AVAILABILITY OF VITAMIN D FOR CONSUMERS AND PATIENTS

Prof. Heike A. Bischoff-Ferrari, MD, DrPH

Centre on Aging and Mobility, University of Zurich

Dept. of Rheumatology, University Hospital Zurich

Overview

- **Why is the availability of vitamin D important to patients and consumers?**
  - **Sources of vitamin D // how many are deficient?**
  - Scientific Evidence
  - Safety
  - Public Health Potential
  - Economic Considerations

Background: How come whole nations are vitamin D deficient?

1.

Main Source of Vitamin D

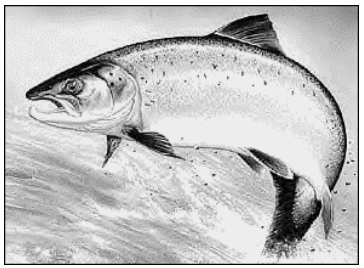
We expose less than 5% of our skin to the sun + we wear sunscreen

Very little vitamin D production from November to May in all of Europe

Vitamin D production in the skin decreases 4 times with age

Seniors avoid the sun: lowest levels in the Mediterranean (SENECA study)

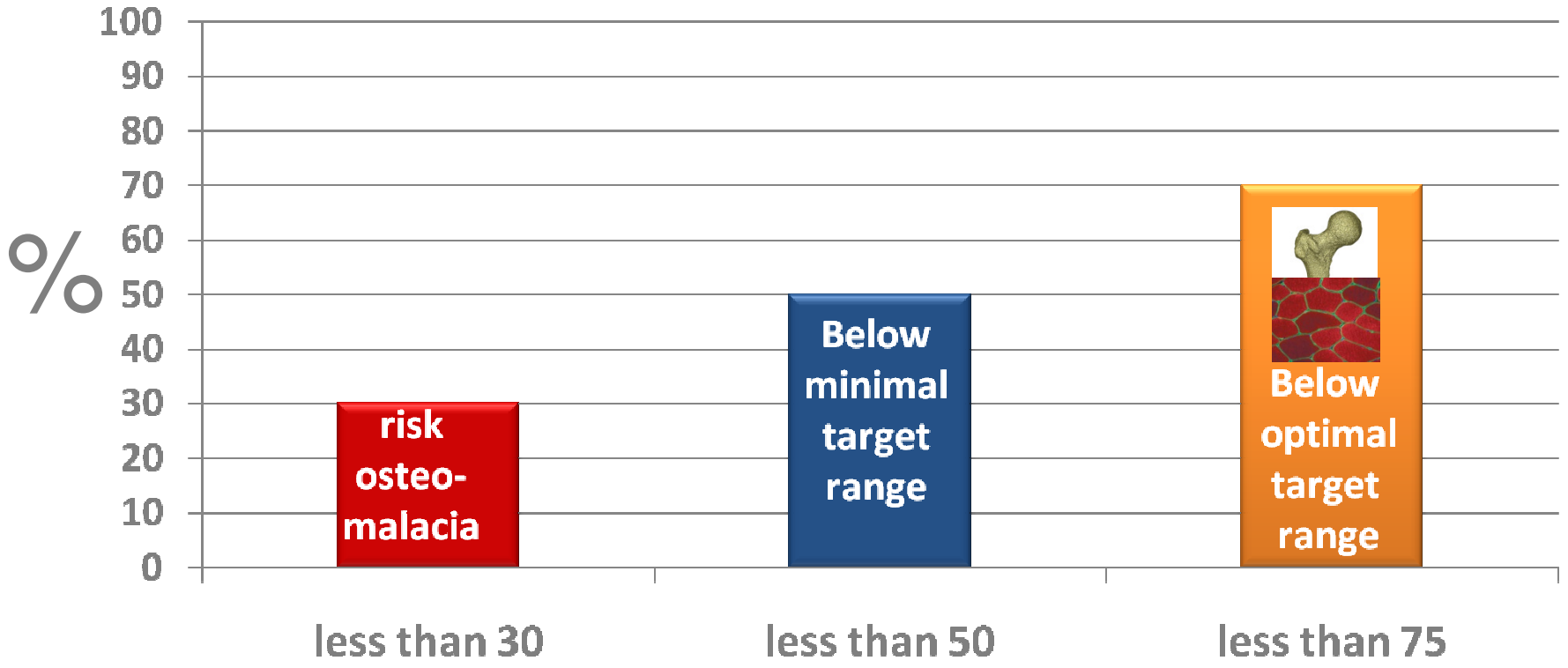
2. Nutritional sources of vitamin D are limited

- not enough  in the sea

Chen TC, Holick MF, et al. Factors that influence the cutaneous synthesis and dietary sources of vitamin D. Arch Biochem Biophys 2007;8:8.

