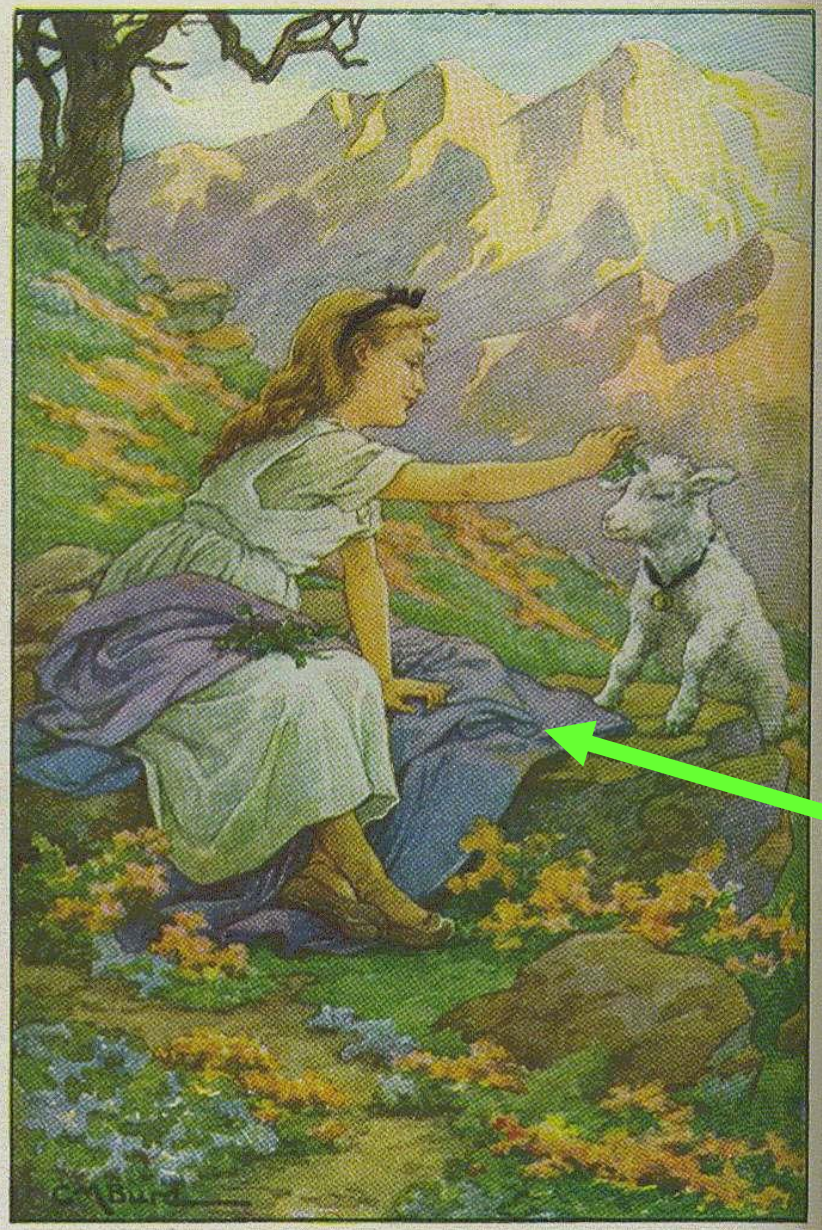
Vitamin D and policy creation.

Reinhold Vieth

Professor, Departments of Nutritional Sciences and Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

November 5/6, 2013



Clara Began to Hold Out the Leaves One by One to Snowflake. (See page 242.)

The Childrens's story
HEIDI

Her friend Clara who lived in the city probably suffered from

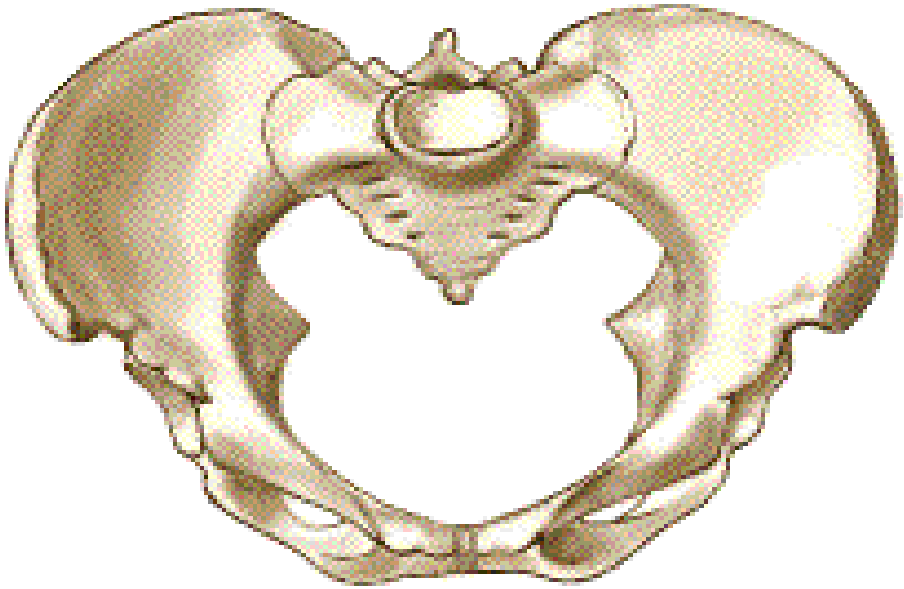
- Rickets (bone)
- Weak muscles
- Infection-prone

Probable serum 25(OH)D < 25 nmol/L

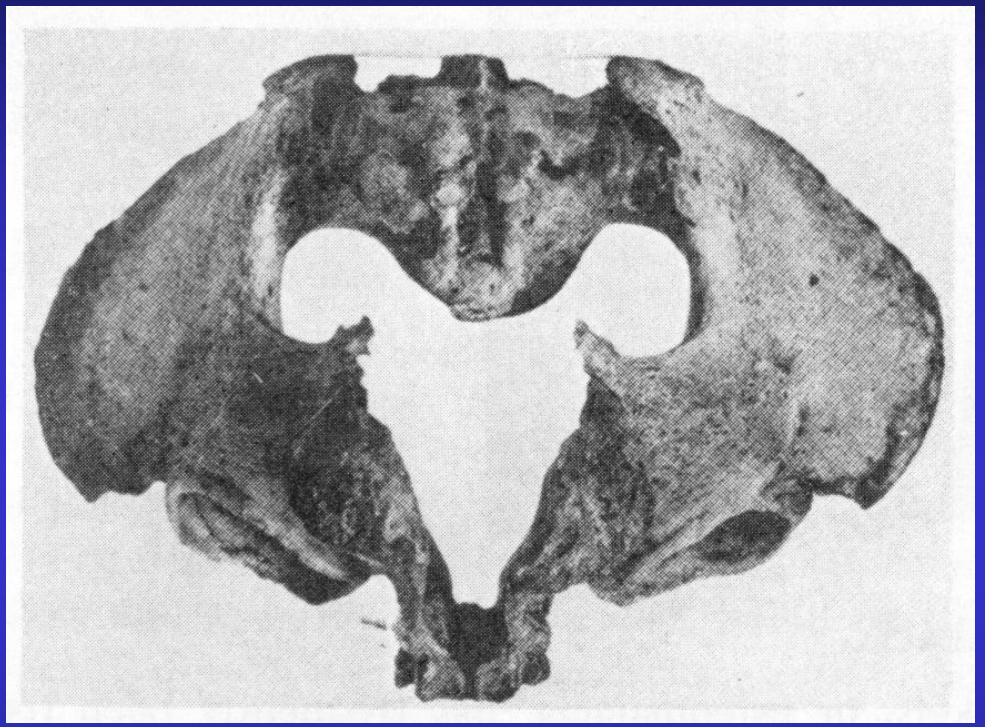
Probable serum 25(OH)D > 75 nmol/L

If shadow TALLER than you are tall, you CANNOT make vitamin D

Childhood lack of vitamin D causes rickets



Normal shape of female pelvis



Contracted pelvis, in a case of osteomalacia (adult rickets). Normal childbirth would be impossible

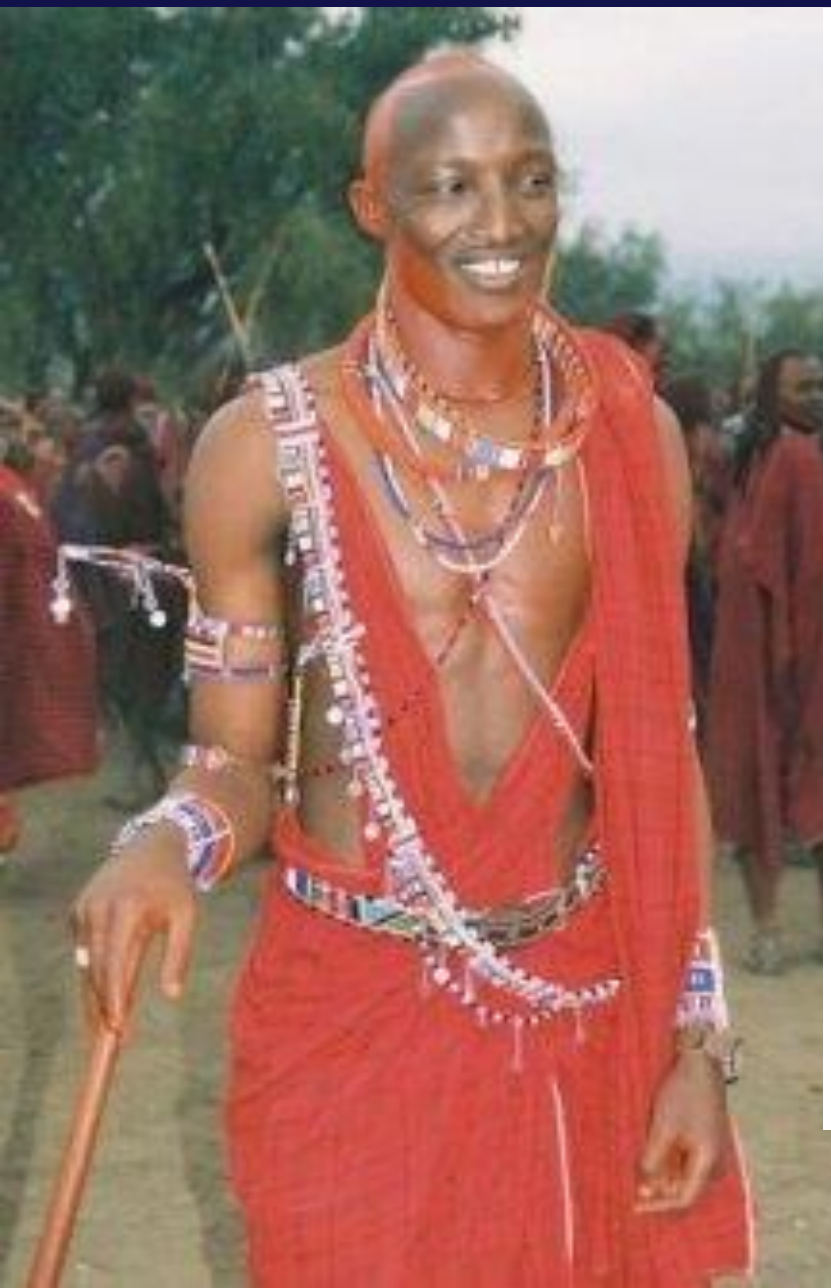
Vieth 2001. Nutritional Aspects of Osteoporosis, Chapter 17, ed P Burckhardt, RP Heaney, B Dawson-Hughes; Academic Press

