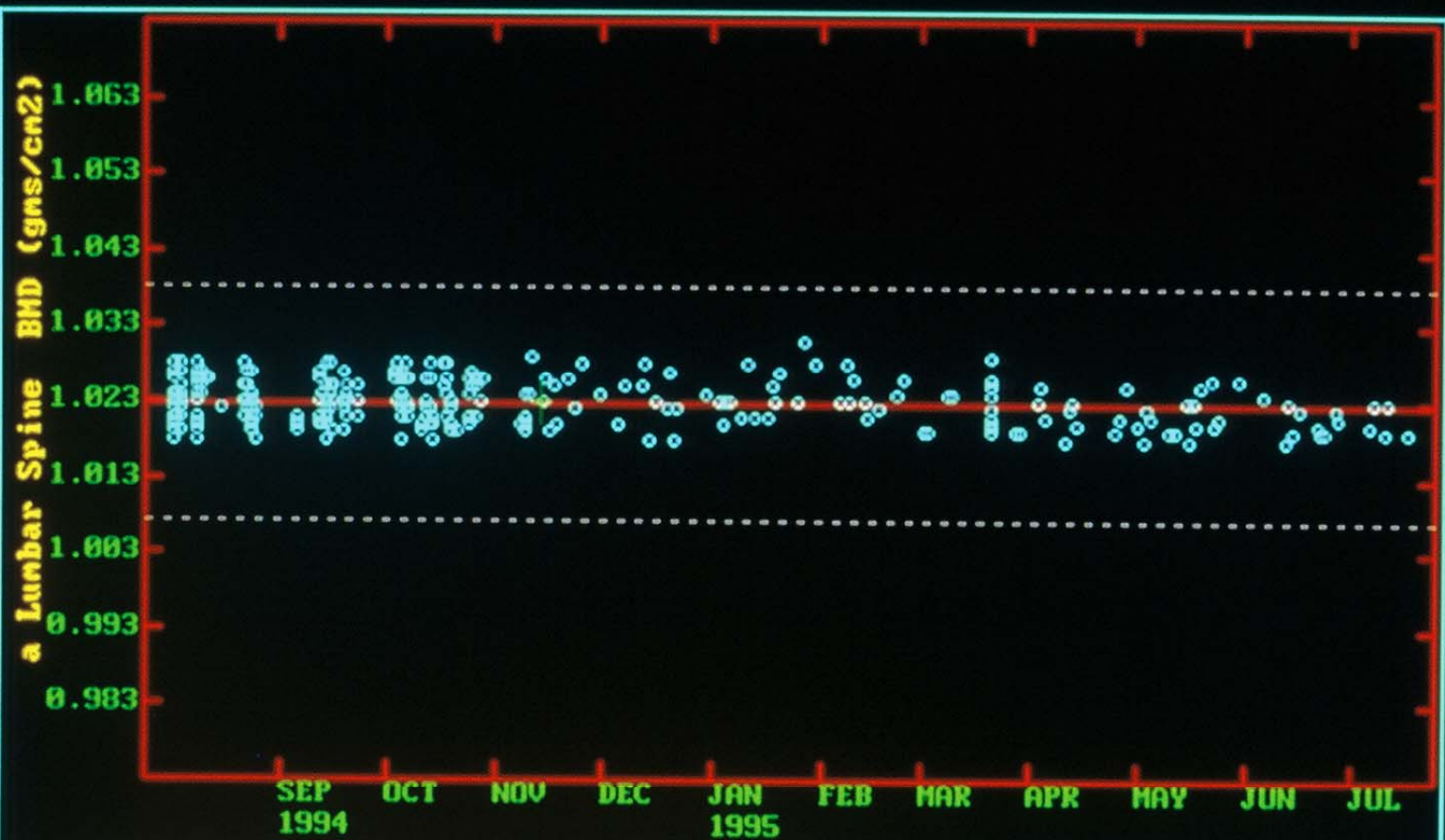
HOLOGIC



# Bone Measurement Techniques

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<u>Technique</u>	<u>Precision (%)</u>	<u>Significant change (%)</u>
Spine DEXA	1	3
Hip DEXA	1.5	4
Q-CT	3	8
p-DEXA	2	5
Ultrasound	4	11



Reference Values	Plot Statistics
spine phantom #2057	n = 313
mean = 1.0227 gms/cn2	mean = 1.0229 gms/cn2
S.D. = 0.0027 gms/cn2	S.D. = 0.0028 gms/cn2
limits = $\pm 1.5\%$ of mean	cv = 0.28%

U Mass Medical Center  
(3004)