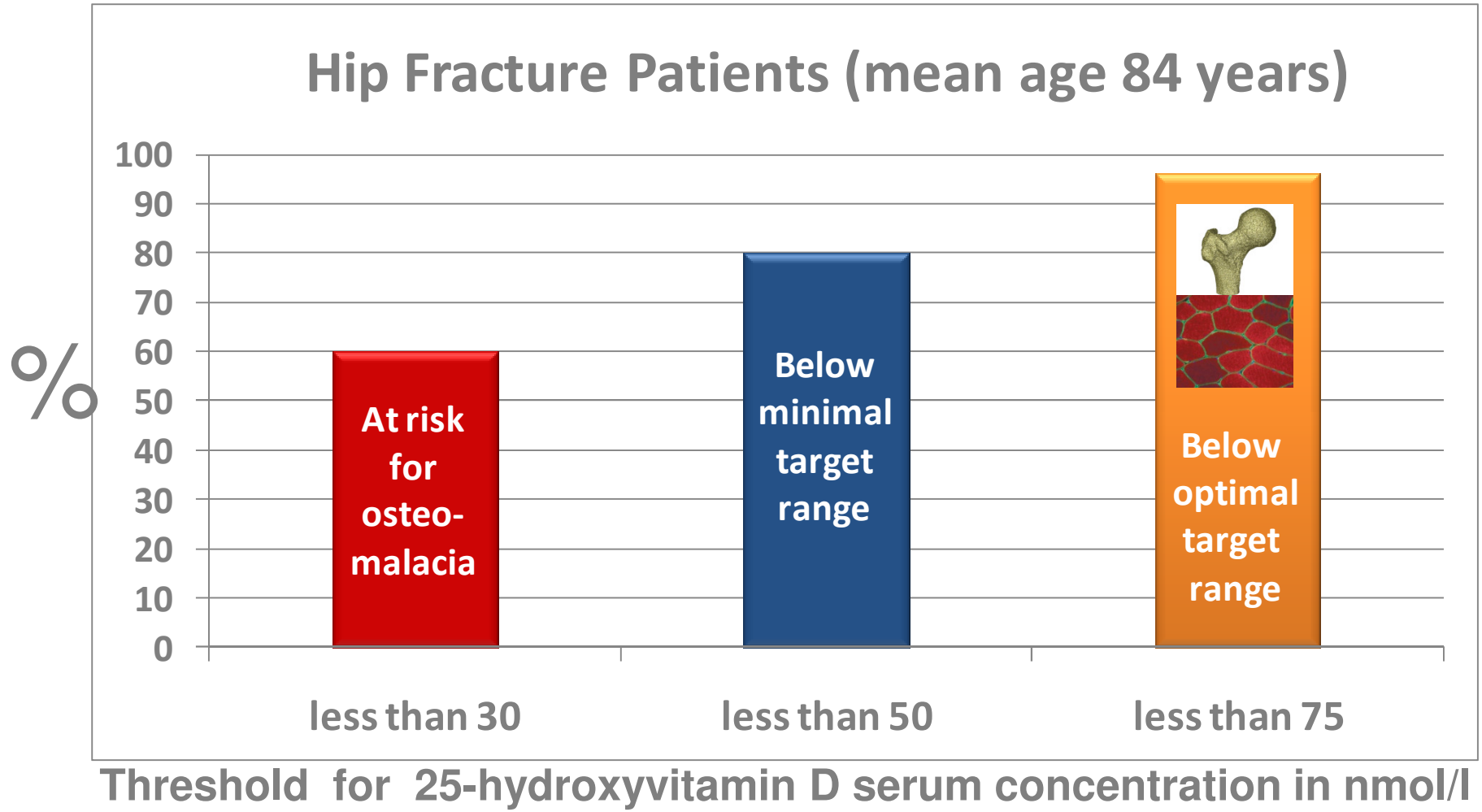
How many are deficient?

Adult European Population



van der Wielen RP, et al. Serum vitamin D concentrations among elderly people in Europe. Lancet 1995;346:207-10 (SENECA).
Burnand B, Burckhardt P et al. Serum 25-hydroxyvitamin D: Swiss population. Am J Clin Nutr 1992;56:537-42.

How many are deficient?



Bischoff-Ferrari HA, Staehelin HB, Theiler R et al.; Severe Vitamin D Deficiency in Swiss Hip Fracture Patients; Bone 2008

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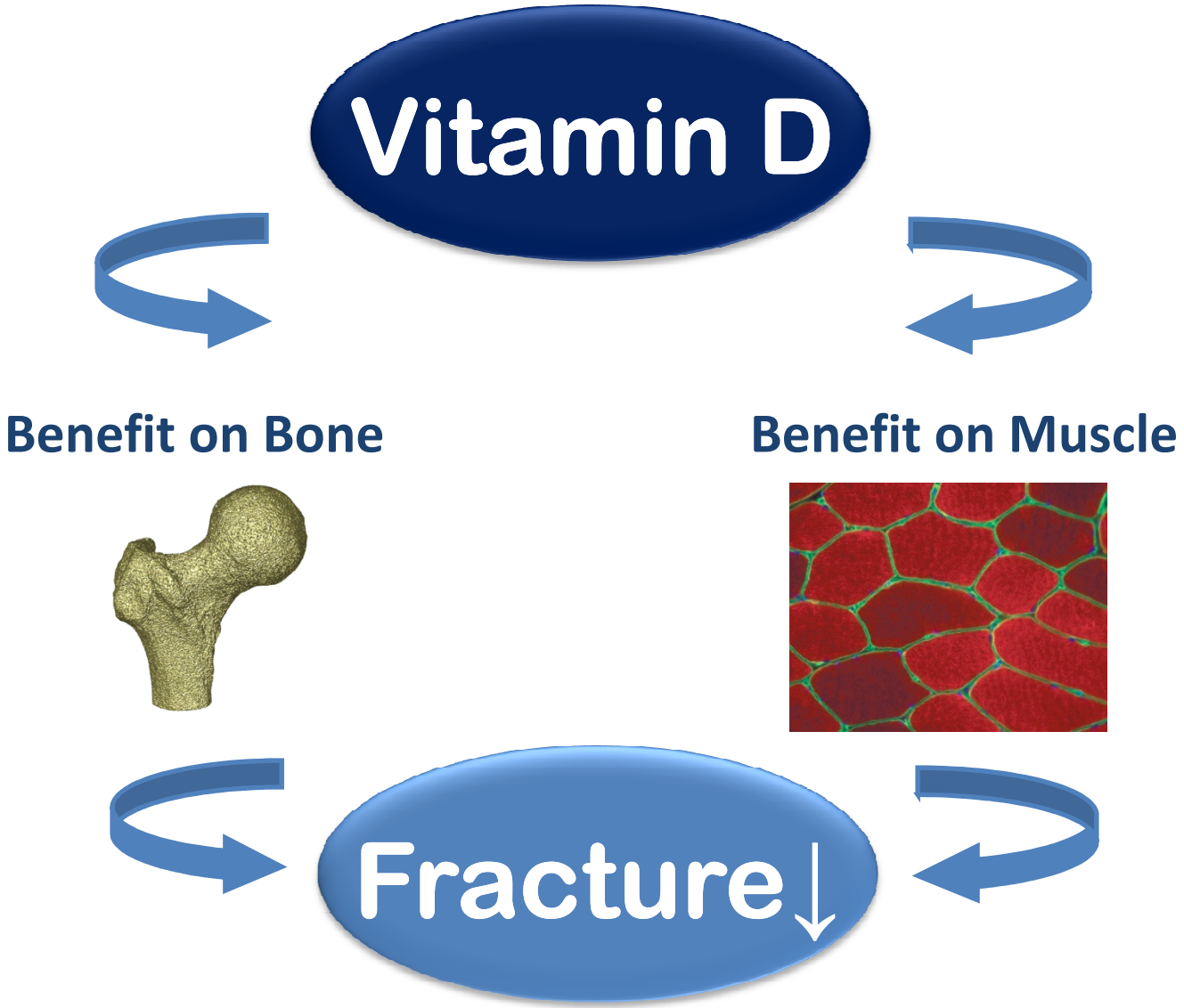
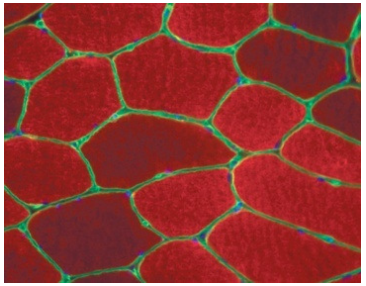
WE HAVE EVIDENCE TODAY



