VITAMIN D

WHAT IT DOES &
HOW MUCH WE NEED

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Working definition:

- a deficiency is any condition in which inadequate intake of a nutrient results in significant dysfunction or disease
- conversely, nutrient adequacy is the situation in which further increases in intake produce no further reduction in dysfunction or disease

What is the operative model for nutrition?

WHAT IS THE OPERATIVE MODEL?

- for the media?
- for regulators?
- for nutritional policy makers?
- for nutritional physiologists?

WHAT IS THE OPERATIVE MODEL?

- *for the media and for regulators*

  - nutrition is about killing yourself with a fork
  - it's about avoiding risks
  - it's about warnings & cautions

Nutrition Facts

Serving Size 1 cup (228g)
Serving Per Container 2

Amount Per Serving

Calories 250	Calories from Fat 110
	% Daily Value*
Total Fat 12g	**18%**
Saturated Fat 3g	**15%**
Cholesterol 30mg	**10%**
Sodium 470mg	**20%**
Total Carbohydrate 31g	**10%**
Dietary Fiber 0g	**0%**
Sugars 5g	
Protein 5g	
Vitamin A	
Vitamin C	2%
Calcium	20%
Iron	4%

* Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs:

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

For a package of macaroni & cheese

http://vm.cfsan.fda.gov/~dms/foodlab.html

Limit these nutrients

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Get enough of these nutrients

MEDIA REPORTING

- most media reports about nutrition emphasize harm and risk
- while the explanation is partly that harm is more newsworthy than benefit (and the media battens on controversy)
- still the impression unwittingly conveyed to the general public is one of concern and danger

WHAT IS THE OPERATIVE MODEL?

- *for nutritional policy makers*

  - nutrition is about determining the least one can get by on without suffering overt disease of a specific type
  - (once called MDRs)

WHAT IS THE OPERATIVE MODEL?

- *for nutritional physiologists*
  - adult nutrition is about preventive maintenance of tissues and organs
  - it's about keeping them from wearing out or breaking down prematurely
  - its referent is the intake that prevailed when human physiology evolved

CHRONIC DISEASE PERSPECTIVE

- chronic disease is the breakdown of structure and/or function of a body system
- its origin is usually multifactorial
  - genes
  - environment
    - ✓ nutrition
    - ✓ infection
    - ✓ toxins
    - ✓ injury

low vitamin D status impairs this protective/ reparative activity

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THE PREVENTIVE MAINTENANCE MODEL

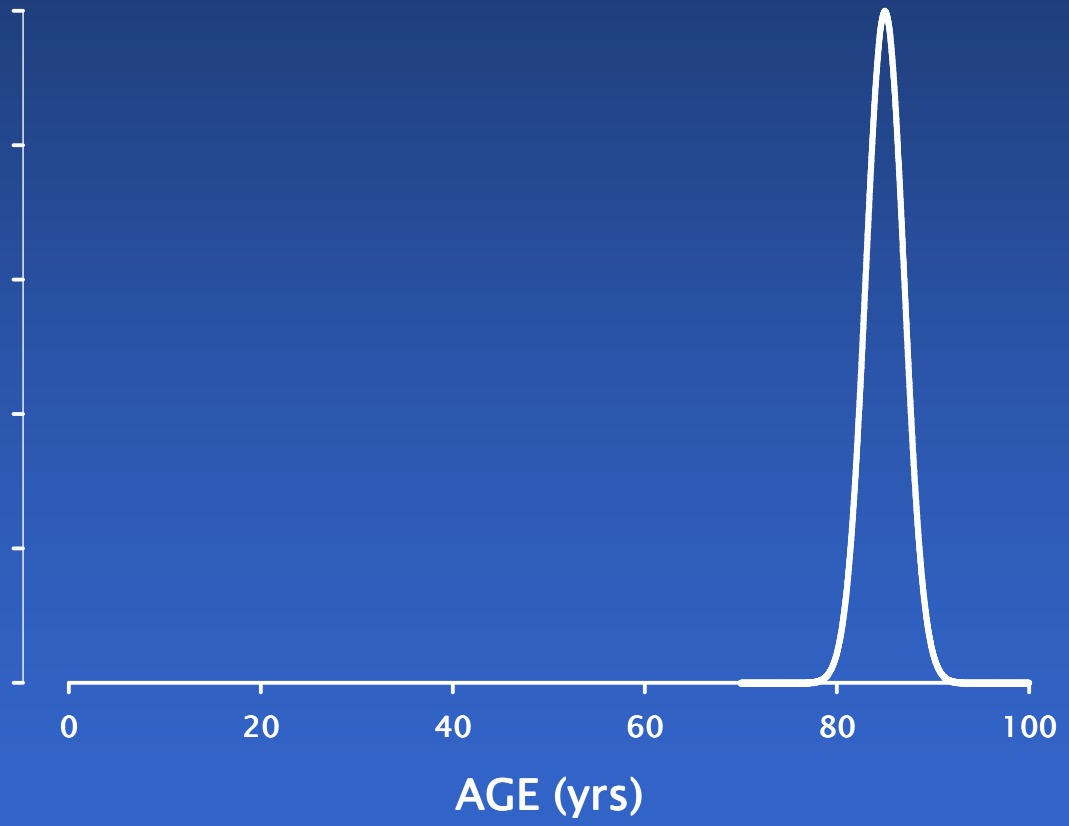
foundational premises:

- all tissues need all nutrients
- shortages impair the functioning of *all* body systems
- premature organ/system "wearing out", as a consequence of nutrient deficiency, will vary from person to person, depending on variable genetic composition

THE PREVENTIVE MAINTENANCE MODEL

- *also recognizes that:*
  - the organism will work perfectly well without maintenance – *for a while . . .*
- it thus reconciles the seeming paradox that an organism can be "deficient" without being clinically "sick"
  - *for a while . . .*
- it's also about squaring the morbidity/ mortality curve

THEORETICAL MORTALITY CURVE



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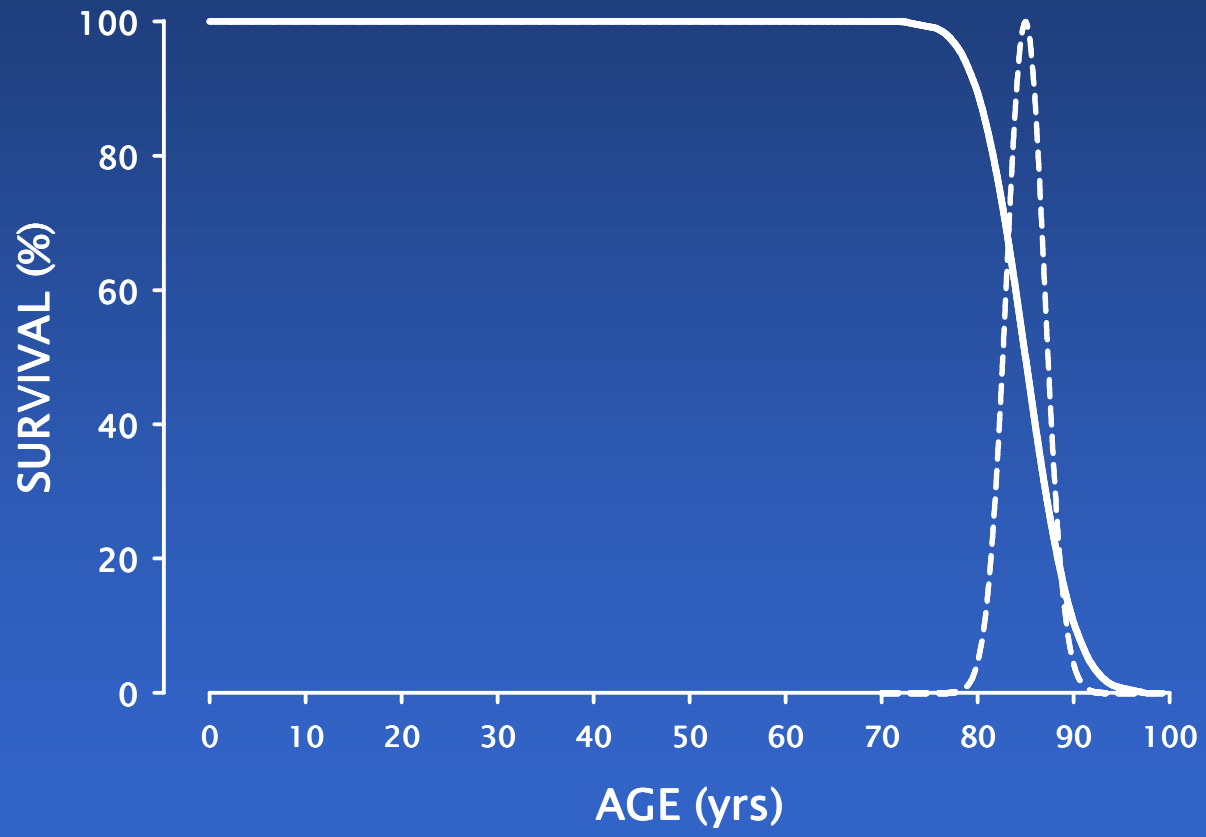
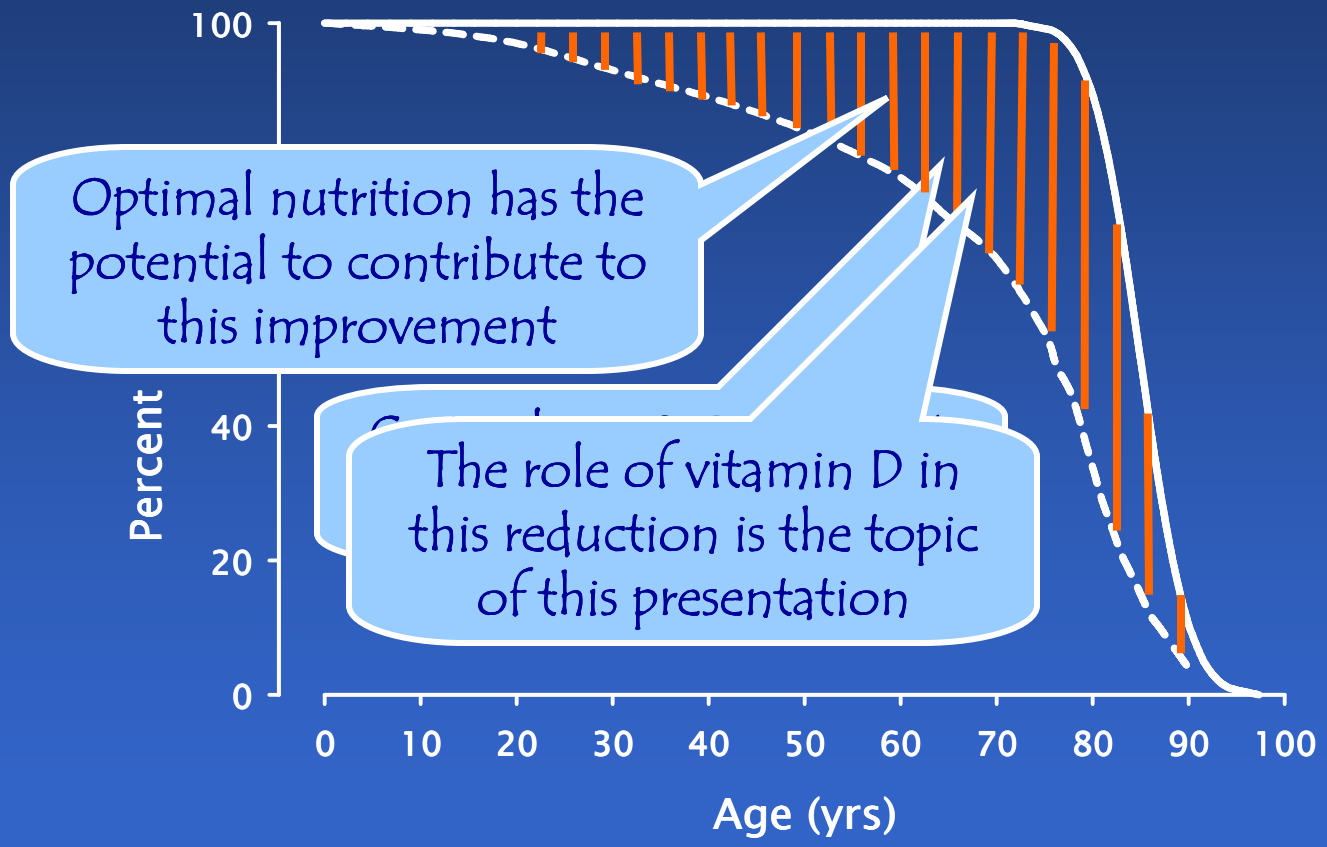
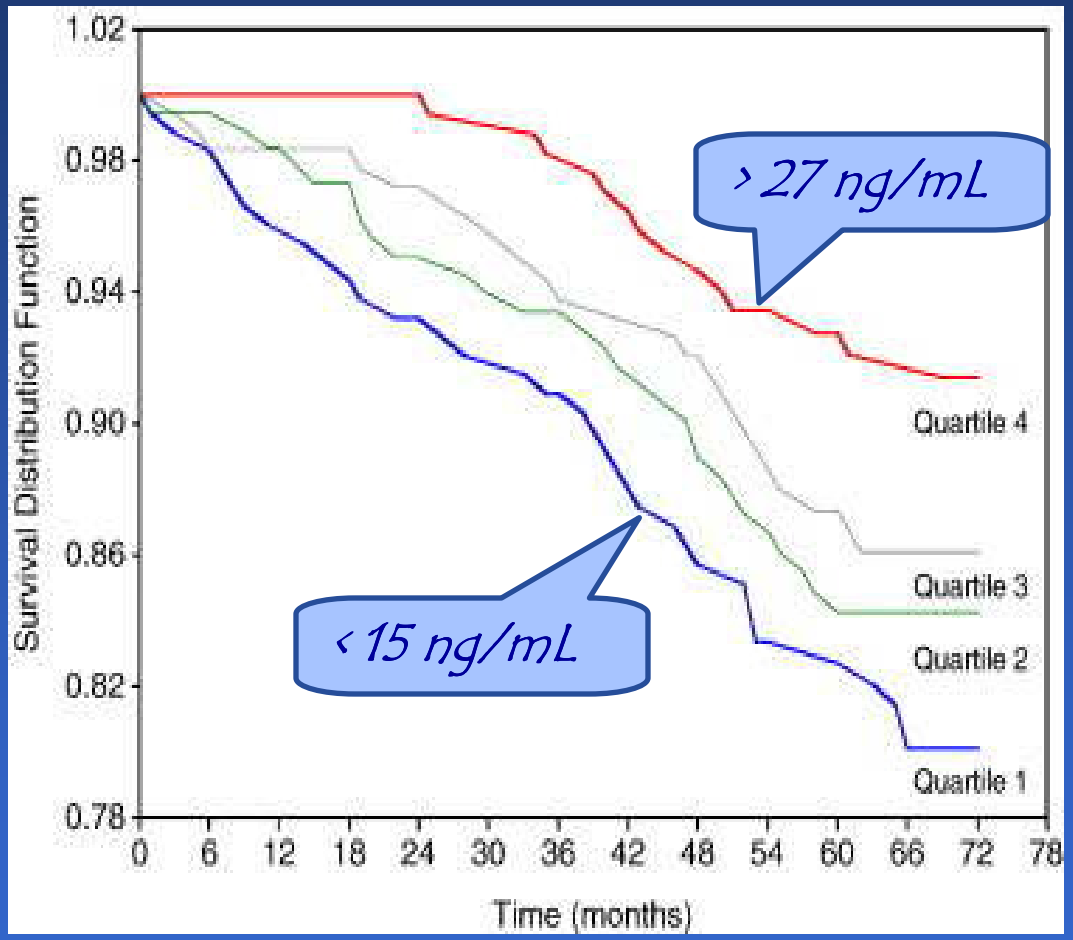


