

Calcium, Vitamin D, Exercise and Bone Health

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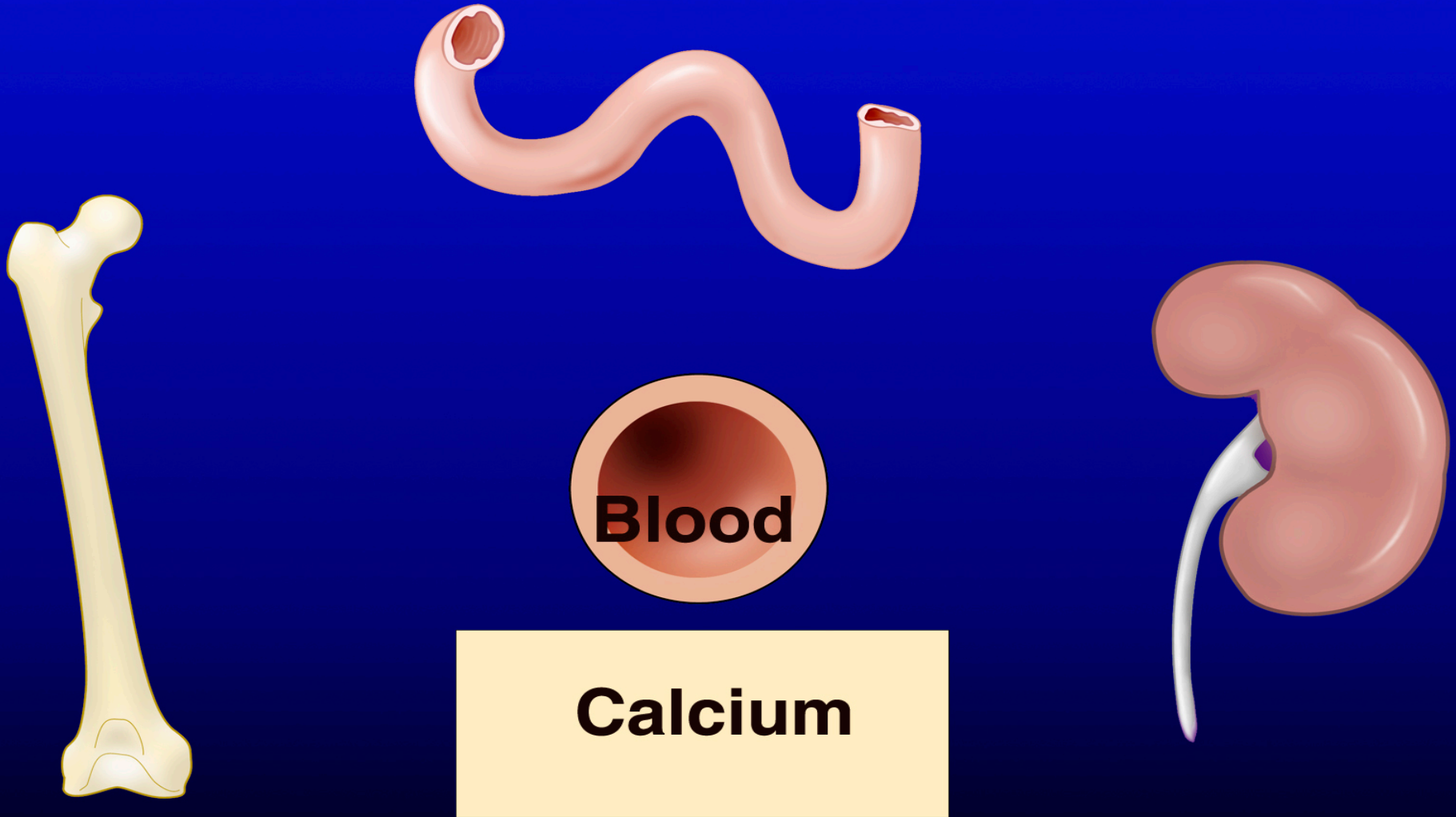
New York, NY USA

2nd International Nutrition Conference

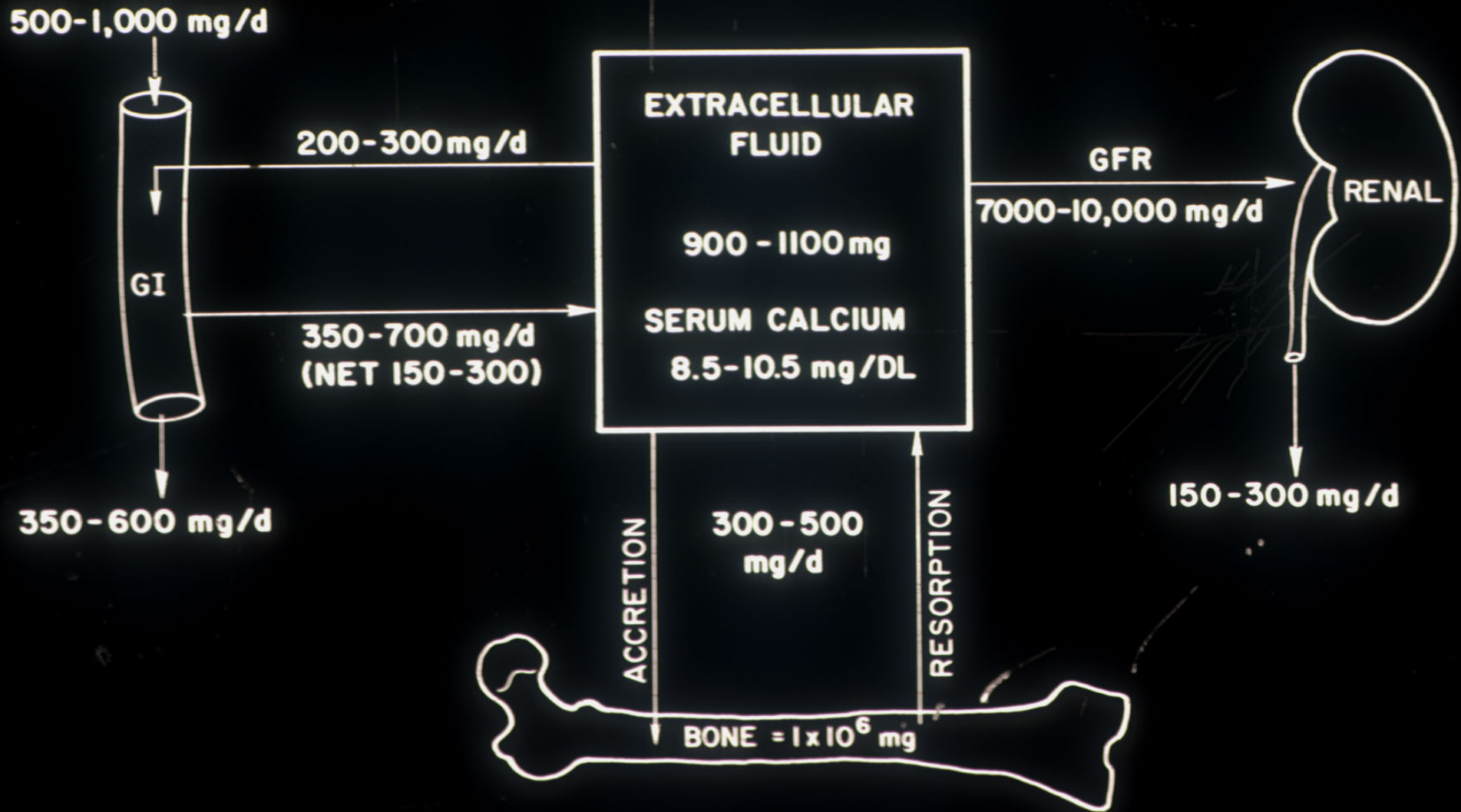
Yerevan, Armenia

May 30-31, 2016

Regulation of Serum Calcium



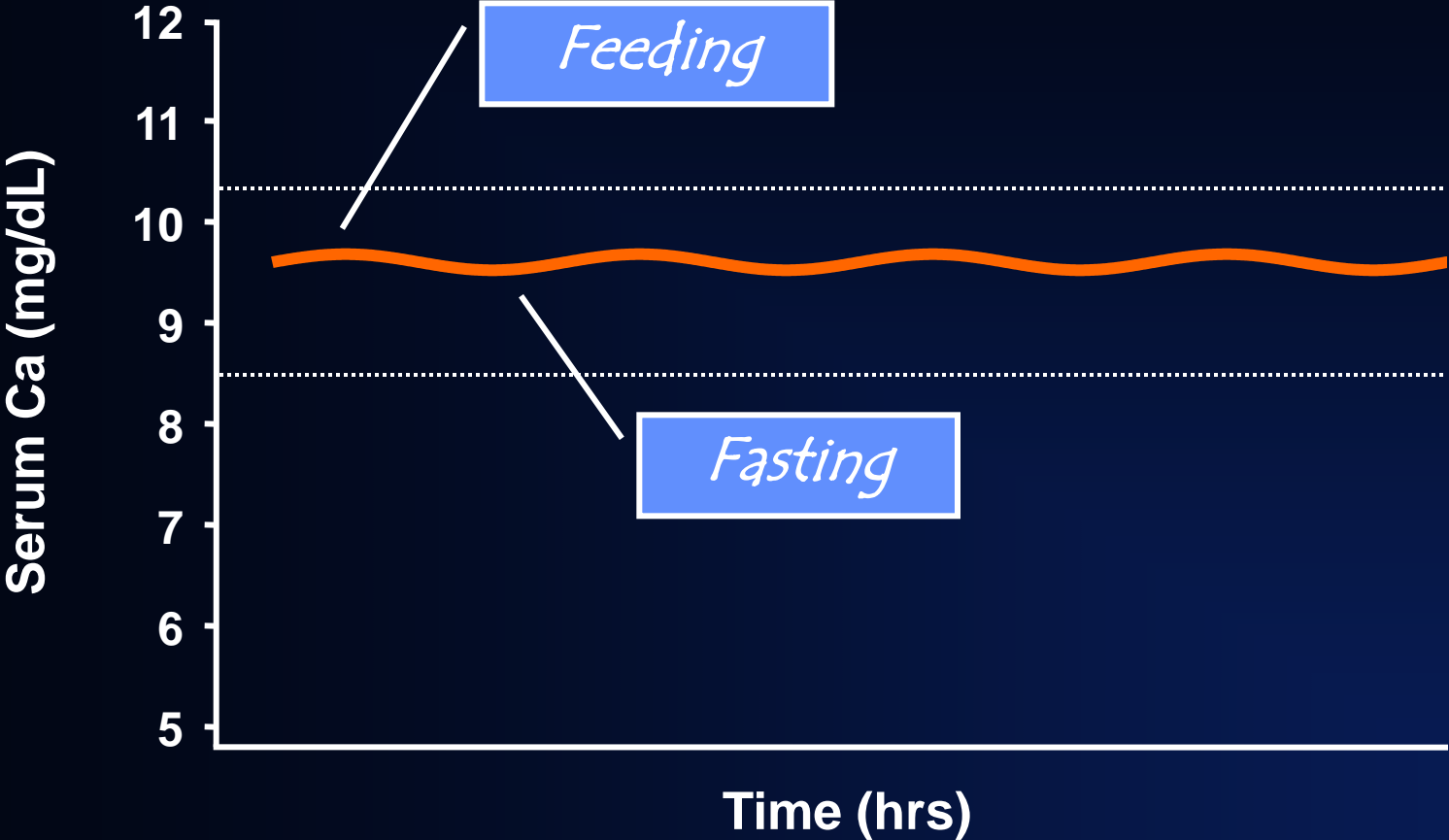
ADULT CALCIUM BALANCE



Key principle #1

Hormonal mechanisms keep the serum calcium within normal limits "at all times" under general homeostatic conditions- even if calcium balance is negative

