

**2/17/11  
PRESENTA-  
TION:  
VITAMIN D**

<TARGET><BILL></BILL><SUBJECT>2-17-11 PRESENTATION  
VITAMIN D</SUBJECT><COMM>HHSS27</COMM></TARGET>



U.S. National Library of Medicine  
NIH National Institutes of Health

## Vitamin D

URL of this page: <http://www.nlm.nih.gov/medlineplus/druginfo/natural/929.html>

### What is it?

Vitamin D is a vitamin. It can be found in small amounts in a few foods, including fatty fish such as herring, mackerel, sardines and tuna. To make vitamin D more available, it is added to dairy products, juices, and cereals that are then said to be "fortified with vitamin D." But most vitamin D – 80% to 90% of what the body gets – is obtained through exposure to sunlight. Vitamin D can also be made in the laboratory as medicine.

Vitamin D is used for preventing and treating rickets, a disease that is caused by not having enough vitamin D (vitamin D deficiency). Vitamin D is also used for treating weak bones (osteoporosis), bone pain (osteomalacia), bone loss in people with a condition called hyperparathyroidism, and an inherited disease (osteogenesis imperfecta) in which the bones are especially brittle and easily broken. It is also used for preventing falls and fractures in people at risk for osteoporosis, and preventing low calcium and bone loss (renal osteodystrophy) in people with kidney failure.

Vitamin D is used for conditions of the heart and blood vessels, including high blood pressure and high cholesterol. It is also used for diabetes, obesity, muscle weakness, multiple sclerosis, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), asthma, bronchitis, premenstrual syndrome (PMS), and tooth and gum disease.

Some people use vitamin D for skin conditions including vitiligo, scleroderma, psoriasis, actinic keratosis, and lupus vulgaris.

It is also used for boosting the immune system, preventing autoimmune diseases, and preventing cancer.

Because vitamin D is involved in regulating the levels of minerals such as phosphorous and calcium, it is used for conditions caused by low levels of phosphorous (familial hypophosphatemia and Fanconi syndrome) and low levels of calcium (hypoparathyroidism and pseudohypoparathyroidism).

Vitamin D in forms known as calcitriol or calcipotriene is applied directly to the skin for a particular type of psoriasis.

If you travel to Canada, you may have noticed that Canada recognizes the importance of vitamin D in the prevention of osteoporosis. It allows this health claim for foods that contain calcium: "A healthy diet with adequate calcium and vitamin D, and regular physical activity, help to achieve strong bones and may reduce the risk of osteoporosis." But the US version of this osteoporosis health claim does not yet include vitamin D.

### How effective is it?

*Natural Medicines Comprehensive Database* rates effectiveness based on scientific evidence according to the following scale: Effective, Likely Effective, Possibly Effective, Possibly Ineffective, Likely Ineffective, Ineffective, and Insufficient Evidence to Rate.

The effectiveness ratings for **VITAMIN D** are as follows:

**Effective for...**

- **Treating conditions that cause weak and painful bones (osteomalacia).**
- **Low levels of phosphate in the blood (familial hypophosphatemia).**
- **Low levels of phosphate in the blood due to a disease called Fanconi syndrome.**
- **Psoriasis (with a specialized prescription-only form of vitamin D).**
- **Low blood calcium levels because of a low parathyroid thyroid hormone levels.**
- **Helping prevent low calcium and bone loss (renal osteodystrophy) in people with kidney failure.**
- **Rickets.**
- **Vitamin D deficiency.**

**Likely effective for...**

- **Treating osteoporosis (weak bones).** Taking a specific form of vitamin D called cholecalciferol (vitamin D3) along with calcium seems to help prevent bone loss and bone breaks.
- **Preventing falls in older people.** Researchers noticed that people who don't have enough vitamin D tend to fall more often than other people. They found that taking a vitamin D supplement reduces the risk of falling by up to 22%. Higher doses of vitamin D are more effective than lower doses. One study found that taking 800 IU of vitamin D reduced the risk of falling, but lower doses didn't.

Also, vitamin D, in combination with calcium, but not calcium alone, may prevent falls by decreasing body sway and blood pressure. This combination prevents more falls in women than men.

- **Reducing bone loss in people taking drugs called corticosteroids.**

**Possibly effective for...**

- **Reducing the risk of multiple sclerosis (MS).** Studies show taking vitamin D seems to reduce women's risk of getting MS by up to 40%. Taking at least 400 IU per day, the amount typically found in a multivitamin supplement, seems to work the best.
- **Preventing cancer.** Some research shows that people who take a high-dose vitamin D supplement plus calcium might have a lower chance of developing cancer of any type.
- **Weight loss.** Women taking calcium plus vitamin D are more likely to lose weight and maintain their weight. But this benefit is mainly in women who didn't get enough calcium before they started taking supplements.
- **Flu.** Some research in school aged children show that taking a vitamin D supplement during winter might reduce the chance of getting seasonal flu.
- **Reducing the risk of rheumatoid arthritis in older women.**
- **Reducing bone loss in women with a condition called hyperparathyroidism.**
- **Preventing tooth loss in the elderly.**

**Possibly ineffective for...**

- **Breast cancer.** Many studies have looked at whether vitamin D can help prevent breast cancer, but their results have not always agreed. The best evidence to date comes from a large study called the Women's Health Initiative, which found that taking 400 IU of vitamin D and 1000 mg of calcium per day does not seem to lower the chance of getting breast cancer. The possibility remains that high doses of vitamin D might lower breast cancer risk in younger women. But the doses needed would be so high that they might not be safe.
- **High blood pressure.**
- **Improving muscle strength in older adults.**
- **Preventing bone loss in people with kidney transplants.**

**Insufficient evidence to rate effectiveness for...**

- **Heart disease.** Research suggests that people with low levels of vitamin D in their blood are much more likely to develop heart disease, including heart failure, than people with higher vitamin D levels. However, taking vitamin D does not seem to extend the life of people with heart failure.
- **High cholesterol.** People with lower vitamin D levels seem to be much more likely to have high cholesterol than people with higher vitamin D levels. Limited research shows that taking calcium plus vitamin D daily, in combination with a low-calorie diet, significantly raises "good (HDL) cholesterol" and lowers "bad (LDL) cholesterol" in overweight women. But taking calcium plus vitamin D alone, does not reduce LDL cholesterol levels.
- **Gum disease.** Higher blood levels of vitamin D seem to be linked with a reduced risk of gum disease in people 50 years of age or older. But, this doesn't seem to be true for adults younger than 50.
- **Diabetes.** People with lower vitamin D levels are significantly more likely to have type 2 diabetes compared to people with higher vitamin D levels. But, there is no reliable evidence that taking vitamin D supplements can treat or prevent type 2 diabetes.
- **Premenstrual syndrome (PMS).** There is some evidence that getting more vitamin D from the diet might help to prevent PMS or reduce symptoms. Taking vitamin D supplements might help reduce symptoms but doesn't seem to help prevent PMS.
- **A blood cell disease called myelodysplastic syndrome.**
- **A muscle disease called proximal myopathy.**
- **Colorectal cancer.**
- **Warts.**
- **Bronchitis.**
- **Asthma.**
- **Breathing disorders.**
- **Metabolic syndrome.**
- **Muscle pain caused by medications called "statins."**
- **Vaginal atrophy.**
- **Other conditions.**

More evidence is needed to rate vitamin D for these uses.

**How does it work?**

Vitamin D is required for the regulation of the minerals calcium and phosphorus found in the body. It also plays an important role in maintaining proper bone structure.

Sun exposure is an easy, reliable way for most people to get vitamin D. Exposure of the hands, face, arms, and legs to sunlight two to three times a week for about one-fourth of the time it would take to develop a mild sunburn will cause the skin to produce enough vitamin D. The necessary exposure time varies with age, skin type, season, time of day, etc.

It's amazing how quickly adequate levels of vitamin D can be restored by sunlight. Just 6 days of casual sunlight exposure without sunscreen can make up for 49 days of no sunlight exposure. Body fat acts like a kind of storage battery for vitamin D. During periods of sunlight, vitamin D is stored in fatty fat and then released when sunlight is gone.

Nevertheless, vitamin D deficiency is more common than you might expect. People who don't get enough sun, especially people living in Canada and the northern half of the US, are especially at risk. Vitamin D deficiency also occurs even in sunny climates, possibly because people are staying indoors more, covering up when outside, or using sunscreens consistently these days to reduce skin cancer risk.

Older people are also at risk for vitamin D deficiency. They are less likely to spend time in the sun, have fewer "receptors" in their skin that convert sunlight to vitamin D, may not get vitamin D in their diet, may have trouble absorbing vitamin D even if they do get it in their diet, and may have more trouble converting dietary vitamin D to a useful form due to aging kidneys. In fact, the risk for vitamin D deficiency in people over 65 years of age is very high. Surprisingly, as many as 40% of older people even in sunny climates such as South Florida don't have enough vitamin D in their systems.

Vitamin D supplements may be necessary for older people, people living in northern latitudes, and for dark-skinned people who need extra time in the sun, but don't get it.

### Are there safety concerns?

Vitamin D is **LIKELY SAFE** when taken by mouth in recommended amounts. Most people do not commonly experience side effects with vitamin D, unless too much is taken. Some side effects of taking too much vitamin D include weakness, fatigue, sleepiness, headache, loss of appetite, dry mouth, metallic taste, nausea, vomiting, and others.

Taking vitamin D for long periods of time in doses higher than 50 mcg (2000 units) per day is **POSSIBLY UNSAFE** and may cause excessively high levels of calcium in the blood. However, much higher doses are often needed for the short-term treatment of vitamin D deficiency. This type of treatment should be done under the supervision of a healthcare provider.

Special precautions & warnings:

**Pregnancy and breast-feeding:** Vitamin D is **LIKELY SAFE** during pregnancy and breast-feeding when used in daily amounts below 50 mcg (2000 units). Do not use higher doses. Using higher doses might cause serious harm to the infant.

**Kidney disease:** Vitamin D may increase calcium levels and increase the risk of "hardening of the arteries" in people with serious kidney disease. This must be balanced with the need to prevent renal osteodystrophy, a bone disease that occurs when the kidneys fail to maintain the proper levels of calcium and phosphorus in the blood. Calcium levels should be monitored carefully in people with kidney disease.

**High levels of calcium in the blood:** Taking vitamin D could make this condition worse.

**"Hardening of the arteries" (atherosclerosis):** Taking vitamin D could make this condition worse.

**Sarcoidosis:** Vitamin D may increase calcium levels in people with sarcoidosis. This could lead to kidney stones and other problems. Use vitamin D cautiously.

**Histoplasmosis:** Vitamin D may increase calcium levels in people with histoplasmosis. This could lead to kidney stones and other problems. Use vitamin D cautiously.

**Over-active parathyroid gland (hyperparathyroidism):** Vitamin D may increase calcium levels in people with hyperparathyroidism. Use vitamin D cautiously.

**Lymphoma:** Vitamin D may increase calcium levels in people with lymphoma. This could lead to kidney stones and other problems. Use vitamin D cautiously.

### Are there interactions with medications?

#### Moderate

Be cautious with this combination.

**Aluminum**

Aluminum is found in most antacids. Vitamin D can increase how much aluminum the body absorbs. This interaction might be a problem for people with kidney disease. Take vitamin D two hours before, or four hours after antacids.

**Atorvastatin (Lipitor)**

Vitamin D might decrease the amount of atorvastatin (Lipitor) that enters the body. This might decrease how well atorvastatin (Lipitor) works.

**Calcipotriene (Dovonex)**

Calcipotriene is a drug that is similar to vitamin D. Taking vitamin D along with calcipotriene (Dovonex) might increase the effects and side effects of calcipotriene (Dovonex). Avoid taking vitamin D supplements if you are taking calcipotriene (Dovonex).

**Digoxin (Lanoxin)**

Vitamin D helps your body absorb calcium. Calcium can affect the heart. Digoxin (Lanoxin) is used to help your heart beat stronger. Taking vitamin D along with digoxin (Lanoxin) might increase the effects of digoxin (Lanoxin) and lead to an irregular heartbeat. If you are taking digoxin (Lanoxin), talk to your doctor before taking vitamin D supplements.

**Diltiazem (Cardizem, Dilacor, Tiazac)**

Vitamin D helps your body absorb calcium. Calcium can affect your heart. Diltiazem (Cardizem, Dilacor, Tiazac) can also affect your heart. Taking large amounts of vitamin D along with diltiazem (Cardizem, Dilacor, Tiazac) might decrease the effectiveness of diltiazem.

**Medications changed by the liver (Cytochrome P450 3A4 (CYP 3A4) substrates)**

Some medications are changed and broken down by the liver. Vitamin D may increase how quickly the liver breaks down some medications. Taking vitamin D along with some medications may decrease the effectiveness of some medications. Before taking vitamin D, talk to your health care provider if you are taking any medications that are changed by the liver.

Some of these medications changed by the liver include lovastatin (Mevacor), clarithromycin (Biaxin), cyclosporine (Neoral, Sandimmune), diltiazem (Cardizem), estrogens, indinavir (Crixivan), triazolam (Halcion), and others.

**Verapamil (Calan, Covera, Isoptin, Verelan)**

Vitamin D helps your body absorb calcium. Calcium can affect the heart. Verapamil (Calan, Covera, Isoptin, Verelan) can also affect the heart. Do not take large amounts of vitamin D if you are taking verapamil (Calan, Covera, Isoptin, Verelan).

**Water pills (Thiazide diuretics)**

Vitamin D helps your body absorb calcium. Some "water pills" increase the amount of calcium in the body. Taking large amounts of vitamin D along with some "water pills" might cause to be too much calcium in the body. This could cause serious side effects including kidney problems.

Some of these "water pills" include chlorothiazide (Diuril), hydrochlorothiazide (HydroDIURIL, Esidrix), indapamide (Lozol), metolazone (Zaroxolyn), and chlorthalidone (Hygroton).

**Minor**

Be watchful with this combination.

**Cimetidine (Tagamet)**

The body changes vitamin D into a form that it can use. Cimetidine (Tagamet) might decrease how well the body changes vitamin D. This might decrease how well vitamin D works. But this interaction probably isn't important for most people.

### **Heparin**

Heparin slows blood clotting and can increase the risk of breaking a bone when used for a long period of time. People taking these medications should eat a diet rich in calcium and vitamin D.

### **Low molecular weight heparins (LMWHs)**

Some medications called low molecular weight heparins can increase the risk of breaking a bone when used for a long periods of time. People taking these medications should eat a diet rich in calcium and vitamin D.

These drugs include enoxaparin (Lovenox), dalteparin (Fragmin), and tinzaparin (Innohep).

## **Are there interactions with herbs and supplements?**

### **Magnesium**

Taking vitamin D can raise the level of magnesium in people who have low magnesium and low vitamin D levels. In people with normal magnesium levels, this doesn't seem to happen.

## **Are there interactions with foods?**

There are no known interactions with foods.

## **What dose is used?**

The following doses have been studied in scientific research:

### **BY MOUTH:**

- For preventing osteoporosis and fractures: 400-1000 IU per day has been used for older adults. Some experts recommended higher doses of 1000-2000 IU daily.
- For preventing falls: 800-1000 IU/day has been used in combination with calcium 1000-1200 mg/day.
- For preventing multiple sclerosis (MS): long-term consumption of at least 400 IU per day, mainly in the form of a multivitamin supplement, has been used.
- For preventing all cancer types: calcium 1400-1500 mg/day plus vitamin D3 (cholecalciferol) 1100 IU/day in postmenopausal women has been used.
- For muscle pain caused by medications called "statins": vitamin D2 (ergocalciferol) or vitamin D3 (cholecalciferol) 50,000 units once a week or 400 IU daily.
- For preventing the flu: vitamin D (cholecalciferol) 1200 IU daily.

Most vitamin supplements contain only 400 IU (10 mcg) vitamin D.

The Institute of Medicine publishes an Adequate Intake (AI) recommendation which is an estimate of the amount of vitamin D that appears to maintain normal functioning. The current daily AI of vitamin D to prevent rickets in healthy children and bone pain (osteomalacia) in adults is based on age. Birth through 50 years of age, 200 IU (5 mcg); Adults ages 51 to 70, 400 IU (10 mcg); Adults greater than 70 years of age, 600 IU (15 mcg) daily. The upper intake levels (UL) for vitamin D are 1000 IU (25 mcg) for infants 0 to 12 months and 2000 IU (50 mcg) for everyone over one year of age.

Some organizations are recommending higher amounts. In 2008, the American Academy of Pediatrics increased the recommended minimum daily intake of vitamin D to 400 IU daily for all infants and children, including adolescents. Parents should not use vitamin D liquids dosed as 400 IU/drop. Giving one dropperful or mL by mistake can deliver 10,000 IU/day. The US Food and Drug Administration (FDA) will force companies to provide

no more than 400 IU per dropperful in the future.

The National Osteoporosis Foundation recommends vitamin D 400 IU to 800 IU daily for adults under age 50, and 800 IU to 1000 IU daily for older adults.

The North American Menopause Society recommends 700 IU to 800 IU daily for women at risk of deficiency due to low sun (e.g., homebound, northern latitude) exposure.

Guidelines from the Osteoporosis Society of Canada recommend vitamin D 400 IU per day for people up to age 50, and 800 IU per day for people over 50.

Osteoporosis Canada now recommends 400-1000 IU daily for adults under the age of 50 years and 800-2000 IU daily for adults over the age of 50 years.

The Canadian Cancer Society recommends 1000 IU/day during the fall and winter for adults in Canada. For those with a higher risk of having low vitamin D levels, this dose should be taken year round. This includes people who have dark skin, usually wear clothing that covers most of their skin, and people who are older or who don't go outside often.

Many experts now recommend using vitamin D supplements containing cholecalciferol in order to meet these intake levels. This seems to be more potent than another form of vitamin D called ergocalciferol.

### Other names

Alfacalcidol: 1-alpha-hydroxycholecalciferol, 1 alpha (OH)D3.

Calcifediol: 25-HCC, 25-hydroxycholecalciferol, 25-hydroxyvitamin D3, 25-OHCC, 25-OHD3.

Calcipotriene: Calcipotriol.

Calcitriol: 1,25-DHCC, 1,25-dihydroxycholecalciferol, 1,25-dihydroxyvitamin D3, 1,25-diOHC, 1,25(OH)2D3.

Cholecalciferol: Activated 7-dehydrocholesterol, colecalciferol, Vitamin D3, Vitamine D3.

Dihydrotachysterol: DHT, dihydrotachysterol 2, dichysterol.

Ergocalciferol: Activated ergosterol, Calciferol, Ergocalciferolum, Irradiated ergosterol, Viosterol, Vitamin D2, Vitamine D2.

Paricalcitol: 19-nor-1,25-dihydroxyvitamin D2, Paracalcin.

Fat-Soluble Vitamin, Vitamina D, Vitamine D.

### Methodology

To learn more about how this article was written, please see the *Natural Medicines Comprehensive Database* methodology (<http://www.nlm.nih.gov/medlineplus/druginfo/natural/methodology.html>).

### References

To see all references for the Vitamin D page, please go to <http://www.nlm.nih.gov/medlineplus/druginfo/natural/929.html>.

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## Janet Ogan

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**From:** Rep. Wes Keller  
**Sent:** Thursday, February 03, 2011 10:26 AM  
**To:** Janet Ogan  
**Subject:** FW: Vitamin D

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**From:** Hurlburt, Ward B (HSS) [mailto:ward.hurlburt@alaska.gov]  
**Sent:** Thursday, February 03, 2011 7:26 AM  
**To:** Rep. Wes Keller  
**Subject:** FW: Vitamin D

Wes – here is the e-mail I sent to bill Streur regarding the Vitamin D material Rep, Seaton shared with us.

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**From:** Hurlburt, Ward B (HSS)  
**Sent:** Tuesday, February 01, 2011 3:40 PM  
**To:** Streur, William J (HSS)  
**Subject:** Vitamin D

There were three short strictly advocacy type news release presentations. There is a “grassroots.com” organization sponsoring all this and there was also reference to some kind of Vitamin D foundation in one of the news releases. A woman who was clearly an advocate and I believe non medical was the moderator for the conference. The conference, which took place at UC San Diego, last April had five presenters with six presentations. The audience based on self identification of those who had questions included physicians, naturalists, students, nutritionists, and others.

The presentations were well done. There were some references to some of the material in the slides being derived from double blinded randomized clinical trials, which can provide the strongest grade of evidence. Some of the presenters were physicians, a couple had public health doctorates. The program was held at UCSD, but at the end of each presentation the material had a slide disclaiming any responsibility for what was said by the presenters. All except one presenter disclaimed any conflicts of interest, but the seminar was clearly one of a series that Grassroots.com has put on and since the presenters were each from a different academic institution around the country I am sure they were at least sponsored for participation.

From one of the questions to the last presenter there was a comment that the sales of Vitamin D have increased five fold in the US, that the use of laboratory testing for Vitamin D levels now far surpasses testing for all other biomarkers put together. I also learned that Mike Huckabee is an advocate.

To the average Paul Seaton I am sure the presentations would be very credible. It was a conference of “experts”. The concepts of evidence based medicine reveal that expert opinion and consensus conferences are the weakest grade of clinical evidence and should not be the source of clinical decisions if other evidence can be found.

Some of the claims for Vitamin D were not credible to me. For example one presenter claimed that if people took Vitamin D supplements to get their blood levels to 40 to 50 ng/dl (nanograms per deciliter) that 80% of breast cancer and 99% of colon cancer would be prevented. A vast array of other benefits was also claimed. Those claims of a vast array of benefits are not dissimilar to what has been claimed for Vitamin E, Vitamin C, and Vitamin B12 just in my professional lifetime – with the hyperenthusiasm passing with time.

The presenters seemed to congregate around daily doses of Vitamin D of up to 30,000 iu as being safe though all agreed there is risk of significant harm from doses at a high enough level.

The National Institutes of Health funded a study to look at Vitamin D and specifically the claims of advocates such as the presenters in this seminar. Their funding led to an Institute of Medicine report that included recommendation to increase the recommended "Adequate Intake" dose of Vitamin D to 400 iu for adults 51 to 70 years and 600 iu for adults over 70. The American Academy of Pediatrics now recommends a 400iu dose for all infants and children.