SQUARING THE MORTALITY CURVE



ALL-CAUSE MORTALITY*

- 714 community dwelling women
- aged 70-79
- Baltimore Women's Health & Aging Studies I & II
- median follow-up: 72 months
- risk adjusted for age, race, BMI, & other factors associated with mortality



* Semba et al. (2009) Nutr Res 29:525-530

VITAMIN D IN NATURE

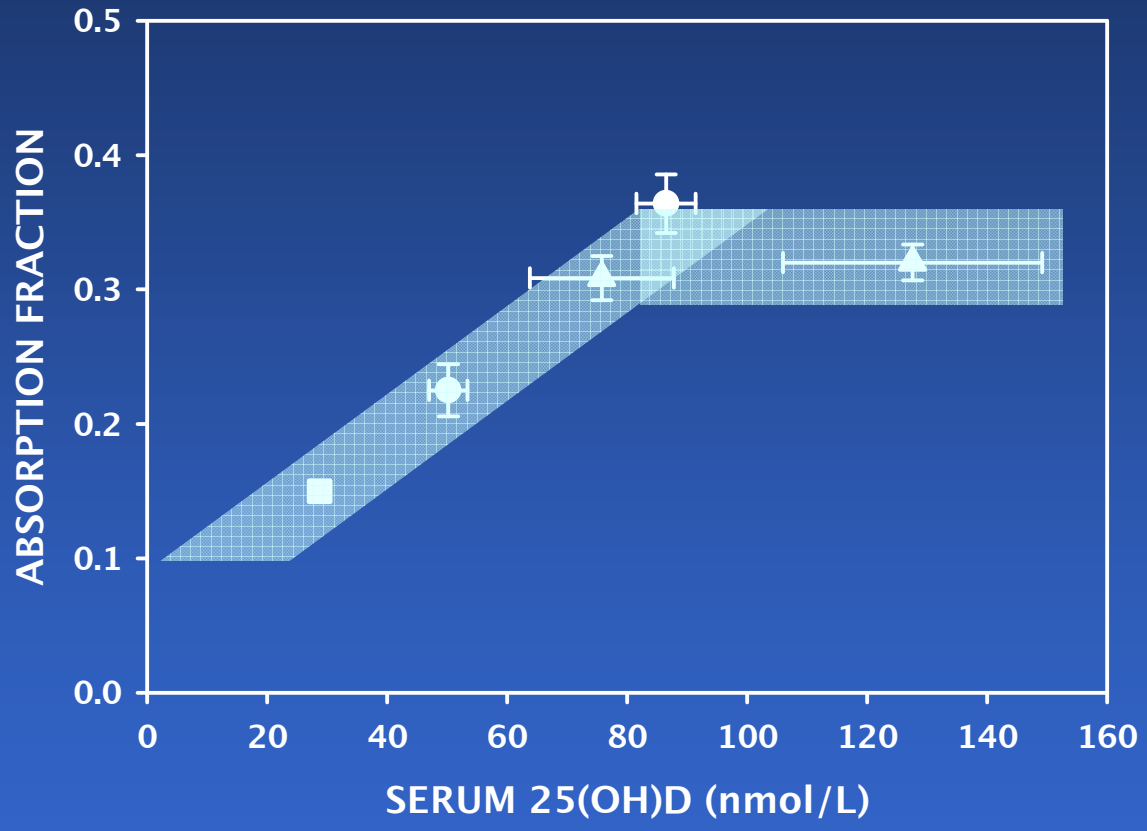
- vitamin D exists in two chemically distinct forms:
  - vitamin D2 – ergocalciferol
  - vitamin D3 – cholecalciferol
- D3 is the natural form in animals; it is what we make in our skins on exposure to UV-B light
- D2, once thought equivalent to D3, is only ~50-60% as potent as D3

VITAMIN D IN NATURE

- serum 25(OH)D is the way vitamin D status is evaluated
- lower end of acceptable range for serum 25(OH)D:
  75–80 nmol/L
  (30–32 ng/mL)

- There has been a gradually growing acceptance of 75–80 nmol/L (30–32 ng/mL) as the lower end of the "normal" range.
- What is the basis for this figure?
- Will it hold?

A VITAMIN D THRESHOLD



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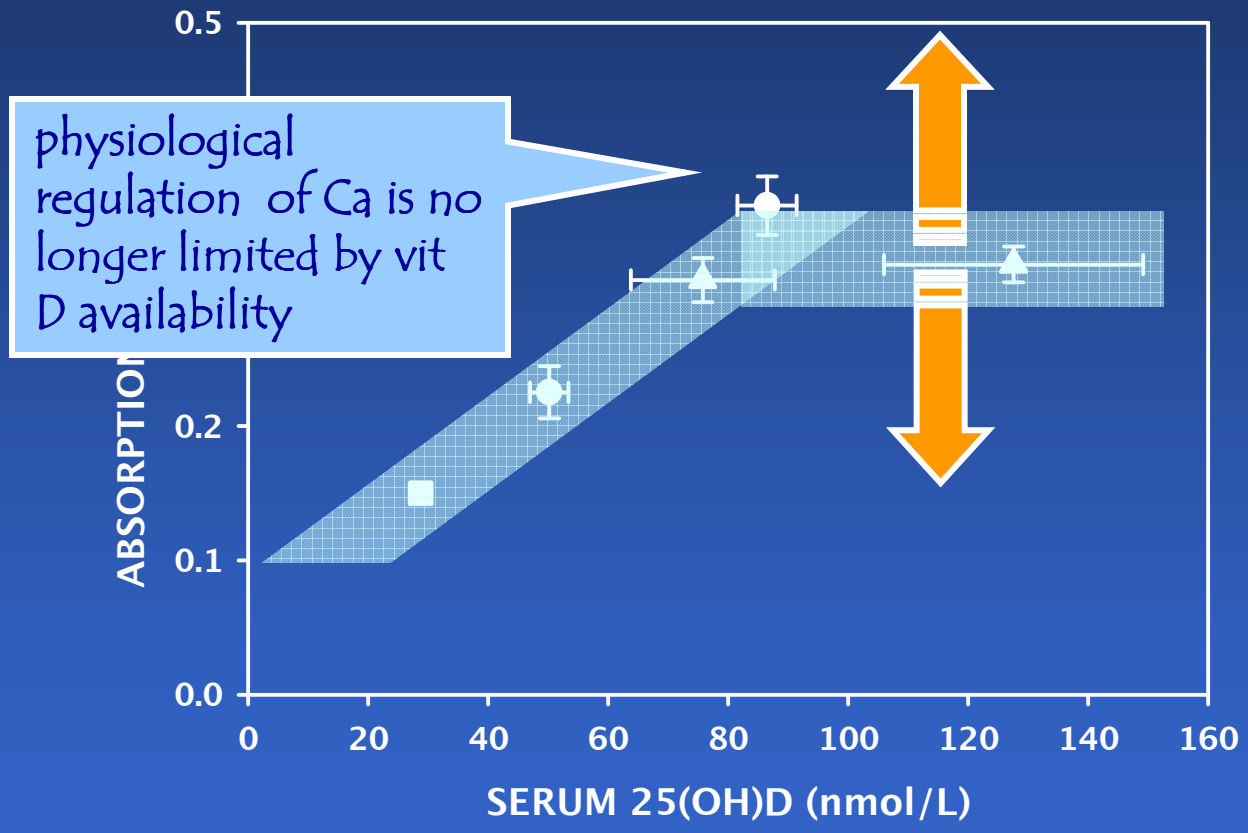