EVIDENCE:two 2009 Meta-analyses of double-blinded Trials

Effect was dose-dependent increasing with dose and vitamin D level

18% Reduction **20% Reduction (33% 65-74 yrs)** **19% Reduction**



Hip fractures **Any non-vertebral fracture**

Received dose (treatment dose*adherence) of > 480 IU vitamin D/d

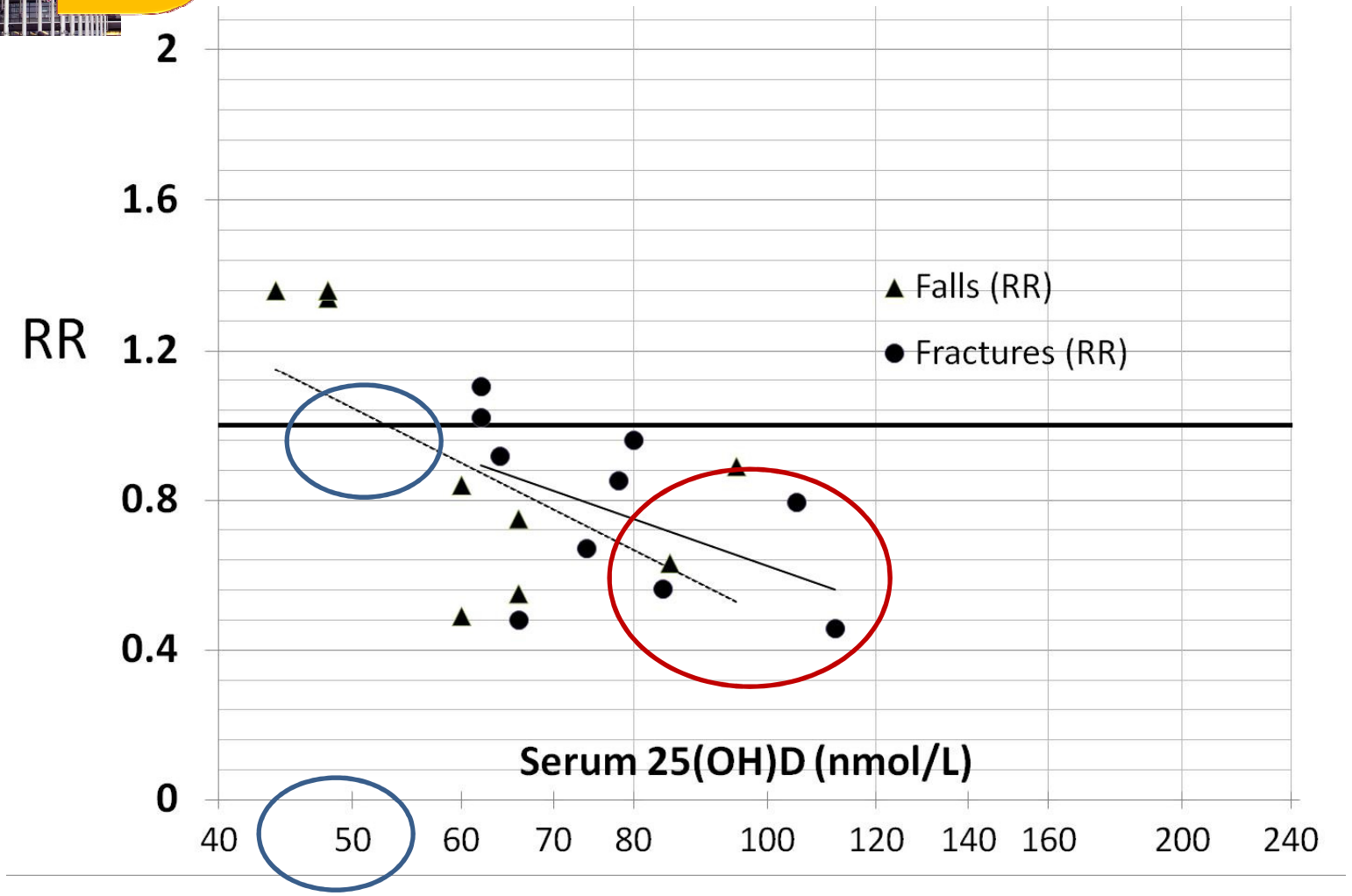
Falls

Treatment dose of 700 to 1000 IU vitamin D/d

Bischoff-Ferrari HA, et al.; Archives of Internal Medicine 2009;

