Sustainable nutrition – do supplements do it better?

Adelaide, 30 August, 2011

Robert Scragg
School of Population Health,
University of Auckland,
New Zealand

Supplement use by Australians

Australian Bureau of Statistics – 1995 National Health Survey

- 30% of the population had recently used a vitamin and mineral supplement, or a natural medication.
- People aged 45-54 years were most likely to have used a vitamin and mineral supplement, or natural medication (37%).
- Among those using vitamin and/or mineral supplements:
  - 82% did so as a preventative health measure
  - 6% did so to treat a respiratory disease (mainly common cold)

Research on vitamins & prevention of chronic disease has found inconsistent results between observational studies & randomised controlled trials (RCTs)

Vitamin	Observational studies: High vitamin level	RCT s: effect of vitamin supplementation
Vitamin A (beta-carotene & retinol)	decreased cancer	increased lung cancer & mortality
Vitamin B	decreased cancer	no effect on cancer
Vitamin C	decreased cancer & CV disease	no effect on cancer & CV disease
Vitamin E	decreased CV disease	No effect on CV disease increased mortality

Meta-analysis: RCTs of anti-oxidant supplementation and all-cause mortality

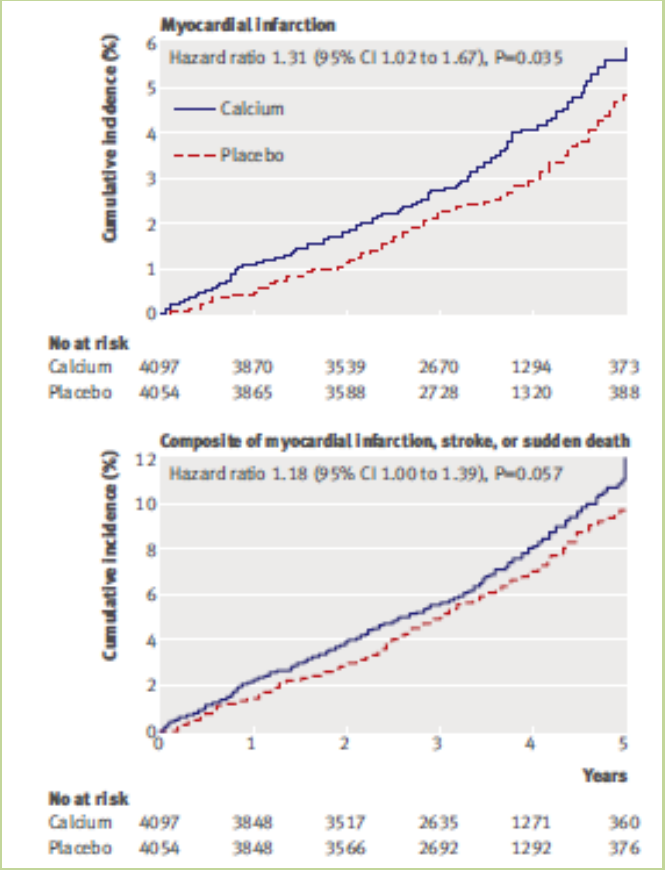
Bjelakovic G, *Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD007176*

Vitamin	Relative Risk (95% CI)
Vitamin A	**1.16** (1.10 – 1.24)
Beta-carotene	**1.07** (1.02 – 1.11)
Vitamin C	1.06 (0.94 – 1.20)
Vitamin E	**1.04** (1.01 – 1.07)
Selenium	0.91 (0.76 – 1.09)

- Current evidence does not support the use of antioxidant supplements in the general population.
- Evidence on vitamin C and selenium not conclusive.

Calcium supplements & cardiovascular disease

- Increased risk of heart attack
- Must be taken daily
  - expensive, low compliance