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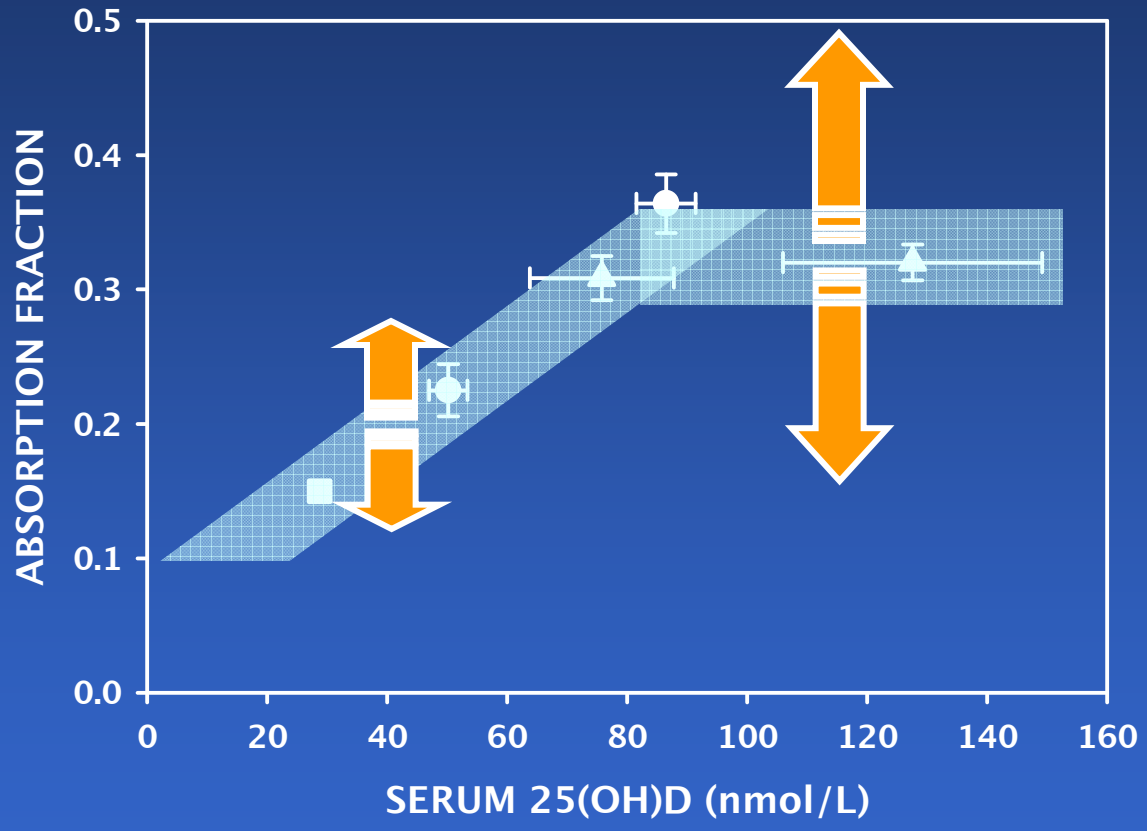

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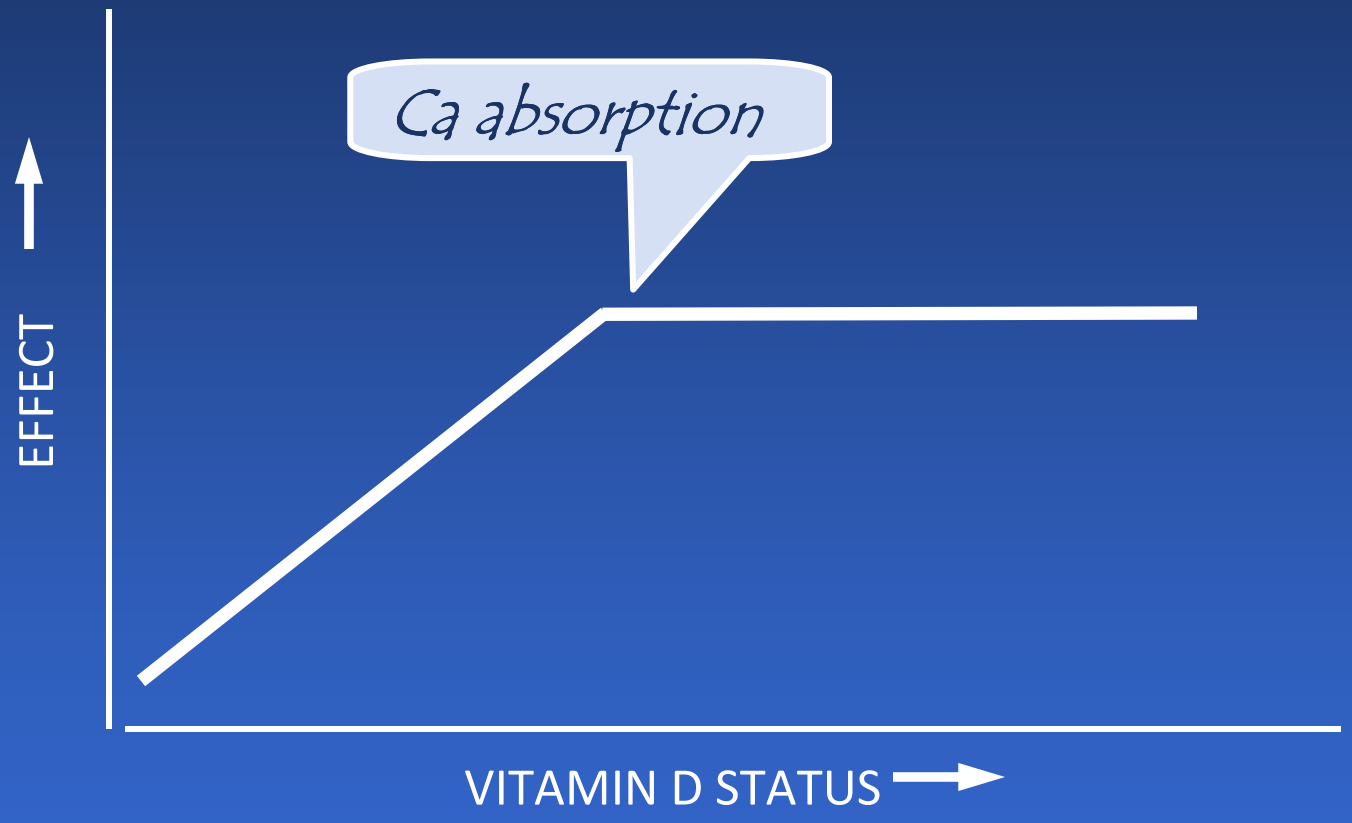
THE RESPONSE THRESHOLD



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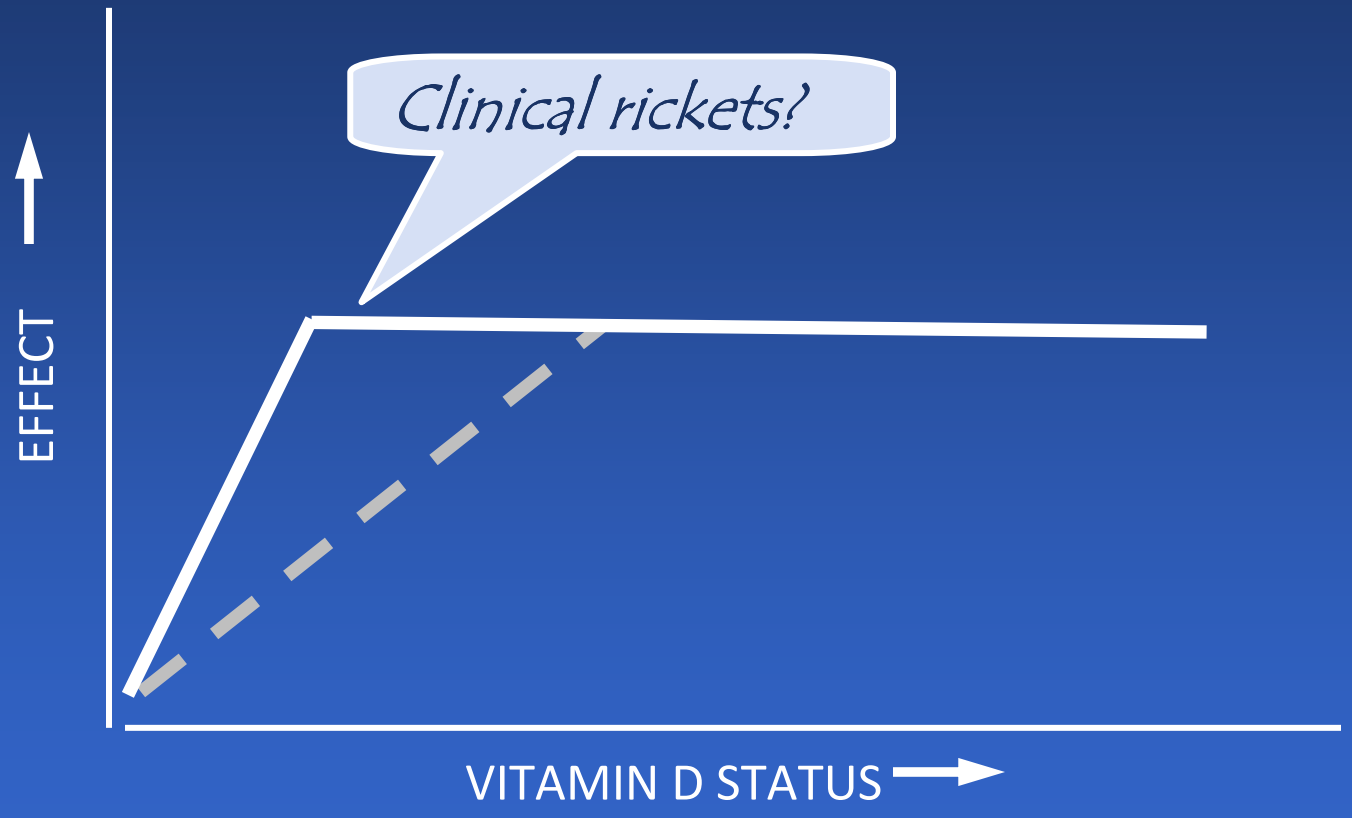

