HCR

5

<TARGET><BILL>HCR 5</BILL><SUBJECT>HCR
5</SUBJECT><COMM>HHSS27</COMM></TARGET>

Alaska State Legislature

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REPRESENTATIVE Paul Seaton
District 35

MEMORANDUM

TO: Representative Wes Keller
Chair, House Health and Social Services Committee

FROM: Representative Paul Seaton

DATE: March 1, 2011

RE: Request for Hearing

I respectfully request that HCR 5, relating to chronic disease prevention and vitamin D, be scheduled for a hearing in the House Health and Social Services Committee.

We will need to be teleconferenced statewide. We will let you know the names of testifiers as we receive this information.

Please feel free to contact me, or my legislative intern, Crystal A. Rogers, with questions or thoughts at 465-6256.

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REPRESENTATIVE Paul Seaton
District 35

HCR 5
Sponsor Statement

Short Title: A resolution relating to prevention of disease and to vitamin D.

HCR 5 urges the State of Alaska to adopt a disease prevention model of health and to increase the awareness of the preventative benefits of vitamin D supplementation, and increase vitamin D availability to reduce health impacts and costs.

Mounting scientific evidence shows a correlation between vitamin D sufficiency and significant decrease in incidence of cancer, diabetes, heart disease, rheumatoid arthritis, chronic pain, Seasonal Affective Disorder, oral disease, influenza, upper respiratory illness, tuberculosis, multiple sclerosis, osteoporosis, fractures in the elderly, autism, rickets, pregnancy complications, and hepatitis C.

For seven months out of the year, the sun angle is too low for Alaskans to be able to produce vitamin D from sunlight. Partly due to this long "vitamin D winter," Alaska has some of the lowest blood serum levels of vitamin D in the country. Correspondingly, Alaska also has relatively high rates of chronic disease. For example, according to the Alaska Division of Public Health, chronic diseases (cancer, heart disease, respiratory disease, and stroke, respectively) make up four of the top five causes of death in the state. These diseases come at a great cost both socially and financially to our state.

Deficiency in vitamin D may contribute heavily to this steep social and financial cost. Two studies mentioned in HCR 5 demonstrate this. The first one, examining the economic burden of vitamin D deficiency, estimated that Canada could lower the death rate by 37,000 deaths and save $14.4 billion dollars per year by increasing the national average of vitamin D blood serum levels. The second, similar study showed that the United States could have 50,000—63,000 fewer deaths and save $40-56 billion per year with sufficient population levels of vitamin D.

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REPRESENTATIVE Paul Seaton

District 35

With higher rates of chronic disease in northern latitudes, and fewer and fewer federal dollars coming in to cover the escalating healthcare and Medicaid costs in Alaska, it is imperative to prevent—rather than just treat—chronic disease. Prevention of chronic disease is a matter of lifestyle: healthy diet, frequent exercise, and adequate levels of vitamins and nutrients. Most people understand this, but are unaware that vitamin D deficiency needs to be addressed in every community of this state.

HCR 5 asks Governor Sean Parnell to establish "prevention of disease" as a primary model of health care in Alaska, and for the Department of Health and Social Services and health care providers to increase attention to vitamin D deficiency and promote supplementation. It also asks the Department to provide vitamin D supplements to the elderly, children, and pregnant women. Vitamin D supplementation is a low-cost measure that could help save lives, and significantly improve the health of many Alaskans, while saving millions of dollars in health treatment costs.

FISCAL NOTE

STATE OF ALASKA
2011 LEGISLATIVE SESSION

Fiscal Note Number
Bill Version **HCR 5**
() Publish Date

Identifier (file name) HCR5-LEG-COU-03-02-2011
Title Relating to Prevention of Disease and to Vitamin D
Sponsor Representative Seaton
Requester House Health and Social Services Committee

Dept. Affected Legislature
Appropriation Legislative Council
Allocation Session Expenses
OMB Component Number 782

Expenditures/Revenues (Thousands of Dollars)

Note: Amounts do not include inflation unless otherwise noted below.

	Appropriation Required	Information					
OPERATING EXPENDITURES	**FY 2012**	**FY 2012**	**FY 2013**	**FY 2014**	**FY 2015**	**FY 2016**	**FY 2017**
Personal Services							
Travel							
Contractual							
Supplies							
Equipment							
Grants & Claims							
Miscellaneous							
TOTAL OPERATING	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
CAPITAL EXPENDITURES							
CHANGE IN REVENUES							

FUND SOURCE (Thousands of Dollars)

1002 Federal Receipts							
1003 GF Match							
1004 GF							
1005 GF/Program Receipts							
1037 GF/Mental Health							
Other Interagency Receipts							
TOTAL	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**

Estimate of any current year (FY2011) cost

POSITIONS

Full-time							
Part-time							
Temporary							

Why this fiscal note differs from previous version

Initial Version

Prepared by Shane Miller, Finance Manager
Division Administrative Services Division
Approved by Pamela Varni, Executive Director
Legislative Affairs Agency

Phone 465-6626
Date/Time 3/2/11 1:51 PM
Date 3/2/2011

(Revised 12/29/2010 OMB)

Analysis

This fiscal note has zero impact on the Legislative Affairs Agency.

FISCAL NOTE

STATE OF ALASKA
2011 LEGISLATIVE SESSION

Fiscal Note Number
Bill Version **HCR005\M**
() Publish Date

Identifier (file name): HCR005-DHSS-PHN-03-09-11
Title Vitamin D Supplements
Sponsor Rep. Seaton
Requester House HSS

Dept. Affected Health and Social Services
Appropriation Public Health
Allocation Nursing
OMB Component Number 288

Expenditures/Revenues (Thousands of Dollars)

Note: Amounts do not include inflation unless otherwise noted below.

	Appropriation Required	Information					
OPERATING EXPENDITURES	**FY 2012**	**FY 2012**	**FY 2013**	**FY 2014**	**FY 2015**	**FY 2016**	**FY 2017**
Personal Services							
Travel							
Services							
Commodities							
Capital Outlay							
Grants							
Miscellaneous							
TOTAL OPERATING	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
CAPITAL EXPENDITURES							
CHANGE IN REVENUES							

FUND SOURCE (Thousands of Dollars)

1002 Federal Receipts							
1003 GF Match							
1004 GF	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1005 GF/Program Receipts							
1037 GF/Mental Health							
Other (please identify)							
TOTAL	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**

Estimate of any current year (FY2011) cost

POSITIONS

Full-time	**0**	0	0	0	0	0	0
Part-time							
Temporary							

Why this fiscal note differs from previous version (if initial version, please note as such)

Not Applicable. Initial version.

Prepared by Ward B. Hurlburt, M.D., MPH - Chief Medical Officer / Director
Division Public Health
Approved by Alison Elgee, Assistant Commissioner
DHSS Finance & Management Services

Phone 269-6680
Date/Time 3/4/11 12:00 AM
Date 3/9/2011

FISCAL NOTE

STATE OF ALASKA **BILL NO.** HCR005
2011 LEGISLATIVE SESSION

Analysis

This House Concurrent Resolution relates to the prevention of disease and the benefits of Vitamin (Vit.)D.

The division is submitting a zero fiscal note because no new authorization is necessarily invoked by passage of this resolution. Should the Legislature decide to require the department to undertake activities through additional legislation, an additional appropriation will be necessary.

This analysis estimates the cost of implementing the four activities in the resolution if the division were to implement them, although the division has no plans to do so at this time. The assumptions used to calculate the fiscal note are detailed on page 3.

The resolution includes language that encourages or urges the Department of Health and Social Services to implement four activities in regards to Vitamin D supplements. The activities are

(1) to increase attention to Vit. D deficiency, Vit. D testing, and to promote awareness of the long-term health benefits of and increased chances of cancer survival with sufficient levels of Vit. D;
(2) investigate substituting Vit. D supplementation for influenza vaccination as a less costly method for preventing influenza;
(3) provide Vit. D supplements to the elderly to prevent bone loss, falls, fractures, and other age-related health problems; and
(4) provide Vit. D supplements to pregnant women and infants to prevent pregnancy complications, preterm births, type 1 diabetes, and rickets.

For the first activity, the department would contract for professional services to create an awareness campaign on the benefits of Vit. D. at an estimated cost of $50.0. This would be an ongoing cost.

For the second activity, the department would require $100.0 for a PhD-level epidemiologist (1 FTE, existing PCN, Range 20/A) plus $35.0 for overhead (rent, utilities, etc.). The epidemiologist would conduct a study investigating subsitution of Vit. D supplemention for influenza vaccination as a less costly method of preventing influenza. This study would take at least three years. This is a conservative estimate and could be double or triple the amount depending on the final study design.

For the third and fourth activities, the department would provide Vit. D supplements through Public Health Nursing Clinics at a cost of $211.2 annually. Elderly, pregnant women, and infants who go to the clinics would receive a limited office visit to determine if Vitamin D supplements were indicated. Of the approximately 17,200 public health clinic clients seen in 2011, it is assumed 3,225 (18.75%) could have received one or more 90-day supplies of Vit. D supplements. The client would receive a limited office visit each time the client came to the clinic for more supplements to determine if Vit. D was still medically necessary and evaluate their health condition. Public Health Nursing would report their results to the epidemiologist conducting the Vit. D study.

The total cost for Years 1 to 3 would be $396.2. Years 4 and 5 would be $261.2 since the second activity for a study would be completed by then.

(Continued on page 3.)

Analysis Continued

Assumptions:

Clients
17,200 total clients served by Public Health Nursing, 2011
75% percent PHN clients who are elderly/pregnant women/infants
12,900 clients eligible for Vit. D supplements
25% percent clients eligible who receive Vit. D
3,225 clients eligible who receive Vit. D
806 clients (25%) visit 1/year
806 clients (25%) visit 2/year
806 clients (25%) visit 3/year
807 clients (25%) visit 4/year

Medical Supply Unit Cost
$ 1.20 Cost is $0.10 per Vit. D pill (over-the-counter, wholesale)
At 1 dose per week, with 12 doses dispensed per clinic visit (90-day supply)
$ 25.00 Cost of 15 min. limited office visit for each clinic visit (max. 4 /year)
$ 26.20 total cost per clinic visit for Vit. D

Total Annual Cost
$ 211,238 medical supplies for dispensing Vit. D
$ 100,000 personal services for 1 FTE epidemiologist (Range 20/A) to investigate Vit. D as substitute for influenza vaccine (Years 1-3)
$ 85,000 contractual costs for awareness campaign of benefits of Vit. D ($50.0); overhead for 1 FTE ($35.0)
$ 396,238 total annual cost Year 1

This analysis includes only the direct medical supply and administrative costs of implementing the resolution. The cost savings if patients opted for Vit. D supplements in lieu of influenza vaccine are not included in this analysis. Nor does it include the additional cost of treating patients who did not get vaccinated for influenza and later became ill.

The annual cost per person for Vit. D supplements (assuming 52 doses, 4 visits) is $104.80. In comparison, the medical supply unit cost of influenza vaccine is approximately $33-$66 annual cost per person (assuming $8/dose plus $25 limited office visit for 1-2 doses/year).

The resolution notes that part of the budget of the Department of Health and Social Services is used to treat illnesses that could be prevented with adequate blood serum levels of Vit. D. Those potential costs savings are not included in this analysis as the amount of avoided costs are indeterminate and would likely not be realized in the time frame covered by the fiscal note.

STATE OF ALASKA

HEALTH & SOCIAL SERVICES

WORK DRAFT REVIEW

Please note: The Department of Health and Social Services strives to provide timely programmatic input on proposed work drafts to assist with an efficient flow of legislation through the committee process. Nothing in this document should be construed as support or opposition for the proposal. A full review is still under way.

DIVISIONS IMPACTED	BILL NUMBER	SPONSOR
Public Health	[Bill Version]HCR005[Committee]	Rep. Seaton

SUBJECT
Vitamin D Supplements

DEPT CONTACT	DATE
Lewis, Jill	3/14/2011

SUMMARY

PRELIMINARY COMMENTS ABOUT BILL/PROGRAM EFFECTS

HSS committee chair, Rep. Keller, asked Dr. Hurlburt to provide alternative language during the hearing on 3/11/11.

AMENDMENTS PROPOSED

Accept the changes suggested by Rep. Keller regarding the "Whereas" statements.

Page 5, Line 28-30: replace with "Be it resolved that the Alaska State Legislature respectfully requests the Governor to support prevention of disease as a primary health model of health care in Alaska; and be it"

Page 5, Line 31 through Page 6, Line 3: replace with "Further resolved that the Department of Health and Social Services and health care providers promote awareness of healthy dietary requirements and continue to monitor the scientific literature regarding dietary and vitamin requirements and recommendations."

Page 6, Lines 4-13: delete all.

PLEASE ATTACH A SEPARATE SHEET FOR ADDITIONAL COMMENTS.

PRELIMINARY COMMENTS (continued from previous page)

Click here to enter text.

Changes between HCR 5 v. M and CSHCR 5 v. B

Three types of changes from the last committee meeting:

1. Changes that soften the language so it is not interpreted as a mandated
    a. Adding the word "potentially" and substituting "promote" for "provide"
        i. P.5 line 26; p.6 line 5; p. 6 line10; p. 6 line 16
    b. In the WHEREAS language referring to influenza vaccine urges the department to look at the effectiveness of vitamin D vs. vaccination through a comparative treatment effective analysis.
        i. P.6 lines 12-13
2. Changes correcting errors/clarifying
    a. Specifying that the 2007 study showing decreased cancer rates was in a group of postmenopausal women.
        i. P. 2 line 1
    b. Add the word "blood" to clarify vitamin D levels are tested through blood testing
        i. P. 5 line 5
    c. Changes IU level for the 2010 study of Japanese School children from 2,000 to 1,200 (typo).
        i. P. 3 line 28
3. Adding a WHEREAS that highlights the significance of the aggregate studies
        i. P.6 lines 28-29

AMENDMENT

OFFERED IN THE HOUSE BY REPRESENTATIVE KELLER

TO: CSHB 78( ), Draft Version "D"

Page 3, line 2, following "department":

Insert "for deposit in the general fund"

Page 3, line 10, following "department":

Insert "from money appropriated for the purpose"

Page 4, following line 6:

Insert a new subsection to read:

"(i) Direct incentive payments, loan repayments, and matching payments shall be made with funds appropriated by the legislature for that purpose."

Page 4, lines 30 - 31:

Delete all material.

Reletter the following subsections accordingly.

Page 5, following line 20:

Insert a new subsection to read:

"(c) If insufficient funds are appropriated in a fiscal year, the department shall prorate payments based on the number of approved participants in the program."

27-LS0504\B
Mischel
3/14/11

CS FOR HOUSE CONCURRENT RESOLUTION NO. 5( )

IN THE LEGISLATURE OF THE STATE OF ALASKA

TWENTY-SEVENTH LEGISLATURE - FIRST SESSION

BY

Offered:
Referred:

Sponsor(s): REPRESENTATIVES SEATON, Tuck, Millett, Gruenberg

A RESOLUTION

Relating to prevention of disease and to vitamin D.

BE IT RESOLVED BY THE LEGISLATURE OF THE STATE OF ALASKA:

WHEREAS the nutrient and pre-hormone vitamin D is manufactured in the skin during exposure to ultraviolet B light from high-angle sunshine; and

WHEREAS, for seven months a year, the angle of the sun's rays is too low for adequate ultraviolet B exposure in the state; and

WHEREAS Alaskans have one of the lowest levels of vitamin D blood serum in the nation because of the state's northern latitude; and

WHEREAS the state has a high incidence of preventable diseases that numerous studies indicate may be correlated with insufficient blood serum levels of vitamin D; and

WHEREAS a 2008 study by the Ketchikan Indian Community Tribal Health Clinic found that blood serum levels of vitamin D of Alaska Natives tested in Ketchikan averaged between 6 and 17 ng/ml; and

WHEREAS a 1986 study by the University of Alaska Fairbanks found the blood serum levels of vitamin D of Caucasian males averaged 27 ng/ml; and

WHEREAS a 2007 article published in the American Journal of Clinical Nutrition

reported that a study that compared cancer rates of a group of postmenopausal women taking 1,100 IU of vitamin D supplements in combination with calcium to cancer rates of a group taking a placebo found the risk of developing any cancer after four years was 60 percent lower in the group taking vitamin D supplements; and

WHEREAS a study presented at the 2008 annual meeting of the American Association for Cancer Research found that blood serum levels of vitamin D of at least 50 ng/ml were associated with an 83 percent reduction in the incidence of breast cancer compared to blood serum levels of vitamin D of 25 ng/ml; and

WHEREAS a 2007 article published in the American Journal of Preventative Medicine reported that a study found that a group with blood serum levels of vitamin D of at least 42 ng/ml had a 60 percent reduction in the incidence of colorectal cancer compared to a group with blood serum levels of vitamin D of 25 ng/ml; and

WHEREAS a 2010 study by the University of San Diego showed that incidence of bladder cancer increases as latitude increases and that the incidence of bladder cancer decreased by 40 percent with adequate blood serum levels of vitamin D; and

WHEREAS a study referenced by Michael F. Holick, Ph.D., M.D., in The Vitamin D Solution found that men with prostate cancer who received 2,000 IU of vitamin D a day for two years had a 50 percent reduction in the rise of prostate-specific antigen, an indicator of prostate cancer activity; and

WHEREAS a 2001 study published in The Lancet found that a group with blood serum levels of vitamin D of 52 ng/ml had a 66 percent reduction in the incidence of type 1 diabetes compared to a group with blood serum levels of vitamin D of 25 ng/ml; and

WHEREAS a 2001 study published in the Lancet found that children in Finland who received 2,000 IU a day of vitamin D for the first year of life were 80 percent less likely to develop type 1 diabetes by age 30 compared to children receiving 400 IU a day of vitamin D; and

WHEREAS a 2006 study published in Diabetes Care found that taking 800 IU of vitamin D in combination with calcium resulted in a 33 percent reduction in the risk of type 2 diabetes; and

WHEREAS a 1998 study published in the Journal of the American College of Cardiology found that the incidence of heart attacks is 53 percent higher during the sun-

deprived winter months than during the summer months; and

WHEREAS a growing body of research from around the world indicates that deficiency in vitamin D correlates with a broad spectrum of conditions, such as high blood pressure, poor insulin sensitivity, inflammation, and other conditions related to heart disease; and

WHEREAS numerous studies have found that vitamin D suppresses the inflammation that plays a role in rheumatoid arthritis, chronic muscle pain, metabolic syndrome, congestive heart failure, and stroke; and

WHEREAS a 2008 study published in the Archives of Internal Medicine showed that the risk for heart attack in men with vitamin D blood serum levels at or below 15 ng/ml is 2.4 times greater than that for men whose vitamin D levels are at or above 30 ng/ml; and

WHEREAS a 1999 study published in the Journal of Nutrition, Health and Aging found that patients with seasonal affective disorder treated with a single dose of 100,000 IU of vitamin D showed significant improvement after one month; and

WHEREAS a 2004 study published in the American Journal of Clinical Nutrition found that low blood serum levels of vitamin D were associated with periodontal disease; and

WHEREAS a 2005 study published in the American Journal of Public Health found that the rate of oral disease among Alaska Natives is disproportionately high; and

WHEREAS a 2010 study published in the Journal of Laryngology and Otology found that low levels of vitamin D are associated with an increased incidence of upper respiratory tract infections; and

WHEREAS the Centers for Disease Control and Prevention report that influenza vaccine effectiveness varies greatly; and

WHEREAS in 2010, the Department of Health and Social Services, reported that the state is no longer subsidizing universal vaccinations for influenza because of a seven-fold increase in cost over 10 years and a decrease in federal funding; and

WHEREAS a 2010 article published in the American Journal of Clinical Nutrition reported that a study of a group of Japanese school children who received 1,200 IU of vitamin D a day showed a 50 percent reduction in the incidence of influenza compared to other school children; and

WHEREAS vitamin D has been shown to influence the immune response to

tuberculosis, and studies have shown that vitamin D deficiency is associated with increased risk of acquiring tuberculosis; and

WHEREAS a 2010 article in The Lancet reported that the risk of multiple sclerosis increases with latitude and with low blood serum levels of vitamin D; and

WHEREAS a 2006 article published in the Journal of American Medical Association reported that a study examining blood samples of more than 7,000,000 army recruits from 1992 - 2004 found that higher blood serum levels of vitamin D were associated with a significantly lower risk of developing multiple sclerosis; and

WHEREAS a 2005 article published in the Journal of the American Medical Association reported that elderly persons who had blood serum levels of vitamin D of at least 45 ng/ml experienced a 50 percent reduction of fractures, and a 2007 article published in the Journal of the American Geriatric Society reported that elderly persons who had blood serum levels of vitamin D of at least 30 ng/ml experienced a 72 percent reduction in falls compared to those who had blood serum levels of vitamin D below 25 ng/ml; and

WHEREAS the elderly are at high risk for vitamin D deficiency because of indoor lifestyle and the reduced ability of aging skin to manufacture vitamin D; and

WHEREAS a 2009 article published in the Journal of Alzheimer's Disease reported that vitamin D reduces the risk of several types of diseases that have been identified as risk factors for or precursors to dementia; and

WHEREAS a 2010 article published in The Journal of Alternative and Complementary Medicine reported that a study in Egypt found that children without autism had blood serum levels of vitamin D averaging 40.1 ng/ml, and children with autism had significantly lower blood serum levels of vitamin D, averaging 28.5 ng/ml; and

WHEREAS Sara B. Arnaud, M.D., found that infants and children with blood serum levels of vitamin D of at least 18 ng/ml have a 99 percent prevention rate of the bone disease rickets; and

WHEREAS a 2007 study published in the Journal of Clinical Endocrinology and Metabolism found that females who received regular vitamin D supplementation during the first year of life are 50 percent less likely to develop preeclampsia in their first pregnancy; and

WHEREAS a 2009 article published in The Journal of Clinical Endocrinology and Metabolism found that pregnant women with low blood serum levels of vitamin D were

nearly four times more likely to deliver by cesarean section than women with blood serum levels of vitamin D of at least 15 ng/ml; and

WHEREAS a 2009 study at the Medical University of South Carolina found that pregnant women who took 4,000 IU a day of vitamin D during pregnancy had a 50 percent reduction in the rate of premature birth and delivered fewer babies with low birth weight than women who took 400 IU a day of vitamin D; and

WHEREAS a 2010 study at the Rebecca Sieff Hospital in Israel found that when patients with hepatitis C were given 1,000 IU a day of vitamin D, the blood of 44 percent of the participants was virus-free after a month of treatment, and the blood of 96 percent of the participants was virus-free after three months; and

WHEREAS, although the Institute of Medicine of the National Academy of Sciences, in 2010, recommended 600 IU a day of vitamin D, levels above 2,000 IU a day and an upper level intake of 4,000 IU a day may be more appropriate for those who live in the northern latitude; and

WHEREAS a 2007 study published in the American Journal of Clinical Nutrition found vitamin D toxicity only above 30,000 IU a day; and

WHEREAS a 2007 article published in the Journal of Photochemistry and Photobiology estimated that the United States economic burden due to vitamin D deficiency from inadequate exposure to ultraviolet B light, inadequate diet, and lack of supplements was estimated at $40,000,000,000 - 56,000,000,000 in 2004; and

WHEREAS a 2010 article published in Molecular Nutrition and Food Research regarding the rate of premature death and the economic burden in Canada found that annual deaths could be reduced by 37,000 and the economic burden reduced by 6.9 percent or $14,400,000,000 if blood serum levels of vitamin D of the population were adequate; and

WHEREAS part of the budget of the Department of Health and Social Services is used to treat illnesses that could potentially be prevented with adequate blood serum levels of vitamin D; and

WHEREAS the above-referenced studies and findings taken in aggregate provide significant evidence for the benefits of vitamin D supplements; and

WHEREAS vitamin D supplements are inexpensive;

BE IT RESOLVED that the Alaska State Legislature respectfully requests the

Governor to establish prevention of disease as a primary model of health care in Alaska; and be it

FURTHER RESOLVED that the Alaska State Legislature encourages the Alaska Department of Health and Social Services and health care providers to increase attention to vitamin D deficiency and vitamin D blood testing and to promote awareness of the potential long-term health benefits of and increased chances of cancer survival with sufficient levels of vitamin D; and be it

FURTHER RESOLVED that the Alaska State Legislature urges the Department of Health and Social Services to

(1) promote vitamin D supplements for the elderly potentially to prevent bone loss, falls, fractures, and other age-related health problems;

(2) determine the relative effectiveness of influenza vaccination as compared with vitamin D supplementation, using the comparative treatment effectiveness analysis;

(3) investigate substituting vitamin D supplementation as a cost-effective method for preventing influenza in the adult population not identified as high risk; and

(4) promote vitamin D supplements for pregnant women and infants to prevent pregnancy complications, preterm births, type 1 diabetes, and rickets.

ALASKA: BURDEN OF CHRONIC DISEASE 2011

THE BURDEN OF CHRONIC DISEASE

Chronic diseases – such as heart disease, stroke, cancer, and diabetes – are among the most prevalent, costly, and preventable of all health problems. Leading a healthy lifestyle (avoiding tobacco use, being physically active, and eating well) greatly reduces a person's risk for developing chronic disease. Access to high-quality and affordable prevention measures (including screening and appropriate follow-up) are essential steps in saving lives, reducing disability and lowering costs for medical care.

HEART DISEASE AND STROKE

Heart disease and stroke, the second and fifth leading causes of death in Alaska, are the most common cardiovascular diseases.

- Heart disease accounted for 18% of deaths in Alaska in 2008, while stroke accounted for 5% of deaths.
- In 2009, 26% of adults in Alaska reported having high blood pressure (hypertension) and 35% of those who had their cholesterol tested reported having high blood cholesterol, which puts them at greater risk for developing heart disease and stroke.

CANCER

Cancer is the leading cause of death in Alaska.

- 25% of all deaths in Alaska in 2008 were due to cancer.
- The most commonly diagnosed cancers in Alaska are: (1) breast, (2) prostate, and (3) lung.

DIABETES

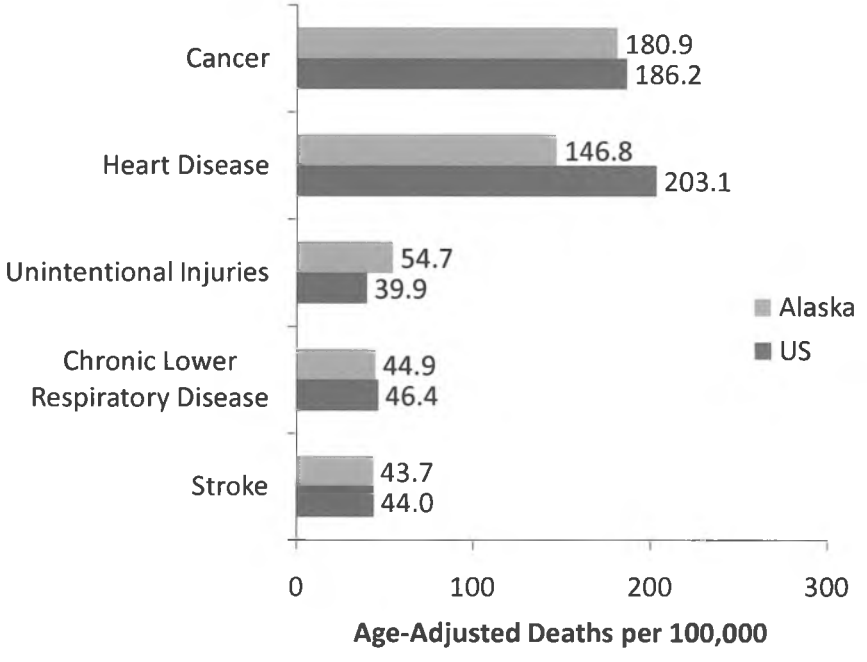
In 2008, diabetes was the 7th leading cause of death in both Alaska and the US. Likely to be underreported as a cause of death, the risk of death among people with diabetes is about twice that of people without diabetes of similar age.

- 93 Alaskans died from diabetes mellitus in 2008.
- In 2009, 6% of adults in Alaska reported being diagnosed with non-pregnancy related diabetes.

ARTHRITIS

- Arthritis is the most common cause of disability in the US, affecting more than 46 million Americans.
- In 2009, 23% of adults in Alaska reported being diagnosed with arthritis.

5 Most Common Causes of Death, Alaska Compared with United States, 2008



ALASKA: RISK FACTORS AND PREVENTIVE SERVICES

TOBACCO

Tobacco use is the single most preventable cause of death and disease in the United States. Each year, an estimated 438,000 people in the US die prematurely from smoking or exposure to secondhand smoke, and another 8.6 million have a serious illness caused by smoking. For every person who dies from smoking, 20 people suffer from at least one serious tobacco-related illness.

- In 2009, 19% of adults and 16% of high school students in Alaska reported being current smokers.

NUTRITION, PHYSICAL ACTIVITY, AND OVERWEIGHT/OBESITY

In the past 30 years, the prevalence of overweight and obesity has increased sharply for both adults and children. Physical inactivity and unhealthy eating contribute to overweight and obesity and a number of chronic diseases, including some cancers, cardiovascular disease, and diabetes.

- In 2009, 65% of adults in Alaska were overweight or obese and 26% of high school students were overweight or obese, based on self-reported height and weight.
- 83% of high school students and 77% of adults in Alaska consumed fewer than 5 servings of fruits and vegetables per day.
- 54% of Alaska high school students did not attend PE class in the past week.
- 26% of adults in Alaska did not get enough physical activity to meet federal recommendations.

EARLY DETECTION

Mammography is a screening method that has been shown to reduce mortality due to breast cancer by approximately 20-25% over 10 years among women 40 years and over.

- In 2008, 32% of women in Alaska aged 40 years or older reported not having had a mammogram within the last 2 years (which was the recommendation at the time).

Up to 60% of deaths from colorectal cancer could be prevented if persons aged 50 and older were screened regularly. Colorectal cancer can be prevented by removing precancerous polyps or abnormal growths, which can be identified during a fecal occult blood test, sigmoidoscopy, or colonoscopy.

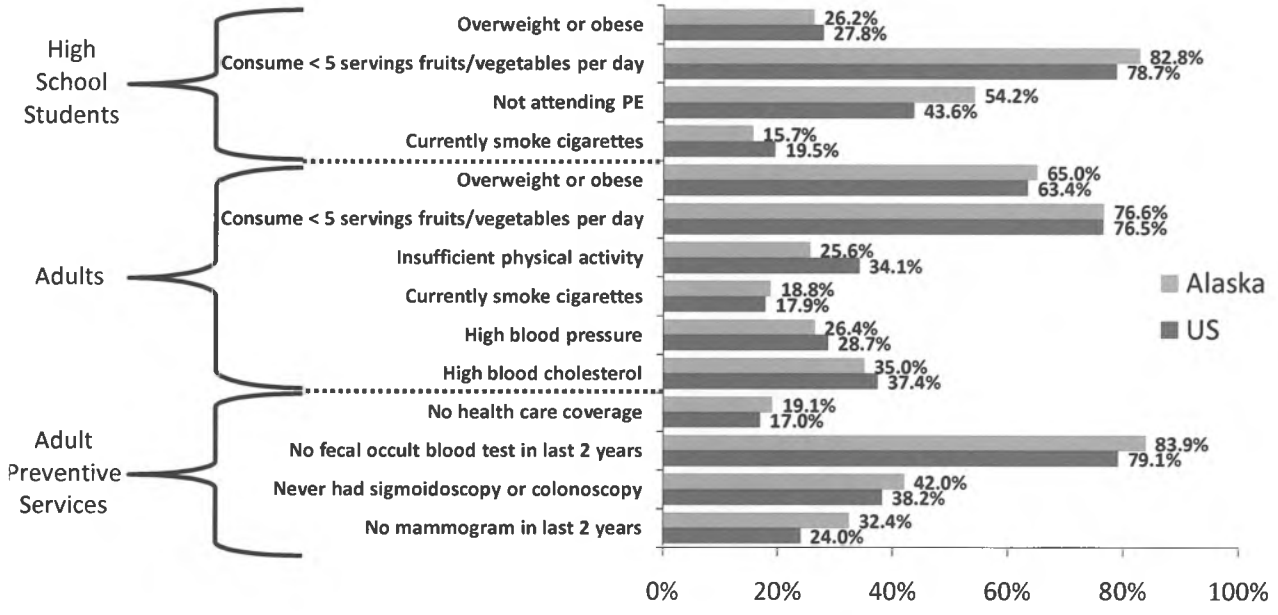
- In 2008, among Alaskans aged 50 years or older 42% reported never having had a sigmoidoscopy or colonoscopy.
- 84% reported not having had a fecal occult blood test within the past two years.

NO HEALTH CARE COVERAGE

With the US health care system changing rapidly, health care plans (e.g., health insurance, HMOs, and Medicaid/Medicare) need to ensure that all Americans have access to affordable, high-quality preventive services.

- In 2009, 19% of adults aged 18-64 in Alaska reported having no health care coverage.