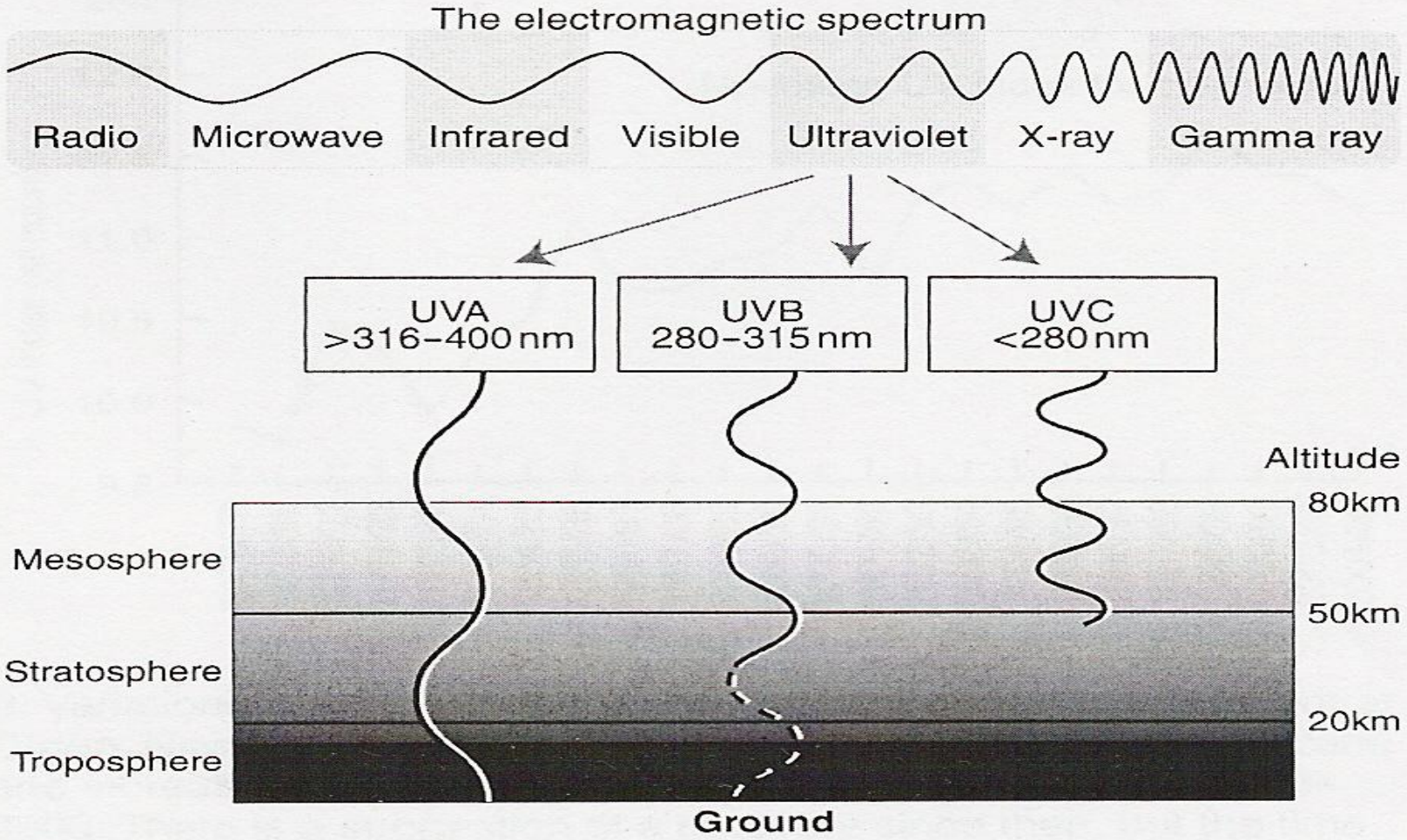
Bolland MJ, et al,
BMJ 2010;341:c3691

Vitamin D supplementation

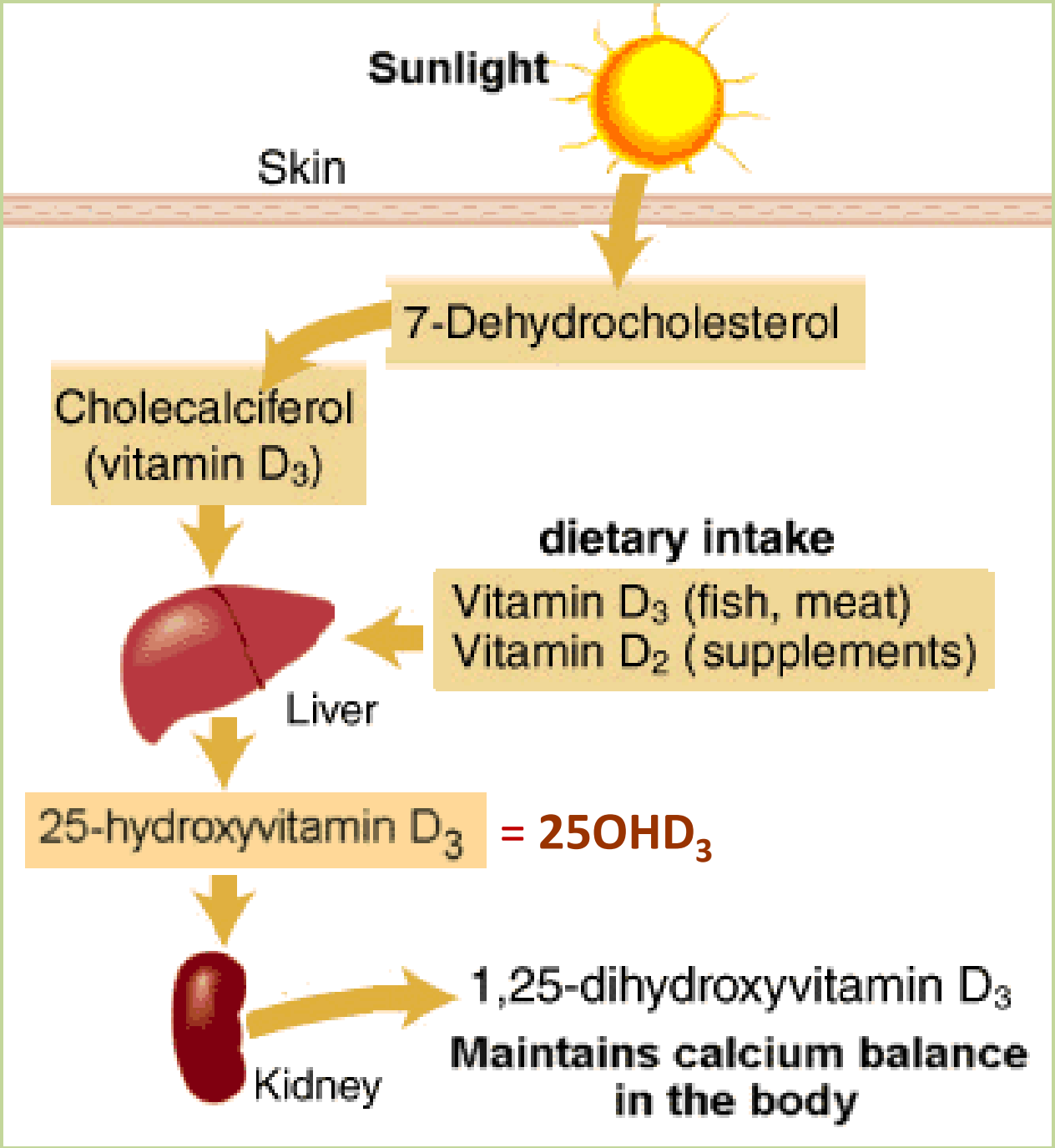
Is it:

- Safe?
- Effective?
- Sustainable?

2: The electromagnetic spectrum and penetration of ultraviolet radiation through the Earth's atmosphere*

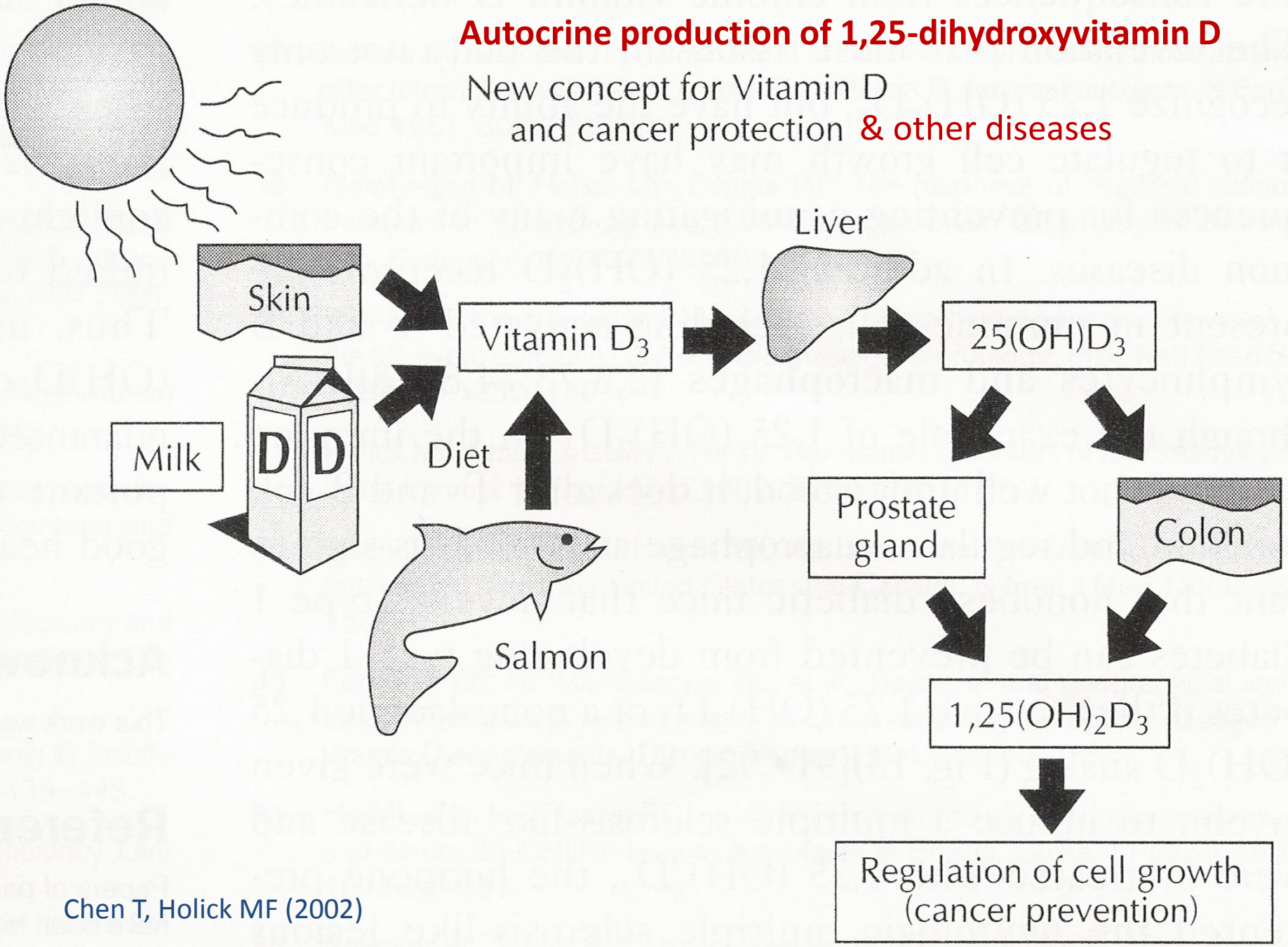


*Adapted from Office of Public Outreach, Space Telescope Science Institute. Amazing space. Available at: <http://amazing-space.stsci.edu/light/ems-frames.html>.