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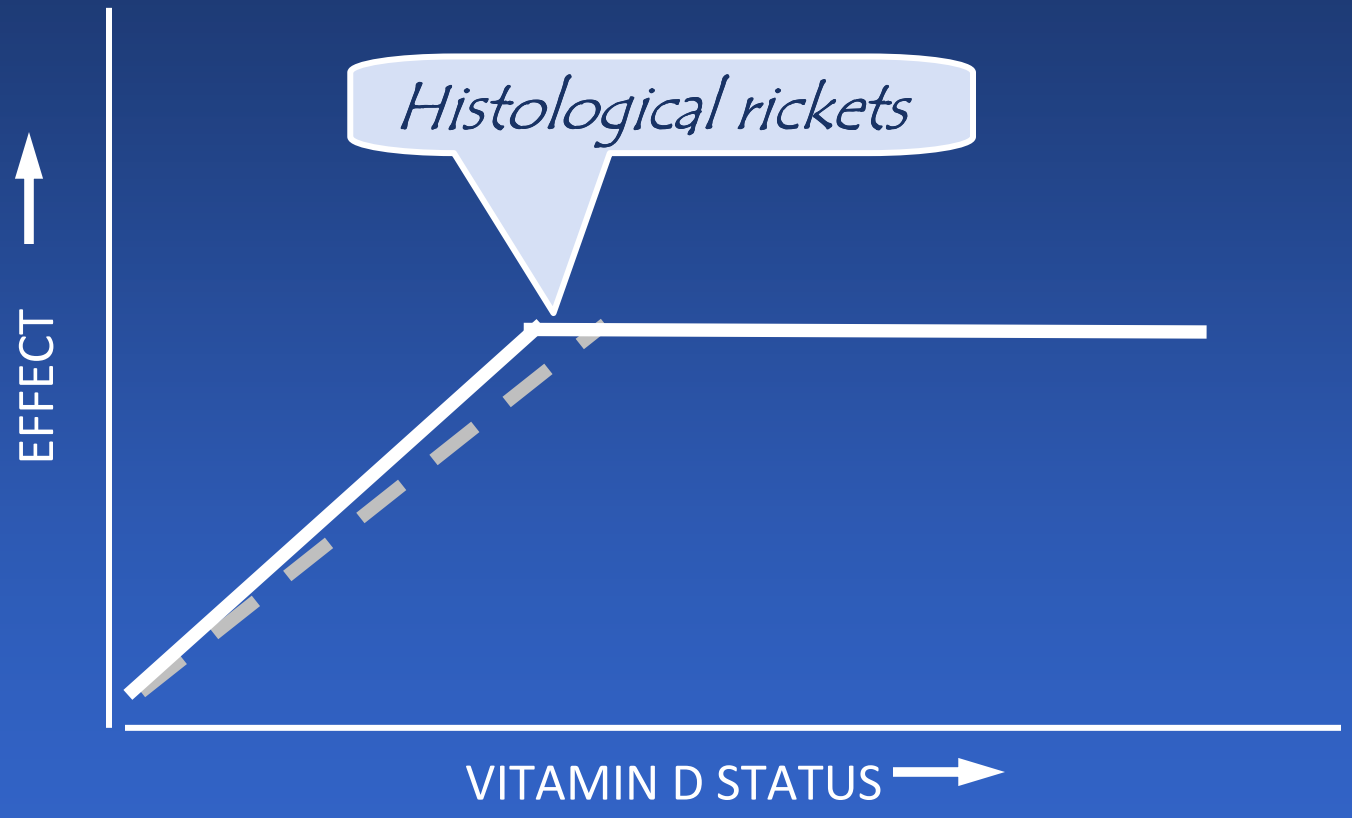
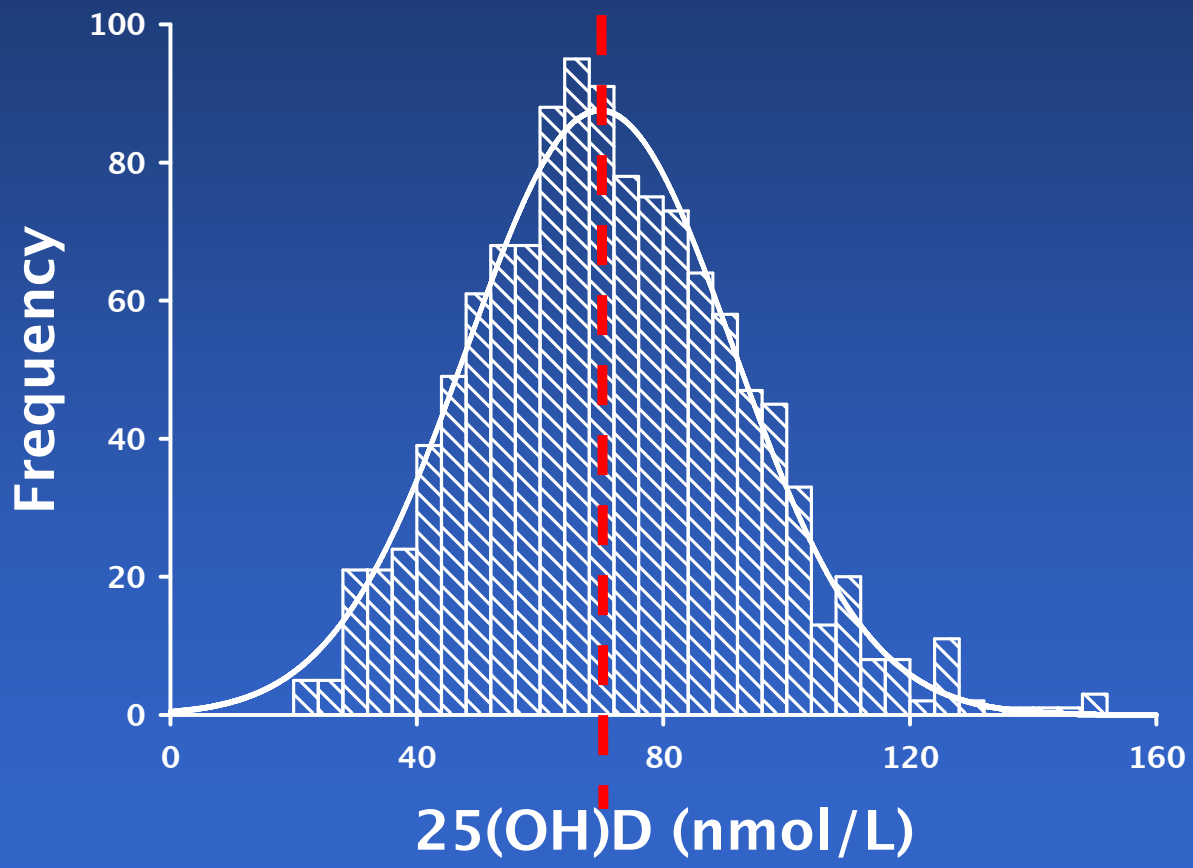


25(OH)D IN OLDER WOMEN*

- 1168 women aged 55 & older
- latitude 41° N
- 25(OH)D values adjusted for season
- median vit D supplement dose = 200 IU



*Lappe et al., JACN 2006

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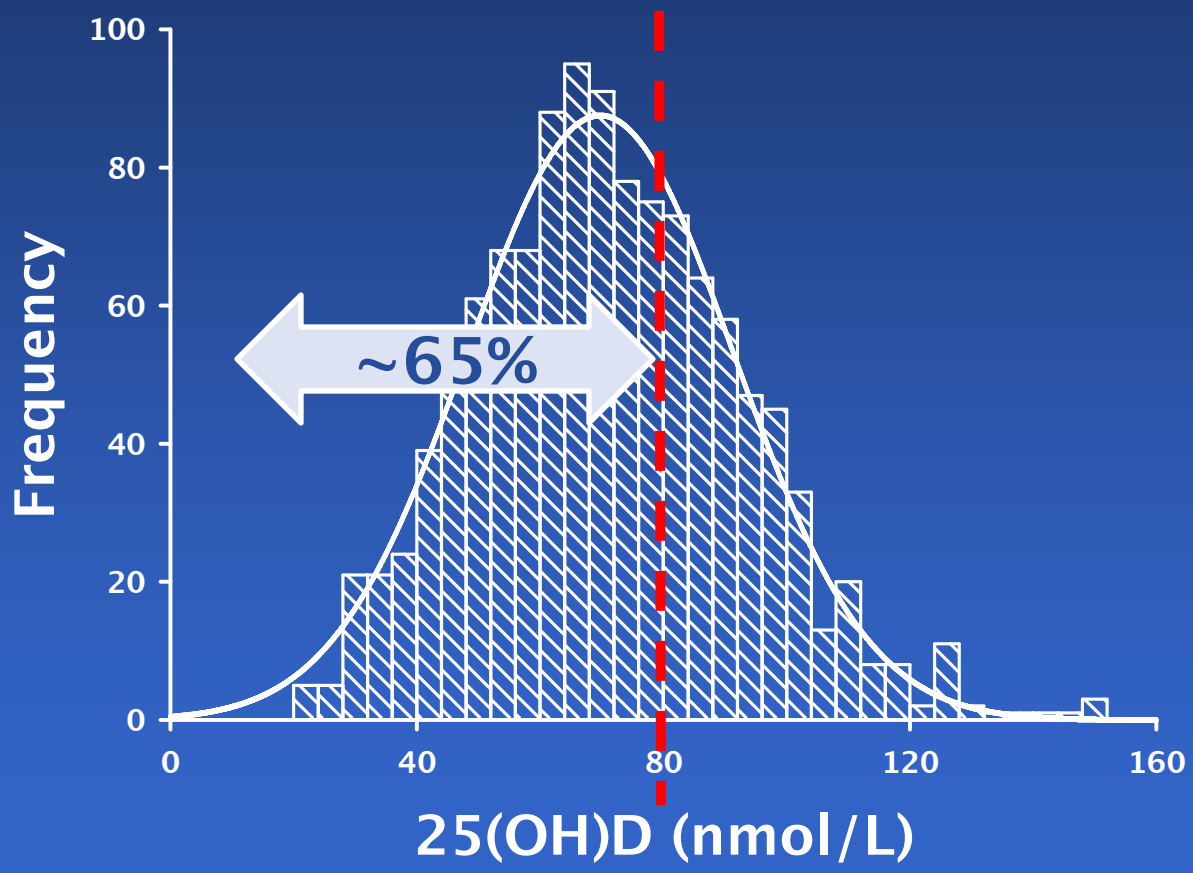