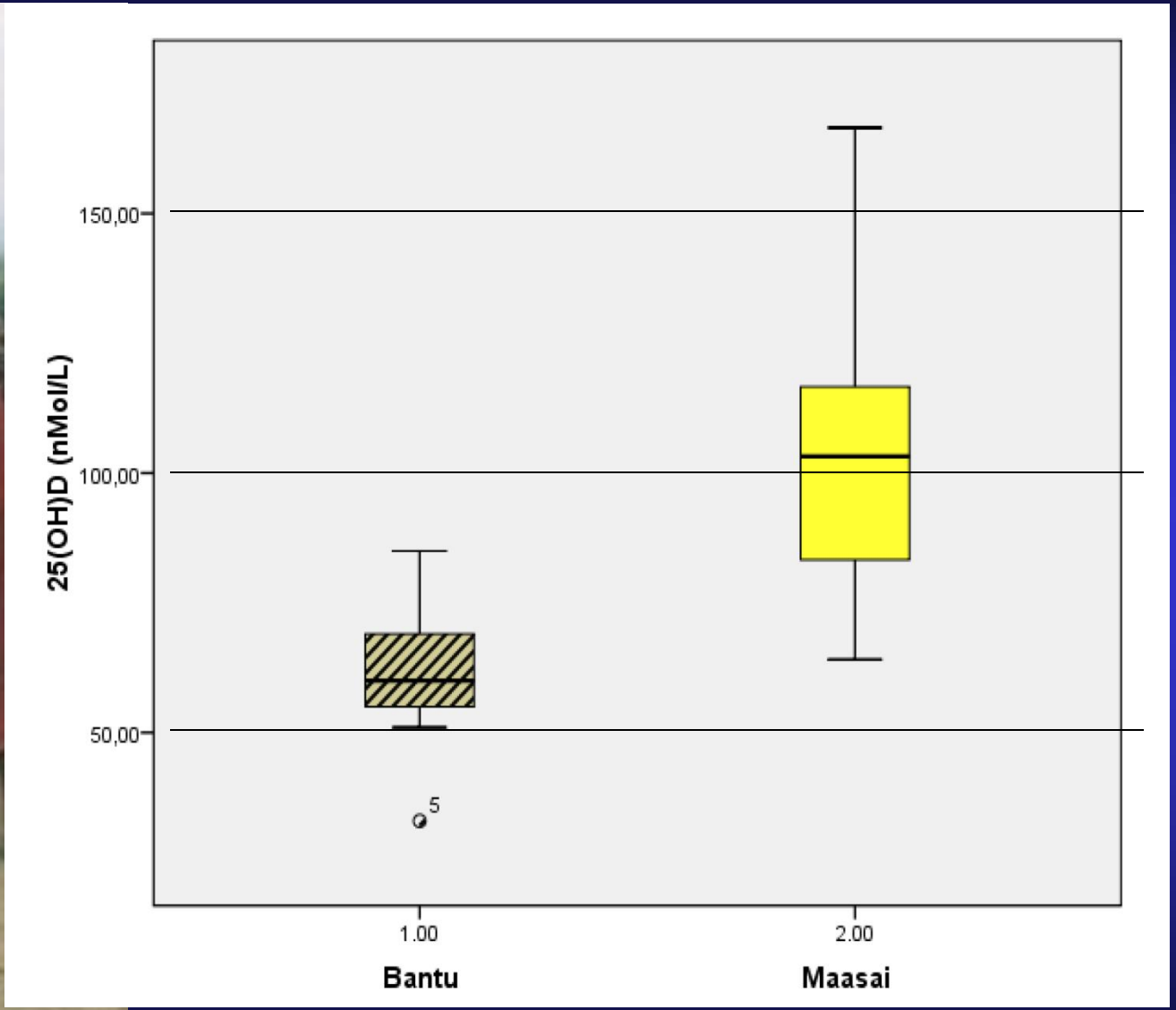
WHAT IS “NORMAL” FOR 25(OH)D ?

World Distribution of Nonhuman Primates

from; Primate Behavior: Field studies of monkeys and apes. I DeVore 1965

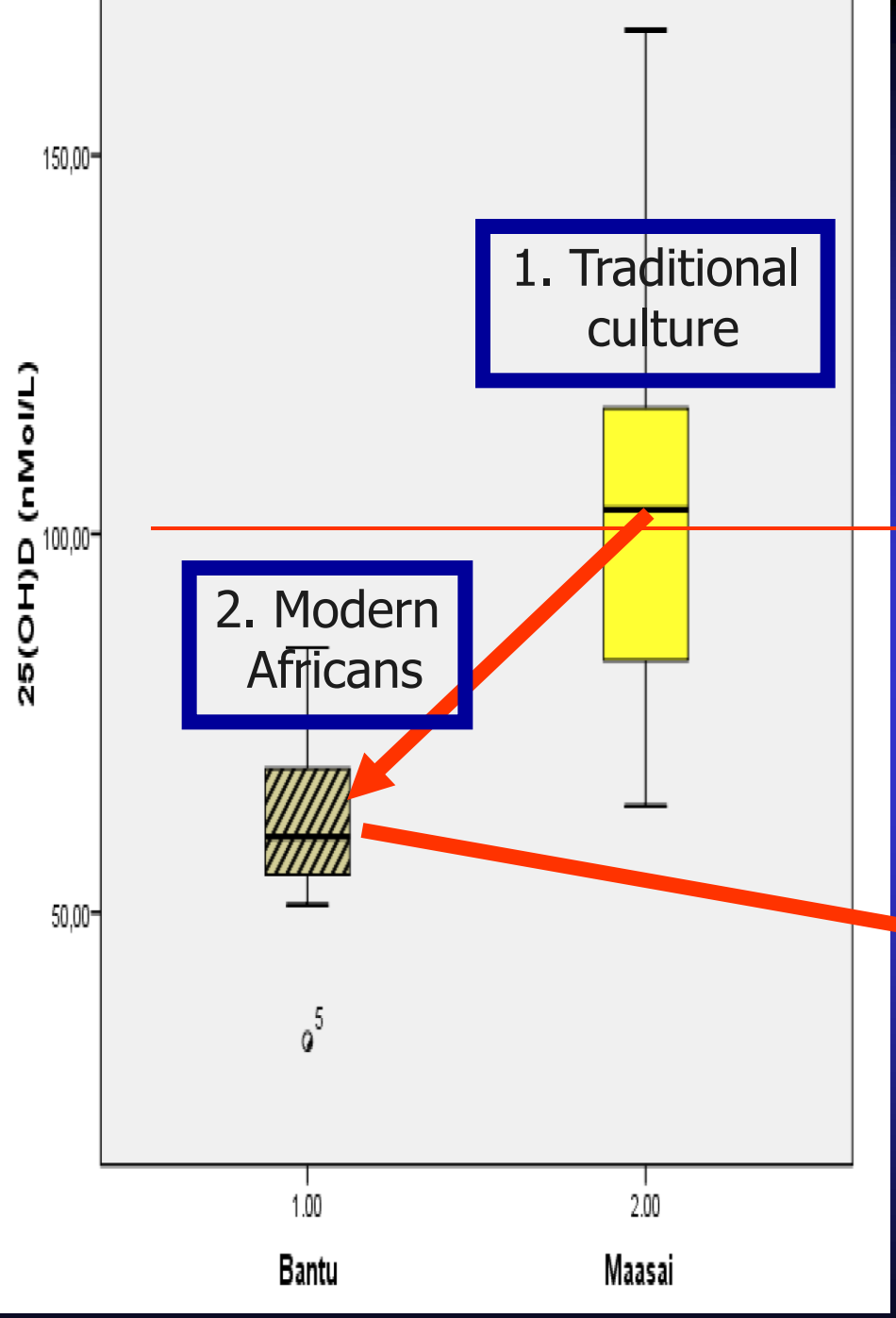
Maasai median 25(OH)D = 104 nmol/L = 41 ng/mL