Normal Function

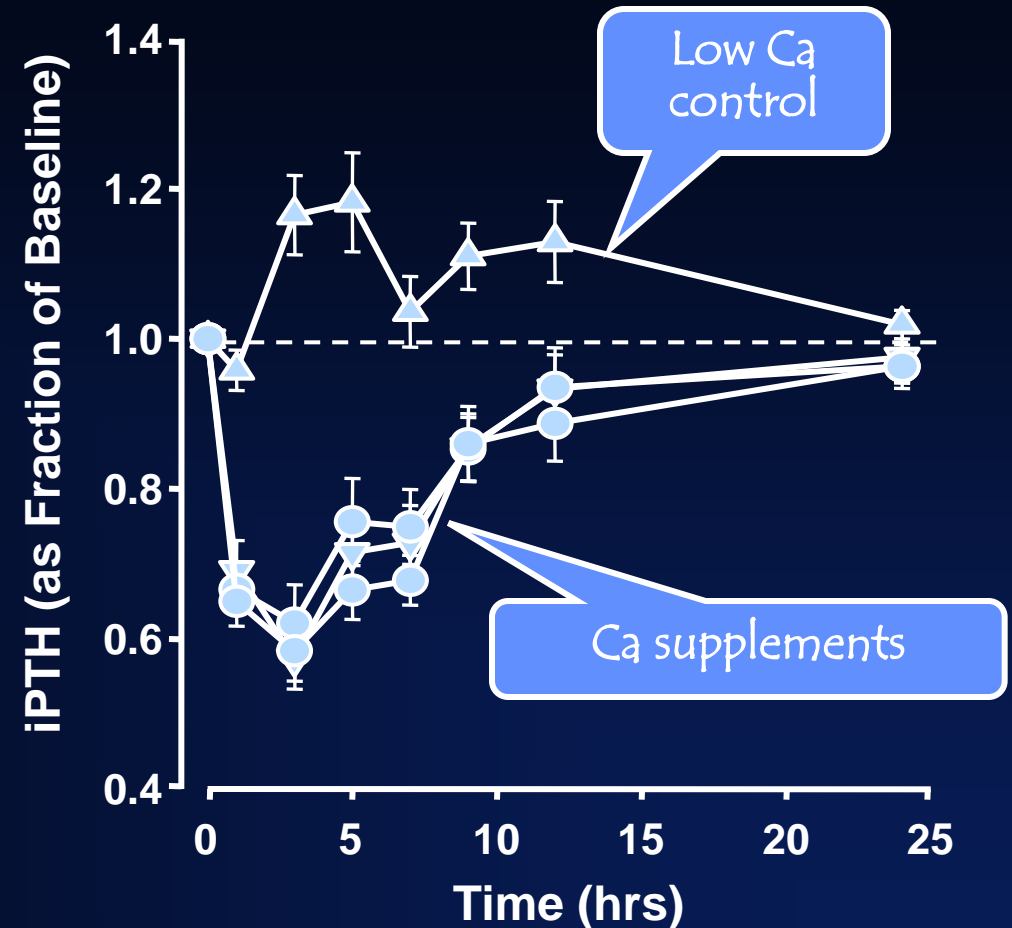


Hormonal regulation of the serum calcium level

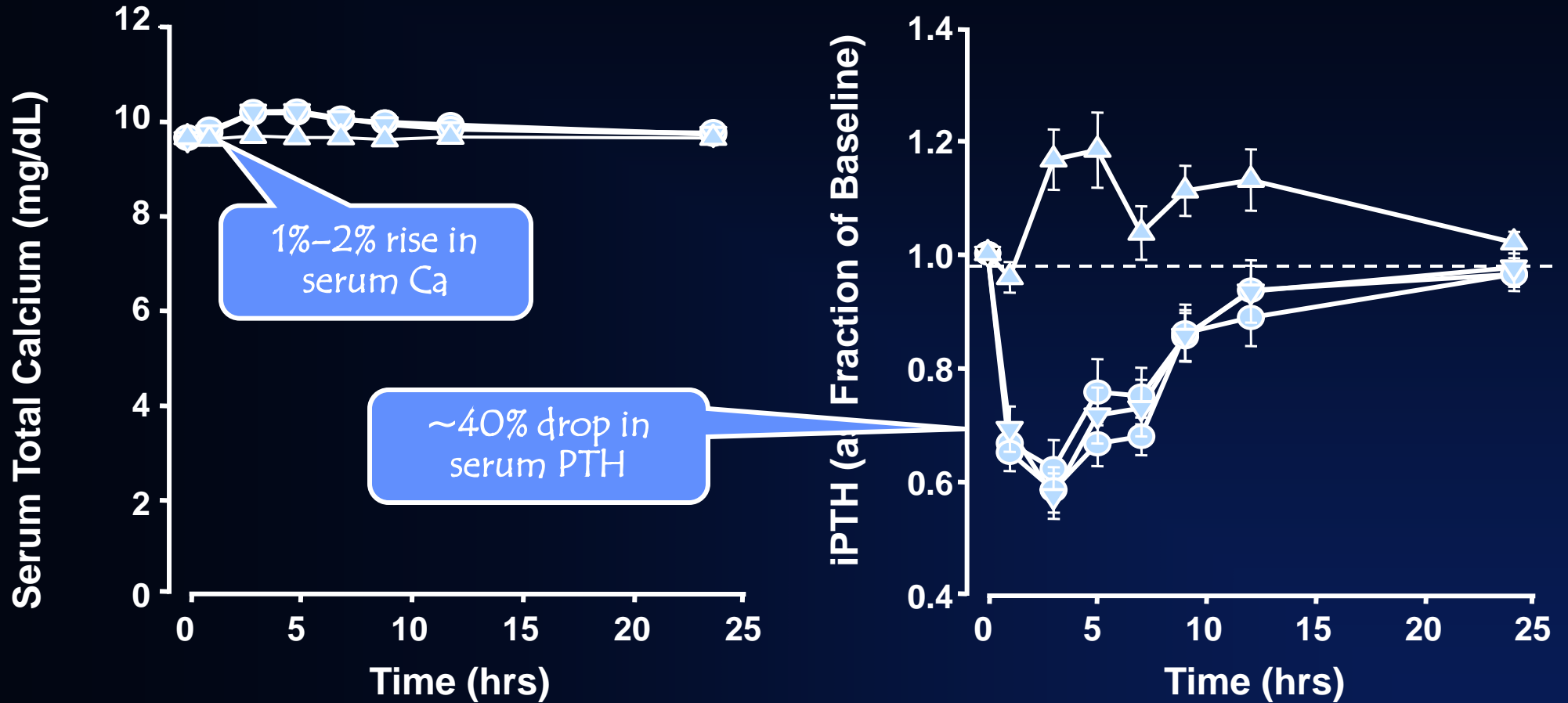
- **Parathyroid hormone**
- Vitamin D

PTH Responsiveness

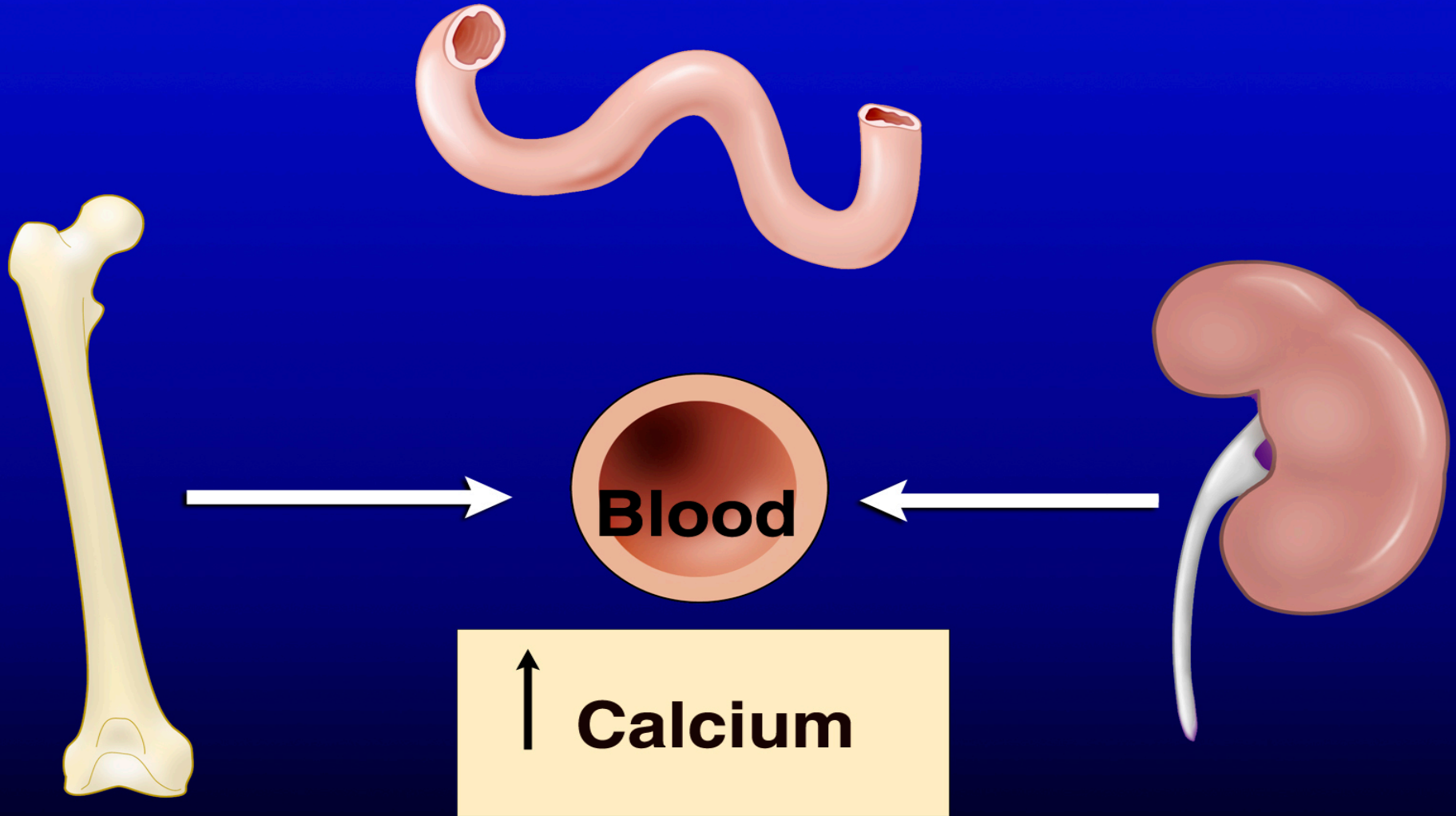
- 24 healthy post-menopausal women
- 500 mg oral Ca load from each of 3 equivalent supplement preparations