Bischoff-Ferrari HA, et al.; British Medical Journal 2009

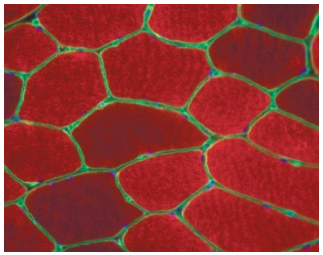
Optimal Vitamin D Levels for Fall and Fracture prevention from Clinical Trials



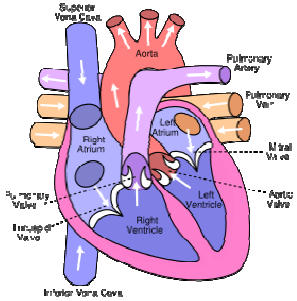
Bischoff-Ferrari , Staehelin HB et al.; Archives of Internal Medicine 2009; Bischoff-Ferrari, Dawson-Hughes et al.; British Medical Journal 2009
Bischoff-Ferrari HA, Shao A , Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; OP International 2009

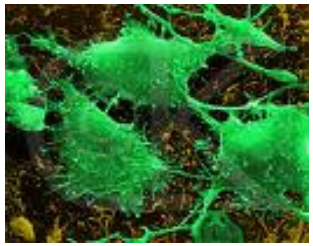
Additional public health potential

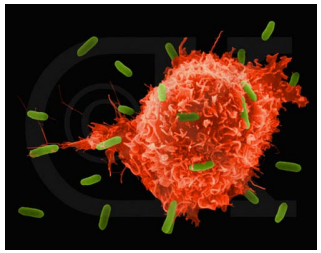
Fracture and Fall Prevention



General Health



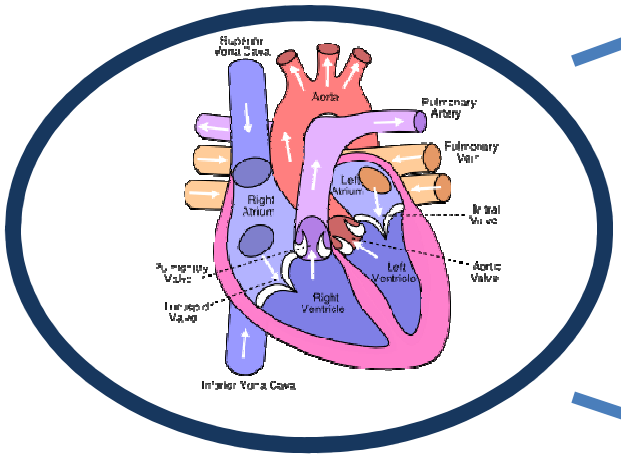




Small clincal trials, mechanistic and large cohort studies suggest

benefit of vitamin D on cardio-vascular health

Large clinical trials needed to confirm such benefits



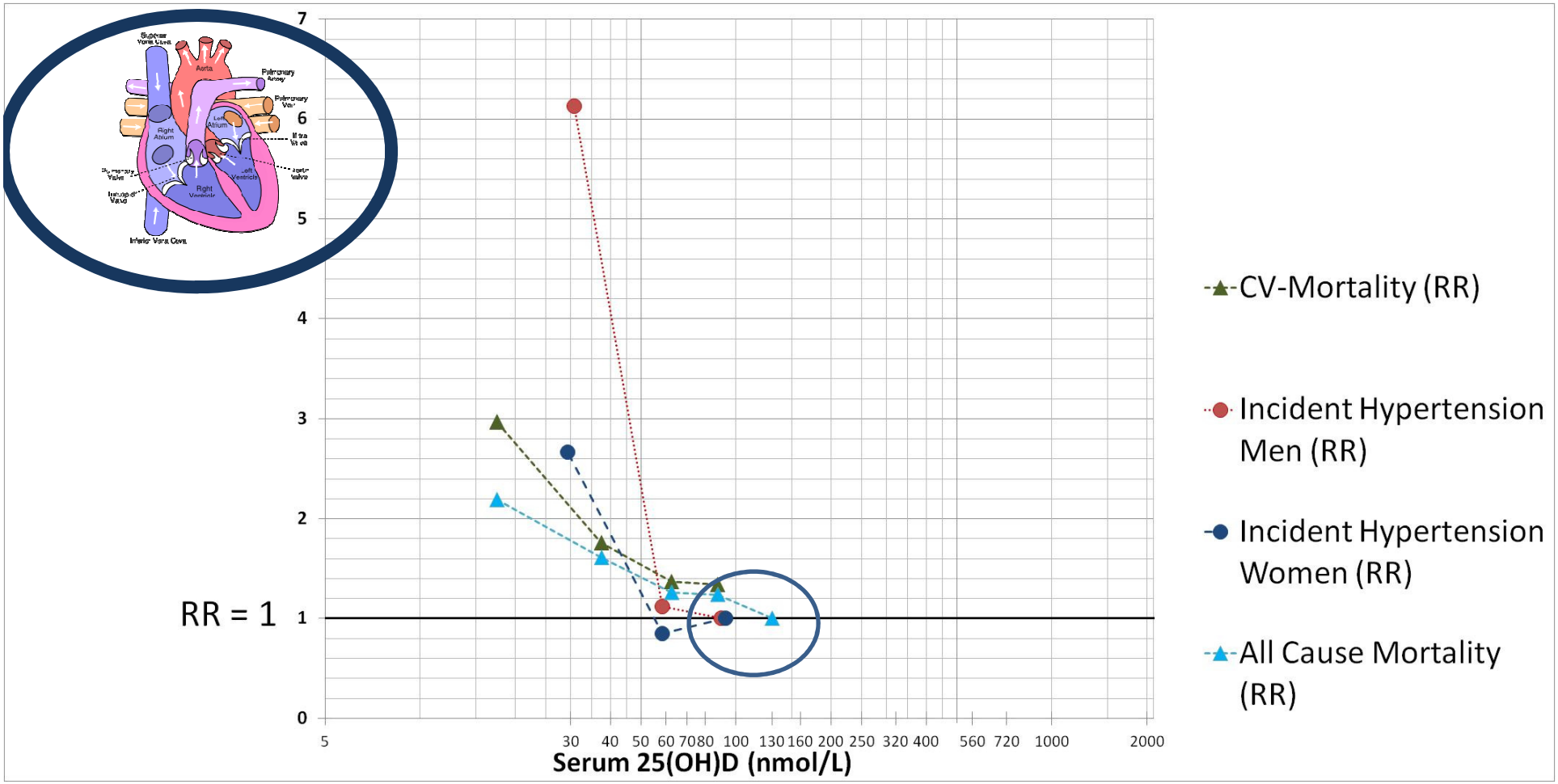
Mouse without the VDR:
has hypertension
and dies from heart failure