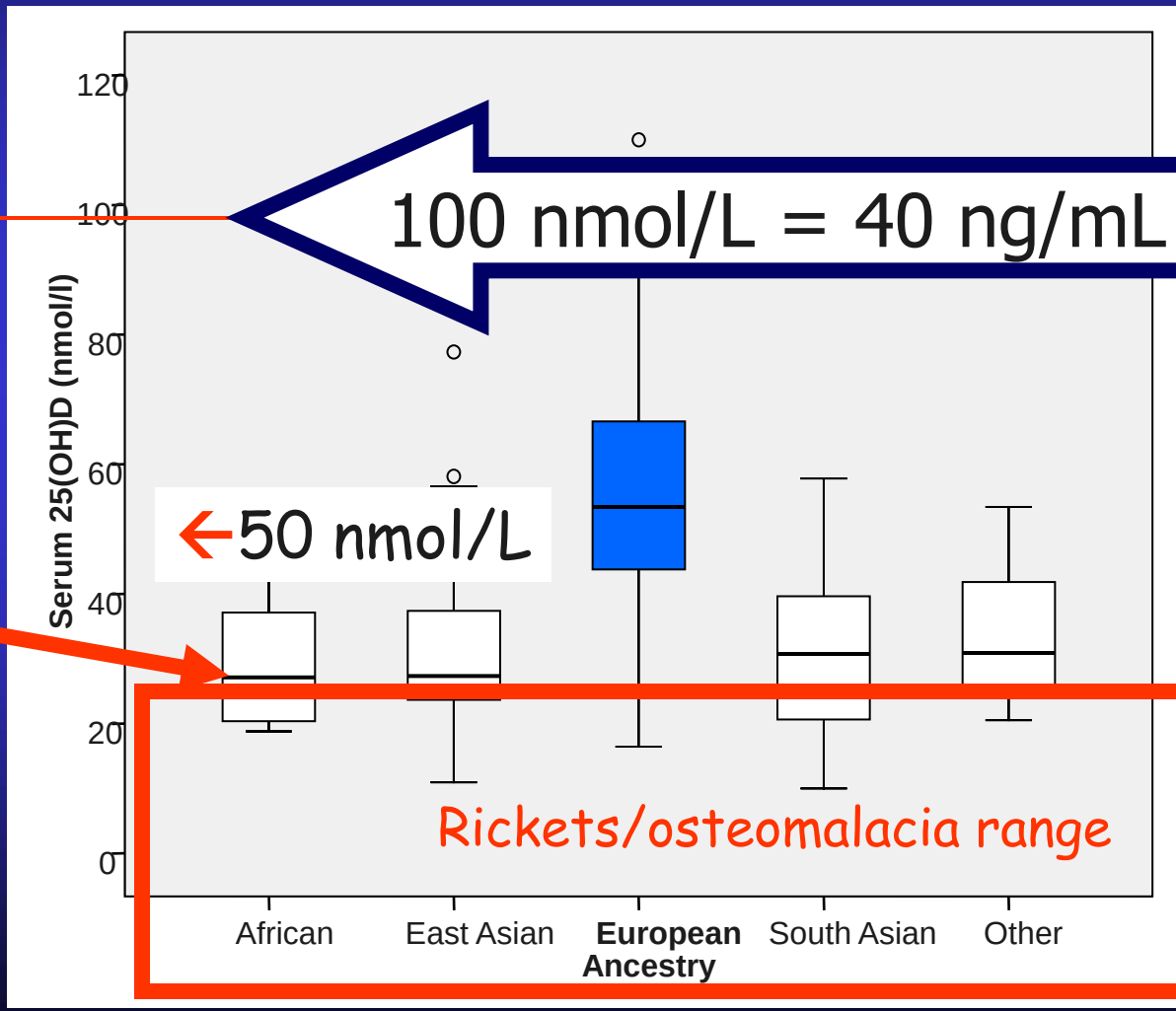




Luxwolda and Muskiet , Brit J Nutrition 2011

Are "Normal" serum 25(OH)D levels healthy?





Gozdzik et al, *BMC Public Health* 2008, **8**:336

To correct the problem of low vitamin D for the general public requires public health policy.

NEW PROBLEM: Policy makers are risk averse. They want certainty.

Standard of care:

1. A diagnostic and treatment **process that a clinician should follow for a certain type of patient…**

"…not necessarily the only standard of care." (New England Journal of Medicine, 2004)

2. In legal terms, the level at which the average, prudent provider in a given community would practice.

how similarly qualified practitioners would have managed the patient's care under the same or similar circumstances.

The medical malpractice **plaintiff must establish the appropriate standard of care and demonstrate that the standard of care has been breached**.

US Website offers 314 policy guidelines that relate to vitamin D

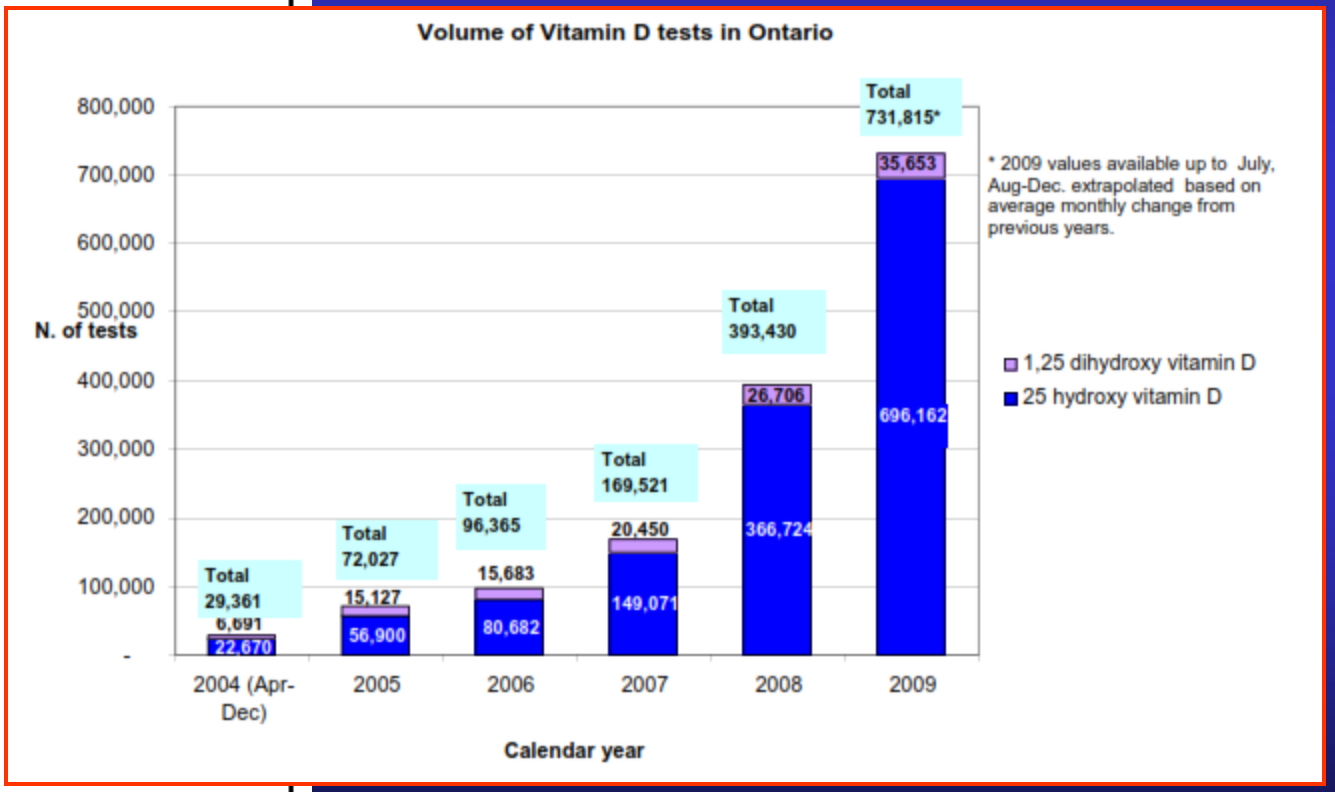
Ontario Health Technology Assessment Series 2010; Vol. 10, No. 2

Clinical Utility of Vitamin D Testing

An Evidence-Based Analysis

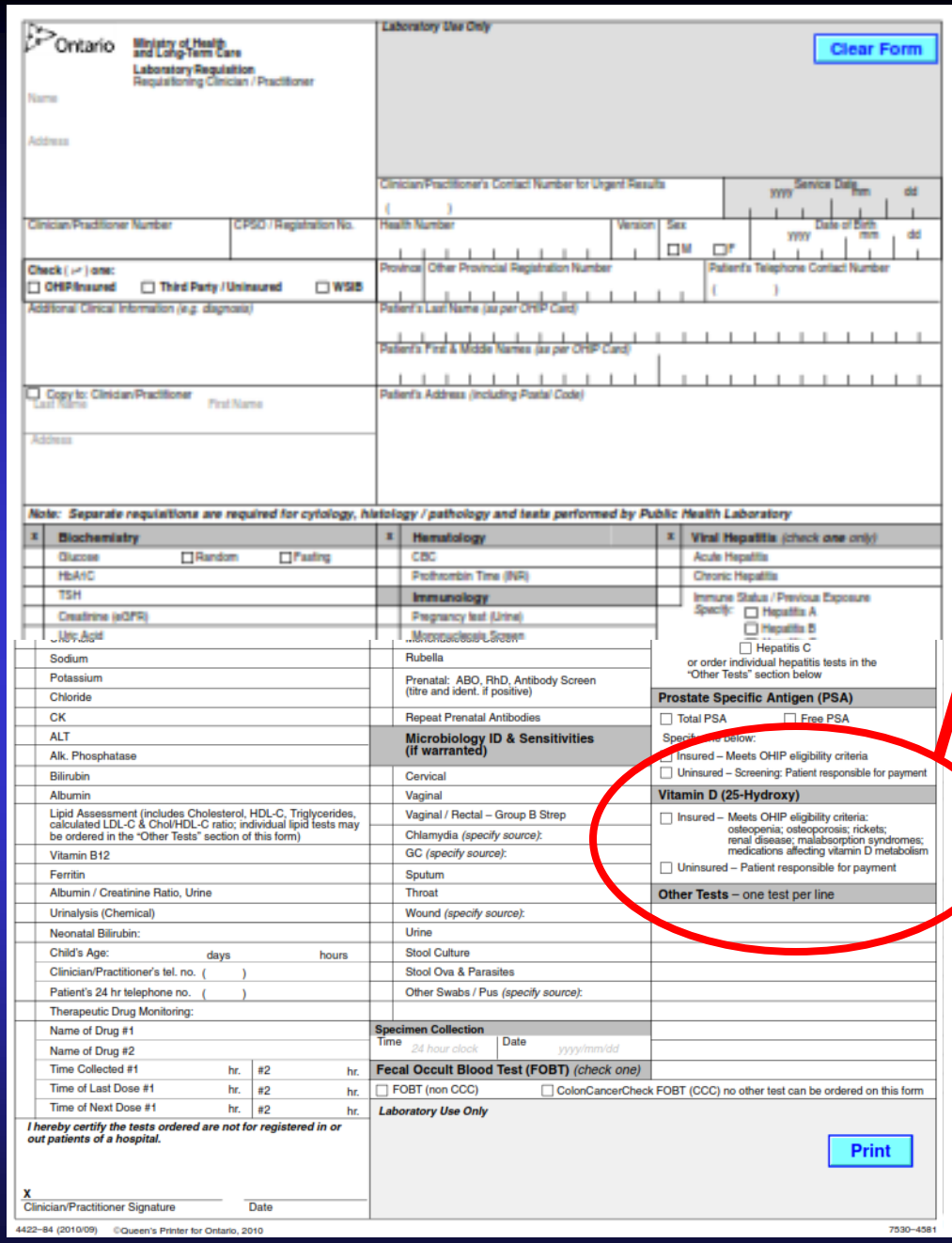
Presented to the Ontario Health Technology Advisory Committee in November 2009