Preventive Services and Risk Factors, Alaska Compared with United States



4/2005 thru 3/2007
Ketchikan

Research and Professional Briefs

Vitamin D Deficiency in a Nonrandom Sample of Southeast Alaska Natives

JOSEPH T. FROST, MPH, RD; LANI HILL, FNP

ABSTRACT

Serum vitamin D has recently been inversely associated with risk for type 2 diabetes. Recent literature suggests that many more individuals than generally thought suffer from vitamin D deficiency. Southeast Alaskan Natives are at an increased risk due to limited sunlight exposure and possible inadequate vitamin D intake. Therefore, the relationship between vitamin D and glucose should be investigated specifically in the southeast Alaska Native population. A review of lab records yielded 83 charts of patients found to have a serum 25-hydroxyvitamin D during a 2-year period. Upon review of these charts, only nine of 83 vitamin D levels were found to exceed the 32 ng/mL (80 nmol/L) threshold. Age and vitamin D levels were associated in a positive linear relationship ($r=0.354$, $P=0.028$). The patients in the lowest vitamin D quartile were younger in age compared to the highest quartile (14.6 years, 95% confidence interval: 4.9, 24.29; $P=0.004$). The high rate of deficiency noted in this sample suggests this population should be further assessed for vitamin D deficiency. Future studies are needed to confirm the association between a vitamin D deficiency and diabetes incidence in this population.
J Am Diet Assoc. 2008;108:1508-1511.

Although traditionally associated with calcium absorption and bone health, expanded roles for vitamin D, including a relationship to diabetes, have recently been reported in the literature. Low serum 25-hydroxyvitamin D levels have been found in individuals with diabetes compared to controls (1,2). The Third Nutrition and Health Examination Survey revealed an inverse association between risk of diabetes and 25-hydroxyvitamin D levels (3). A similar association was seen in the Nurses' Health Study (4). Serum 25-hydroxyvitamin D levels were found to be inversely associated with pancreatic beta cell function, thus suggesting a cause and effect relationship with diabetes (5). Recent research suggests that many more individuals than generally thought, especially those in northern latitudes or with other sunlight restrictions, are deficient in vitamin D (6-9). Both the recommended levels of serum vitamin D and the Adequate Intake from food sources have recently been suggested to be inadequate. At these levels it is thought the beneficial effect of vitamin D cannot be achieved. (6,8,10-12). Despite being at an increased risk for vitamin D deficiency due to limited sunlight exposure (13,14) and lactose intolerance (up to 80%) (15), southeast Alaskan Natives have not been included in vitamin D deficiency studies. The objectives of this study were to investigate vitamin D deficiency in the southeast Alaskan Native population and its possible role in the incidence of diabetes.

METHODS

A manual review of lab records for the 2-year time period of April 1, 2005, to March 30, 2007, was used to identify patients who had 25-hydroxyvitamin D tests completed as part of their care received at the Ketchikan Indian Community Tribal Health Clinic, a native health clinic on an Alaskan island that receives an annual rainfall of 12.5 feet per year. (Natives with varying degrees of native ancestry and who belong to one of 557 federally recognized tribes qualify for health care through Indian Health Service policies. In general, the term *American Indian* or *Alaskan Native* refers to those with native, although not necessarily exclusive, ancestry. Therefore, degree of Native blood varies in this population.)

This review yielded a nonrandom sample of 83 charts of Alaskan Natives. We conducted a retrospective electronic and manual review of these charts to investigate the possible relationship between serum vitamin D levels and abnormal glucose levels.

Electronic and paper charts of individuals known to have the test performed were reviewed, and test results for serum vitamin D and glucose, sex, age, and body mass index (BMI) were recorded. In the event of multiple vitamin D tests, only the initial test was used in data analysis. In all cases, the fasting glucose measured closest to the date of the initial vitamin D test was recorded. Glucose values obtained more than 1 year apart from the vitamin D test were excluded from the analysis. Of the 83 patients, fasting blood glucoses were recorded for 51.

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Table. Demographic data, 25-hydroxyvitamin D levels, and fasting glucose levels of patients with and without diabetes (n=83 except where otherwise noted)

	Patients with diabetes (n)	Patients without diabetes (n)	*P* value
Sex			
Male	12	16	
Female	16	39	
	← mean±SD[a] →		
Age[b] (y)	56±14	45±16	0.004
BMI[bc]	38.9±9.2	31.9±7.2	0.001
25-hydroxyvitamin D (ng/mL)	15.7±8.6	17.8±12.1	0.348
Fasting glucose[ab] (mg/dL)	139.8±49.9 (n=16)	96.2±11.1 (n=35)	<0.001

[a]SD=standard deviation.
[b]Denotes category of statistical significance at the α=.05 level.
[c]BMI=body mass index; calculated as kg/m^2.

Data from 2-hour oral glucose tolerance tests are not reported because only five were recorded. Random glucose levels were not analyzed due to multiple variables affecting their results. Vitamin D samples were drawn in-house and sent to a commercial laboratory for analysis using immunochemiluminometric assay. The threshold for the laboratory's vitamin D assay is 7.0 ng/mL (17.5 nmol/L); for data analysis all "undetectable" values were assigned 7.0 ng/mL (17.5 nmol/L).

Minitab version 15 (2007, Minitab Inc, State College, PA) was used for statistical analysis. Univariate regression calculations were done. Subjects were divided into quartiles based on vitamin D levels and comparisons were made using two-sample *t* tests with regard to glucose values, sex, age, and BMI. Results were considered significant at the α=.05 level.

The protocol for this study was granted expedited status under 45 CFR 46.110 by the Alaska Area Institutional Review Board in Anchorage. It was also approved by Ketchikan Indian Community Tribal Health Clinic Administration staff, the Ketchikan Indian Community Health Board, and the Ketchikan Indian Community Tribal Council.

RESULTS AND DISCUSSION

Of the 83 Native patients found to have received a 25-hydroxyvitamin D test during the 2-year period, 55 were female and 28 were male, with a mean age of 49 years (range=19 to 94 years) (Table). Twenty-eight of these patients were diagnosed with diabetes, of which all but two were vitamin D–deficient. Of the 55 without diabetes, only seven were vitamin D–sufficient (Figure). Subjects without diabetes were younger (−10.39, 95% confidence interval [CI]: −17.31, −3.47; *P*=0.004), had a lower BMI (−7.05, 95% CI: −11.06, −3.05; *P*=0.001), and had lower fasting blood glucose values (−43.63, 95% CI: −61.29, −25.97; *P*=<0.001). The mean (±standard deviation) 25-hydroxyvitamin D level was 17.1±11.0 ng/mL (42.8±27.5 nmol/L). Using two-sample *t* tests, no significant differences were found between sexes. Results indicated a significant positive linear relationship of age with respect to vitamin D levels (r=0.354, *P*=0.028).

Subjects were divided into quartiles based on 25-hydroxyvitamin D levels. These quartiles were compared in terms of sex, age, BMI, and fasting blood glucose values. With the exception of age, no statistically significant differences were observed between quartiles. The lowest quartile was on average 14.6 years younger compared with the highest quartile (95% CI: −24.29, −4.91; *P*=0.004). Patients known to have diabetes were then removed from the analysis (to control for confounding from the diabetes disease process or treatment, which may affect vitamin D), yielding similar results.

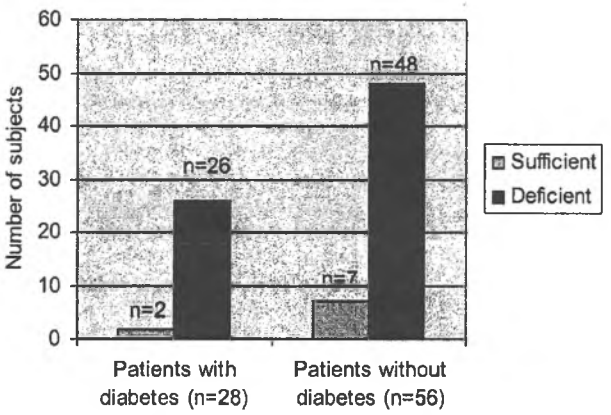

Figure. Vitamin D sufficiency of patients with and without diabetes using 32 ng/mL (80 nmol/L) as the minimum value for sufficiency.

No statistically significant relationships between vitamin D levels and blood glucose levels were observed. However, only nine of 83 vitamin D values were more than the recommended threshold of 32 ng/mL (80 nmol/L), and 18 of the vitamin D levels were so low that their actual value was undetectable. Although we cannot extrapolate these results to say that 89% of the population is vitamin D–deficient, the data suggest a basis for further investigation. It would seem unlikely to observe such a high rate of deficiency in this study, if there were not a high prevalence of vitamin D deficiency, even with perceptive clinicians ordering vitamin D tests for patients they thought to be at high risk for deficiency. The intent

of the study to compare serum glucose values between individuals of high and low serum vitamin D levels was somewhat undermined by the fact that so few normal values were observed. In fact, even the highest quartile of vitamin D values included values much less than the threshold of vitamin D deficiency.

The high prevalence of vitamin D deficiency found in this study is supported by studies reporting vitamin D deficiency in populations at higher latitudes or with otherwise limited sunlight exposure (although not at the magnitude found in this convenience sample) (7,8,12,13). The positive linear correlation between age and vitamin D levels found in this study differs from the common belief that vitamin D levels decrease with age. However, this positive correlation has been reported previously (7).

The finding related to subjects with known diabetes is also intriguing; only two of the 28 patients had 25-hydroxyvitamin D levels more than the 32 ng/mL (80 nmol/L) threshold. This is consistent with previous reports of vitamin D deficiency in patients with diabetes (1,2). Again, this is not a random sample but it does represent 20% of the known patients with diabetes per the Ketchikan Indian Community Diabetes Management System database. From a chart review we cannot determine that low vitamin D levels were a risk factor for diabetes in these individuals; however, this possibility deserves further investigation.

There are clear limitations to the design of this study. First, the study is retrospective in nature and therefore cannot determine causality. Second, this study did not assess known contributors to serum 25-hydroxyvitamin D levels, such as diet, supplementation, sunlight exposure, and medications that may interfere with vitamin D absorption and/or utilization. The results include 59 vitamin D levels measured during autumn and winter months, when vitamin D levels are thought to be lowest. Furthermore, the study consisted of a convenience sample of patients who were likely tested by providers on their suspicion that the patients had low vitamin D status. The study was not powered to detect differences; however, these data support the need for a larger study to investigate this association.

Despite these limitations, this study design offered a cost-effective opportunity to explore the possibility of vitamin D deficiency in this population and its relationship with diabetes. Given southeast Alaskan Natives' high risk for vitamin D deficiency, the increasing incidence of diabetes (100% to 125% in 14 years) (16), and recent research associating diabetes and vitamin D status, these results should not be dismissed. Although it is tempting to disregard vitamin D deficiency in this population as a genetic difference in normal values, it must be noted that African Americans also have lower vitamin D levels and have a 33% higher risk for cancer (17). Nor should Chiu and colleagues' conclusion that increasing a person's blood concentration of 25-hydroxyvitamin D from 10 ng/mL (25 nmol/L) to approximately 30 ng/mL (75 nmol/L) would improve insulin sensitivity by 60% be easily dismissed as not applicable to the native population (5).

Future efforts to explain the increase in incidence of diabetes should consider decreasing vitamin D–rich fish and fish oil consumption in the native population and the potential resultant decrease in serum vitamin D levels. It has been reported that in at least one group of Alaskan Natives that the consumption of traditional foods is much less common in younger natives compared with elders: 50% less in some categories of native food (18). Decreased traditional food consumption combined with additional lifestyle changes (eg, increased automobile use, more indoor activities, sedentary lifestyle) may be promote vitamin D deficiency.

CONCLUSIONS

This study suggests southeast Alaskan Natives may be at risk for vitamin D deficiency. To the extent that vitamin D plays a role in the etiology of diabetes and other chronic disorders, Alaskan Natives with vitamin D deficiency may be at increased risk for these diseases. This study's finding of decreased vitamin D levels in younger individuals is of concern from a public health standpoint and should be further evaluated. Specifically, the possibility that elder natives consume more fish and fish oils and therefore have higher vitamin D levels should be considered. Registered dietitians should be aware of the emerging expanded role of vitamin D in chronic diseases such as diabetes, and should consider vitamin D status in their nutrition assessments, especially for patients with limited sun exposure.

The corresponding author is a commissioned officer in the United States Public Health Service but is submitting this manuscript as an individual and not on behalf of the Federal Government.

The authors thank Carolyn E. Ford, PhD, for her contribution to the conceptual design of the protocol, and the Ketchikan Indian Community/Official Village of Saxman Health Board and the Ketchikan Indian Community Tribal Council for their permission to conduct this research.

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SEASONAL VARIATION IN SERUM 25-HYDROXYVITAMIN D IN HEALTHY FAIRBANKS, ALASKA RESIDENTS: RELATION TO DIET AND SUNLIGHT EXPOSURE

A

THESIS

Presented to the Faculty of the University of Alaska

in Partial Fulfillment of the Requirements

for the Degree of

MASTER OF SCIENCE

By

Meredith Grant Tallas, B.S.

Fairbanks, Alaska

December 1986

ABSTRACT

This study tested the hypothesis that lower UV radiation during the Fairbanks winter may cause seasonal vitamin D deficiencies. Forty-seven adult Caucasians (mean age, 34 years) donated monthly blood samples and gave 4-day food and sunlight exposure records during one year. There was a highly significant seasonal variation in serum 25-(OH)vitamin D (25-OHD), with the lowest mean mid-winter value above deficiency levels, and a yearly mean of 27 ng/ml for the full group. Analyses of variance indicated significant effects of vitamin D intake, sunlight exposure and sex on serum 25-OHD. Vitamin D intake appeared to be a more important factor determining year-round 25-OHD levels than sunlight exposure. Males had yearly mean 25-OHD levels 16% higher than females and 25% of the females, but none of the males, had yearly means less than 20 ng/ml indicating that females were at greater risk for the development of vitamin D deficiency.

Record: 1

Title: Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial.

Authors: Lappe JM; Travers-Gustafson D; Davies KM; Recker RR; Heaney RP

Author Address: Osteoporosis Research Center, Creighton University, Omaha, NE 68131, USA. jmlappe@creighton.edu

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Publication Type: Journal Article; Randomized Controlled Trial; Research Support, N.I.H., Extramural

Language: English

Journal Information: *Country of Publication:* United States *NLM ID:* 0376027 *Publication Model:* Print *Cited Medium:* Print *ISSN:* 0002-9165 (Print) *Linking ISSN:* 00029165 *NLM ISO Abbreviation:* Am. J. Clin. Nutr. *Subsets:* Core Clinical (AIM); MEDLINE

MeSH Terms: Dietary Supplements*
Calcium/*therapeutic use
Neoplasms/*prevention & control
Vitamin D/*therapeutic use
Calcifediol/blood; Double-Blind Method; Female; Fractures, Bone/prevention & control; Humans; Incidence; Kaplan-Meier Estimate; Logistic Models; Middle Aged; Neoplasms/epidemiology

Abstract: **Background:** Numerous observational studies have found supplemental calcium and vitamin D to be associated with reduced risk of common cancers. However, interventional studies to test this effect are lacking.
Objective: The purpose of this analysis was to determine the efficacy of calcium alone and calcium plus vitamin D in reducing incident cancer risk of all types.
Design: This was a 4-y, population-based, double-blind, randomized placebo-controlled trial. The primary outcome was fracture incidence, and the principal secondary outcome was cancer incidence. The subjects were 1179 community-dwelling women randomly selected from the population of healthy postmenopausal women aged >55 y in a 9-county rural area of Nebraska centered at latitude 41.4 degrees N. Subjects were randomly assigned to receive 1400-1500 mg supplemental calcium/d alone (Ca-only), supplemental calcium plus 1100 IU vitamin D3/d (Ca + D), or placebo.
Results: When analyzed by intention to treat, cancer incidence was lower

in the Ca + D women than in the placebo control subjects (P < 0.03). With the use of logistic regression, the unadjusted relative risks (RR) of incident cancer in the Ca + D and Ca-only groups were 0.402 (P = 0.01) and 0.532 (P = 0.06), respectively. When analysis was confined to cancers diagnosed after the first 12 mo, RR for the Ca + D group fell to 0.232 (CI: 0.09, 0.60; P < 0.005) but did not change significantly for the Ca-only group. In multiple logistic regression models, both treatment and serum 25-hydroxyvitamin D concentrations were significant, independent predictors of cancer risk. **Conclusions:** Improving calcium and vitamin D nutritional status substantially reduces all-cancer risk in postmenopausal women. This trial was registered at clinicaltrials.gov as NCT00352170.

Comments: Comment in: Am J Clin Nutr. 2007 Dec;86(6):1804-5; author reply 1805-6. (PMID: 18065602)
Comment in: Am J Clin Nutr. 2007 Nov;86(5):1549; author reply 1549-50. (PMID: 17991672)
Comment in: Am J Clin Nutr. 2008 Mar;87(3):792-3; author reply 793-4. (PMID: 18326620)
Comment in: Am J Clin Nutr. 2008 Mar;87(3):792; author reply 793-4. (PMID: 18326621)
Erratum in: Am J Clin Nutr. 2008 Mar;87(3):794.

Grant Information: AG14683-01A2 United States AG NIA NIH HHS

Molecular Sequence: ClinicalTrials.gov NCT00352170

Substance Nomenclature: 1406-16-2 (Vitamin D)
19356-17-3 (Calcifediol)
7440-70-2 (Calcium)

Entry Dates: *Date Created:* 20070608 *Date Completed:* 20070711 *Latest Revision:* 20101118

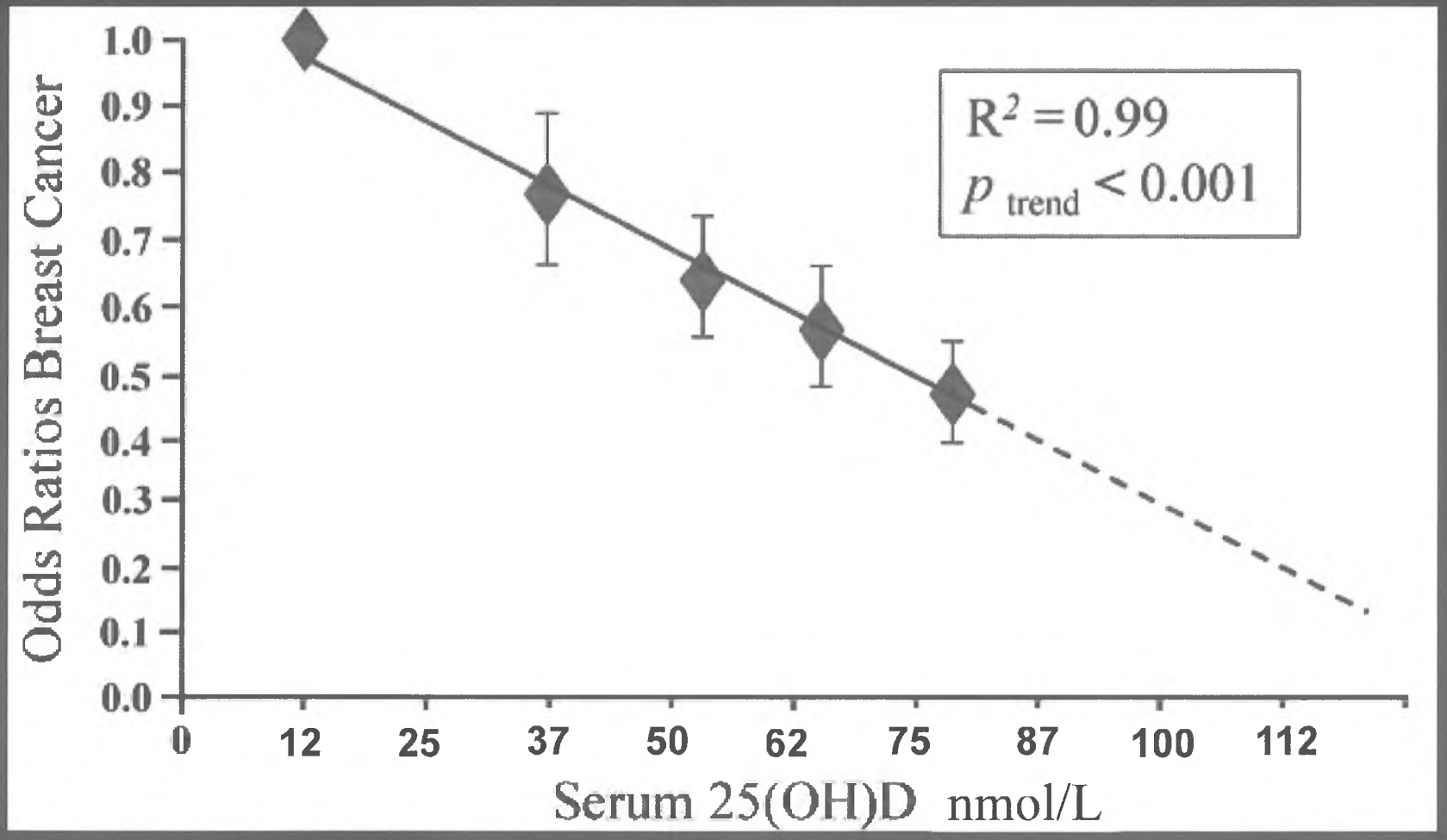
Update Code: 20101124

PMID: 17556697

Database: MEDLINE

Breast Cancer Dose Response Risk Reduction

Garland, et al. Meta-Analysis of Dose Response, 2008



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Record: 1

Title: Optimal Vitamin D Status for Colorectal Cancer Prevention: A Quantitative Meta Analysis.

Authors:
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Mohr, Sharif B.[1]
Lipkin, Martin[3]
Newmark, Harold L.[4]
Giovannucci, Edward[5]
Wei, Melissa[5]
Holick, Michael F.[6]

Source: American Journal of Preventive Medicine; Mar2007, Vol. 32 Issue 3, p210-216, 7p

Document Type: Article

Subject Terms:
*VITAMIN D
*CALCIUM regulating hormones
*COLON (Anatomy) -- Cancer
*CANCER -- Prevention

Abstract: Background: Previous studies, such as the Women's Health Initiative, have shown that a low dose of vitamin D did not protect against colorectal cancer, yet a meta-analysis indicates that a higher dose may reduce its incidence. Methods: Five studies of serum 25(OH)D in association with colorectal cancer risk were identified using PubMed. The results of all five serum studies were combined using standard methods for pooled analysis. The pooled results were divided into quintiles with median 25(OH)D values of 6, 16, 22, 27, and 37 ng/mL. Odds ratios were calculated by quintile of the pooled data using Peto's Assumption-Free Method, with the lowest quintile of 25(OH)D as the reference group. A dose–response curve was plotted based on the odds for each quintile of the pooled data. Data were abstracted and analyzed in 2006. Results: Odds ratios for the combined serum 25(OH)D studies, from lowest to highest quintile, were 1.00, 0.82, 0.66, 0.59, and 0.46 (p _{trend}<0.0001) for colorectal cancer. According to the DerSimonian-Laird test for homogeneity of pooled data, the studies were homogeneous (chi²=1.09, df=4, p=0.90. The pooled odds ratio for the highest quintile versus the lowest was 0.49 (p<0.0001, 95% confidence interval, 0.35–0.68). A 50% lower risk of colorectal cancer was associated with a serum 25(OH)D level ≥33 ng/mL,

compared to ≤12 ng/mL. Conclusions: The evidence to date suggests that daily intake of 1000–2000 IU/day of vitamin D₃ could reduce the incidence of colorectal with minimal risk. [Copyright &y& Elsevier]

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Record: 1

Title: Ultraviolet B Irradiance and Incidence Rates of Bladder Cancer in 174 Countries.

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Gorham, Edward D.[1,2]
Grant, William B.[3]
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Source: American Journal of Preventive Medicine; Mar2010, Vol. 38 Issue 3, p296-302, 7p

Document Type: Article

Subject Terms: *ULTRAVIOLET radiation -- Physiological effect
*MULTIPLE regression analysis
*SMOKING
*MEDICAL care
*PUBLIC health
*BLADDER
*CANCER
DISEASE incidence
NAICS/Industry Codes525120 Health and Welfare Funds

Abstract: Background: Although nearly half of bladder cancer cases are due to smoking, the cause of nearly half is unexplained. Purpose: This study aims to determine whether an inverse association exists between ultraviolet B (UVB) irradiance and incidence rates of bladder cancer worldwide. Methods: This study used an ecologic approach. Age-adjusted incidence rates of bladder cancer from 2002 were obtained for all 174 countries in GLOBOCAN, a database of the International Agency for Research on Cancer. The relationship of latitude and estimated serum 25-hydroxyvitamin D [25(OH)D] with incidence rates was determined. The independent contributions to incidence rates of bladder cancer of UVB, per capita cigarette consumption in 1980, and per capita health expenditure for 2001 were assessed using multiple regression. The analyses were performed in July 2008. Results: Bladder cancer incidence rates were higher in countries at higher latitudes than those nearer to the equator ($r=-0.66$, 95% CI=−0.74, −0.57, $p<0.01$). Ultraviolet B irradiance was independently inversely associated with incidence rates of bladder cancer after controlling for per capita cigarette consumption ($\beta=-0.28$, 95% CI=−0.51, −0.05; R ² for model=0.38, $p<0.0001$). Further, UVB irradiance was also inversely associated with incidence rates after

controlling for per capita health expenditure (β=−0.23, 95% CI=−0.36, −0.01; R ² for model=0.49, p<0.0001) in a separate regression model. Conclusions: Further investigation is needed to confirm the associations identified in this study using observational studies of individuals. The focus of this research should include the association of serum 25(OH)D levels with risk of bladder cancer. [Copyright &y& Elsevier]

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LifeExtension® http://www.lef.org/

Life Extension Magazine September 2010

BOOK
EXCERPT

The Vitamin D Solution

By Michael F. Holick, PhD, MD

If I had to give you a single secret ingredient that could apply to the prevention—and treatment, in many cases—of heart disease, common cancers, stroke, infectious diseases from influenza to tuberculosis, type 1 and 2 diabetes, dementia, depression, insomnia, muscle weakness, joint pain, fibromyalgia, osteoarthritis, rheumatoid arthritis, osteoporosis, psoriasis, multiple sclerosis, and hypertension, it would be this: vitamin D.

I have been traveling around the world not only lecturing about vitamin D but also hearing from physicians how common vitamin D deficiency is. It's not only the most common nutritional deficiency in the world, but it's also the most common medical condition, affecting at least one billion people. Three out of every four Americans are deficient in vitamin D, up from one out of two twenty years ago.

A HORMONE, NOT A VITAMIN

Naturally, we're disposed to think about vitamin D as a vitamin—a substance that we get from our diets, like vitamin C or niacin, and that participates in biological reactions to help the body operate optimally. But despite its name, vitamin D isn't really a vitamin. Vitamin D is in a class by itself; its far-reaching effects on the body are aligned with how hormones act to influence metabolic pathways, cellular functions, and the expression of myriad genes. Vitamin D's active metabolic product in the body, in fact, is a molecule called 1,25-dihydroxyvitamin D (let's call it 1,25-vitamin D for simplicity), which is a secosteroid hormone that directly or indirectly targets more than two thousand genes, or about 6 percent of the human genome.

FROM BONE HEALTH TO BRAIN HEALTH

Contrary to what was previously believed—that vitamin D receptors were only in bones, intestines, and kidneys—we now know that vitamin D receptors are *everywhere* in the body. There is even proof that vitamin D receptors exist in the brain and that the active form of vitamin D stimulates the production of mood-elevating serotonin. This explains how it may help reduce depression (or just a chronically foul mood). Fat cells, too, have vitamin D receptors, and fat cells can be more metabolically active (burn more calories) if they have more vitamin D. People tend to think that fat cells are like inanimate blobs of lard when in fact they are active participants in the process by which your brain learns that you're full and don't need to take another bite of food. When you've had enough, fat cells secrete a hormone called leptin that allows you to push away from the table. A lack of vitamin D will interfere with this appetite-suppressing hormone whose job it is to regulate your body weight. And we all know what an unchecked appetite can lead to: weight gain and a higher risk of developing type 2 diabetes. Speaking of which, vitamin D deficiency has also been shown to exacerbate type 2 diabetes, impair insulin production in the pancreas, and increase insulin resistance.

BENEFITS OF VITAMIN D IN BRIEF

Bone health: prevents osteopenia, osteoporosis, osteomalacia, rickets, and fractures.

Cellular health: prevents certain cancers, such as prostate, pancreatic, breast, ovarian, and colon; prevents infectious diseases and upper-respiratory-tract infections, asthma, and wheezing disorders.

Organ health: prevents heart disease and stroke; prevents type 2 diabetes, periodontitis and tooth loss, and other inflammatory diseases.

Muscular health: supports muscle strength.

Autoimmune health: prevents multiple sclerosis, type 1 diabetes mellitus, Crohn's disease, and rheumatoid arthritis.

Brain health: prevents depression, schizophrenia, Alzheimer's disease, and dementia.

Mood-related health: prevents seasonal affective disorder, premenstrual syndrome (PMS, also known as premenstrual tension), and sleeping disorders.

VITAMIN D AND OBESITY

Because vitamin D is stored in fat cells, you'd think that people with excess fat would have plenty of extra vitamin D on hand to make up any shortage. As it turns out, that thinking is wrong, and a parallel relationship exists between vitamin D deficiency and obesity. The fatter you are, the higher your risk for a deficiency. Why? The vitamin D essentially gets locked inside the fat cells, unavailable for use.

In one of my studies, we exposed obese and nonobese individuals to the same amount of UVB radiation and showed that obese people can only raise their blood levels of vitamin D by about 45 percent compared to a normal-weight person. Obese people (defined as those with a body mass index, or BMI, above 30) often need at least twice as much vitamin D to satisfy their body's needs. With the majority of Americans overweight or obese these days, it's not a stretch to understand why a similar number of people are vitamin D deficient. The two epidemics have worsened in unison.

WHAT CONSTITUTES A DEFICIENCY?

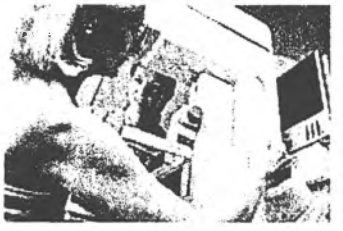
My extensive studies have helped redefine what it means to be vitamin D deficient. Before one of my publications in the *Lancet* in 1998, vitamin D deficiency was defined as a having 25-vitamin D levels below **10** nanograms per milliliter. I demonstrated, however, that a blood level of twice that—20 nanograms per milliliter—is needed to prevent an unhealthy elevation in parathyroid hormone level, a sign of vitamin D deficiency.

Obesity-related conditions now account for nearly 10 percent of all medical spending, having doubled in the last decade. It's hard to believe that the obesity rate could rise 37 percent in just eight years alone, but that's exactly what happened between 1998 and 2006—bringing a breathtaking one third of the adult American population into the obese camp. Why the spike in such a short time frame?

We've evolved to store vitamin D in fat. This allows us to have ample supplies on hand during the long winter months, when it's virtually impossible to make vitamin D—when the active synthesis of vitamin D from the sun is in hibernation until the spring. But humans did not evolve to carry such copious amounts of excessive fat. The result is that this fat begins to have negative effects on the body's metabolism and hormonal balance.

Contrary to what you might think, overweight people don't have higher levels of 25-vitamin D due to their higher fat content. They have lower levels, because the excess fat absorbs and holds onto the vitamin D so that it cannot be used for bone building and cellular health. Unlike a normal-weight person, whose fat is continually being recycled so the vitamin D can be released, those with relatively immobile fat stores cannot access their vitamin D, which is literally locked up in their adipose tissue. Making matters worse, obese people are frequently vitamin D deficient to start with because they go outside much less. Obese people need two to three times more vitamin D a day than those of normal weight, so I advise such patients to take between 3,000 and 6,000 IU of vitamin D a day.

CRACKING ONE OF CANCER'S CODES BREAST CANCER



Here's a staggering statistic: Women who are deficient in vitamin D at the time they are diagnosed with breast cancer are nearly 75 percent more likely to die from the disease than women with sufficient vitamin D levels. What's more, their cancer is twice as likely to metastasize to other parts of the body.

In the United States, more than forty thousand women die from breast cancer every year—making it the deadliest killer of women after heart disease. One woman in eight either has or will develop breast cancer in her lifetime. There are 214,000 new cases and 41,000 deaths from breast cancer each year in the United States. A 2008 study found that women who had a vitamin D deficiency at the time they were diagnosed with breast cancer were 94 percent more likely to have their cancer spread than women with adequate 25-vitamin D levels in their bodies.

In May 1999, a landmark study by Dr. Esther John, based on the meticulous analysis of breast cancer statistics from the

National Health and Nutrition Examination Survey, was published. The authors conclude definitively that sun exposure and a vitamin D–rich diet significantly lower the risk of breast cancer.

PROSTATE CANCER

Only heart attacks and lung cancer kill more men than cancer of the prostate. Cancer of the prostate is especially feared by men because surgical treatment for this form of cancer frequently results in impotence. A study in the August 2001 issue of the *Lancet* proves that the risk of developing prostate cancer is directly related to sunlight exposure. The study divided people into four groups according to how much sunlight they had been exposed to. The lowest quarter, or quartile, of the study participants were three times more likely to develop prostate cancer than those in the highest quartile of sun exposure. The results show that those in the highest quartile reduced their risk of developing prostate cancer by 66 percent. Those in the second and third quartiles also had a significantly lower chance of getting prostate cancer compared with those in the lowest quartile, who received the least sun exposure. Another study took a long look, over almost two years, at men with prostate cancer who received 2,000 IU of vitamin D a day and found that overall the men had a 50 percent reduction in the rise of their levels of prostate specific antigen (PSA), which is an indicator of prostate cancer activity.

COLON CANCER

Cancer of the colon and its neighboring area, known sometimes as colorectal cancer, affects both men and women. Like breast cancer and prostate cancer, colorectal cancer is seen much more frequently than skin cancers and is much more deadly. About 150,000 Americans are told each year that they have colon cancer, and about 35 percent of these will die of it.