The IOM findings do not corroborate the claims of substantiation of the benefits by the presenters for Vitamin D beyond some bone related issues such as rickets or osteomalacia, prevention of falls, psoriasis, for individuals taking corticosteroids, or for certain metabolic defects.

Sun exposure was found to be beneficial by the IOM (Toby could have told them that). Ten minutes a day at noon with 40% body exposure with no sunscreen two or three times a week produces sufficient Vitamin D according to the IOM statement. Because Vitamin D is a fat stored vitamin, six days of casual sunlight exposure without sunscreen can make up for 50 days of no sunlight exposure.

The recommendations from the "non-advocates" for an upper limit seem to be that 2000iu a day does not present a risk and the IOM report stated that for those over eight years of age 4000 iu a day was a reasonable "upper limit".

The IOM report did not comment on Vitamin D level testing and clearly did not recommend it on a population or screening basis.

So I still do not believe there is potential for Rep. Seaton to think he may be wrong in his passion, but I believe an argument that the legislature is not the place for clinical or coverage decisions might be more acceptable.

Ward

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# VITAMIN D: MIRACLE NUTRIENT OR SNAKE OIL

## The Challenge for Alaska

Robert P. Heaney, M.D.

*Creighton University Osteoporosis Research Center*



# OUT OF AFRICA

- humans evolved in equatorial E. Africa, wearing no clothes and were originally dark-skinned
- they made an abundance of vitamin D, year-round, in their skins



# CUTANEOUS VITAMIN D SYNTHESIS

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*ultra-violet B  
radiation*

7-dehydro-  
cholesterol



pre-vitamin D



vitamin D

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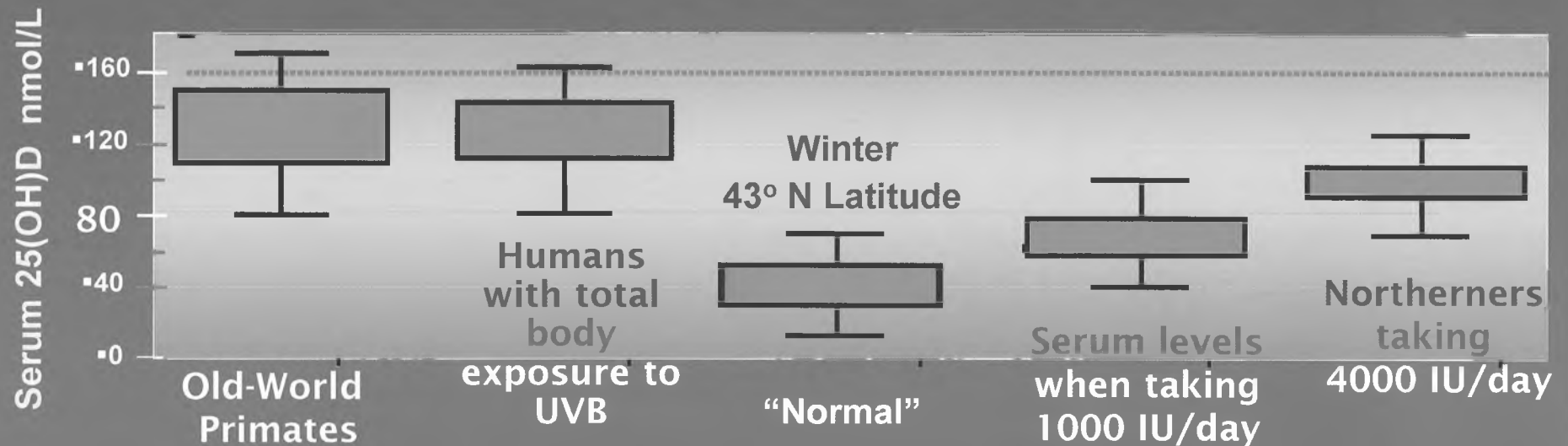
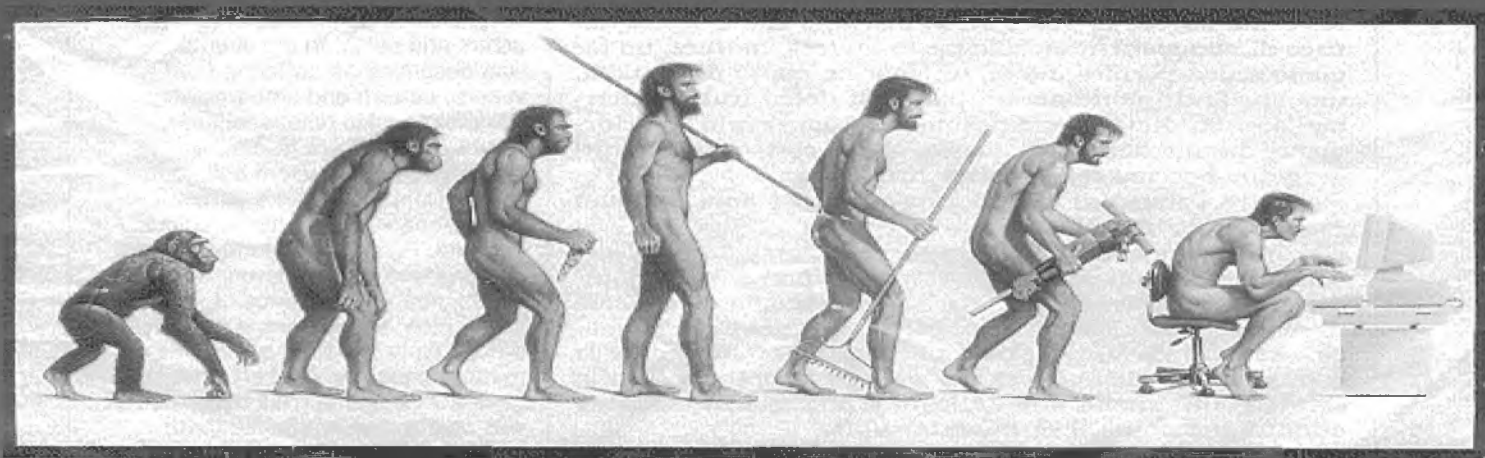
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# VITAMIN D & PRIMATE PROGRESS (?)

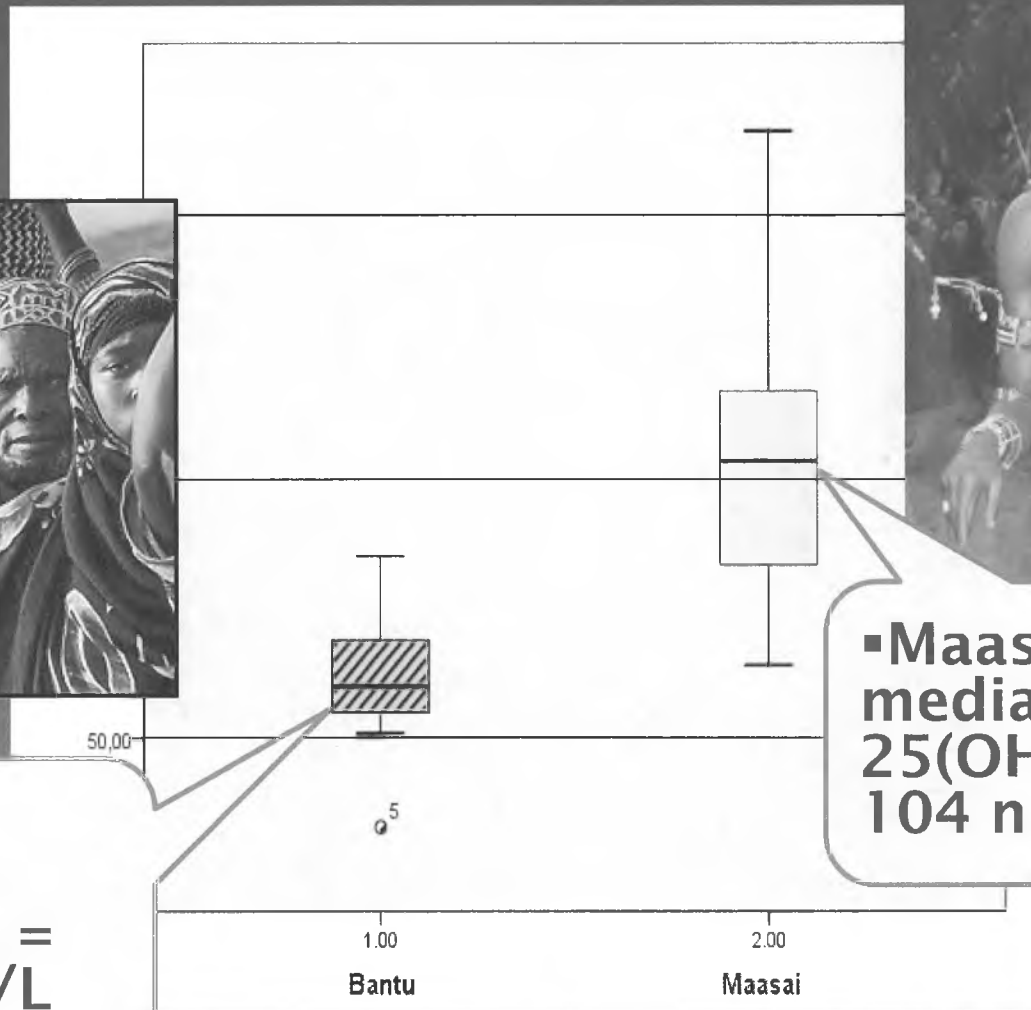


- Sources include: Cosman Osteoporosis Int 2000; Fuleihan NEJM 1999;
- Scharla Osteoporosis Int 1998; Vieth AJCN 1999, 2000

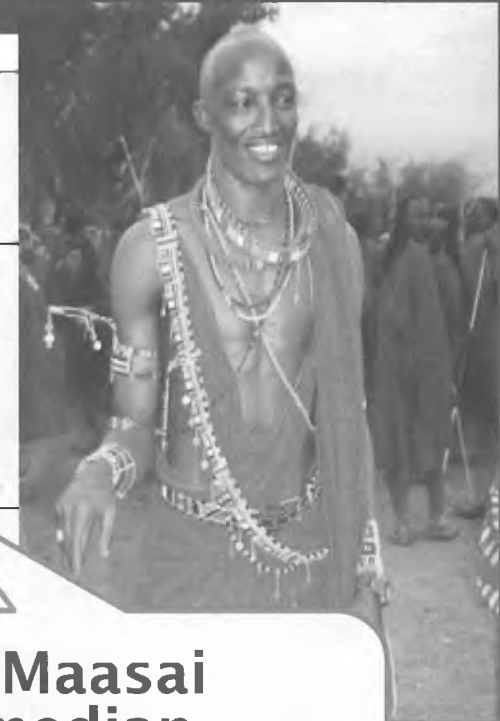
# THE PRIMITIVE LEVEL



▪ Bantu  
median  
25(OH)D =  
59 nmol/L



▪ Maasai  
median  
25(OH)D =  
104 nmol/L



▪ Luxwolda and Muskiet, submitted manuscript

# 25(OH)D IN THE TROPICS\*

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- 42 older Mayan men in Guatemala
- latitude: 15° N
- altitude: 2300 m
- studied in summer 2008
- mean serum 25(OH)D: 60.2 nmol/L (25 ng/mL)



▪\*Collaboration with N. Solomon, CeSSIAM

# OUT OF AFRICA

- migration north out of Africa led to reduced vitamin D availability
  - clothing covered skin surface that had formerly been exposed to the sun
  - latitude and cloud cover reduced solar irradiance
  - skin pigmentation acted as a sunscreen



# RICKETS & GROUP SURVIVAL

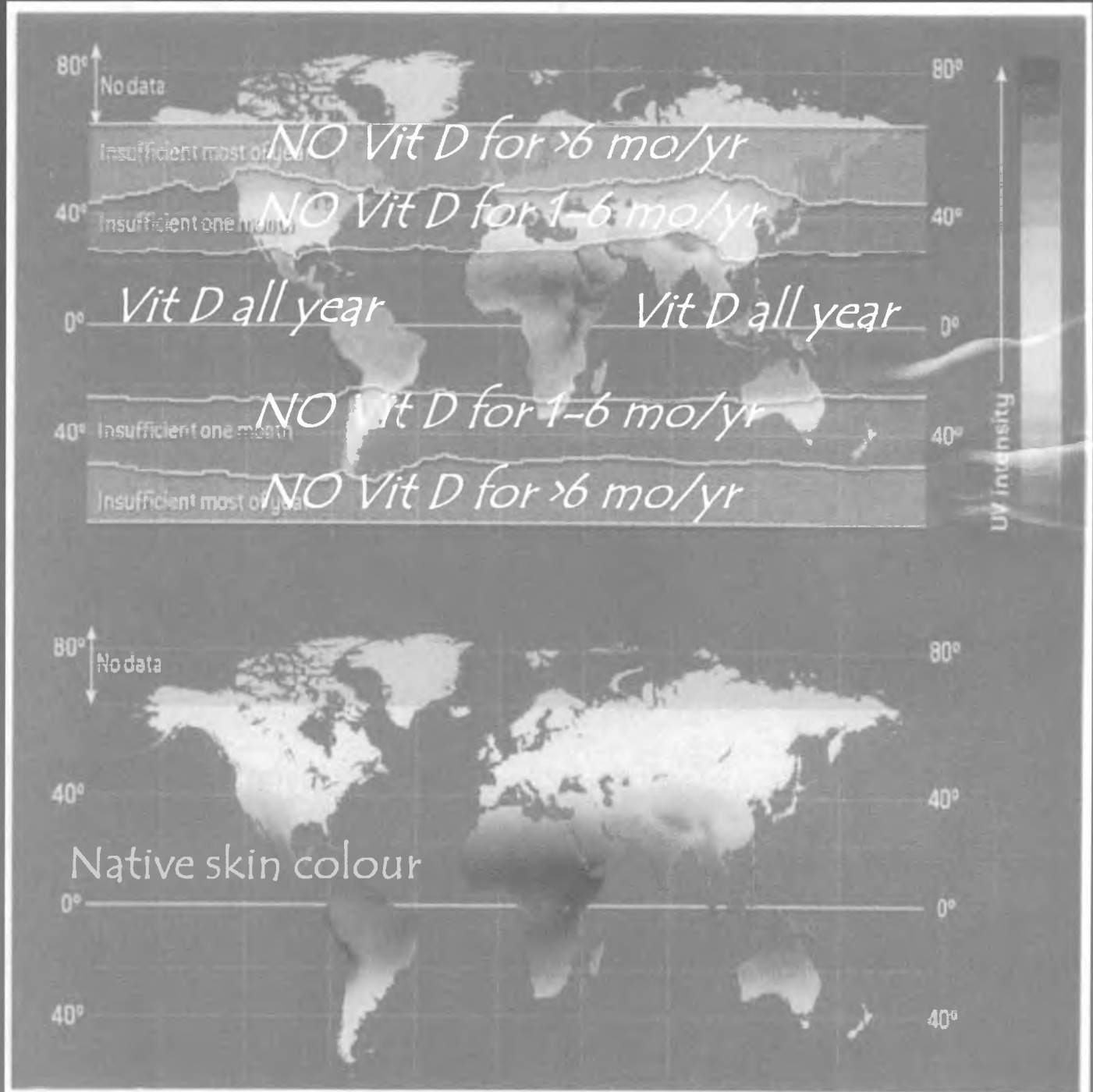
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- the reduced vitamin D availability led to rickets
- distortion of the pelvis in severe rickets prevented childbirth
- only paler skinned migrants were able to reproduce



Number of months in which solar UV-B can induce cutaneous vitamin D synthesis

Distribution of melanin in native populations



# VIT D – CANONICAL SCHEME

skin

liver

kidney

gut



principal storage form of  
the vitamin at prevailing  
inputs

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# VIT D – CANONICAL SCHEME

skin

liver

kidney

gut



the functional indicator of  
vitamin D status

produced by the kidney  
when the body senses a  
need for Ca

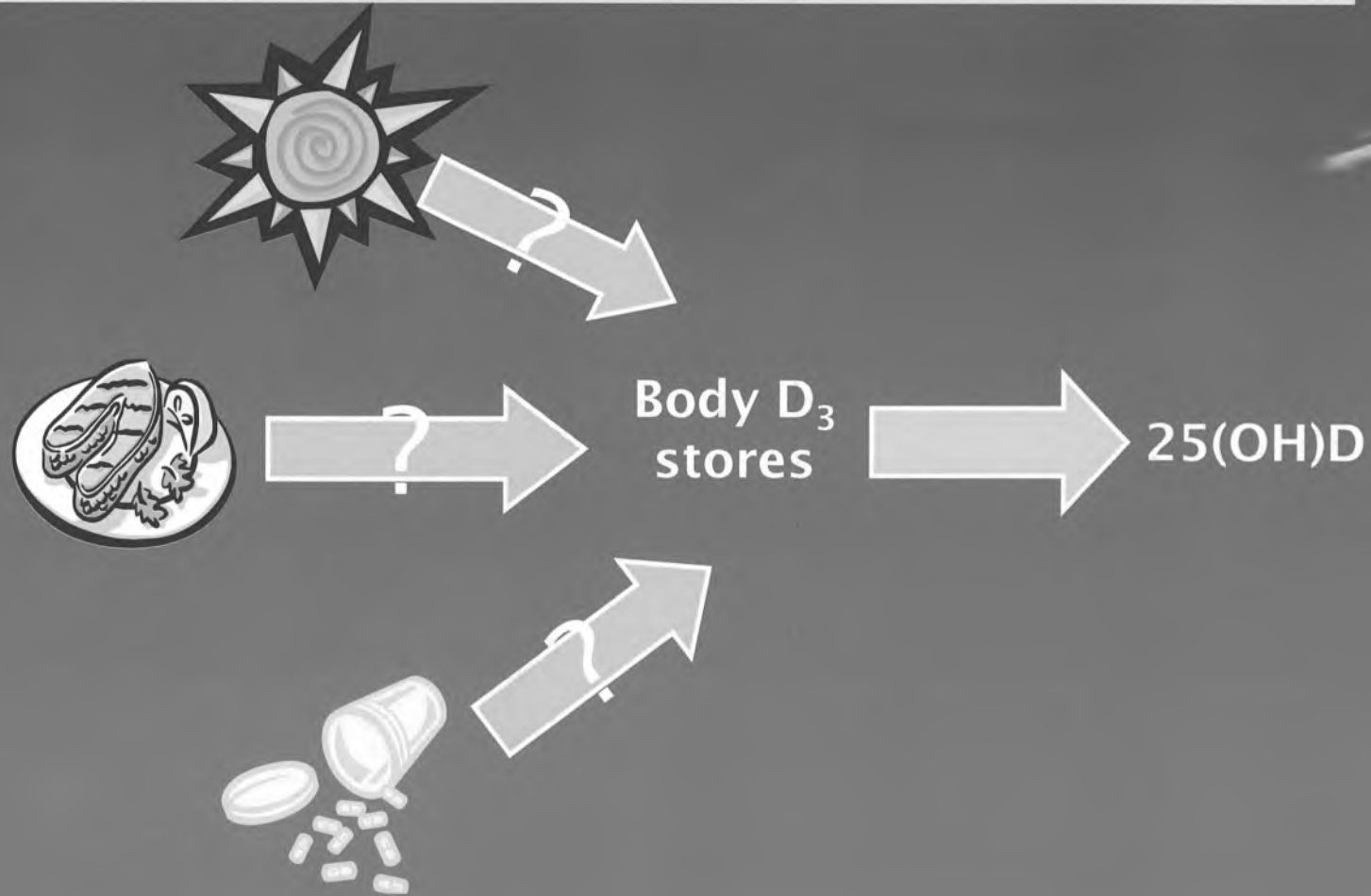
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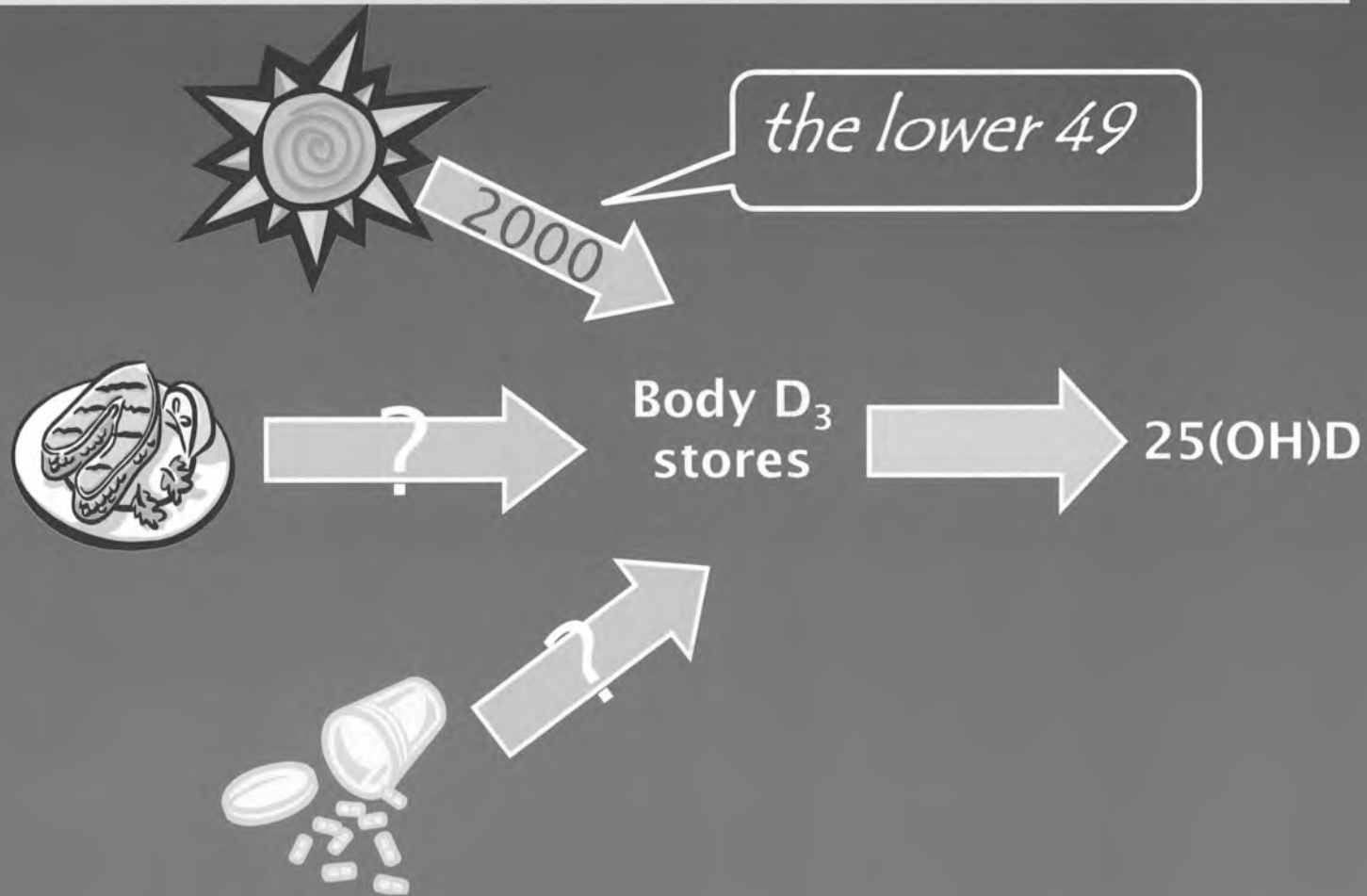
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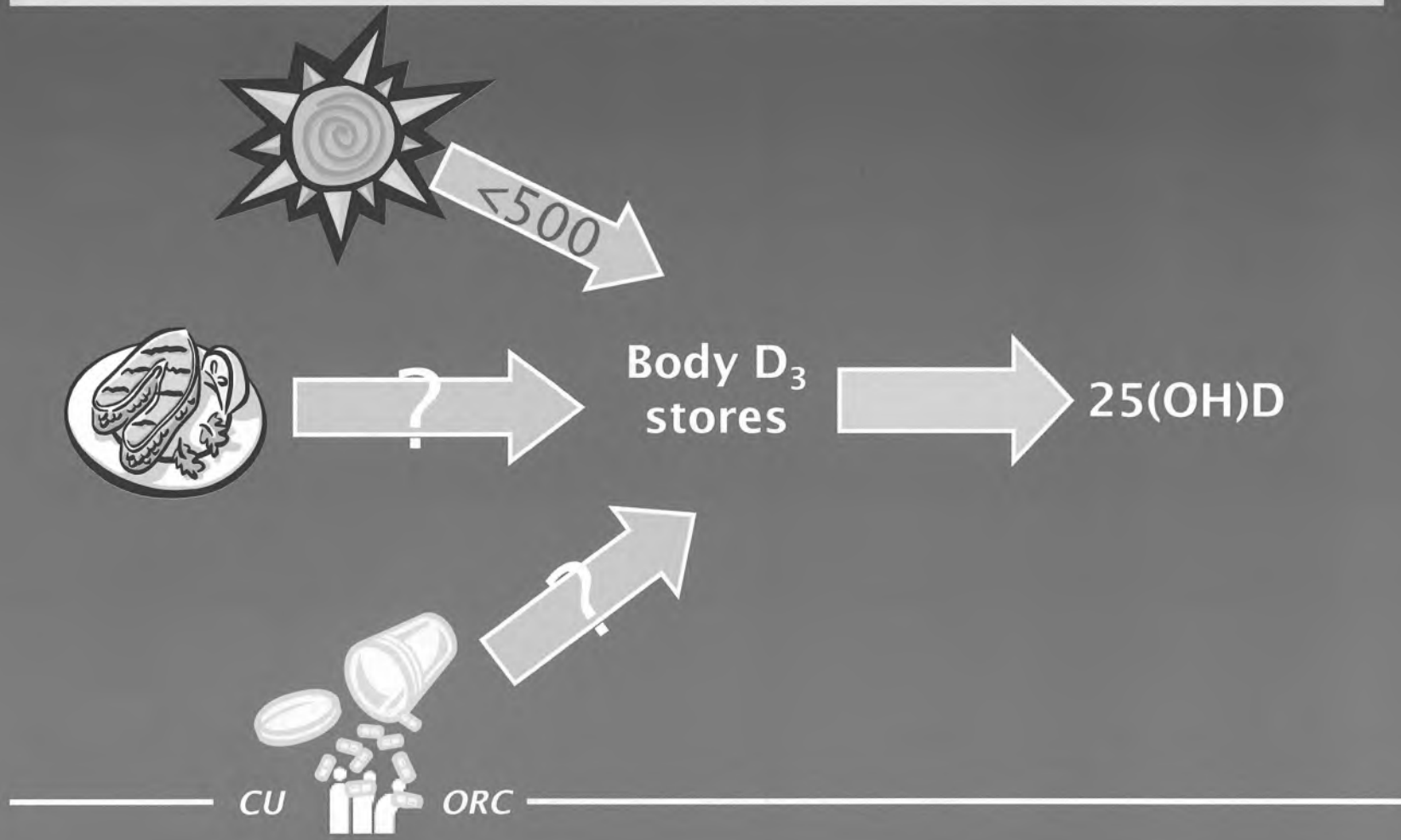