PTH Responsiveness

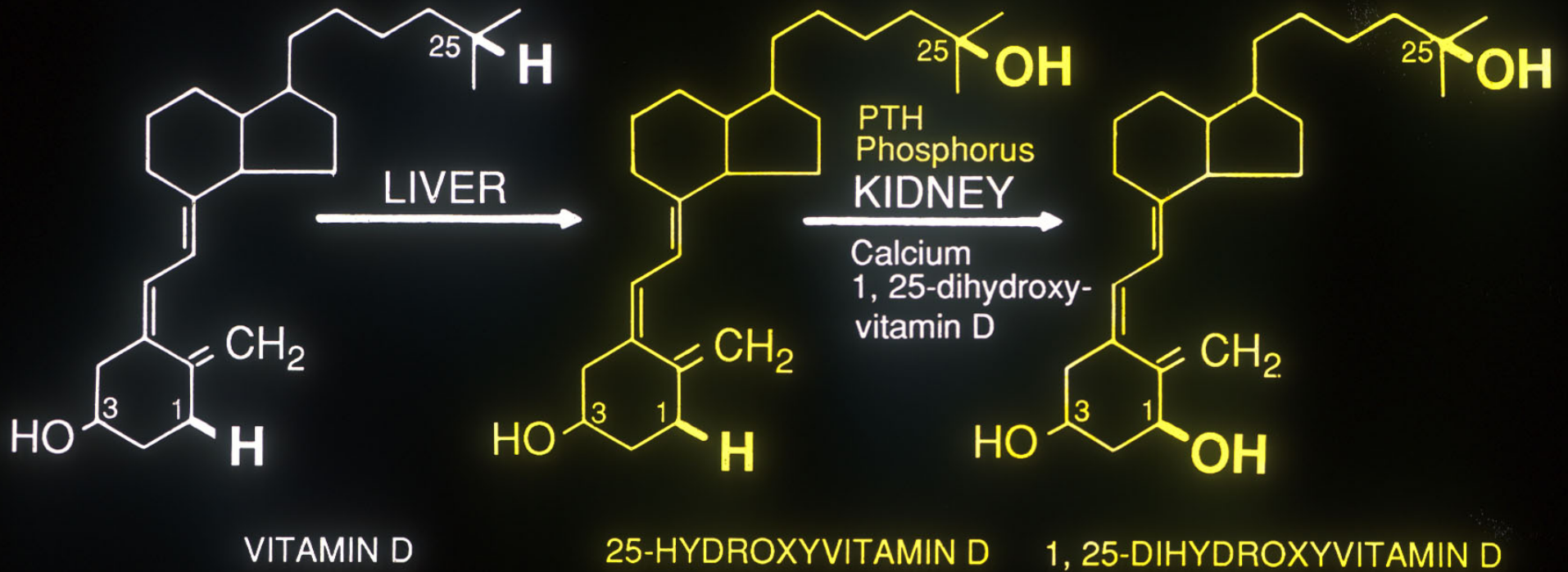


PTH: Effect on Serum Calcium



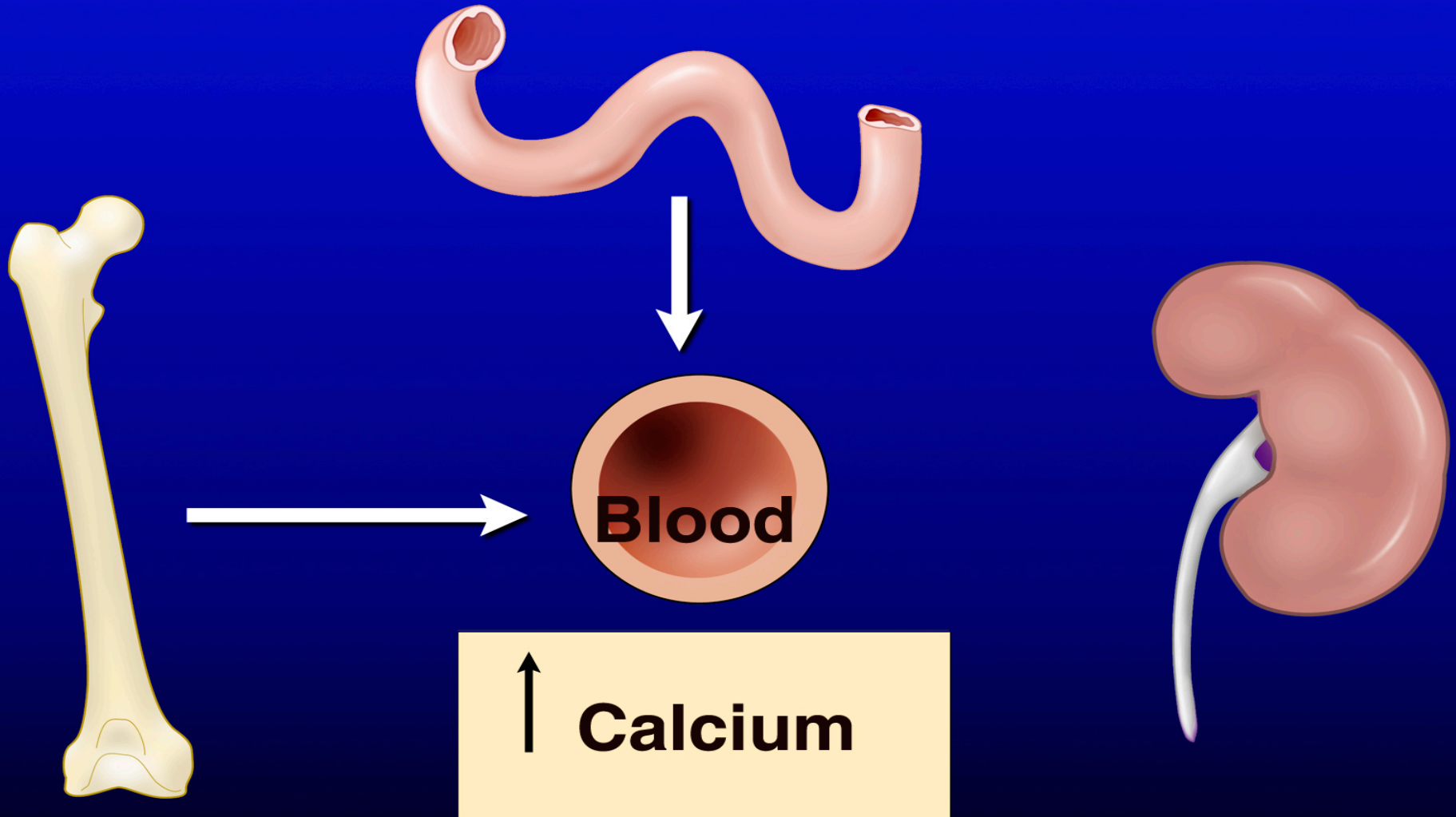
Hormonal regulation of the serum calcium level

- Parathyroid hormone
- Vitamin D



**Storage form: index of vitamin D
sufficiency or insufficiency**

1,25(OH)₂D: Effect on Serum Calcium

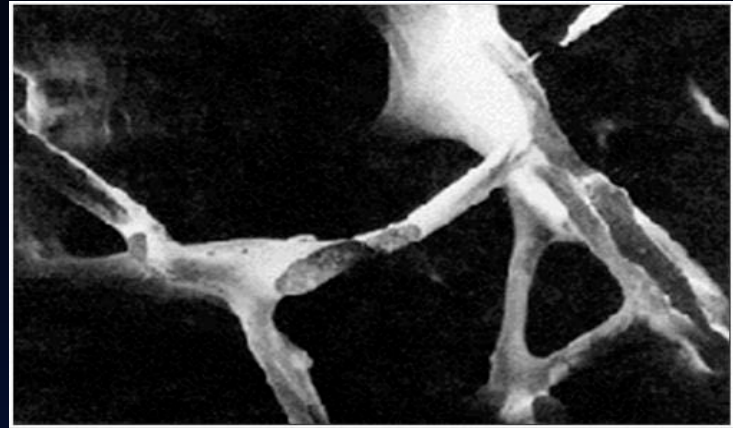


Principle #2

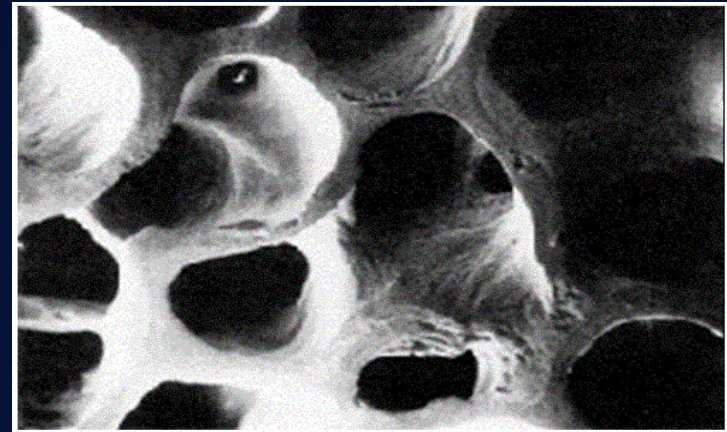
- Osteoporosis is a state of *skeletal* calcium deficiency; not of abnormalities in the serum calcium
- The serum calcium in osteoporosis is typically:
 - Normal
 - High
 - Low

Osteoporosis: Identifying the Problem

“ A skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.”



Osteoporotic bone



Healthy bone

Osteoporosis

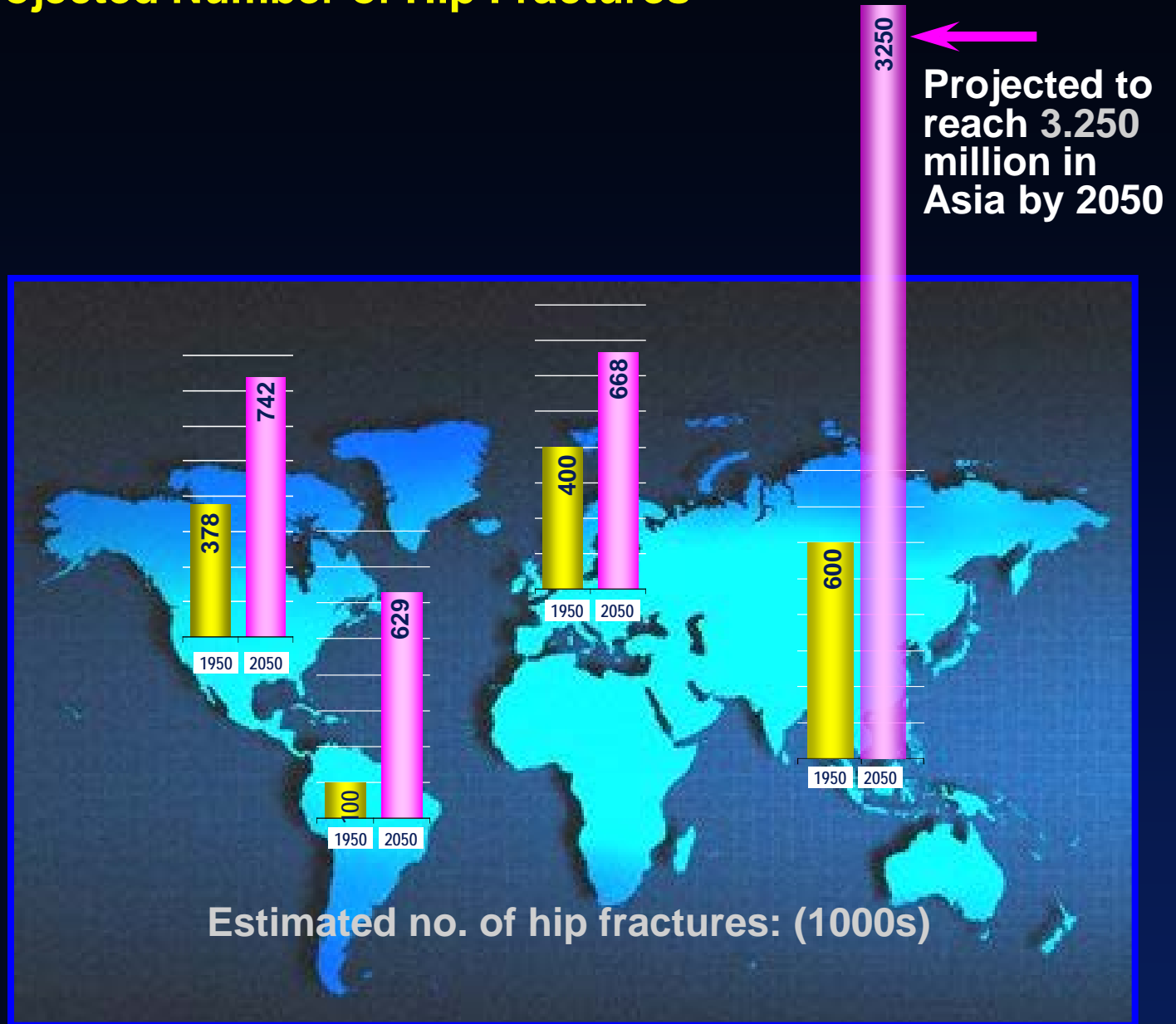
- A skeletal calcium deficiency state (not a state of abnormal serum calcium concentration) associated with bone loss and microarchitectural deterioration