A study published in the *Journal of Clinical Oncology* in 2008, conducted by lead researcher Dr. Kimmie Ng of the Dana-Farber Cancer Institute in Boston found that high blood levels of 25-vitamin D increased colon cancer patients' survival rate by 48 percent. In this study, Dr. Ng and her team collected data on 304 patients who had been diagnosed with colon cancer between 1991 and 2002. Everyone in the study had had their 25-vitamin D blood levels measured a minimum of two years before being diagnosed with the disease. The patients were tracked until they died or until the study ended in 2005; 123 patients died, 96 of them from colon or rectal cancer during the follow-up period. Dr. Ng and her team found that the patients with the highest 25-vitamin D levels were 39 percent less likely to die from colorectal cancer than the patients who had the lowest levels.

These findings are consistent with dozens and dozens of other observations that have been made in the past decade, including those by Dr. Cedric Garland. His lab reports that you are three times less likely to die from colon cancer if you have healthy levels of 25-vitamin D in your bloodstream.

A NEW MODEL FOR CANCER?

Though it's a stretch to say vitamin D can totally prevent and cure cancer, some scientists have been bold enough to suggest a whole new theory about cancer. Just last year, the Garland brothers raised the possibility that there's another story behind cancer's genesis in the body. The current scientific model assumes that a genetic mutation is cancer's point of origin. But what if that assumption is wrong? What if there is another way to explain how cancer develops? Those are the questions the Garlands put forth, which were published in the *Annals of Epidemiology* and immediately picked up by the media.

First, Dr. Cedric Garland and his team pointed to a host of research that suggests cancer develops when cells lose the ability to stick together in a healthy, normal way. He went on to argue that the key factor in this initial triggering of a malignancy could well be a lack of vitamin D. According to Dr. Garland, researchers have documented that with enough activated vitamin D present, cells adhere to one another in tissue and act as normal, mature cells. But if there is a deficiency of activated vitamin D, cells can lose this stick-to-each-other quality, as well as their identity as differentiated cells. The result? They may revert to a dangerous, immature state and become cancerous.

What can stop this process from occurring, says Dr. Garland, is ample supplies of vitamin D in the body. Whether or not this theory can be proven true will be told by future studies and research.

TESTING, TESTING, 1-2-3

The only surefire way to know for certain the extent of your vitamin D deficiency is to ask for a *25-hydroxyvitamin D* test, also called a 25(OH) D test. This is the circulating form of vitamin D that the liver generates and that then becomes activated by the kidneys. While it's intuitive to think you'd want to test for the body's "active form" rather than just a precursor, testing for the activated vitamin D (1,25-vitamin D) does not give an accurate portrayal of your vitamin D status.

And here's the rub: many doctors order the wrong test, and when the results come back showing a normal level of activated vitamin D, they think everything is D-okay. You could, however, be suffering from a serious deficiency even though your activated levels appear normal—or even elevated.

FOLLOWING DR. HOLICK'S RECOMMENDATIONS

Dr. Holick uses vitamin D supplements, milk, and sensible sun exposure to keep his ***25-hydroxyvitamin D*** blood levels at **50** ng/mL. Dr. Holick believes that this and higher levels of 25-hydroxyvitamin are optimal.

Life Extension® has always used the more accurate ***25-hydroxyvitamin D*** blood test recommended by Dr. Holick. Foundation members can order this ***25-hydroxyvitamin* D blood test** for **$47** by calling **1-800-208-3444.**

To order a copy of *The Vitamin D Solution* by Dr. Michael F. Holick, call 1-800-544-4440 or visit www.LifeExtension.com
Item#33824 • Retail price $25.95 Member price $18.17

LifeExtension®

Record: 1

Title: Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study.

Authors: Hypponen, Elina
Laara, Esa
Reunanen, Antti
Jarvelin, Marjo-Riitta
Virtanen, Suvi M

Source: Lancet; 11/3/2001, Vol. 358 Issue 9292, p1500, 4p, 2 Charts

Document Type: Article

Subject Terms: *VITAMIN D
*DIABETES
*DIETARY supplements
*MEDICINE, Preventive

Abstract: Summary: Background: Dietary vitamin D supplementation is associated with reduced risk of type 1 diabetes in animals. Our aim was to ascertain whether or not vitamin D supplementation or deficiency in infancy could affect development of type 1 diabetes. Methods: A birth-cohort study was done, in which all pregnant women (n=12 055) in Oulu and Lapland, northern Finland, who were due to give birth in 1966 were enrolled. Data was collected in the first year of life about frequency and dose of vitamin D supplementation and presence of suspected rickets. Our primary outcome measure was diagnosis of type 1 diabetes by end of December, 1997. Findings: 12 058 of 12 231 represented live births, and 10 821 (91% of those alive) children were followed-up at age 1 year. Of the 10 366 children included in analyses, 81 were diagnosed with diabetes during the study. Vitamin D supplementation was associated with a decreased frequency of type 1 diabetes when adjusted for neonatal, anthropometric, and social characteristics (rate ratio [RR] for regular vs no supplementation 0.12, 95% CI 0.03-0.51, and irregular vs no supplementation 0.16, 0.04-0.74. Children who regularly took the recommended dose of vitamin D (2000 IU daily) had a RR of 0.22 (0.05-0.89) compared with those who regularly received less than the recommended amount. Children suspected of having rickets during the first year of life had a RR of 3.0 (1.0-9.0) compared with those without such a suspicion. Interpretation: Dietary vitamin D supplementation is associated with reduced risk of type 1 diabetes. Ensuring adequate vitamin D supplementation for infants could help to reverse the increasing trend in the incidence of type 1 diabetes. [ABSTRACT FROM AUTHOR]

Full Text Word Count: 3664

ISSN: 00995355

Accession Number: 5448201

Database: Academic Search Premier

Record: 1

Title: Vitamin D and Calcium Intake in Relation to Type 2 Diabetes in Women.

Authors: Pittas, Anastassios G.[1] *apittas@tufts-nemc.org*
Dawson-Hughes, Bess[1,2]
Li, Tricia[3]
Van Dam, Rob M.[3]
Willett, Walter C.[3]
Manson, Joann E.[3,4]
Hu, Frank B.[3]

Source: Diabetes Care; Mar2006, Vol. 29 Issue 3, p650-656, 7p, 4 Charts

Document Type: Article

Subject Terms: *VITAMIN D
*CALCIUM
*NON-insulin-dependent diabetes
*DIABETES
*ENDOCRINE glands -- Diseases

Abstract: OBJECTIVE -- The purpose of this study was to prospectively examine the association between vitamin D and calcium intake and risk of type 2 diabetes. RESEARCH DESIGN AND METHODS -- In the Nurses' Health Study, we followed 85,779 women who had no history of diabetes, cardiovascular disease, or cancer at baseline for the development of type 2 diabetes. Vitamin D and calcium intake from diet and supplements was assessed every 2-4 years. During 20 years of follow-up, we documented 4,843 incident cases of type 2 diabetes. RESULTS -- After adjusting for multiple potential confounders, there was no association between total vitamin D intake and type 2 diabetes. However, the relative risk (RR) of type 2 diabetes was 0.87 (95% CI 0.75-1.00; P for trend = 0.04) comparing the highest with the lowest category of vitamin D intake from supplements. The multivariate RRs of type 2 diabetes were 0.79 (0.70-0.90; P for trend <0.001) comparing the highest with the lowest category of calcium intake from all sources and 0.82 (0.72-0.92; P for trend <0.001) comparing the highest with the lowest category of calcium intake from supplements. A combined daily intake of >1,200 mg calcium and >800 IU vitamin D was associated with a 33% lower risk of type 2 diabetes with RR of 0.67 (0.49-0.90) compared with an intake of <600 mg and 400 IU calcium and vitamin D, respectively. CONCLUSIONS -- The results of this large prospective study suggest a potential beneficial role for both vitamin D and calcium intake in reducing the risk of type 2 diabetes. [ABSTRACT FROM AUTHOR]

Author Affiliations: [1]Division of Endocrinology, Diabetes and Metabolism, Tufts-New England Medical Center, Boston, Massachusetts
[2]Bone Metabolism Laboratory, Jean Mayer U.S. Department of Agriculture Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts
[3]Harvard School of Public Health and Channing Laboratory, Boston, Massachusetts
[4]Division of Preventive Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Full Text Word Count: 5731
ISSN: 01495992
Accession Number: 20210227
Database: Academic Search Premier

Record: 1

Title: Seasonal distribution of acute myocardial infarction in the second National Registry of Myocardial Infarction.

Authors: Spencer FA; Goldberg RJ; Becker RC; Gore JM

Author Address: Cardiovascular Thrombosis Research Center, Department of Medicine, University of Massachusetts Medical Center, Worcester 01655, USA. fred.spencer@banyan.ummed.edu

Source: Journal Of The American College Of Cardiology [J Am Coll Cardiol] 1998 May; Vol. 31 (6), pp. 1226-33.

Publication Type: Journal Article; Research Support, Non-U.S. Gov't

Language: English

Journal Information: *Country of Publication:* UNITED STATES *NLM ID:* 8301365 *Publication Model:* Print *Cited Medium:* Print *ISSN:* 0735-1097 (Print) *Linking ISSN:* 07351097 *NLM ISO Abbreviation:* J. Am. Coll. Cardiol. *Subsets:* Core Clinical (AIM); MEDLINE

MeSH Terms: Registries*
Seasons*
Myocardial Infarction/*epidemiology
Aged; Female; Hospitalization; Humans; Male; Middle Aged; Myocardial Infarction/etiology; United States/epidemiology

Abstract: **Objectives:** This observational study sought to determine whether cases of acute myocardial infarction (AMI) reported to the second National Registry of Myocardial Infarction (NRMI-2) varied by season.
Background: The existence of circadian variation in the onset of AMI is well established. Examination of this periodicity has led to new insights into pathophysiologic triggers of atherosclerotic plaque rupture. Although a seasonal pattern for mortality from AMI has been previously noted, it remains unclear whether the occurrence of AMI also displays a seasonal rhythmicity. Documentation of such a pattern may foster investigation of new pathophysiologic determinants of plaque rupture and intracoronary thrombosis.
Methods: We analyzed the number of cases of AMI reported to NRMI-2 by season during the period July 1, 1994 to July 31, 1996. Data were normalized so that seasonal occurrence of AMI was reported according to a standard 90-day length.
Results: A total of 259,891 cases of AMI were analyzed during the study period. Approximately 53% more cases were reported in winter than during the summer. The same seasonal pattern (decreasing occurrence of

reported cases from winter to fall to spring to summer) was seen in men and women, in different age groups and in 9 of 10 geographic areas. In-hospital case fatality rates for AMI also followed a seasonal pattern, with a peak of 9% in winter.

Conclusion: The present results suggest that there is a seasonal pattern in the occurrence of AMIs reported to NRMI-2 that is characterized by a marked peak of cases in the winter months and a nadir in the summer months. This pattern was seen in all subgroups analyzed as well as in different geographic areas. These findings suggest that the chronobiology of seasonal variation in AMI may be affected by variables independent of climate.

Comments: Comment in: J Am Coll Cardiol. 1999 Jun;33(7):2088-9. (PMID: 10362222)
Comment in: J Am Coll Cardiol. 1998 Dec;32(7):2103-4. (PMID: 9857903)

Entry Dates: *Date Created:* 19980522 *Date Completed:* 19980522 *Latest Revision:* 20061115

Update Code: 20101124

PMID: 9581712

Database: MEDLINE

Record: 1

Title: 25-Hydroxyvitamin D and Risk of Myocardial Infarction in Men.

Authors: Giovannucci, Edward[1,2] *egiovann@hsph.harvard.edu*
Yan Liu[1]
Hollis, Bruce W.[3]
Rimm, Eric B.[1,2]

Source: Archives of Internal Medicine; 6/9/2008, Vol. 168 Issue 11, p1174-1180, 7p, 3 Charts

Document Type: Article

Subject Terms:
*MYOCARDIAL infarction
*CORONARY heart disease
*HEART -- Diseases
*MEN -- Health & hygiene
*MEDICINE
*HEALTH
*CARDIOVASCULAR system -- Diseases
*INTERNAL medicine
*CARDIOLOGY

Abstract: The article assesses prospectively whether plasma 25-hydroxyvitamin D (25[OH]D) concentrations are associated with risk of coronary heart disease. It shows that men who are deficient in 25[OH]D were at increased risk for myocardial infarction compared with those who are considered to be sufficient in 25[OH]D. It emphasizes that even men with intermediate 25 [OH]D levels were at elevated risk relative to those with sufficient 25[OH]D levels. It concludes that low levels of 25[OH]D are associated with higher risk of myocardial infarction in a graded manner, even after controlling for factors known to be associated with coronary artery disease.

Author Affiliations: [1]Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts
[2]Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston
[3]Department of Pediatrics, Medical University of South Carolina, Charleston

ISSN: 00039926

Accession Number: 32681692

Database: Academic Search Premier

Record: 1

Title: Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder.

Authors: Gloth FM 3rd; Alam W; Hollis B

Author Address: The Department of Medicine, The Union Memorial Hospital, Baltimore, Maryland 21218-2895, USA.

Source: The Journal Of Nutrition, Health & Aging [J Nutr Health Aging] 1999; Vol. 3 (1), pp. 5-7.

Publication Type: Clinical Trial; Journal Article; Randomized Controlled Trial

Language: English

Journal Information: *Country of Publication:* FRANCE *NLM ID:* 100893366 *Publication Model:* Print *Cited Medium:* Print *ISSN:* 1279-7707 (Print) *Linking ISSN:* 12797707 *NLM ISO Abbreviation:* J Nutr Health Aging *Subsets:* MEDLINE

MeSH Terms: Phototherapy*
Seasonal Affective Disorder/*drug therapy
Seasonal Affective Disorder/*therapy
Vitamin D/*therapeutic use
Adolescent; Adult; Analysis of
Variance; Female; Humans; Hydroxycholecalciferols/blood; Male; Middle Aged; Psychological Tests; Vitamin D/biosynthesis

Abstract: Seasonal Affective Disorder (SAD) is prevalent when vitamin D stores are typically low. Broad-spectrum light therapy includes wavelengths between 280-320 nm which allow the skin to produce vitamin D. This study was designed to test the hypothesis that vitamin D deficiency might play a role in SAD. A prospective, randomized controlled trial was conducted in a group of 15 subjects with SAD. Eight subjects received 100,000 I.U. of vitamin D and seven subjects received phototherapy. At the onset of treatment and after 1 month of therapy subjects were administered the Hamilton Depression scale, the SIGH-SAD, and the SAD-8 depression scale. All subjects also had serum levels of 25-hydroxyvitamin D (25-OH D) measured before and 1 week after intervention therapy. All subjects receiving vitamin D improved in all outcome measures. The phototherapy group showed no significant change in depression scale measures. Vitamin D status improved in both groups (74% vitamin D group, $p < 0.005$ and 36% phototherapy group, $p < 0.01$). Improvement in 25-OH D was significantly associated with improvement in depression scale scores ($r2=0.26$; $p=0.05$). Vitamin D may be an important treatment for SAD. Further studies will be necessary to confirm these findings.

Record: 1

Title: Association between serum concentrations of 25-hydroxyvitamin D3 and periodontal disease in the US population.

Authors: Dietrich T; Joshipura KJ; Dawson-Hughes B; Bischoff-Ferrari HA

Author Address: Department of Periodontology and the Department of Oral Surgery and Oral Radiology, Charité, Humboldt University of Berlin, Germany. tdietric@bu.edu

Source: The American Journal Of Clinical Nutrition [Am J Clin Nutr] 2004 Jul; Vol. 80 (1), pp. 108-13.

Publication Type: Journal Article; Research Support, Non-U.S. Gov't

Language: English

Journal Information: *Country of Publication:* United States *NLM ID:* 0376027 *Publication Model:* Print *Cited Medium:* Print *ISSN:* 0002-9165 (Print) *Linking ISSN:* 00029165 *NLM ISO Abbreviation:* Am. J. Clin. Nutr. *Subsets:* Core Clinical (AIM); MEDLINE

MeSH Terms: Bone Density*
Calcifediol/*blood
Periodontal Diseases/*epidemiology
Vitamin D Deficiency/*complications
Adult; Age Factors; Female; Humans; Linear Models; Male; Middle Aged; Nutrition Surveys; Periodontal Diseases/blood; Periodontal Diseases/prevention & control; Prevalence; Risk Factors; United States/epidemiology; Vitamin D Deficiency/blood

Abstract: **Background:** Periodontal disease (PD) is a common chronic inflammatory disease and an important risk factor for tooth loss. Vitamin D might affect periodontal disease risk via an effect on bone mineral density (BMD) or via immunomodulatory effects.
Objective: The objective was to evaluate whether serum 25-hydroxyvitamin D(3) [25(OH)D(3)] concentrations are associated with PD in the third National Health and Nutrition Examination Survey.
Design: We analyzed data on periodontal attachment loss (AL) and serum 25(OH)D(3) concentrations from 11 202 subjects aged > or =20 y. Mean AL was modeled in a multiple linear regression with quintile of serum 25 (OH)D(3) concentration as an independent variable. The model was stratified by age and sex and was adjusted for age within age groups, race or ethnicity, smoking, diabetes, poverty income ratio, body mass index, estrogen use, and gingival bleeding.
Results: 25(OH)D(3) concentrations were significantly and inversely

associated with AL in men and women aged > or =50 y. Compared with men in the highest 25(OH)D(3) quintile, those in the lowest quintile had a mean AL that was 0.39 mm (95% CI: 0.17, 0.60 mm) higher; in women, the difference in AL between the lowest and highest quintiles was 0.26 mm (0.09, 0.43 mm). In men and women younger than 50 y, there was no significant association between 25(OH)D(3) and AL. The BMD of the total femoral region was not associated with AL and did not mediate the association between 25(OH)D(3) and AL.
Conclusions: Low serum 25(OH)D(3) concentrations may be associated with PD independently of BMD. Given the high prevalence of PD and vitamin D deficiency, these findings may have important public health implications.

Substance Nomenclature: 19356-17-3 (Calcifediol)

Entry Dates: *Date Created:* 20040623 *Date Completed:* 20040713 *Latest Revision:* 20061115

Update Code: 20101124

PMID: 15213036

Database: MEDLINE

Record: 1

Title: Improving the Oral Health of Alaska Natives.

Authors: Sekiguchi, Eugene
Guay, Albert H.
Brown, L. Jackson
Spangler Jr., Thomas J.

Source: American Journal of Public Health, May2005, Vol. 95 Issue 5, p769-773, 5p, 1 Chart, 2 Graphs

Document Type: Article

Subject Terms: MOUTH -- Care & hygiene
INDIANS of North America -- Alaska
MOUTH -- Diseases
DENTAL health education

Geographic Terms: ALASKA

Abstract: There is a high prevalence of oral disease in the Alaska Native population, much of which goes untreated, creating a large discrepancy between the level of their oral health and that of the general population. The causes of this discrepancy are multiple--a major cause being the lack of access to care, especially in remote Alaska Native villages. Improving the oral health status of Alaska Natives will require treatment of current disease and initiation of an effective program to prevent oral disease. Cooperation between the Alaska Native organizations, dental health aides, the dental profession, and the government will be important. A strategy that combines addressing the disease currently present and preventing the occurrence of disease in the long run is the only strategy that offers a sustainable solution. [ABSTRACT FROM AUTHOR]

Lexile: 1260

Full Text Word Count: 3414

ISSN: 00900036

DOI: 10.2105/AJPH.2004.053546

Record: 1

Title: Vitamin D, innate immunity and upper respiratory tract infection.

Authors: Bartley J

Author Address: Department of Otolaryngology-Head and Neck Surgery, Counties-Manukau District Health Board, Auckland, New Zealand. jbartley@ihug.co.nz

Source: The Journal Of Laryngology And Otology [J Laryngol Otol] 2010 May; Vol. 124 (5), pp. 465-9. *Date of Electronic Publication:* 2010 Jan 13.

Publication Type: Journal Article; Review

Language: English

Journal Information: *Country of Publication:* England *NLM ID:* 8706896 *Publication Model:* Print-Electronic *Cited Medium:* Internet *ISSN:* 1748-5460 (Electronic) *Linking ISSN:* 00222151 *NLM ISO Abbreviation:* J Laryngol Otol *Subsets:* Core Clinical (AIM); MEDLINE

MeSH Terms: Respiratory Tract Infections/*prevention & control
Vitamin D/*pharmacology
Vitamins/*pharmacology
Antimicrobial Cationic Peptides/physiology; Heliotherapy; Humans; Immunity, Innate/drug effects; Immunity, Mucosal/drug effects; Respiratory Tract Infections/immunology; Tuberculosis, Cutaneous/therapy; Vitamin D/blood; Vitamin D/physiology; Vitamins/blood

Abstract: **Introduction:** At the turn of the twentieth century, ultraviolet light was successfully used to treat tuberculosis of the skin. Upper respiratory tract infections had been inversely associated with sun exposure. During the last decade, basic scientific research demonstrated that vitamin D has an important anti-infective role.
Method: Review of the relevant literature on the influence of vitamin D on innate immunity and respiratory tract infection.
Results: Vitamin D is involved in the production of defensins and cathelicidin - antimicrobial peptides that provide a natural defence against potential microbiological pathogens. Vitamin D supplementation increases cathelicidin production. Low vitamin D levels are associated with an increased incidence of upper respiratory tract infections.
Conclusions: Vitamin D appears to play an important role in the regulation of innate immunity in the upper respiratory tract. Optimal vitamin D levels and appropriate dosing schedules have yet to be determined.

63

Number of References:	0 (Antimicrobial Cationic Peptides) 0 (Vitamins)
Substance Nomenclature:	1406-16-2 (Vitamin D)
Entry Dates:	*Date Created:* 20100428 *Date Completed:* 20100804
Update Code:	20101124
PMID:	20067648
Database:	MEDLINE

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Flu Vaccine Effectiveness: Questions and Answers for Health Professionals

How is influenza vaccine effectiveness measured?

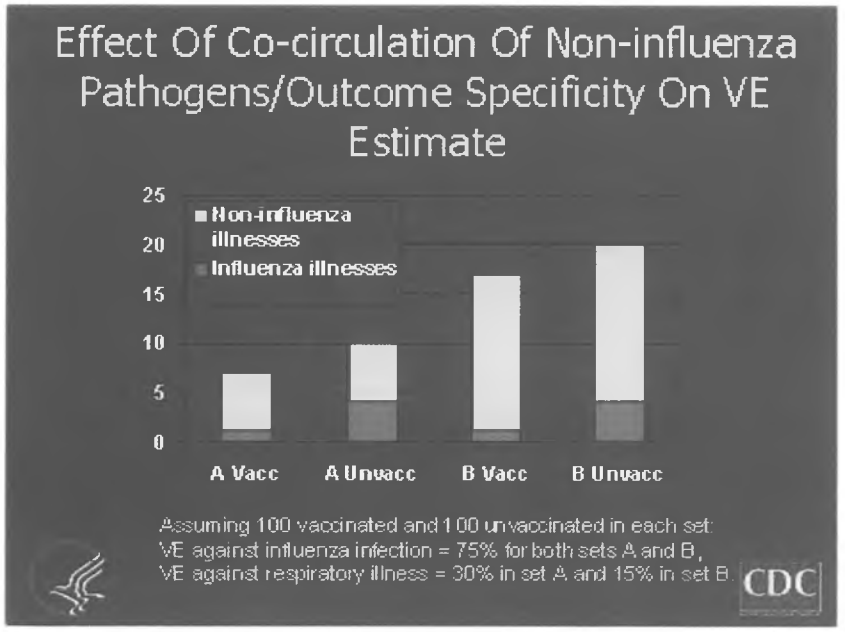
Vaccine efficacy and effectiveness studies use various endpoints or outcomes, which influence how we interpret the results. These endpoints may include the prevention of medically attended acute respiratory illness (MAARI), prevention of laboratory-confirmed influenza virus illness or hospitalization, prevention of influenza-like illness (ILI, such as illness with fever and cough or sore throat), or influenza-associated hospitalizations or deaths. Studies that use outcomes such as an influenza laboratory-confirmed outcome provide the most specific estimates of the impact of the vaccine in preventing influenza. The more non-specific the outcome being measured (*e.g.*, all pneumonia hospitalizations or influenza-like illness that include many illnesses not caused by the influenza virus), the lower the estimates of vaccine effectiveness. For example, a study by Bridges et al. (JAMA 2000) among healthy adults found that the inactivated influenza was 86% effective against laboratory-confirmed influenza, but only 10% effectiveness against all respiratory illnesses in the same population and year.

Why does influenza vaccine effectiveness vary?

The effectiveness of inactivated influenza vaccine depends primarily on the age and immunocompetence of the vaccine recipient, and the degree of similarity between the viruses in the vaccine and those in circulation. In years when the vaccine strains are not well matched to circulating strains, vaccine effectiveness is generally lower. The vaccine may also be lower among persons with chronic medical conditions and among the elderly, as compared to healthy young adults and children. In addition, estimates of vaccine effectiveness vary, based on the specificity of the outcome that is being measured in the study.

It is also important to keep in mind that measurement of vaccine effectiveness against a non-laboratory confirmed outcome is at least partially determined by how much of that outcome is actually caused by influenza viruses, as compared to other pathogens. For example, one non-laboratory confirmed outcome that is often used is ILI. The proportion of ILI's caused by influenza versus other pathogens can vary by year, or even within a year.

As illustrated in the theoretical example graphed below, there is a relationship between our estimates of vaccine efficacy and the proportion of all ILI's caused by influenza versus other pathogens. In this example, the vaccine was 75% effective against laboratory-confirmed influenza, but was 30% effective against ILI when influenza caused 40% of ILI's in the unvaccinated group. The vaccine would be only 15% effective, however, if influenza caused only 20% of ILI's. This is an important relationship to keep in mind, since there can be wide variation in the percentage of ILIs caused by influenza.



How effective is the inactivated influenza vaccine (IIV)?

Overall

Overall, in years when the vaccine and circulating viruses are well-matched, influenza vaccines can be expected to reduce laboratory-confirmed influenza by approximately 70% to 90% in healthy adults <65 years of age. Several studies have also found reductions in febrile illness, influenza-related work absenteeism, antibiotic use, and doctor visits.

In years when the vaccine strains are not well matched to circulating strains, vaccine effectiveness can be variably reduced. For example, in a study among persons 50-64 years during the 2003-04 season, when the vaccine strains were not optimally matched, inactivated influenza vaccine effectiveness against laboratory-confirmed influenza was 60% among persons without high-risk conditions, and 48% among those with high risk conditions, but it was 90% against laboratory-confirmed influenza hospitalization (Herrera, et al Vaccine 2006). A study in children during the same year found vaccine effectiveness of about 50% against medically diagnosed influenza and pneumonia without laboratory confirmation (Ritzwoller, Pediatrics 2005). However, in some years when vaccine and circulating strains were not well-matched, no vaccine effectiveness can be demonstrated in some studies, even in healthy adults (Bridges, JAMA 2000). It is not possible in advance of the influenza season to predict how well the vaccine and circulating strains will be matched, and how that match may affect the degree of vaccine effectiveness.

Immunocompromised

The immune competence of the person being vaccinated can also affect vaccine effectiveness. For example, the vaccine may be only 30%-40% effective against influenza-related respiratory illness among nursing home residents. However, even in this group of frail elderly, the vaccine still provides substantial protection against more severe outcomes, such as influenza-related hospitalization (effectiveness of 50-60%) and deaths (80%). The presence of chronic medical conditions may also affect vaccine effectiveness. In a study of persons 50-64 years of age, the vaccine was 60% effective among otherwise healthy adults 50-64 years of age, but only 48% effective among those with high-risk medical conditions (Herrera, et al Vaccine 2006).

Adults 65 years or older

Among elderly persons *not* living in nursing homes or similar long-term care facilities, influenza vaccine has been reported to be 30%-70% effective in preventing hospitalization for pneumonia and influenza. Among older persons who reside in nursing homes, influenza vaccine is most effective in preventing severe illness, secondary complications, and deaths. Among this population, the vaccine has been reported to be 50%-60% effective in preventing influenza-related hospitalization or pneumonia, and 80% effective in preventing influenza-related death, although the effectiveness in preventing illness from influenza often ranges from 30% to 40%. In years when the vaccine is not well- matched to circulating influenza strains, vaccine effectiveness (VE) is often lower.

For nursing homes, vaccination rates of 80% or more among residents can reduce the risk of influenza outbreaks in the facility. In addition, other studies suggest that the vaccination of the health care workers in nursing homes, as well as the residents, is important to prevent influenza outbreaks (Potter et al., J Infect Dis 1997;175:1—6. Carman et al., Lancet 2000;355 (9198):93—7. Shugarman et al., J Am Med Dir Assoc. 2006 Nov;7(9):562-7).

Children

A 4-year randomized, placebo-controlled trial of children aged 1-15 years found vaccine effectiveness ranging from 77% to 91%, following only one dose of vaccine given to previously unvaccinated children (Neuzil, Pediatric Infectious Diseases Journal, 2001).

Another 2-year study of children aged 6-24 months found that the vaccine was 66% effective against laboratory-confirmed influenza in year 1 of the study. Only children who were fully vaccinated (*i.e.* had either 2 doses if not previously vaccinated, or 1 dose if previously vaccinated) versus unvaccinated children were included in the analysis. In the other year, few cases of influenza occurred, making it difficult to assess the vaccine's effectiveness.

A study of influenza vaccine effectiveness among >5,000 children aged 6-23 months found vaccine effectiveness of 49% against clinically diagnosed pneumonia or influenza among fully vaccinated children (Ritzwoller, Pediatrics 2005).

All of these studies together suggest substantial benefit from influenza vaccination of children.

How does the number of doses of vaccine that a child receives affect vaccine effectiveness?

Children <9 years of age who have not been vaccinated previously are recommended to receive 2 doses the first year they get vaccinated. In subsequent years, they need only 1 dose. This is because many children <9 years of age have not been infected with influenza viruses previously, and a booster dose is needed in children previously not exposed to influenza infections or vaccine in order for them to have a good immune response.

For the inactivated vaccine, no VE has been demonstrated for children who needed 2 doses but who received only one. (Ritzwoller et al. Pediatrics 2003; Allison MA, et al. J Pediatrics 2006). A study of live attenuated vaccine by Belshse et al of children <5 years, however, did show VE among children administered only 1 dose. However, the live vaccine is not licensed for use in children <5 years of age.

Chronic medical conditions

A limited number of influenza vaccine studies have been conducted in groups with underlying medical conditions. In a study of adults aged 50—64 years with laboratory-confirmed influenza

during the 2003-04 season, when vaccine and circulating viruses were not well-matched, vaccine effectiveness was estimated to be 48% among those with one or more high-risk conditions. A study of high-risk adults aged 18-64 found vaccine effectiveness against influenza -related hospitalization and deaths of 87% and 78%, respectively (Hak, 2005). A study of diabetic persons estimated that influenza vaccine reduced influenza, pneumonia, or diabetes-related hospitalizations by 79% (95% CI: 19% to 95%) during two influenza seasons (Colquhoun, 1997). However, the control group had a significantly lower proportion of insulin-dependent diabetics, which could have inflated the vaccine effectiveness estimates.

Overall, vaccine efficacy and effectiveness estimates among persons with high-risk conditions are somewhat lower compared to similar age groups of persons without high-risk conditions. However, the risk of influenza-related complications among this group is much higher, so vaccination provides substantial benefit, even given the lower effectiveness.

How effective is the live attenuated influenza vaccine (LAIV)?

(As of 2007, this vaccine is licensed only for healthy, non-pregnant persons between 5 and 49 years.)

Healthy Children

A randomized, double-blind, placebo-controlled trial among 1,602 healthy children initially aged 15--71 months assessed the efficacy of trivalent LAIV against culture-confirmed influenza during two seasons (Belshe et al., N Engl J Med 1998;338:1405—12. Belshe et al, J Pediatr 2000;136:168--75). In season one, when vaccine and circulating virus strains were well-matched, efficacy in preventing confirmed illness from influenza was 93% for participants who received 2 doses of LAIV. In season two, when the A (H3N2) component was not well-matched between vaccine and circulating virus strains, efficacy was 86% overall.

Other non-laboratory confirmed, less specific outcome results included a 21% reduction in all febrile illnesses, 27% reduction in febrile otitis media, and a 28% reduction in otitis media with concomitant antibiotic use. A review of LAIV effectiveness in children aged 18 months—18 years found effectiveness against medically attended acute respiratory illness (MAARI), a non-laboratory confirmed outcome, of 18%, but greater estimated efficacy against laboratory confirmed influenza-- 92% against influenza A (H1N1), and 66% against an influenza B drift variant (Halloran et al., Am J Epidemiol 2003;158:305--11).

Healthy Adults

A randomized, double-blind, placebo-controlled trial among 4,561 healthy working adults aged 18--64 years assessed multiple endpoints, including reductions in self-reported respiratory tract illness without laboratory confirmation, absenteeism, healthcare visits, and medication use during peak and total influenza outbreak periods (Nichol et al., JAMA 1999;282:137--44). The study was conducted during the 1997--98 influenza season, when the vaccine and circulating A (H3N2) strains were not well-matched. Vaccination was associated with reductions in severe febrile illnesses of 19%, and febrile upper respiratory tract illnesses of 24%.