Small clinical trials in humans:
UVB-irradiation or
800 IU vitamin D reduces blood pressure
by about 6 mmHG

Large cohort studies:
vitamin D levels of at least 75 nmol/l
compared to levels below 36 nmol/l
6-fold lower risk of hypertension among men
3-fold lower risk among women
2.5-fold lower risk of myocardial infarction

Giovannucci E et al. Archives of Int. Med. 2008; Pfeifer M et al. J Clin Endocrinol Metab. 2001 ; Krause et al. The Lancet 1998
Bouillon R, Bischoff-Ferrari H, Willett W. JBMR 2008; Endo I et al. Endocrinology 2003

Large Cohort Studies: Optimal Vitamin D Levels for cardio-vascular health



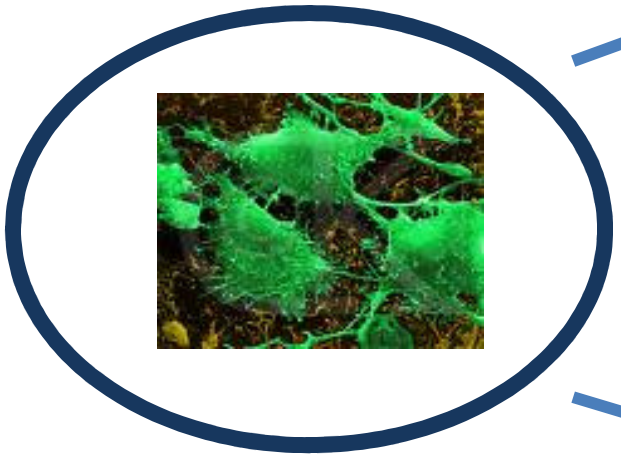
Incident hypertension: Forman JP et al. (NHS + HP); Hypertension 2007.
All-cause and cardiovascular mortality: Ginde AA (NHANES III); Am J Prev. Med. 2007

Bischoff-Ferrari HA, Shao A , Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; Osteoporosis International 2009

One small clincal trial, mechanistic studies and large cohort studies suggest a benefit of vitamin D on

cancer prevention

Large clinical trials needed to confirm such benefits



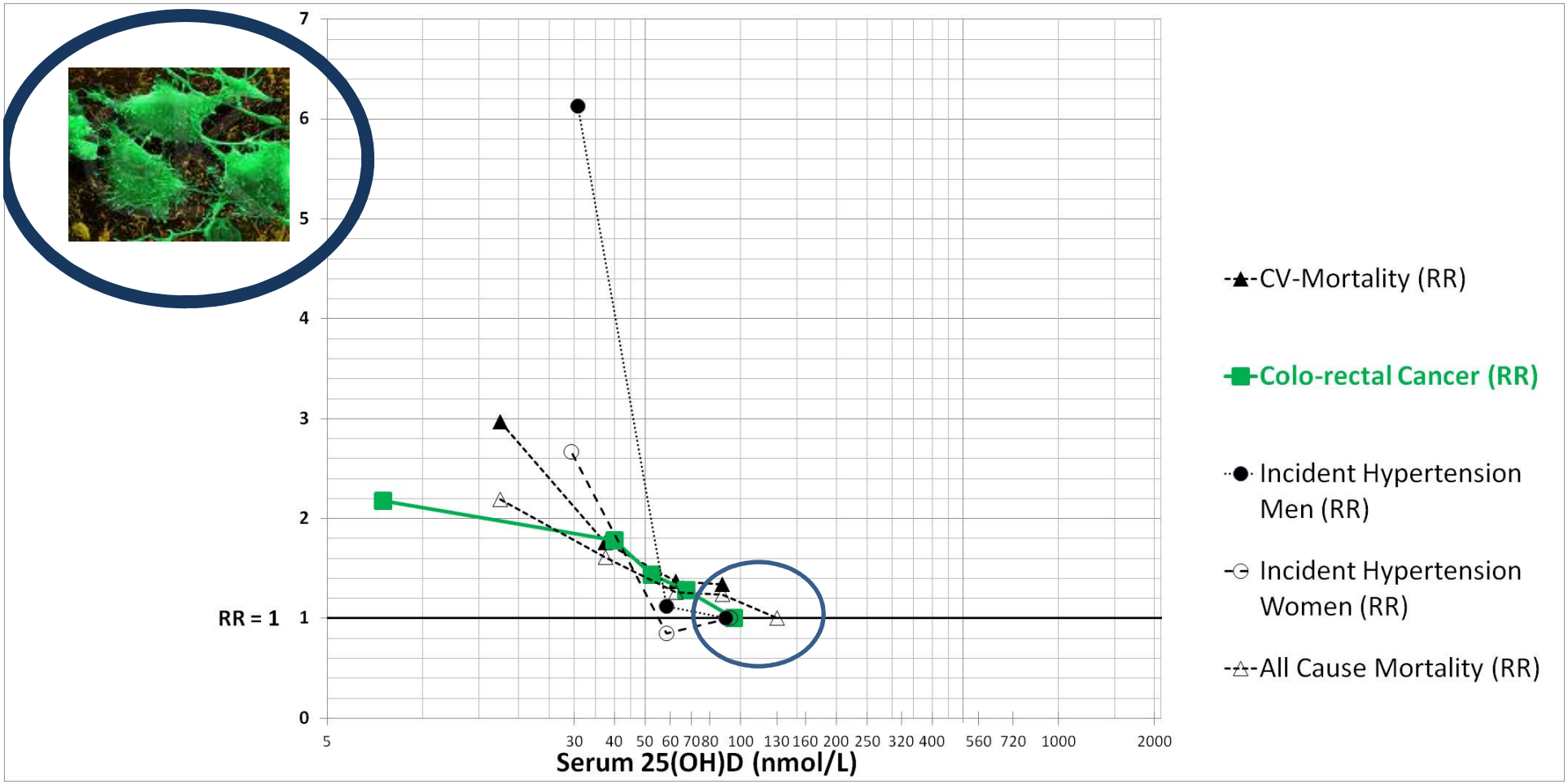
Vitamin D inhibits cell proliferation:
Shown for fibroblasts, colo-rectal, breast and prostate cancer cells