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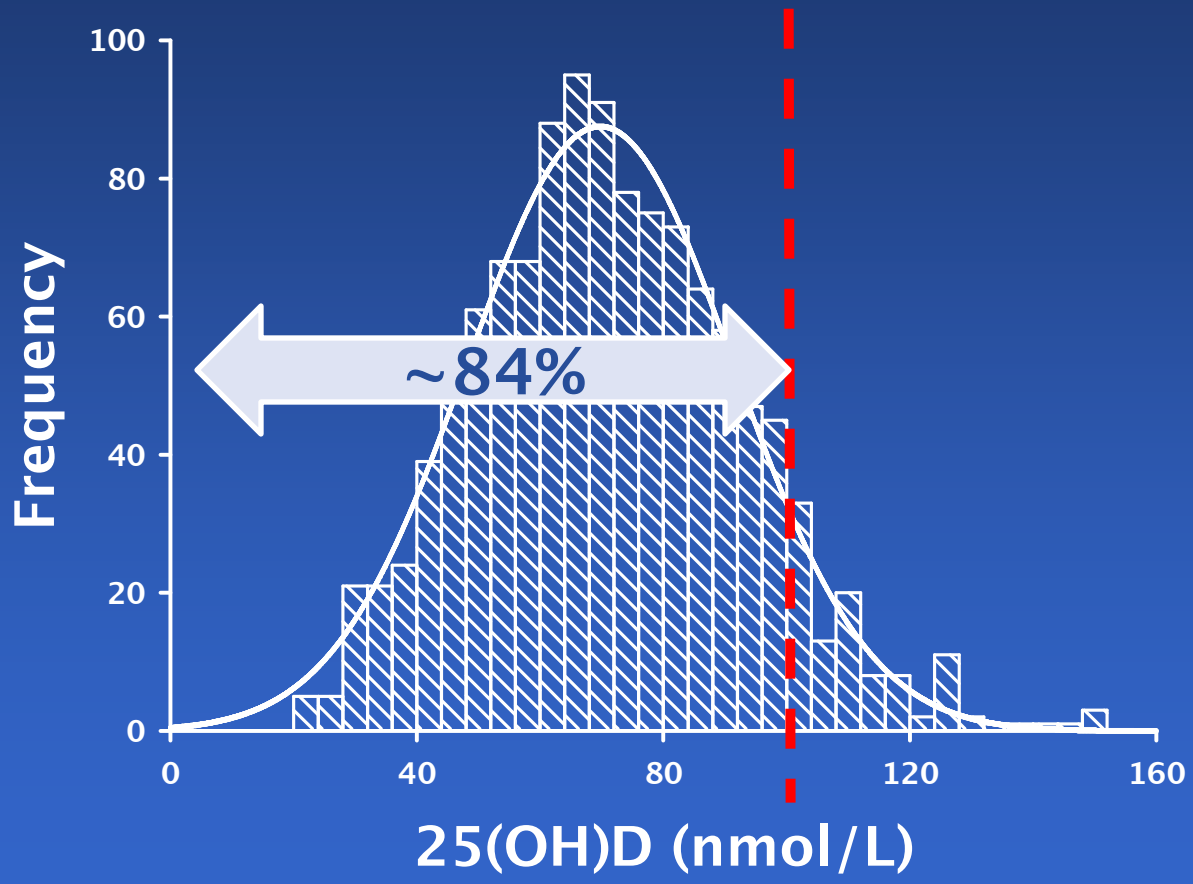
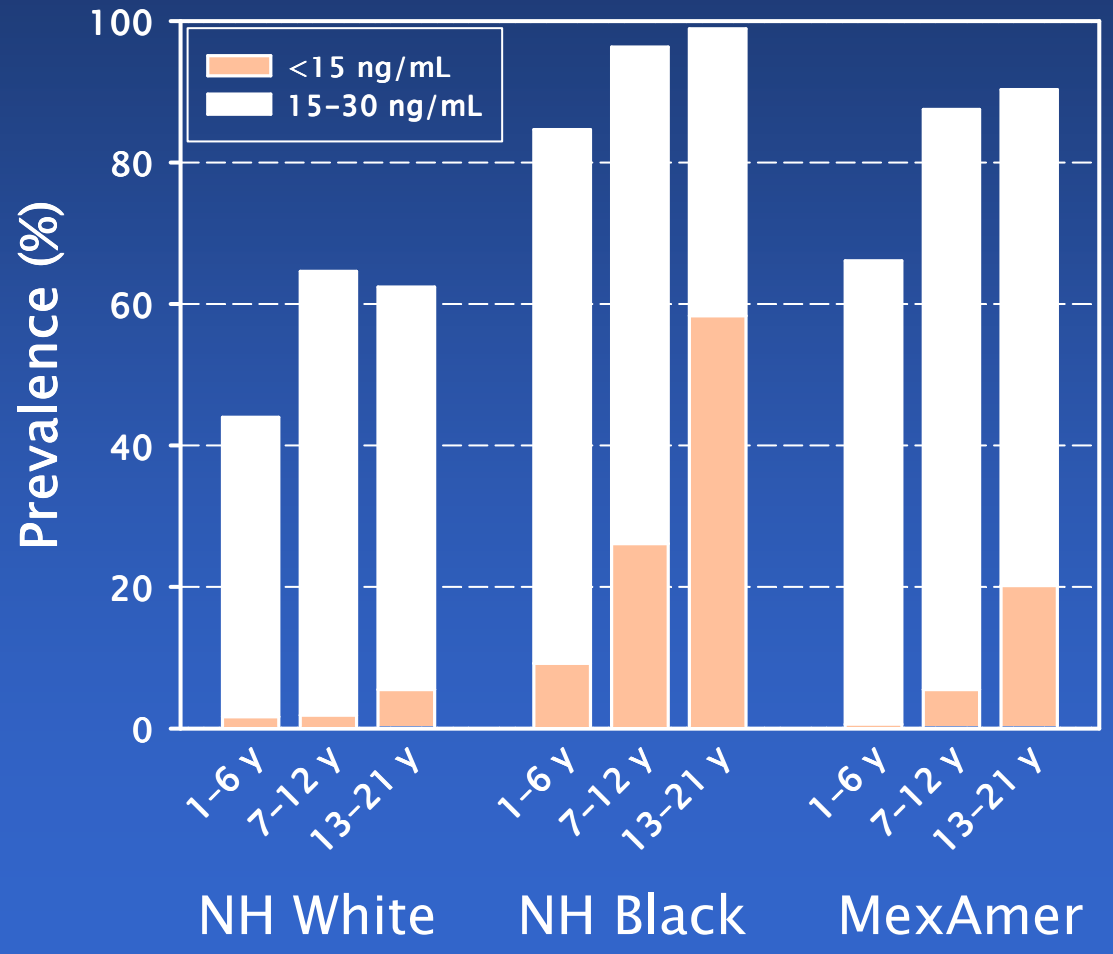


*Lappe et al., JACN 2006

VIT D DEFICIENCY IN CHILDREN

- NHANES 2001–2004
- girls
- n=3012
- Kumar et al. Pediatrics 2009

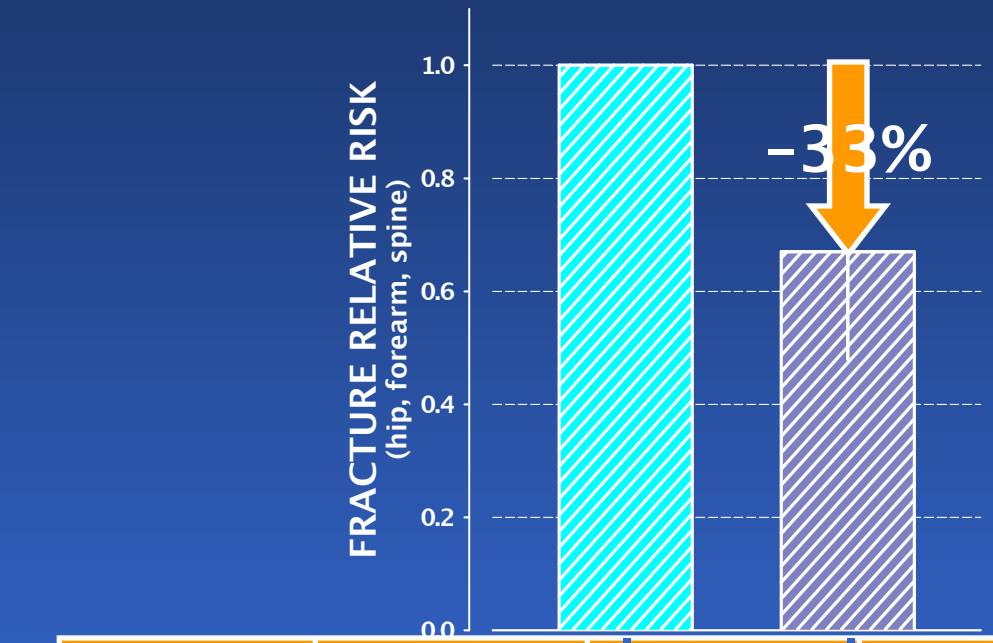


All studies, in virtually all nations, irrespective of latitude, show that the majority of the world's population has inadequate vitamin D status.

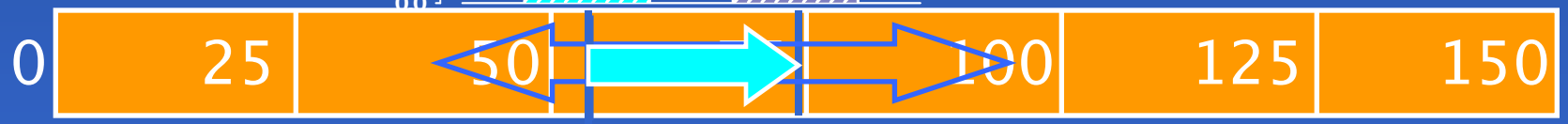
WHAT ARE THE CONSEQUENCES?