Vaccination was also associated with fewer days of illness, fewer days of work lost, fewer days with healthcare provider visits, and reduced use of prescription antibiotics and over-the-counter medications. Among a subset of 3,637 healthy adults aged 18--49 years, LAIV recipients (n = 2,411) had 26% fewer febrile upper-respiratory illness episodes; 27% fewer lost work days as a result of febrile upper respiratory illness; and 18%--37% fewer days of

healthcare provider visits caused by febrile illness, compared with placebo recipients (n = 1,226). Days of antibiotic use were reduced by 41%--45% in this age subset.

A randomized, double-blind, placebo-controlled challenge study among 92 healthy adults (LAIV, n = 29; placebo, n = 31; inactivated influenza vaccine, n = 32) aged 18--41 years assessed the efficacy of both LAIV and inactivated vaccine (Treanor et al., Vaccine 1999;18:899--906.). The overall efficacy of LAIV and inactivated influenza vaccine in preventing laboratory-documented influenza from all three influenza strains combined was 85% and 71%, respectively. This was on the basis of experimental challenge by viruses to which study participants were susceptible before vaccination. The difference in efficacy between the two vaccines was not statistically significant.

How does vaccine efficacy/effectiveness (VE) compare between live attenuated vaccine and inactivated vaccine?

Few studies directly comparing LAIV and IIV have been done, and results appear to differ for adults versus children. A randomized, placebo-controlled trial among 876 healthy adults 18-46 years old found overall VE of 75% for IIV, which was statistically significant, and 48% VE for LAIV, which was not statistically significant in a year with a drifted strain (Ohmit NEJM 2006). However, a small randomized, double-blind, placebo-controlled challenge study among 92 healthy adults (LAIV, n = 29; placebo, n = 31; inactivated influenza vaccine, n = 32) aged 18-41 years found overall efficacy of LAIV and inactivated influenza vaccine in preventing laboratory-documented influenza of 85% and 71%, respectively (Treanor et al., Vaccine 1999;18:899--906.). The difference in efficacy between the two vaccines was not statistically significant.

However, in 3 studies among children where inactivated vaccine was compared with a refrigerator-stable experimental form of the LAIV, referred to as CAIV-T, which is not yet licensed in the U.S., the LAIV vaccine was overall of greater benefit. However, none of the studies included a placebo group, so overall effectiveness could not be assessed. One study included 2187 children aged 6-71 months who had recurrent respiratory tract infections (Ashkenazi et al. Pediatric Infect Dis J 2006) and found overall influenza rates of 2.3% among CAIV-T recipients, and 4.8% for TIV, for a 52.7% decrease. In a randomized study of 2229 children 6-17 years with asthma, 4.1% of CAIV-T recipients and 6.2% of TIV recipients developed influenza, for a reduction of 34.7% for CAIV-T over TIV (Fleming DM, et al. Pediatric Infect Dis J 2006). Publication of the results of a third study among 7852 children 6-59 months is pending.

What information is necessary for yearly surveillance of vaccine effectiveness?

Ideally, influenza vaccine effectiveness (VE) would be assessed on a yearly basis, using a consistent methodology and population. This would allow for comparison of clinical VE outcomes with laboratory data on the relatedness of influenza vaccine viruses with those contained in the vaccine. Use of a laboratory-confirmed outcome to assess VE is very important to provide the most specific results of the benefit of the vaccine, and to limit the impact of the co-circulation of non-influenza respiratory pathogens on the influenza VE estimate. Ideal populations for assessment would include different analyses of pediatric populations, healthy adults, and older adults. Because a proportion of older adults have co-morbidities and may be differentially motivated to seek medical care for influenza-related symptoms, analyses and interpretation of influenza VE in this population are difficult. Thus, this should not be the only population assessed for influenza VE.

What types of vaccine effectiveness studies are being conducted by CDC now?

(/flu/images/professionals/map_eip_nvsn_counties.jpg) Map: Emerging Infections Program and New Vaccine Surveillance Network Participating Counties, 2005-2006

Because of the changing nature of influenza viruses and the vaccine, annual assessment of the effectiveness of influenza vaccines is important. Vaccine effectiveness studies can look at various target populations (*e.g.*, children, the elderly), and determine how well the vaccine prevents against different outcomes (*e.g.*, hospitalization, illness, death, and laboratory-confirmed infection). CDC is currently conducting studies that have only a laboratory-confirmed outcome. The findings of these studies are then used to enhance vaccine recommendations or support the need for new methods of vaccine production.

In 2004, a 3-year CDC-funded pilot study with the Marshfield Clinic Research Foundation was initiated to develop an assessment system of the vaccine's effectiveness across all groups for whom influenza vaccine is targeted. This study is in its final year.

Through CDC's Emerging Infections Program Network and the New Vaccine Surveillance Network, other vaccine effectiveness studies are being conducted during the 2006-07 influenza season among children 6-59 months of age. These studies will assess the effectiveness of the vaccine in preventing laboratory-confirmed influenza hospitalizations.

Influenza Vaccine Effectiveness Studies Currently Being Conducted by CDC

Table 1. Marshfield Clinic Studies

Study Design	Cohort and case-control
Seasons	2004-05, 2005-06, 2006-07
Setting	Clinic population in north-central WI
Age	All ACIP-recommended groups
Cases	Patients with acute respiratory illness (ARI) symptoms and influenza positive by culture or RT-PCR
Cohort Controls	Cohort of adults and children for whom ACIP recommended annual influenza vaccination. Age-matched persons with ARI symptoms in same healthcare system.

Vaccination data	Obtained from regional electronic vaccine registry and patient report
Source of other data	Electronic medical record and interview of adult or parent/guardian
Other patient characteristics included in analyses	Age, gender, race, high- risk condition, use of health care

Table 2. Emerging Infections Program Studies

Study Design	Case-control
Seasons	2005-06, 2006-07
Setting	Hospitals in 8 (05-06) and 9 (06-07) states
Age	6-23 mo (05-06), 6-59 mo (06-07)
Cases	Children hospitalized with laboratory confirmed influenza test. Testing done as ordered by clinicians.
Controls	Age- and zip-code matched children not hospitalized with influenza
Vaccination data	Obtained from health care providers and parent report
Source of other data	Medical chart review, interview of parent/guardian
Other patient characteristics included in analyses	Age, gender, race, insurance status, high- risk conditions, socioeconomic status

Table 3. New Vaccine Surveillance Network Studies

Study Design	Case-control
Seasons	2003-04, 2004-05, 2005-06, 2006-07
Setting	Hospitals, Emergency Departments, and outpatient clinics in 3 counties (TN, NY, OH)
Age	6-59 months
Cases	Children prospectively enrolled with fever or ARI who test positive for influenza by culture or RT-PCR
Controls	Children prospectively enrolled with fever or ARI who test negative for influenza by culture and RT-PCR
Vaccination data	Obtained from health care providers
Source of other data	Medical chart review, interview of parent/guardian
Other patient characteristics included in analyses	Date enrolled, age, gender, race, insurance status, high-risk conditions, socioeconomic status and other risk factors.

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State of Alaska Epidemiology **Bulletin**

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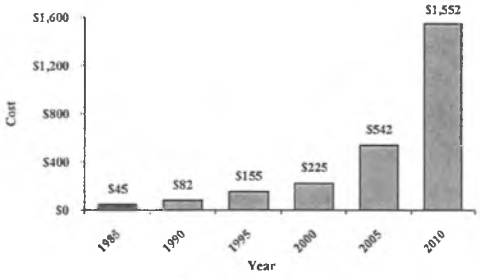
Bulletin No. 31 October 6, 2010

Only Pediatric/Adolescent Vaccines to be Supplied by State Beginning in 2011

For over 30 years the Alaska Immunization Program maintained a "universal" vaccine program, distributing at no cost all Advisory Committee on Immunization Practices (ACIP)-recommended pediatric and selected adult vaccines to public and private providers in Alaska. This vaccine distribution has been supported almost entirely with two sources of federal funding. The *Vaccines for Children (VFC) Program* pays for vaccines for children who meet certain federal criteria. *Section 317 of the U.S. Public Health Service Act (317)* covers the cost of vaccines for the approximately one-third of Alaska children who are not VFC-eligible, as well as adult vaccines. As a federal entitlement program, VFC funding increases to support newly recommended vaccines for children; however, 317 funding has not kept pace with rapidly rising vaccine costs, which have risen almost seven-fold in the last 10 years (Figure 1).

Figure 1: Alaska Immunization Program Estimated Cost to Purchase Recommended Vaccines for One Child from their Year of Birth through Age 18 Years, for Selected Years from 1985 through 2010



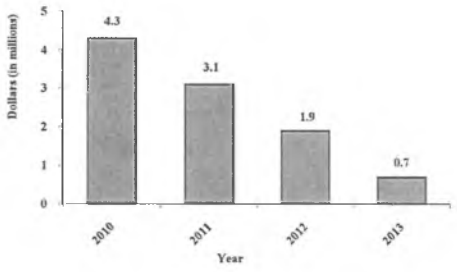
has made it increasingly challenging for Alaska to maintain its vaccine distribution policy; however, these challenges are not unique to Alaska. Almost one-half (23/50) of U.S. states supply vaccines only for VFC-eligible children, i.e., vaccines are not supplied for children who do not meet program eligibility criteria or for adults. Other state vaccine supply policies include *universal purchase* (all vaccines for all children), *universal purchase select* (vaccines for all children except selected expensive vaccines available for VFC-eligibles only), and *VFC and underinsured* and *VFC and underinsured select* (varying levels of coverage for underinsured children) (Figure 2).

Figure 2: Public Purchase Pediatric Vaccine Supply Policy — United States, July 2010[1]

Alaska's vaccine purchases are supported almost entirely with funding from the U.S. Centers for Disease Control and Prevention (CDC). In 2008, CDC informed Alaska that the state had been "significantly overfunded" relative to other state and local immunization programs for many years, and the agency could no longer support Alaska's universal immunization program. CDC agreed to maintain 317 funding at ~$4.3 million through 2010, with the understanding that funding would decrease in subsequent years.

To meet the challenges presented by increased vaccine costs and reduced funding, Alaska has taken incremental steps to reduce vaccine expenditures while trying to maintain maximum availability of pediatric vaccines. In 2007, the Immunization Program discontinued shipments of adult influenza vaccine to private providers. In January 2009, the state limited the provision of human papillomavirus (HPV) and meningococcal conjugate vaccines to children who met the federal eligibility requirements of the Vaccines for Children (VFC) Program.[2] These program modifications helped trim vaccine costs by more than $2 million per year. However, CDC has notified Alaska that, beginning in 2011, the state's 317 vaccine dollars will be reduced by ~$1.2 million for each of the next 3 years, at which time Alaska's funding will be proportionate to that received by other immunization programs in the United States (Figure 3). Therefore, a change in Alaska's vaccine supply policy is necessary (Box).

Figure 3: Projected 317 Vaccine Funding for Alaska, 2010–2013



Box. The Alaska Immunization Program's 2011 Vaccine Supply Policy

Due to the increased cost of vaccines and federal 317 funding cuts, the following Alaska Immunization Program vaccine supply policy will become effective on **January 1, 2011**:

- All ACIP-recommended pediatric vaccines except HPV and MCV4 will continue to be supplied for all children through age 18 years. HPV and MCV4 will continue to be available for VFC-eligible children only.
- **Adult vaccines that historically have been provided by the Alaska Immunization Program (i.e., influenza, pneumococcal, tetanus/diphtheria) will no longer be supplied to public or private sector providers.**

Alternate Resources Available for Adult Vaccines

Private insurance policies and Medicare frequently support the cost of adult vaccines. Resource information related to Medicare billing and other potential funding sources is posted on the Section of Epidemiology website.[3] Manufacturer contact information for vaccine ordering also is included.

Conclusion

Although the Alaska Immunization Program regrets this policy change for adult vaccines, we are pleased that we can continue to provide pediatric vaccines at the current level throughout 2011. As the state's 317 funding levels continue to decrease over the next 3 years, this pediatric policy may need to be reconsidered. We will also continue to monitor the implementation of the Patient Protection and Affordable Care Act to determine its potential impact on vaccine funding in the future. To the greatest extent possible, we will continue our commitment to eliminate vaccine-preventable diseases in Alaska's children.

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(Contributed by Laurel Wood, MPA, Immunization Program Manager, Section of Epidemiology)

Record: 1

Title: Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren.

Authors: Urashima M; Segawa T; Okazaki M; Kurihara M; Wada Y; Ida H

Author Address: Division of Molecular Epidemiology, Jikei University School of Medicine, Nishi-shimbashi 3-25-8, Minato-ku, Tokyo 105-8461, Japan. urashima@jikei.ac.jp

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Language: English

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MeSH Terms: Dietary Supplements*
Cholecalciferol/*administration & dosage
Influenza, Human/*prevention & control
Adolescent; Body Height; Body Weight; Child; Cholecalciferol/adverse effects; Cholecalciferol/therapeutic use; Double-Blind Method; Female; Humans; Influenza A virus; Influenza, Human/epidemiology; Japan/epidemiology; Male; Patient Selection; Placebos; Risk

Abstract: **Background:** To our knowledge, no rigorously designed clinical trials have evaluated the relation between vitamin D and physician-diagnosed seasonal influenza.
Objective: We investigated the effect of vitamin D supplements on the incidence of seasonal influenza A in schoolchildren.
Design: From December 2008 through March 2009, we conducted a randomized, double-blind, placebo-controlled trial comparing vitamin D(3) supplements (1200 IU/d) with placebo in schoolchildren. The primary outcome was the incidence of influenza A, diagnosed with influenza antigen testing with a nasopharyngeal swab specimen.
Results: Influenza A occurred in 18 of 167 (10.8%) children in the vitamin D(3) group compared with 31 of 167 (18.6%) children in the placebo group [relative risk (RR), 0.58; 95% CI: 0.34, 0.99; P = 0.04]. The reduction in influenza A was more prominent in children who had not been taking other

vitamin D supplements (RR: 0.36; 95% CI: 0.17, 0.79; P = 0.006) and who started nursery school after age 3 y (RR: 0.36; 95% CI: 0.17, 0.78; P = 0.005). In children with a previous diagnosis of asthma, asthma attacks as a secondary outcome occurred in 2 children receiving vitamin D(3) compared with 12 children receiving placebo (RR: 0.17; 95% CI: 0.04, 0.73; P = 0.006).

Conclusion: This study suggests that vitamin D(3) supplementation during the winter may reduce the incidence of influenza A, especially in specific subgroups of schoolchildren. This trial was registered at https://center.umin.ac.jp as UMIN000001373.

Substance Nomenclature: 0 (Placebos)
67-97-0 (Cholecalciferol)

Entry Dates: *Date Created:* 20100421 *Date Completed:* 20100528

Update Code: 20101124

PMID: 20219962

Database: MEDLINE

Record: 1

Title: Vitamin D and tuberculosis.

Authors: Chocano-Bedoya, Patricia
Ronnenberg, Alayne G.

Source: Nutrition Reviews, May2009, Vol. 67 Issue 5, p289-293, 5p

Document Type: Article

Subject Terms: VITAMIN D
TUBERCULOSIS
IMMUNE response
GENETIC polymorphisms
HUMAN genetics -- Variation
NUCLEOTIDE sequence
EPIDEMIOLOGY -- Research

Abstract: Tuberculosis is highly prevalent worldwide, accounting for nearly two million deaths annually. Vitamin D influences the immune response to tuberculosis, and vitamin D deficiency has been associated with increased tuberculosis risk in different populations. Genetic variability may influence host susceptibility to developing active tuberculosis and treatment response. Studies examining the association between genetic polymorphisms, particularly the gene coding for the vitamin D receptor (VDR), and TB susceptibility and treatment response are inconclusive. However, sufficient evidence is available to warrant larger epidemiologic studies that should aim to identify possible interactions between VDR polymorphisms and vitamin D status. [ABSTRACT FROM AUTHOR]

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Title: Vitamin D and multiple sclerosis.

Authors: Ascherio, Alberto[1,2,3] *aascheri@hsph.harvard.edu*
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Source: Lancet Neurology; Jun2010, Vol. 9 Issue 6, p599-612, 14p

Document Type: Article

Subject Terms:
*VITAMIN D in human nutrition
*MULTIPLE sclerosis
*PREVENTION
*MEDICAL geography
*NERVOUS system -- Diseases
*PROGNOSIS
*HUMAN genetics -- Variation
*RESEARCH

Abstract: Summary: The hypothesis that adequate vitamin D nutrition can contribute to the prevention of multiple sclerosis (MS) was originally proposed to explain the geographical distribution of MS, but only recently has the relation between various measures of vitamin D (eg, sun exposure, dietary sources, and serum concentrations of 25-hydroxyvitamin D) and risk of developing MS been rigorously investigated. Overall, the results of these studies support a protective effect of vitamin D, but there are uncertainties and many unanswered questions, including how vitamin D exerts a protective effect, how genetic variations modify the effect, and whether vitamin D can influence the course of MS progression. [Copyright &y& Elsevier]

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ISSN: 14744422

DOI: 10.1016/S1474-4422(10)70086-7

Accession Number: 50964808

Database: Academic Search Premier

Record: 1

Title: Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis.

Authors: Munger KL; Levin LI; Hollis BW; Howard NS; Ascherio A

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Source: JAMA: The Journal Of The American Medical Association [JAMA] 2006 Dec 20; Vol. 296 (23), pp. 2832-8.

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MeSH Terms: Multiple Sclerosis/*blood
Vitamin D/*analogs & derivatives
Adolescent; Adult; African Continental Ancestry Group/statistics & numerical data; Case-Control Studies; European Continental Ancestry Group/statistics & numerical data; Female; Humans; Male; Middle Aged; Multiple Sclerosis/epidemiology; Prospective Studies; Risk; Vitamin D/blood

Abstract: **Context:** Epidemiological and experimental evidence suggests that high levels of vitamin D, a potent immunomodulator, may decrease the risk of multiple sclerosis. There are no prospective studies addressing this hypothesis.

Objective: To examine whether levels of 25-hydroxyvitamin D are associated with risk of multiple sclerosis.

Design, Setting, and Participants: Prospective, nested case-control study among more than 7 million US military personnel who have serum samples stored in the Department of Defense Serum Repository. Multiple sclerosis cases were identified through Army and Navy physical disability databases for 1992 through 2004, and diagnoses were confirmed by medical record review. Each case (n = 257) was matched to 2 controls by age, sex, race/ethnicity, and dates of blood collection. Vitamin D status was estimated by averaging 25-hydroxyvitamin D levels of 2 or more serum samples collected before the date of initial multiple sclerosis symptoms.

Main Outcome Measures: Odds ratios of multiple sclerosis associated with continuous or categorical levels (quantiles or a priori-defined categories) of serum 25-hydroxyvitamin D within each racial/ethnic group.
Results: Among whites (148 cases, 296 controls), the risk of multiple sclerosis significantly decreased with increasing levels of 25-hydroxyvitamin D (odds ratio [OR] for a 50-nmol/L increase in 25-hydroxyvitamin D, 0.59; 95% confidence interval, 0.36-0.97). In categorical analyses using the lowest quintile (<63.3 nmol/L) as the reference, the ORs for each subsequent quintile were 0.57, 0.57, 0.74, and 0.38 (P = .02 for trend across quintiles). Only the OR for the highest quintile, corresponding to 25-hydroxyvitamin D levels higher than 99.1 nmol/L, was significantly different from 1.00 (OR, 0.38; 95% confidence interval, 0.19-0.75; P = .006). The inverse relation with multiple sclerosis risk was particularly strong for 25-hydroxyvitamin D levels measured before age 20 years. Among blacks and Hispanics (109 cases, 218 controls), who had lower 25-hydroxyvitamin D levels than whites, no significant associations between vitamin D and multiple sclerosis risk were found.
Conclusion: The results of our study suggest that high circulating levels of vitamin D are associated with a lower risk of multiple sclerosis.

Grant Information: NS042194 United States NS NINDS NIH HHS; NS46635 United States NS NINDS NIH HHS

Substance Nomenclature: 1406-16-2 (Vitamin D)
64719-49-9 (25-hydroxyvitamin D)

Entry Dates: *Date Created:* 20061220 *Date Completed:* 20061222 *Latest Revision:* 20071203

Update Code: 20101124

PMID: 17179460

Database: MEDLINE

Record: 1

Title: Fracture Prevention With Vitamin D Supplementation: A Meta-analysis of Randomized Controlled Trials.

Authors: Bischoff-Ferrari, Heike A.
Willett, Walter C.
Wong, John B.
Giovannucci, Edward
Dietrich, Thomas
Dawson-Hughes, Bess

Source: JAMA: Journal of the American Medical Association, 5/11/2005, Vol. 293 Issue 18, p2257-2264, 8p, 1 Diagram, 2 Charts, 6 Graphs

Document Type: Article

Subject Terms: VITAMIN D -- Therapeutic use
FRACTURES -- Prevention
DIETARY supplements -- Research
CLINICAL trials
BONES -- Wounds & injuries
VITAMIN therapy
VITAMINS -- Research

Abstract: Context The role and dose of oral vitamin D supplementation in nonvertebral fracture prevention have not been well established. Objective To estimate the effectiveness of vitamin D supplementation in preventing hip and nonvertebral fractures in older persons. Data Sources A systematic review of English and non-English articles using MEDLINE and the Cochrane Controlled Trials Register (1960-2005), and EMBASE (1991-2005). Additional studies were identified by contacting clinical experts and searching bibliographies and abstracts presented at the American Society for Bone and Mineral Research (1995-2004). Search terms included randomized controlled trial (RCT), controlled clinical trial, random allocation, double-blind method, cholecalciferol, ergocalciferol, 25-hydroxyvitamin D, fractures, humans, elderly, falls, and bone density. Study Selection Only double-blind RCTs of oral vitamin D supplementation (cholecalciferol, ergocalciferol) with or without calcium supplementation vs calcium supplementation or placebo in older persons (≥60 years) that examined hip or nonvertebral fractures were included. Data Extraction Independent extraction of articles by 2 authors using predefined data fields, including study quality indicators. Data Synthesis All pooled analyses were based on random-effects models. Five RCTs for hip fracture (n = 9294) and 7 RCTs for nonvertebral fracture risk (n = 9820) met our

inclusion criteria. All trials used cholecalciferol. Heterogeneity among studies for both hip and nonvertebral fracture prevention was observed, which disappeared after pooling RCTs with low-dose (400 IU/d) and higher -dose vitamin D (700-800 IU/d), separately. A vitamin D dose of 700 to 800 IU/d reduced the relative risk (RR) of hip fracture by 26% (3 RCTs with 5572 persons; pooled RR, 0.74; 95% confidence interval [CI], 0.61-0.88) and any nonvertebral fracture by 23% (5 RCTs with 6098 persons; pooled RR, 0.77; 95% CI, 0.68-0.87) vs calcium or placebo. No significant benefit was observed for RCTs with 400 IU/d vitamin D (2 RCTs with 3722 persons; pooled RR for hip fracture, 1.15; 95% CI, 0.88-1.50; and pooled RR for any nonvertebral fracture, 1.03; 95% CI, 0.86-1.24). Conclusions Oral vitamin D supplementation between 700 to 800 IU/d appears to reduce the risk of hip and any nonvertebral fractures in ambulatory or institutionalized elderly persons. An oral vitamin D dose of 400 IU/d is not sufficient for fracture prevention. [ABSTRACT FROM AUTHOR]

ISSN: 00987484

Accession Number: 17013420

Database: MasterFILE Premier

Record: 1

Title: A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study.

Authors: Broe, Kerry E.[1] *broe@hrca.harvard.edu*
Chen, Tai C.[2]
Weinberg, Janice[3]
Bischoff-Ferrari, Heike A.[4,5]
Holick, Michael F.[2]
Kiel, Douglas P.[6]

Source: Journal of the American Geriatrics Society; Feb2007, Vol. 55 Issue 2, p234 -239, 6p, 3 Charts

Document Type: Article

Subject Terms: *VITAMIN D
*CALCIUM regulating hormones
*STEROID hormones
*NURSING homes
*HEALTH facilities
*CLINICAL trials

Author-Supplied Keywords: falls
nursing home
randomized clinical trial
vitamin D

NAICS/Industry Codes621498 All Other Outpatient Care Centers
623110 Nursing Care Facilities
623311 Continuing Care Retirement Communities

Abstract: OBJECTIVES: To determine the effect of four vitamin D supplement doses on falls risk in elderly nursing home residents. DESIGN: Secondary data analysis of a previously conducted randomized clinical trial. SETTING: Seven hundred twenty-five-bed long-term care facility. PARTICIPANTS: One hundred twenty-four nursing home residents (average age 89). INTERVENTION: Participants were randomly assigned to receive one of four vitamin D supplement doses (200 IU, 400 IU, 600 IU, or 800 IU) or placebo daily for 5 months. MEASUREMENTS: Number of fallers and number of falls assessed using facility incident tracking database. RESULTS: Over the 5-month study period, the proportion of participants with falls was 44% in the placebo group (11/25), 58% (15/26) in the 200 IU group, 60% (15/25) in the 400 IU group, 60% (15/25) in the 600 IU group, and 20% (5/23) in the 800 IU group. Participants in the 800 IU group had a

72% lower adjusted-incidence rate ratio of falls than those taking placebo over the 5 months (rate ratio=0.28; 95% confidence interval=0.11–0.75). No significant differences were observed for the adjusted fall rates compared to placebo in any of the other supplement groups. CONCLUSION: Nursing home residents in the highest vitamin D group (800 IU) had a lower number of fallers and a lower incidence rate of falls over 5 months than those taking lower doses. Adequate vitamin D supplementation in elderly nursing home residents could reduce the number of falls experienced by this high falls risk group. [ABSTRACT FROM AUTHOR]

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DOI: 10.1111/j.1532-5415.2007.01048.x

Accession Number: 23827663

Database: Academic Search Premier

Record: 1

Title: Does Vitamin D Reduce the Risk of Dementia?

Authors: Grant, William B.[1] *wbgrant@infionline.net*

Source: Journal of Alzheimer's Disease; 2009, Vol. 17 Issue 1, p151-159, 9p, 2 Charts

Document Type: Article

Subject Terms:
*VITAMIN D
*ALZHEIMER'S disease
*DEMENTIA
*NEUROBEHAVIORAL disorders
*PERIODONTAL disease
*TOOTH loss
*ULTRAVIOLET radiation -- Physiological effect

Author-Supplied Keywords:
Alzheimer's disease
cardiovascular disease
cathelicidin
periodontal disease
tooth loss
ultraviolet-B
vascular dementia
vitamin D

Abstract: The understanding of the role of vitamin D in maintaining optimal health has advanced sharply in the past two decades. There is mounting evidence for beneficial roles for vitamin D in reducing the risk of bone diseases and fractures, many types of cancer, bacterial and viral infections, autoimmune diseases, and cardiovascular diseases. Recently, several reports have also been published regarding the role of vitamin D in neuroprotection. This article develops the hypothesis that vitamin D can reduce the risk of developing dementia, presenting the evidence from observational and laboratory studies. The observational evidence includes that low serum 25-hydroxyvitamin D [25(OH)D] has been associated with increased risk for cardiovascular diseases, diabetes mellitus, depression, dental caries, osteoporosis, and periodontal disease, all of which are either considered risk factors for dementia or have preceded incidence of dementia. The laboratory evidence includes several findings on the role of vitamin D in neuroprotection and reducing inflammation. Although this evidence is supportive, there do not appear to be observational studies of incidence of dementia with respect to prediagnostic serum 25(OH)D or

vitamin D supplementation. Such studies now appear to be warranted. [ABSTRACT FROM AUTHOR]

Author Affiliations: [1]Sunlight, Nutrition, and Health Research Center (SUNARC), P.O. Box 641603, San Francisco, CA 94164-1603, USA

ISSN: 13872877

DOI: 10.3233/JAD-2009-1024

Accession Number: 40647040

Database: Academic Search Premier

Record: 1

Title: Reduced Serum Levels of 25-Hydroxy and 1,25-Dihydroxy Vitamin D in Egyptian Children with Autism.

Authors: Meguid, Nagwa A.
Hashish, Adel F.
Anwar, Mona
Sidhom, Gloria

Source: Journal of Alternative & Complementary Medicine, Jun2010, Vol. 16 Issue 6, p641-645; , 5p

Document Type: Article

Subject Terms: VITAMIN D -- Therapeutic use
AUTISM in children -- Treatment
CHILDREN with disabilities -- Care
SERUM
CROSS-sectional method

Abstract: Objective: The aim of this study was to investigate the potential role of vitamin D in autism through serum level assessment. Design: This was a case-controlled cross-sectional study. Setting: The study was conducted at the Out-patient Clinic for "Children with Special Needs" at the Medical Services Unit of the National Research Centre in Cairo, Egypt. Subjects: Seventy (70) children with autism diagnosed according to the DSM-IV criteria of the American Psychiatric Association were recruited for this study. The mean age ± standard deviation (SD) of the patients was 5.3 ± 2.8 years. Controls included 42 age-matched randomly selected healthy children of the same socioeconomic status (mean age ± SD, 6.1 ± 1.8 years). Methods: Circulating levels of both forms of vitamin D (25(OH)D and 1,25(OH)₂D) and serum calcium were measured for all subjects. Associations between vitamin D status, birth season, and clinical characteristics of autism were examined. Results: Children with autism had significantly lower 25(OH)D ($p < 0.00001$) and 1,25(OH)₂D ($p < 0.005$) as well as lower calcium ($p < 0.0001$) serum values than the controls. A significant positive correlation was obtained between 25(OH)D and calcium (correlation coefficient $r = 0.309$, $p < 0.01$) within the children with autism. No significant difference was found on comparison of birth month and season of birth between children with autism and healthy controls. Furthermore, associations linking parental consanguinity or convulsions with vitamin D could not be established. Conclusions: Serum values of 25(OH)D in the children with autism of this study could classify them as being "vitamin D inadequate," which lends support to the

hypothesis that autism is a vitamin D deficiency disorder. [ABSTRACT FROM AUTHOR]

ISSN: 1075-5535

DOI: 10.1089/acm.2009.0349

Accession Number: 51600131

Database: Alt HealthWatch

Record: 1

Title: Serum 25-Hydroxyvitamin D in Infantile Rickets.

Authors: Arnaud, Sara B.
Stickler, Gunnar B.
Haworth, James C.

Source: Pediatrics; Feb76, Vol. 57 Issue 2, p221, 5p

Document Type: Article

Subject Terms: *VITAMIN D deficiency
*RICKETS
*HYPOPHOSPHATEMIA, Familial
*PARATHYROID hormone

Abstract: Abstract. In small children with nutritional vitamin D deficiency, the serum concentration of 25-hydroxyvitamin D (25-OH-D), the major circulating metabolite of vitamin D, was correlated with the stage of clinical disease. It was low (16 to 20 ng/ml) but within the normal range in the earliest (hypocalcemic) stage of the deficiency syndrome and den creased (< 15 ng/ml) in the more advanced stages. In patients with familial hypophosphatemia (X-linked dominant), mean serum 25-OH-D concentration was the same as in age-matched normal controls. Evidence is presented that endogenous parathyroid hormone may have a role in the depletion of serum 25-OH-D in deficiency states. Pediatrics, 57:221-225, 1976, RICKETS, VITAMIN D DEFICIENCY, FAMILIAL HYPOPHOSPHATEMIA (X-LINKED DOMINANT), SERUM 25-HYDROXYVITAMIN D, PARATHYROID HORMONE. [ABSTRACT FROM AUTHOR]

ISSN: 00314005

Accession Number: 4747288

Database: Academic Search Premier

Record: 1

Title: Maternal vitamin D deficiency increases the risk of preeclampsia.

Authors: Bodnar LM; Catov JM; Simhan HN; Holick MF; Powers RW; Roberts JM

Author Address: Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, A742 Crabtree Hall, 130 DeSoto Street, Pittsburgh, Pennsylvania, 15261, USA. bodnar@edc.pitt.edu

Source: The Journal Of Clinical Endocrinology And Metabolism [J Clin Endocrinol Metab] 2007 Sep; Vol. 92 (9), pp. 3517-22. *Date of Electronic Publication:* 2007 May 29.

Publication Type: Journal Article; Research Support, N.I.H., Extramural

Language: English

Journal Information: *Country of Publication:* United States *NLM ID:* 0375362 *Publication Model:* Print-Electronic *Cited Medium:* Print *ISSN:* 0021-972X (Print) *Linking ISSN:* 0021972X *NLM ISO Abbreviation:* J. Clin. Endocrinol. Metab. *Subsets:* Core Clinical (AIM); MEDLINE

MeSH Terms: Pre-Eclampsia/*etiology
Vitamin D Deficiency/*complications
Adolescent; Adult; Calcitriol/blood; Case-Control Studies; Female; Gestational Age; Humans; Infant, Newborn; Mothers; Motor Activity/physiology; Pre-Eclampsia/blood; Pre-Eclampsia/ethnology; Pregnancy; Pregnancy Complications/blood; Pregnancy Outcome; Pregnancy Trimester, First/blood; Risk Factors; Socioeconomic Factors; Vitamin D Deficiency/blood

Abstract: **Context:** Vitamin D has direct influence on molecular pathways proposed to be important in the pathogenesis of preeclampsia, yet the vitamin D-preeclampsia relation has not been studied.

Objectives: We aimed to assess the effect of maternal 25-hydroxyvitamin D [25(OH)D] concentration on the risk of preeclampsia and to assess the vitamin D status of newborns of preeclamptic mothers.

Design and Setting: We conducted a nested case-control study of pregnant women followed from less than 16 wk gestation to delivery (1997-2001) at prenatal clinics and private practices.