Clinical trial in humans:
Among 1179 women age 55+
1100 IU vitamin D + calcium compared to placebo reduced cancer risk by 60% in 4 yrs

Large cohort studies:
Higher vitamin D levels associated with lower cancer risk, and less mortality from cancer, strongest data for colo-rectal cancer

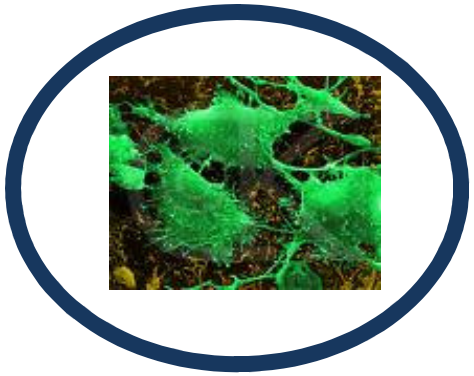
Lappe JM et al. Am J Clin Nutr 2007; Giovannucci E. et al.; JNCI 2006; Feskanich D et al. CEBP 2004; Bouillon R, Bischoff-Ferrari H, Willett W; Perspectives from Mice and Men; JBMR 2008

Large Cohort Studies: Optimal Vitamin D Levels for colo-rectal cancer

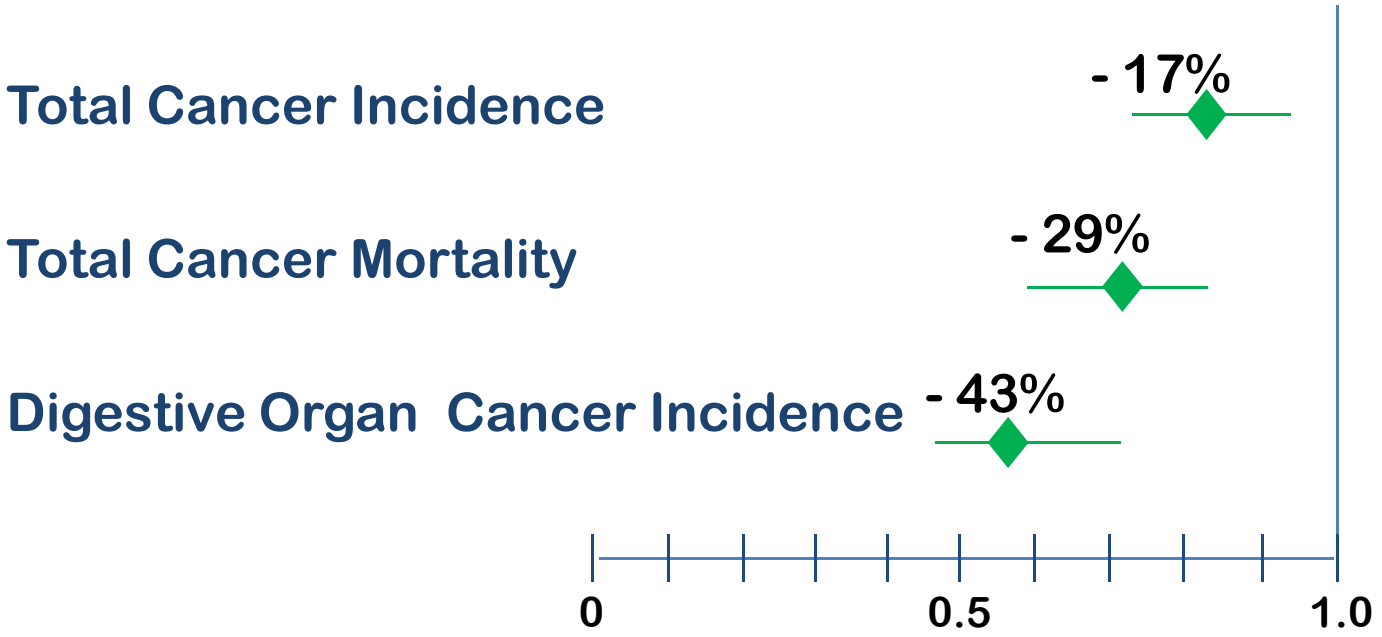


Colorectal cancer: Goreham ED (a quantitative meta-analysis of 5 studies; Am J Prev. Med. 2007

Bischoff-Ferrari HA, Shao A , Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; Osteoporosis International 2009



Multivariable* RR for a 25 nmol/l increment in vitamin D status in men (1986-2000)

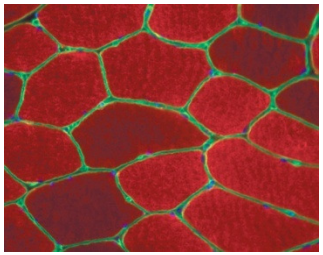


age, smoking, height, alcohol, calories, red meat, calcium, retinol, fruits and vegetables

Giovannucci E. et al., JNCI 2006

Additional public health potential

Fracture and Fall Prevention



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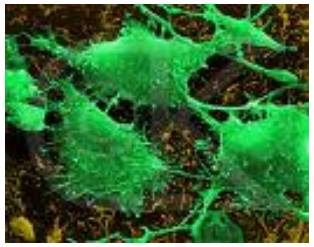

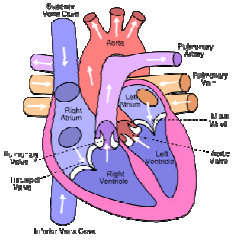

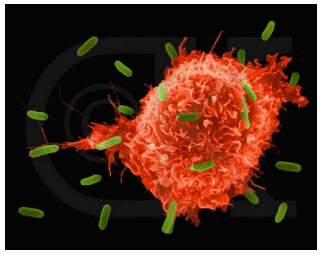

↓Type 1 diabetes
↓ Multiple Sclerosis
↓ Infections
↓ Asthma

Heaney RP. The Vitamin D requirement in health and disease. J Steroid Biochem Mol Biol 2005. Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. Am J Clin Nutr 2004. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes; AJCN 2006.