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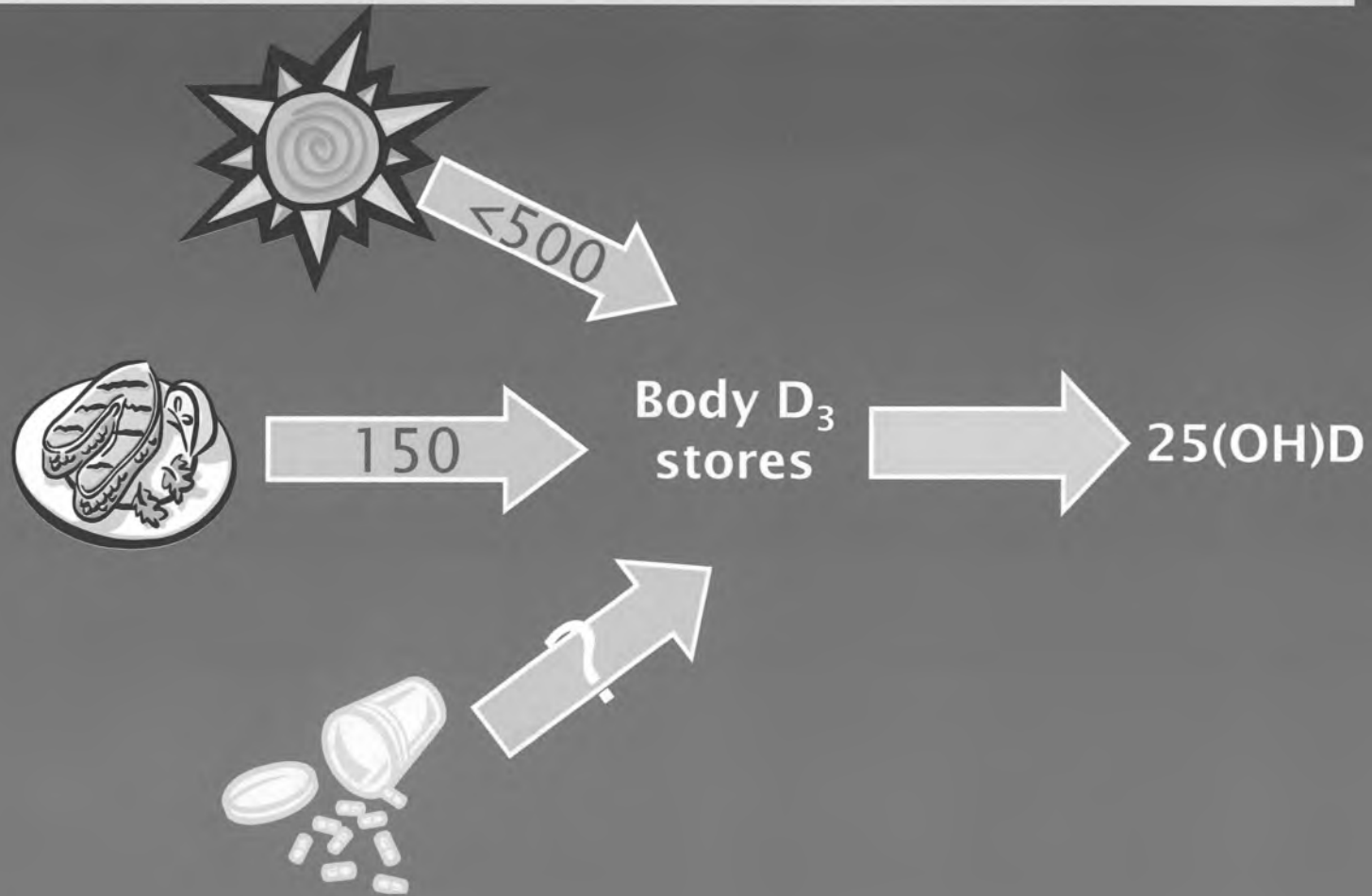


# VITAMIN D – Sources



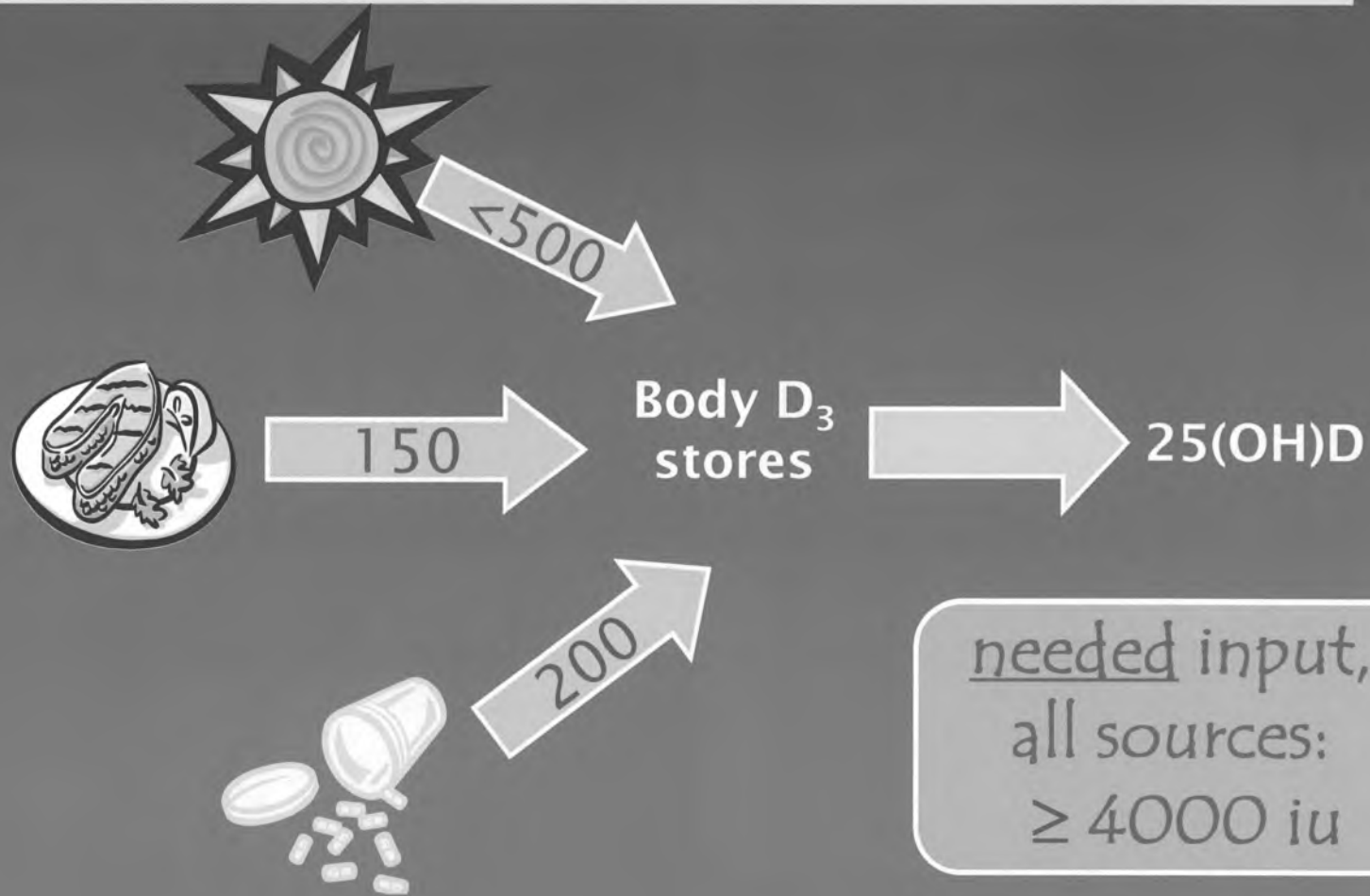
# VITAMIN D – Sources

---



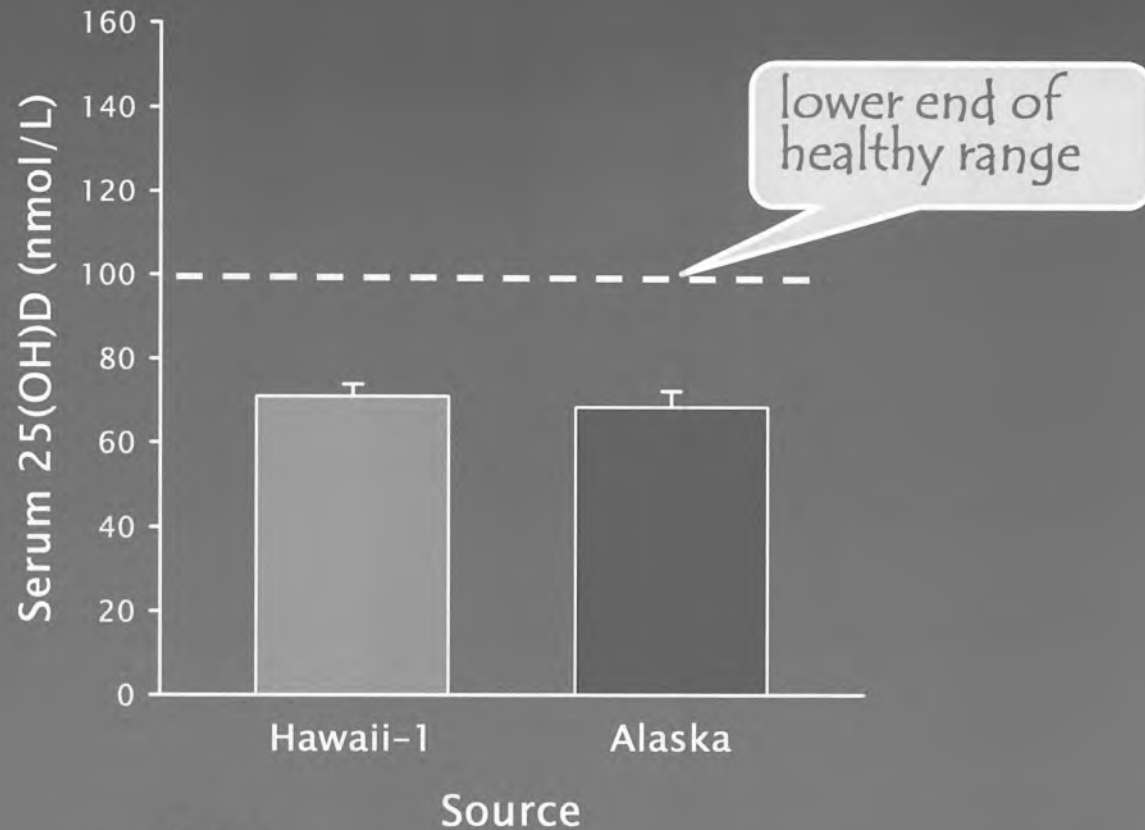
# VITAMIN D – Sources

---



# LATITUDE vs. SUN

---



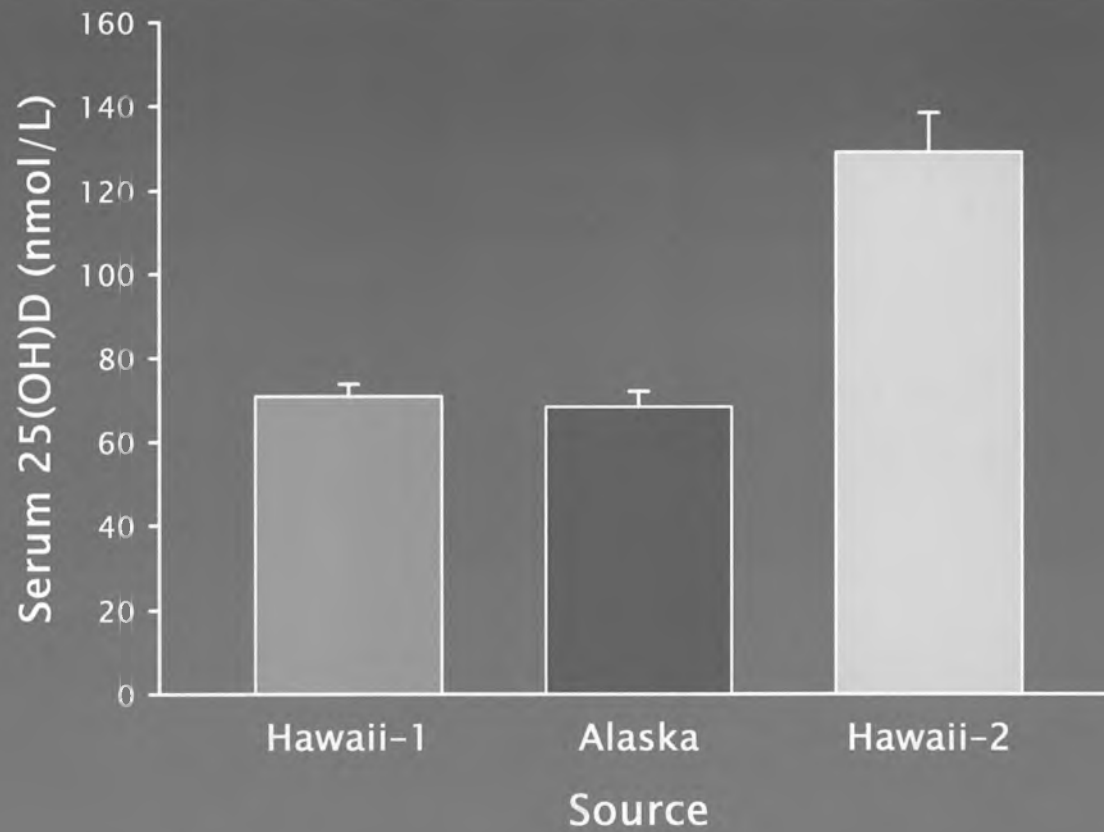
CU



ORC

# LATITUDE vs. SUN

---



---

CU



ORC

---

What is the evidence that this  
low vitamin D status matters?