Patients: Patients included nulliparous pregnant women with singleton pregnancies who developed preeclampsia (n = 55) or did not develop preeclampsia (n = 219). Women's banked sera were newly measured for 25(OH)D.

Main Outcome Measure: The main outcome measure was preeclampsia

(new-onset gestational hypertension and proteinuria for the first time after 20 wk gestation). Our hypotheses were formulated before data collection.
Results: Adjusted serum 25(OH)D concentrations in early pregnancy were lower in women who subsequently developed preeclampsia compared with controls [geometric mean, 45.4 nmol/liter, and 95% confidence interval (CI), 38.6-53.4 nmol/liter, vs. 53.1 and 47.1-59.9 nmol/liter; $P < 0.01$]. There was a monotonic dose-response relation between serum 25(OH)D concentrations at less than 22 wk and risk of preeclampsia. After confounder adjustment, a 50-nmol/liter decline in 25(OH)D concentration doubled the risk of preeclampsia (adjusted odds ratio, 2.4; 95% CI, 1.1-5.4). Newborns of preeclamptic mothers were twice as likely as control newborns to have 25(OH)D less than 37.5 nmol/liter (adjusted odds ratio, 2.2; 95% CI, 1.2-4.1).
Conclusions: Maternal vitamin D deficiency may be an independent risk factor for preeclampsia. Vitamin D supplementation in early pregnancy should be explored for preventing preeclampsia and promoting neonatal well-being.

Comments: Comment in: J Clin Endocrinol Metab. 2007 Sep;92(9):3402-3. (PMID: 17823275)

Grant Information: 5M01 RR00056 United States RR NCRR NIH HHS; K01 MH074092 United States MH NIMH NIH HHS; P30 DK046204 United States DK NIDDK NIH HHS; PPG 2P01 HD30367 United States HD NICHD NIH HHS; R01 HD041663 United States HD NICHD NIH HHS; R01 HD052732 United States HD NICHD NIH HHS

Substance Nomenclature: 32222-06-3 (Calcitriol)

Entry Dates: *Date Created:* 20070907 *Date Completed:* 20071101 *Latest Revision:* 20071203

Update Code: 20101124

PMID: 17535985

Database: MEDLINE

Record: 1

Title: Association between vitamin D deficiency and primary cesarean section.

Authors: Merewood A; Mehta SD; Chen TC; Bauchner H; Holick MF

Author Address: Department of Pediatrics, Division of Endocrinology, Diabetes, and Nutrition, Boston University School of Medicine, and Division of General Pediatrics, Boston Medical Center, Boston, Massachusetts 02118, USA.

Source: The Journal Of Clinical Endocrinology And Metabolism [J Clin Endocrinol Metab] 2009 Mar; Vol. 94 (3), pp. 940-5. *Date of Electronic Publication:* 2008 Dec 23.

Publication Type: Journal Article; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.

Language: English

Journal Information: *Country of Publication:* United States *NLM ID:* 0375362 *Publication Model:* Print-Electronic *Cited Medium:* Internet *ISSN:* 1945-7197 (Electronic) *Linking ISSN:* 0021972X *NLM ISO Abbreviation:* J. Clin. Endocrinol. Metab. *Subsets:* Core Clinical (AIM); MEDLINE

MeSH Terms: Cesarean Section/*statistics & numerical data
Vitamin D Deficiency/*complications
Adult; Calcium/blood; Female; Humans; Infant, Newborn; Logistic Models; Male; Pregnancy; Vitamin D/analogs & derivatives; Vitamin D/blood

Abstract: **Background:** At the turn of the 20th century, women commonly died in childbirth due to rachitic pelvis. Although rickets virtually disappeared with the discovery of the hormone vitamin D, recent reports suggest vitamin D deficiency is widespread in industrialized nations. Poor muscular performance is an established symptom of vitamin D deficiency. The current U.S. cesarean birth rate is at an all-time high of 30.2%. We analyzed the relationship between maternal serum 25-hydroxyvitamin D [25(OH)D] status, and prevalence of primary cesarean section.
Methods: Between 2005 and 2007, we measured maternal and infant serum 25(OH)D at birth and abstracted demographic and medical data from the maternal medical record at an urban teaching hospital (Boston, MA) with 2500 births per year. We enrolled 253 women, of whom 43 (17%) had a primary cesarean.
Results: There was an inverse association with having a cesarean section and serum 25(OH)D levels. We found that 28% of women with serum 25 (OH)D less than 37.5 nmol/liter had a cesarean section, compared with only 14% of women with 25(OH)D 37.5nmol/liter or greater (P = 0.012). In

multivariable logistic regression analysis controlling for race, age, education level, insurance status, and alcohol use, women with 25(OH)D less than 37.5 nmol/liter were almost 4 times as likely to have a cesarean than women with 25(OH)D 37.5 nmol/liter or greater (adjusted odds ratio 3.84; 95% confidence interval 1.71 to 8.62).
Conclusion: Vitamin D deficiency was associated with increased odds of primary cesarean section.

Comments:

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Grant Information: R40MC03620-02-00 United States PHS HHS

Substance Nomenclature: 1406-16-2 (Vitamin D)
64719-49-9 (25-hydroxyvitamin D)
7440-70-2 (Calcium)

Entry Dates: *Date Created:* 20090305 *Date Completed:* 20090407 *Latest Revision:* 20100922

Update Code: 20101124

PubMed Central ID: PMC2681281

PMID: 19106272

Database: MEDLINE

From The Times

October 10, 2009

Vitamin D 'may cut premature birth risk and protect newborn babies'

Oliver Gillie in Bruges

Powerful new evidence about the way that vitamin D can reduce the risk of premature births and boost the health of newborn babies has emerged from an international research conference in Bruges. Delegates were told that mothers who were given ten times the usual dose of vitamin D during pregnancy had their risk of premature birth reduced by half and had fewer small babies.

The findings emerge after evidence, revealed in The Times, that vitamin D — the "sunshine vitamin" — could have a dramatic effect in combating Scotland's appalling health record. Statistics showing that Scots — particularly in the west — are exposed to less sunshine than those living farther south correlate exactly with higher incidences of heart disease, some cancers and multiple sclerosis. The Times has campaigned to have vitamin D recommended and prescribed as part of a national health programme.

The vitamin's benefits have been observed previously in uncontrolled studies of pregnant women and babies, but this is the first time they have been found in a scientific trial which met the most stringent criteria for "evidence-based inquiry". The findings may make it necessary for health departments to revise advice presently given to pregnant and breastfeeding women in the UK.

The investigators, Dr Bruce Hollis and Dr Carol Wagner of the Medical University of South Carolina, Charleston, met rigorous safety tests which were required by the Federal Drug Administration. The study was funded by the National Institutes of Health. The women, who all lived around Charleston, South Carolina, began taking 4,000 IUs per day of vitamin D after their first clinic visit at about three months of pregnancy. (4,000 IUs or international units equals 100 microgms). A control group took 400 IUs,equivalent to the normal recommended dose in the US and UK. The women had their blood and urine tested monthly to ensure calcium and vitamin D levels were within safe limits.

Over the 2½ years of the study thousands of tests were made and monitored by an external safety committee. No test showed any adverse effect of the large dose of vitamin D. The average level of vitamin D in the women's blood increased by about 50 per cent.

About 600 women took part in the trial which included similar numbers of African Americans, Hispanic Americans and whites. Premature babies born to women taking high doses of vitamin D were reduced by half at both 32 and 37 weeks, and there were also fewer babies who were born "small for dates" — that is smaller than would be expected considering the length of time spent in the womb.

The women had a 25 per cent reduction in infections, particularly respiratory infections such as colds and flu as well as fewer infections of the vagina and the gums. The "core morbidities of pregnancy" were also reduced by 30 per cent in the women who took the high-dose vitamin D.

These included diabetes, raised blood pressure, and pre-eclampsia, an increase in blood pressure and fluid which may, if untreated, cause the death of the mother and/or the baby. Babies getting most vitamin D after birth suffered from fewer colds and less eczema.

The Charleston team is running another trial in breastfeeding women who are taking 6,400 IUs per day, a dose 16 times the amount of vitamin D recommended in the UK. This high dose enables women to make breast milk which has sufficient vitamin D for the baby's needs, 400 IUs per day.

The American investigations used vitamin D3, the human form of the vitamin which is more potent than the vitamin D2, the plant form present in Abidec, the vitamin mixture usually recommended for babies in the UK.

"I'm telling every pregnant mother I see to take 4,000 IUs and every nursing mother to take 6,400 IUs of vitamin D a day," said Dr Hollis. "I think it is medical malpractice for obstetricians not to know what the vitamin D level of their patients is. This study will put them on notice."

Five years ago the UK National Institute of Clinical Excellence told doctors that women in Britain did not need to take vitamin D in pregnancy advice later overruled by the Chief Medical Officer.

Page 1 of 2 NEXT PAGE

BEHIND THE STORY

The normally recommended level of sun exposure in the UK does not produce enough vitamin D, according to a separate study reported at the Bruges meeting (Oliver Gillie writes). Sunlight is the main source of vitamin D in the UK as elsewhere and so advice on sun exposure is crucial for health. Food cannot supply more than 10 per cent of what is needed.

Dr Jackie Berry, and Dr Ann Webb and others from the University of Manchester studied the effect of sunlamp treatment, which simulated summer sun in the UK, on 120 white volunteers who wore only a T-shirt and shorts. The treatments were given three times a week for six weeks in winter when blood levels of vitamin D are low and only 26 per cent of the volunteers obtained optimum blood levels as a result of the treatments.

This new research shows that advice, still given in the UK, that casual exposure of hands and face provides sufficient vitamin D is completely wrong. Revised advice from the Department of Health in December 2007 suggested that pregnant women would get sufficient vitamin D if they exposed shoulders as well as arms and legs. But this too is now shown to be insufficient by the study of simulated "British sunlight".

To get optimum benefit from sunbathing as many clothes as possible should be removed, or it should be done more often than three times a week, or for longer than 13 minutes a day. All these increases in exposure can be difficult to achieve especially when sunny weather seldom lasts for six consecutive weeks in the UK.

In wintertime in the UK the optimal level of vitamin D can only be obtained by taking a supplement because the sun is too weak. The Standing Committee of European Doctors is preparing a report on vitamin D which is expected to recognise, contrary to advice in the UK, that everyone, apart from young children, needs a vitamin D supplement of at least 1,000 IUs a day and probably 2,000 for full health.

The higher 2000 figure is supported by observational studies of groups of people showing higher levels of vitamin D are associated with a reduced risk of cancer, heart disease and immune system diseases as well as classic bone diseases, but as yet there are relatively few controlled scientific trials of higher doses.

Patients with hip fractures in Boston, in the US, taking 2000 IUs of vitamin D had 60 per cent fewer complications and 90 per cent fewer infections than patients who received a placebo in a double blind randomised trial, the Bruges workshop was told. They were also 40 per cent less likely to be readmitted to hospital, said the study leader Dr Beth Dawson-Hughes of Tufts University, Boston.

PREVIOUS PAGE Page 2 of 2

HAARETZ.com

Published 01:14 14.01.10 | Latest update 01:34 14.01.10

Study: Vitamin D could help fight hepatitis C

Already heralded in battling cancer, Vitamin D may also be key to curing hepatitis. But Israelis, especially the ultra-Orthodox, are woefully deficient.

By Dan Even
Tags: Israel health Israel news

A new study has found that administering vitamin D to hepatitis C patients dramatically reduces the presence of the virus in the blood.

The study, carried out at Rebecca Sieff Hospital in Safed and Hillel Yaffeh Medical Center in Hadera by Dr. Assy Nimer and Dr. Saif Abu-Mouch covered 90 hepatitis C patients.

The findings were presented in late November at a conference of the American Association for the Study of Liver Diseases.

For six months, in addition to the standard treatment, which included Interferon once a week and a daily dose of the antiviral drug Ribavirin, 30 patients were also treated with 1,000 units of vitamin D a day. A control group of 60 patients went without the vitamin.

In order to assess the impact of vitamin D on the treatment of the disease, before starting the study, all patients, including those from the control group and those who were found to have a vitamin D deficiency, were given supplements, so that all participants began the study from the same point.

A month after the start of treatment, the virus had disappeared from the blood in 44 percent of the group receiving vitamin D supplements, as opposed to just 18 percent among the control group.

After three months, the success rate for the group getting the supplement rose to 96 percent, compared to 48 percent in the control group.

Other findings from the study, which will be presented next month in Kfar Blum at a conference of the Israeli Association for the Study of the Liver, indicate that this trend continues even after the end of drug treatment.

The initial results show that six months after the end of treatment, 90 percent of patients treated with drug therapy and vitamin D supplements had the virus disappear and completely recovered.

"The drug treatment for hepatitis C patients is usually administered for around a year, and occasionally the virus disappears from the blood, but remains in other places, for example, in the liver and lymph glands," explained Nimer, the director of the Liver Disease Unit at Rebecca Sieff Hospital. "At the end of the treatment, the virus may return to the blood, but we found that in patients who were also given the vitamin D supplement, the virus did not return, that is, it was excreted by the body."

How vitamin D helps improve the condition of hepatitis patients is not entirely clear. However, according to Nimer, "It has already been proven that vitamin D benefits the immune system by increasing the activity of T cells [white blood cells that help in the fight against pathogens], improves the body's reaction to the insulin hormone, and reduces the level of pro-inflammatory proteins that cause liver infections caused by viruses."

The findings have important ramifications, mainly in light of the difficulty in effectively treating all patients with hepatitis C, a disease that has become the leading cause of cirrhosis of the liver and the need for liver transplants, and thereby the number one cause of liver cancer.

It is the only form of hepatitis for which no vaccine has been developed yet.

"The proteins surrounding the virus change constantly and it is difficult to create a vaccine against it," Nimer said.

There are some 300 people believed to be living in Israel with hepatitis C and receiving drug therapy. World Health Organization data indicates that this is an infectious disease with global reach: in the United States, 2 million-4 million patients are diagnosed annually, 5 million-15 million patients in Europe, and 12 million patients in India. Most of them are unaware they have been infected and are not receiving drug therapy, which increases the risk of a worsening of liver function.

There is also an incidence of disease in Japan, where some 350,000 new cases are diagnosed annually, and in Egypt, where 20 percent of blood donors are rejected as carriers of hepatitis C.

The virus is spread primarily by coming into contact with tainted blood, either through blood donation or unsterilized syringes, mainly among narcotics users.

The risk of being infected during unprotected sex is low - around 2-3 percent.

In recent years medical literature has highlighted vitamin D as effective in reducing the risk of various diseases, including infectious diseases, diabetes and even breast cancer, prostate cancer and colon cancer. It also increases the effectiveness of treatment for cancer patients.

An article published in 2006 suggested the possibility that a vitamin D deficiency during the sunless days of winter is the cause of flu outbreaks and increases the risk of respiratory illness in children, even though articles published later countered those findings.

Let the sunshine in

Vitamin D is absorbed from the sun's rays, but according to recently conducted studies over the past few years, even in sunny Israel, a substantial part of the population suffers from a Vitamin D deficiency.

A survey conducted at Rambam Medical Center in Haifa found that there is a severe shortage of vitamin D in the ultra-Orthodox community due to their modest dress, which shields most of the body from the sun's rays.

A survey conducted a year and a half ago at the Kupat Holim Meuhedet health maintenance organization, which checked vitamin levels in the blood in children up to the age of 19, found an average level of 22 nanograms per milliliter of vitamin D. This amount is only two-thirds of the recommended level (32 units).

In the ultra-Orthodox Kiryat Sanz neighborhood in Netanya, an especially severe shortage was found, with an average of 18.5 units. However even in the Jerusalem neighborhood of Baka, which is partially secular, the average level measured was still only 29 units.

About two years ago, Prof. Sophia Ish-Shalom of Rambam found that young high-tech workers also have a vitamin D deficiency, due to the many hours spent working in offices during daylight hours.

Around 5-10 percent of vitamin D levels are obtained from foods, especially salmon, sardines, mackerel, cod, tuna and egg yolks. Vitamin D levels are measured in international units.

At the U.S. National Academy of Science's National Institute of Health, the recommended daily consumption is 200 units of vitamin D up until age 40, 500 units from age 51-70 and 600 units from age 71 on.

Many experts argue that the recommendations are too low, and the issue is under discussion in professional medical associations in the West.

In recent months, the Health Ministry has begun promoting a plan to increase vitamin D levels among Israelis, by enriching milk drinks, approving the import of nutritional supplements that contain vitamin D in higher doses and increasing awareness of the importance of the vitamin among pregnant women and among children, among other tactics.

This story is by: Dan Even

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Dietary Reference Intakes for Calcium and Vitamin D

Calcium and vitamin D are two essential nutrients long known for their role in bone health. Over the last ten years, the public has heard conflicting messages about other benefits of these nutrients—especially vitamin D—and also about how much calcium and vitamin D they need to be healthy.

To help clarify this issue, the U. S. and Canadian governments asked the Institute of Medicine (IOM) to assess the current data on health outcomes associated with calcium and vitamin D. The IOM tasked a committee of experts with reviewing the evidence, as well as updating the nutrient reference values, known as Dietary Reference Intakes (DRIs). These values are used widely by government agencies, for example, in setting standards for school meals or specifying the nutrition label on foods. Over time, they have come to be used by health professionals to counsel individuals about dietary intake.

The committee provided an exhaustive review of studies on potential health outcomes and found that the evidence supported a role for these nutrients in bone health but not in other health conditions. Further, there is emerging evidence that too much of these nutrients may be harmful.

The committee provided an exhaustive review of studies on potential health outcomes and found that the evidence supported a role for these nutrients in bone health but not in other health conditions.

Health Effects of Vitamin D and Calcium Intake

The new reference values are based on much more information and higher-quality studies than were available when the values for these nutrients were first set in 1997. The committee assessed more than one thousand studies and reports and listened to testimony from scientists and stakeholders before making its conclusions. It reviewed a range of health outcomes, including but not limited to cancer, cardiovascular disease and hypertension, diabetes

and metabolic syndrome, falls, immune response, neuropsychological functioning, physical performance, preeclampsia, and reproductive outcomes. This thorough review found that information about the health benefits beyond bone health—benefits often reported in the media—were from studies that provided often mixed and inconclusive results and could not be considered reliable. However, a strong body of evidence from rigorous testing substantiates the importance of vitamin D and calcium in promoting bone growth and maintenance.

Dietary Reference Intakes

The DRIs are intended to serve as a guide for good nutrition and provide the basis for the development of nutrient guidelines in both the United States and Canada. The science indicates that on average 500 milligrams of calcium per day meets the requirements of children ages 1 through 3, and on average 800 milligrams daily is appropriate for those ages 4 through 8 (see table for the Recommended Dietary Allowance—a value that meets the needs of most people). Adolescents need higher levels to support bone growth: 1,300 milligrams per day meets the needs of practically all adolescents. Women ages 19 through 50 and men up to 71 require on average 800 milligrams daily. Women over 50 and both men and women 71 and older should take in 1,000 milligrams per day on average to ensure they are meeting their daily

TABLE: Dietary Reference Intakes for Calcium and Vitamin D

	Calcium			Vitamin D		
Life Stage Group	Estimated Average Requirement (mg/day)	Recommended Dietary Allowance (mg/day)	Upper Level Intake (mg/day)	Estimated Average Requirement (IU/day)	Recommended Dietary Allowance (IU/day)	Upper Level Intake (IU/day)
Infants 0 to 6 months	*	*	1,000	**	**	1,000
Infants 6 to 12 months	*	*	1,500	**	**	1,500
1–3 years old	500	700	2,500	400	600	2,500
4–8 years old	800	1,000	2,500	400	600	3,000
9–13 years old	1,100	1,300	3,000	400	600	4,000
14–18 years old	1,100	1,300	3,000	400	600	4,000
19–30 years old	800	1,000	2,500	400	600	4,000
31–50 years old	800	1,000	2,500	400	600	4,000
51–70 year old males	800	1,000	2,000	400	600	4,000
51–70 year old females	1,000	1,200	2,000	400	600	4,000
>70 years old	1,000	1,200	2,000	400	800	4,000
14–18 years old, pregnant/lactating	1,100	1,300	3,000	400	600	4,000
19–50 years old, pregnant/lactating	800	1,000	2,500	400	600	4,000

*For infants, Adequate Intake is 200 mg/day for 0 to 6 months of age and 260 mg/day for 6 to 12 months of age.
**For infants, Adequate Intake is 400 IU/day for 0 to 6 months of age and 400 IU/day for 6 to 12 months of age.

Higher levels of both nutrients have not been shown to confer greater benefits, and in fact, they have been linked to other health problems, challenging the concept that "more is better."

needs for strong, healthy bones.

Determining intake levels for vitamin D is somewhat more complicated. Vitamin D levels in the body may come from not only vitamin D in the diet but also from synthesis in the skin through sunlight exposure. The amount of sun exposure one receives varies greatly from person to person, and people are advised against sun exposure to reduce the risk of skin cancer. Therefore, the committee assumed minimal sun exposure when establishing the DRIs for vitamin D, and it determined that North Americans need on average 400 International Units (IUs) of vitamin D per day (see table for the Recommended Dietary Allowances—values sufficient to meet the needs of virtually all persons). People age 71 and older may require as much as 800 IUs per day because of potential changes in people's bodies as they age.

Questions About Current Intake

National surveys in both the United States and Canada indicate that calcium may remain a nutrient of concern, especially for girls ages 9-18. Some postmenopausal women taking supplements may be getting too much calcium, thereby increasing their risk for kidney stones.

Information from national surveys shows vitamin D presents a complicated picture. While the average total intake of vitamin D is below the median requirement, national surveys show that average blood levels of vitamin D are above the 20 nanograms per milliliter that the IOM committee found to be the level that is needed for good bone health for practically all individuals. These seemingly inconsistent data suggest that sun exposure currently contributes meaningful amounts of vitamin D to North Americans and indicates that a majority of the population is meeting its needs for vitamin D. Nonetheless, some subgroups—particularly those who are older and living in institutions or who have dark skin pigmentation—may be at increased risk for getting too little vitamin D.

Before a few years ago, tests for vitamin D were conducted infrequently. In recent years, these tests have become more widely used, and confusion has grown among the public about how much vitamin D is necessary. Further, the measurements, or cut-points, of sufficiency and deficiency used by laboratories to report results have not been set based on rigorous scientific studies, and no central authority has determined which cut-points to use. A single individual might be deemed deficient or sufficient, depending on the laboratory where the blood is tested. The number of people with vitamin D deficiency in North America may be overestimated because many laboratories appear to be using cut-points that are much higher than the committee suggests is appropriate.

Tolerable Upper Levels of Intake

The upper level intakes set by the committee for both calcium and vitamin D represent the safe boundary at the high end of the scale and should not be misunderstood as amounts people need or should strive to consume. While these values

vary somewhat by age, as shown in the table, the committee concludes that once intakes of vitamin D surpass 4,000 IUs per day, the risk for harm begins to increase. Once intakes surpass 2,000 milligrams per day for calcium, the risk for harm also increases.

As North Americans take more supplements and eat more of foods that have been fortified with vitamin D and calcium, it becomes more likely that people consume high amounts of these nutrients. Kidney stones have been associated with taking too much calcium from dietary supplements. Very high levels of vitamin D (above 10,000 IUs per day) are known to cause kidney and tissue damage. Strong evidence about possible risks for daily vitamin D at lower levels of intake is limited, but some preliminary studies offer tentative signals about adverse health effects.

Conclusion

Scientific evidence indicates that calcium and vitamin D play key roles in bone health. The current evidence, however, does not support other benefits for vitamin D or calcium intake. More targeted research should continue. Higher levels have not been shown to confer greater benefits, and in fact, they have been linked to other health problems, challenging the concept that "more is better."

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Record: 1

Title: Risk assessment for vitamin D.

Authors: Hathcock JN; Shao A; Vieth R; Heaney R

Author Address: Council for Responsible Nutrition, Washington, DC 20036-5114, USA. jhathcock@crnusa.org

Source: The American Journal Of Clinical Nutrition [Am J Clin Nutr] 2007 Jan; Vol. 85 (1), pp. 6-18.

Publication Type: Journal Article; Meta-Analysis; Review

Language: English

Journal Information: *Country of Publication:* United States *NLM ID:* 0376027 *Publication Model:* Print *Cited Medium:* Print *ISSN:* 0002-9165 (Print) *Linking ISSN:* 00029165 *NLM ISO Abbreviation:* Am. J. Clin. Nutr. *Subsets:* Core Clinical (AIM); MEDLINE

MeSH Terms: Nutrition Policy*
Vitamin D*/administration & dosage
Vitamin D*/adverse effects
Bone Density Conservation Agents/*administration & dosage
Bone and Bones/*metabolism
Vitamin D Deficiency/*prevention & control
Bone Density Conservation Agents/adverse effects; Dietary Supplements; Evidence-Based Medicine; Female; Food, Fortified; Humans; Hypercalcemia/chemically induced; Hypercalcemia/prevention & control; Male; Maximum Tolerated Dose; No-Observed-Adverse-Effect Level; Nutritional Requirements; Risk Assessment; United States; Vitamin D Deficiency/complications; Vitamins/administration & dosage; Vitamins/adverse effects

Abstract: The objective of this review was to apply the risk assessment methodology used by the Food and Nutrition Board (FNB) to derive a revised safe Tolerable Upper Intake Level (UL) for vitamin D. New data continue to emerge regarding the health benefits of vitamin D beyond its role in bone. The intakes associated with those benefits suggest a need for levels of supplementation, food fortification, or both that are higher than current levels. A prevailing concern exists, however, regarding the potential for toxicity related to excessive vitamin D intakes. The UL established by the FNB for vitamin D (50 microg, or 2000 IU) is not based on current evidence and is viewed by many as being too restrictive, thus curtailing research, commercial development, and optimization of nutritional policy. Human

clinical trial data published subsequent to the establishment of the FNB vitamin D UL published in 1997 support a significantly higher UL. We present a risk assessment based on relevant, well-designed human clinical trials of vitamin D. Collectively, the absence of toxicity in trials conducted in healthy adults that used vitamin D dose > or = 250 microg/d (10,000 IU vitamin D3) supports the confident selection of this value as the UL.

Number of References: 99

Substance Nomenclature: 0 (Bone Density Conservation Agents)
0 (Vitamins)
1406-16-2 (Vitamin D)

Entry Dates: *Date Created:* 20070108 *Date Completed:* 20070215

Update Code: 20101124

PMID: 17209171

Database: MEDLINE

Record: 1

Title: Comparisons of estimated economic burdens due to insufficient solar ultraviolet irradiance and vitamin D and excess solar UV irradiance for the United States.

Authors: Grant WB; Garland CF; Holick MF

Author Address: Sunlight, Nutrition and Health Research Center (SUNARC), 2107 Van Ness Avenue, Suite 403B, San Francisco, CA 94109-2529, USA. wgrant@sunarc.org

Source: Photochemistry And Photobiology [Photochem Photobiol] 2005 Nov-Dec; Vol. 81 (6), pp. 1276-86.

Publication Type: Comparative Study; Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't

Language: English

Journal Information: *Country of Publication:* United States *NLM ID:* 0376425 *Publication Model:* Print *Cited Medium:* Print *ISSN:* 0031-8655 (Print) *Linking ISSN:* 00318655 *NLM ISO Abbreviation:* Photochem. Photobiol. *Subsets:* MEDLINE

MeSH Terms: Cost of Illness*
Health Expenditures*
Ultraviolet Rays*/adverse effects
Vitamin D/*physiology
Cataract/economics; Dietary Supplements; Great Britain; Humans; Keratosis/economics; Melanoma/economics; Melanoma/etiology; Multiple Sclerosis/economics; Neoplasms/economics; Neoplasms/etiology; Osteoporosis/economics; Risk Reduction Behavior; Skin Neoplasms/economics; Skin Neoplasms/etiology; Sunlight; United States; Vitamin D/pharmacology

Abstract: Vitamin D sufficiency is required for optimal health, and solar ultraviolet B (UVB) irradiance is an important source of vitamin D. UVB and/or vitamin D have been found in observational studies to be associated with reduced risk for over a dozen forms of cancer, multiple sclerosis, osteoporotic fractures, and several other diseases. On the other hand, excess UV irradiance is associated with adverse health outcomes such as cataracts, melanoma, and nonmelanoma skin cancer. Ecologic analyses are used to estimate the fraction of cancer mortality, multiple sclerosis prevalence, and cataract formation that can be prevented or delayed. Estimates from the literature are used for other diseases attributed to excess UV irradiation, additional cancer estimates, and osteoporotic fractures. These results are used to estimate the economic burdens of insufficient UVB irradiation and vitamin D insufficiency as well as excess UV irradiation in the United States for these diseases and conditions. We estimate that 50,000-63,000 individuals in the United States and 19,000-25,000 in the UK die prematurely from cancer annually due to insufficient vitamin D. The U.S. economic burden due to vitamin D insufficiency from inadequate exposure to solar UVB irradiance, diet, and supplements was estimated at $40-56 billion in 2004, whereas the economic burden for excess UV irradiance was estimated at $6-7 billion. These results suggest that increased vitamin D through UVB irradiance, fortification of food, and supplementation could reduce the health care burden in the United States, UK, and elsewhere. Further research is required to confirm these estimates.

Grant Information: AR3696312 United States AR NIAMS NIH HHS; M01RR00533 United States RR NCRR NIH HHS

Substance Nomenclature: 1406-16-2 (Vitamin D)

Entry Dates: *Date Created:* 20051215 *Date Completed:* 20060609 *Latest Revision:* 20071114

Record: 1

Title: An estimate of the economic burden and premature deaths due to vitamin D deficiency in Canada.

Authors: Grant WB; Schwalfenberg GK; Genuis SJ; Whiting SJ

Author Address: Sunlight, Nutrition, and Health Research Center (SUNARC), San Francisco, CA 94164-1603, USA. wbgrant@infionline.net

Source: Molecular Nutrition & Food Research [Mol Nutr Food Res] 2010 Aug; Vol. 54 (8), pp. 1172-81.

Publication Type: Journal Article; Research Support, Non-U.S. Gov't; Review

Language: English

Journal Information: *Country of Publication:* Germany *NLM ID:* 101231818 *Publication Model:* Print *Cited Medium:* Internet *ISSN:* 1613-4133 (Electronic) *Linking ISSN:* 16134125 *NLM ISO Abbreviation:* Mol Nutr Food Res *Subsets:* MEDLINE

MeSH Terms:
Health Care Costs*
Mortality*
Vitamin D/*administration & dosage
Vitamin D/*physiology
Vitamin D Deficiency/*economics
Vitamin D Deficiency/*physiopathology
25-Hydroxyvitamin D
2/blood; Adult; Calcifediol/blood; Canada/epidemiology; Child; Female; Humans; Infant; Male; Nutrition Policy; Pregnancy; Vitamin D Deficiency/epidemiology; Vitamin D Deficiency/prevention & control

Abstract: The objective of this work is to estimate the economic burden and premature death rate in Canada attributable to low serum 25-hydroxyvitamin D (25(OH)D) levels. Vitamin D deficiency has been linked to many diseases and conditions in addition to bone diseases, including many types of cancer, several bacterial and viral infections, autoimmune diseases, cardiovascular diseases, and adverse pregnancy outcomes. Canadians have mean serum 25(OH)D levels averaging 67 nmol/L. The journal literature was searched for papers reporting dose-response relationships for vitamin D indices and disease outcomes. The types of studies useful in this regard include randomized controlled trials, observational, cross-sectional, and ecological studies, and meta-analyses. The mortality rates for 2005 were obtained from Statistics Canada. The economic burden data were obtained from Health Canada. The estimated benefits in disease reduction were based on increasing the mean serum 25(OH)D level to 105 nmol/L. It is estimated that the death rate could fall by 37,000 deaths (22,300-52,300 deaths), representing 16.1% (9.7-22.7%) of annuals deaths and the economic burden by 6.9% (3.8-10.0%) or $14.4 billion ($8.0 billion-$20.1 billion) less the cost of the program. It is recommended that Canadian health policy leaders consider measures to increase serum 25(OH)D levels for all Canadians.

Substance Nomenclature:
1406-16-2 (Vitamin D)
19356-17-3 (Calcifediol)
21343-40-8 (25-Hydroxyvitamin D 2)

Entry Dates: *Date Created:* 20100810 *Date Completed:* 20101130

Update Code: 20101209

PMID: 20352622

Database: MEDLINE

Take Magnesium AND Vitamin D To Avoid Vitamin D Side Effects

If you are taking Vitamin D, it's important that you understand the **Magnesium and Vitamin D** connection in order to avoid vitamin d side effects and to maximize absorption.

Nutrients don't work alone, and when it comes to taking vitamin d, it's important that you take magnesium and vitamin d together and not JUST vitamin d alone in large doses as this can lead to what people **BELIEVE** are vitamin d side effects, but are really just magnesium deficiency symptoms that have been induced because of how vitamin d 'uses up' magnesium in its conversion to its 'active form' in the bloodstream from supplements and sunlight.

This is a **BIG** problem because as more and more people, and their doctors, begin to realize the amazing health benefits that Vitamin D has to offer and to understand the seriousness of the long term Symptoms of Vitamin D Deficiency, more people are taking vitamin d with the effect of there being an increase in people having these so called 'vitamin d side effects'.

But what is **Not** being addressed by health care practitioners, however, is that many of these 'Vitamin D Side Effects' are not problems with the vitamin d, but are problems with not getting enough magnesium! There would be a significant reduction in problems with taking vitamin d if only people would take magnesium and vitamin d were taken **TOGETHER**.