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- **Why is the availability of vitamin D important to patients and consumers?**
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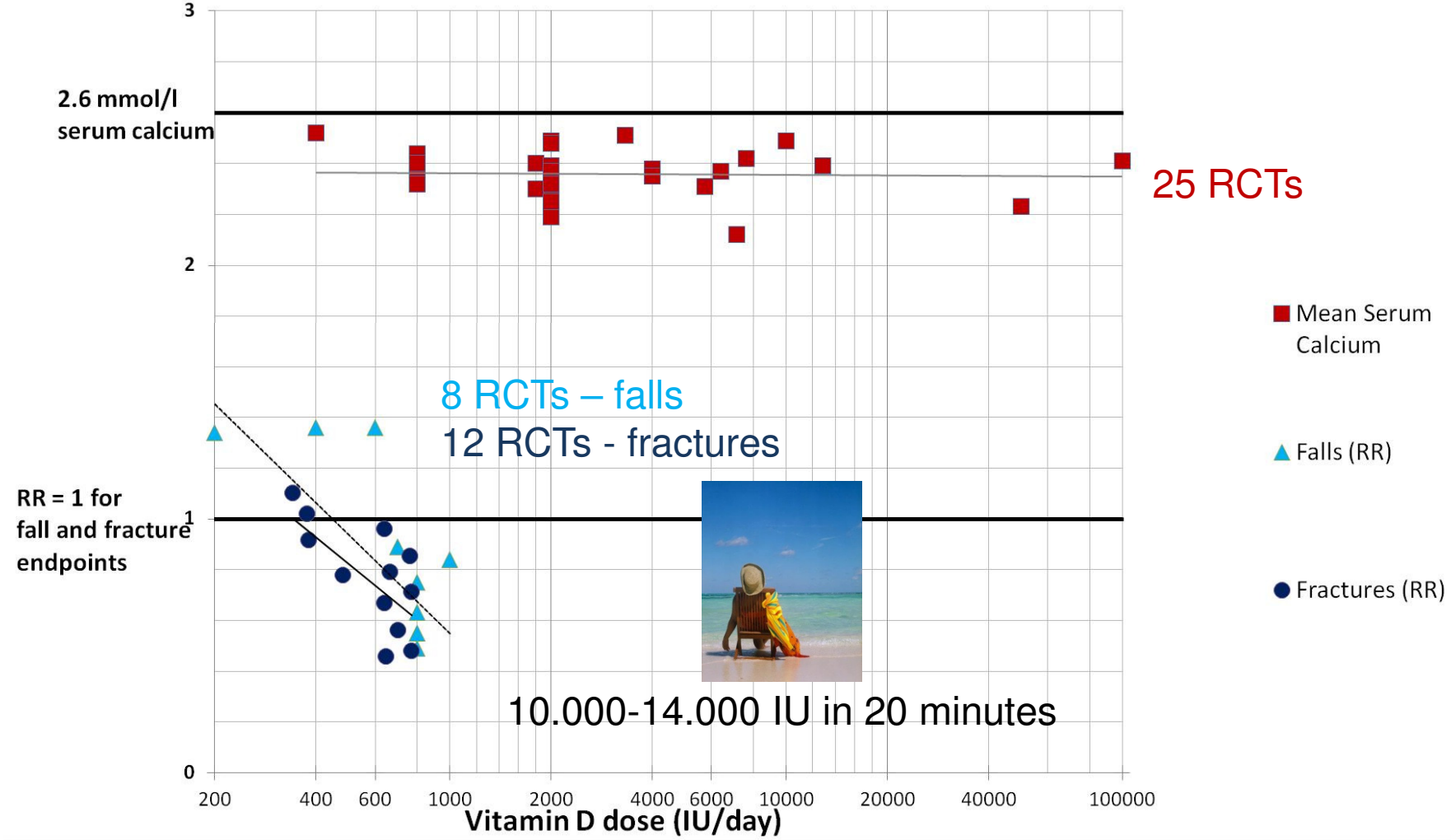
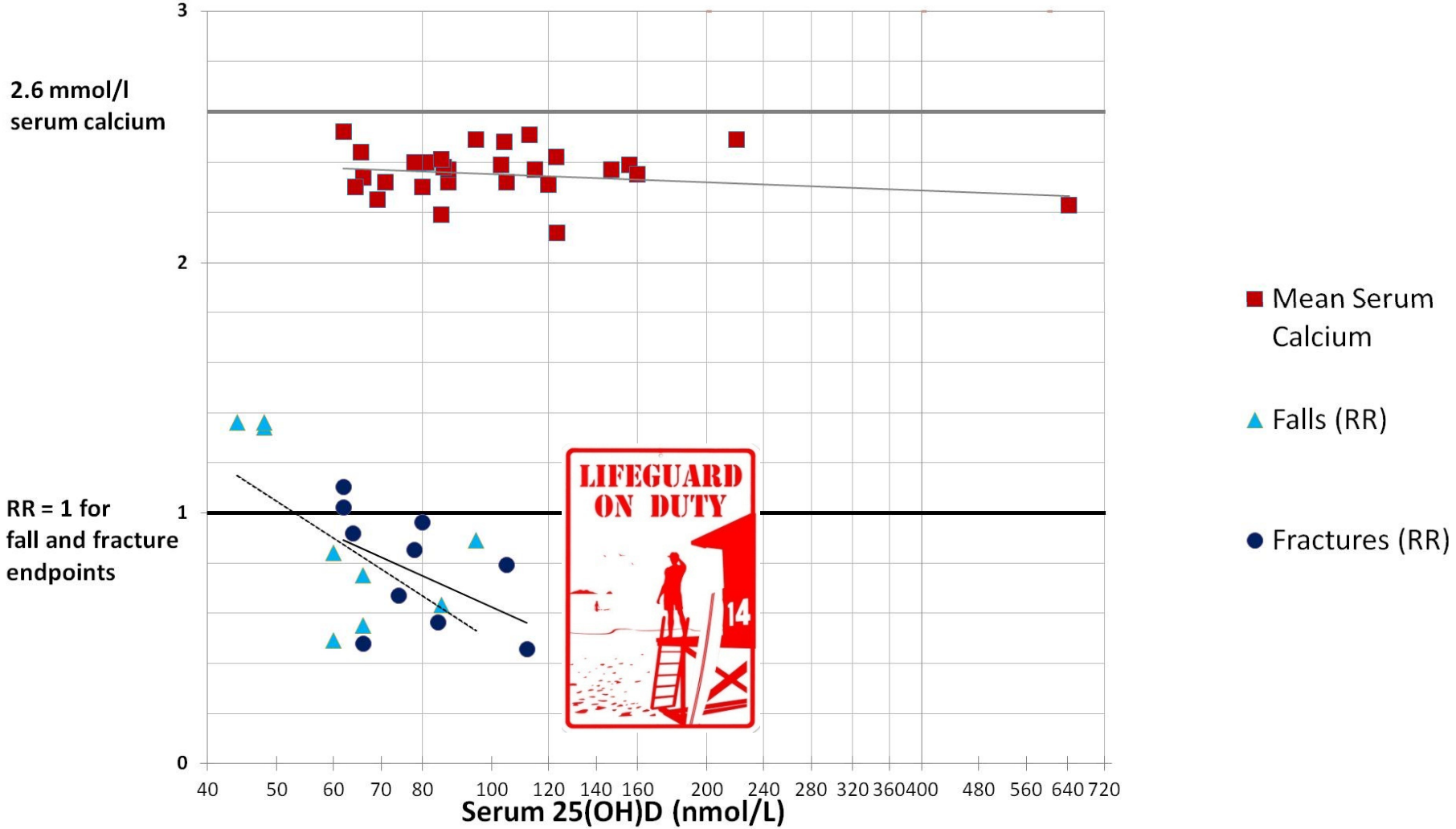
Safety based on Trials with Vitamin D // dose



Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC ; Benefit-Risk Assessment of Vitamin D; OP International 2009

Safety based on Trials with Vitamin D // levels



Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC ; Benefit-Risk Assessment of Vitamin D; OP International 2009

Summary safety

- Vitamin D intakes of 800 to 1000 IU vitamin D per day or vitamin D levels of about 75 to 110 nmol/l provide optimal benefits for fall and fracture prevention **without increasing health risks** (Evidence-based).
- Vitamin D levels of about 75 to 110 nmol/l **also** provide optimal benefits on cardiovascular health and cancer prevention **without increasing health risks** (Epidemiologic data).
- 800 to 1000 IU vitamin D per day, will bring about **50% to 75 - 110 nmol/l --** Higher intakes are needed to bring all adults to **75 to 100 nmol/l** (1800 to 4000 IU per day based on benefit risk assessment – not tested for important endpoints)

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC ; Benefit-Risk Assessment of Vitamin D; OP International 2009

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Public Health Potential based on Fall and Fracture Prevention with Vitamin D – we have **EVIDENCE**

- **Hip fractures are the most frequent fracture at age 75+**
  - In the first 12 months after hip fracture
    - 50% of seniors are less mobile
    - 30% of seniors loose their independence
    - 10% of seniors fracture their other hip
    - 30-50 % of seniors are re-admitted to acute care for any reason
    - 15 to 25% die
- **30% of seniors age 65 and 50% of seniors age 80 fall each year**
    - Falls are the primary cause of hip fracture
    - Falls are independent predictors of functional decline
    - 9% of emergency room visits are due to a fall
    - 5% of falls lead to a fracture
    - 40% of nursing home admissions are due to a fall

With 800 to 1000 IU vitamin D per day we could reduce these events and their serious consequences by about 20%

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Economic Considerations

- **Economic benefits of having all Europeans reach a desirable 25-hydroxyvitamin D threshold of 100nmol/l** (40ng/ml) were estimated by Grant et al. based on epidemiological data on the expected reduction of chronic disease.
- For a daily dose between 2000–3000 IU of vitamin D3, the reduction in health care expenditures was estimated to be 187,000 million Euro per year (2007 €) , while the estimated cost of 2000–3000 IU of vitamin D3 per day along with costs for education and testing was estimated to be 10,000 million Euro per year.
- As epidemiologic estimates often appear inflated due to artificially defined control populations, more clarity on health economic savings will be achieved from a large-scale clinical trial of the health benefits and health resource savings associated with vitamin D.
- Ongoing cost-efficacy analysis for fracture and fall prevention by Dawson-Hughes, Wong and Bischoff-Ferrari

Grant WB, Cross HS, Garland CF, et al. Estimated benefit of increased vitamin D status in reducing the economic burden of disease in western Europe. Prog Biophys Mol Biol 2009;99:104-13.

Time to D

- We have evidence today that in seniors 800 to 1000 IU Vitamin D could reduce 20% of hip fractures, any non-vertebral fractures and falls

- Potential additional benefit on general health

- Yet, 50% to 70% of the adult population is vitamin D deficient

- **Action at a public health level:**
  (1) recommend 800 to 1000 IU vitamin D to all seniors age 60 – 65 +
  (2) to all adults?
  (3) large trial to confirm additional health benefits