# 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

# CLASSICAL VIT D DEFICIENCY

---

- rickets in children
- caused by poor absorption of calcium
  - leading to high PTH levels,
  - lowered renal phosphate threshold
  - hypophosphatemia
- serum 25(OH)D: < 10 ng/mL
- preventable by 200–400 IU D<sub>3</sub>/day
- that dose does *not* restore full Ca absorptive function

# RICKETS RISES AGAIN

---

- decreased sun exposure of babies
- maternal vitamin D deficiency
- failure to supplement infant feedings with vitamin D
- weaning infants to non-milk liquids

# CRANIOTABES IN “NORMAL” INFANTS\*

---

Note “hot cross bun” skull in this 5 mo old

1120 consecutive neonates in Japan  
22% had craniotabes  
median 25(OH)D at 1 mo: < 10 ng/mL

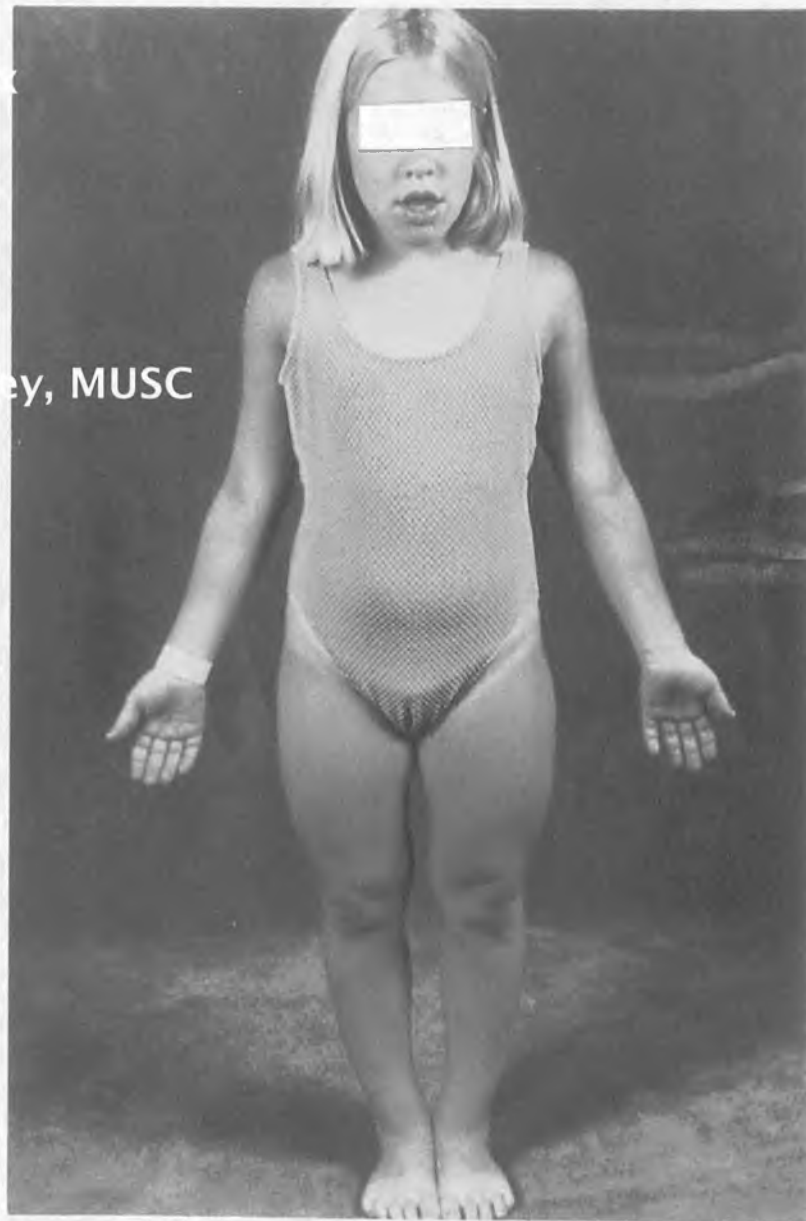
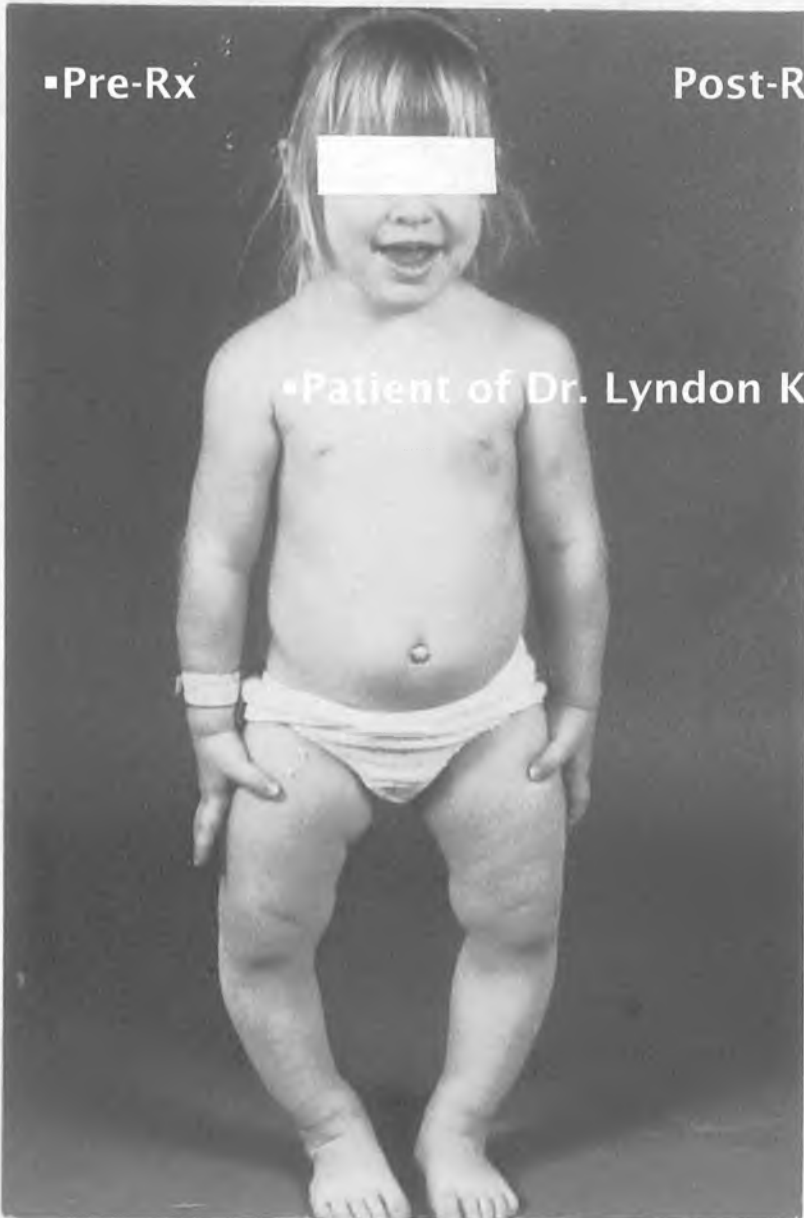
\*Yorifuji et al., JCEM; 93:1784-88 (2008)



▪Pre-Rx

Post-Rx

▪Patient of Dr. Lyndon Key, MUSC

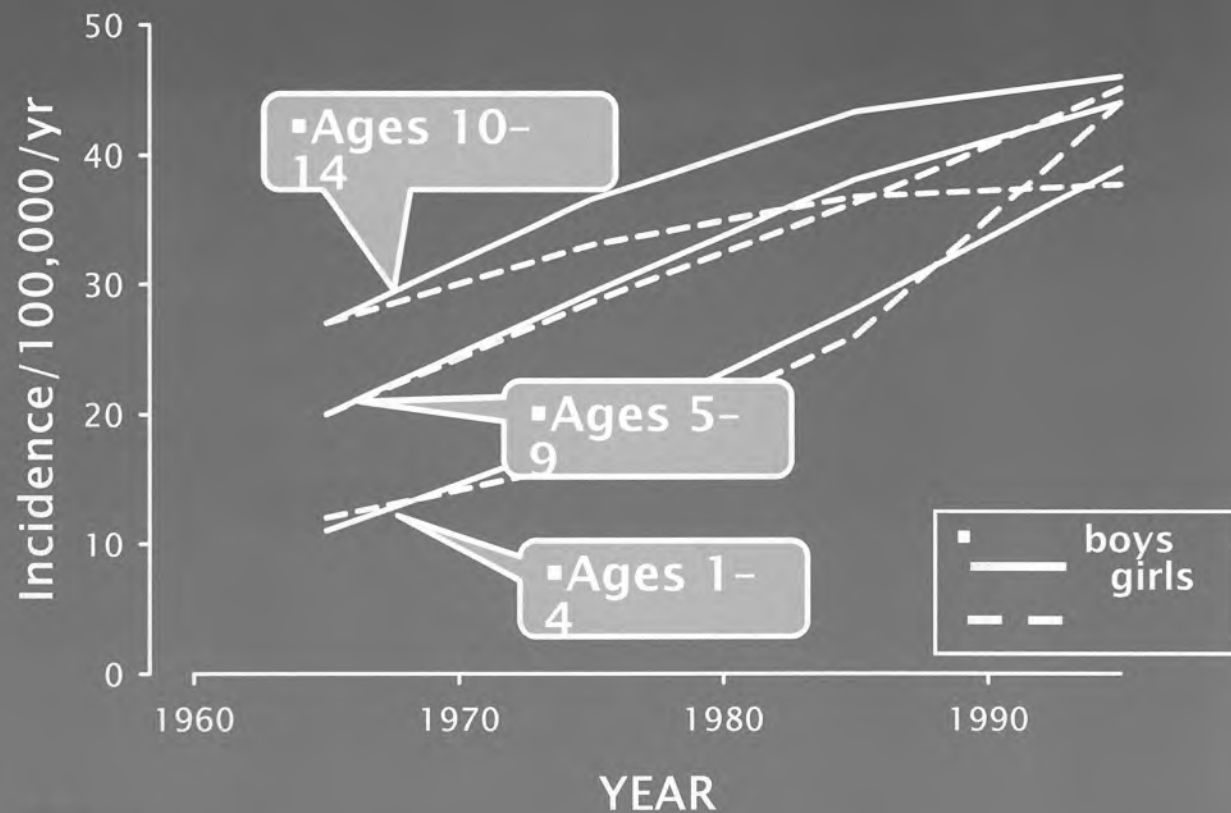


*Her rickets have healed*

*but –*

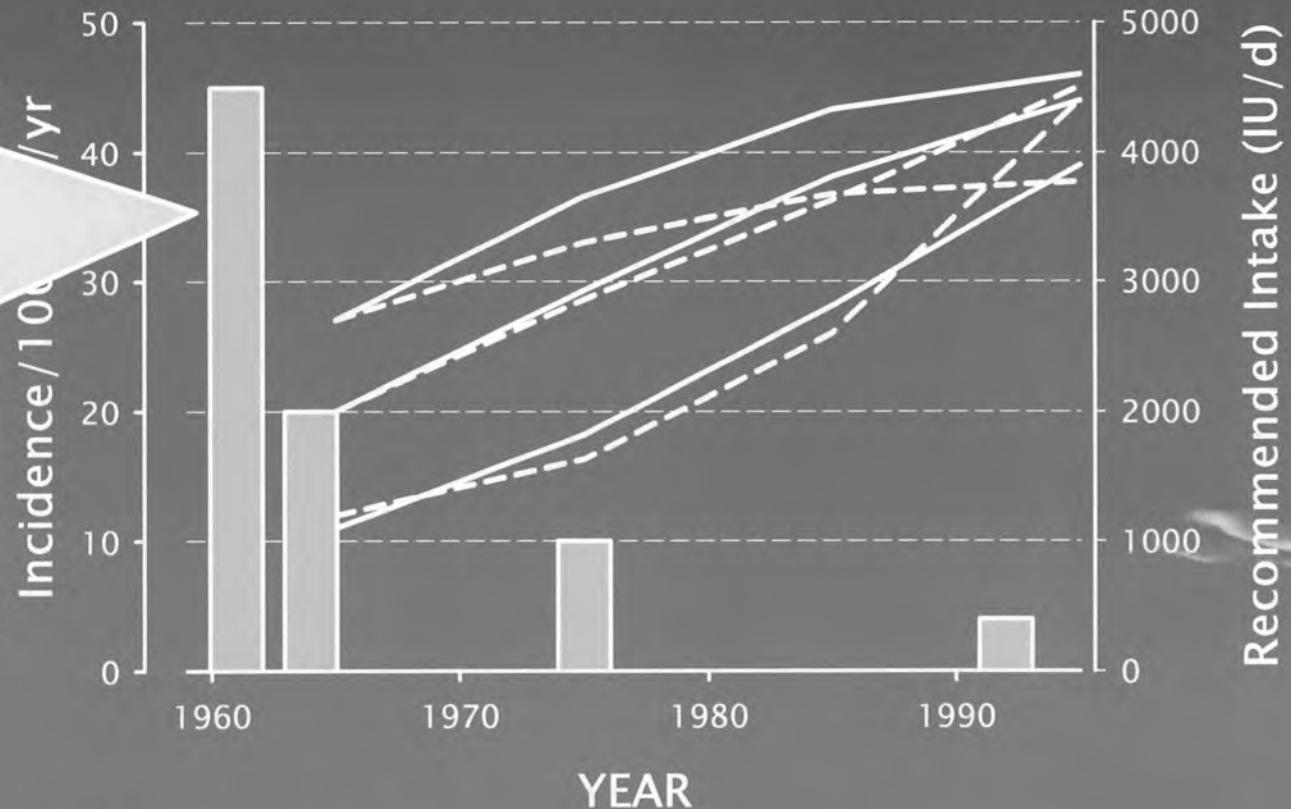
*does she have subtle long-term  
consequences of early life vitamin  
D deficiency?*

# JUVENILE DIABETES IN FINLAND\*



# JUVENILE DIABETES IN FINLAND\*

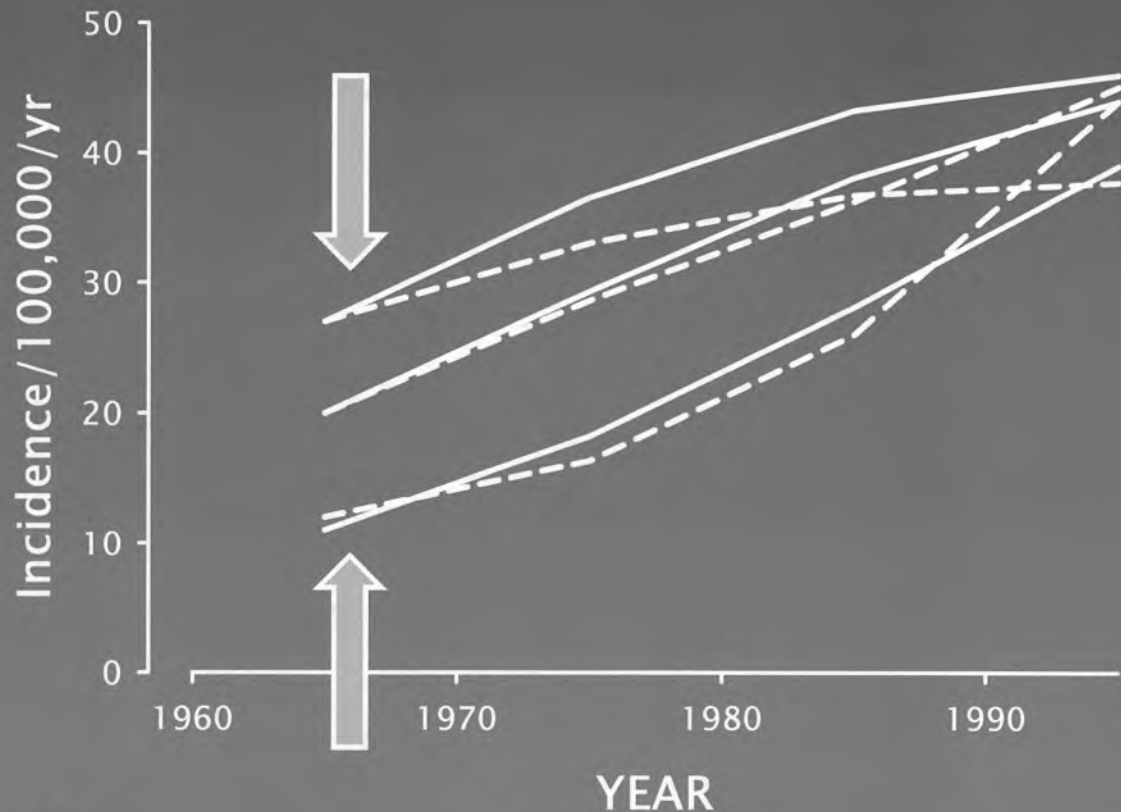
This dosage reflects the then common practice in E. Europe of giving 600,000 IU 3x per year during infancy



— CU  — ORC

\*Karvonen et al., (1999) Diabetes Care 22:1066-70

# JUVENILE DIABETES IN FINLAND\*

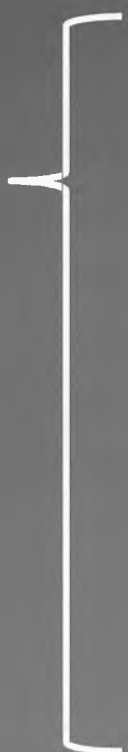


— CU  — ORC

\*Karvonen et al., (1999) Diabetes Care 22:1066-70

# NEONATAL VIT D & DIABETES\*


---

- 10,366 northern Finnish children
  - 2000 IU Vit D/d 1<sup>st</sup> year of life
- 
- those who got the recommended amount regularly
  - those who got it sometimes
  - those who got it never
  - those who got little or no vit D at all & were thought to have rickets

\*Hypponen et al., Lancet 2001;358:1500-03

# NEONATAL VIT D & DIABETES\*

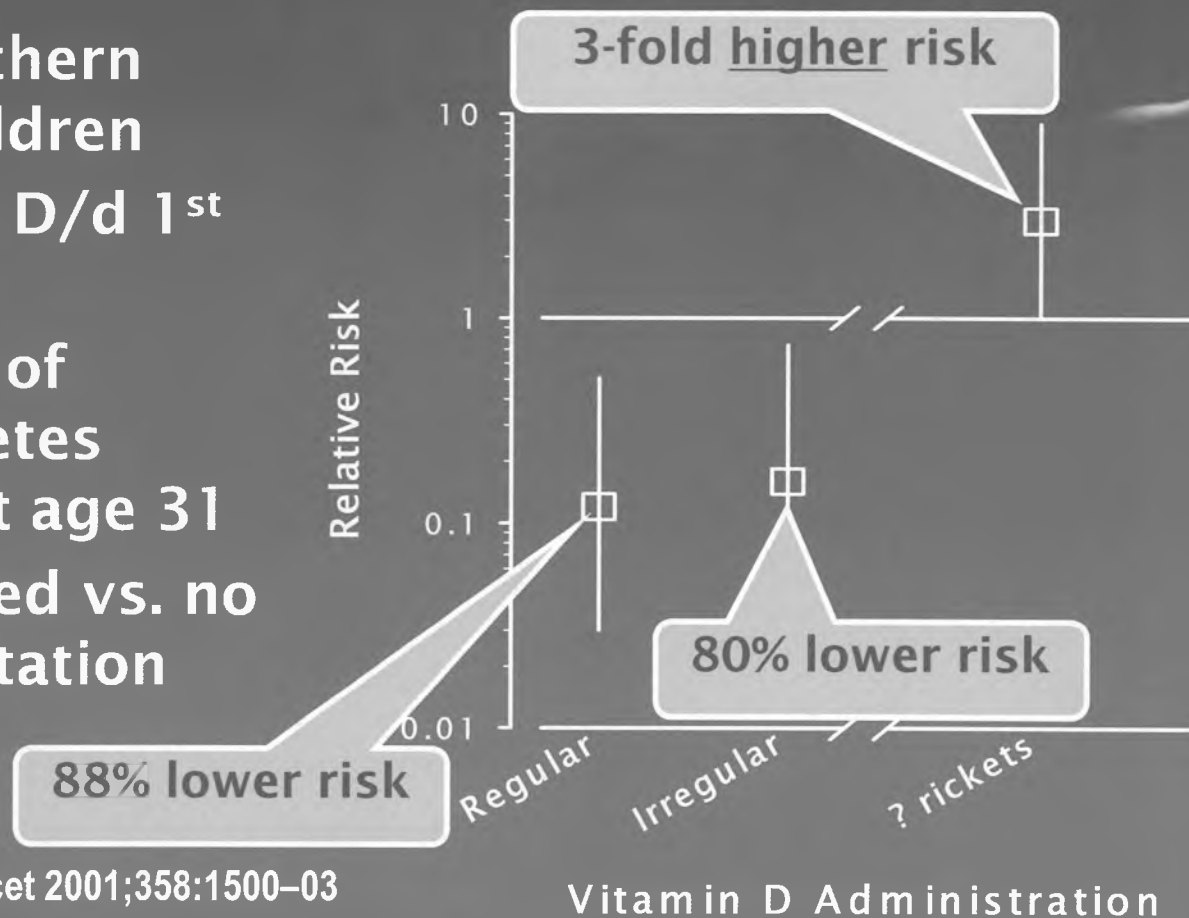
---

- 10,366 northern Finnish children
  - 2000 IU Vit D/d 1<sup>st</sup> year of life
  - prevalence of type I diabetes assessed at age 31
  - RR calculated vs. no supplementation
- 
- those who got the recommended amount regularly
  - those who got it sometimes
  - those who got it never
  - those who got little or no vit D at all & were thought to have rickets

▪\*Hypponen et al., Lancet 2001;358:1500-03

# NEONATAL VIT D & DIABETES\*

- 10,366 northern Finnish children
- 2000 IU Vit D/d 1<sup>st</sup> year of life
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▪\*Hypponen et al., Lancet 2001;358:1500-03

# WHAT ARE THE CONSEQUENCES?

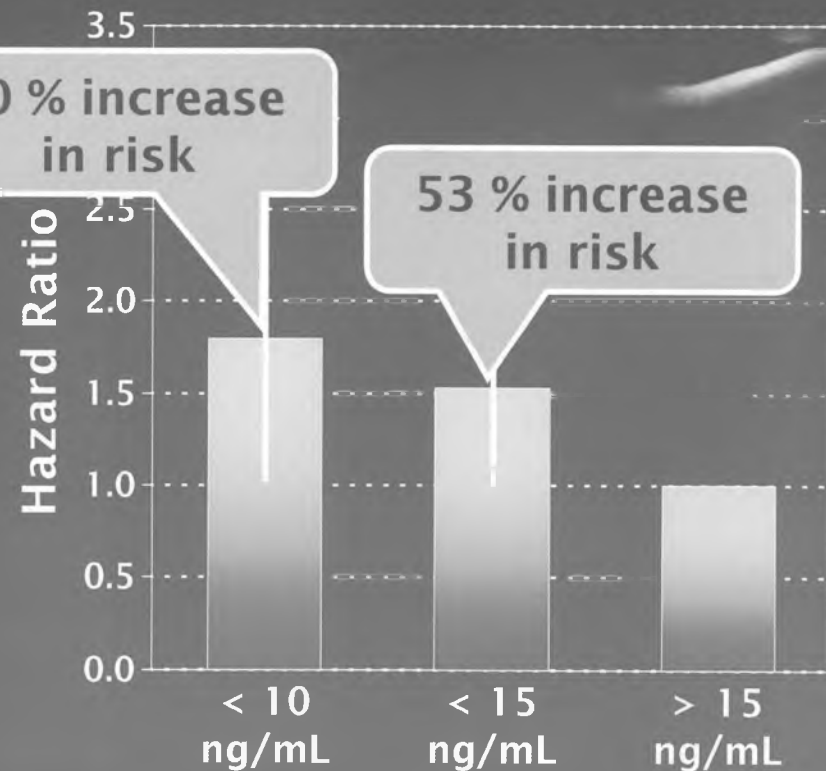
---

- the burden of chronic diseases, most of which are multi-factorial, is made worse by inadequate vitamin D status
- we won't be able to know the true size of that burden until we eradicate vitamin D deficiency
- for some disorders the vitamin D component may account for as much as half (or more) of the total burden