Part of this problem is that nearly as many people have undiagnosed magnesium deficiencies as do people with vitamin d deficiencies. And unfortunately, blood Magnesium Levels are virtually worthless and can't tell you if you really are magnesium deficient!

In fact, Signs of Magnesium Deficiency are SO prevalent that Dr. Carolyn Dean calls this problem an 'Epidemic'. And if you have even a **MILD** unrecognized magnesium deficiency, your Signs of Magnesium Deficiency are going to be amplified greatly when vitamin d is taken- particularly in the large doses commonly used for vitamin d deficiency treatment. And this is creating some uncomfortable Side Effects of Vitamin D that are actually **NOT** problems with taking vitamin d itself, but symptoms of an induced magnesium deficiency!

Some of the problems being experienced by those taking vitamin D are: • Headaches

- Insomnia
- Jitteriness
- Muscle Cramps
- Anxiety
- Heart Palpitations
- Constipation

All of which are exactly the same as Signs of Magnesium Deficiency!! While certainly there are always going to be those who simply can't tolerate taking Vitamin D Supplements for one reason or another, the good news is that the vast majority of these problems can be

cleared up or easily prevented by being sure to take magnesium, in a dosage that is outlined on the Magnesium Dosage page, along with your vitamin d. This is equally true of those who get their vitamin d from the sun as well.

Vitamin D Absorption Problems
How Magnesium and Vitamin D Work Together

Since magnesium is required for the conversion of vitamin d into its active form, it's also true that taking vitamin d may not raise Vitamin D Blood Levels in those who are magnesium deficient!! Be sure that you read this again and understand this magnesium and vitamin d interrelationship:

- Magnesium is 'Used Up' when Vitamin D is converted into its active form in the blood
- Magnesium is 'Required' to convert Vitamin D into its active form in the blood

It works **BOTH ways**. Magnesium is not JUST depleted, but you won't convert vitamin d unless you have enough magnesium in order to allow vitamin d to **BE** converted!! In many cases where large doses of vitamin d are taken but the vitamin d level does not come up, both the person deficient and their doctor believe that they are having Vitamin D Absorption problems. This ends up causing:

1) A lot of fear that an underlying serious medical problem exists

2) Unnecessarily high dosages of Vitamin D are often taken causing worsening of the magnesium deficiency

3) Thousands and sometimes tens of thousands of dollars are spent in unnecessary medical testing to find the 'absorption' problem

4) The underlying magnesium deficiency is often never found and addressed because testing for magnesium levels is not a useful test to determine need for that nutrient

Unlike drugs, nutrients are 'synergistic' and interconnected with each other. Especially in the case of *Magnesium and Vitamin D* it's EXTREMELY important that you take magnesium if you are taking vitamin d on a regular basis.

Vitamin D

Its role in promoting public health and decreasing the incidence of disease

By

Representative Paul Seaton

What is Vitamin D?

Vitamin D3: A vitamin produced by the body when exposed to ultraviolet light or obtained from dietary sources. Vitamin D3 is a hormone that has an important role in calcium and phosphorus metabolism. Technically, vitamin D3 is not a vitamin because the body can produce it. Also known as cholecalciferol.

UV and Dietary sources

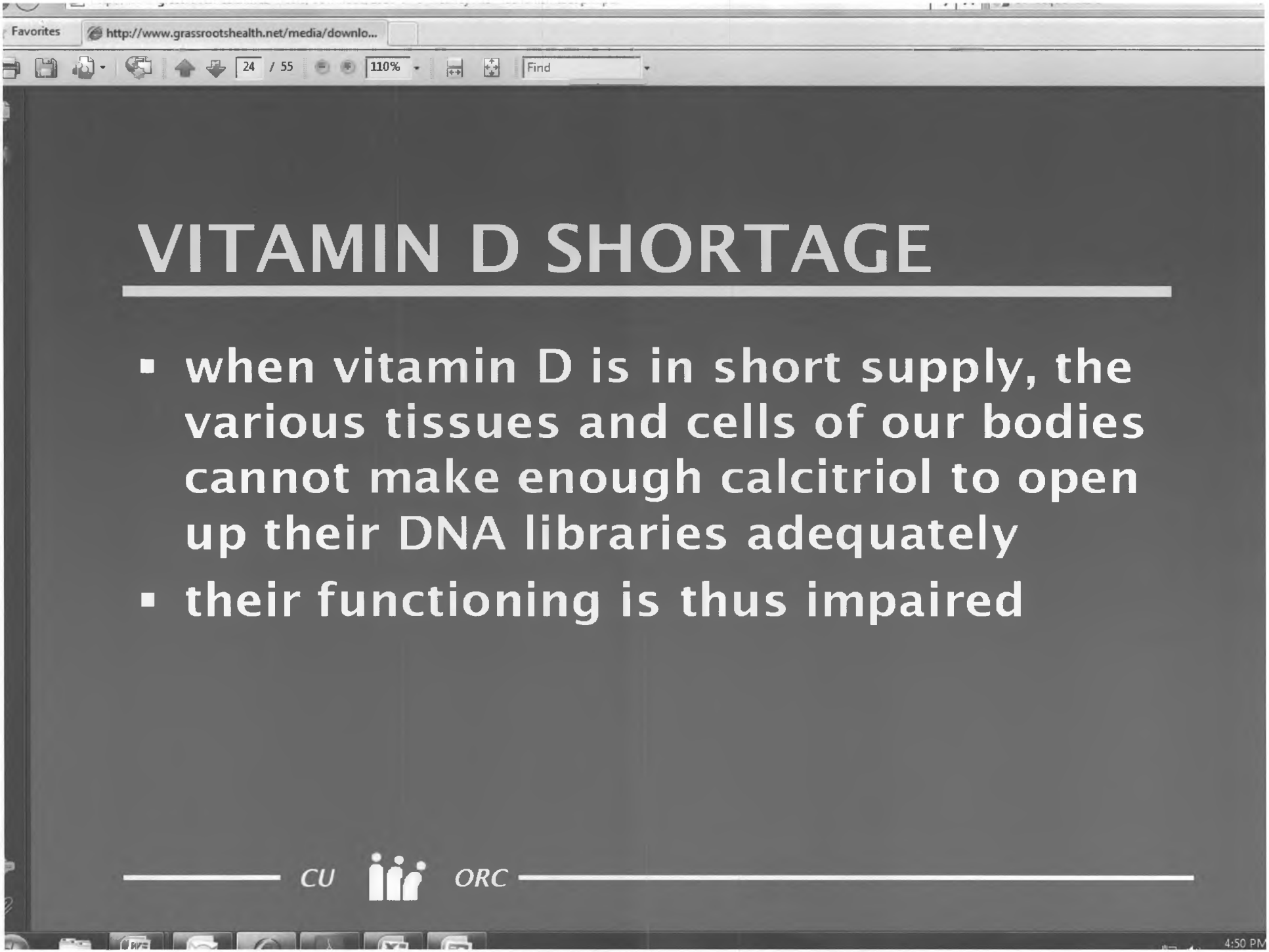
Caucasian skin produces approximately 10,000 International Units (IU) of vitamin D in response to 20–30 minutes summer sun exposure

People with darker skin pigmentation require significantly more sun exposure to get the same amount of vitamin D

Source	Approx Vitamin D Content
Salmon	
Fresh, wild (3.5 oz)	600-1000 IU
Fresh, farmed (3.5 oz)	100-250 IU
Canned (3.5 oz)	300-600 IU
Sardines, Canned (3.5 oz)	300 IU
Mackerel, canned (3.5 oz)	250 IU
Tuna, canned (3.6 oz)	230 IU
Exposure to Sunlight	3000 IU
Fortified milk (8oz)	100 IU
Fortified orange juice (8 oz)	100 IU
Infant formulas (8 oz)	100 IU
Prescription vitamin d	50,000 IU

Source: New England Journal of Medicine Vol 357:266-281 July 19, 2007

Despite your Best Efforts it is hard to get adequate Vitamin D from UV during the Alaska Winter


Favorites
http://www.grassrootshealth.net/media/downlo...
24 / 55
110%
Find
VITAMIN D SHORTAGE
when vitamin D is in short supply, the various tissues and cells of our bodies cannot make enough calcitriol to open up their DNA libraries adequately
their functioning is thus impaired
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ORC
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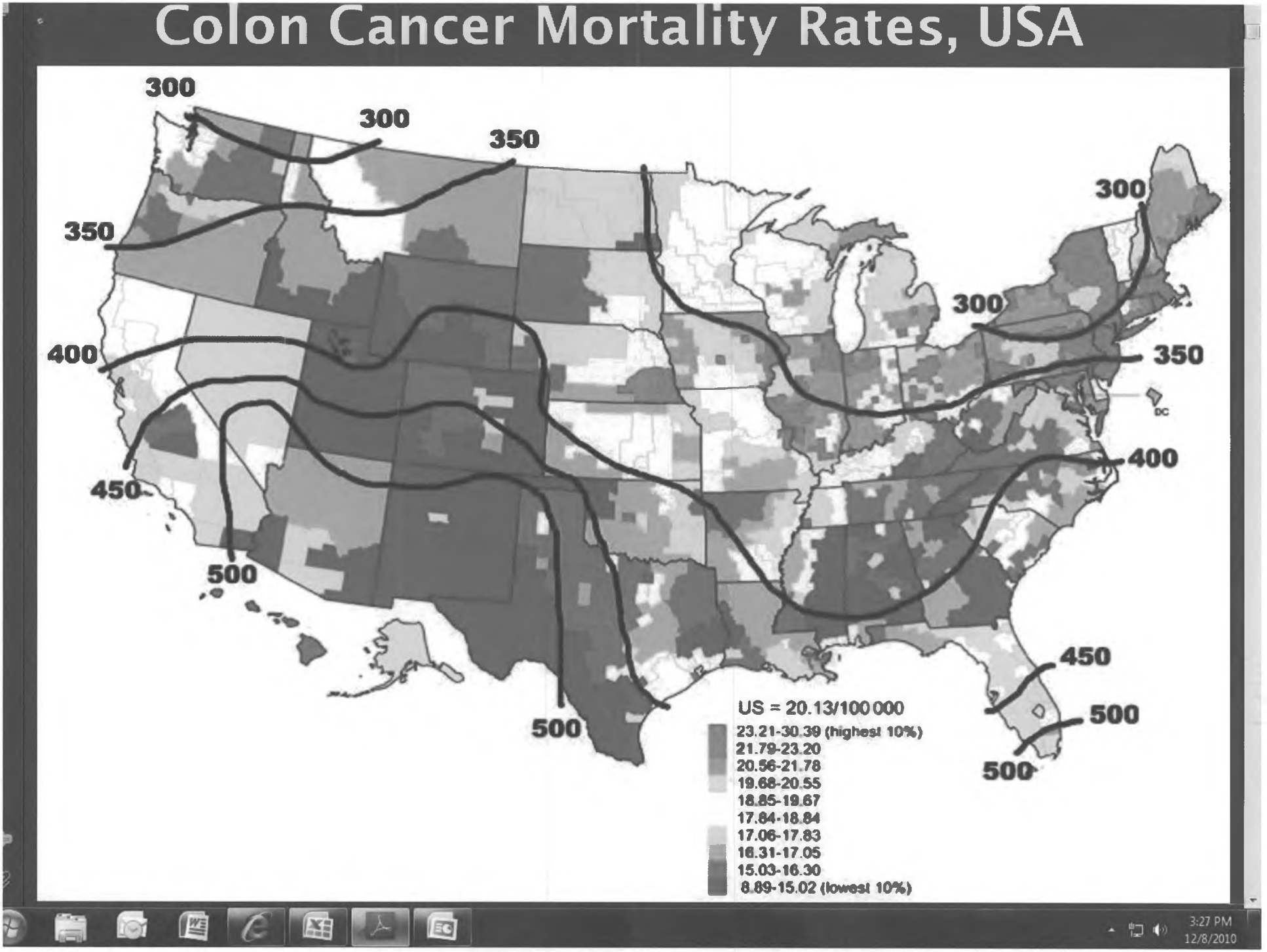
WHAT ARE THE CONSEQUENCES?

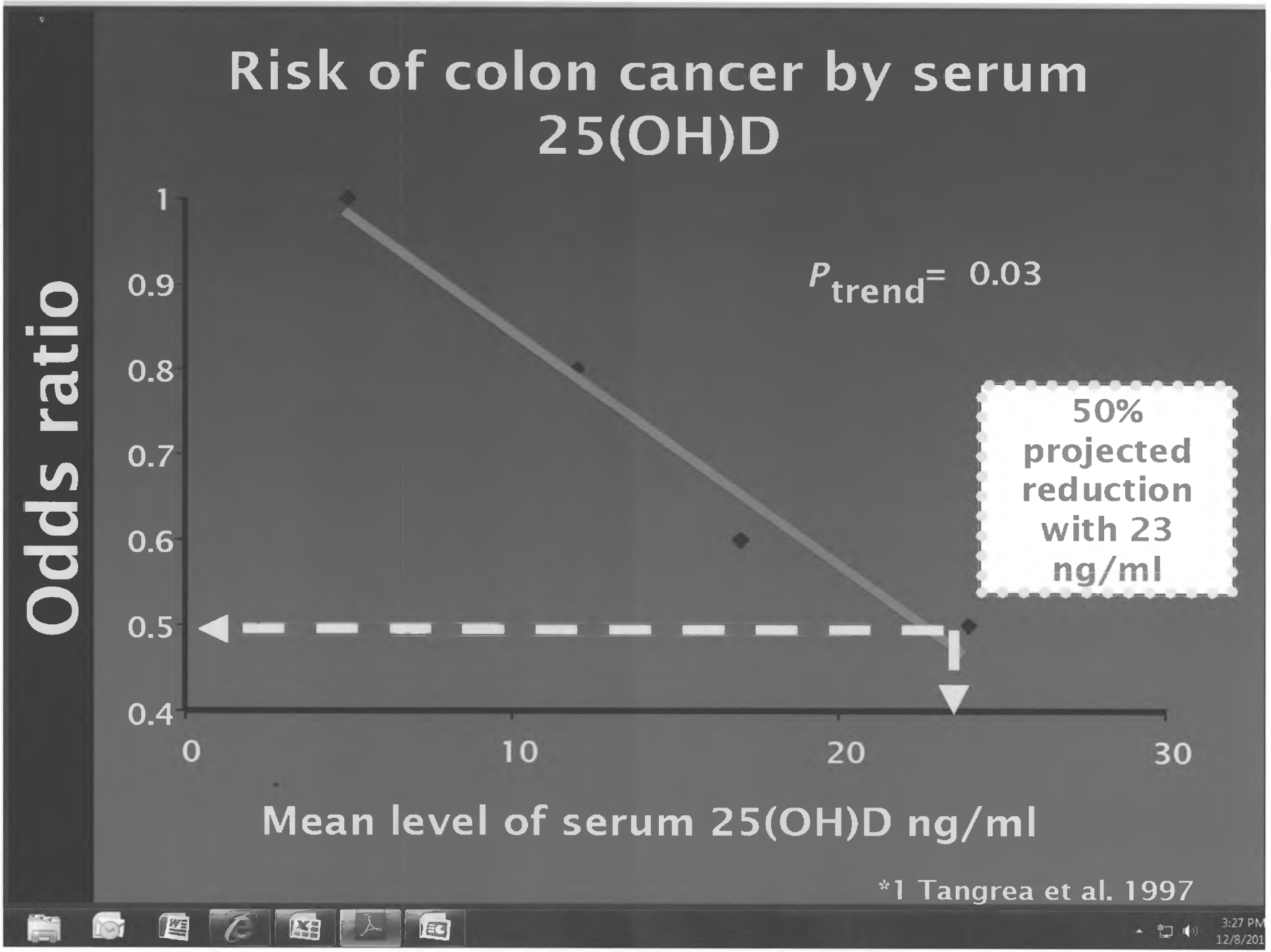
- bone diseases, falls, & fractures
- hypertension
- ↑ risk of cardiac disease & death
- prematurity, low birth weight, & ↑ Caesareans
- diabetes & metabolic syndrome
- periodontal disease
- decreased resistance to infection
- various cancers
- ↑ risk of multiple sclerosis

State Health Policy

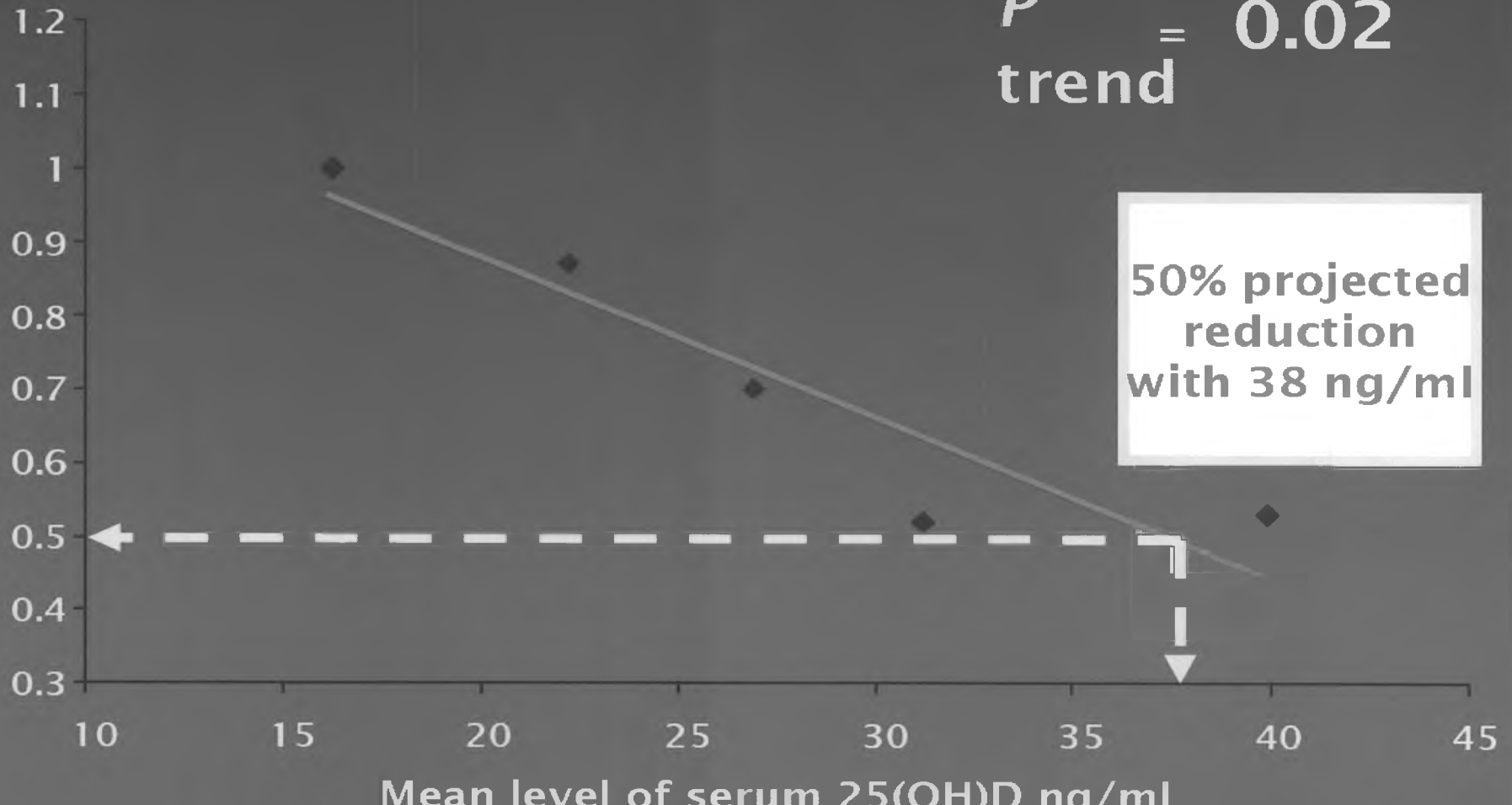
- Do we need a new statewide health policy that concentrates on prevention of disease instead of current policy focusing on treatment?

Colon Cancer Mortality Rates, USA




Risk of colon cancer by serum 25(OH)D
Odds ratio
1
0.9
0.8
0.7
0.6
0.5
0.4
0
10
20
30
P_{trend}= 0.03
50% projected reduction with 23 ng/ml
Mean level of serum 25(OH)D ng/ml
*1 Tangrea et al. 1997
3:27 PM
12/8/201

Risk of colon cancer by serum 25(OH)D



*2 Feskanich et al. 200

Meta-analysis

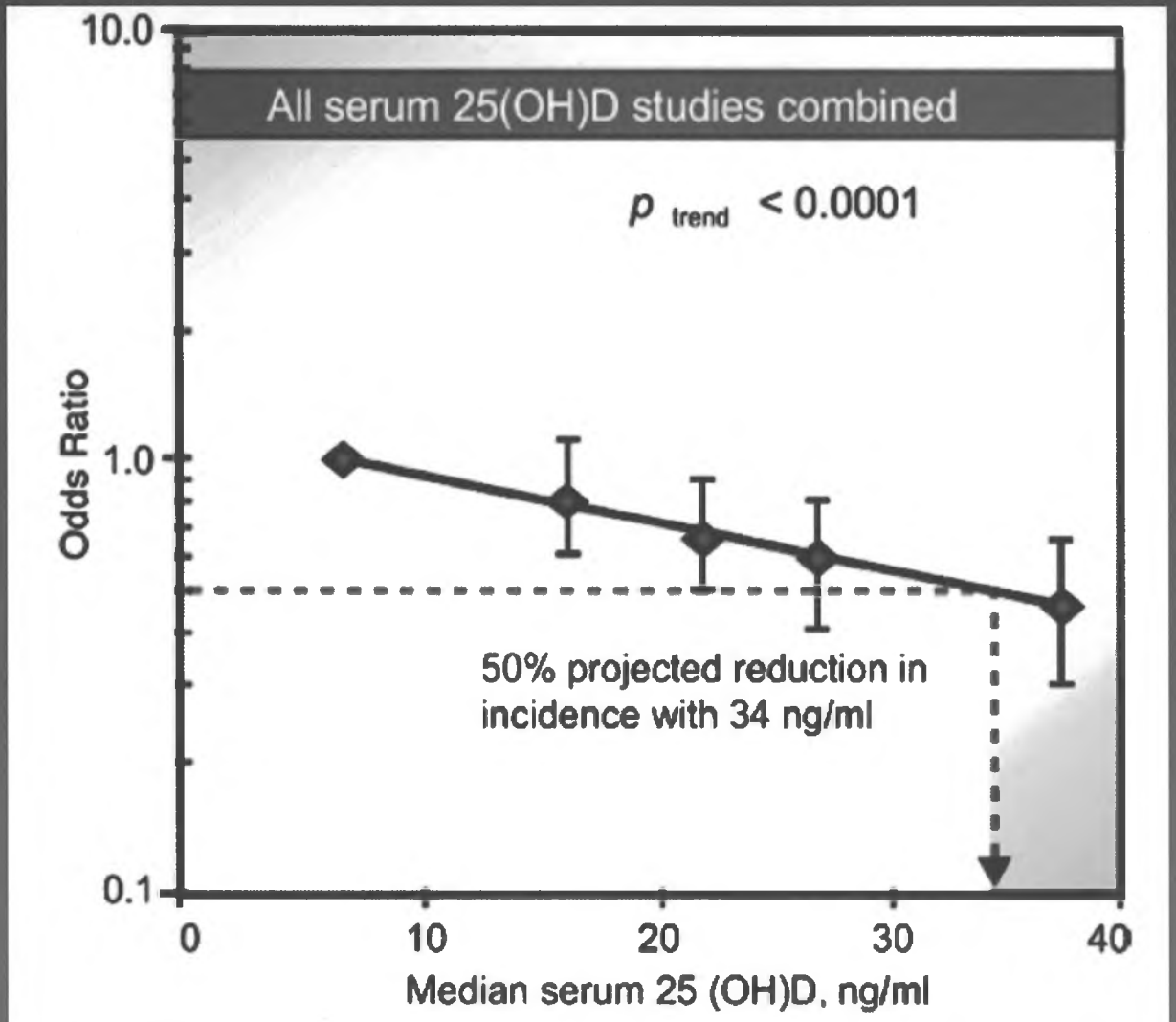
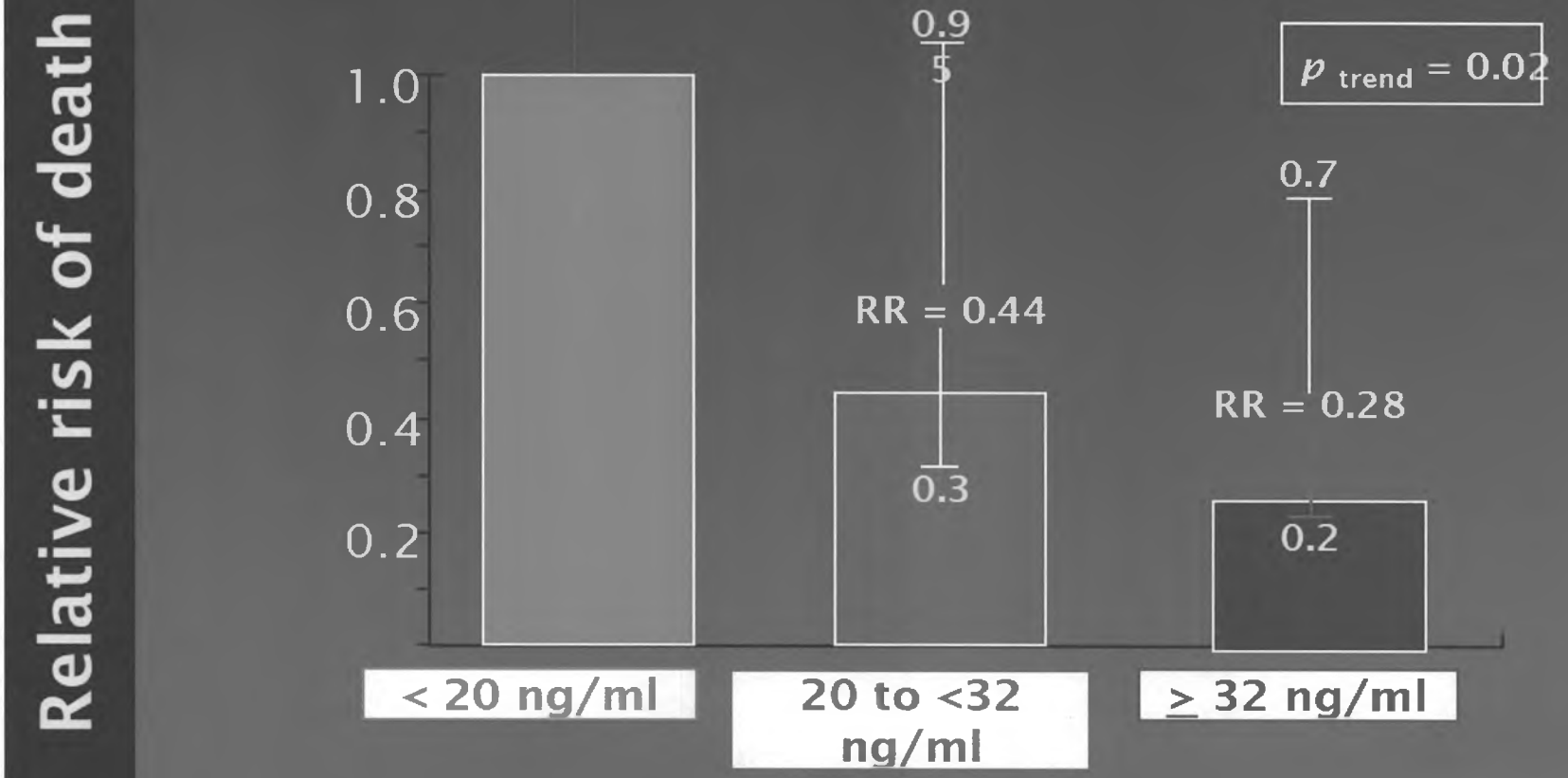


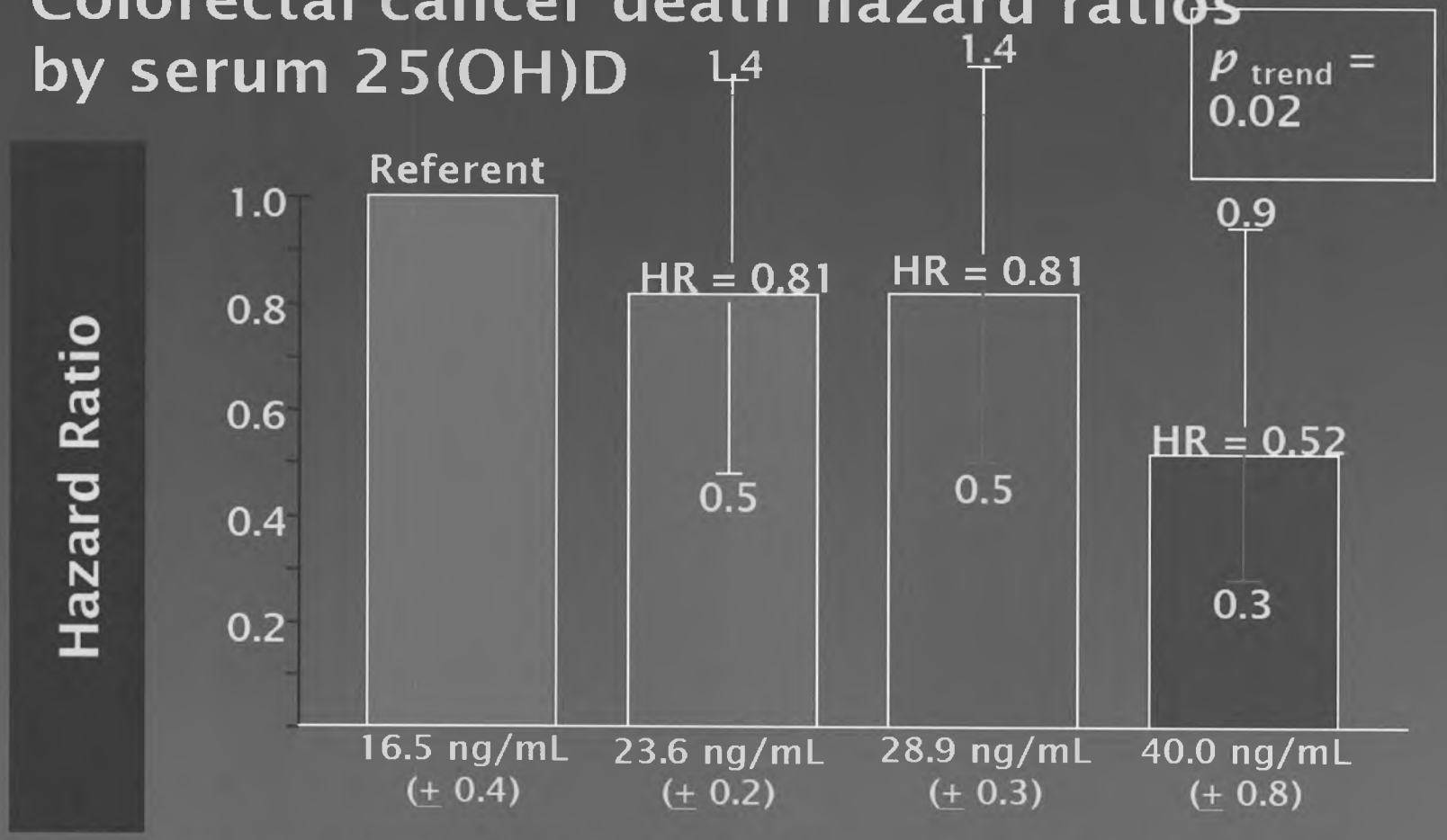
Figure 1. Dose–response gradient for colorectal cancer according to serum 25(OH)D concentration, all five studies combined.[1,4–7] The five points are the odds ratios for each quintile of 25(OH)D based on combined data from the five studies.