Sunlight
Skin
7-Dehydrocholesterol
Cholecalciferol
(vitamin D_3)
dietary intake
Vitamin D_3 (fish, meat)
Vitamin D_2 (supplements)
Liver
25-hydroxyvitamin D_3
= 25OHD$_3$
1,25-dihydroxyvitamin D_3
Maintains calcium balance
in the body
Kidney

Autocrine production of 1,25-dihydroxyvitamin D

New concept for Vitamin D
and cancer protection & other diseases



Chen T, Holick MF (2002)

Tissues with the vitamin D receptor

Norman & Bouillon, *Experimental Biology & Medicine* 2010

- Adipose
- Adrenal
- Bone, osteoblasts
- Brain, general
- Brain, amygdala
- Brain, hypothalamus
- Brain, glial cells
- Breast
- Cartilage
- Colon
- Eggshell gland
- Epididymus, seminiferous tubules
- Gills (fish)
- Hair follicle
- Intestine
- Kidney
- Liver
- Lung
- Lymphocytes (B&T)
- Muscle, cardiac
- Muscle, embryonic
- Muscle, smooth
- Ovary
- Pancreas b-cell
- Parathyroid
- Parotid
- Pituitary
- Placenta
- Prostate
- Retina
- Skin
- Sperm
- Stomach
- Testis
- Thymus
- Thyroid
- Tonsils, dendritic cells
- Uterus
- Yolk sac (bird)

25(OH)D levels in Australians

AusDiab Study

- Population sample of people ≥ 25 years in 1999-2000
- Mean 25(OH)D = 65 nmol/L in people without diabetes

Gagnon C, et al, *Diabetes Care* 2011

Population surveys

≤ 50 nmol/L in winter/spring:

- Sth-east Qld 40.5%
- Geelong 37.4%
- Tasmania 67.3%

Van der Mei I, et al, *Environ Health Perspec*t 2007; 115: 1132

Vitamin D & cancer

colorectal
prostate
breast

IARC report: meta-analysis of nested case control studies - baseline 25OHD & colorectal cancer risk

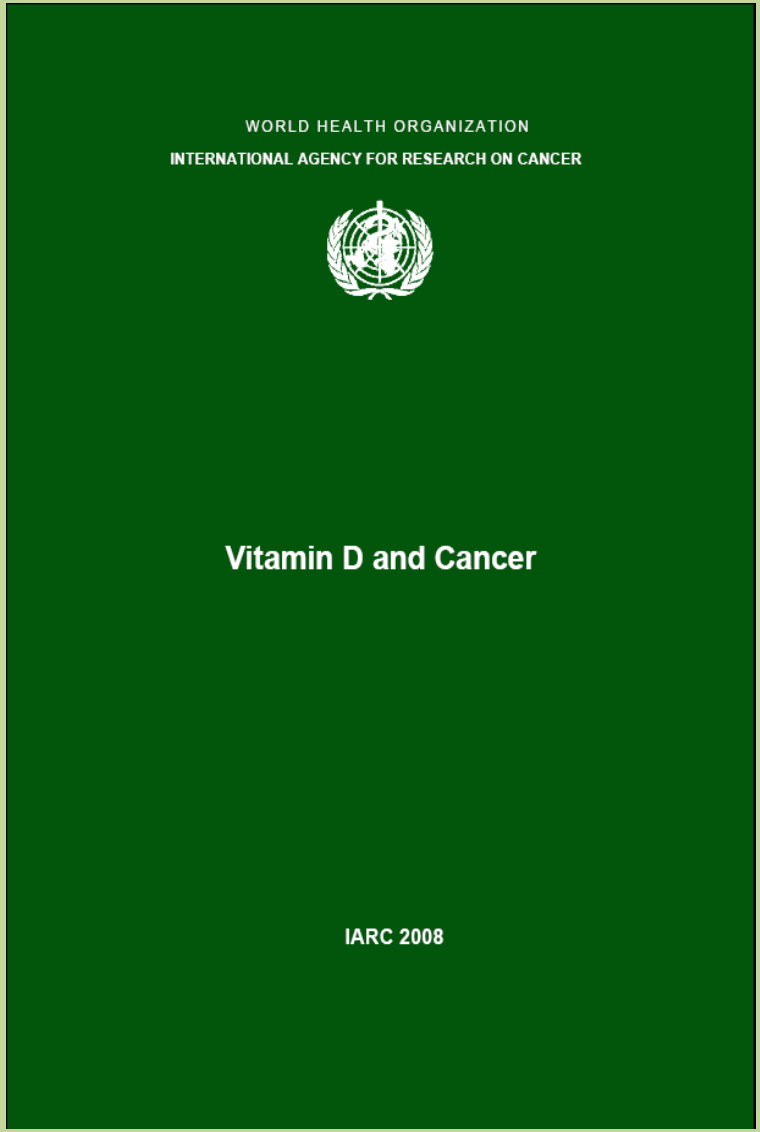
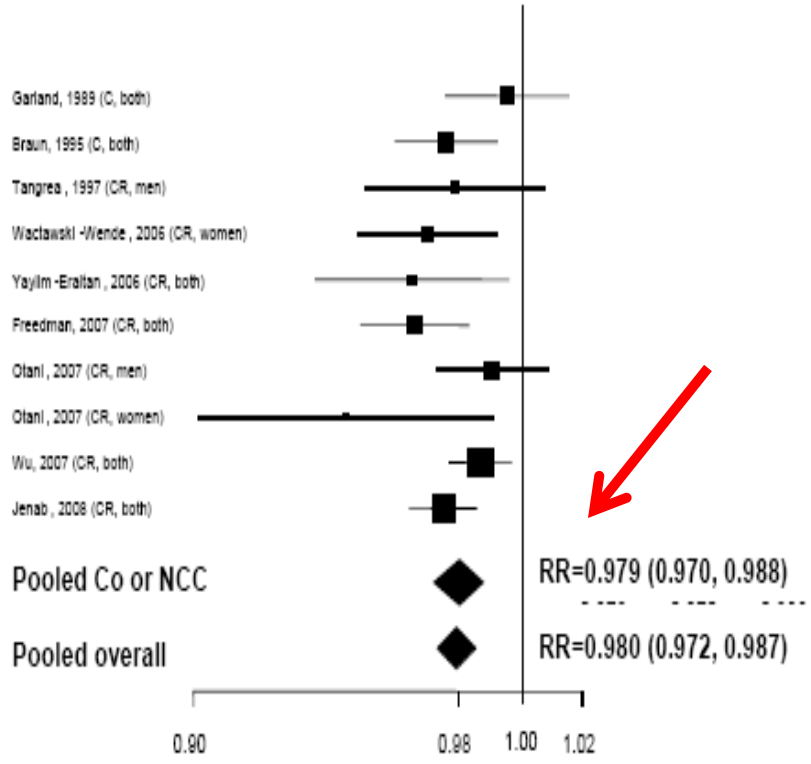


Figure 13.2 - Dose-response relative risks for colorectal cancer due to an increase of 1 unit of ng/mL serum level of 25-hydroxyvitamin D. Aggregated estimates. The relative risk "pooled Co or NCC" is calculated after exclusion of case-control studies (C is colon, R is rectum, Co is cohort studies, NCC is nested case-control studies)



Possible reduction in colon cancer risk for various increases in serum 25-hydroxyvitamin D

– from IARC meta-analysis (Fig 13.2)

Increase in 25(OH)D			Relative risk	Reduction in risk
(nmol/L)	For example:	ng/mL		
2.5	from 25 to 27.5 nmol/L	1	0.98	2%
25	from 25 to 50 nmol/L	10	$0.98^{10} = 0.82$	18%
50	from 25 to 75 nmol/L	20	$0.98^{20} = 0.67$	33%
75	from 25 to 100 nmol/L	30	$0.98^{30} = 0.55$	45%

IARC report conclusion on vitamin D & **colon** cancer

"The results show evidence for an increased risk of colorectal cancer and colorectal adenoma with low serum 25-hydroxyvitamin D levels." (page 2)