February 2010



Ontario
Medical Advisory Secretariat
Ministry of Health and Long-Term Care

http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series



Ontario — Ministry of Health and Long-Term Care

Laboratory Requisition

Requisitioning Clinician / Practitioner

Name

Address

Laboratory Use Only

Clear Form

Clinician/Practitioner's Contact Number for Urgent Results

Service Date (yyyy mm dd)

Clinician/Practitioner Number | CPSO / Registration No. | Health Number | Version | Sex ☐M ☐F | Date of Birth (yyyy mm dd)

Check (✓) one: ☐ OHIP Insured ☐ Third Party / Uninsured ☐ WSIB

Province | Other Provincial Registration Number | Patient's Telephone Contact Number

Additional Clinical Information (e.g. diagnosis)

Patient's Last Name (as per OHIP Card)

Patient's First & Middle Names (as per OHIP Card)

☐ Copy to: Clinician/Practitioner — Last Name | First Name

Address

Patient's Address (including Postal Code)

Note: Separate requisitions are required for cytology, histology / pathology and tests performed by Public Health Laboratory

x	Biochemistry
	Glucose ☐ Random ☐ Fasting
	HbA1C
	TSH
	Creatinine (eGFR)
	Uric Acid
	Sodium
	Potassium
	Chloride
	CK
	ALT
	Alk. Phosphatase
	Bilirubin
	Albumin
	Lipid Assessment (includes Cholesterol, HDL-C, Triglycerides, calculated LDL-C & Chol/HDL-C ratio; individual lipid tests may be ordered in the "Other Tests" section of this form)
	Vitamin B12
	Ferritin
	Albumin / Creatinine Ratio, Urine
	Urinalysis (Chemical)
	Neonatal Bilirubin:
	Child's Age: days hours
	Clinician/Practitioner's tel. no. ( )
	Patient's 24 hr telephone no. ( )
	Therapeutic Drug Monitoring:
	Name of Drug #1
	Name of Drug #2
	Time Collected #1 hr. #2 hr.
	Time of Last Dose #1 hr. #2 hr.
	Time of Next Dose #1 hr. #2 hr.

x	Hematology
	CBC
	Prothrombin Time (INR)
	Immunology
	Pregnancy test (Urine)
	Mononucleosis Screen
	Rubella
	Prenatal: ABO, RhD, Antibody Screen (titre and ident. if positive)
	Repeat Prenatal Antibodies
	Microbiology ID & Sensitivities (if warranted)
	Cervical
	Vaginal
	Vaginal / Rectal – Group B Strep
	Chlamydia *(specify source)*:
	GC *(specify source)*:
	Sputum
	Throat
	Wound *(specify source)*:
	Urine
	Stool Culture
	Stool Ova & Parasites
	Other Swabs / Pus *(specify source)*:

Specimen Collection — Time (24 hour clock) | Date (yyyy/mm/dd)

Fecal Occult Blood Test (FOBT) *(check one)*

☐ FOBT (non CCC) ☐ ColonCancerCheck FOBT (CCC) no other test can be ordered on this form

x	Viral Hepatitis (check one only)
	Acute Hepatitis
	Chronic Hepatitis
	Immune Status / Previous Exposure Specify: ☐ Hepatitis A ☐ Hepatitis B ☐ Hepatitis C

or order individual hepatitis tests in the "Other Tests" section below

Prostate Specific Antigen (PSA)

☐ Total PSA ☐ Free PSA

Specify below:

☐ Insured – Meets OHIP eligibility criteria

☐ Uninsured – Screening: Patient responsible for payment

Vitamin D (25-Hydroxy)

☐ Insured – Meets OHIP eligibility criteria: osteopenia; osteoporosis; rickets; renal disease; malabsorption syndromes; medications affecting vitamin D metabolism

☐ Uninsured – Patient responsible for payment

Other Tests – one test per line

Laboratory Use Only

Print

I hereby certify the tests ordered are not for registered in or out patients of a hospital.

x Clinician/Practitioner Signature — Date

4422–84 (2010/09) ©Queen's Printer for Ontario, 2010 — 7530–4581

Vitamin D (25-Hydroxy)

☐ Insured – Meets OHIP eligibility criteria: osteopenia; osteoporosis; rickets; renal disease; malabsorption syndromes; medications affecting vitamin D metabolism

☐ Uninsured – Patient responsible for payment

Conclusion: OHIP insures 25(OH)D testing only for those conditions that justify a prescription for vitamin D

But…

"rickets" = "osteomalacia"

= muscle weakness & pain

Ministry of Health and Long-Term Care

Laboratories and Diagnostics
880 Bay St., 4th Floor, Room 433
Toronto ON M7A 1R3
Tel.: 416 326-3611
Fax: 416 326-3617

Ministère de la Santé et des Soins de longue durée

Laboratoires et Diagnostic
880, rue Bay, 4e étage, Salle 433
Toronto ON M7A 1R3
Tél: 416 326-3611
Téléc.:416 326-3617

Ontario

DEC 1 5 2010

Dr. Rienhold Vieth
Mount Sinai Hospital
600 University Avenue
Toronto ON M5G 1X5

Dear Dr. Vieth:

Thank you for your e-mail to Gary Ross, Program Manager, Registration and

3. I was very surprised to note that osteomalacia is not included among the eligibility criteria on the requisition form, for coverage of serum 25-hydroxyvitamin D. This surely was an oversight. Rickets and osteomalacia are essentially synonyms, differing only in the age group affected by the nutrient deficiency.

Adult rickets is the equivalent of osteomalacia and rickets is a covered indication for vitamin D testing. To be eligible for an OHIP-insured vitamin D test, a clinical diagnosis of rickets (or osteomalacia) is sufficient to have the test insured as a component of the necessary work-up for the patient.

The „Waddling Gait“ of Osteomalacia

62 yr old patient

S.creatinine	2.13 mg/dL (-1.3)
S.calcium (corr)	**1.50 mmol/L (2.2-2.6)**
S.phosphate	1.81 mmol/L (0.84-1.45)
S.magnesium	0.65 mmol/L (0.7-1.1)
1,25(OH)2D	**163 pg/ml (30-70)**

25(OH)D 15 nmol/L

(Desirable: >50 or >75 nmol/L)

PTH	1082 pg/ml (<65)

CKD stage III
PAOD stage II
arterial hypertension
chronic pancreatitis (MRI diagnosis)

RECOMMENDATIONS FOR 25(OH)D TESTING:

ONTARIO VS THE ENDOCRINE SOCIETY

Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline

Michael F. Holick, N
Catherine M. Gordo
and Connie M. Wea

Boston University School
(N.C.B.), Madison, Wiscon
Children's Hospital Boston
Medicine (D.A.H.), Calgary
68178; Mayo Clinic (M.H.
Lafayette, Indiana 47907

Objective: The objective
vention of vitamin D defic

OHIP COVERS ONLY FOR:

Specify one below:

☐ Insured – Meets OHIP eligibility criteria

☐ Uninsured – Screening: Patient responsible for payment

Vitamin D (25-Hydroxy)

☐ Insured – Meets OHIP eligibility criteria: osteopenia; osteoporosis; rickets; renal disease; malabsorption syndromes; medications affecting vitamin D metabolism

☐ Uninsured – Patient responsible for payment

Other Tests – one test per line

OHIP DOES NOT COVER →

TABLE 2. Indications for 25(OH)D measurement (candidates for screening)

- Rickets
- Osteomalacia
- Osteoporosis
- Chronic kidney disease
- Hepatic failure
- Malabsorption syndromes
  - Cystic fibrosis
  - Inflammatory bowel disease
  - Crohn's disease
  - Bariatric surgery
  - Radiation enteritis
- Hyperparathyroidism
- Medications
  - Antiseizure medications
  - Glucocorticoids
  - AIDS medications
  - Antifungals, *e.g.* ketoconazole
  - Cholestyramine
- African-American and Hispanic children and adults
- Pregnant and lactating women
- Older adults with history of falls
- Older adults with history of nontraumatic fractures
- Obese children and adults (BMI > 30 kg/m^2)
- Granuloma-forming disorders
  - Sarcoidosis
  - Tuberculosis
  - Histoplasmosis
  - Coccidiomycosis
  - Berylliosis
- Some lymphomas

THE COCHRANE LIBRARY

Independent high-quality evidence for health care de

THE TOP REVIEW SYSTEM OF EVIDENCE BASED MEDICINE CONCLUDES MULTIPLE BENEFITS OF VITAMIN D

Record Information Issue: Current | All Restrict to: Reviews |

Vitamin D supplementation for prevention of mortality in adults Goran Bjelakovic August 2011

Vitamin D supplementation for improving bone mineral density in children Tania M Winzenberg, October 2010

Vitamin D compounds for people with chronic kidney disease requiring dialysis Suetonia C Palmer, October 2009

Vitamin D compounds for people with chronic kidney disease not requiring dialysis Suetonia C Palmer October 2009

Vitamin D for the treatment of chronic painful conditions in adults Sebastian Straube, November 2010

Vitamin D and vitamin D analogues for preventing fractures D for associated with involutional and post-menopausal osteoporosis Alison Avenell, April 2009

Vitamin D for the management of multiple sclerosis Vanitha A Jagannath, December 2010

Calcium and vitamin corticosteroid-induced osteoporosis Joanne Homik, July 2010

Interventions for the prevention of nutritional rickets in term born children Christian Lerch, Thomas Meissner January 2009