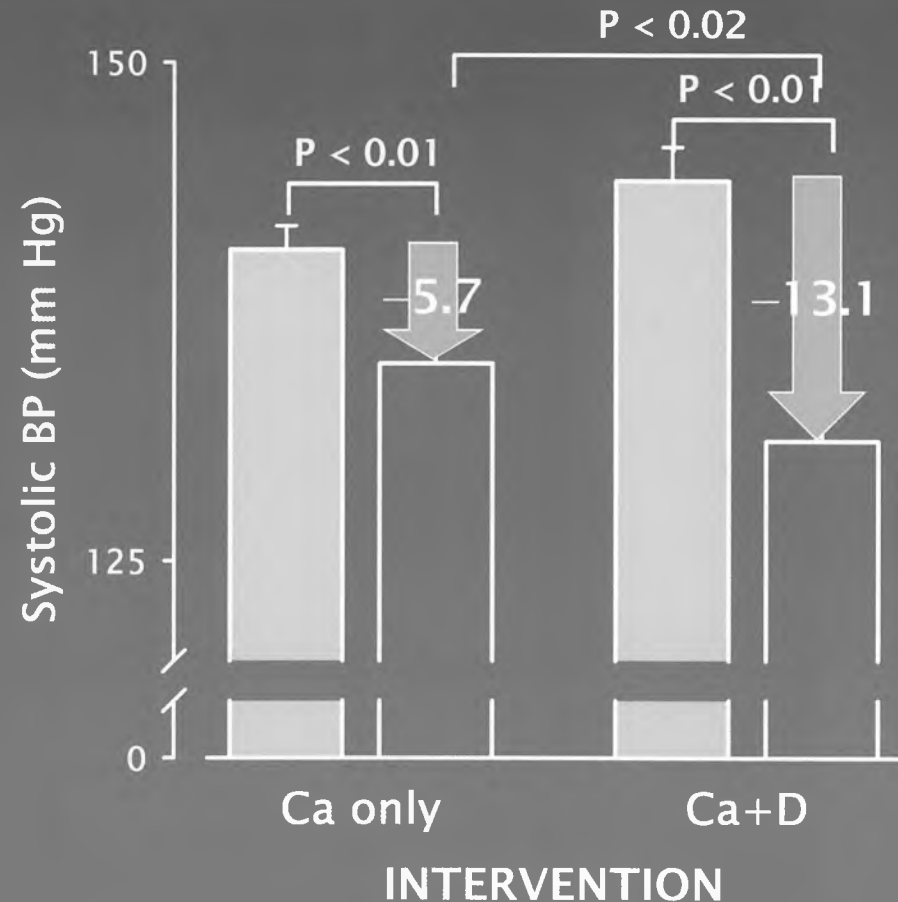
# VIT D & CARDIOVASCULAR DISEASE

- 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*



# CALCIUM, VIT D, & BLOOD PRESSURE\*

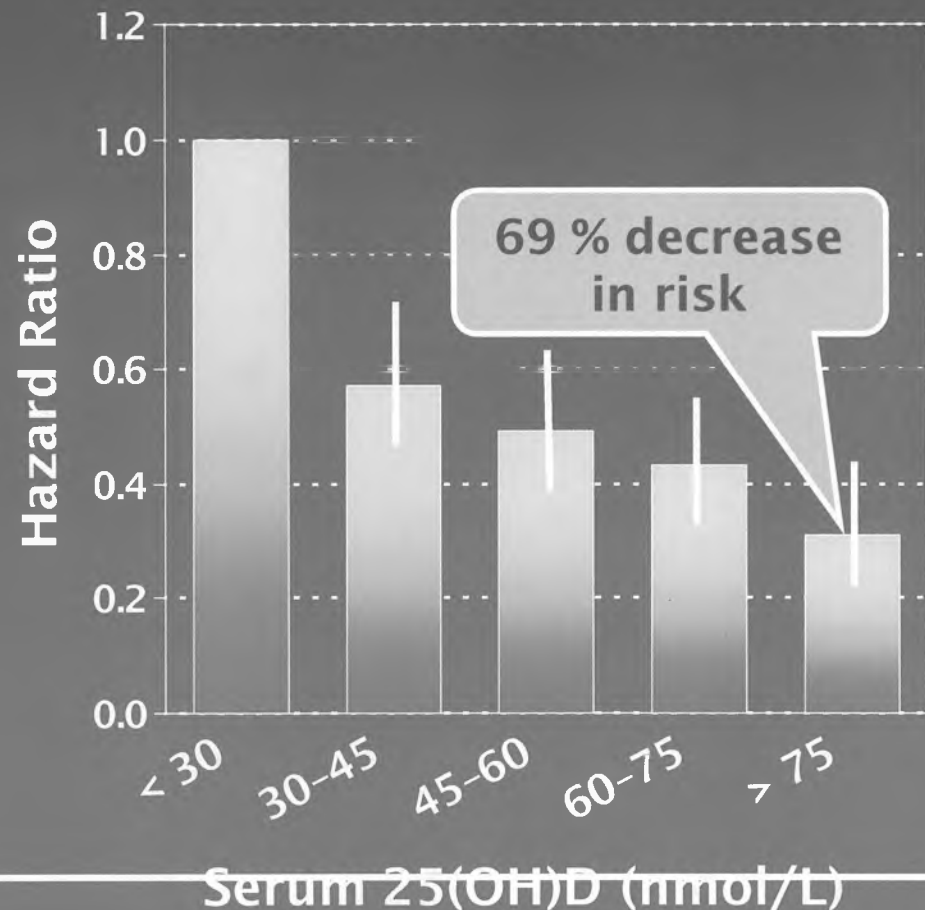
- 148 women, aged  $74 \pm 1$
- DB-RCT
- baseline 25(OH)D  $< 50$  nmol/L
- treated for 8 wks with:  
Ca 1200 mg/d or  
Ca + 800 IU vit D/d



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

# 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*



CU

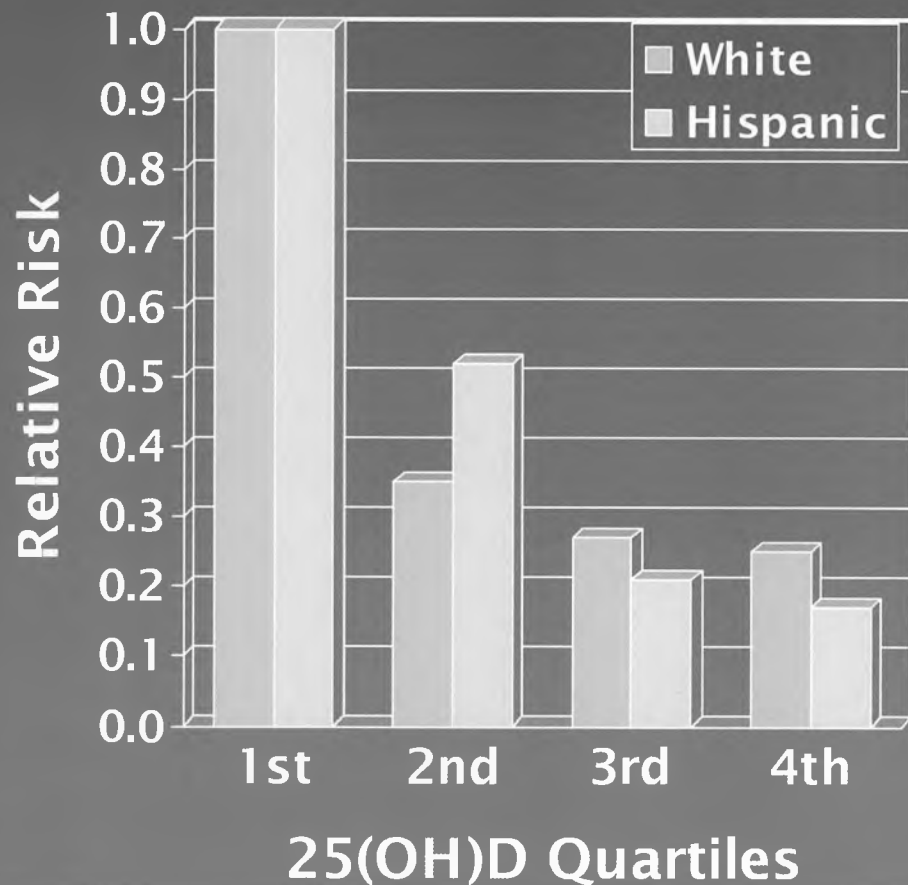


ORC

Serum 25(OH)D (nmol/L)

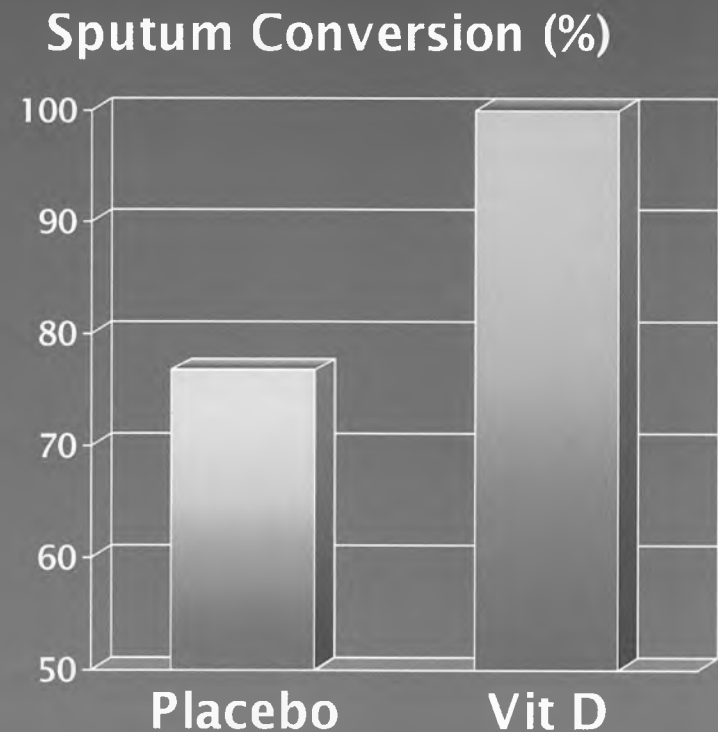
# DIABETES & 25(OH)D

- Scragg et al., 2004  
Diabetes Care  
27:2813-18
- NHANES-III
- 6,228 adults
- plasma glucose independently predicted by BMI & serum 25OHD (fasting and 2 hr post load)



# VITAMIN D & INFLUENZA\*

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



CU

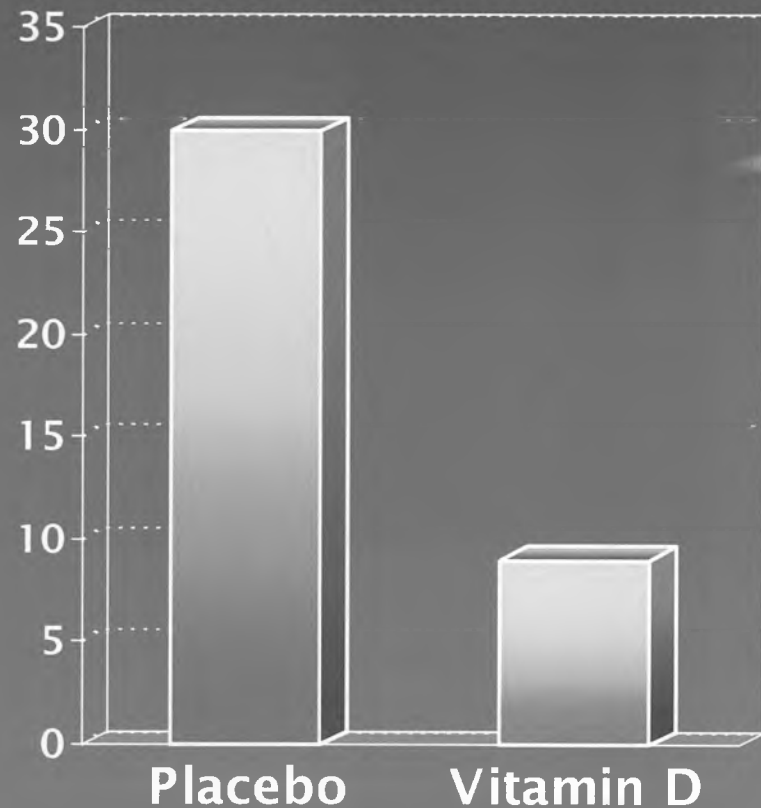


ORC

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

# VITAMIN D & CAESAREANS\*

- 253 women
- Boston Med Cntr
- 43 primary caesareans
  - 17 failure to progress
  - 14 fetal signs
  - 6 malpresentation
  - 6 miscellaneous
- 25(OH)D measured shortly after birth



CU

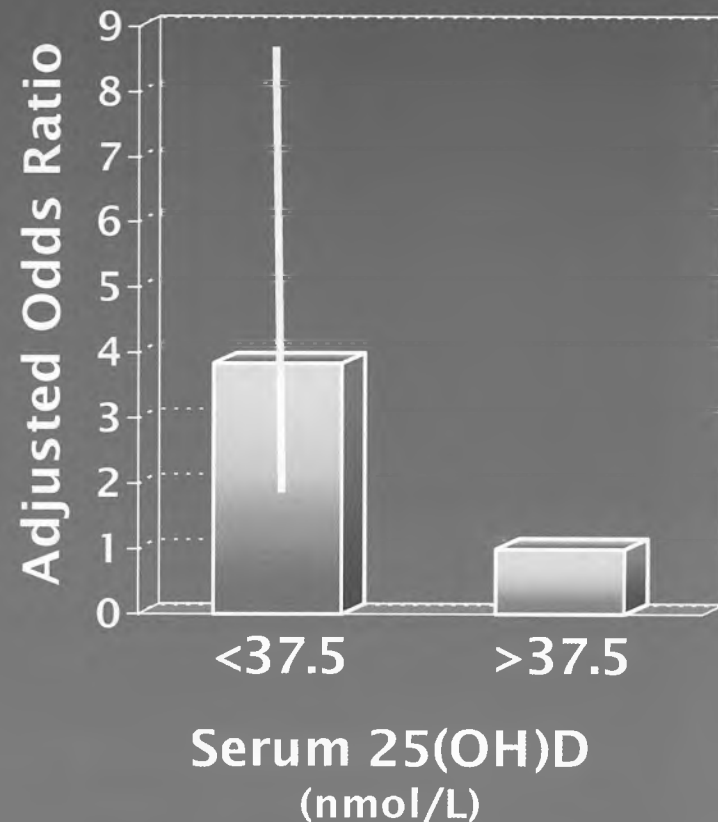


ORC

\*Merewood et al., JCEM (epub Dec 2008)

# VITAMIN D & CAESAREANS\*

- 253 women
- Boston Med Cntr
- 43 primary caesareans
- multiply adjusted OR for Caesarean in women above or below < 37.5: 3.84
- P < 0.001



CU

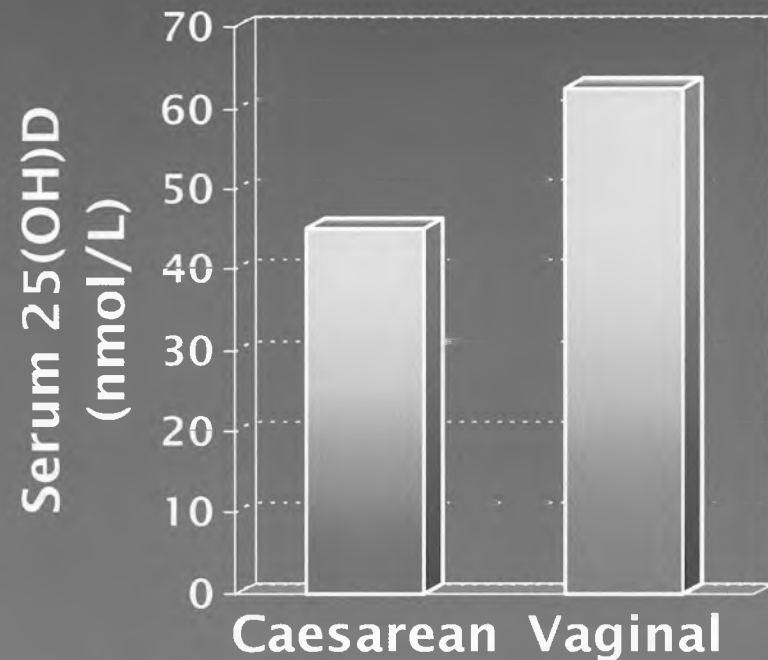


ORC

\*Merewood et al., JCEM (epub Dec 2008)

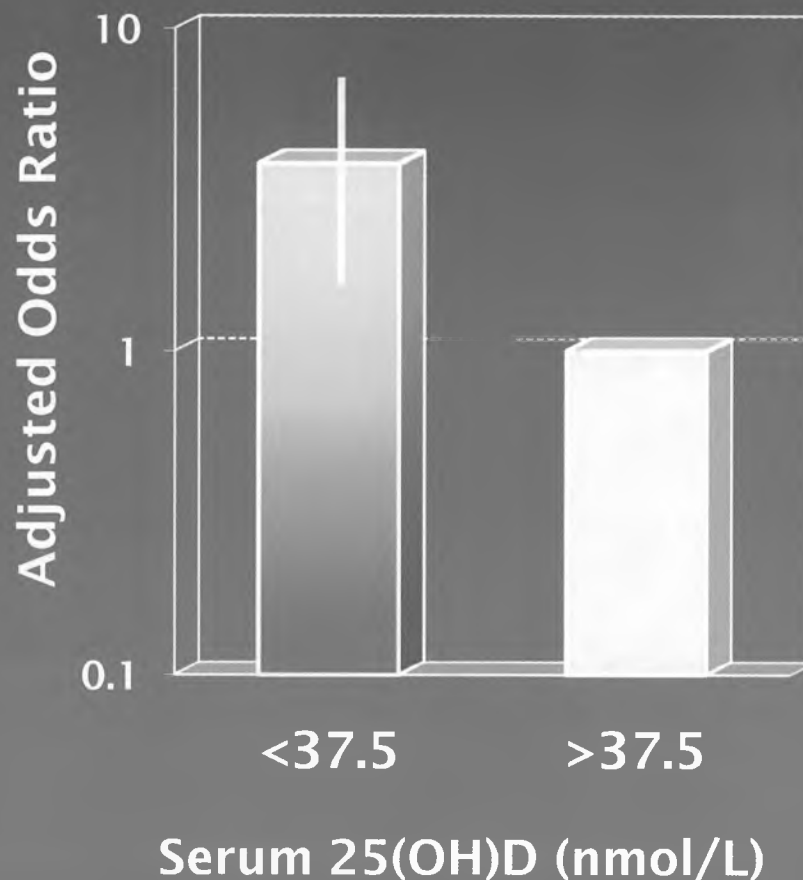
# VITAMIN D & CAESAREANS\*

- 253 women
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- 25(OH)D measured shortly after birth



# VITAMIN D & CAESAREANS\*

- 253 women
- Boston Med Cntr
- 43 primary caesareans
- multiply-adjusted OR for Caesarean in women with 25(OH)D < 37.5: 3.84 (CI: 1.71–8.62; P < 0.001)



▪\*Merewood et al., JCEM (epub Dec 2008)

# VIT D & PREGNANCY OUTCOMES\*

---

- DB-RCT; N = 690 pregnant women
- dosed with 400, 2000, & 4000 IU/d from wk 12 to delivery