Osteoporosis

A GLOBAL PROBLEM

Projected Number of Hip Fractures

Total number of hip fractures:
1950 = 1.66 million
2050 = 6.26 million



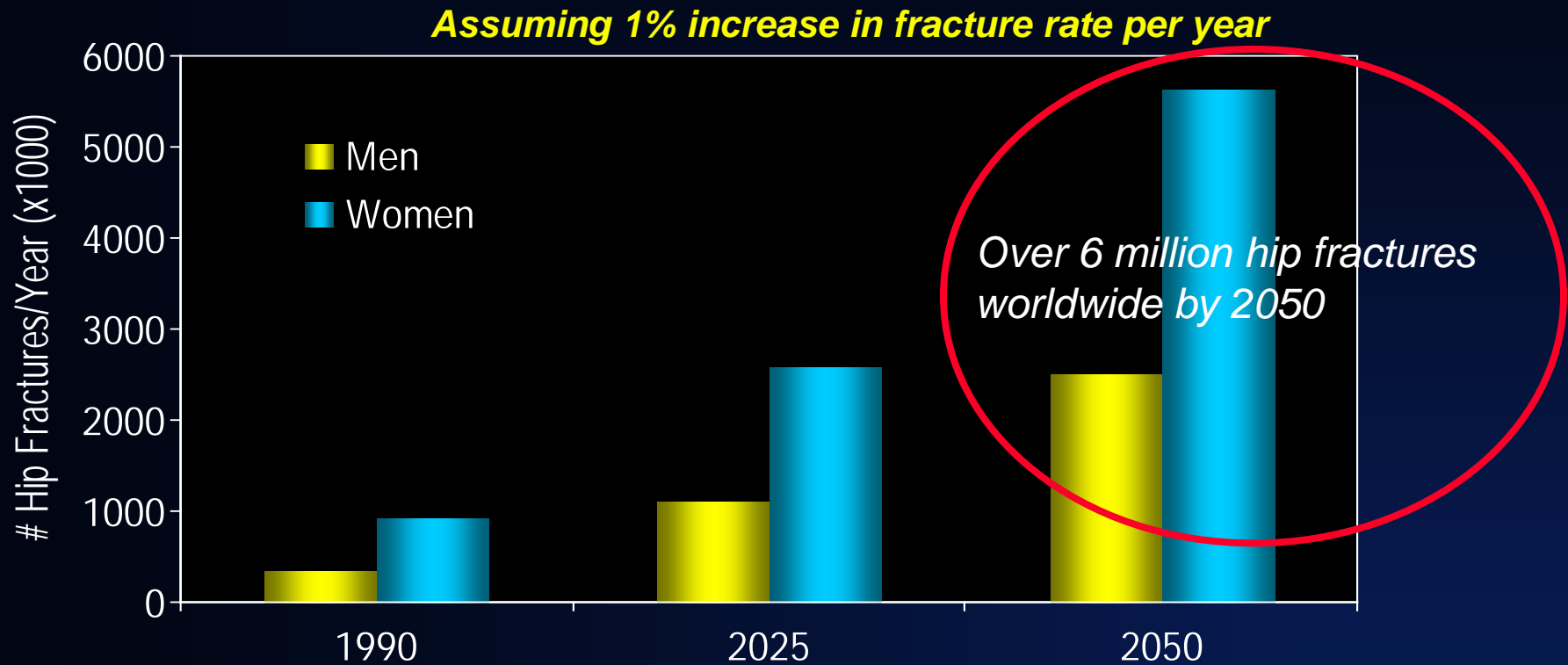
Osteoporosis: Worldwide Prevalence

- **Affects 200 million women worldwide¹**
 - **1/3 of women aged 60 to 70**
 - **2/3 of women aged 80 or older**
- **Approximately 30 % of women over the age of 50 have one or more vertebral fractures²**

1. International Osteoporosis Foundation Osteoporos Int 1996, 6:233

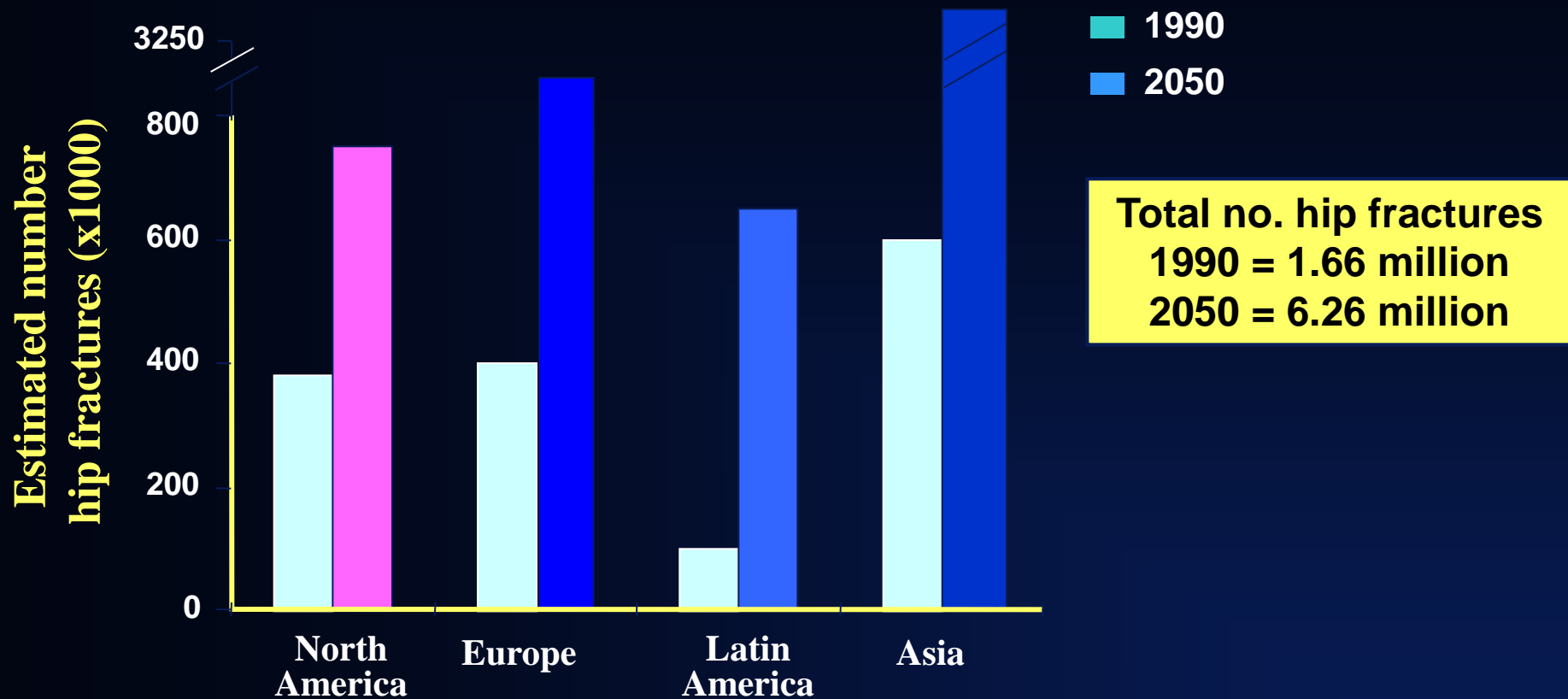
2. Dennison, 2000

Predicted Number of Hip Fractures Worldwide



Socioeconomic impact of hip fractures will increase markedly, particularly in Asia.

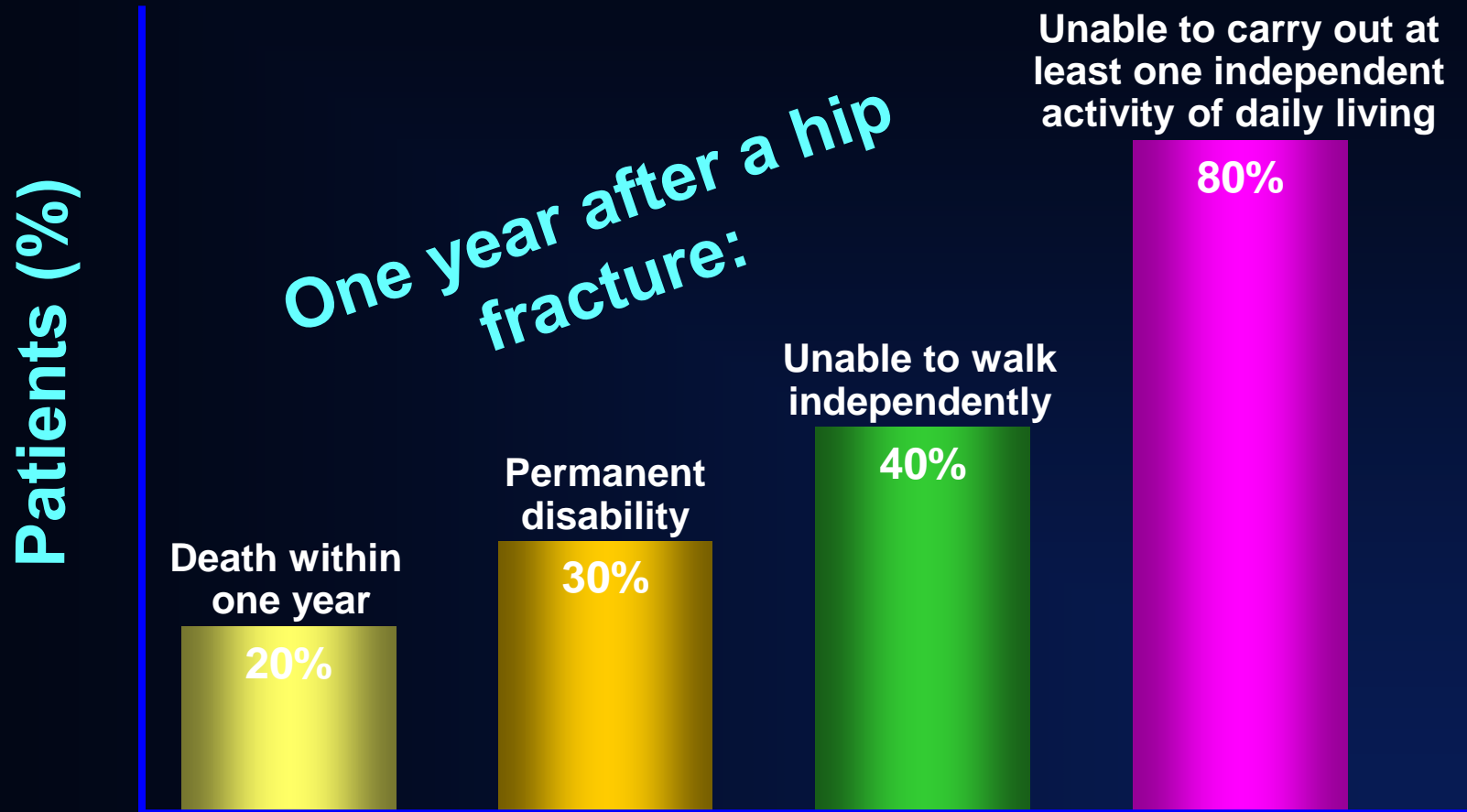
Projected number of hip fractures worldwide



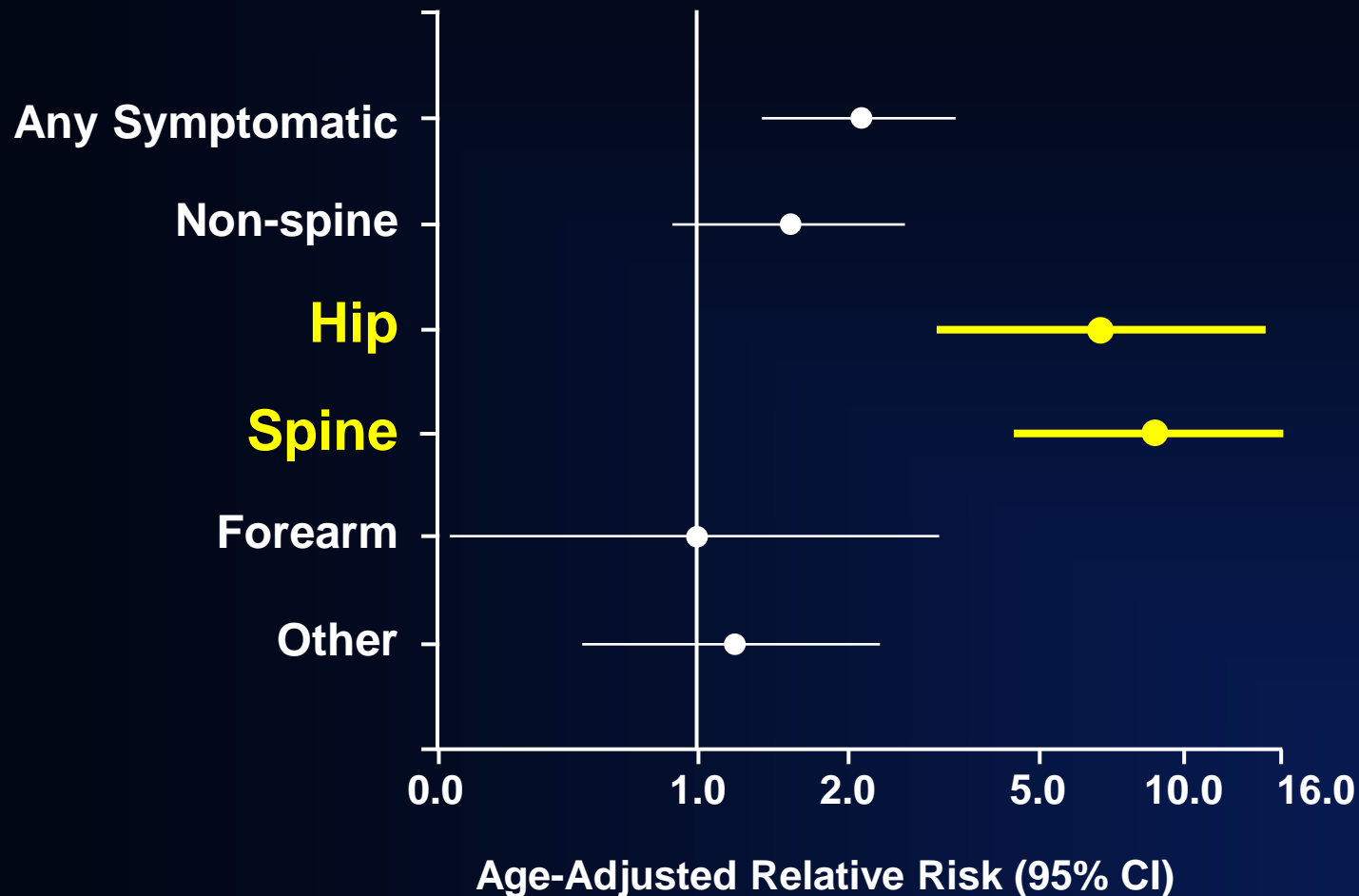
**BY THE YEAR 2050, MORE THAN HALF
OF THE WORLD'S 6 MILLION HIP
FRACTURES WILL OCCUR IN ASIA**

Cooper C et al. Hip fractures in the elderly
Osteoporosis Int'l 1992;2;285-289

Morbidity After Hip Fractures



Relative Risk of Death Following Clinical Fractures Fracture Intervention Trial (FIT)*



*6459 postmenopausal women ages 55-81 years followed for an average of 3.8 years

Importance of the Hip Fracture

- Increased morbidity and mortality
- Without treatment ,the risk of another fracture with the first year is significant
- Another fracture leads to another fracture
- Impaired Quality of Life

Human Costs of Osteoporosis

- Impaired function, decreased mobility
- More bone loss due to decreased activity
- Compressed abdomen, reduced appetite
- Reduced pulmonary function
- Sleep disorders
- Shortened survival
- Poor self esteem



Ross PD et al. *Ann Intern Med* 1991;114:23.
Silverman SL. *Bone* 1992;13 (suppl 2):S27-31.
Cooper C, et al. *Am J Epidemiol* 1993;137:1001-5.
Lyles et al. *Am J Med* 1993;94:595-601.
Schlaich C, et al. *Osteoporos Int* 1998;8:261-7.