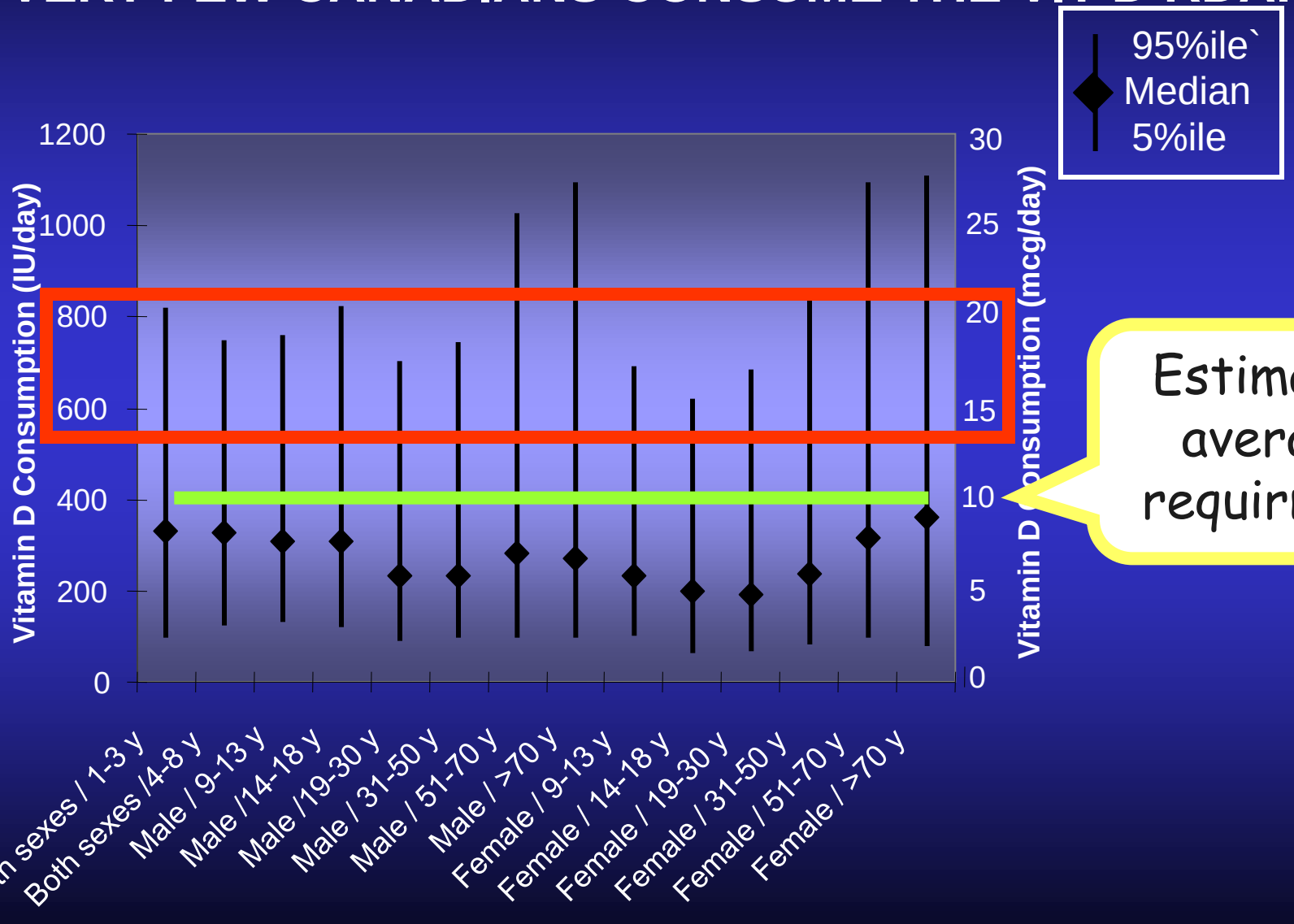
Interventions for preventing falls in older people living in the community Lesley D Gillespie, October 2010

Interventions for preventing falls in older people in nursing care facilities and hospitals Ian D Cameron February 2010

VITAMIN D A MODERN EXAMPLE OF THE FORTIFICATION VS SUPPLEMENTATION DILEMMA

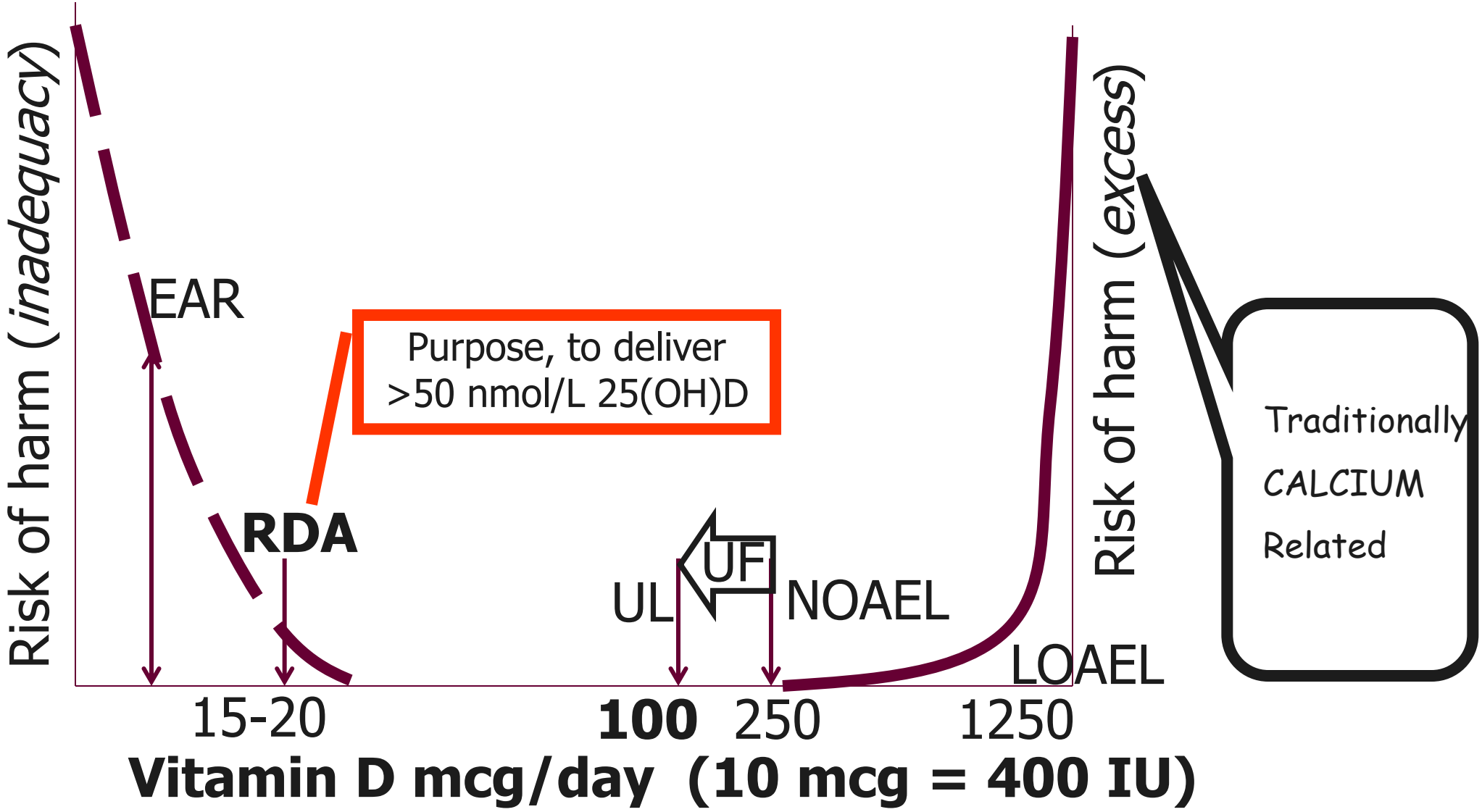
Canada Total Vitamin D intakes from food (fortification) and supplements (non-prescription):

VERY VERY FEW CANADIANS CONSUME THE VIT D RDA.



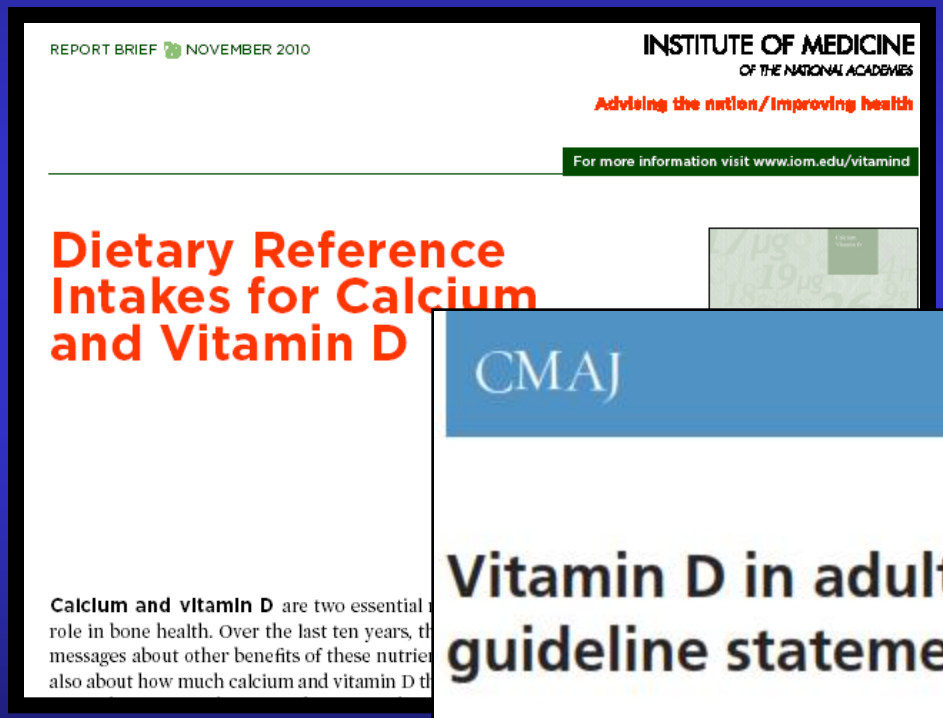
DO DOSAGE RECOMMENDATIONS FOR VITAMIN D MAKE SENSE?