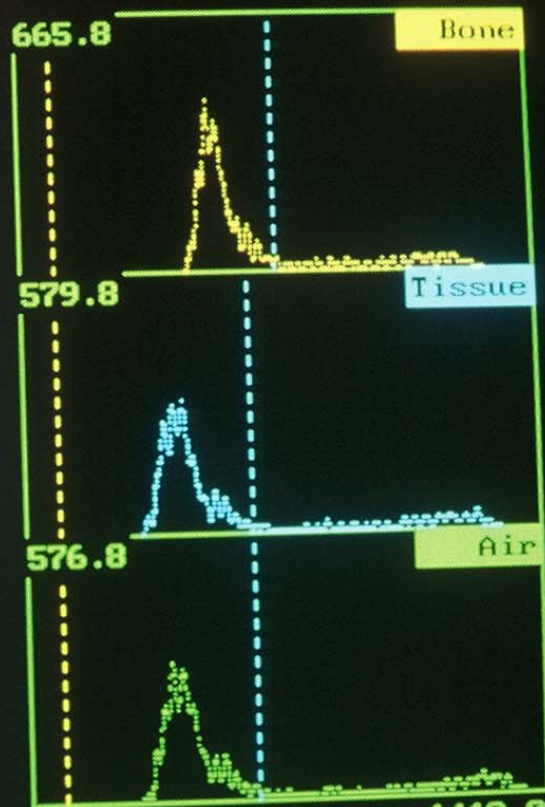


CALCULATION IN PROGRESS

k = 1.105 d0 = 95.1(1.000)[11]



104 x 159



-96.0 1412.0  
Select Metal Threshold  
TH B 10652 T 9277 A 9229  
Left or Right to move threshold 128  
Up/Down to select ( Bone)  
End to End, ESC to ESCape  
CoHome to update tissuenap

Name: BETTY

Hip Implant

## Fracture Risk as a Function of Bone Mass

	Bone Mass	Fracture Risk
Spine	▼ 1 SD*	▲ 1.9 times
Hip	▼ 1 SD*	▲ 2.4 times

\*SD = Standard deviation below aged matched mean

Melton, L.J. III et al.: Long-term fracture prediction by bone mineral assessed at different skeletal sites, *J. Bone Miner. Res.* 8(10):1227-1233, 1993.

Ross, P.D. et al.: Pre-existing fractures and bone mass predict vertebral fracture incidence in women, *Ann. Intern. Med.* 114(11):919-923, June 1, 1991.

# Osteoporosis: A potential risk of chronic LT4 overdosage

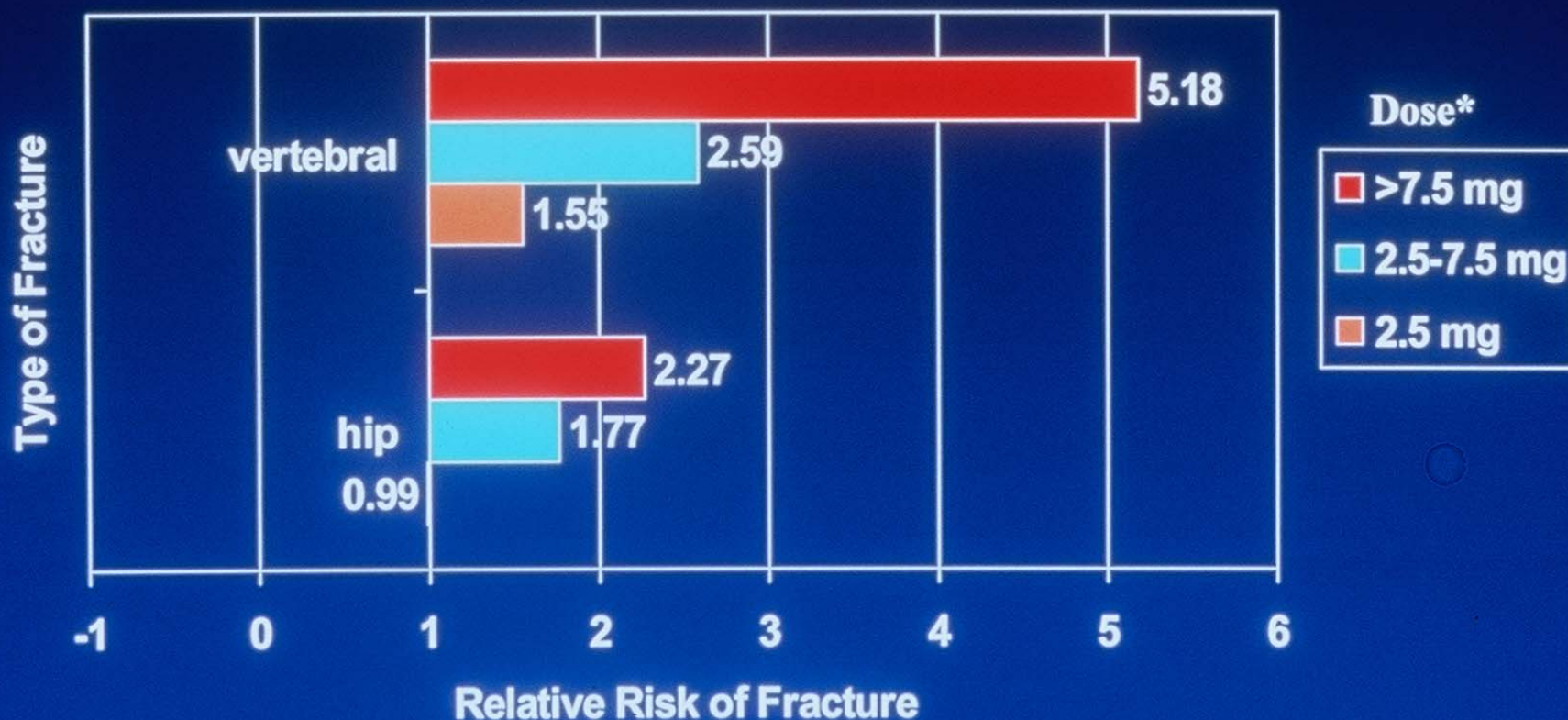
- ▶ **Overdosed premenopausal women:**
  - 12.8% decreased femoral neck density\*
  - TSH levels  $<0.5$ , "normal" T4 (subclinical hyperthyroidism)
- ▶ **Conclusion: Prudence suggests lower LT4 doses, so TSH=0.5-5**