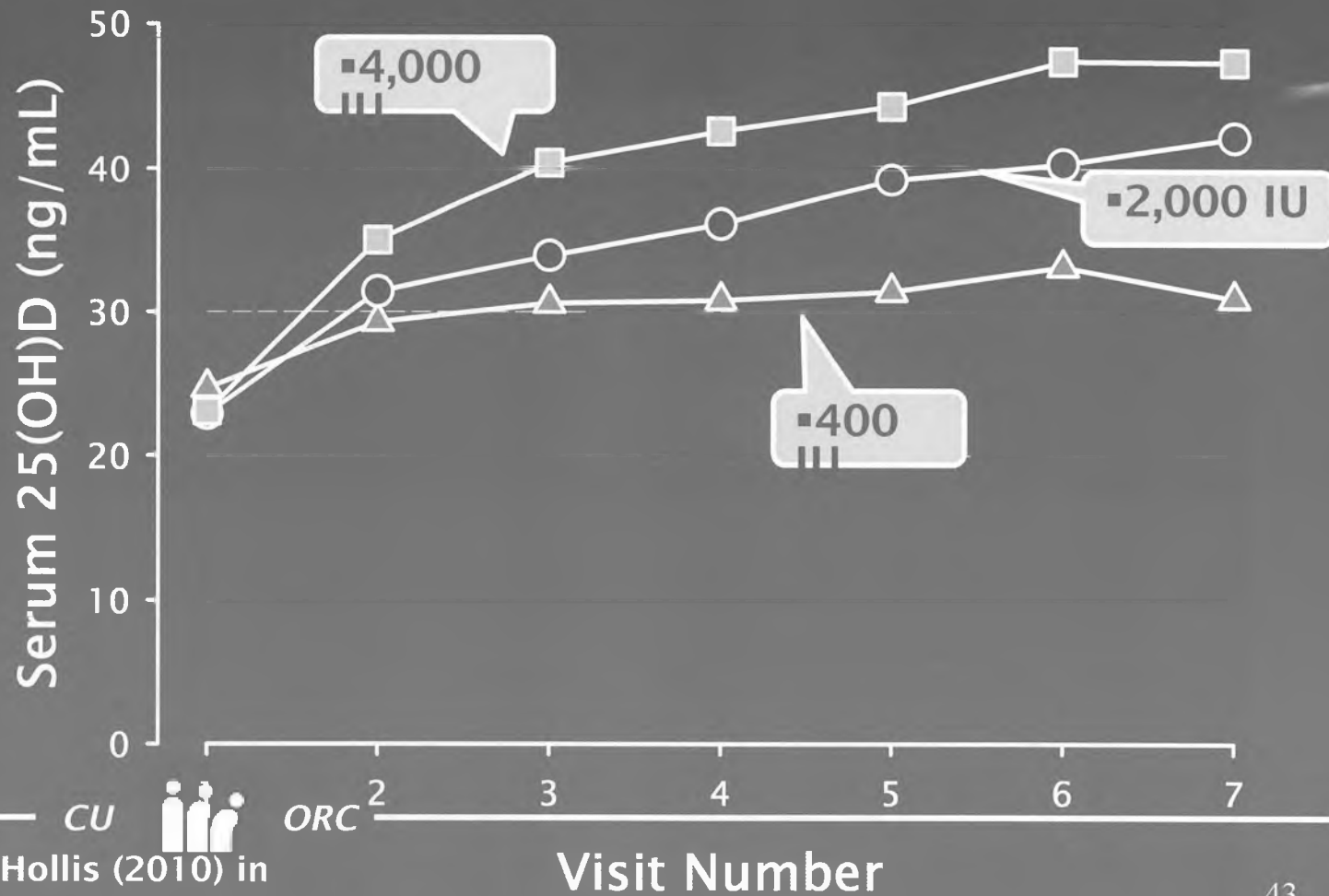
CU



ORC

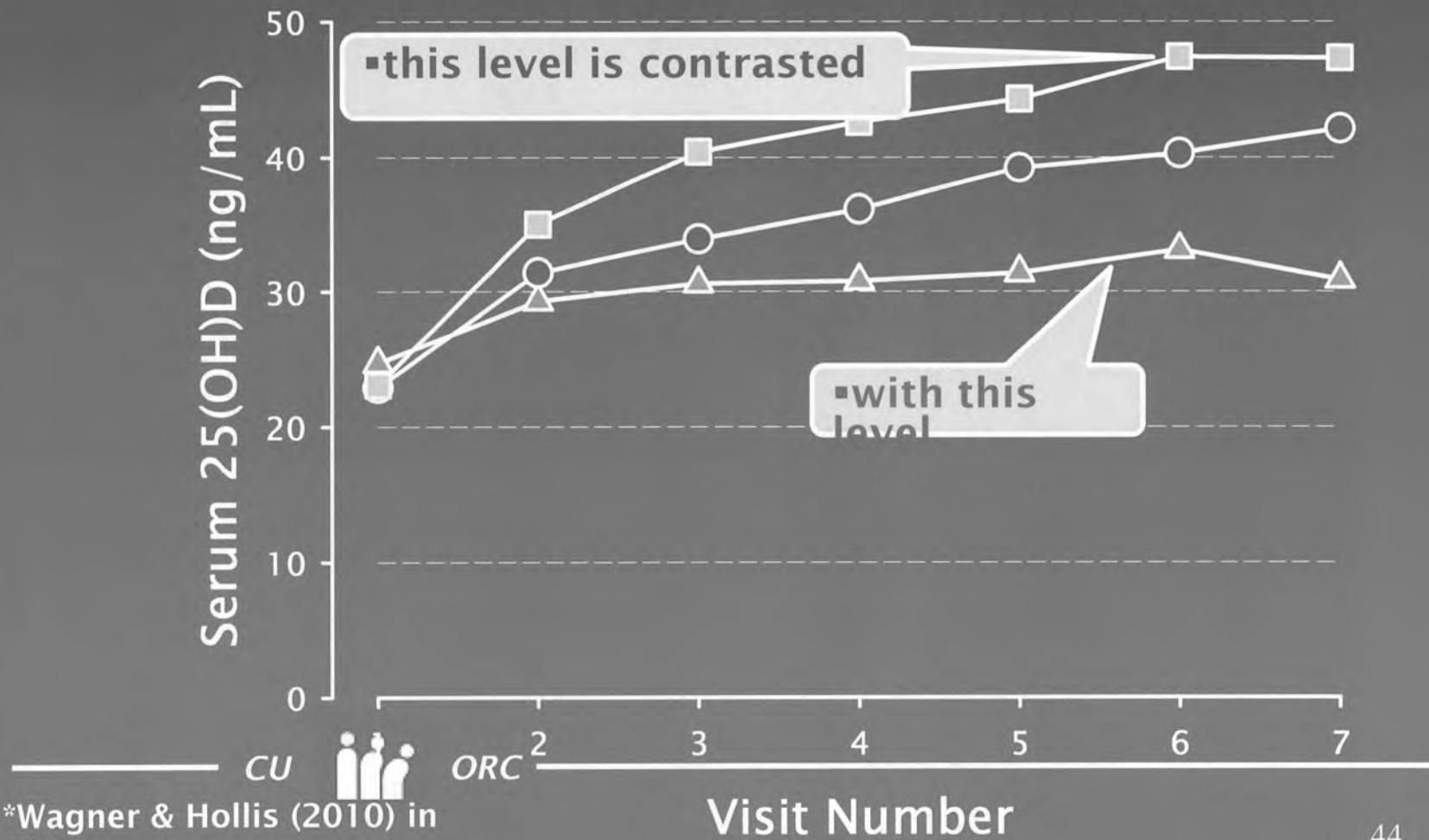
▪\*Wagner & Hollis (2010) in press

# VIT D & PREGNANCY OUTCOMES\*



\*Wagner & Hollis (2010) in press

# VIT D & PREGNANCY OUTCOMES\*



\*Wagner & Hollis (2010) in press

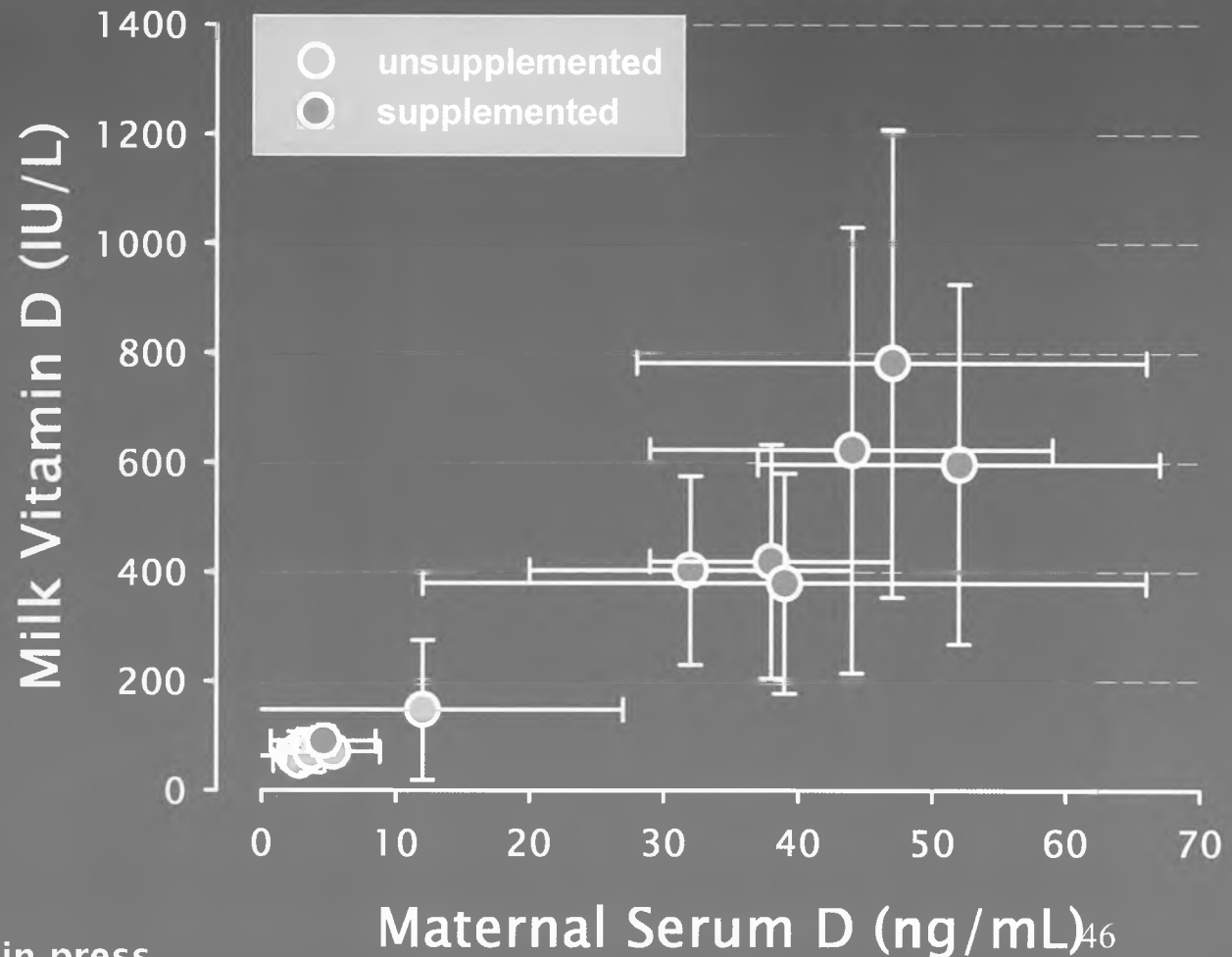
# VIT D & PREGNANCY OUTCOMES\*

---

- DB-RCT; N = 690 pregnant women
- dosed with 400, 2000, & 4000 IU/d from wk 12 to delivery
- risk of untoward outcomes reduced by half:
  - pre-term delivery (P < 0.01)
  - gestational diabetes, pre-eclampsia, hypertension (P < 0.01)
  - periodontal disease (P < 0.05)
  - neonatal infection (P < 0.05)

# VIT D & NURSING OUTCOMES\*

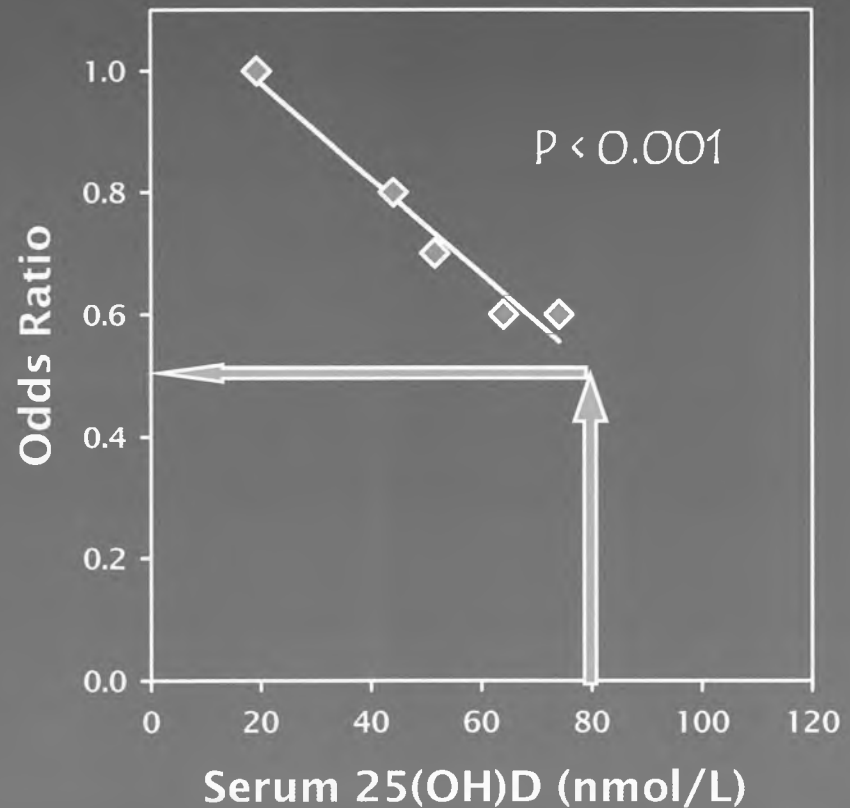
- n = 12
- dose:  
6400  
IU/d



▪\*Hollis & Wagner (2009) in press

# COLORECTAL CANCER

- 5 prospective studies
- > 200,000 individuals
- 430 cases
- ORs computed for 25(OH)D quantiles
- Garland et al, 2005



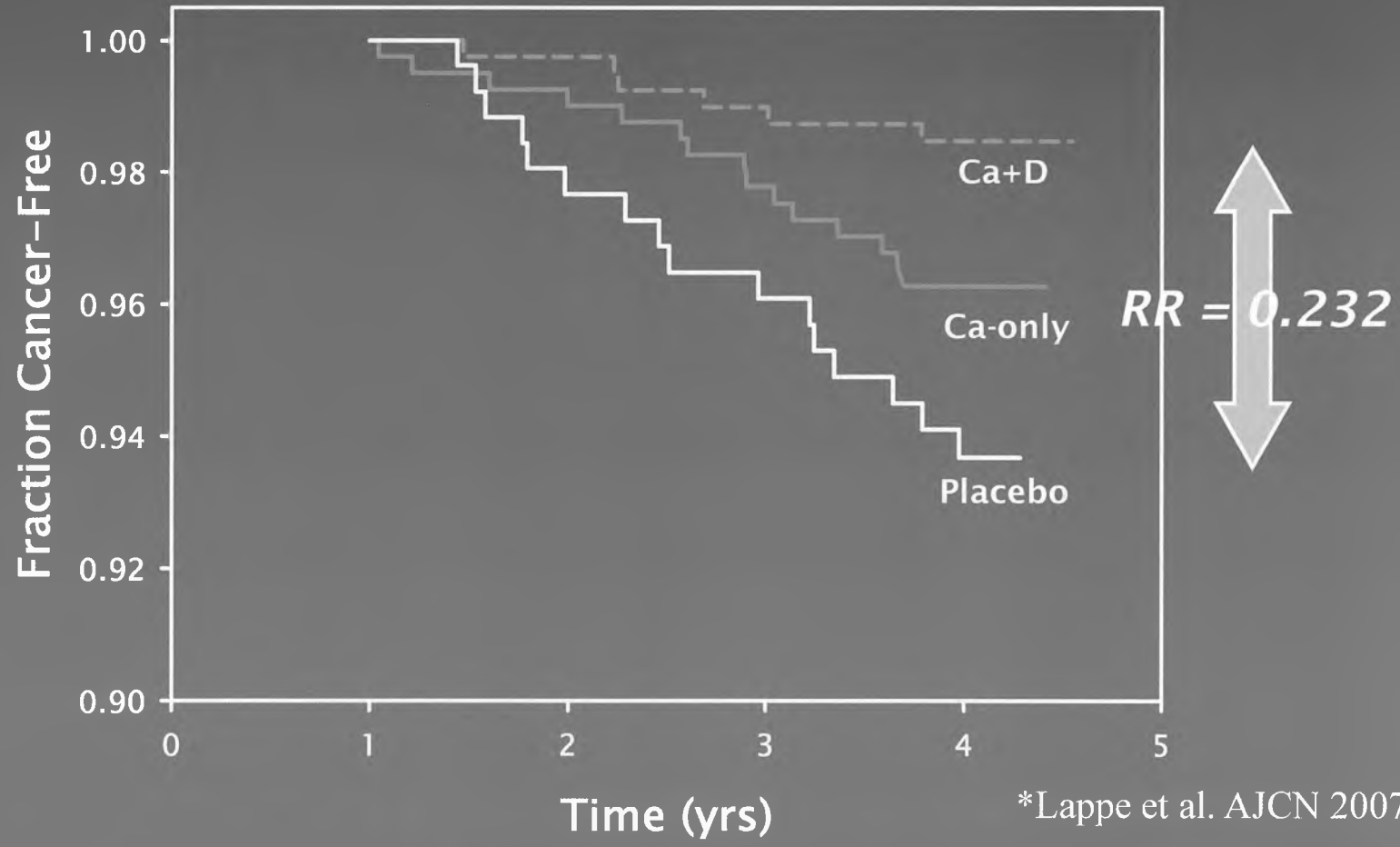
# VITAMIN D & CANCER\*

---

- 1179 healthy women
- aged  $66.7 \pm 7.3$
- four year trial
- 1032 finished (87.5%)
- baseline 25(OH)D:  $71.8 \text{ nmol/L} \pm 20.3$
- three treatment groups:
  - control
  - Ca (1400–1500 mg/d)
  - Ca plus D<sub>3</sub> (1100 IU/d)
- achieved 25(OH)D:  $96 \text{ nmol/L} \pm 21.4$



# VITAMIN D & CANCER\*



\*Lappe et al. AJCN 2007

## **CANCERS BY TREATMENT (YRS 2-4)**

<b>Site</b>	<b>Placebo (n=266)</b>	<b>Ca+D (n = 403)</b>
<b>Breast</b>	<b>7 (2.6%)</b>	<b>4 (1.0%)</b>
<b>Colon</b>	<b>2 (0.7%)</b>	<b>0 (0.0%)</b>
<b>Lung</b>	<b>3 (1.1%)</b>	<b>1 (0.2%)</b>
<b>Marrow/Lymphoma</b>	<b>4 (1.5%)</b>	<b>2(0.5%)</b>
<b>Other</b>	<b>2 (0.7%)</b>	<b>1 (0.2%)</b>
<b>Total*</b>	<b>18 (6.8%)</b>	<b>8 (2.0%)*</b>

\* P < 0.05

# STATUS OF THE EVIDENCE

---

- there are now more than 40 randomized controlled trials evaluating a causal connection between serum 25(OH)D levels and various health outcomes
  - 15+ osteoporotic fractures
  - 7+ falls
  - 3 hypertension
  - 1 cancer
  - 1 adjuvant tuberculosis therapy
  - 3 respiratory infection risk
  - 3 pregnancy outcomes
  - 1 periodontal disease
  - 3 insulin sensitivity & diabetes

Two questions: –

How can a single nutrient have such diverse effects in so many different tissues ?

If these effects are correct, why haven't they been apparent previously ?

# CELL MODELS

---

*old:*



- DNA in somatic cells functions mainly to make faithful copies for tissue repair or replacement

*new:*

- DNA functions constantly in synthesis of needed cellular apparatus

# CELL MODELS

---

*old:*

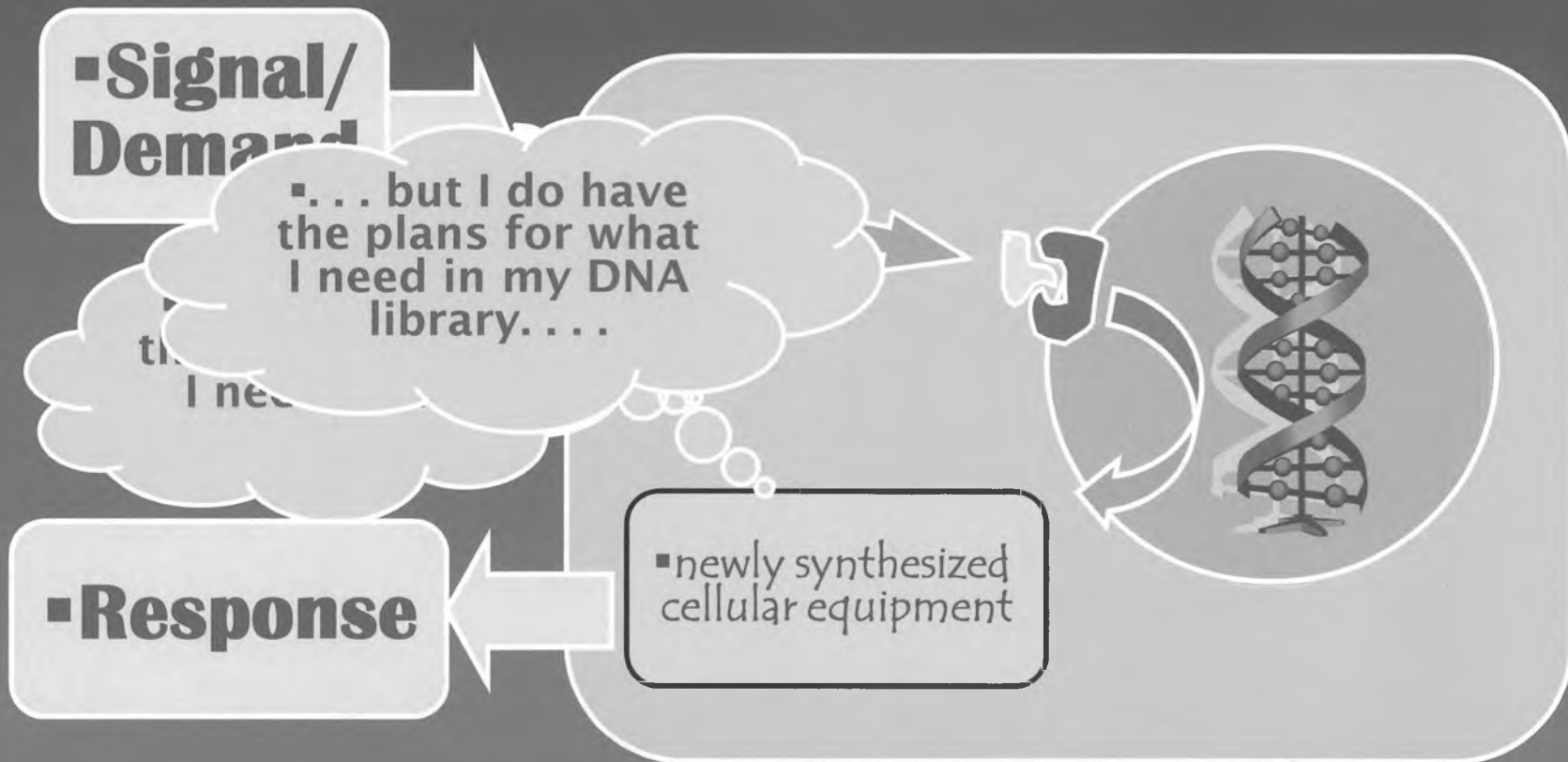


- cell/tissue differentiation meant that each cell type contained different cytoplasmic apparatus