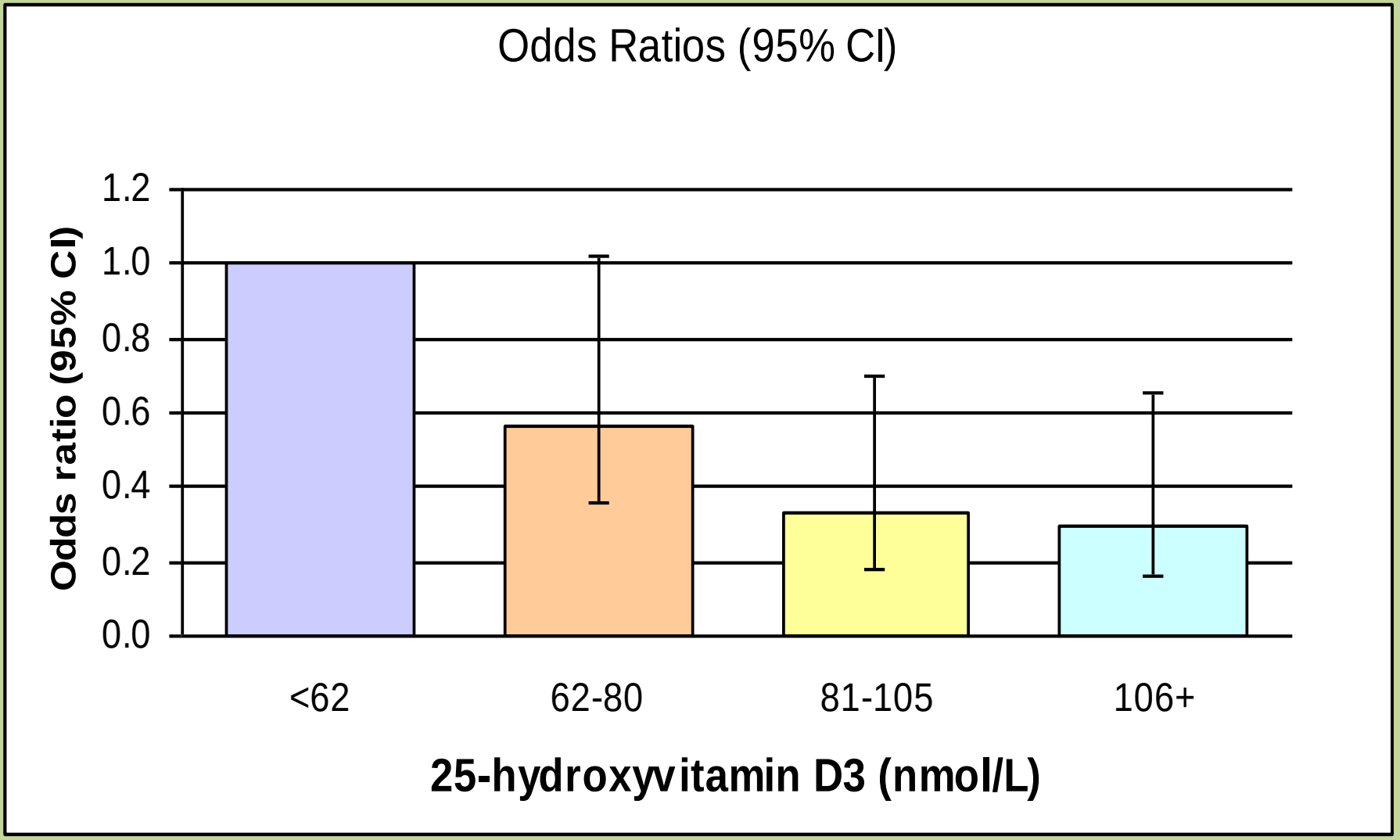
"There is however only **limited evidence** of a **causal link** due to confounding by other dietary or lifestyle factors." (page 305)

Vitamin D & cardiovascular disease

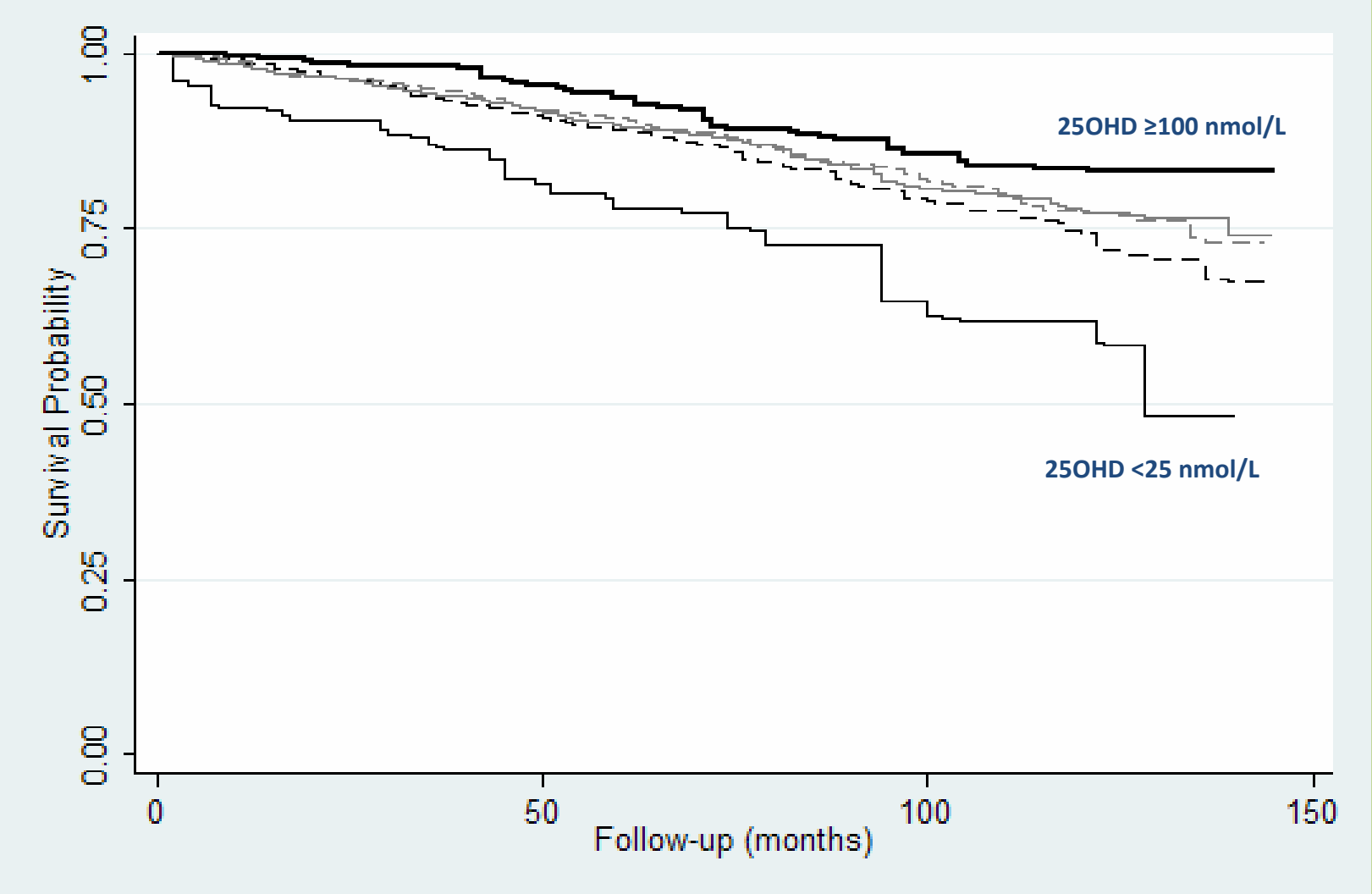
Observational studies of vitamin D & CV disease

Plasma 25-hydroxyvitamin D_3 & myocardial infarction risk

Auckland Heart Study (Scragg, *Int J Epidemiol* 1990; 19: 559)



Survival from CV disease in follow-up of NHANES III cohort ≥ 65 years – Ginde AA, et al, *J Am Geriatr Soc* 2009; 57: 1595 2009



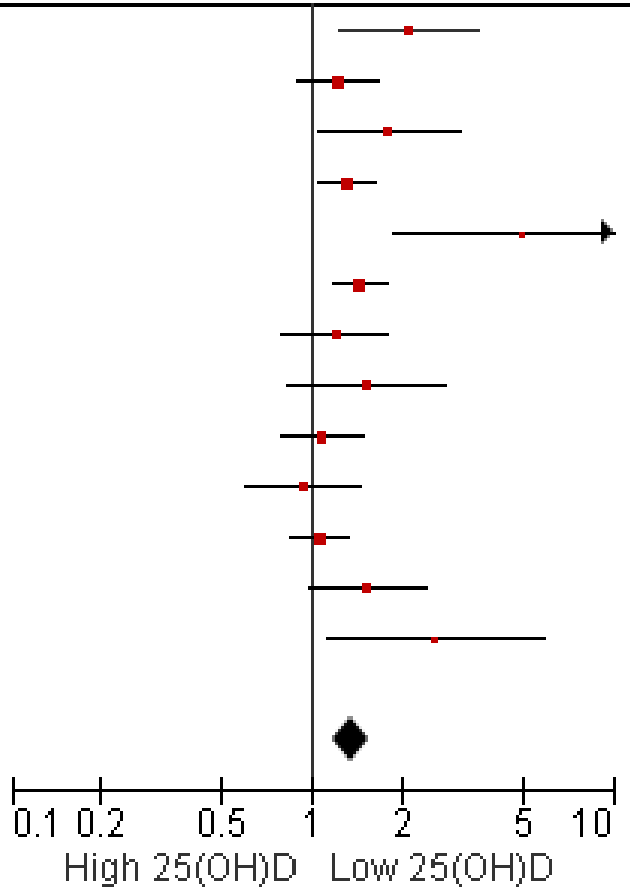
Forest plot of RR from **cohort studies** of **CV disease**:

lowest 25(OH)D category v. highest (reference) : >4000 CV events

Study or Subgroup	Weight	Risk Ratio IV, Random, 95% CI
Giovannucci 2008	5.4%	2.09 [1.24, 3.54]
Melamed 2008	10.2%	1.22 [0.90, 1.65]
Wang 2008	5.2%	1.80 [1.05, 3.08]
Kilkkinen 2009	12.9%	1.32 [1.05, 1.64]
Pilz 2009	1.9%	5.02 [1.88, 13.42]
Anderson 2010	13.5%	1.45 [1.18, 1.78]
Bolland 2010	7.5%	1.20 [0.80, 1.80]
Cawthon 2010	4.3%	1.52 [0.83, 2.80]
Hutchinson 2010 nonsmoker	9.9%	1.08 [0.79, 1.48]
Hutchinson 2010 smoker	7.0%	0.93 [0.61, 1.44]
Jassal 2010	13.0%	1.07 [0.86, 1.33]
Michaelsson 2010	6.5%	1.53 [0.97, 2.41]
Semba 2010	2.6%	2.57 [1.12, 5.91]
Total (95% CI)	**100.0%**	**1.35 [1.17, 1.56]**

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 23.17$, df = 12 (P = 0.03); $I^2 = 48\%$

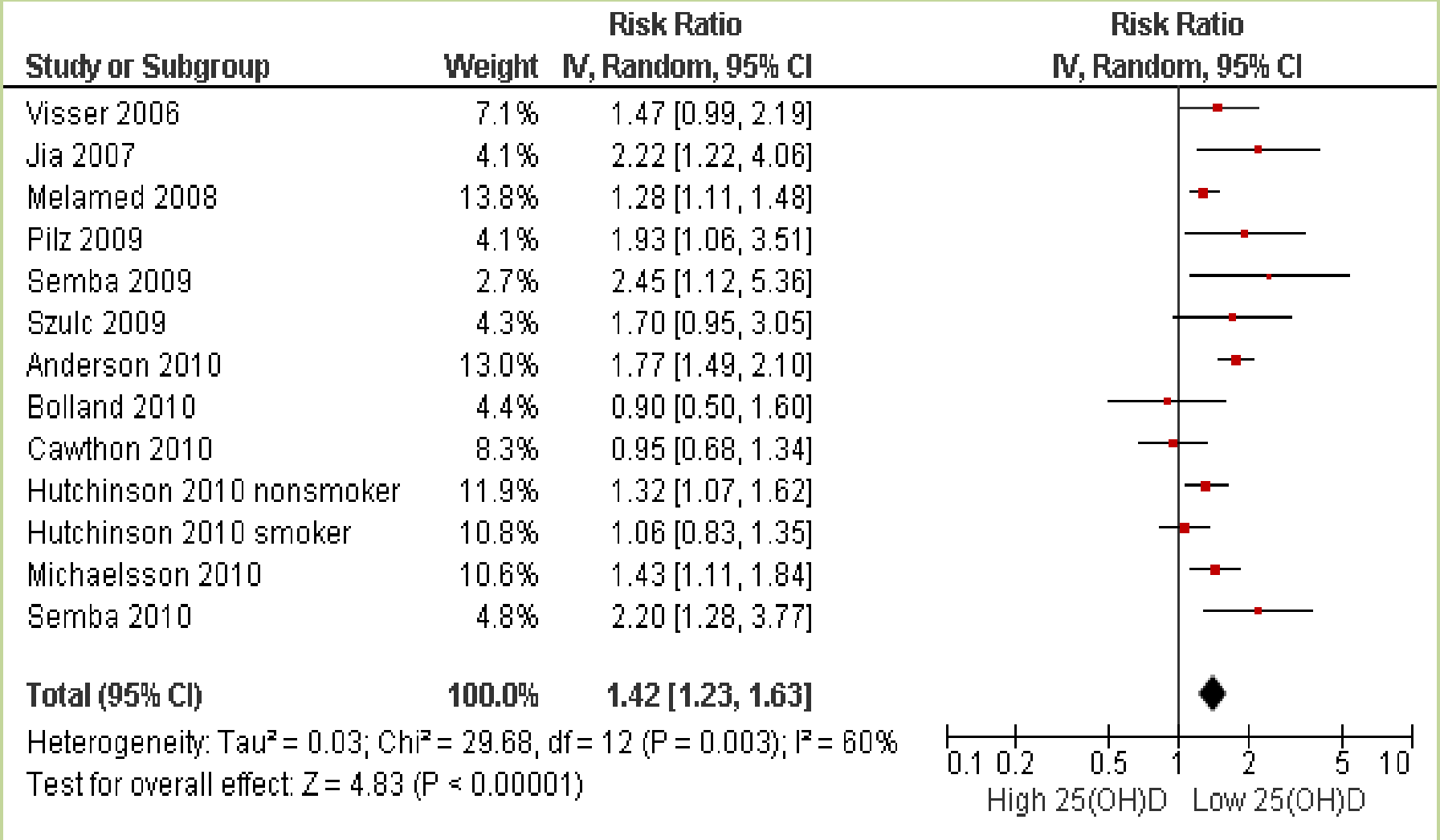
Test for overall effect: Z = 4.11 (P < 0.0001)



Scragg, *Public Health Nutrition* 2011; 14: 1515

Forest plot of RR from **cohort studies** of **all-cause mortality**:

lowest 25(OH)D category v. highest (reference) : >6,500 deaths



Scragg, *Public Health Nutrition* 2011; 14: 1515

RCTs of
Vitamin D supplementation &

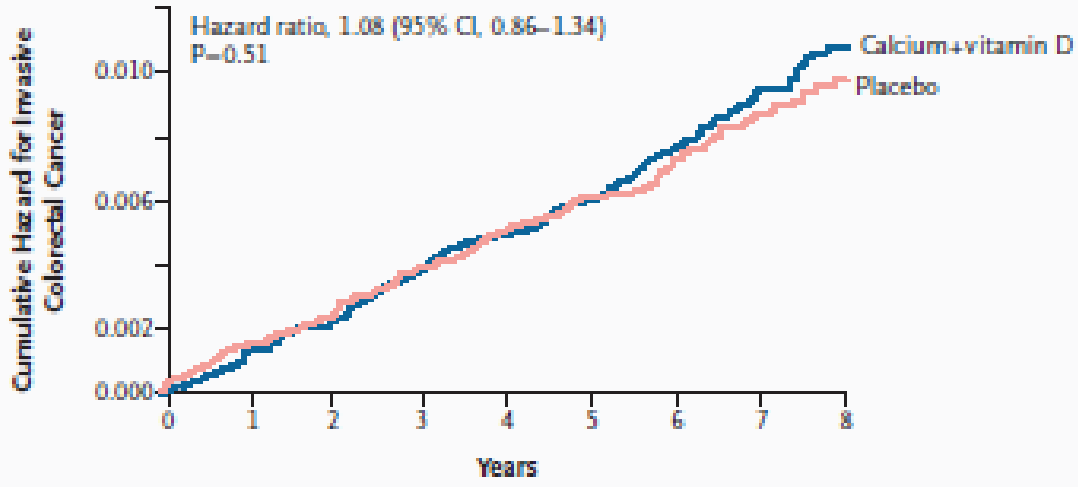
colorectal cancer

cardiovascular disease

Women's Health Initiative RCT

- Enrolled 36,282 women aged 50-79 years
- Treatment (each day):
  - vitamin D 400 IU & calcium 1000 mg (or placebo)
- Followed for an average of 7 yrs

Women's Health Initiative: **no effect** of **Vitamin D** (400 IU/day) & Calcium (1 gm/day) on **colorectal cancer** – Wactawski-Wende, N Engl J Med 2006;354:684