\*JAMA 269:3137-3141, 1988



# Corticosteroid Dose-Dependent Effect on Fracture Risk

N = 488,470



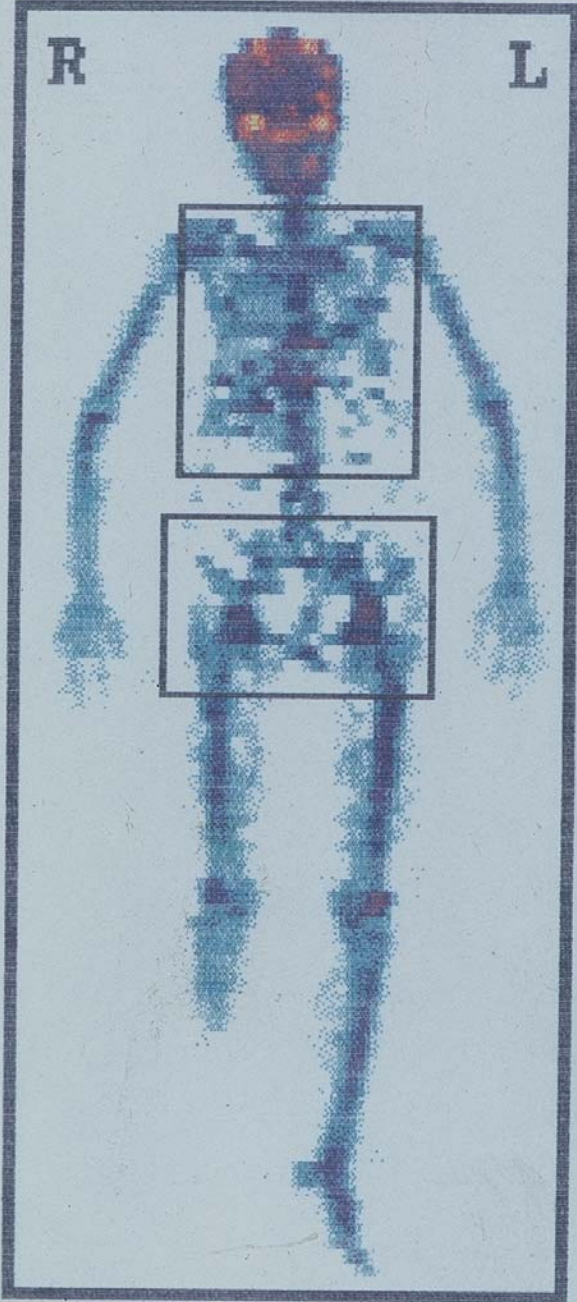
DM 3026L  
26 1 88







L  H









# 350,000 Hip Fractures Each Year



- Only 25% of hip fracture patients will make a full recovery
- 40% will require nursing home care
- 50% will need a cane or walker; and
- 24 % of those over age 50 will die within 12 months
- Nearly 1/4 hip fracture patients will die within 12 months because of complications related to the injury and the recovery period
- The cost of hip fracture care averages \$33,000 per patient
  
- The cost of one year risedronate treatment is about \$700-800