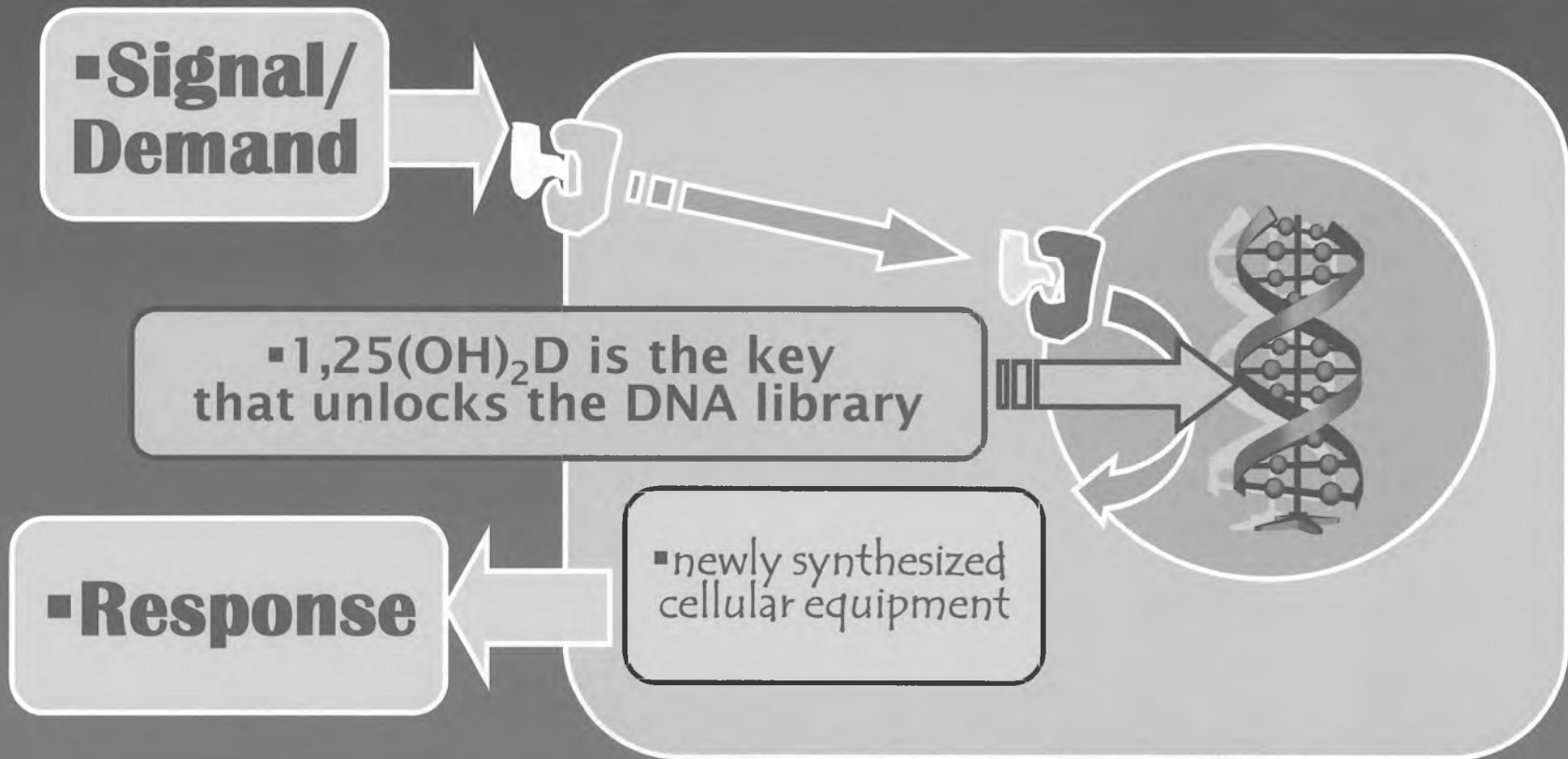
*new:*

- cell/tissue differentiation meant that only certain genes can be accessed in each tissue

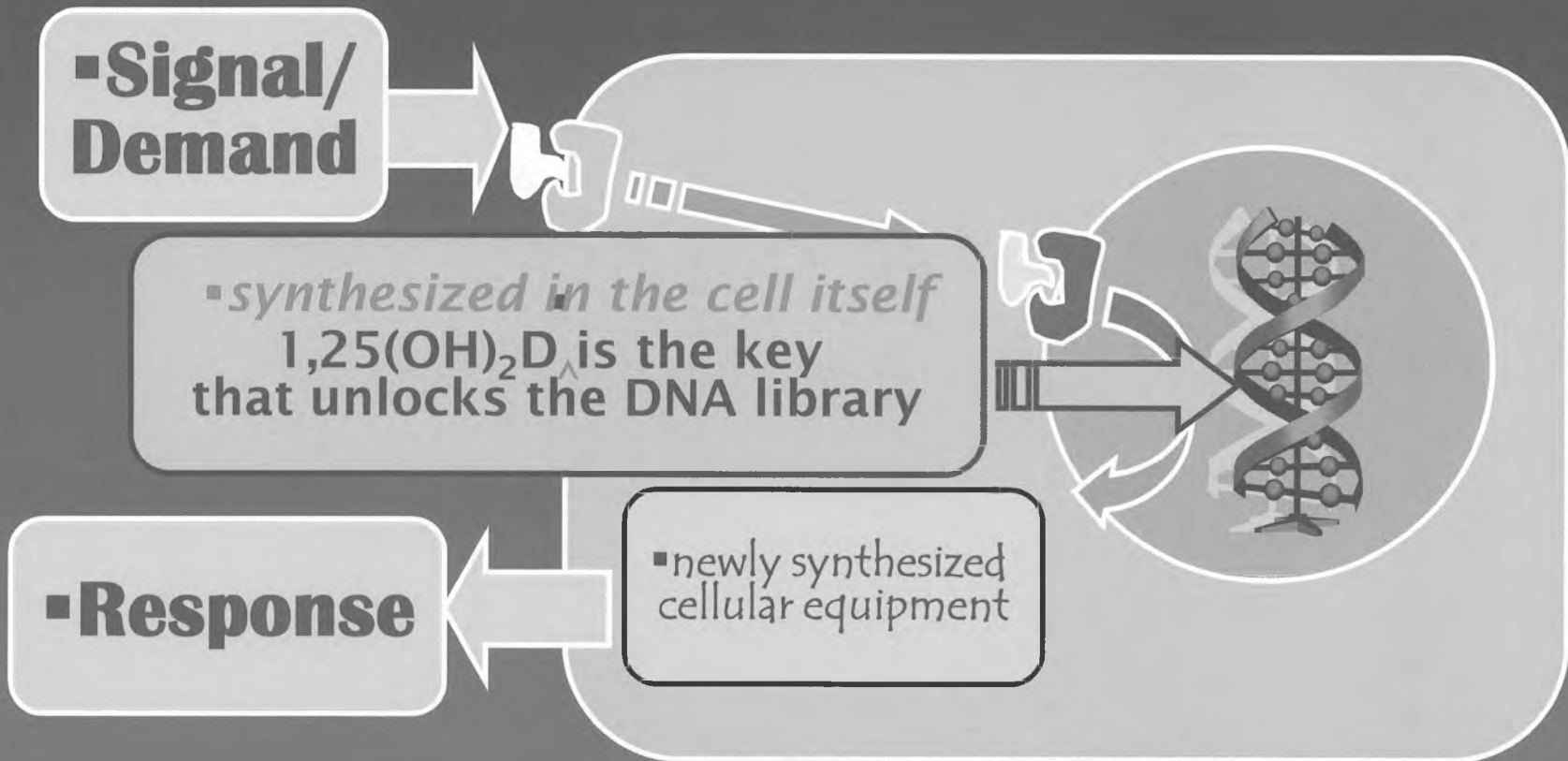
# HOW A CELL RESPONDS



# HOW A CELL RESPONDS



# HOW A CELL RESPONDS



things go  
better  
with  
**Vitamin D**

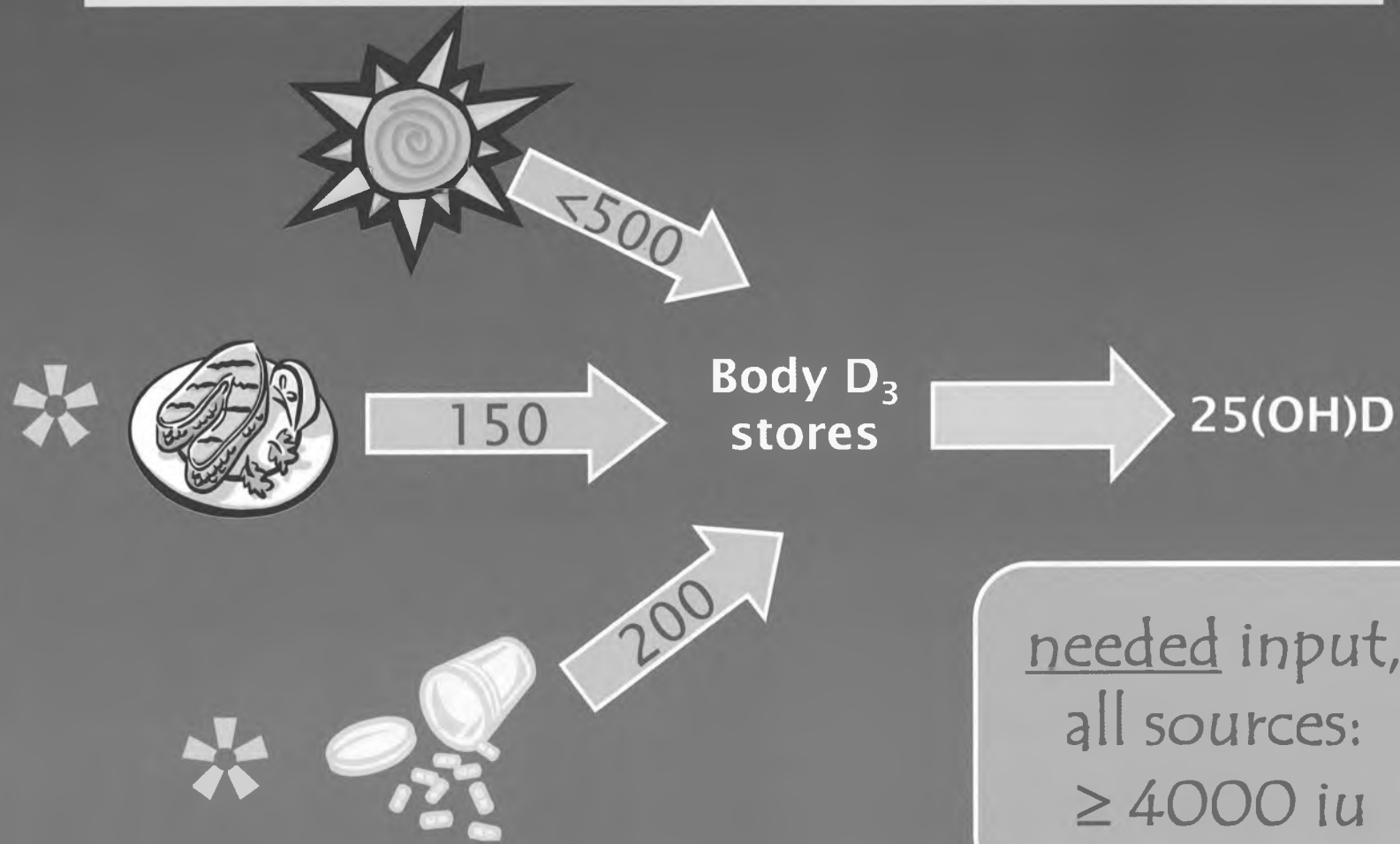
# PERSPECTIVE

---

- vitamin D is an integral component of the mechanism whereby cells control gene transcription in response to a variety of extracellular stimuli
- adequate vitamin D status enables optimal response to a broad variety of signals
- expression of deficiency status will vary from person to person depending upon tissue-specific sensitivity



# VITAMIN D – Sources



*needed input,  
all sources:  
≥ 4000 iu*

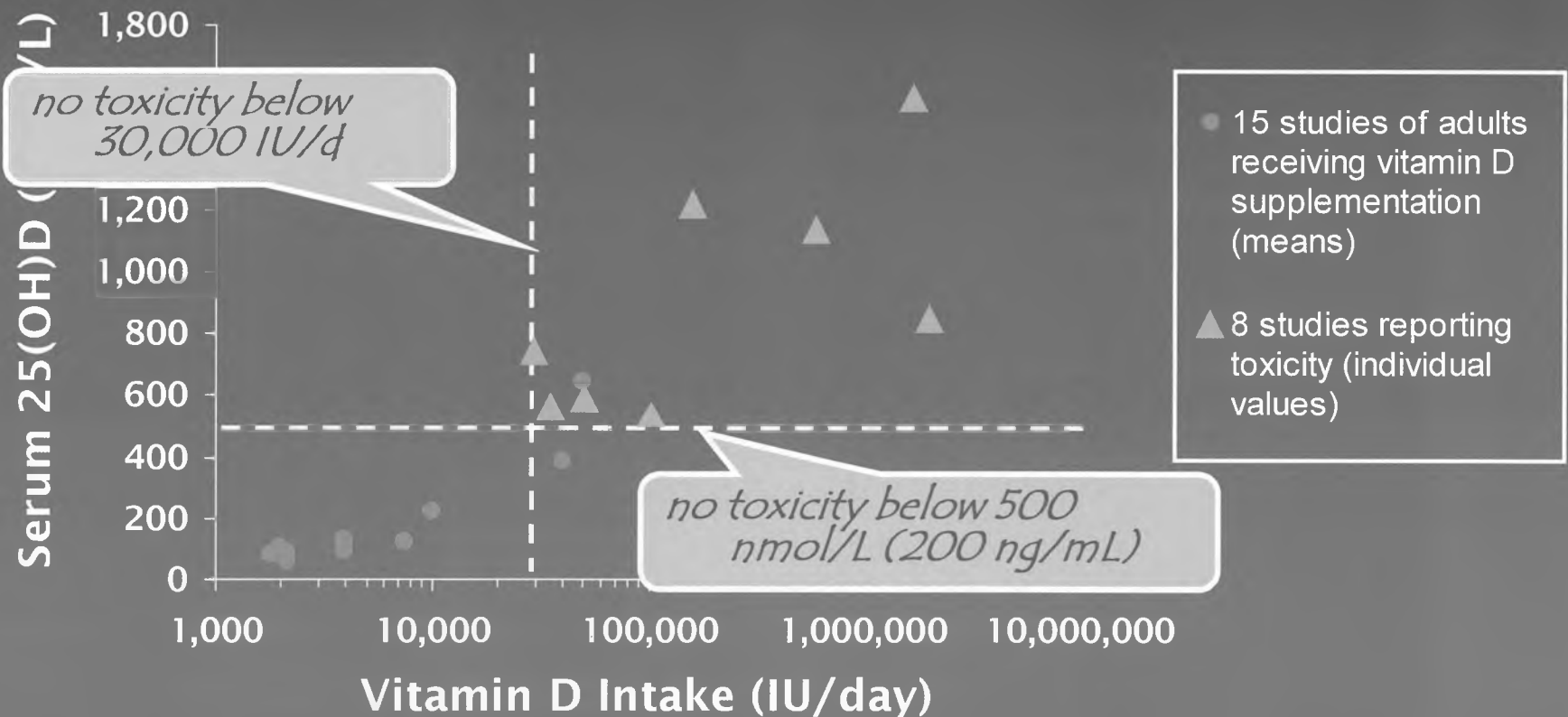
# FORTIFICATION vs. SUPPLEMENTATION

---

- both will work, at least in theory
- supplementation –
  - requires continued voluntary compliance
  - emphasis on education and promotion
- fortification –
  - offers best long-term effectiveness
  - should strive to add ~1000 IU/day to the diets of most Alaskans (e.g., by adding D to all wheat flour products)



# VITAMIN D INTAKE & TOXICITY\*



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

# THE NAAMAN SYNDROME

---

"Are not the rivers of Damascus, the Abana and the Pharpar, better than all the waters of Israel? Could I not wash in them?"  
With this he said to the king of Syria.

But his servants said to him: "My Father, if he would, he would have done it? All that he said." So Naaman went down and plunged into the Jordan. His flesh became like the flesh of a child.

... if something is easy,  
inexpensive, and safe, it  
can't be any good ...

Right?

2 Kings 5:12-14

Thank you . . .



**Vitamin**  
**D**<sup>\*</sup>**action**



A Consortium of Scientists, Institutions, and Individuals  
Committed to Solving the Worldwide Vitamin D Deficiency Epidemic

# Vitamin D Prevents What's Next?

**Carole A Baggerly**  
*Director, GrassrootsHealth*

# Alaska Statistics

---

- **Breast Cancer**

- 372 to be diagnosed each year
- \$75,000 cost/case (one time)
- Total Cost/year: \$27,911,341

**20% Potential Prevention (up to 80%)**

**74-297 people wouldn't get it**

**Cost savings/year: \$5,582,268**

# Alaska Statistics

---

- Falls with injuries
  - 5,500 expected/year (10% over 65)
  - \$10,555 cost/each
  - Total Cost/year: \$58,052,500

20-80% Potential Prevention

1100-4400 wouldn't be hospitalized

Cost savings/year (20%): \$11,610,500

# Alaska Statistics

---

- Pre-term births/pregnancy conditions
- (<34 wks)
  - 1281 expected/year (11% of births)
  - \$50,000 cost/each (initial)
  - Total cost/year: \$64,075,200

**50% Potential Prevention (maximum)**

**640 wouldn't happen**

**Cost savings/year: \$32,037,600**

# Potential Benefit of 3 Conditions

---

▪ Breast Cancer (20%)	\$5,582,268
▪ Falls (20%)	\$11,610,500
▪ Pregnancy (50%)	\$32,037,600
<b>Total</b>	<b>\$49,230,368</b>

# Cost of supplementation for 626,932 people/year

---

- Cost of vitamin D/day/person: \$0.10
- 365 days: \$36.00
- 626,932 population\*\$36.00 = \$22,883,000
- *Special program for supplementation for the pregnant women, all over 65, all cancer conditions*

Potential Benefit \$49,230,368-22,883,000

**\$26,347,368 net savings**

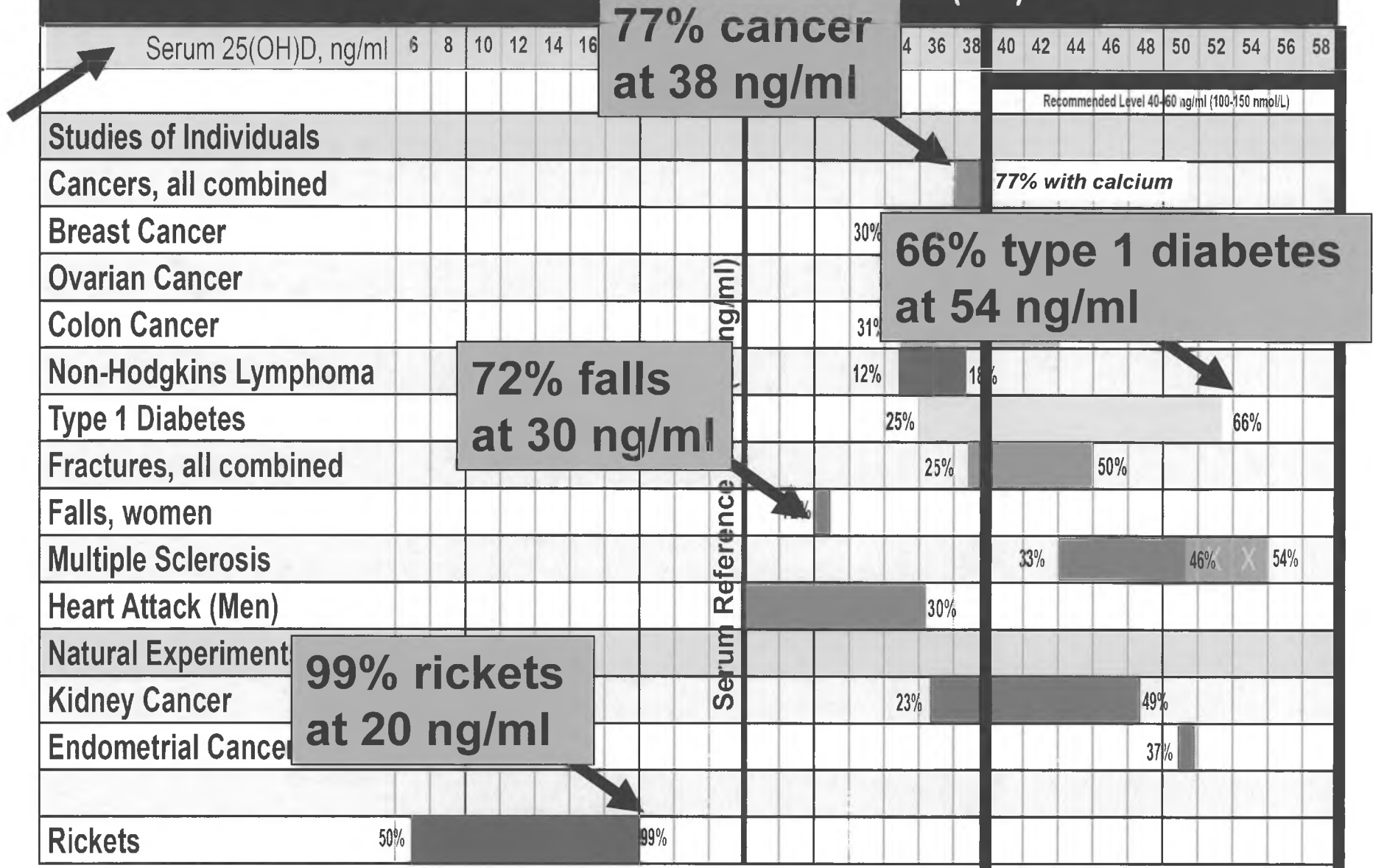
*Room for testing, education programs*

# HOW to prevent these conditions?

---

Get vitamin D serum level to  
40-60 ng/ml

# Disease Incidence Prevention by Serum 25(OH)D Level





*What's in place to solve this problem?*

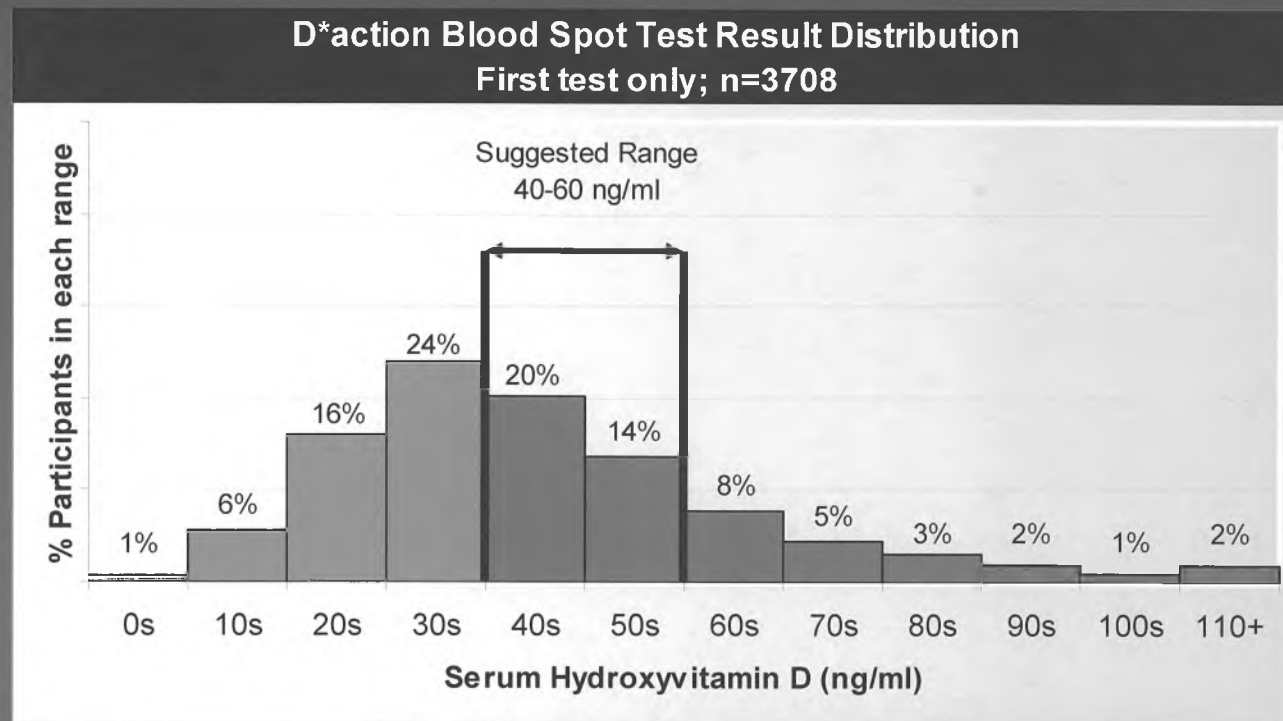
## The Vitamin D\*action Community Project