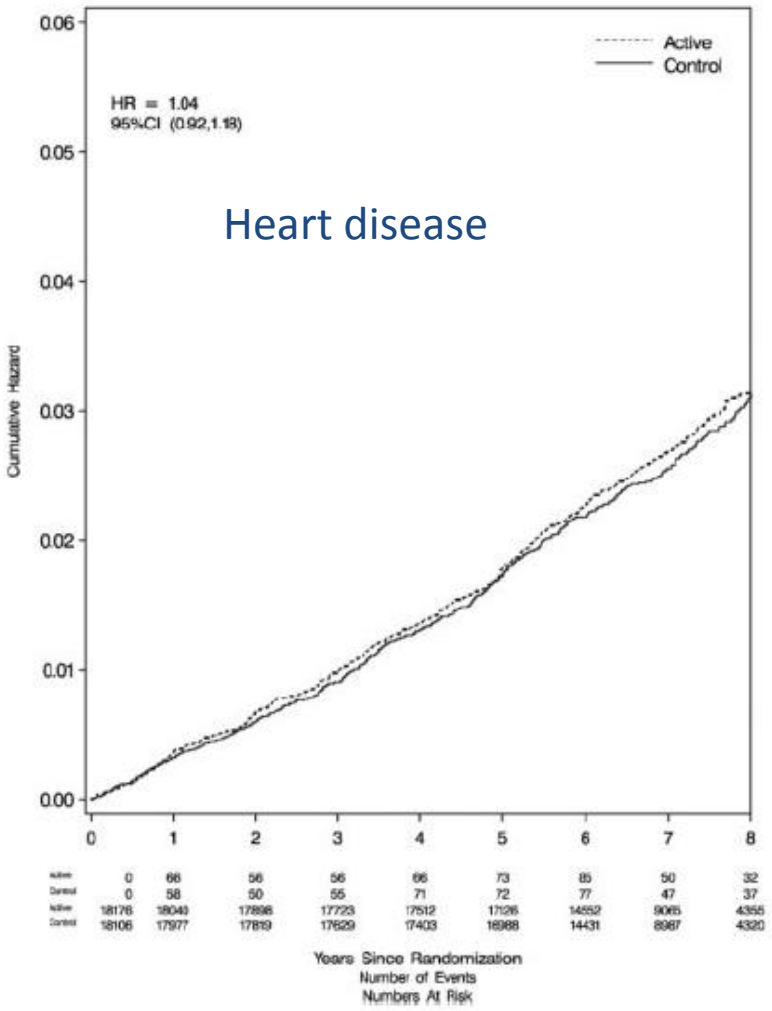
Calcium+vitamin D									
No. of events	0	23	17	28	20	19	27	23	9
No. at risk	18,176	18,048	17,936	17,780	17,605	17,248	14,680	9138	4403
Placebo									
No. of events	0	27	16	27	20	18	20	17	7
No. at risk	18,106	17,967	17,832	17,663	17,471	17,093	14,530	9041	4351

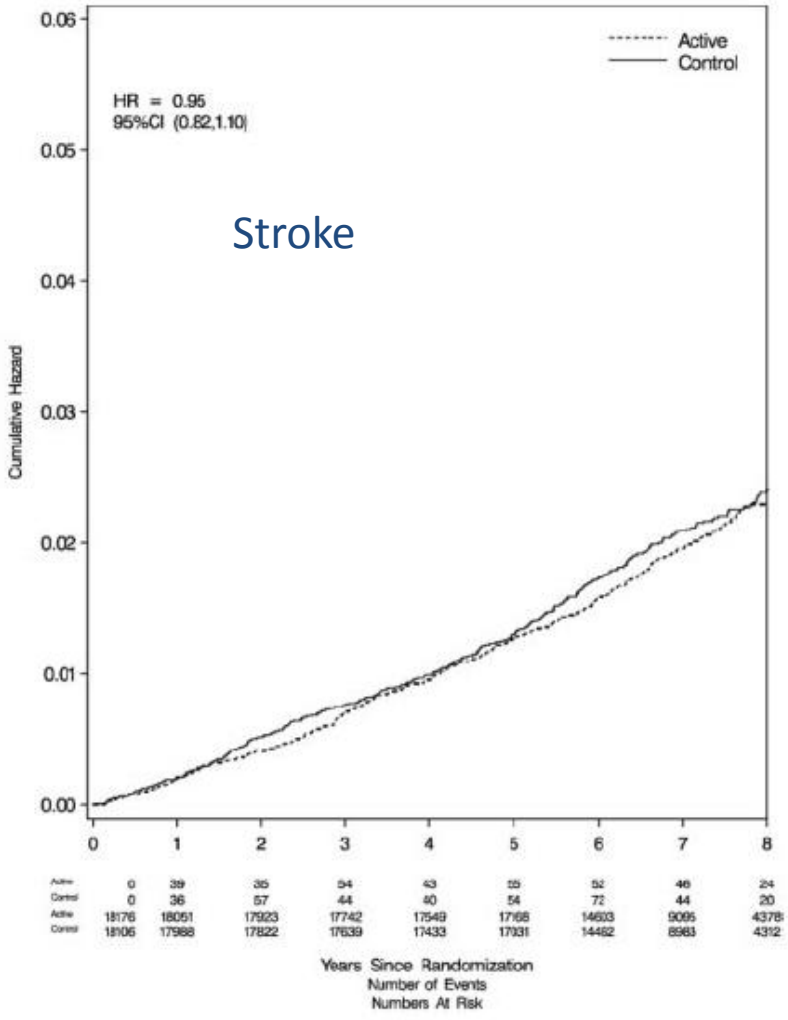
Figure 3. **Kaplan–Meier Estimates of the Cumulative Hazard for Invasive Colorectal Cancer with Supplemental Calcium plus Vitamin D, as Compared with Placebo.**

CI denotes confidence interval. Two events in each group that occurred after year 8 are not shown.

Women's Health Initiative: **no effect** of **Vitamin D** (400 IU/day) & Calcium (1 gm/day) on **CV disease**

– Hsia, Circulation 2007; 115: 846





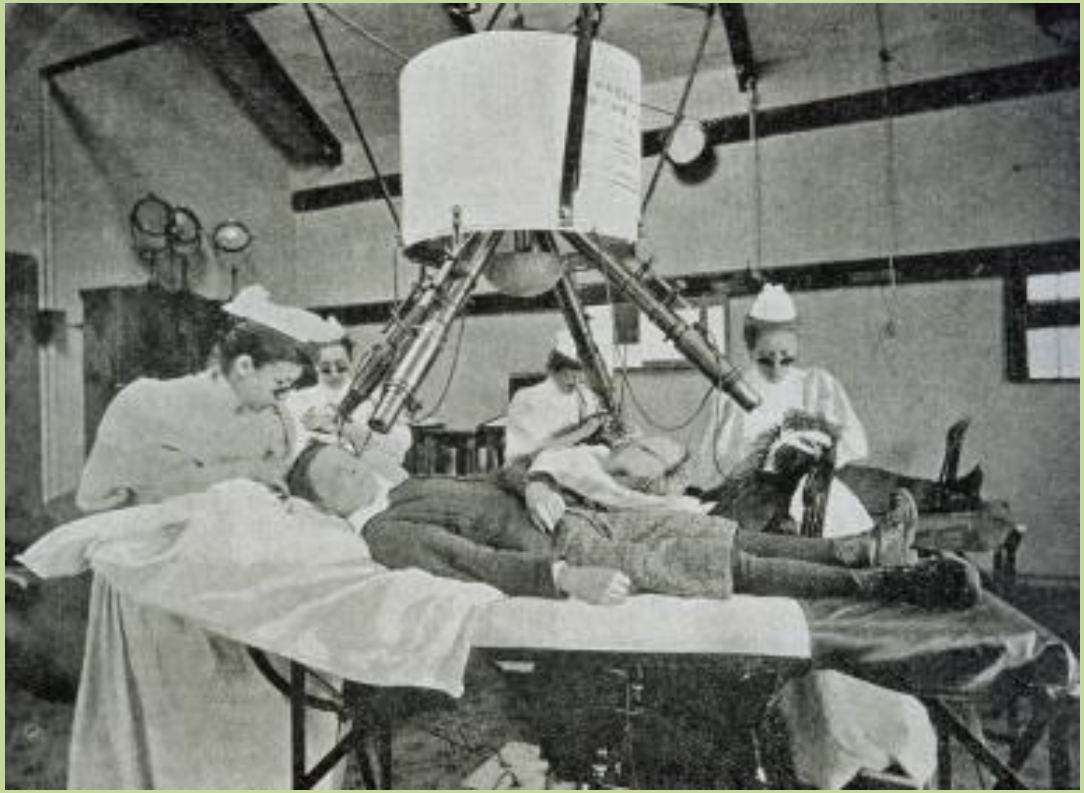
Limitations **of WHI RCT of vitamin D & calcium**

- ***Low dose*** of vitamin D (400 IU/day):
  - Increase serum 25OHD levels by only 7 nmol/L.
- ***Low compliance***:
  - 70% of participants taking supplements 50% or more of the time ≈ 35% or more of the target dose, or about 140 IU/day.
- ***Contamination*** of the control group since many were taking vitamin D supplements on entry and continued to take them throughout the study.