NEW 2011 USA/Canada IOM POLICY FOR VITAMIN D



VITAMIN D INTAKE RECOMMENDATIONS:

IOM VS ENDOCRINE SOCIETY


REPORT BRIEF NOVEMBER 2010

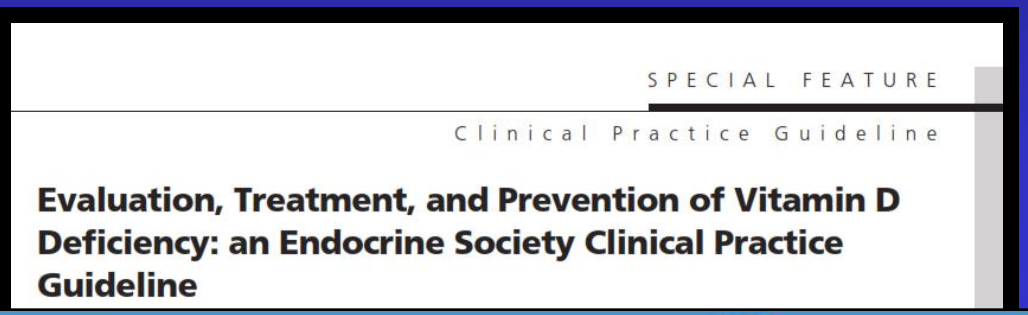
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the nation/Improving health

For more information visit www.iom.edu/vitamind

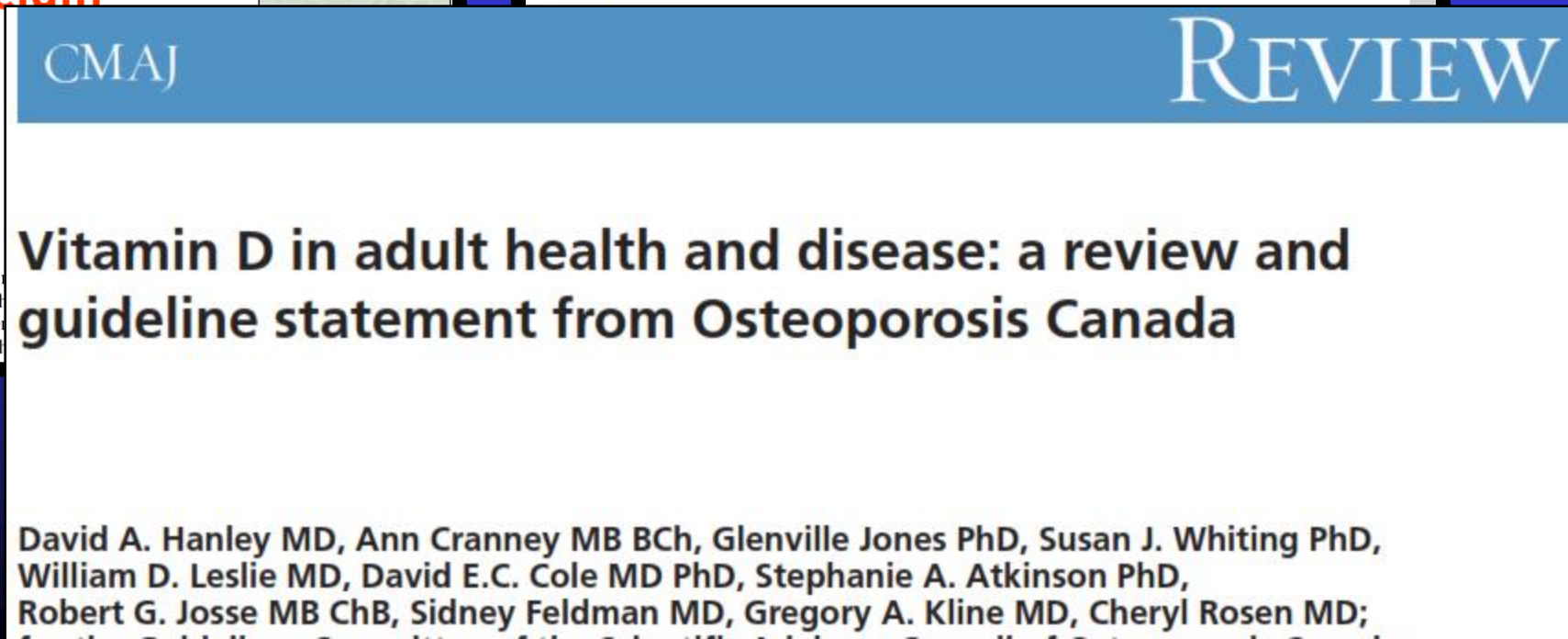
Dietary Reference Intakes for Calcium and Vitamin D

Calcium and vitamin D are two essential
role in bone health. Over the last ten years, th
messages about other benefits of these nutrie
also about how much calcium and vitamin D th


SPECIAL FEATURE

Clinical Practice Guideline

Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline


CMAJ REVIEW

Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada

David A. Hanley MD, Ann Cranney MB BCh, Glenville Jones PhD, Susan J. Whiting PhD, William D. Leslie MD, David E.C. Cole MD PhD, Stephanie A. Atkinson PhD, Robert G. Josse MB ChB, Sidney Feldman MD, Gregory A. Kline MD, Cheryl Rosen MD;

TABLE 3. Vitamin D intakes recommended by the IOM and the Endocrine Practice Guidelines Committee

Life stage group	IOM recommendations				Committee recommendations for patients at risk for vitamin D deficiency	
	AI	EAR	RDA	UL	Daily requirement	UL
Infants						
0 to 6 months	400 IU (10 μg)			1,000 IU (25 μg)	400–1,000 IU	2,000 IU
6 to 12 months	400 IU (10 μg)			1,500 IU (38 μg)	400–1,000 IU	2,000 IU
Children						
1–3 yr		400 IU (10 μg)	600 IU (15 μg)	2,500 IU (63 μg)	600–1,000 IU	4,000 IU
4–8 yr		400 IU (10 μg)	600 IU (15 μg)	3,000 IU (75 μg)	600–1,000 IU	4,000 IU
Males						
9–13 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
14–18 yr		400 IU (10 μg)	600 IU (15		600–1,000 IU	4,000 IU
19–30 yr		400 IU (10 μg)	600 IU (		1,500–2,000 IU	10,000 IU
31–50 yr		400 IU (10 μg)	600 IU (15		1,500–2,000 IU	10,000 IU
51–70 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
>70 yr		400 IU (10 μg)	800 IU (20 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
Females						
9–13 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μg)	600–1,000 IU	4,000 IU
14–18 yr		400 IU (10 μg)	600 IU (15		600–1,000 IU	4,000 IU
19–30 yr		400 IU (10 μg)	600 IU		1,500–2,000 IU	10,000 IU
31–50 yr		400 IU (10 μg)	600 IU (15		1,500–2,000 IU	10,000 IU
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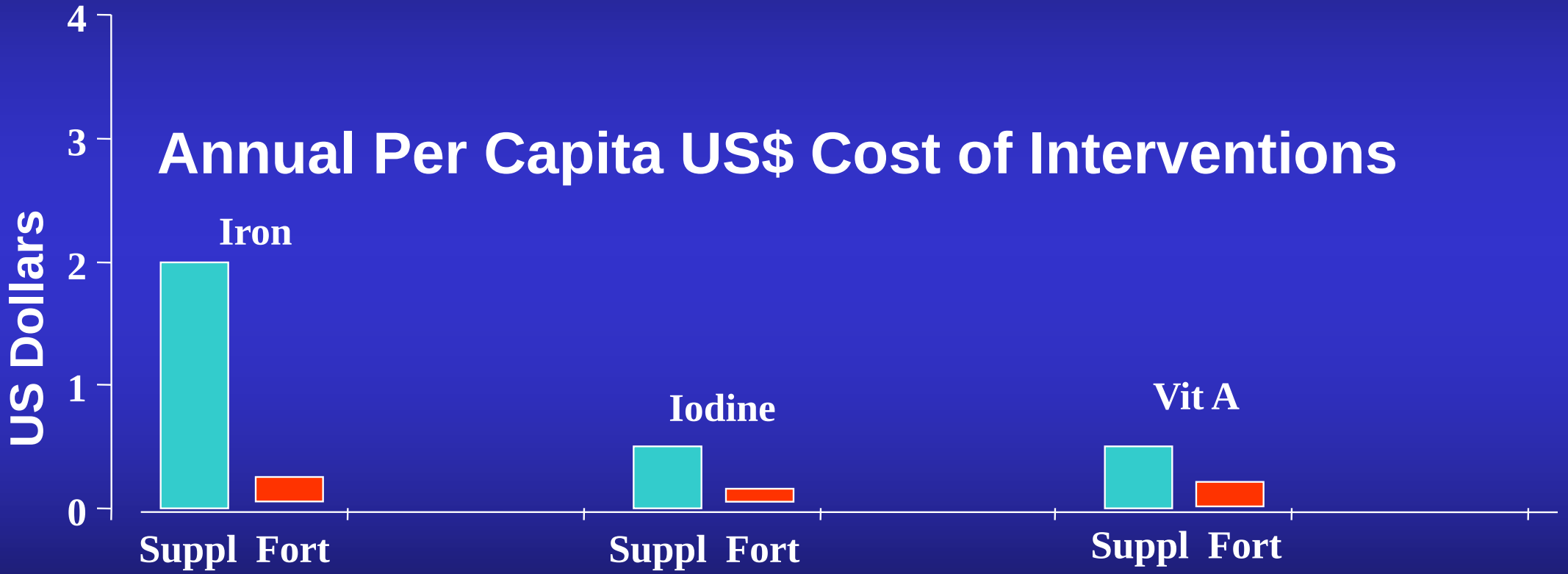
>70 yr		400 IU (10 μg)	800 IU (20 μg)	4,000 IU (100 μg)	1,500–2,000 IU	10,000 IU
Pregnancy						
14–18 yr		400 IU (10 μg)	600 IU (15		600–1,000 IU	4,000 IU
19–30 yr		400 IU (10 μg)	600 IU (1		1,500–2,000 IU	10,000 IU
31–50 yr		400 IU (10 μg)	600 IU (15 μg)	4,000 IU (100 μ	1,500–2,000 IU	10,000 IU

RISKS/BENEFITS FOR GOVERNMENT POLICY: "Political Controversy"