- bone diseases, falls, & fractures
- hypertension
- ↑ risk of cardiac disease & death
- prematurity, low birth weight, & ↑ Caesareans
- diabetes & metabolic syndrome
- periodontal disease
- decreased resistance to infection
- various cancers
- ↑ risk of multiple sclerosis

THE 25(OH)D CONTINUUM



- N = 2,686
- ages 65–85
- 5 yr RCT
- Vit D ≅ 800 IU/d
- Trivedi et al. BMJ 2003; 326:469



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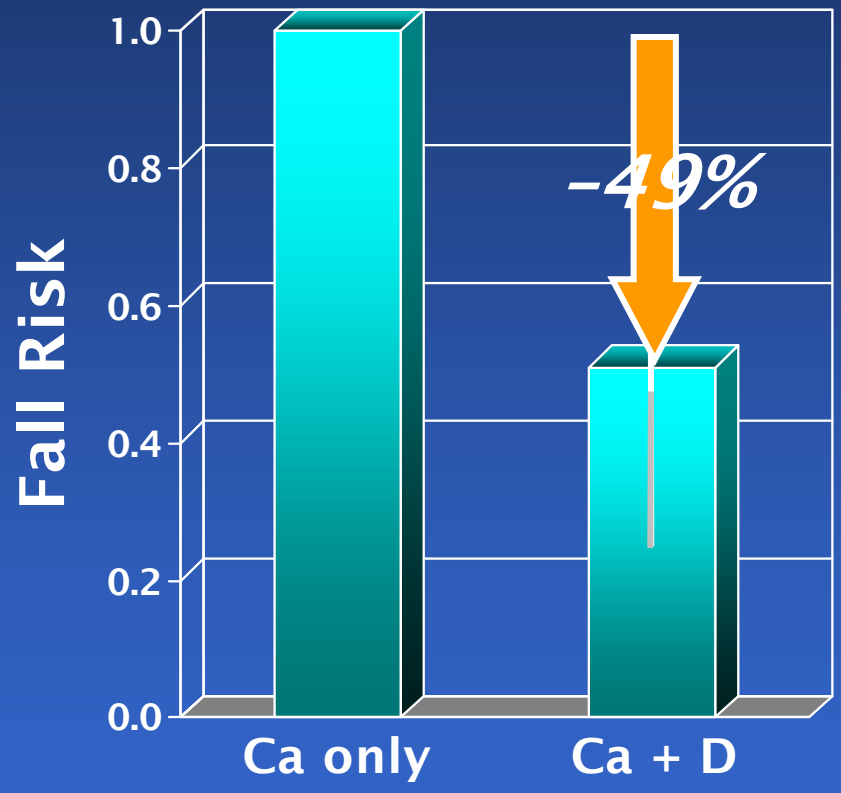
VITAMIN D & RISK OF FALLING*

- 122 women
- Age: 63–99
- DB–RCT
  - Ca 1,200 mg/d
  - Ca + 800 IU Vit D
- 12 week duration
- 25(OH)D 12 ng/mL at baseline



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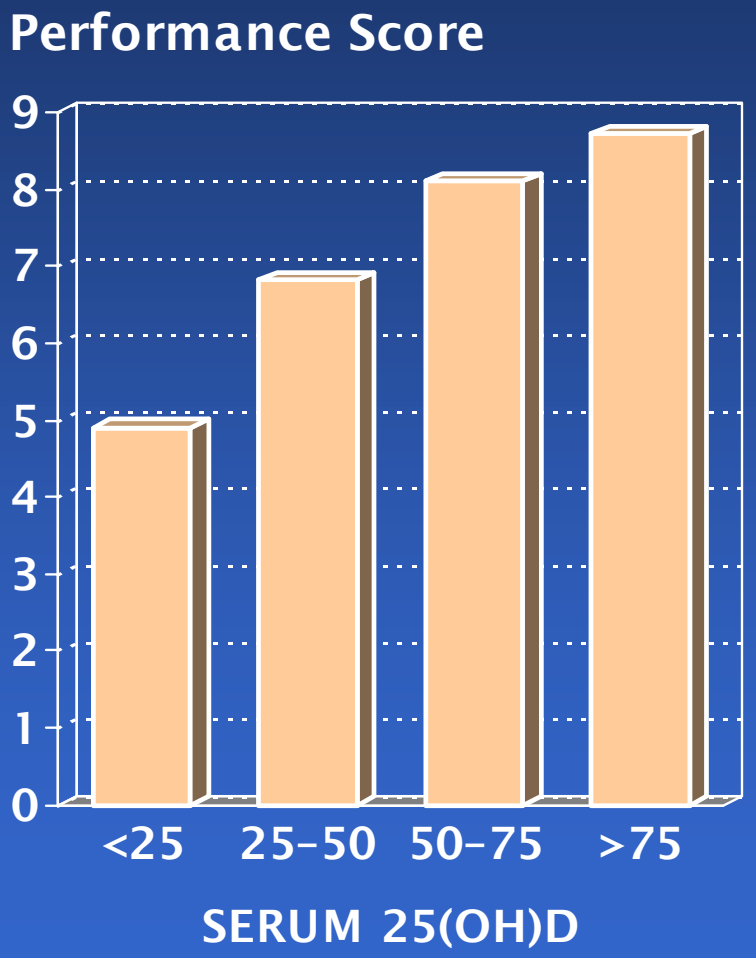
*Bischoff et al. *JBMR*. 2003;18:343–351.

VIT D & NEUROMUSCULAR FUNCTION*

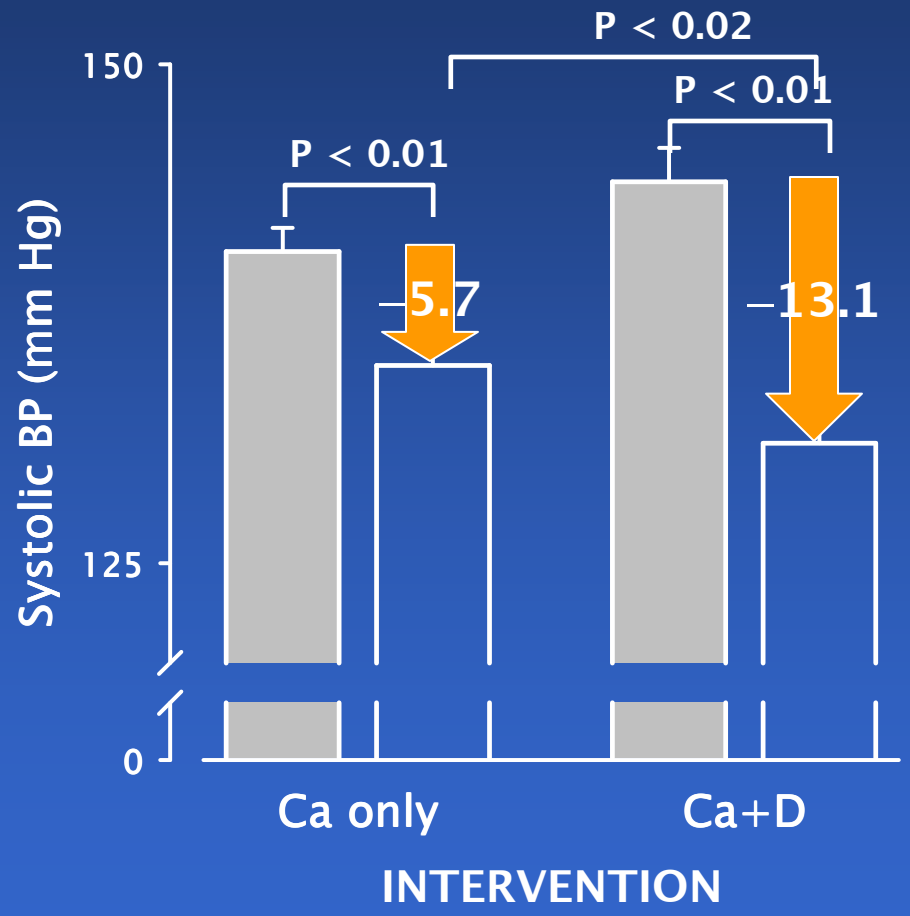
- 1359 men & women; mean age 75.5
- Amsterdam longitud. aging study
- neuromuscular performance measured on a scale of 0 to 12 (higher is better)
- each step statistically significant



*Wicherts et al. *JBMR*. 2005.

VIT D & BLOOD PRESSURE*

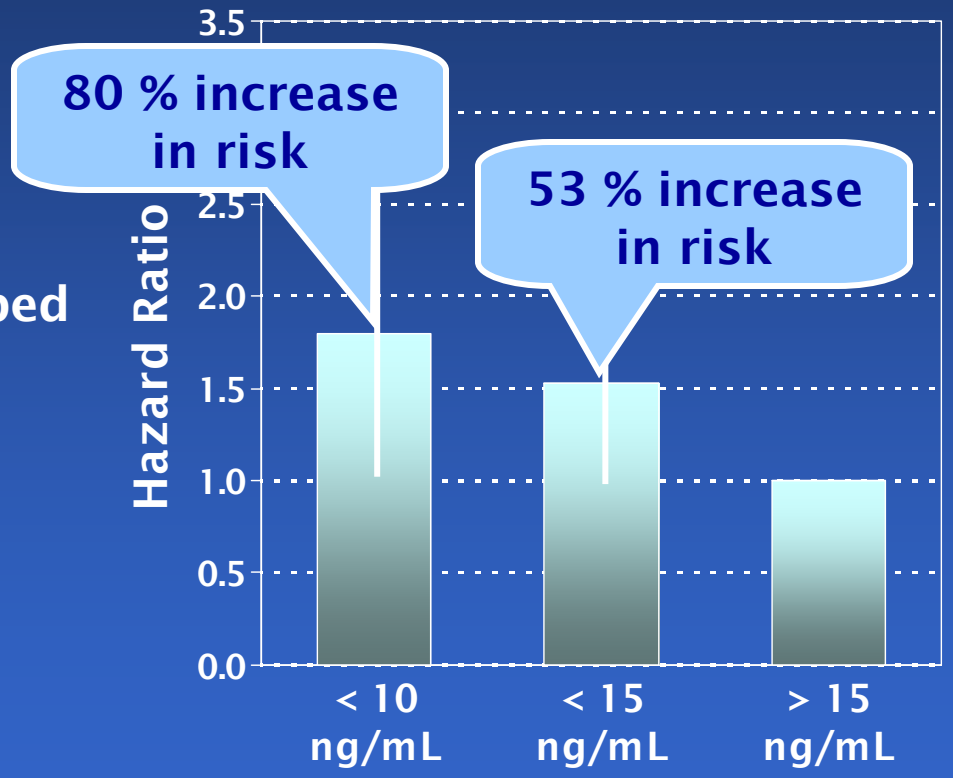
- 148 women, aged 74 ± 1
- DB-RCT
- baseline 25(OH)D < 50 nmol/L
- treated for 8 wks with:
  Ca 1200 mg/d or
  Ca + 800 IU vit D/d



*Pfeifer et al., JCEM 2001; 86:1633–37

VIT D & CARDIOVASCULAR DISEASE

- 1739 Framingham Offspring members
- age: 59 yrs
- follow-up: 5.4 yrs
- 120 individuals developed a CV event
- HR calculated against 25(OH)D values > 15 ng/mL
- *Wang et al. Circulation 2008*



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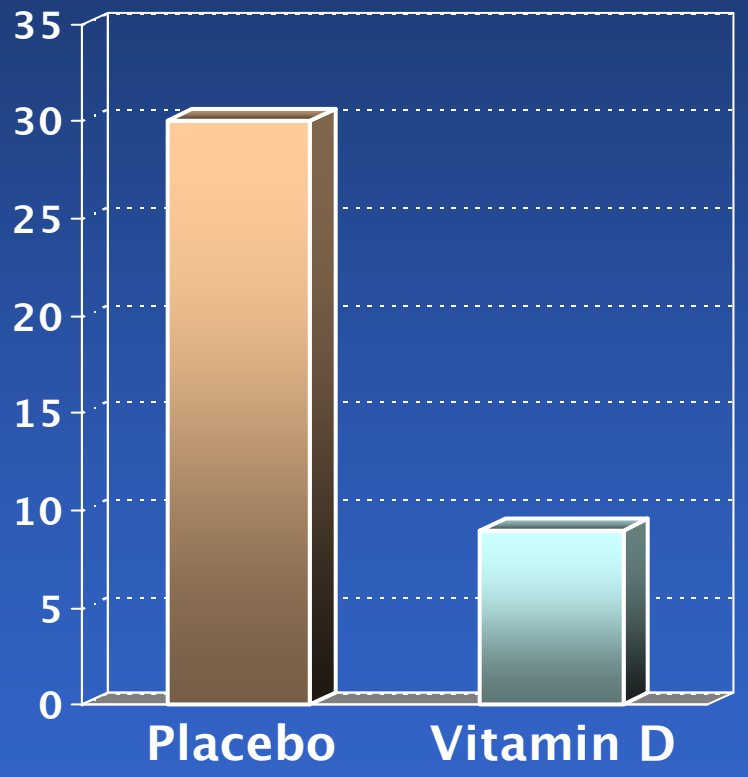
VITAMIN D & INFLUENZA*