Photo courtesy of the National Osteoporosis Foundation

Primary Goal of Therapy Is to Stop the Fracture Cascade



The key epidemiological message:

“Osteoporosis is one of the most dangerous diseases of the 21st century*”

**Narine Mamikonyan, Armenian Osteoporosis Association, 2015*

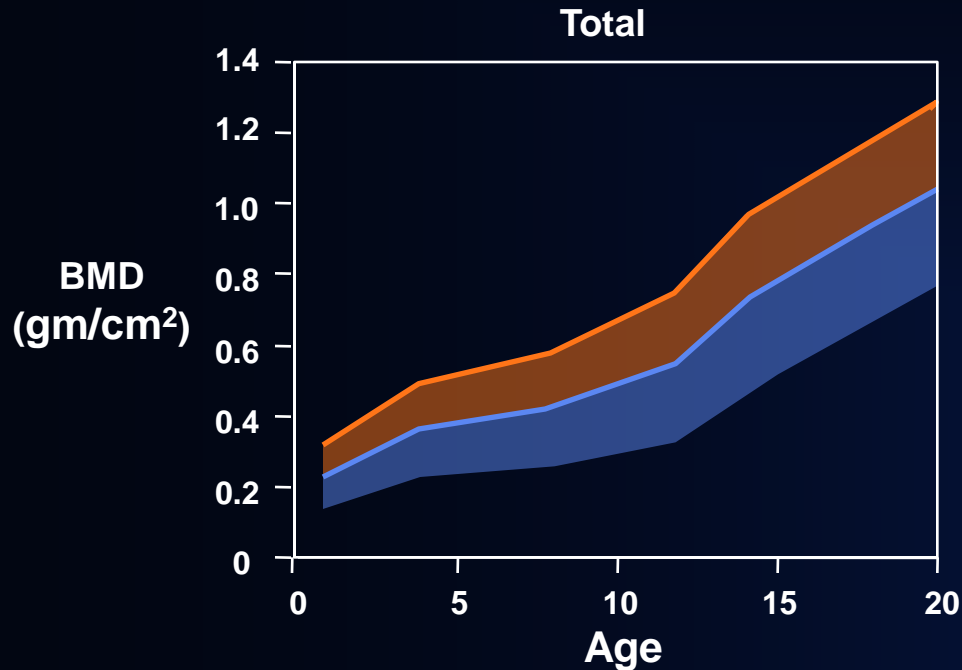
Osteoporosis

- A skeletal calcium deficiency state (not a state of abnormal serum calcium concentration) associated with bone loss and microarchitectural deterioration
- Childhood nutrition is a key element in the disease that is seen in adulthood

**Osteoporosis is a problem that has its
roots in**

CHILDHOOD!

Increase in Bone Mass with Age in Children



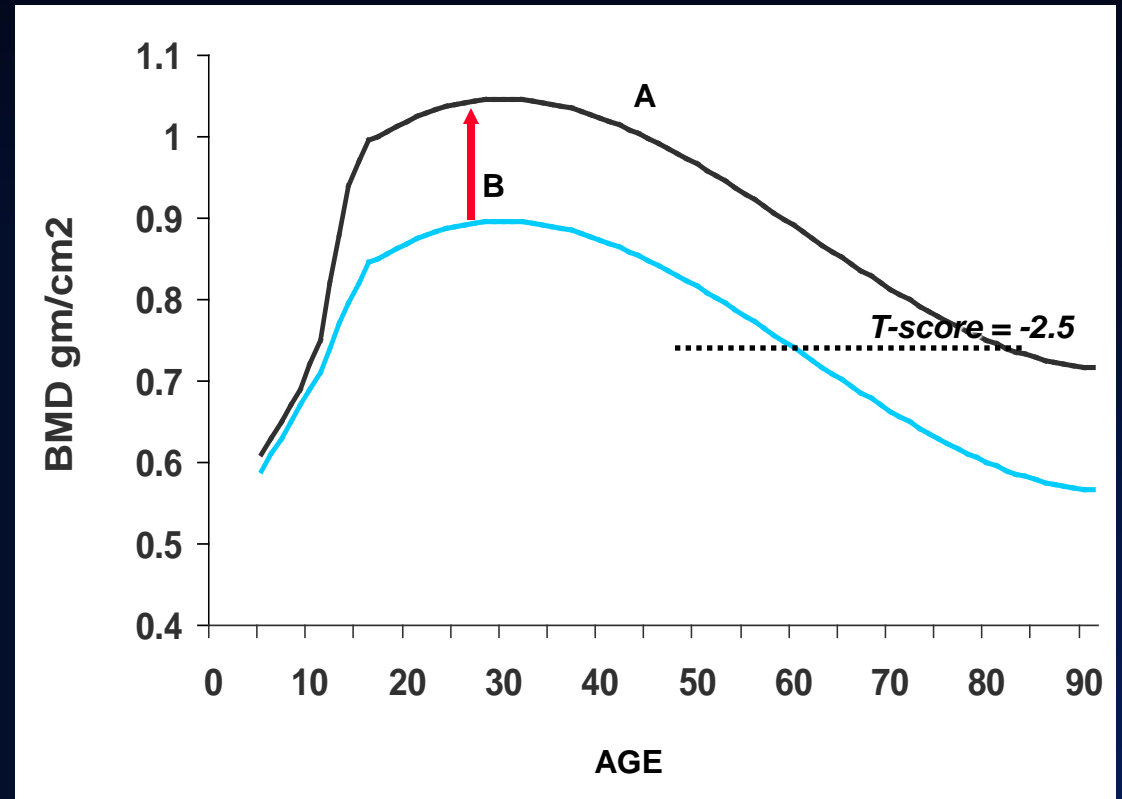
Peak attained in early 20s-30

Maintained until 30s or 40s

Peak bone mass is a major determinant of bone density and strength throughout life

The beginning of the end result: Failure to Achieve Optimal Peak Bone Mass

- A. Optimal Peak Bone Mass
- B. Low normal peak bone mass

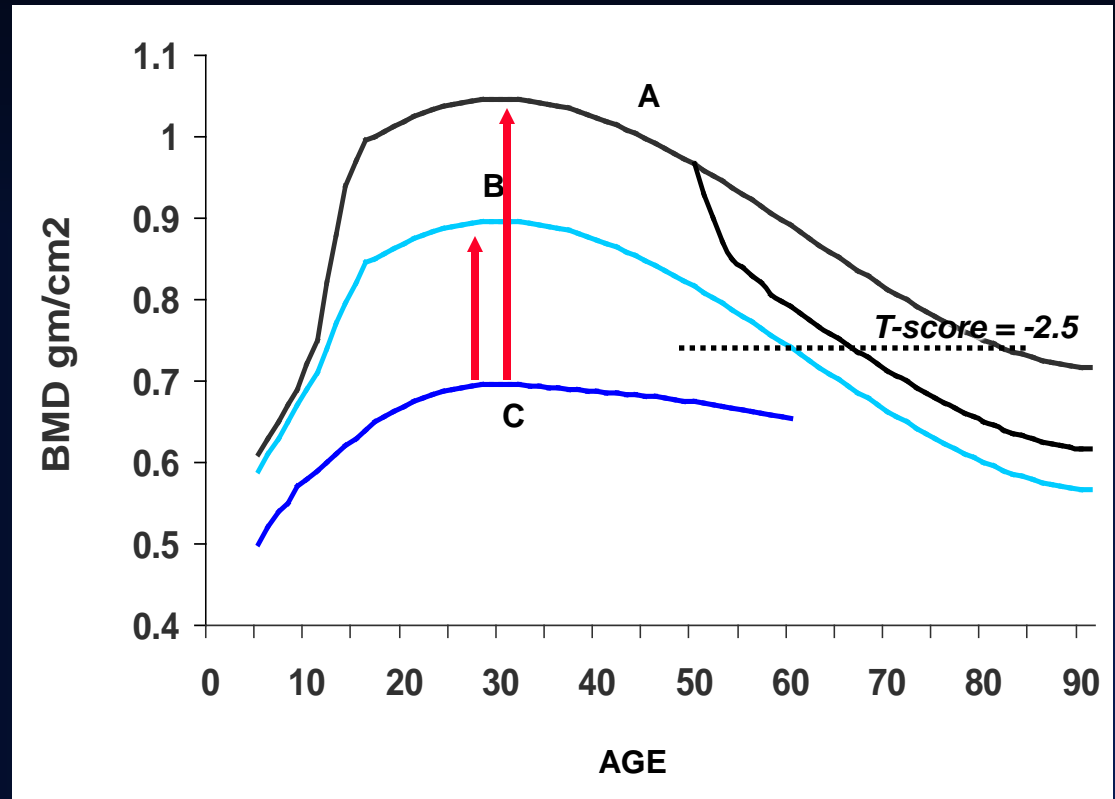


The beginning of the end result: Failure to reach even low normal peak bone mass

A. Optimal Peak Bone Mass

B. Low normal peak bone mass

C. Failure to acquire bone mass even in the low normal range:
• small size
• heredity
• late or missed puberty
• *Stunting?*



Patient seen by Dr. Bilezikian on May 11, 2016: Case in point?