Preventing Goiter and Iodine Deficiency Disorders

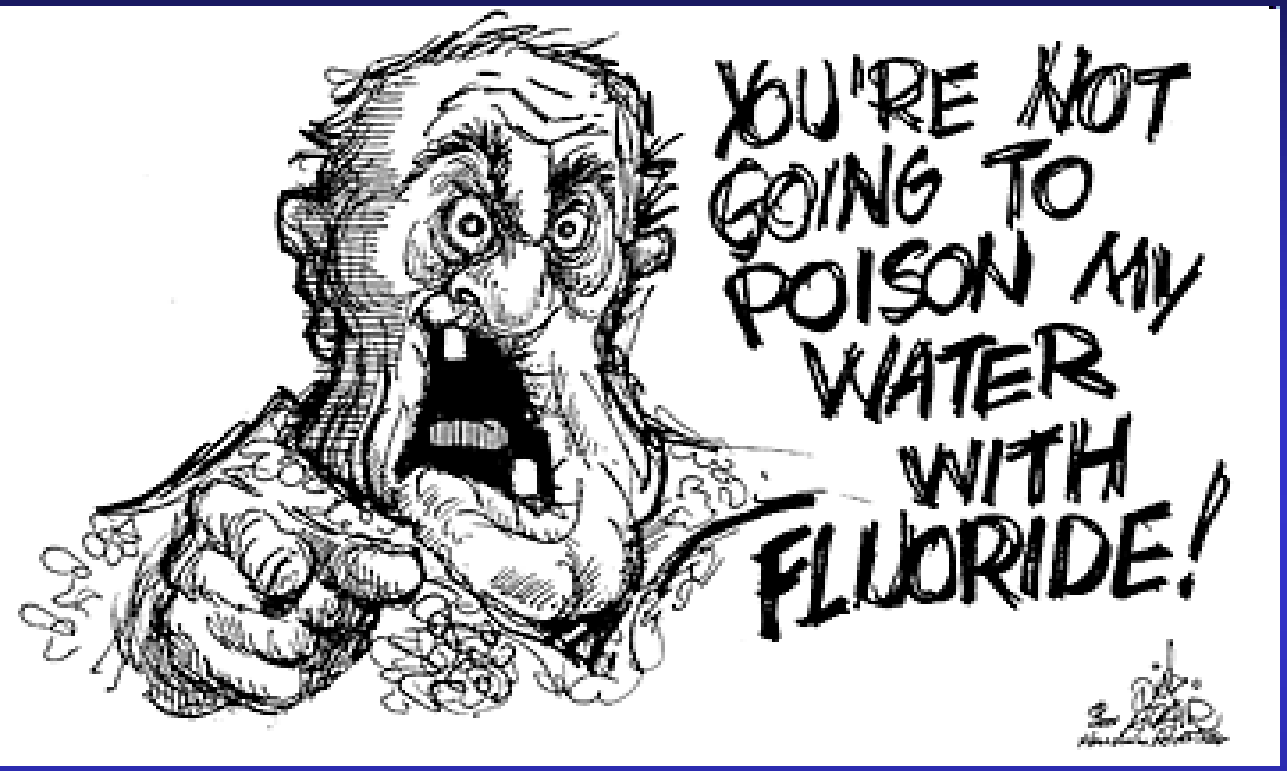
- 1917, high % US draftees rejected - goiter
- 1922-27, goiter rates fall from 39% to 9% by statewide prevention programs
- 1924, Morton's Iodized Salt (N America)
- 1979, Iodization mandatory in Canada
- 1980s, WHO - universal iodization of salt
- Many countries achieved iodization

Cost Comparison: Supplementation vs Fortification



Source: World Bank, 1994

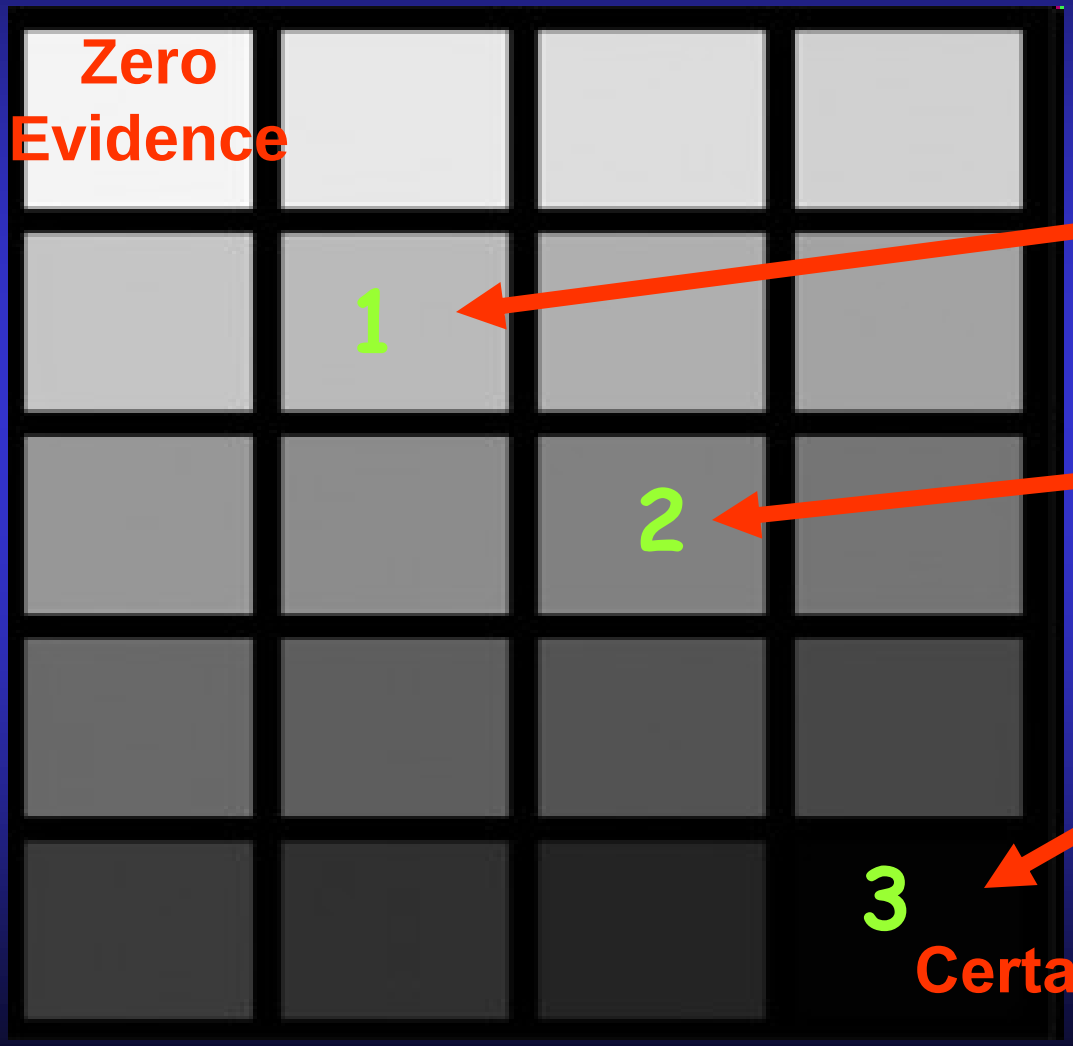
Difficulties in Establishing Policy



- Perception that Government is Paternalistic
- Resistance to "mandatory medication"
- Risk of Overriding Individual choice
- Clinical vs. population approaches
- Professionals in nutrition focus on the clinical (supplementation) approach
- WHO ambivalence/opposition
- Desire for Natural, "Green" foods.

TH Tulchinsky 2004 European Journal of Public Health, Vol. 14 : 226-228

The shades of grey of healt/medical decisions



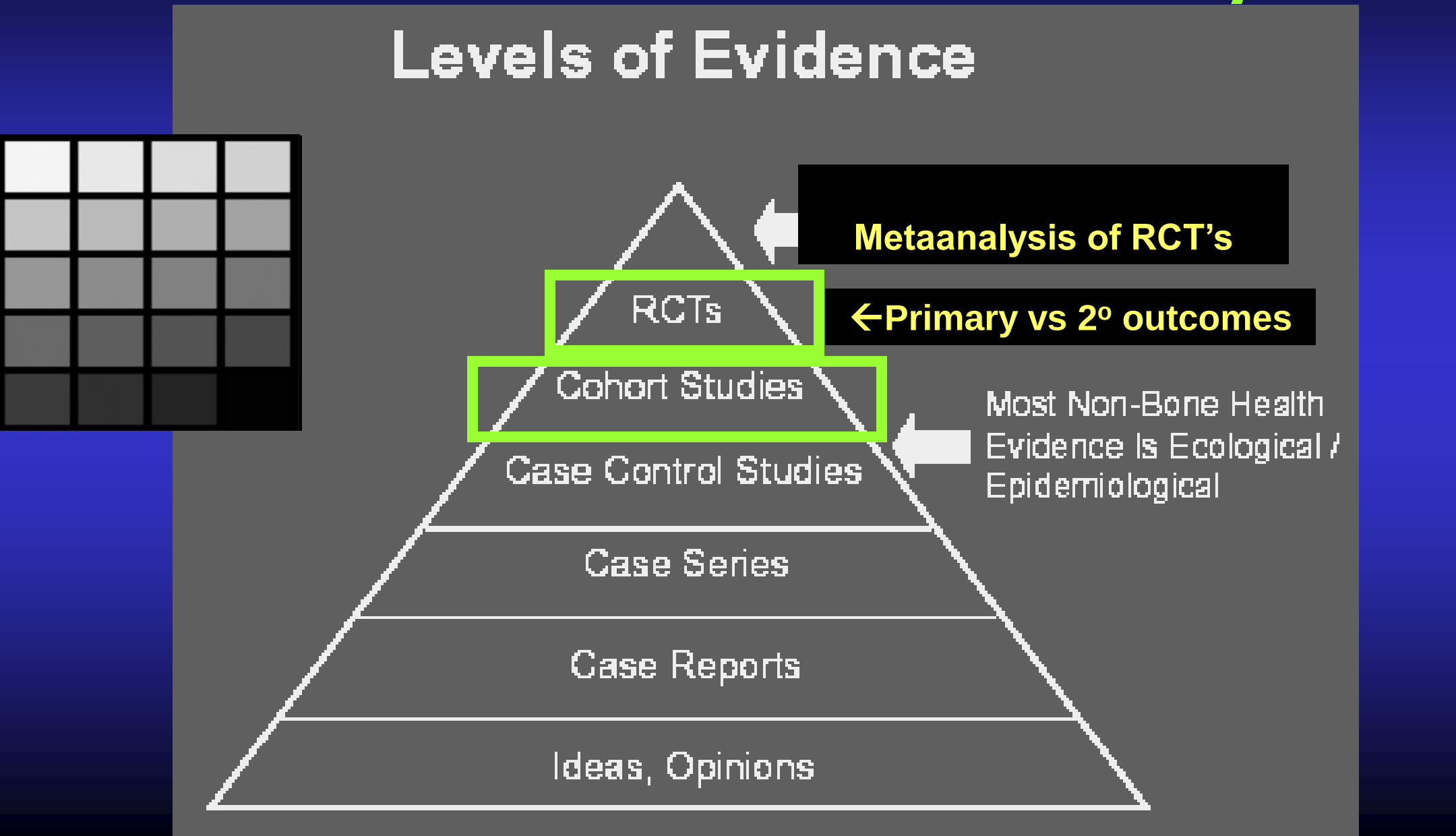
1. Personal care decisions (flexible and possibly only during sickness).