- 208 African-American, postmenopausal women
- 3 yr DB-RCT
- placebo or vit D_3
  - 800 IU/d – 2 yrs
  - 2000 IU/d – 3rd yr
- basal 25(OH)D: 18.8 ± 7.5
- $P < 0.002$



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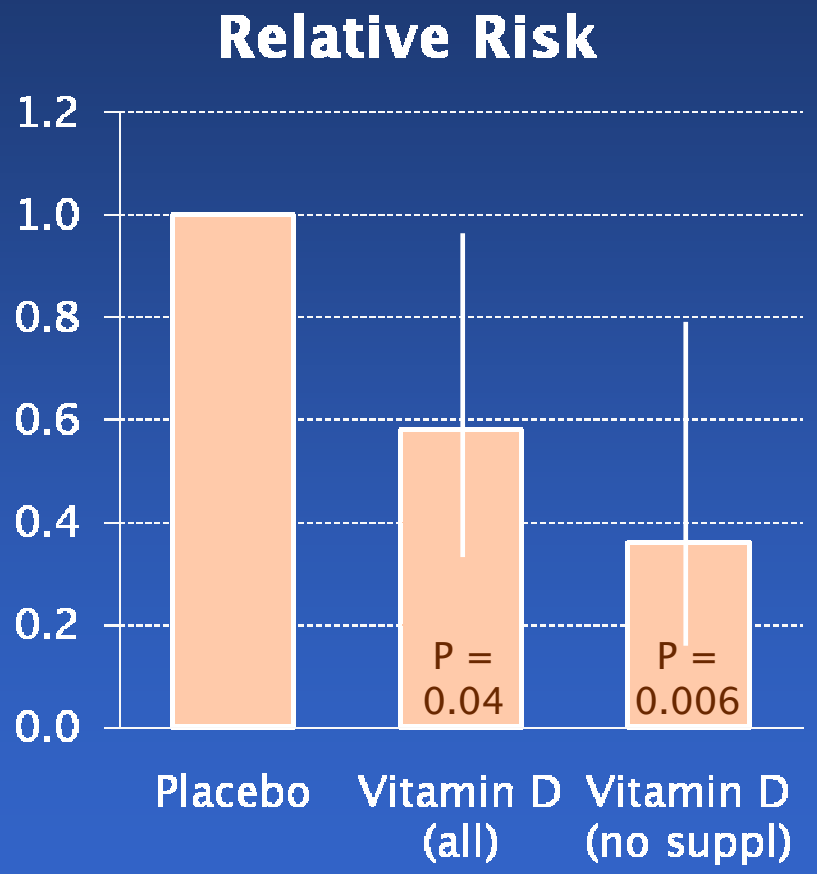
*Aloia & U-Ng (2007) Epidemiol & Infect

VITAMIN D & INFLUENZA*

- DB-RCT
- winter 2008-2009
- 334 Japanese school children, aged 6-15
- mean wt: 35.5 kg
- 1200 IU D_3/d in addition to self-supplementation



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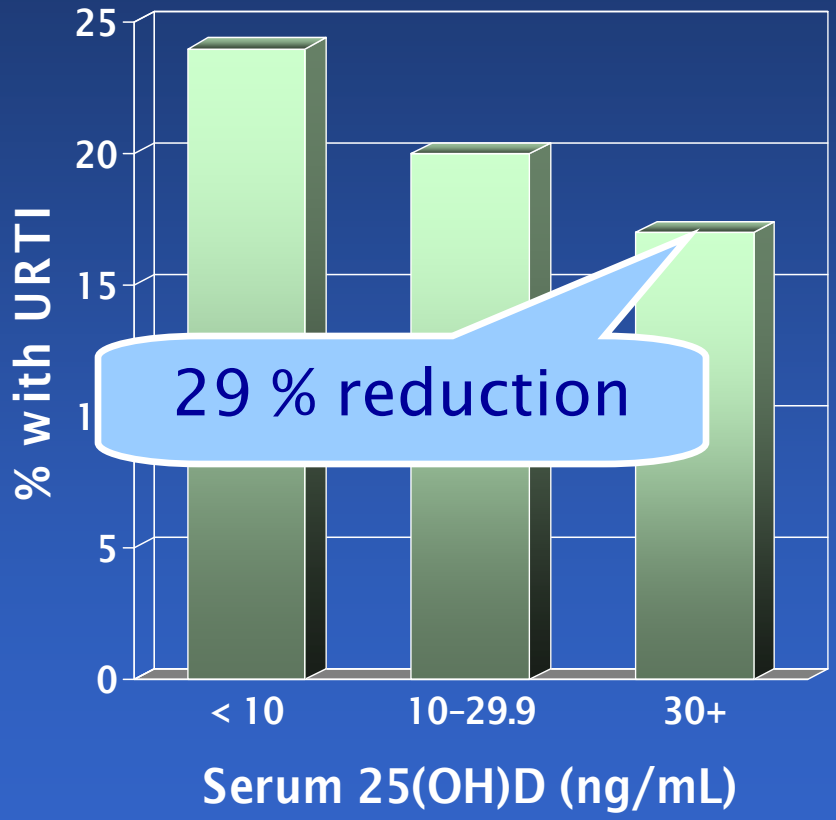
*Urashima et al., AJCN 2010

VITAMIN D & THE COMMON COLD*

- 18,883 individuals in NHANES-III
- tested association between serum 25(OH)D & recent URTI
- P < 0.001
- association stronger for those with asthma & COPD

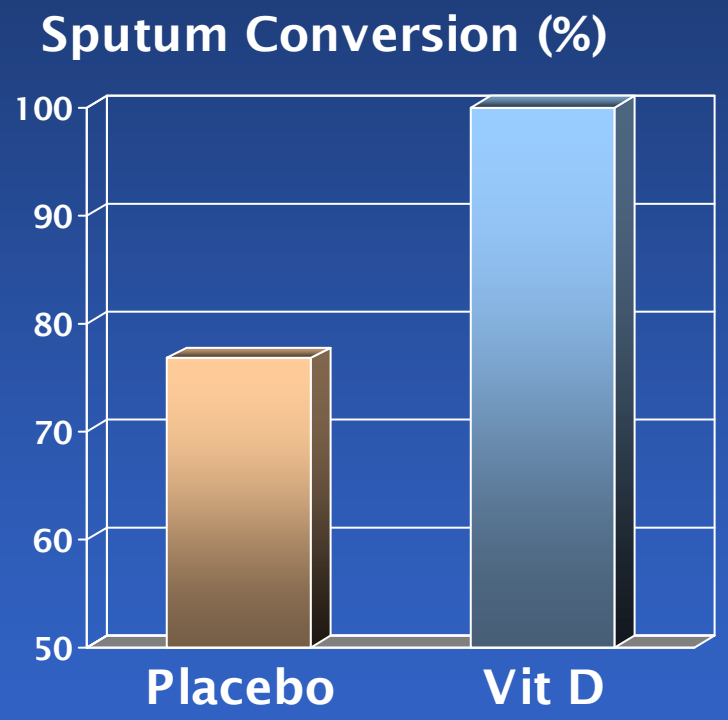


CU ORC

Ginde et al., Arch Int Med 2009 169:

VITAMIN D & TUBERCULOSIS*

- 67 pts with pulmonary TB
- standard treatment for all
- in addition, randomized to either vit D 10,000 IU/d or placebo
- P = 0.002