# D\*action Project Results

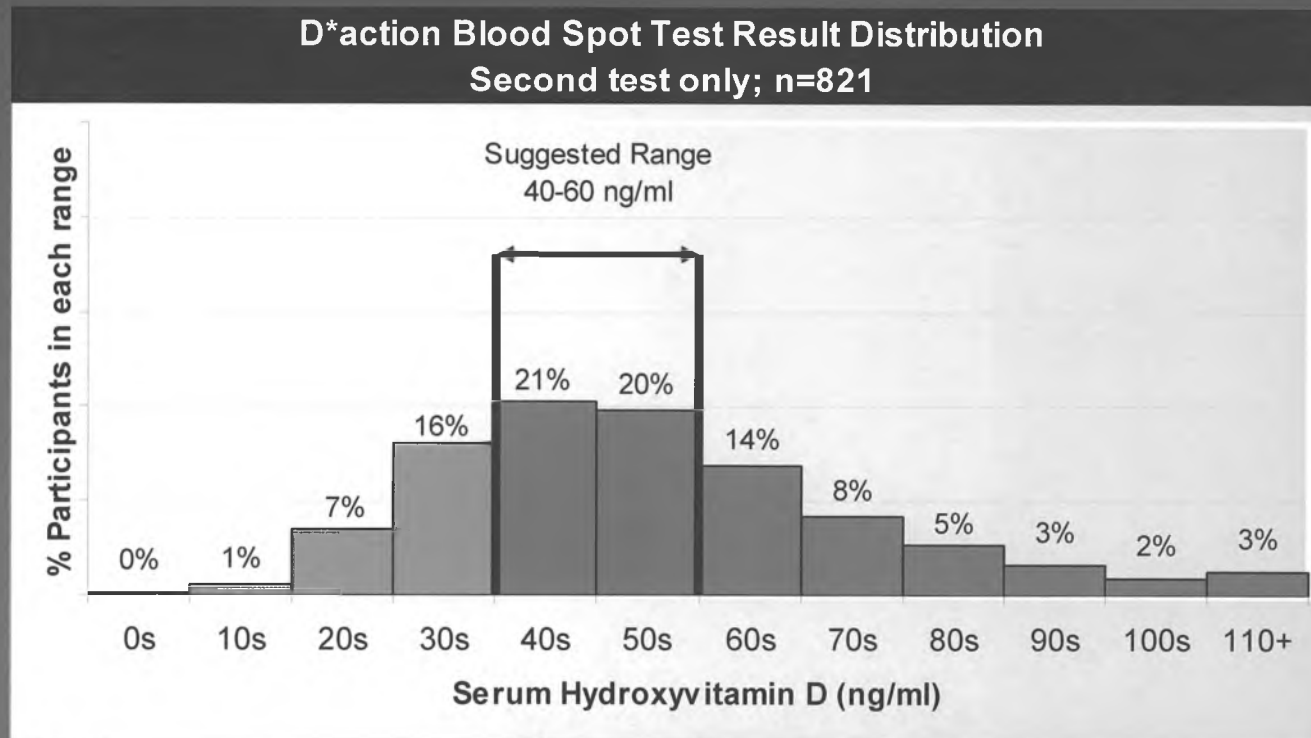
# Blood Spot Test Result Distribution (first test only)

47% Deficient



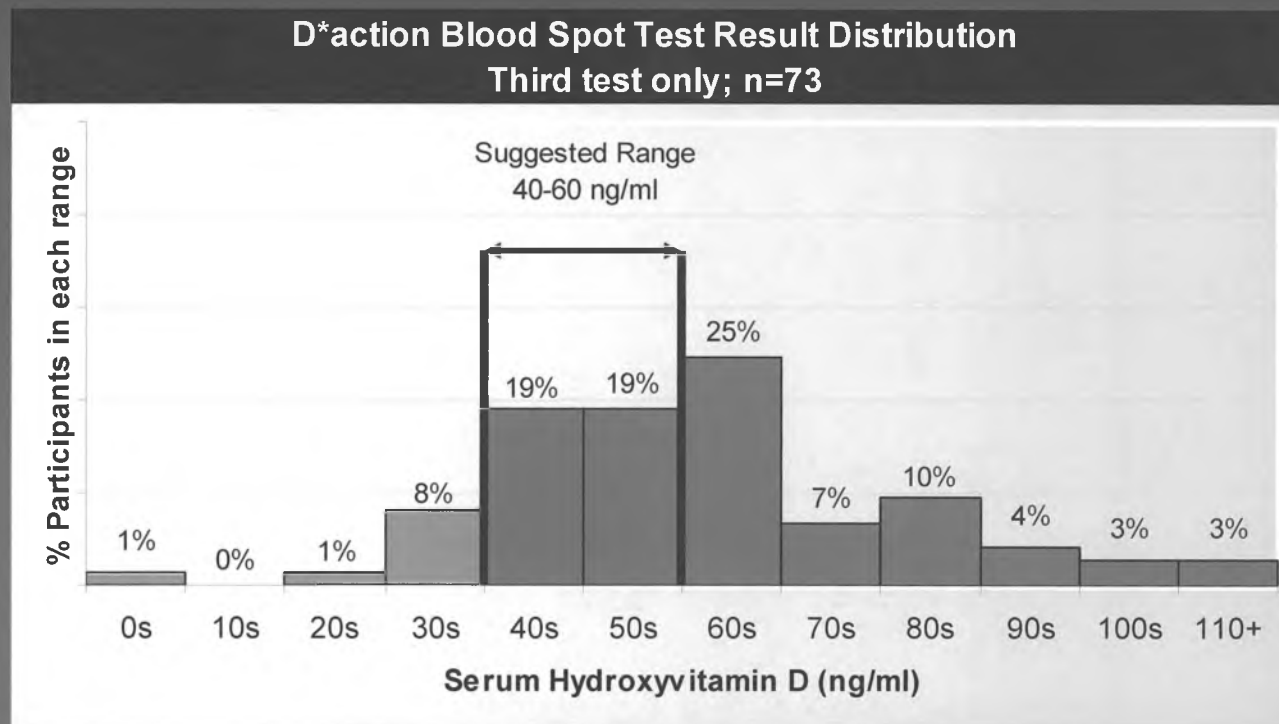
# Blood Spot Test Result Distribution (second test)

From 47% to only 24% Deficient (6 months)

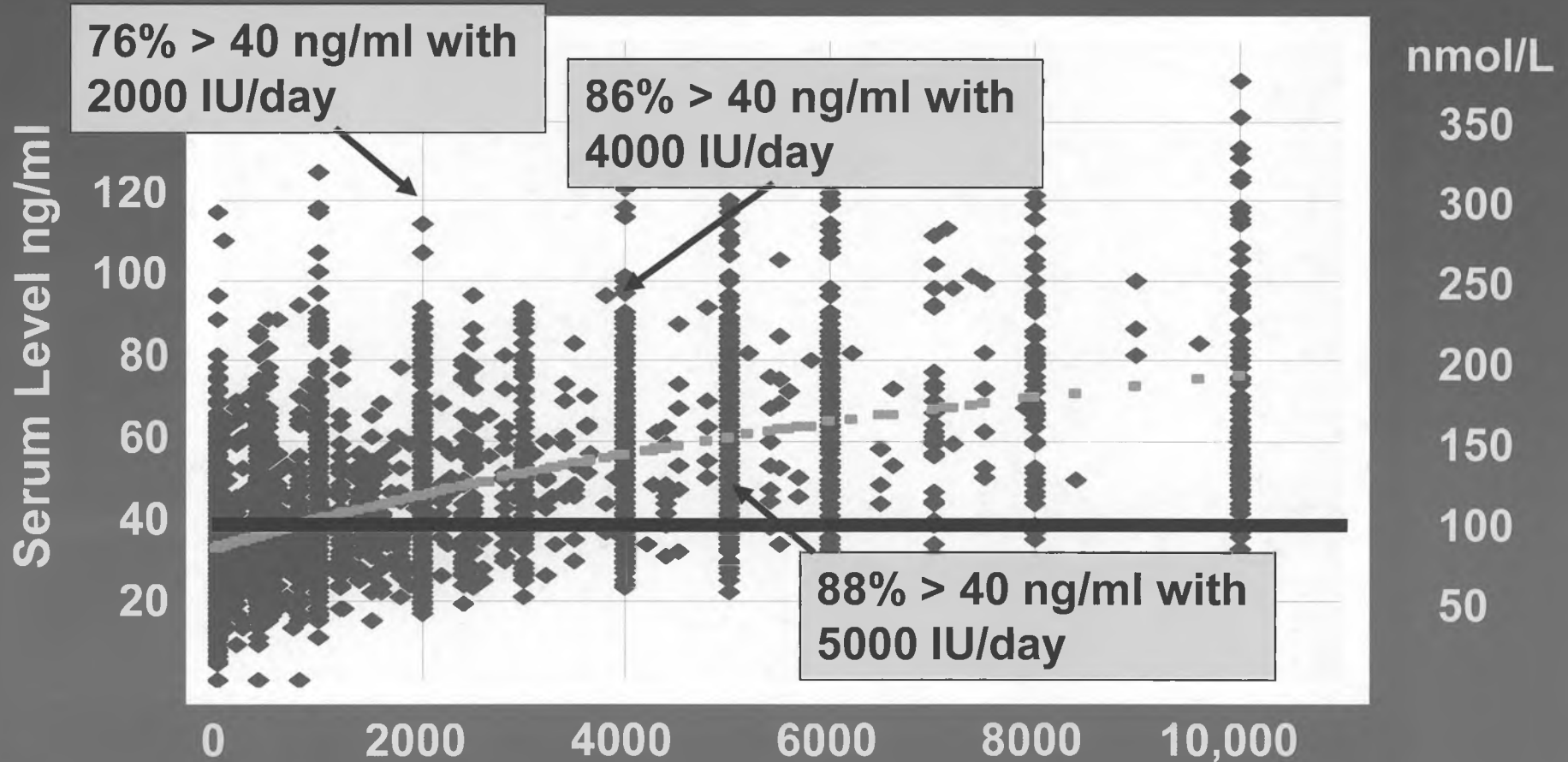


# Blood Spot Test Result Distribution (third test)

From 47% to 24% to 10% (12 months)



# D\*action Project: Serum Level vs Intake



# Key Results of D\*action Project

---

- Public is READY! “Thanks for helping me take charge of my health!”
- Tools (internet) are ready!
- 12 months works: 47% deficient to 10%: *~80% improvement!*
- It takes 5000 IU/day to get 88% > 40 ng/ml
- There was NO toxicity observed at <40,000 IU/day



## Major Goals with D\*action in 5 Years in Any Community

- Reduce the incidence by at least 25% of
  - Breast cancer, colon cancer
  - Pre-term births/preeclampsia
  - Falls
  - +Additional D sensitive diseases
- Educate public, healthcare personnel
- Develop Public Health Policy Actions



## How Does GrassrootsHealth do this?

- Education—Healthcare AND Community Sessions
- Vitamin D Test (2x/year) and health questionnaire
- Feedback to individuals/supplementation
- Development of Community Policy/Action Plan



## WHO?

- **Participation:**
  - **At least 1000 people in the community/year**



**We know enough to reduce  
diseases today!**

***Let us know how we can help!***

**“Action springs not from thought but from a  
readiness for responsibility”**

**Dietrich Bonhoeffer**

# Special Thanks

---

- Cedric F. Garland, Dr. P.H.
- Robert P. Heaney, MD
- Leo L. Baggerly, Ph.D.
- ALL 8000 sponsors!



## International Panel formed in 2007

University of California  
Los Angeles  
John Adams, M.D.  
Milan Fiala, M.D.  
Martin Hewison, Ph.D.  
H. Phillip Koeffler, M.D.  
Keith C. Norris, M.D.

University of California Riverside  
Mathew Mizwicki, Ph.D.  
Anthony W. Norman, Ph.D.  
Laura P. Zanello, Ph.D.

University of California San Francisco  
David Gardner, M.S., M.D.  
Bernard P. Halloran, Ph.D.

University of California San Diego  
Richard L. Gallo, M.D., Ph.D.  
Cedric F. Garland, Dr. P.H.  
Frank C. Garland, Ph.D.  
Edward D. Gorham, Ph.D.  
Tissa Hata, M.D.

University of California Davis  
Bruce D. Hammock, Ph.D.  
Hari A. Reddy, Ph.D.  
Ray Rodriguez, Ph.D.



## International Panel, continued

Atascadero State Hospital  
John J. Cannell, M.D.

Boston University School of Medicine  
Michael F. Holick, Ph.D., M.D.

Creighton University  
Joan M. Lappe, Ph.D., R.N.  
Robert P. Heaney, M.D.

Harvard School of Public Health  
Edward Giovannucci, M.D., ScD.  
Walter C. Willett, Dr. P.H., M.D.

International Medical  
Center of Japan  
Tetsuya Mizoue, M.D., Ph.D.

McGill University  
John H. White, Ph.D.

Medical University of South Carolina  
Bruce W. Hollis, Ph.D.  
Carol Wagner, M.D.

Roswell Park Cancer Institute  
Candace Johnson, Ph.D.  
Donald L. Trump, M.D.

Sunlight, Nutrition and Health Research Center  
William B. Grant, Ph.D.

University at Albany—SUNY  
JoEllen Welsh, Ph.D.

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# References

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## *Page 2 Breast Cancer:*

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## *Page 8 Disease Incidence Prevention Chart References:*

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*Pages 11-14 all data from GrassrootsHealth study*

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## Actions

### What's needed to Solve the vitamin D Deficiency?

- Measure the 25-hydroxyvitamin D serum levels.
- Provide intake from UVB exposure, supplements, fortified foods, to get serum levels to 40-60 ng/ml (100-150 nmol/L).

### D\*action Project

- An international study to assess the health effects of large populations who have serum levels in the 40-60 ng/ml (100-150 nmol/L) range.
- Cedric F. Garland, Dr. P.H., F.A.C.E., Moores Cancer Center, University of California San Diego is the study's principal investigator.
- Participants will provide health information and do a vitamin D test every 6 months for a period of 5 years.
- Physicians, clinics, research groups and other health interested groups are encouraged to join the project. Individuals can also enroll in the project.
- There are currently over 7000 individual participants from all over the world in the study; approximately 50% of them started with levels below 40 ng/ml (100 nmol/L).
- Diagnosis & Treatment of Vitamin D Deficiency seminars are held for medical professionals.
- Custom studies are done for research groups. Contact Carole Baggerly, Director, [info@grassrootshealth.org](mailto:info@grassrootshealth.org) for further information.

Join D\*action: [www.joinaction.org](http://www.joinaction.org)  
Get your blood level tested, take action!

Download the Disease Incidence Prevention Chart showing serum levels required to prevent many diseases: [www.grassrootshealth.net/diseasepreventionchart.pdf](http://www.grassrootshealth.net/diseasepreventionchart.pdf)

D\*action is a public health project of GrassrootsHealth, a 501c3 non-profit organization. [www.grassrootshealth.net](http://www.grassrootshealth.net)  
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## Call to D\*action Scientists

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### International Scientists Panel

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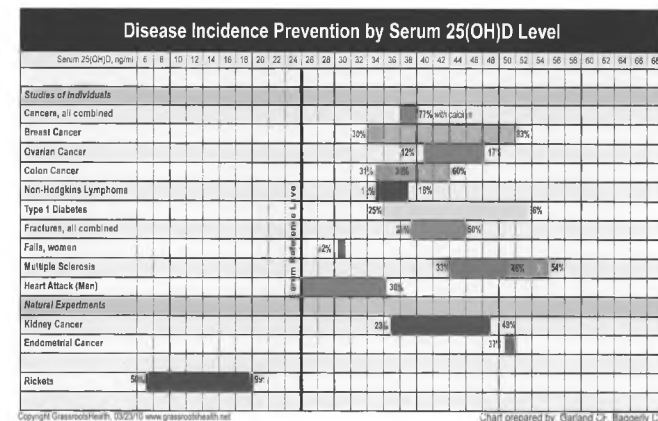
Vitamin **D\*action**

A Consortium of Scientists, Institutions and Individuals  
Committed to Solving the Worldwide Vitamin D Deficiency Epidemic

FAQ's

(Frequently Asked Questions)

Vitamin D



# Vitamin D Frequently Asked Questions

## Why do we need vitamin D?

Every tissue in our bodies needs vitamin D and will not work correctly if we do not get enough. In its most extreme forms, vitamin D deficiency produces rickets in children and osteomalacia (bone softening) in adults.

Milder degrees of deficiency are now understood to be one of the causes of a vast array of chronic diseases, including osteoporosis, impaired immune competence, various autoimmune diseases (such as diabetes and multiple sclerosis), several cancers (breast, colon, lung, lymphoma and prostate, among others) high blood pressure, pregnancy complications and cardiovascular disease. All may develop because of, or be exacerbated by, vitamin D deficiency. Asking the body to deal with these disorders without adequate vitamin D is like asking a fighter to enter battle with one hand tied behind his/her back.

## What is vitamin D?

Vitamin D is one of the chemicals that the tissues of our body use to unlock the DNA blueprints which each tissue contains and which are needed for our cells to produce the many biochemical products required for their day-to-day functioning.

## Where do I get vitamin D?

The principal source of vitamin D is your own skin. A chemical compound naturally present in the superficial layers of skin is converted, on exposure to UVB radiation, to cholecalciferol (vitamin D<sub>3</sub>). However, we manufacture this vitamin D only if we expose our skin to UVB radiation. If we spend all day indoors or go out only in the early morning or late afternoon, we don't produce any vitamin D. You can also get vitamin D from food (limited), supplements and other UVB sources.

## How long should I be outdoors?

There is no single right answer. A light skinned person, wearing a bathing suit, will make about 15,000 IU of vitamin D in 15-20 minutes in July at midday. Darker-skinned individuals can do the same, but it will take twice as long.

## What is the effect of sunscreen?

Sunscreen blocks UVB radiation and prevents the manufacture of vitamin D.

## What about skin cancer?

The brief exposure needed to produce adequate vitamin D is not enough to cause skin cancer. However, if you are worried about that risk, apply sunscreen after the first 15 minutes of exposure.

## Does the body have to process vitamin D before it becomes active?

The body converts vitamin D, whether by mouth or made in the skin, to a compound called 25-hydroxyvitamin D [25(OH)D]. This compound circulates in the blood and is the measure physicians or scientists use to assess vitamin D status. High levels of serum 25(OH)D show that you are getting enough vitamin D, while low levels indicate deficiency.

## How much vitamin D do I need?

The body needs at least 4000 IU/day in order to maintain a healthy concentration of 25(OH)D in the blood. Because most of us don't get enough sun exposure, the little vitamin D we get that way, plus food and fortified food sources, totals no more than about 2000 IU/day. Thus in order to meet the body's need for about 4000 IU/day, most adults should take supplements providing 1000-3000 IU daily.

## Is vitamin D safe?

Vitamin D is safe, if consumed in reasonable quantities. (See 'How much vitamin D do I need?') It is instructive to know that outdoor summer workers by the end of summer will typically have serum levels of 60-80 ng/ml (150-200 nmol/L). However vitamin D is an extremely potent compound, and if taken in abnormally high doses, can produce severe toxicity leading even to death. However, there have been no reported cases of vitamin D toxicity at serum levels of 25(OH)D below 200 ng/ml (500 nmol/L).

## What about calcium and vitamin D?

Vitamin D enables the body's regulation of calcium absorption. With inadequate calcium or vitamin D intake, there is insufficient calcium absorption. However, there is no hyper-absorption with high vitamin D levels. There is also a substantial body of evidence indicating there is an inverse relationship between calcium intake and kidney stone risk.

## Is it important to take vitamin D daily?

As long as the total dose is sufficient, vitamin D does not have to be taken every day. Some physicians prescribe weekly or monthly dosing. **The important thing is to achieve and maintain a range of 40-60 ng/ml (100-150 nmol/L).**

## What about the current IOM (Institute of Medicine) published requirements for vitamin D?

The IOM recently (2010) increased the 'no observable adverse event level' from 2000 IU/day to 10,000 IU/day. This is significant progress. They tripled the intake for all individuals up to age 50. Their focus was limited, however, to skeletal health, not the full array of diseases considered by the D\*action Scientists' Panel.