2. Physician care of patient (flexible and possibly only during sickness).

3. Government Health policy: for all society and for years to come.

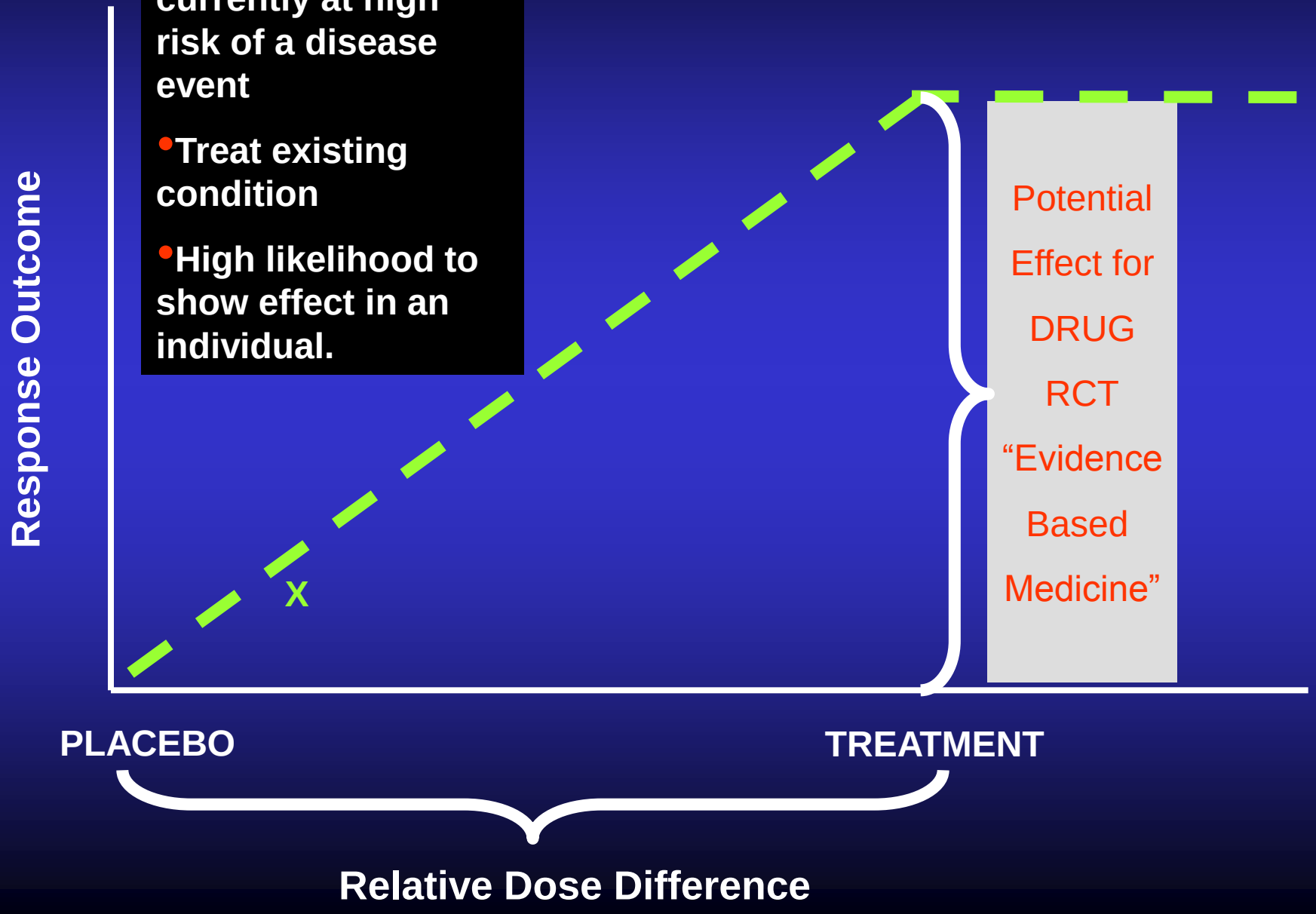
Certainty = "Causality" = RCT only

Policy is slow to adapt because it demands the Ultimate in Evidence: RCT + meta-analysis



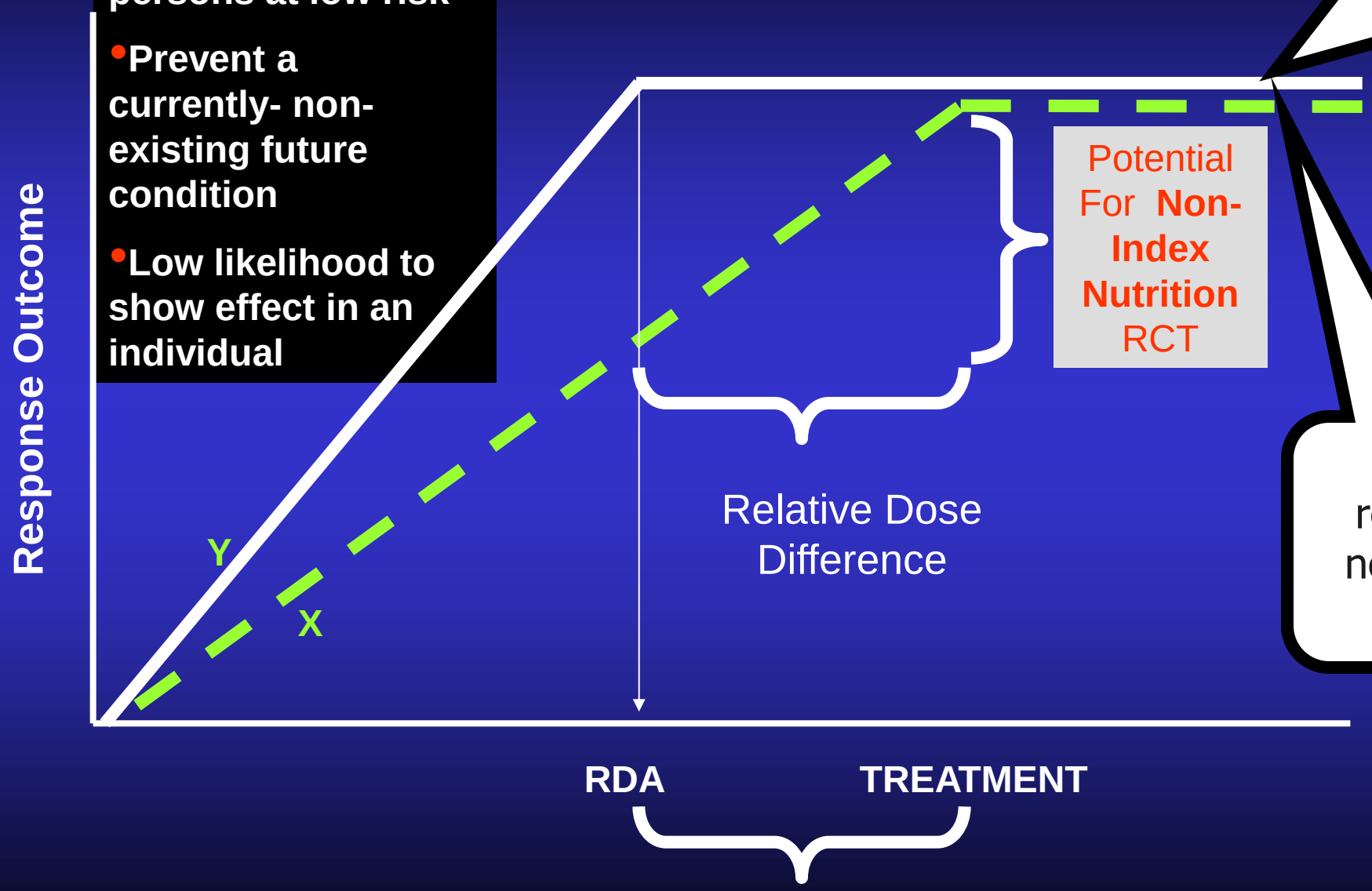
CLASSIC DRUG CLINICAL TRIAL

- Recruit persons currently at high risk of a disease event
- Treat existing condition
- High likelihood to show effect in an individual.



CLASSIC NUTRIENT CLINICAL TRIAL

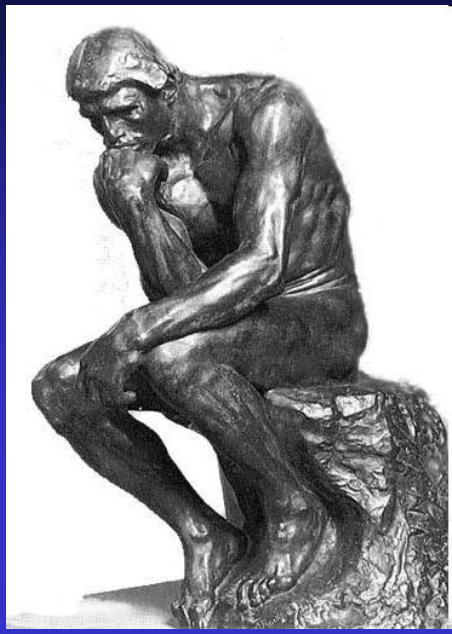
- Recruit Healthy persons at low risk
- Prevent a currently- non-existing future condition
- Low likelihood to show effect in an individual



White response curve is the "index", classic effect of the nutrient.

Green represents a new, putative effect.

For Vitamin D, the perfect clinical trials evidence that policy makers expect is unrealistic.



Policy depends on CONTEXT:

a) personal decisions

b) doctor-patient decisions, vs "standard of care" guidance

c) public health, eg RDA, and regulation for the food industry

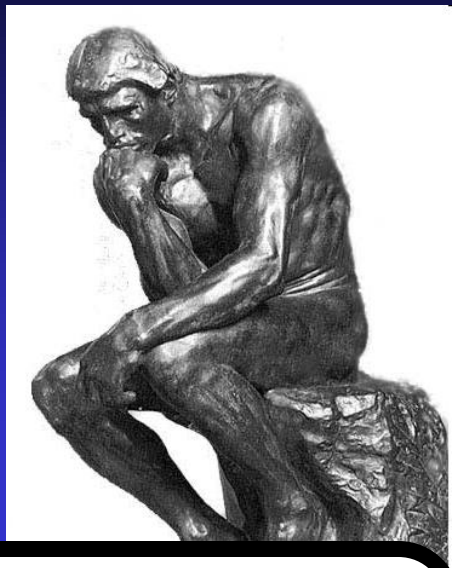
1 THE INDIVIDUAL → take a supplement

2 HEALTH PROFESSIONALS → advise a supplement or PRESCRIPTION

3 GOVERNMENT POLICY → Fortification (mandatory/optional)

For Vitamin D.

THINK ABOUT THE OPTIONS:



- Change the BEHAVIOR of society to consume an ideal diet
- To advise more sunshine is not generally an option
- Change diets through FORTIFICATION
- Advise all of society to take a SUPPLEMENT
- Health is a responsibility of:

1 THE INDIVIDUAL → take a supplement

2 HEALTH PROFESSIONALS → advise a supplement or PRESCRIPTION

3 GOVERNMENT POLICY → Fortification (mandatory/optional)

RV personal perspective on the Future solution to vitamin D