Vitamin D & infection

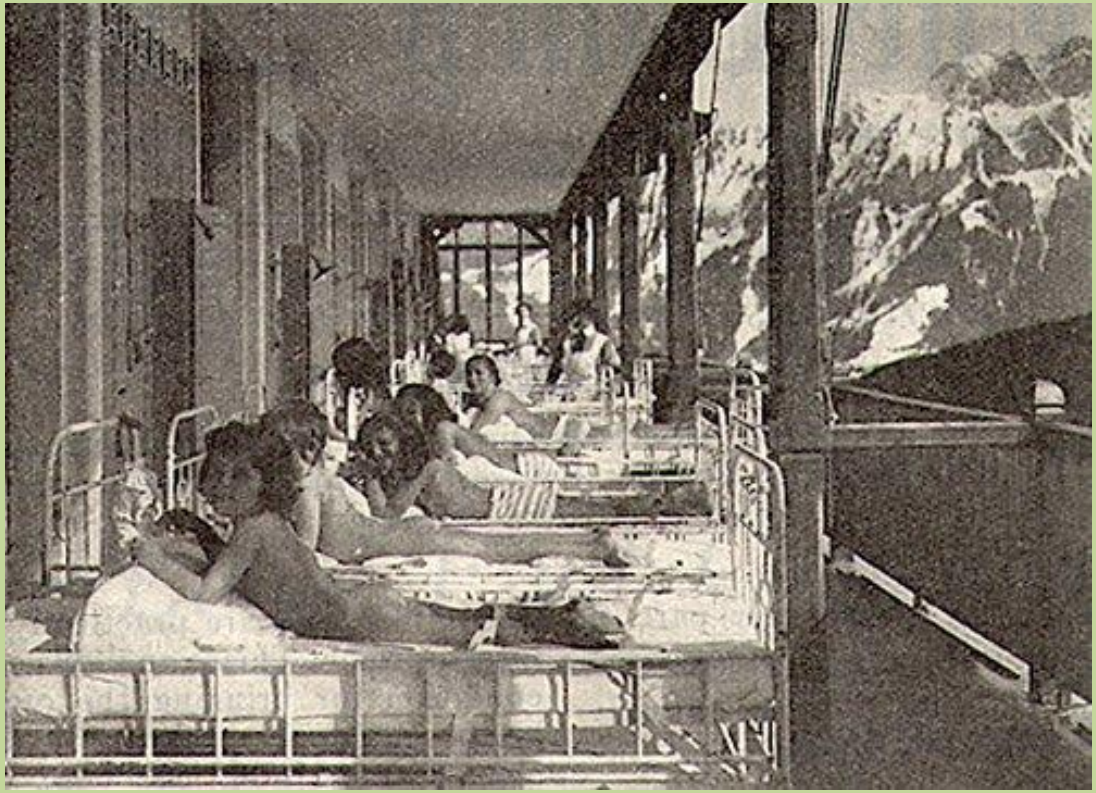
Niels Finsen – 1903 Nobel Prize for Medicine

Finsen lamp – therapy for lupus vulgaris (TB of the skin)



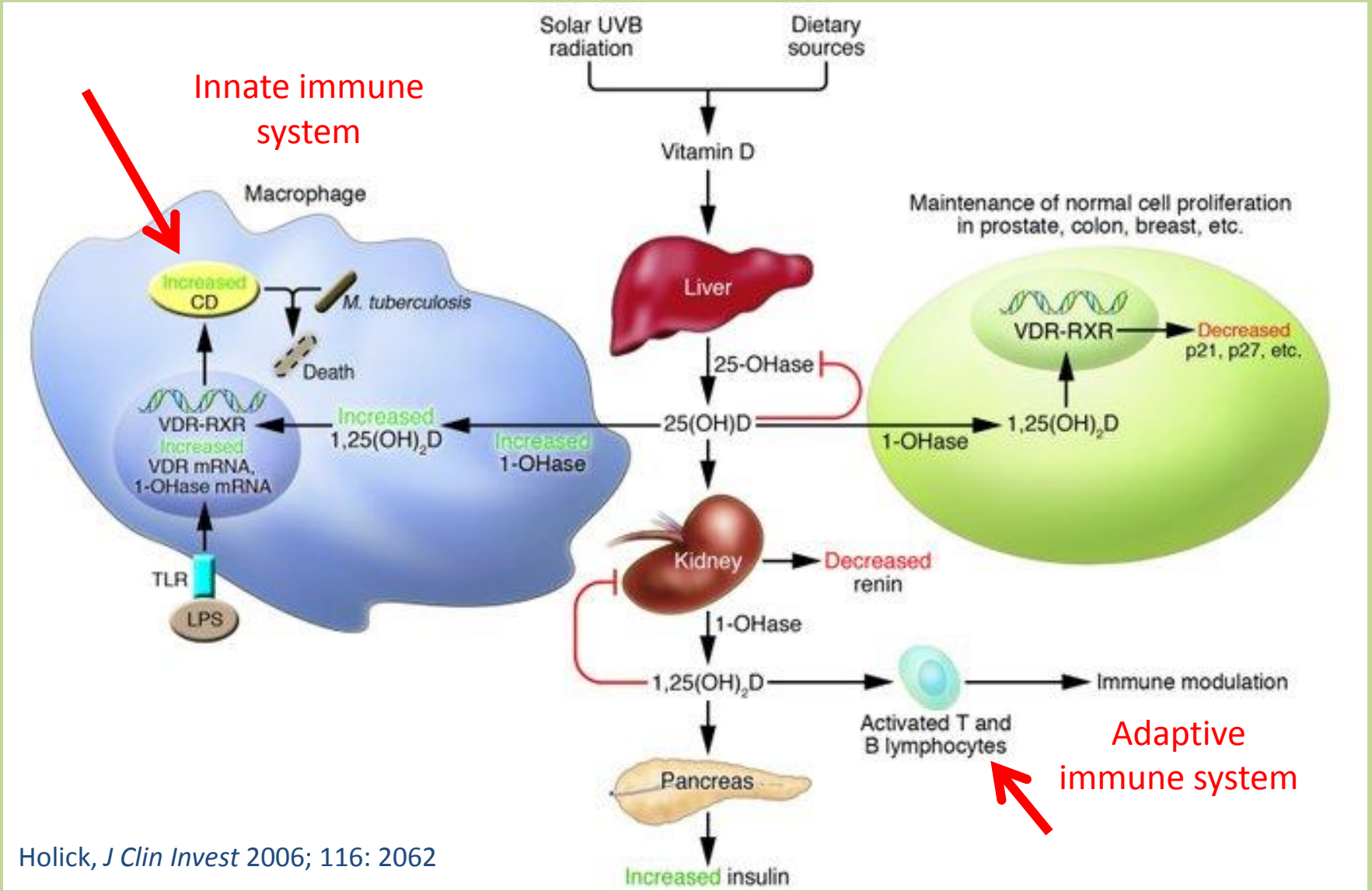
TB Sanataria

www.lung.ca/tb/tbhistory/sanatoriums/type.html



Vitamin D & **cathelicidin** (antimicrobial peptide)