Colon cancer mortality risk by prediagnostic serum 25(OH)D in the USA



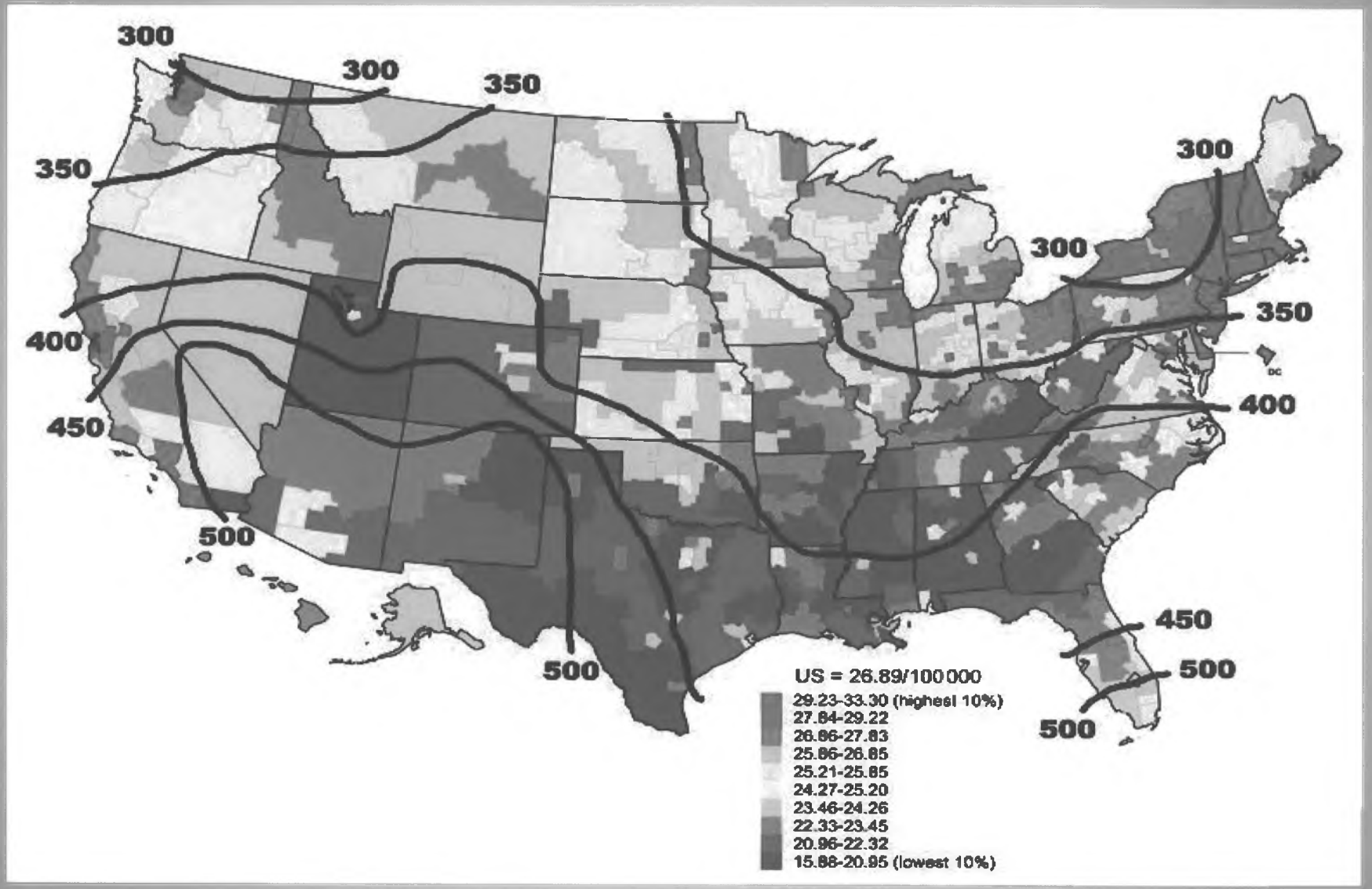
Relative risk of colon cancer mortality, by baseline serum 25-hydroxyvitamin D concentration tertiles, NHANES III cohort, 1988-2000

Colorectal cancer death hazard ratios by serum 25(OH)D

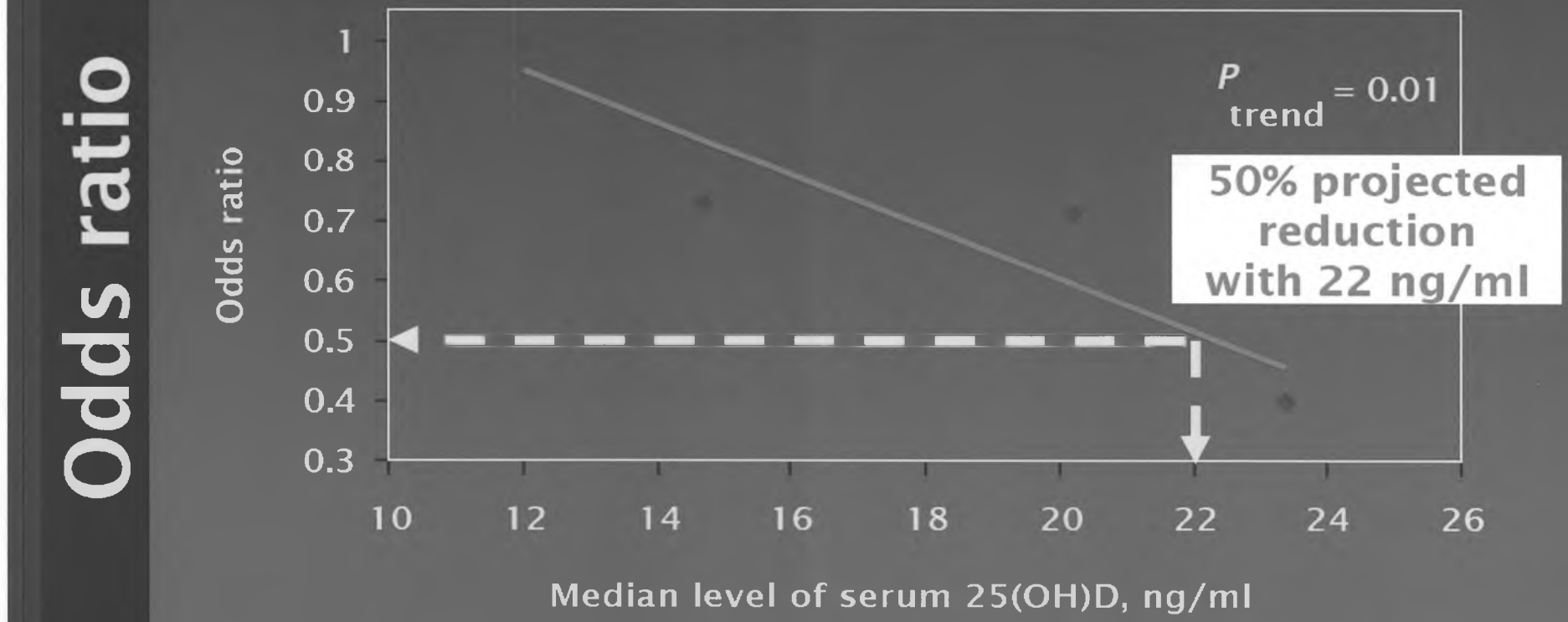


Multivariate-adjusted hazard ratios for death, 304 colorectal cancer patients, by prediagnostic mean plasma 25-hydroxyvitamin D concentration quartiles, Nurses Health and Health Professionals Study Cohorts * 6

Breast cancer mortality in the USA

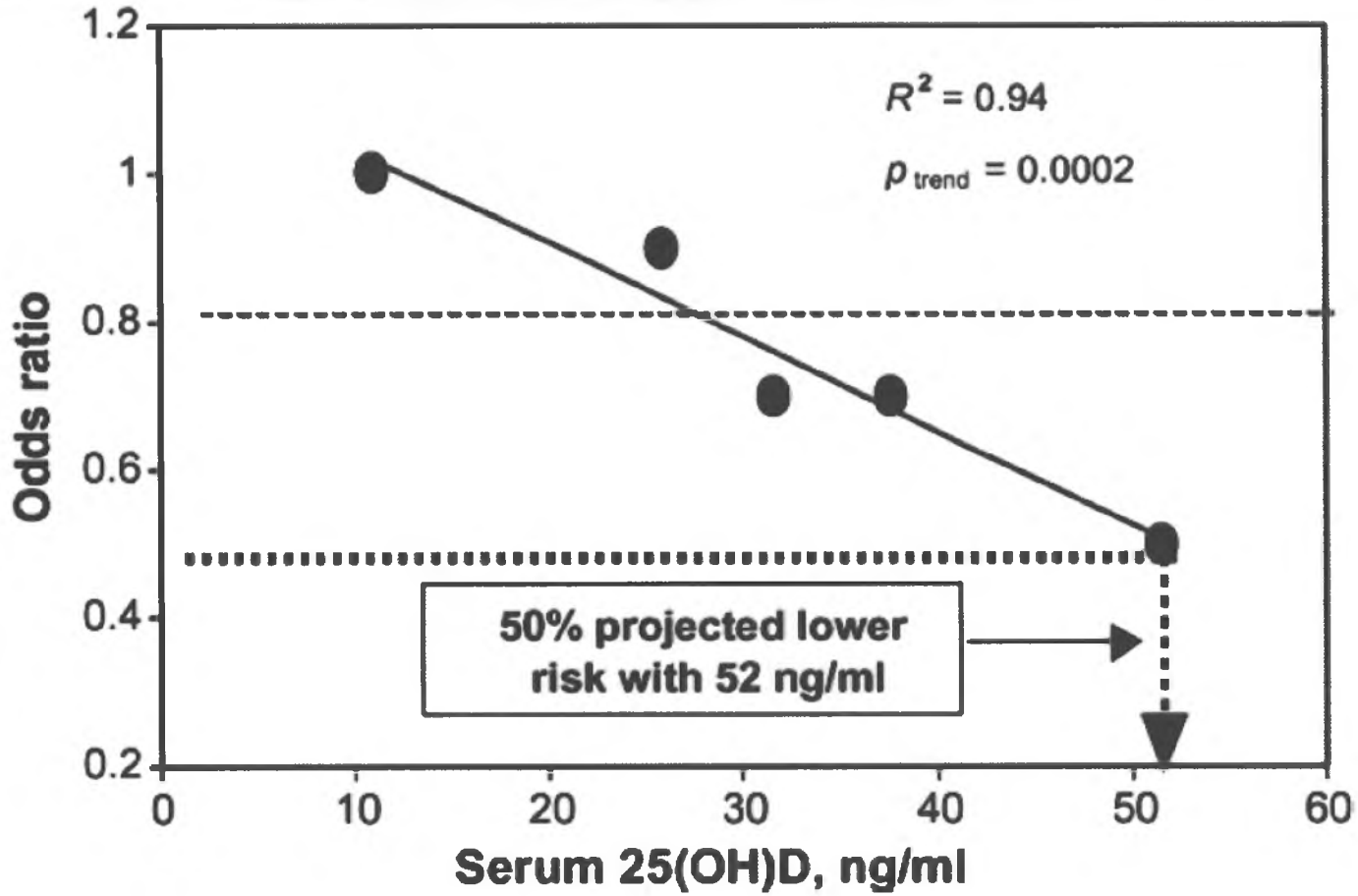


Women's Health Initiative Nested Study (N=295)



*3 Wactawski-Wende

Meta-analysis of breast cancer risk



Dose–response gradient of risk of breast cancer according to serum 25-hydroxyvitamin D concentration, pooled analysis.

Breast cancer risk by 25(OH)D

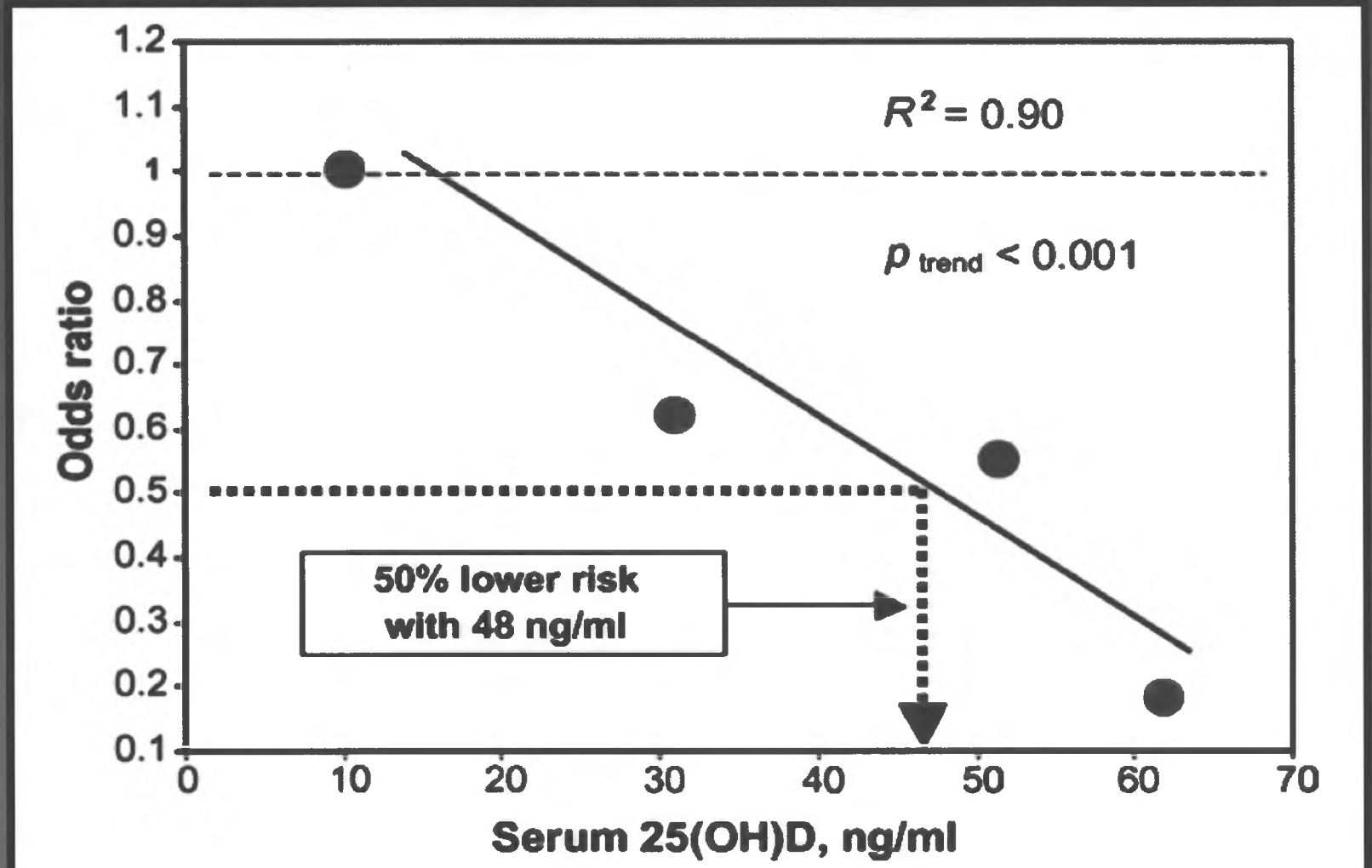
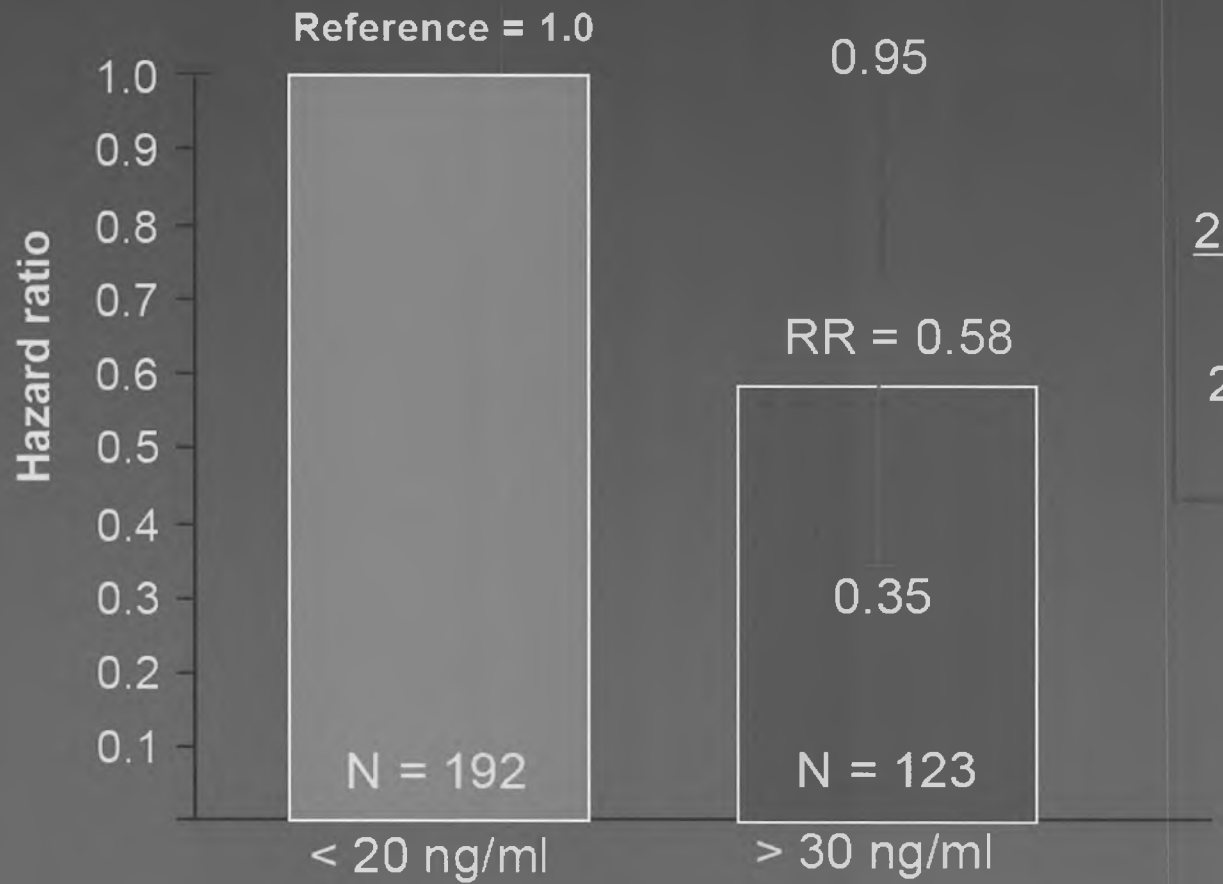


Fig. 2. Dose–response gradient of risk of breast cancer according to serum 25-hydroxyvitamin D concentration, St. George's Hospital, London

Hazard of death, 512 women with breast cancer, by 25(OH)D level at diagnosis, median follow-up 11.6 years, Toronto, Canada



$p = 0.02$

25 (OH)D at dx (ng/ml)

< 20	N= 192
20 - 29.9	N= 197
> 30	N= 123

Hazard ratio and 95% confidence intervals for overall survival by 25(OH)D serum level at diagnosis, Toronto, Canada (latitude 43^0 40 N')

VITAMIN D:

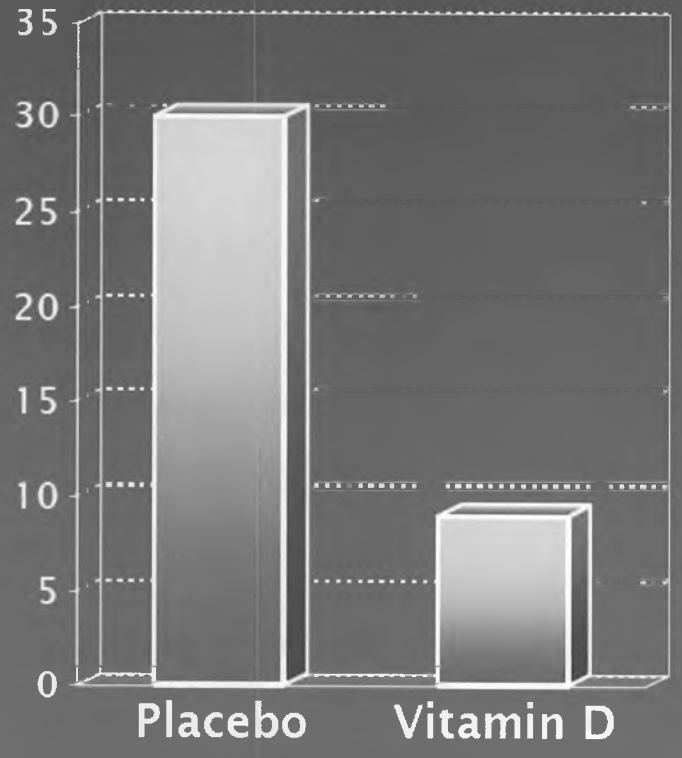
Mechanism of Action
Status of the Evidence

Robert P. Heaney, M.D., F.A.S.N.

Creighton University Osteoporosis Research Center

VITAMIN D & INFLUENZA*

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

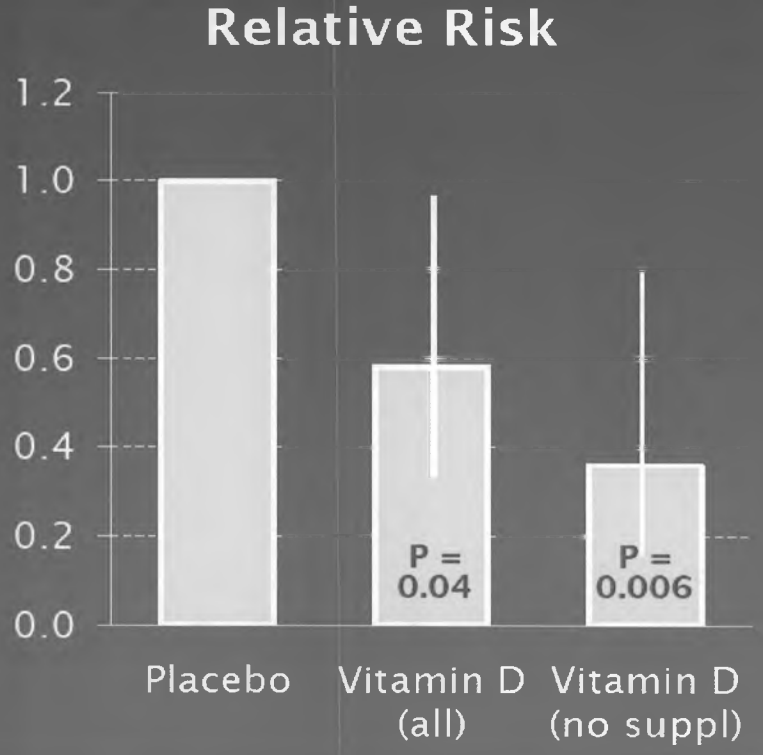


CU ORC

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

VITAMIN D & INFLUENZA*

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

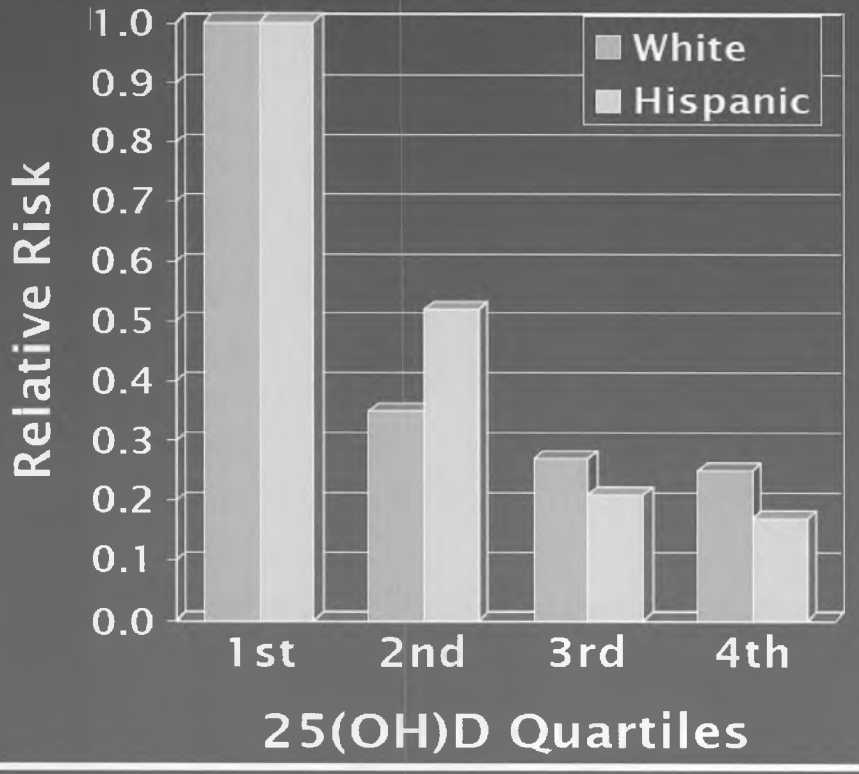


CU ORC

*Urashima et al., AJCN 2010

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)



CU ORC

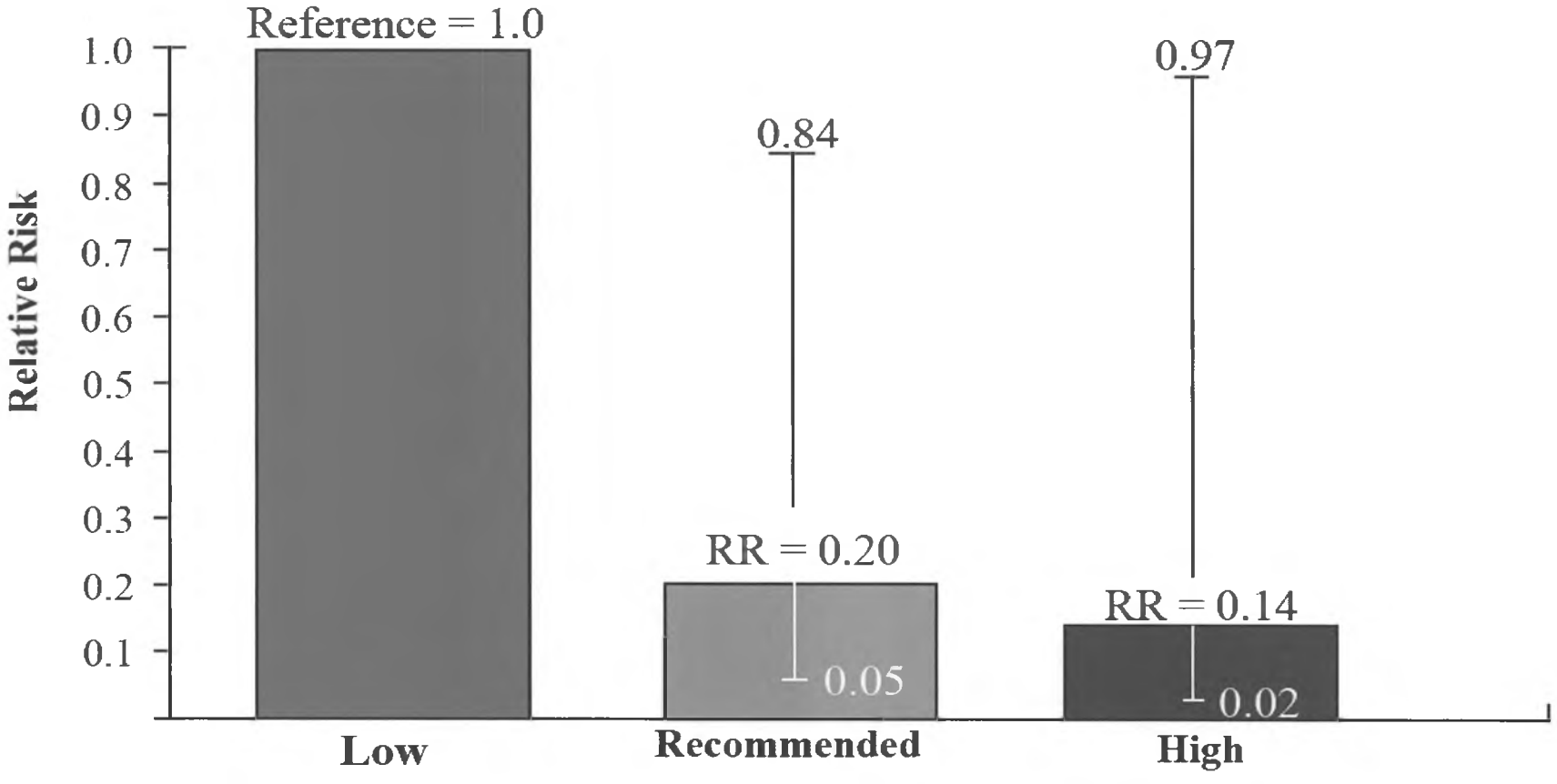
Can Diabetes be Prevented with Vitamin D?

Dr. Frank Garland

Department of Family and Preventive Medicine,
UCSD School of Medicine,
Rebecca and John Moores Cancer Center, and
Technical Director
Naval Health Research Center, San Diego

December 2, 2008

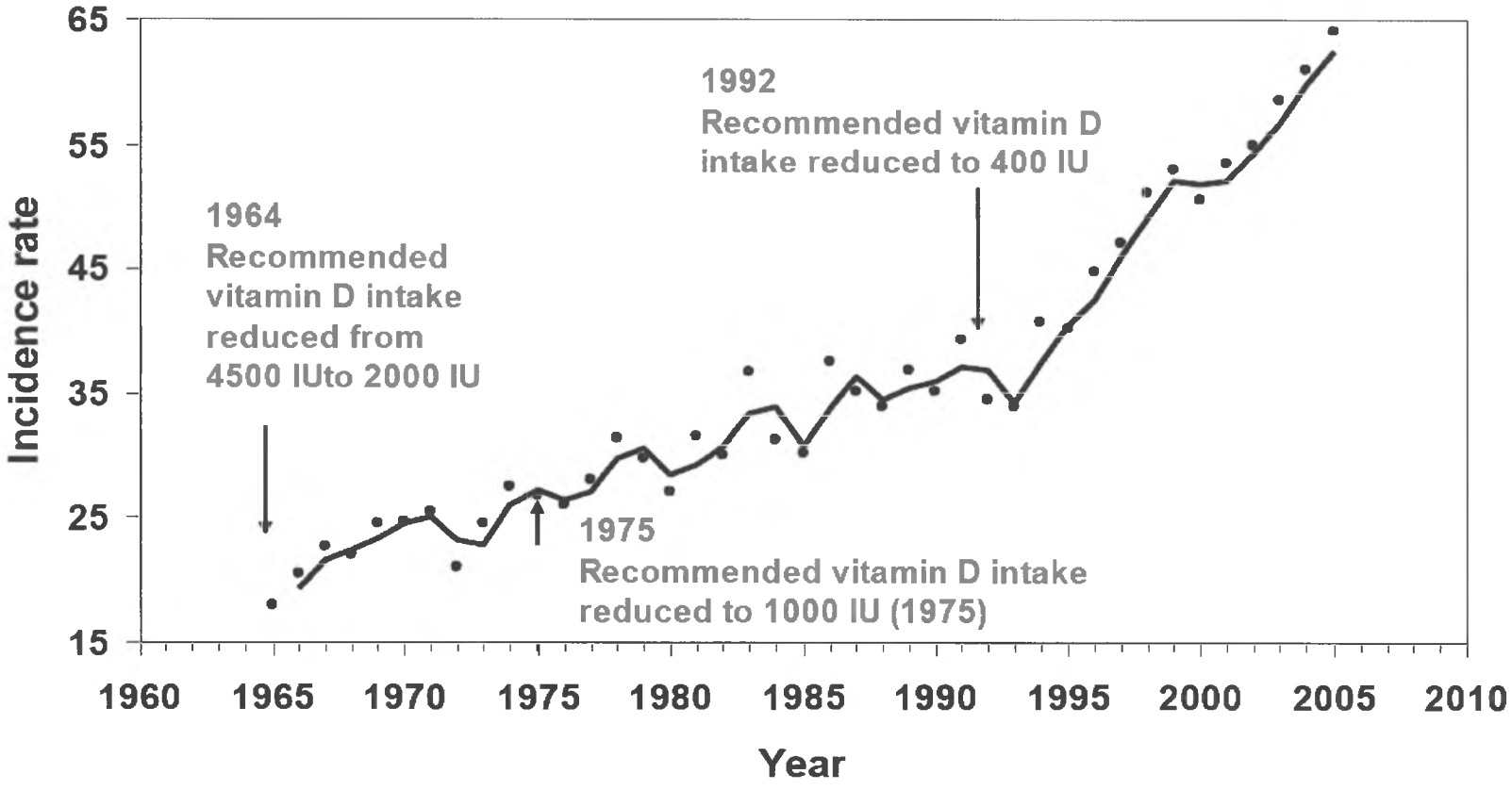
Infants' Vitamin D Supplementation Dose and Incidence of Type I Diabetes in Children in Northern Finland



Relative Risk and 95% confidence intervals for diabetes by vitamin D supplementation dose, Birth Cohort study, N=12,055 pregnant women

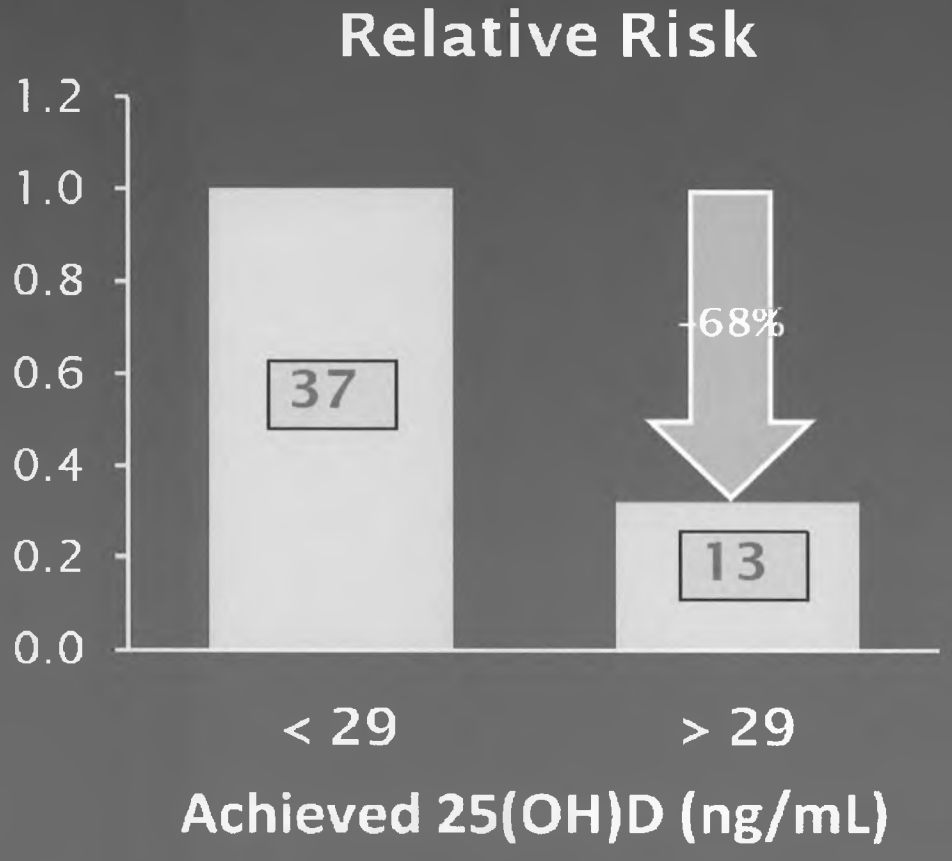
Source: Hyppönen E, Läärä E, Reunanen A, Järvelin MR, Virtanen SM.Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. Lancet. 2001;358:1500-3.