53 YO Caucasian woman with strong family history of osteoporosis
(mother and father)

Menopause 2 years ago. No estrogen Rx

G1 P1

No fragility fractures

No other risk factors

No secondary causes

BMD done because of FH

T-scores: LS -3.0; TH -1.1; FN -2.1; distal radius -0.8

Labs including Chem screen, serum calcium, 25-OH D, PTH, P,
BTMs are all normal. Celiac screen- neg

**Patient seen by Dr. Bilezikian
on May 11, 2016:
Case in point?**

Is this postmenopausal bone loss? (It is hard to imagine that her bone density would fall so quickly in the two years since menopause)

It would seem more likely that her bone density was low well before the menopause

It is possible that she did not achieve the desired optimal peak bone mass in her young adult years

Principle #3

Strongest predictor of bone mineral density in the later years is low bone mineral density at younger ages

Determinants of Peak Bone Mass

- Factors that determine peak bone mass
 - Genetic (approximately 60-80%)
 - Disease susceptibility genes, “high BMD” gene
 - **Exercise**
 - **Nutrition - calcium, vitamin D and protein**
 - Body size and weight
 - Smoking
 - Sex hormones during adolescence

EXERCISE

Childhood

- Stay active
- Stay active
- Stay active
- Stay active
- Stay active

Adulthood

- Walking
- Jogging
- Treadmill
- Weight training
- Tai Chi
- Swimming

Effect of Exercise on Bone Mass

Childhood

- Exercise has been clearly shown to increase bone mass in the growing skeleton

Adulthood

- Exercise has not been clearly shown to increase bone mass in the adult skeleton
- Exercise, though, is helpful for muscle strength, balance, and overall fitness

#1064: Coster et al. Increased Physical Activity in Childhood Reduces Fracture Risk- an 8-Year interventional Study in 3534 Children (ASBMR, 2015)

Background: Exercise increases bone mass in children

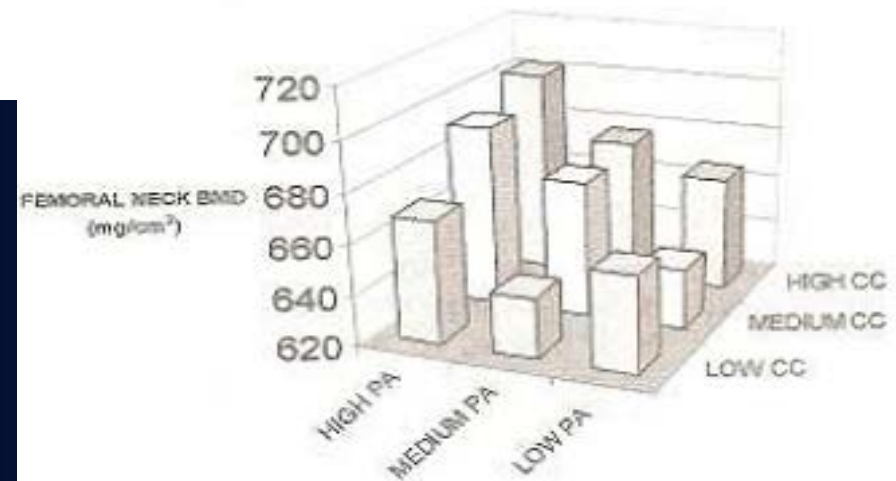
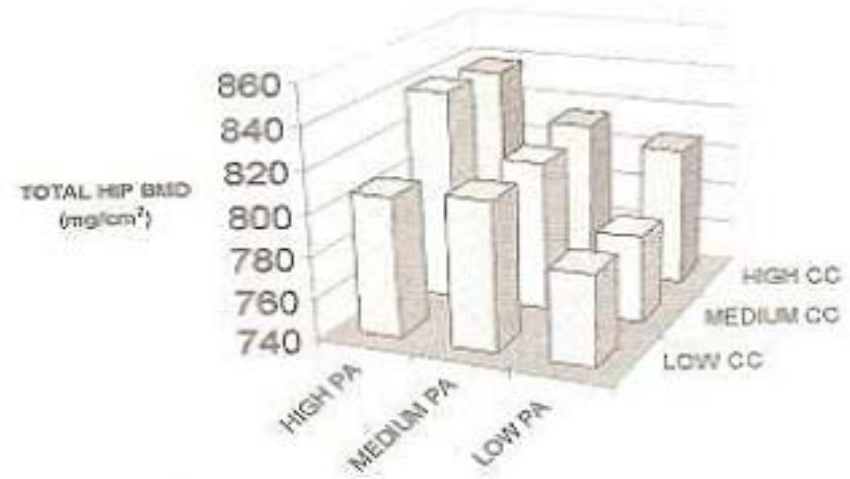
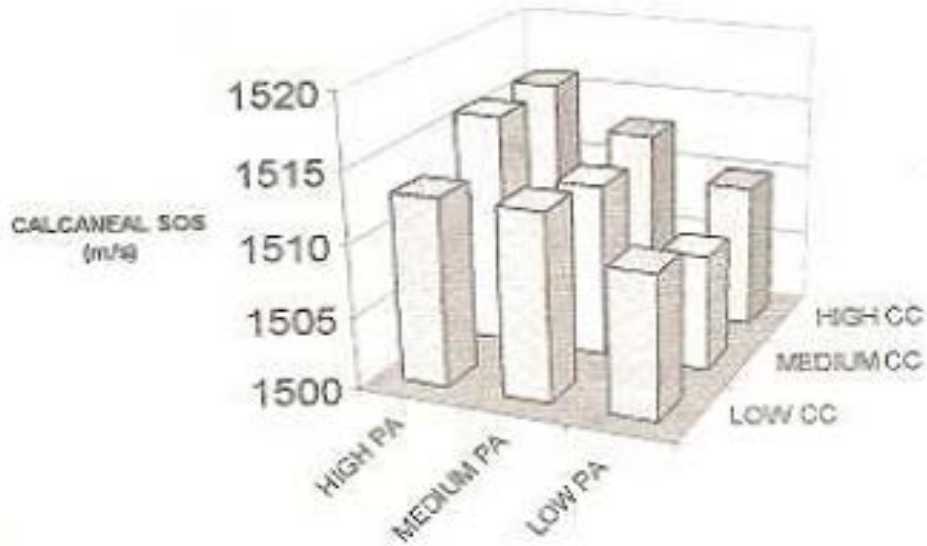
Question: Does it influence fracture risk?

Design: 40' of exercise/school day x 8 yrs in 1339 children (6-8 yrs old).
Control: 2,195 children in other schools 60 minutes/school week.

Results: RR for fx fell every year: at end RR reduction 0.48 (CI 0.25-0.91). Bone mass higher in the exercisers. Muscle strength greater

Conclusion: EXERCISE LEADS TO BETTER SKELETAL HEALTH
IN CHILDREN.

Physical Activity and Calcium Intake work together to increase bone density



Kerr et al. J Bone Miner Res 2001;16:175-181.

Roles of Exercise in Bone Health

- induces growth of larger bones in children and influences peak bone mass
- important for bone health in young adults
- increasingly important with aging
 - slows but does not prevent bone loss
 - maintains muscle strength
 - decreases risk of falling

Children and Adults are not getting enough exercise: Why?

Children

- Urban environment
- Television
- The computer
- Limited exercise programs in schools

Adults

- Urban environment
- Television
- The computer
- The Automobile
- Fewer bicycles

CALCIUM

Calcium intake in Childhood in Armenia

- By UN survey in 2005, the average intake of dairy was 2.5 servings per week (8% of caloric intake) and well under nutritional recommendations

Institute of Medicine Recommended Requirements for Calcium

RDA	mg/d*	Upper Limit (mg/d)
1–3 yr	700	2500
4–8 yr	1000	2500
9–18 yr	1300	3000
Pregnant or lactating (Female)		
14–18 yr	1300	3000
19–50 yr	1000	2500
Infants		
0–6 months	200	1000
6–12 months	260	1500

*Intake that covers needs of $\geq 97.5\%$ of population

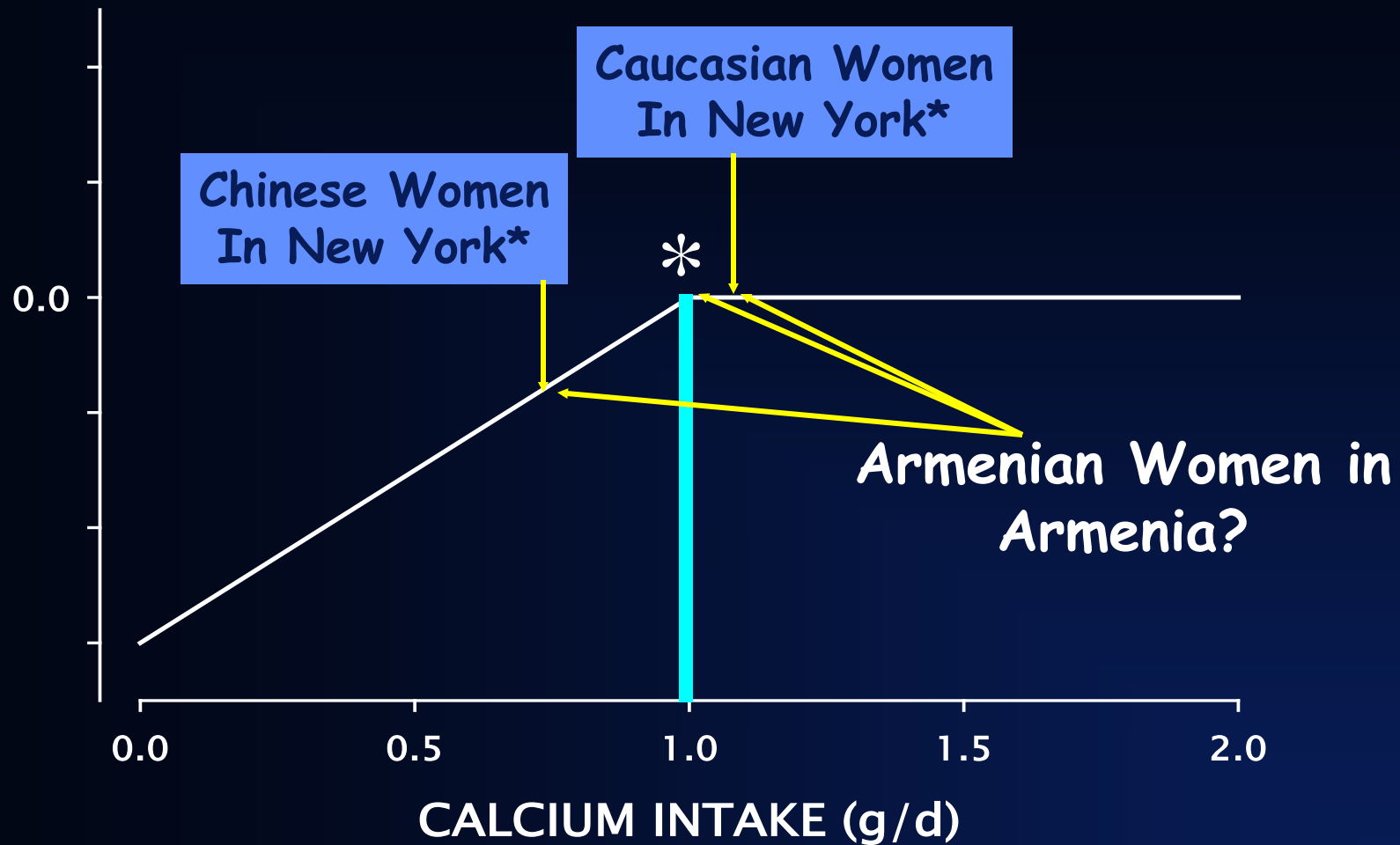
Calcium

- Preferably, calcium intake should come from natural sources (i.e., dairy)
- Calcium supplementation is used only to make up the difference between amount in foods (including calcium-supplemented foods) and what is needed.
- Only 500-600 mg advised at a time for better absorption
- Should be taken with food (protein meal) for better absorption efficiency

The best sources of Calcium

- **Dietary**
 - Dairy products
 - Green vegetables
 - Certain nuts like almonds
- **Calcium Supplements**
 - Calcium carbonate (40% calcium)
 - Requires a source of acid (gastric or food)
 - Absorption is enhanced by food
 - Calcium Citrate (20% calcium)
 - Does not require acid for absorption
 - Absorption is enhanced with food
 - Is thought to cause fewer GI issues

Calcium is a Threshold Nutrient (Heaney, 2006)





DRINK YOUR LOW OR
NON-FAT MILK;
EAT YOUR LOW OR
NON-FAT YOGURT, CHEESE;
USE CALCIUM SUPPLEMENTS
ONLY TO SUPPLEMENT!

CALCIUM

Recent Claims: Calcium may be bad for your cardiovascular health and will not improve your bone mineral density! (Bolland, Reid et al, 2006)

Why this view is not correct:

- The reports are based upon retrospective and meta-analyses
- The CV end points are not consistent
- Little attention has been paid to the amounts of calcium in these reports: often greater than recommended (<2.5 g/day)

Calcium is good for you!

- In moderation
- Dietary calcium is preferred
- Supplements should be used to supplement dietary calcium
- There is no evidence that dietary and supplemental calcium less than 2.5 g/day is harmful

A photograph of a log cabin with a yellow sign that says "VITAMIN D". The sign is rectangular with rounded corners and is mounted on a wooden post. The cabin has horizontal log siding and a window with a dark frame. The background is a bright, overcast sky.