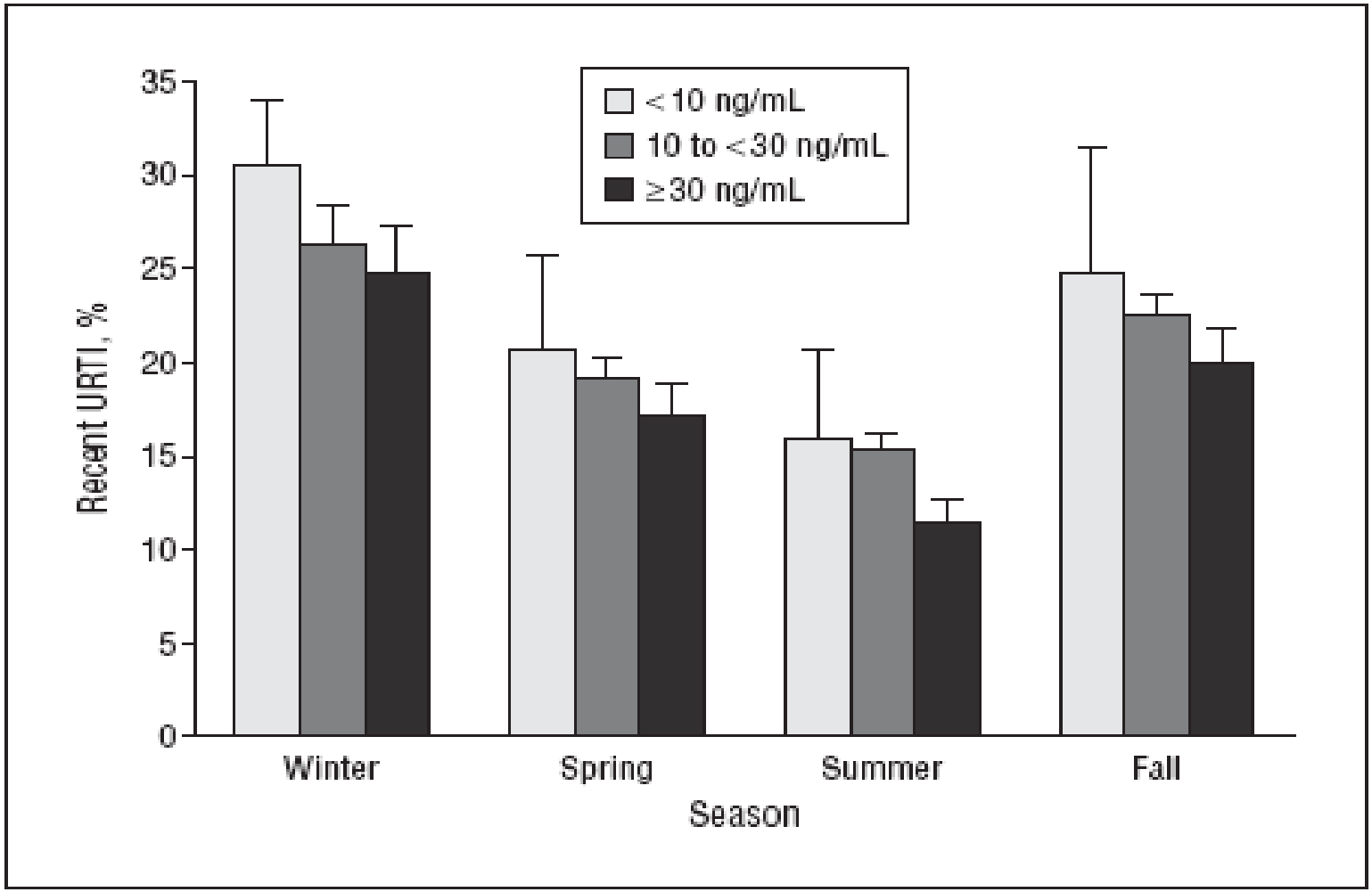
Liu, P.T. et al. *Science* 2006, 311, 1770



Holick, *J Clin Invest* 2006; 116: 2062

Prevalence of **upper respiratory tract infection** in the last few days, by season & 25OHD level: NHANES III

(Ginde, *Arch Intern Med* 2009; 169: 384)



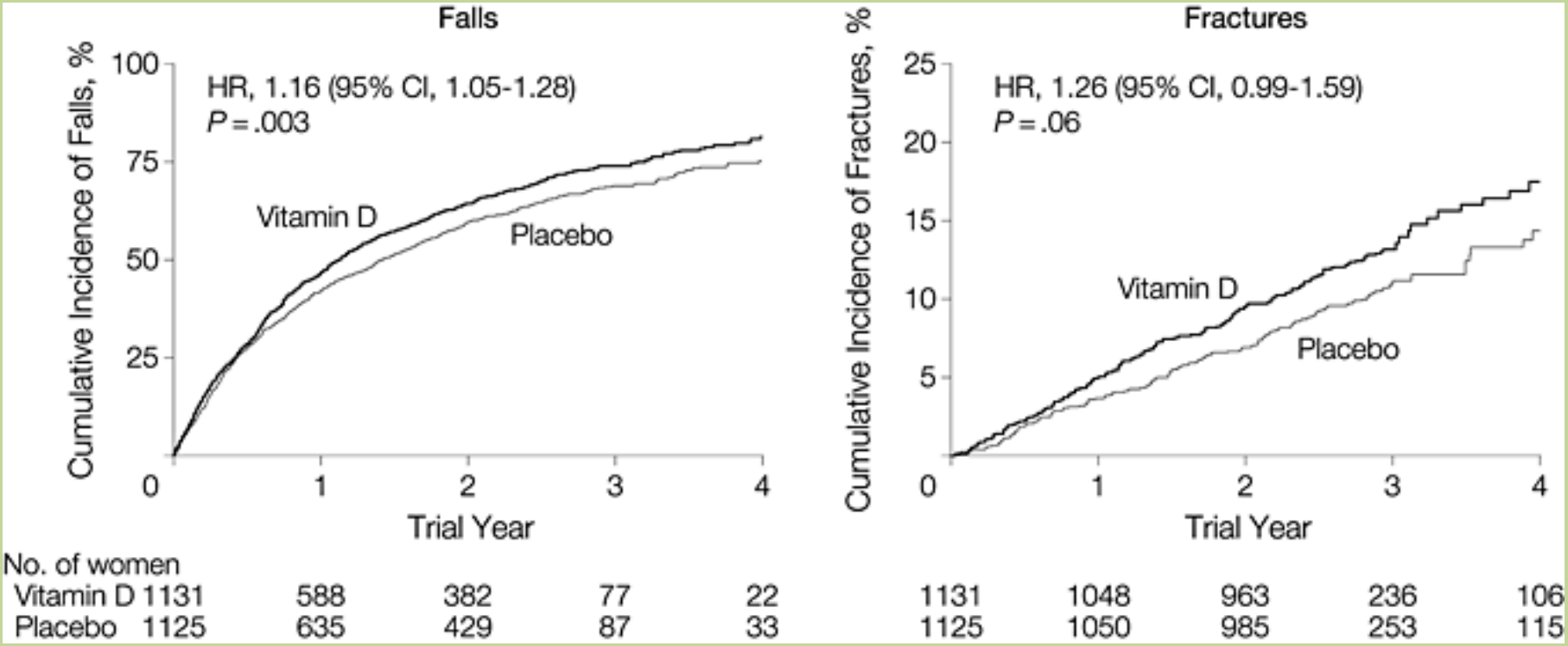
Summary of Previous Slides

Observational studies indicate that low vitamin D is a risk factor for:

- colorectal cancer
- cardiovascular disease
- infectious disease

RCTs needed to determine if vitamin D is beneficial & safe

Annual vitamin D dose of 500,000 IU



Sanders KM, et al, *JAMA* 2010;303:1815

Currently funded vitamin D RCTs

	ViDA (NZ)*	VITAL (USA)
Sample size	5,100	20,000
Vitamin D dose	100,000 IU per month	2000 IU per day
Co-intervention	None	omega-3 fatty acids 1 gram of per day
Primary aim	Cardiovascular disease	Colorectal cancer
Secondary aims (main)	Respiratory disease Fractures	All-cause mortality CV disease
Follow-up period	4 years	5 years
Results due	2015	2017

* ViDA = Vitamin D Assessment Study

Is Vitamin D a sustainable nutrient?

YES: cheap public health strategies are available to increase Vitamin D levels

- Sun exposure
- Dietary sources (lanolin from sheep wool)
  - Fortification of food
  - Supplements (fat soluble, so can be taken monthly)

However, RCTs are required to show that vitamin D is both safe & beneficial