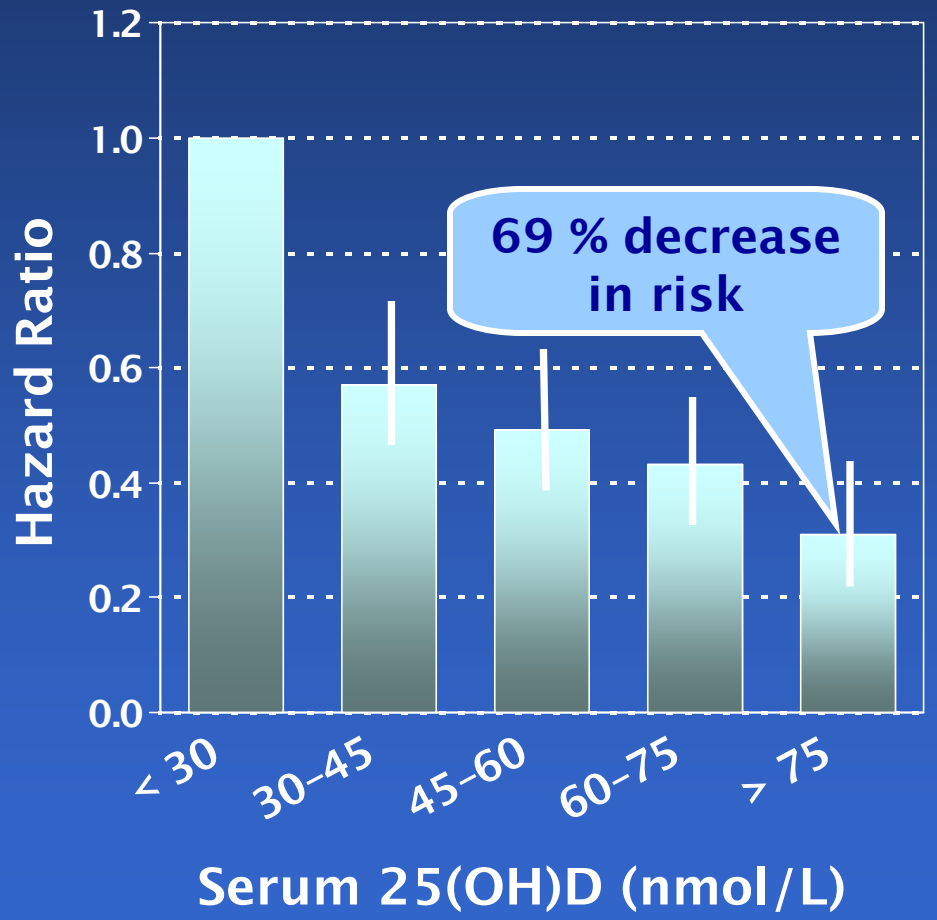
*Nursyam et al., Acta Med Indones 2006

things go better with

Vitamin D

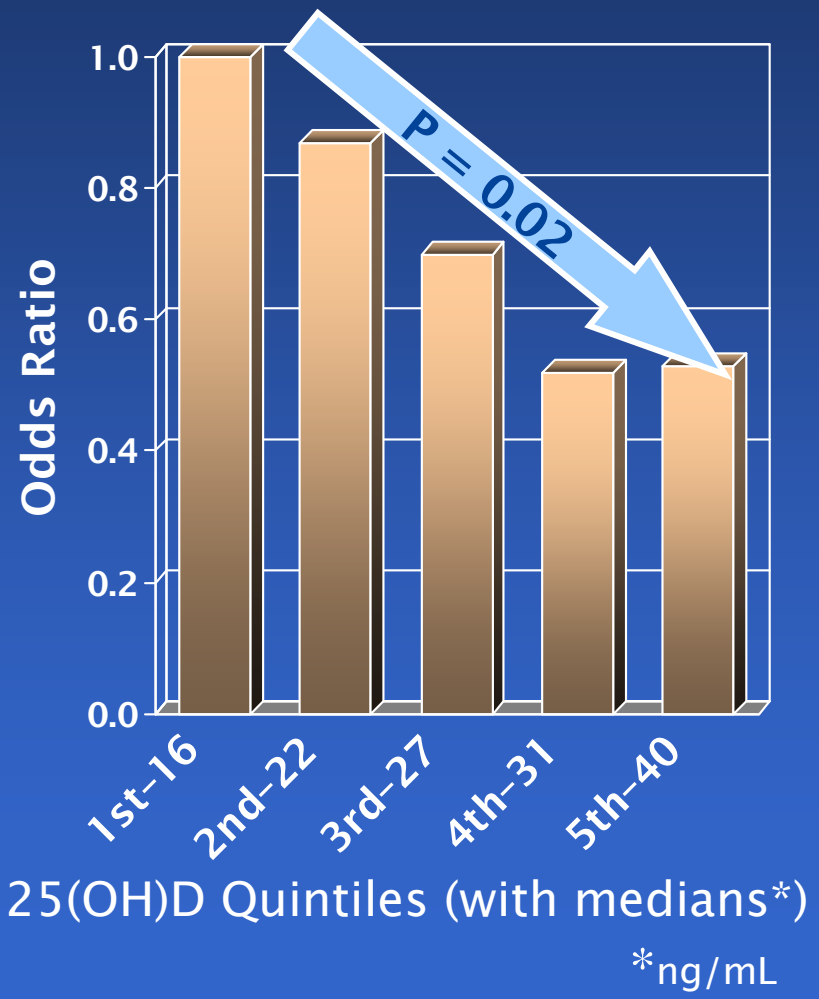
BREAST CANCER RISK

- Case-control study
  - 1394 cases
  - 1365 controls
- Odds ratio for CA inversely associated with vit D status [25(OH)D]
- *Abbas et al., Carcinogenesis (2008) 29:93-99*

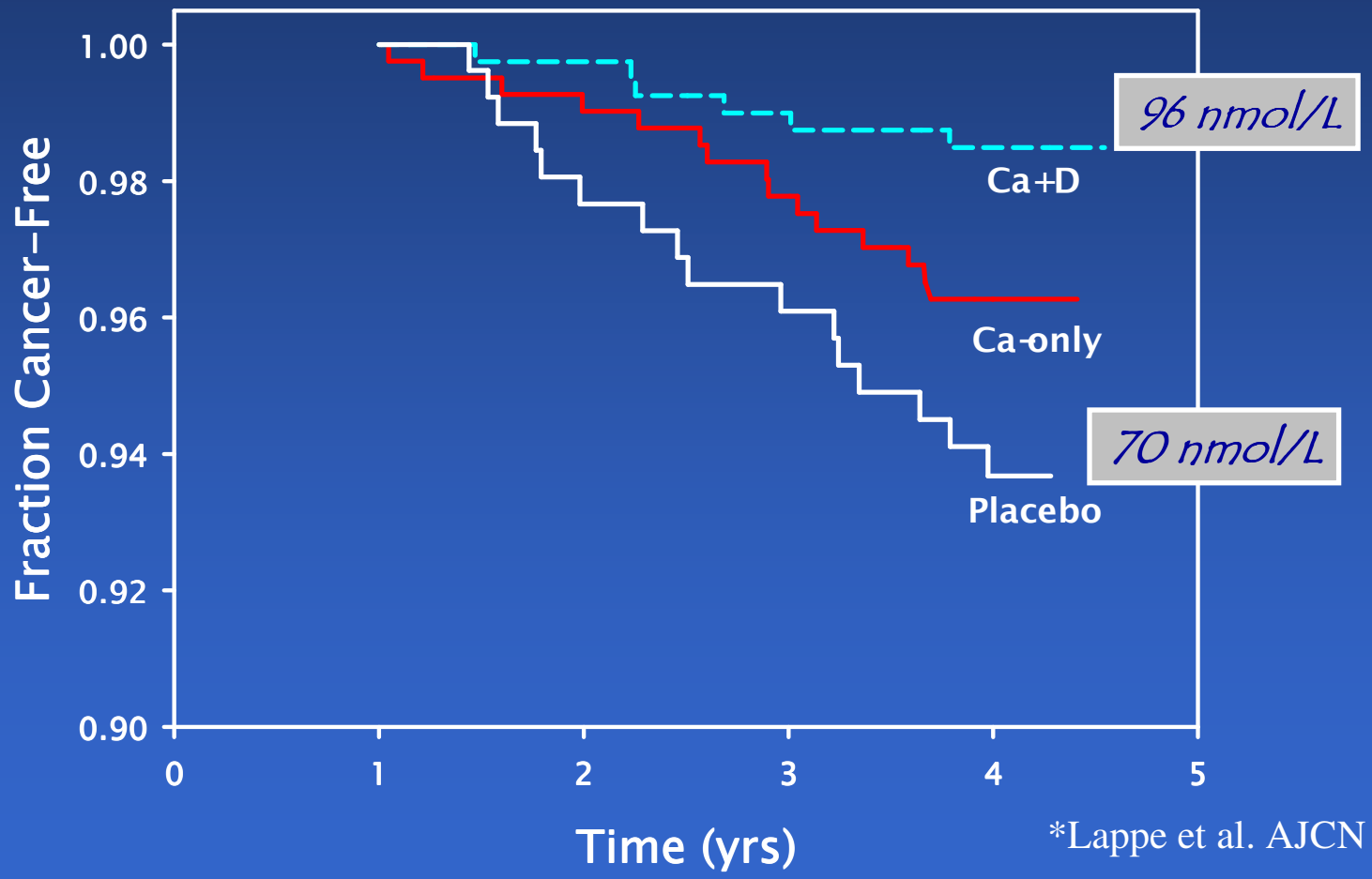


COLORECTAL CANCER

- Nurses' Health Study
- ages 46–78
- nested case-control study
- 193 incident cases
- 25(OH)D measured twice, prior to diagnosis
- Feskanich et al., Cancer Epidemiol Biomarkers Prev 2004 13:1502–08



VITAMIN D & CANCER*



*Lappe et al. AJCN 2007

HOW MUCH IS ENOUGH?

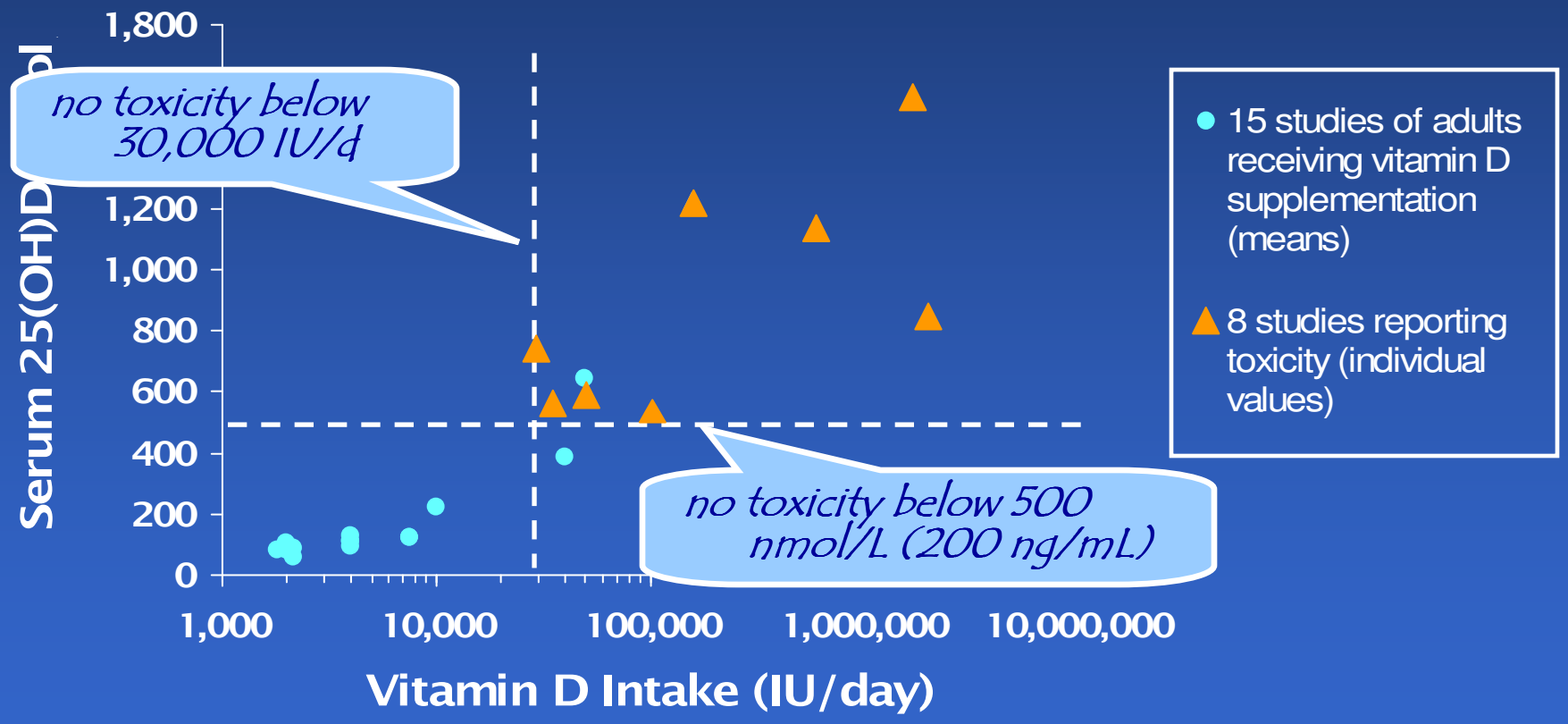
▪ rickets & osteomalacia	▪ 75 nmol/L
▪ Ca absorption	▪ 80 nmol/L
▪ pregnancy outcomes	▪ 120 nmol/L
▪ some cancers	▪ 100 nmol/L
▪ other	▪ ????

MANAGEMENT

- all-input requirement ≅75 IU/kg/d
- most adults will need 1000-3000 IU/d in addition to all other inputs
- 25(OH)D response varies widely
- it is the serum 25(OH)D concentration that must be optimized, not the oral dose
- the correct oral dose is the one that produces and maintains the desired 25(OH)D level

Safety

VITAMIN D INTAKE & TOXICITY*



* Hathcock JN et al. *Am J Clin Nutr.* 2007;85:6–18.

CONCLUSIONS

- serum 25(OH)D levels below 80 nmol/L are not adequate for any body system
- levels of as high as 125 nmol/L may be closer to optimal
- inputs from all sources combined are in the range of:
  - ~4,000 IU/d to sustain 80 nmol/L, and ~5,000 IU/d to sustain 100 nmol/L

Thank you