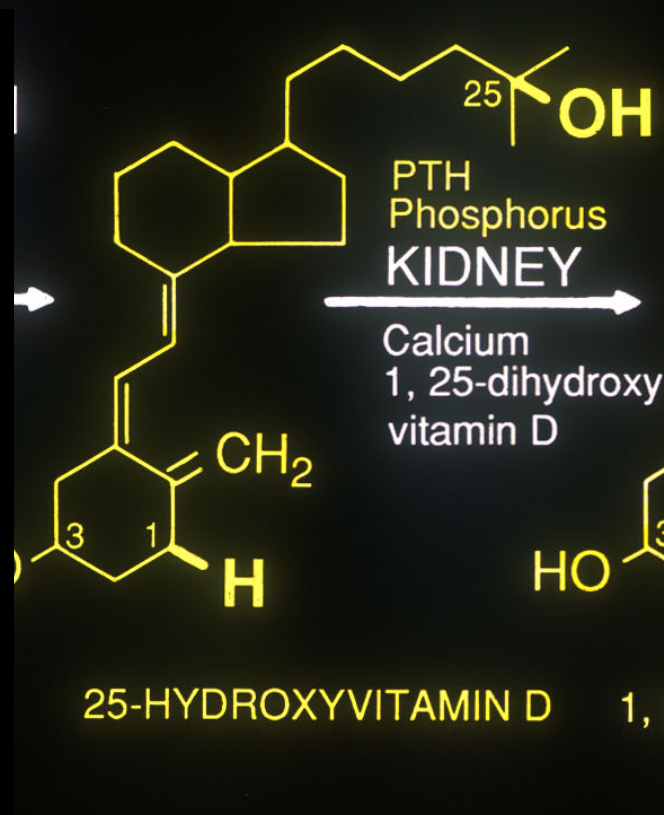
VITAMIN D

Without sufficient vitamin D

- Calcium absorption is reduced
- Even a calcium sufficient diet, therefore will not be adequate, in the presence of vitamin D deficiency

Vitamin D:

What is the metabolite to measure?



In Armenia

- It is very expensive to measure 25-hydroxyvitamin D: (\$25-US per sample)
- Essentially no data, therefore, on vitamin D adequacy here
- Abundant data, though, throughout the world

VITAMIN D DEFICIENCY IS COMMON

- How common is vitamin D deficiency?
- What are common sources of Vitamin D
 - The sun?
 - Dairy? What dairy?
 - Other sources
- How is Vitamin D deficiency defined?
- The stages of Vitamin D deficiency
 - Early, moderate, severe

Sources of Vitamin D: THE SUN

but why is it difficult to get sufficient Vitamin D from the sun?

THE SUN IS NO LONGER A
MAJOR SOURCE OF VITAMIN
D THROUGHOUT THE WORLD

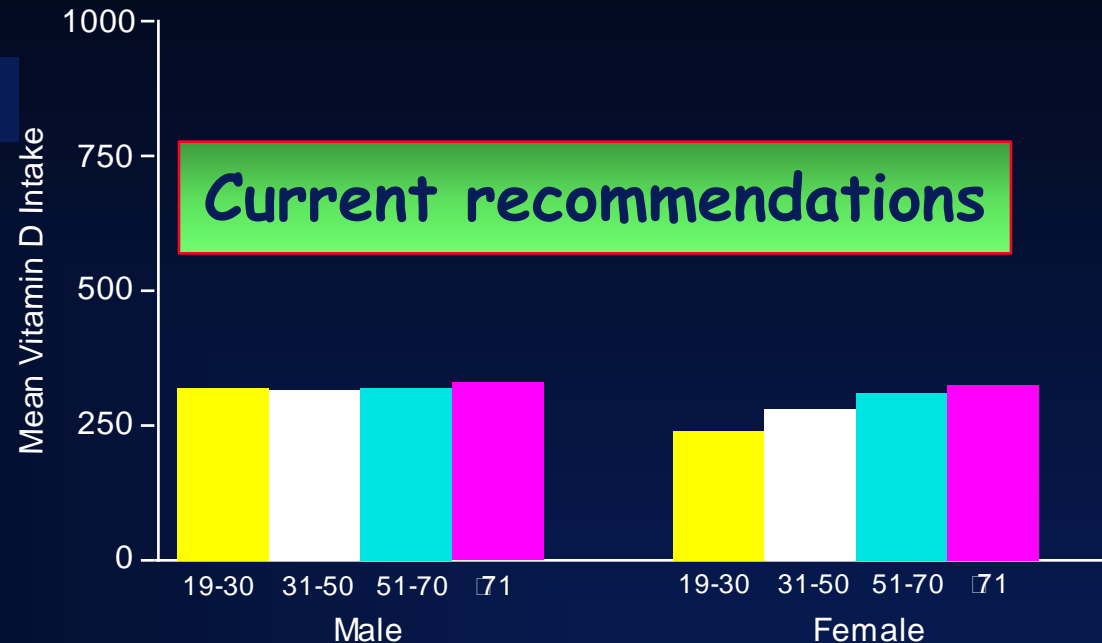
A sunset over a body of water. The sun is low on the horizon, creating a bright orange and red glow. The sky transitions from orange near the horizon to a pale blue at the top. The water is dark blue with some ripples. A small boat is visible on the left side of the horizon.

**If we do not get our
Vitamin D from Sunlight...**

**Is food an alternative
source of Vitamin D?**

Vitamin D is Rare in Food; as a Result, Intake is Low At All Ages

<u>Food</u>	<u>IU</u>
Cod Liver Oil, 1 Tsp	400
Salmon, 3.5 oz	360
Mackerel, 3.5 oz	345
Milk, 1 cup fortified	100
Fortified cereal, 3/4 cup	50
Liver, 3.5 oz	30
Egg, one whole	25

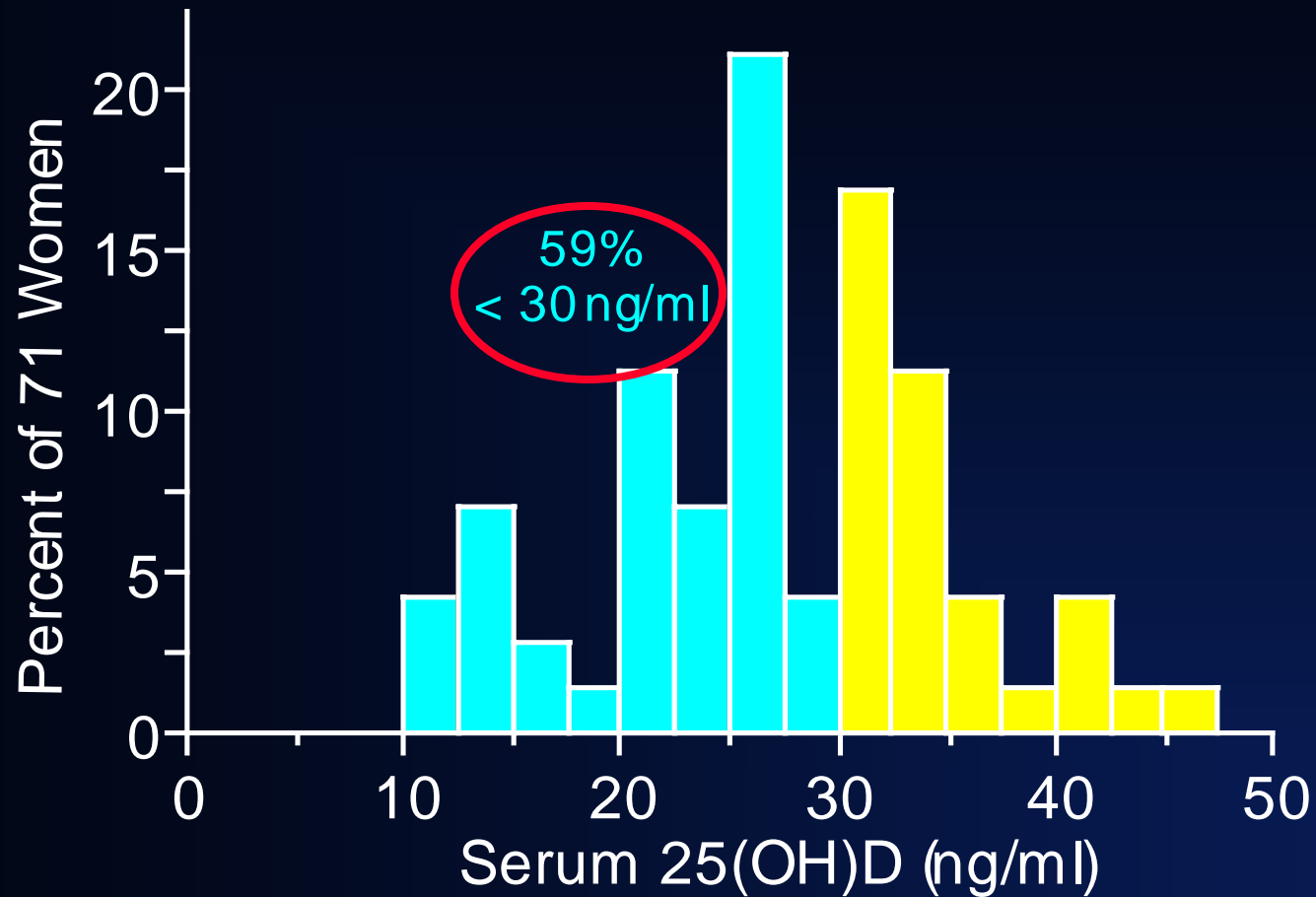


NHANES III data; mean vitamin D intake from food plus supplements

**Without sunlight as a source
Without food as a source...**

**We are all likely to be
deficient in Vitamin D**

Low Vitamin D Status is Endemic



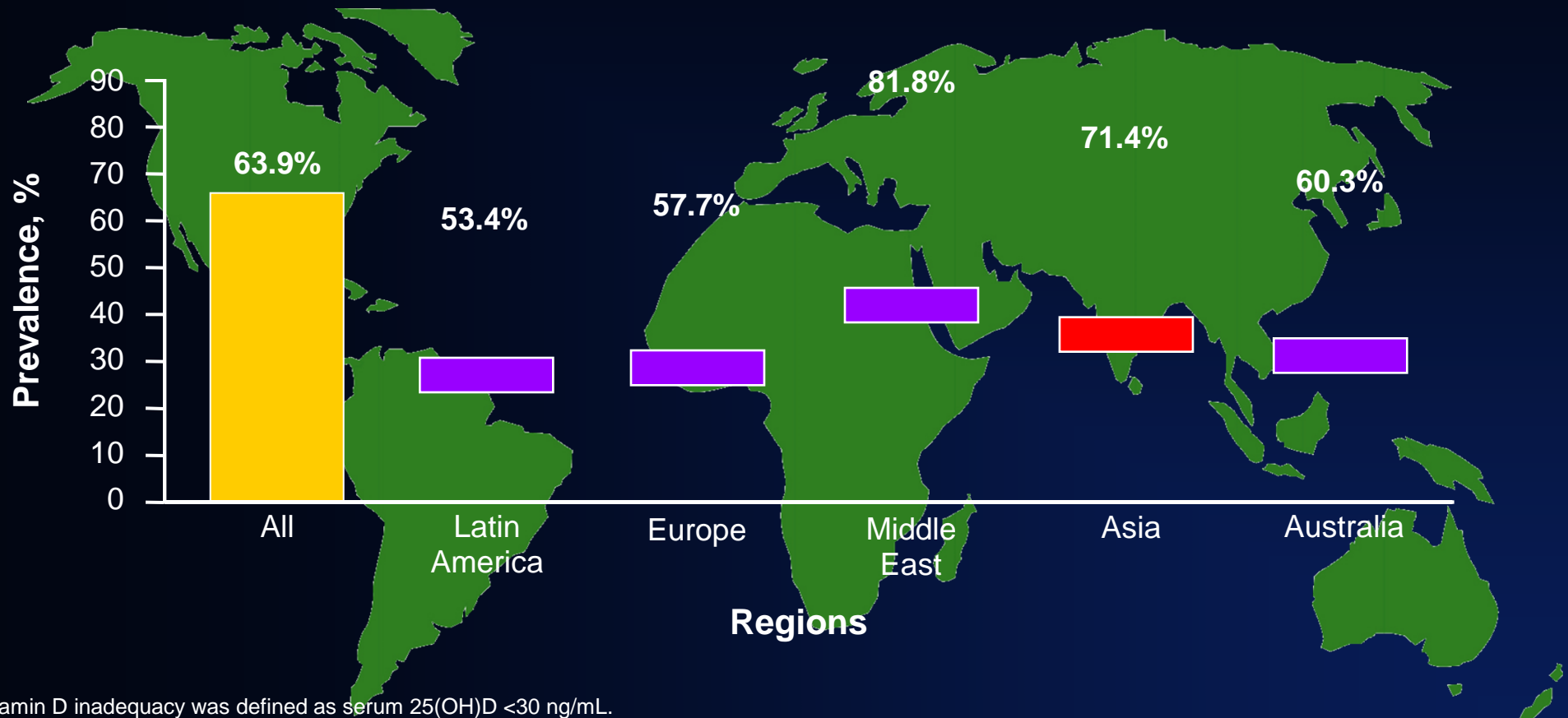
Vitamin D Inadequacy is Common Worldwide



A convenience sample of 2,589
postmenopausal women with osteoporosis
18 countries from 64° N to 38° S latitude

**Overall, 64% had serum 25(OH)D < 30
ng/ml**

Global Prevalence of Vitamin D Inadequacy



*Vitamin D inadequacy was defined as serum 25(OH)D <30 ng/mL.

Study Design: Cross-sectional, international study of 2589 women with osteoporosis from 18 countries to evaluate serum 25(OH)D distribution

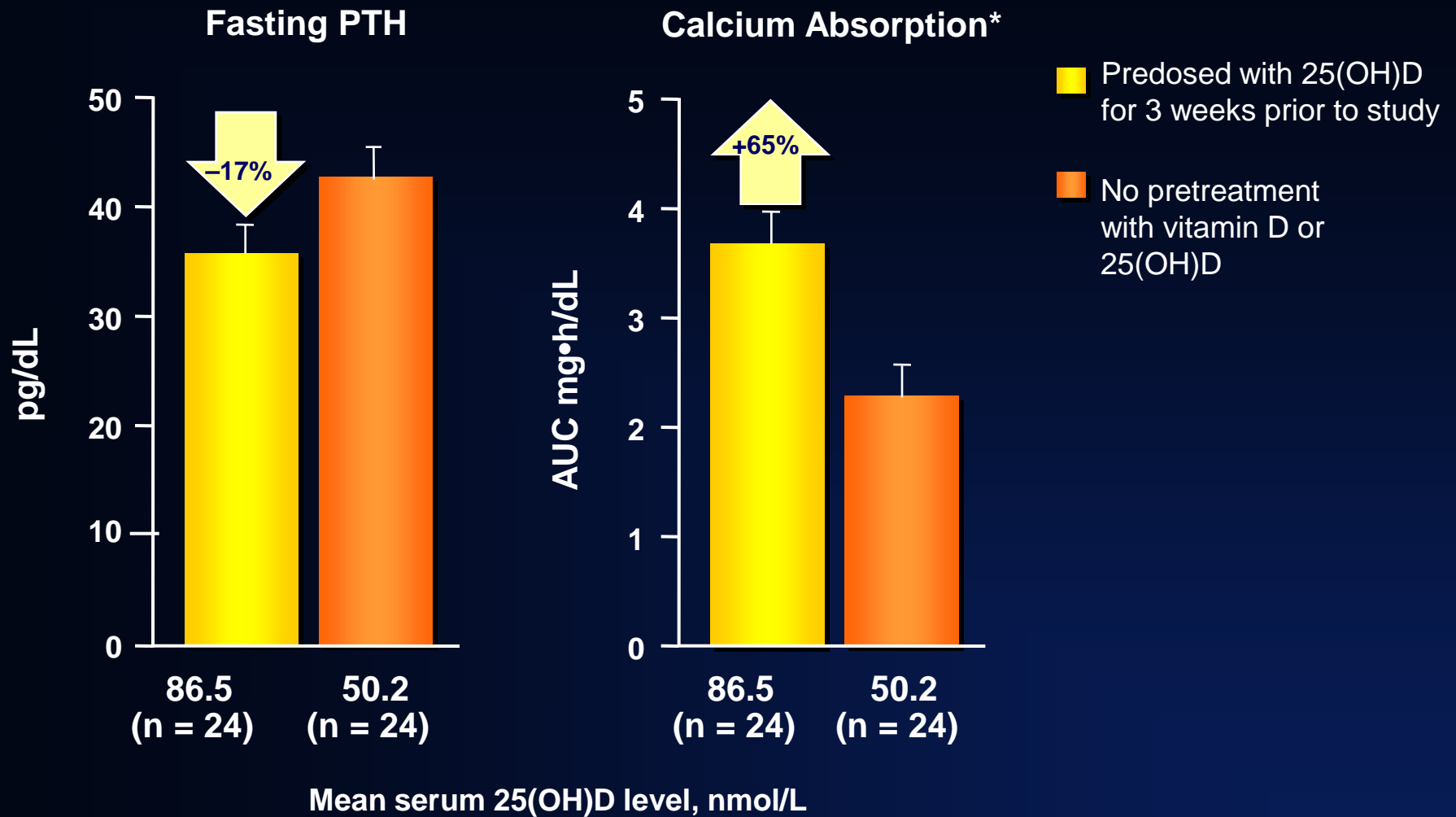
Adapted from Lips P, et al. *J Intern Med.* 2006;260:245–254.

How does one determine what is a normal and what is abnormal re 25-hydroxyvitamin D?

What value of circulating 25-hydroxyvitamin D should we aim for?

- **>20 ng/mL (50 nmol/l)?**
- **>30 ng/mL (75 nmol/l)?**

Vitamin D Status: Impact on Calcium Absorption and PTH

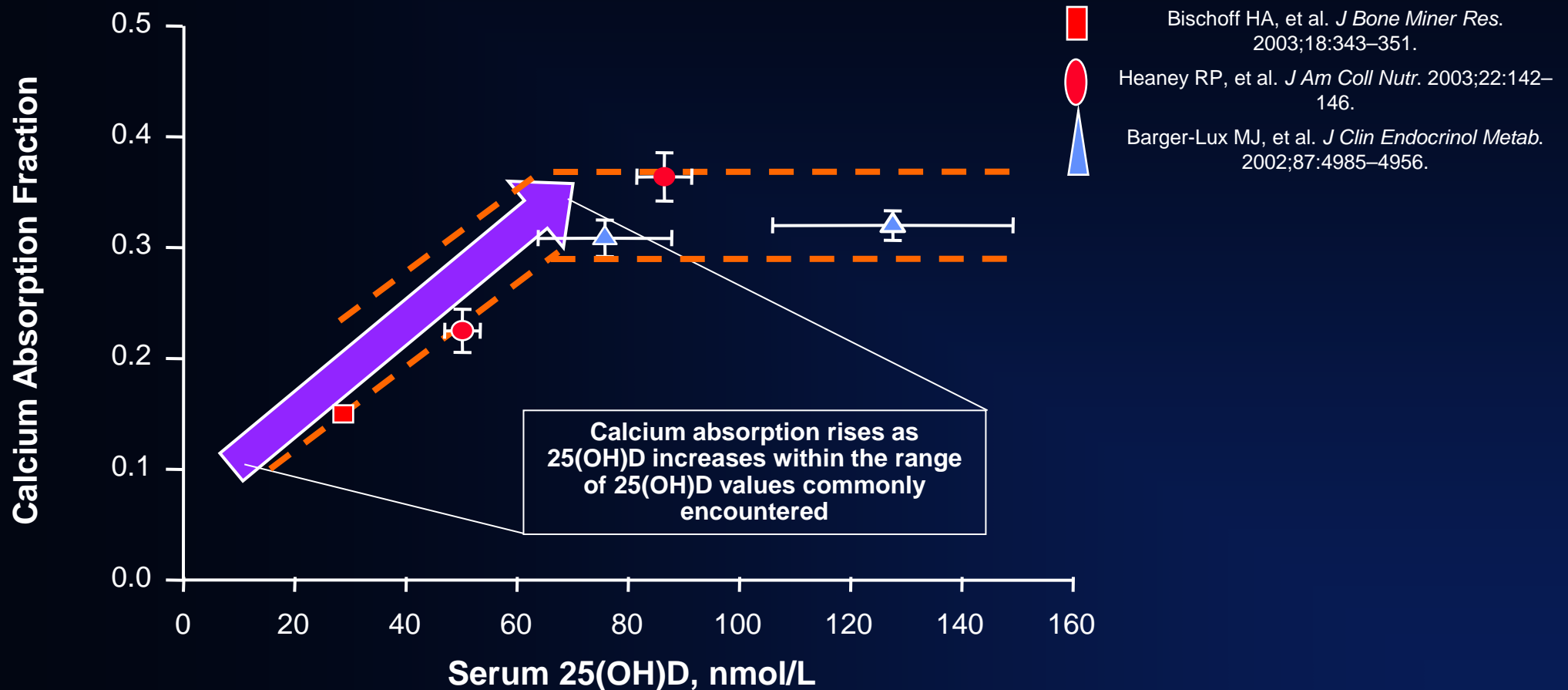


* $P < 0.001$.

Mean serum 25(OH)D level, nmol/L

Vitamin D Is Essential for Calcium Absorption

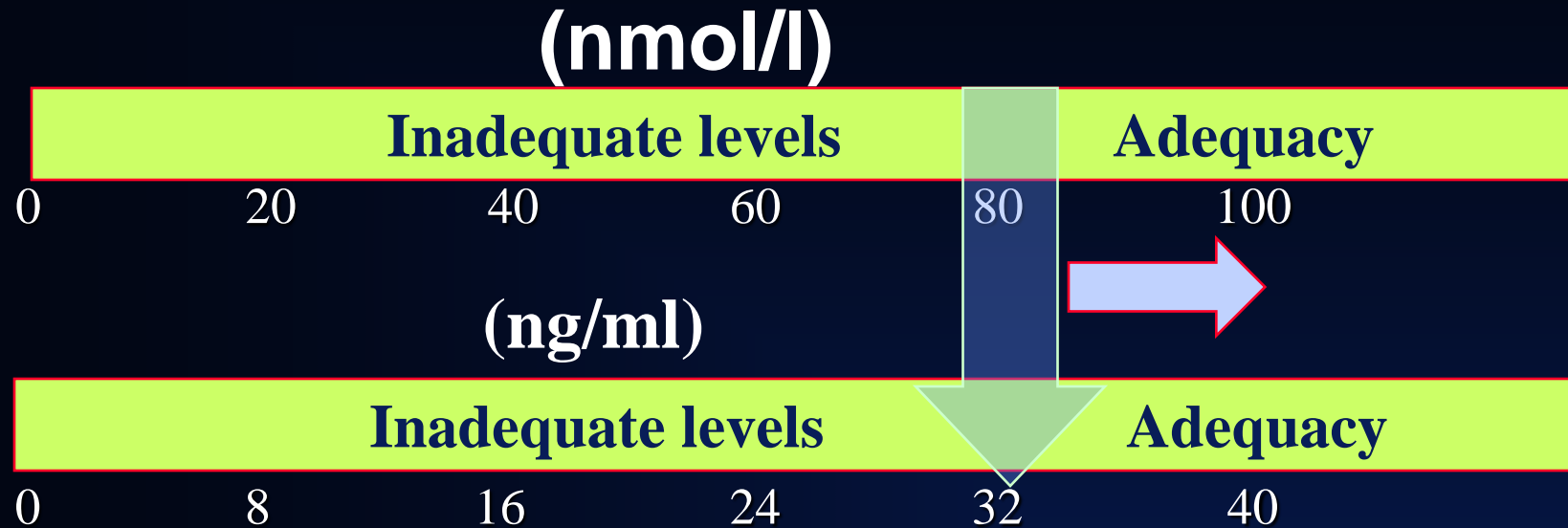
Calcium absorption plateaus at serum 25(OH)D levels ≥ 32 ng/mL.



25-hydroxyvitamin D: what is recommended by most professional societies?

- Lower limit: 30 ng/mL (75 nmol/l)
- Upper limit: 50-80 ng/L (125-200 nmol/l)

25-Hydroxyvitamin D: Threshold values for adequacy



The IOM Report (November 2010)*

- Recommended daily intake: 600 IU (under 70 yrs); 800 IU (over 70 yrs old)
- Maximal daily intake: 4,000 IU

In Armenia

Since Vitamin D measurements are not practical because of expense, how should we ensure vitamin D adequacy in the population?

In Armenia- a suggestion

- Perhaps larger doses 2,000 IU per day for 2 months is advisable
- Then nutritional intake according to the Institute of Medicine guidelines is reasonable

Vitamin D Supplementation and Fracture Risk

- Some studies have found a reduction in fractures with supplementation
- Others have not seen an effect
- Conflicting results may relate to differences in baseline vitamin D status of participants, range of doses used, and compliance

Major points

- Good nutrition in childhood (and throughout life) is a key to optimal skeletal health
- Poor calcium intake and vitamin D deficiency in childhood could lead to suboptimal skeletal calcium and contribute to osteoporosis later in life
- Vitamin D sufficiency is a key element to good skeletal health
- There is an epidemic of vitamin D deficiency, and thus calcium deficiency, throughout the world

What can we do?

- ❑ Pediatricians and Nutritionists in Armenia:
Pay attention to calcium and vitamin D!
Make sure your children are getting enough exercise!
- ❑ Primary care physicians in Armenia:
Pay attention to calcium and vitamin D!
Make sure your patients are getting enough exercise!



Shnorhagalutyun!