Annual age-adjusted incidence rates of type 1 diabetes, children ≤ 14 years old, per 100,000 population, and dates of changes in recommended daily intake of vitamin D in infants, Finland, 1965-2005



CANCER RISK (ALL)

- N = 1,179
- ages 55-85
- 4 yr RCT
- Vit D ≅ 1100 IU/d
- *median* achieved serum 25(OH)D = 29 ng/mL
- Lappe et al. AJCN 2007



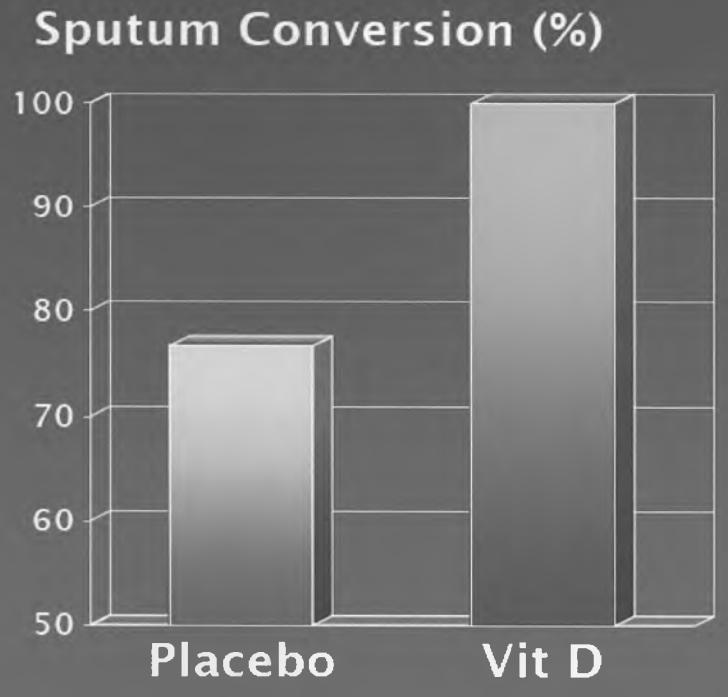
VITAMIN D & TUBERCULOSIS

these experiments show that:

- vit D is an essential mediator in the innate immune response
- serum 25(OH)D is the critical variable
- at least some of the increased sensitivity to infection in vit D-deficiency is due to reduction in response to infectious agents because 25(OH)D is rate-limiting
- the greater tuberculosis susceptibility of blacks is due in part to their low vit D status

VITAMIN D & TUBERCULOSIS*

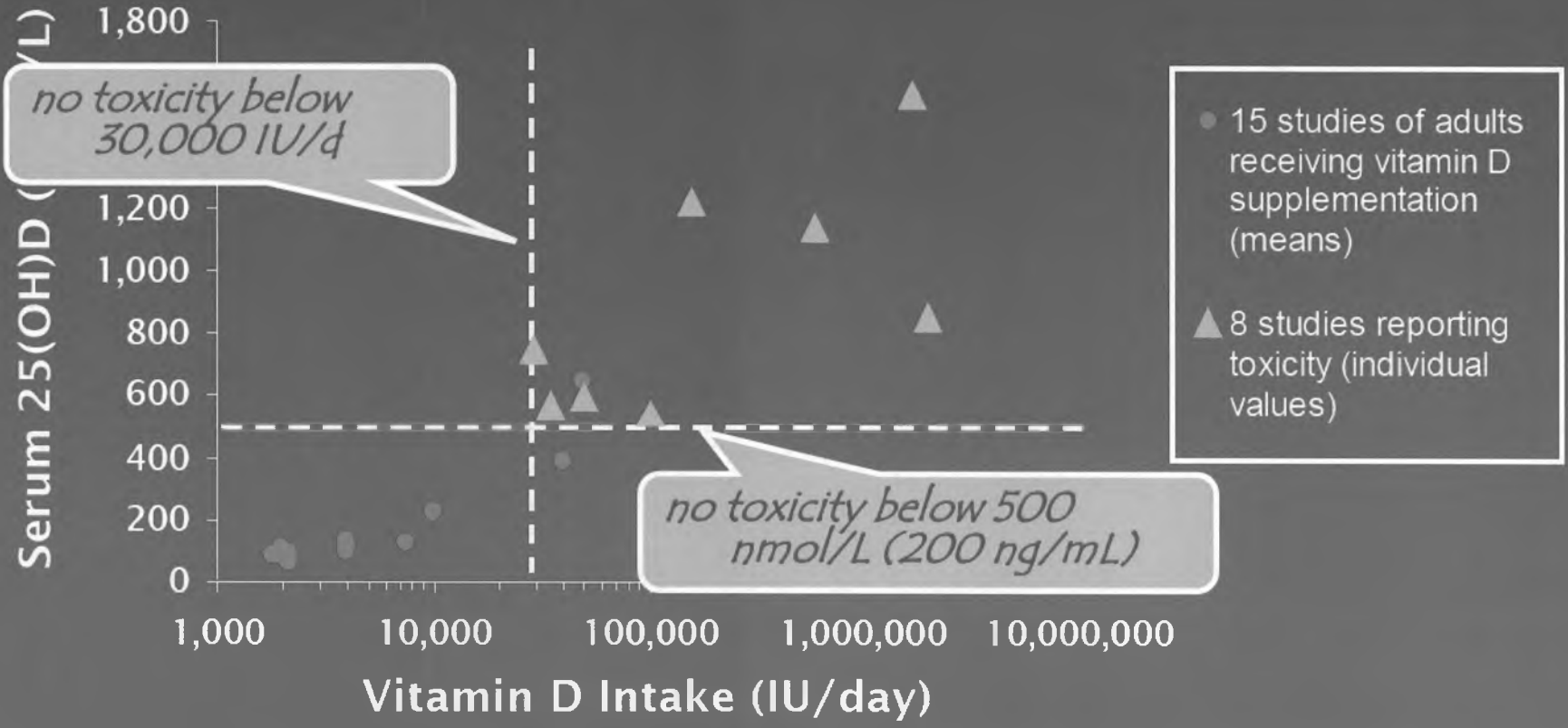
- 67 pts with pulmonary TB
- standard treatment for all
- In addition, randomized to either vit D 10,000 IU/d or placebo
- P = 0.002



CU ORC

*Nursyam et al., Acta Med Indones 2006

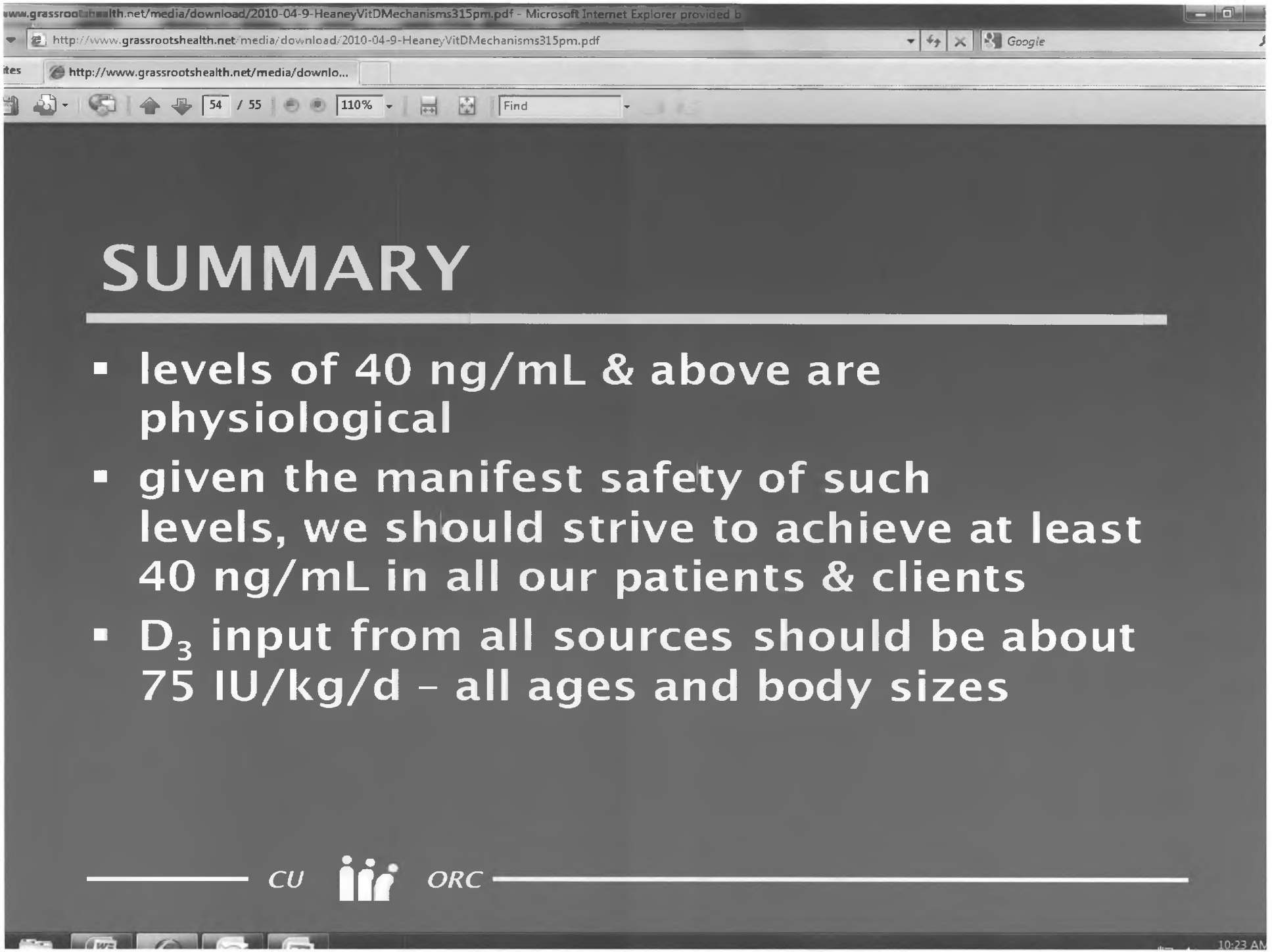
VITAMIN D INTAKE & TOXICITY*



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

SUMMARY

- for several body systems the preponderance of the evidence indicates that ≥32 ng/mL is needed for the full benefits of vitamin D
- observational studies support this conclusion and strengthen the level 1 evidence by insuring the generalizability of the RCTs
- for some endpoints (e.g., cancer) the data suggest that even 32 ng/mL is not high enough (40 – 60 is preferable)


www.grassrootshealth.net/media/download/2010-04-9-HeaneyVitDMechanisms315pm.pdf - Microsoft Internet Explorer provided b
http://www.grassrootshealth.net/media/download/2010-04-9-HeaneyVitDMechanisms315pm.pdf
Google
http://www.grassrootshealth.net/media/downlo...
54 / 55
110%
Find
SUMMARY
levels of 40 ng/mL & above are physiological
given the manifest safety of such levels, we should strive to achieve at least 40 ng/mL in all our patients & clients
D_3 input from all sources should be about 75 IU/kg/d – all ages and body sizes
CU
ORC
10:23 AM

Disease Incidence Prevention by Serum 25(OH)D Level

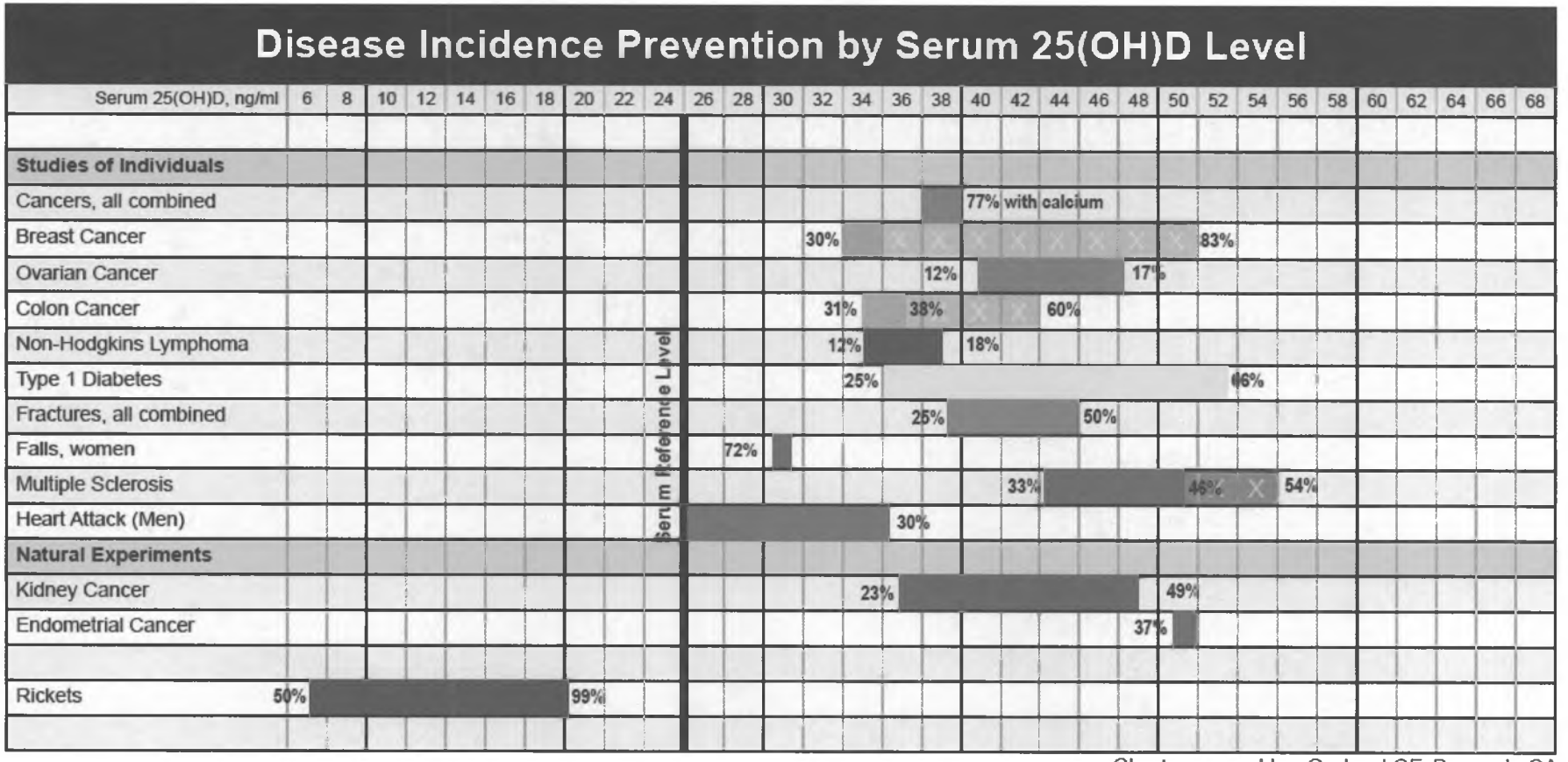
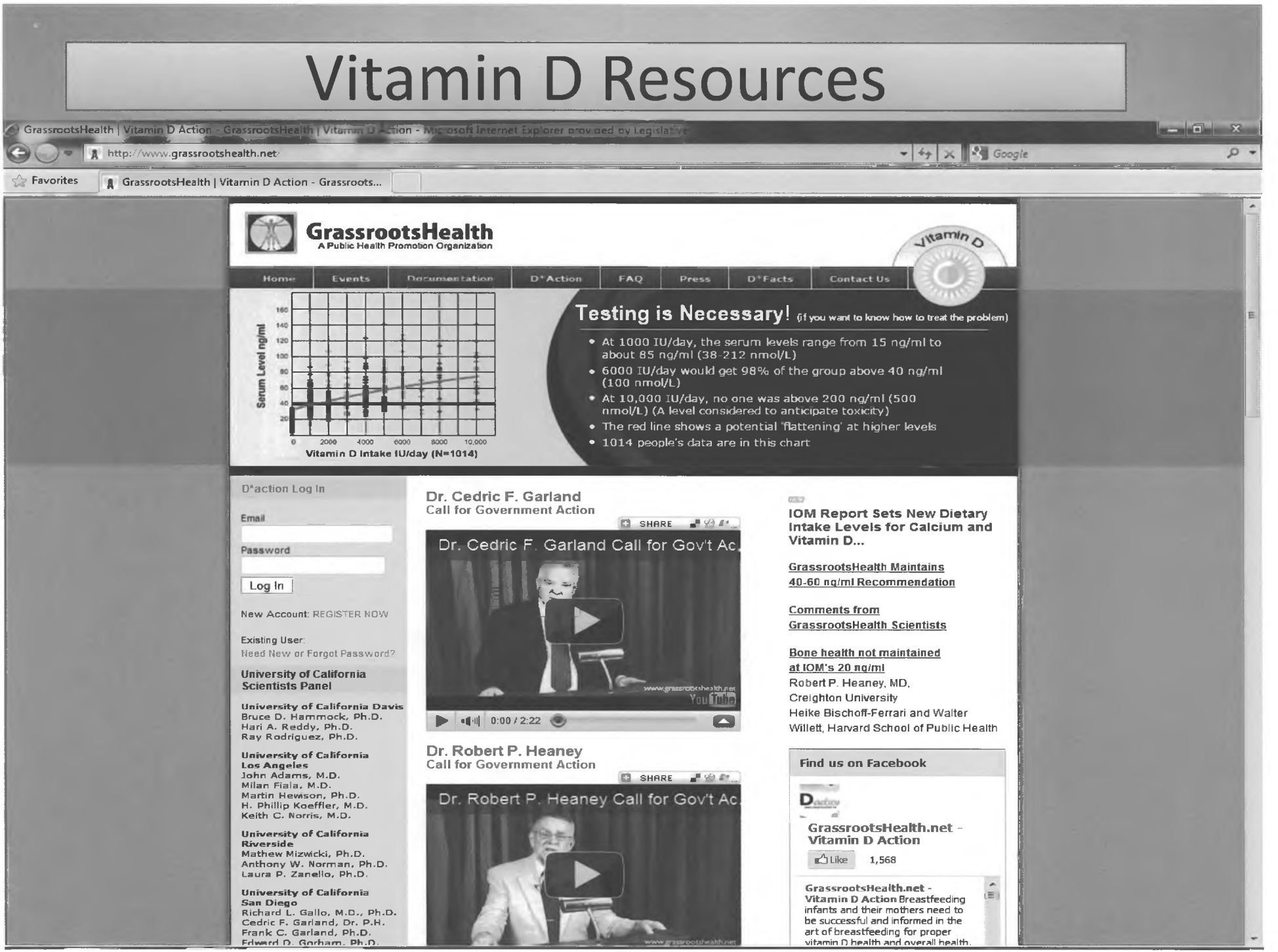


Chart prepared by: Garland CF, Baggerly CA

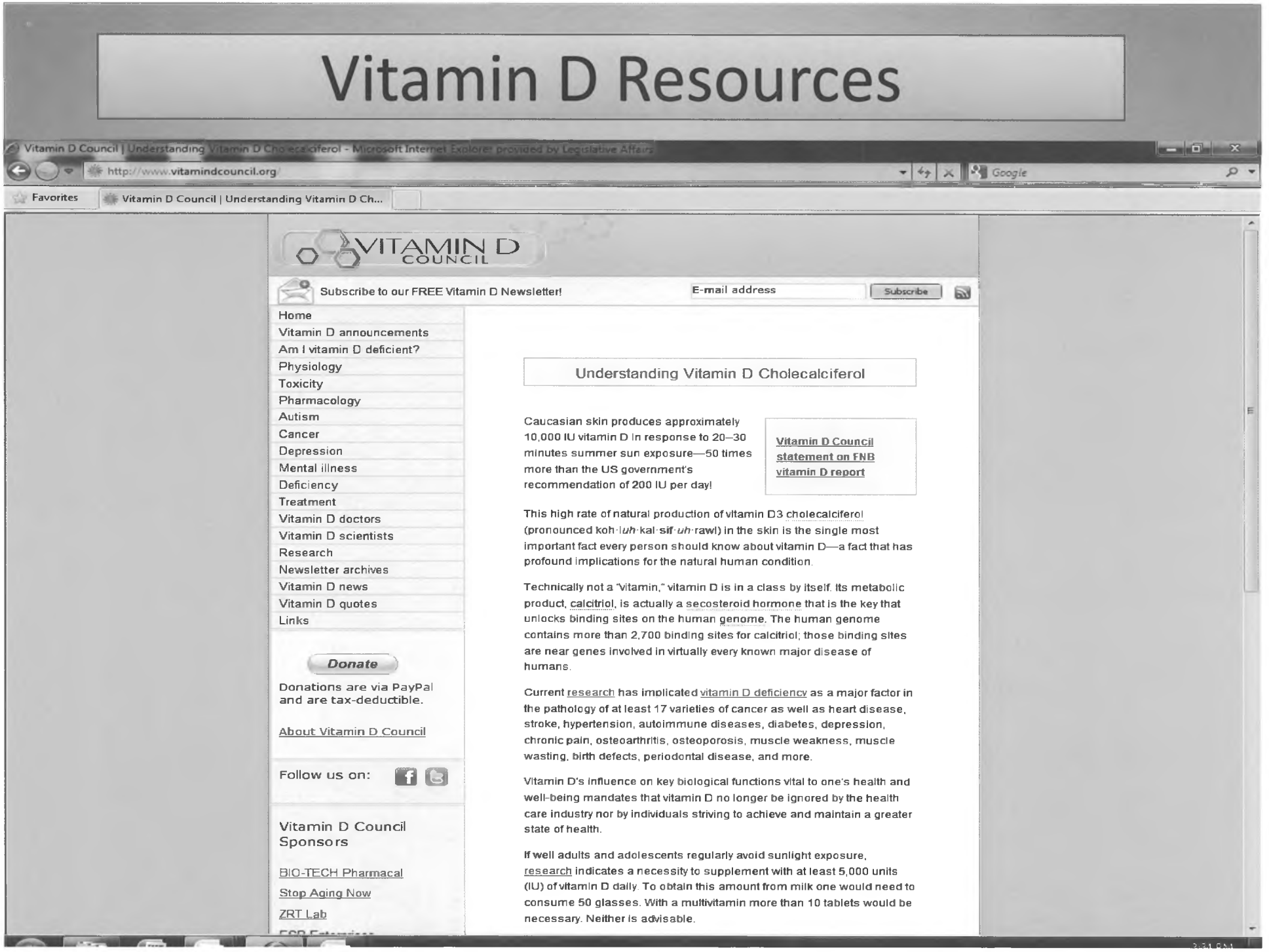
Legend:
All percentages reference a common baseline of 25 ng/ml as shown on the chart.
%'s reflect the disease prevention % at the beginning and ending of available data. Example: Breast cancer incidence is reduced by 30% when the serum level is 34 ng/ml vs the baseline of 25 ng/ml. There is an 83% reduction in incidence when the serum level is 50 ng/ml vs the baseline of 25 ng/ml.
The x's in the bars indicate 'reasonable extrapolations' from the data but are beyond existing data.

References:
All Cancers: Lappe JM, et al. Am J Clin Nutr. 2007;85:1586-91. Breast: Garland CF, Gorham ED, Mohr SB, Grant WB, Garland FC. Breast cancer risk according to serum 25-Hydroxyvitamin D: Meta-analysis of Dose-Response (abstract).American Association for Cancer Research Annual Meeting, 2008. Reference serum 25(OH)D was 5 ng/ml. Garland, CF, et al. Amer Assoc Cancer Research Annual Mtg, April 2008,. Colon: Gorham ED, et al. Am J Prev Med. 2007;32:210-6. Diabetes: Hyppönen E, et al. Lancet 2001;358:1500-3. Endometrium: Mohr SB, et al. Prev Med. 2007;45:323-4. Falls: Broe KE, et al. J Am Geriatr Soc. 2007;55:234-9. Fractures: Bischoff-Ferrari HA, et al. JAMA. 2005;293:2257-64. Heart Attack: Giovannucci et al. Arch Intern Med/Vol 168 (No 11) June 9, 2008. Multiple Sclerosis: Munger KL, et al. JAMA. 2006;296:2832-8. Non-Hodgkin's Lymphoma: Purdue MP, et al. Can Causes Control. 2007;18:989-99. Ovary: Tworoger SS, et al. Cancer Epidemiol Biomarkers Prev. 2007;16:783-8. Renal: Mohr SB, et al. Int J Cancer. 2006;119:2705-9. Rickets: Arnaud S

Vitamin D Resources



Vitamin D Resources



Thank You!

- For further information please contact me at Rep.Paul.Seaton@legis.state.ak.us

  or at 1-800-665-2689

Dr Emily A. Kane ND, LAc
Natural Healthcare
Juneau AK 99801

3-8-11

I strongly support any legislation or resolutions that would promote awareness of, and apply remedies to, Vitamin D deficiency which is rampant in Alaska.

We have become an indoor society. I have been checking Vit D levels routinely in my primary care practice for five years. Not one Alaskan who does not supplement with 3-6,000 IU's daily is replete. The fix is cheap: a year's worth of Vit D_3 drops costs about $20.

Sincerely,

Dr Emily A. Kane

The FNB Has Failed Millions

After 13 year of silence, on Nov. 30, 2010, the quasi-governmental agency the Institute of Medicine's (IOM) Food and Nutrition Board (FNB) recommended that a 3-pound premature infant take virtually the same amount of vitamin D as a 300-pound pregnant woman. While that 400 IU/day dose is close to adequate for infants, 600 IU/day in pregnant women will do nothing to help the three childhood epidemics most closely associated with gestational and early childhood vitamin D deficiencies: asthma, autoimmune disorders, and – as recently reported in the largest pediatric journal in the world – autism. Professor Bruce Hollis of the Medical University of South Carolina has shown that pregnant and lactating women need at least 5000 IU/day, not 600.

The FNB also reported that vitamin D toxicity might occur at an intake of 10,000 IU/day (250 micrograms/day), although it could produce no reproducible evidence that 10,000 IU/day has ever caused toxicity in humans and only one poorly conducted study indicating that 20,000 IU/day may cause mild elevations in serum calcium, but not clinical toxicity.

Viewed with a different measure, this FNB report recommends that an infant should take 10 micrograms/day (400 IU) and a pregnant woman 15 micrograms/day (600 IU). As a single, 30-minute dose of summer sunshine gives adults more than 10,000 IU (250 micrograms), the FNB is apparently also warning that natural vitamin D input – as occurred from the sun before the widespread use of sunscreen – is dangerous. That is, the FNB is implying that God does not know what she is doing.

Disturbingly, this FNB committee focused on bone health, just as it did 14 years ago. It ignored the thousands of studies from the last 10 years that showed higher doses of vitamin D help: heart health, brain health, breast health, prostate health, pancreatic health, muscle health, nerve health, eye health, immune health, colon health, liver health, mood health, skin health, and especially fetal health. Tens of millions of pregnant women and their breast-feeding infants are severely vitamin-D deficient, resulting in a great increase in the medieval disease rickets. The FNB report seems to reason that if so many pregnant women have low vitamin D blood levels then it must be OK because such low levels are so common. However, such circular logic simply represents the caveman existence (never exposed to the light of the sun) of most modern-day pregnant women.

Hence, if you want to optimize your vitamin D levels – not just optimize the bone effect – supplementing is crucial. But it is almost impossible to significantly raise your vitamin D levels when supplementing at only 600 IU/day (15 micrograms). Pregnant women taking 400 IU/day have the same blood levels as pregnant women not taking vitamin D; that is, 400 IU is a meaninglessly small dose for pregnant women. Even taking 2000 IU/day of vitamin D will only increase the vitamin D levels of most pregnant women by about 10 points, depending mainly on their weight. Professor Bruce Hollis has shown that 2000 IU/day does not raise vitamin D to healthy or natural levels in either pregnant or lactating women. Therefore supplementing with higher amounts – like 5000 IU/day – is crucial for the woman who wants her fetus to enjoy optimal vitamin D levels, and the future health benefits that go along with it.

For example, taking only two of the hundreds of recently published studies: Professor Urashima and colleagues in Japan gave 1200 IU/day of vitamin D3 for six months to Japanese 10-year-olds in a randomized controlled trial. They found that vitamin D dramatically reduced the incidence of influenza A as well as the episodes of asthma attacks in the treated kids, while the placebo group was not so fortunate. If Dr. Urashima had followed the newest FNB recommendations, it is unlikely that 400 IU/day treatment arm would have done much of anything and some of the treated young teenagers may have come to serious harm without the vitamin D. Likewise, a randomized controlled prevention trial of adults by Professor Joan Lappe and colleagues at Creighton University, which showed dramatic improvements in the health of internal organs, used more than twice the FNB's new adult recommendations.

Finally, the FNB committee consulted with 14 vitamin D experts and – after reading these 14 different reports – decided to suppress them. Many of these 14 consultants are either famous vitamin D researchers, like Professor Robert Heaney at Creighton or, as in the case of Professor Walter Willett at Harvard, the single best-known nutritionist in the world. So, the FNB will not tell us what Professors Heaney and Willett thought of its new report? Why not?

Today, the Vitamin D Council directed our attorney to file a federal Freedom of Information (FOI) request to the IOM's FNB for the release of these 14 reports.

Most of my friends, hundreds of patients, and thousands of readers of the Vitamin D Council newsletter (not to mention myself) have been taking 5000 IU/day for up to eight years. Not only have they reported no significant side effects, indeed, they have reported greatly improved health in multiple organ systems. My advice, especially for pregnant women: continue taking 5000 IU/day until your 25(OH)D is between 50 and 80 ng/mL (the vitamin D blood levels obtained by humans who live and work in the sun and the midpoint of the current reference ranges at all American laboratories). Gestational vitamin D deficiency is associated not only with rickets, but a significantly increased risk of neonatal pneumonia, a doubled risk for preeclampsia, a tripled risk for gestational diabetes, and a quadrupled risk for primary cesarean section.

The FNB has failed millions of pregnant women whose as-yet unborn babies will pay the price. Let us hope that the FNB will comply with the spirit of "transparency" by quickly responding to our Freedom of Information requests.

John Cannell, MD
Vitamin D Council
1241 Johnson Avenue, #134
San Luis Obispo, California 93401

◆

February 7, 2011

Sharon L. Norton, RN
Suicide Prevention Council Member
PMHNP Graduate Student
61025 Ohlson Mountain Road
Homer, AK 99603

Representative Paul Seaton
345 W. Sterling Hwy. Suite 102B
Homer, Alaska 99603

RE: Preventative Health - Vitamin D Resolution

I appreciate your efforts and agree that research links Vitamin D deficiency and insufficiency to depression, bone disorders, cancer, immune disease, diabetes, and coronary disease, at the very least. Therefore, I support your resolution.

Perhaps, an addendum to your resolution might address a list of micronutrients including Vitamins and Minerals be drawn annually by all primary healthcare providers and with all initial mental health assessments. I would suggest expanding, at the very least, to include Niacin, B12, folate (folic acid), thiamine, Vitamin D and trace minerals including iron, magnesium, and selenium. Scientific evidence links a variety of psychiatric symptoms with deficiency and insufficiency as components to psychiatric syndromes.

I receive healthcare through Indian Health Services and have had few of these labs drawn to my knowledge as late as age 60. My Father is 83, a diabetic, with hypertension, hyperlipidemia, skin cancer, and situational depression who receives services through the VA. The labs listed below were not drawn, any time recently that I am aware of, *until* I made a request of a local practitioner October of 2010. Which found the labs to be: Vitamin D 25 OH Total level of 21, optimum levels range from 30-100 with <20 deficient and 20-30 insufficient, B12 was 127, low was indicated at 180 and high 914, and his Iron was 23, low indicated at 45 and high 182. I plan to request a recheck at his next VA visit this month. His diet has improved and he has been taking supplements I would like to evaluate any improvement or lack thereof. Additionally, I am awaiting my own lab results as we speak.

A large majority of Alaska's citizens would not know to request these labs. It is, therefore, up to the State of Alaska to protect the physical & mental

health and wellbeing of Alaska's people, of all ages. We seek as healthcare professionals and legislative representative's to address the prevention of medical and mental illness; not only personal and family short and long term impact, but as our obligation to address and curb the economic impact on Alaska as a whole.

Additionally, I would support, as an indication of need, an Alaskan research study to evaluate levels of vitamins and minerals, using a very large sample group of both rural and urban Alaskans (not less than 20,000), with a variety of ages, listing medical and psychiatric diagnoses, and comparing regions, those consuming the traditional Native diet compared to Western diet, and those taking supplements with those not. *Including,* those individuals of all ages having threatened and attempted suicide. In order to discover whether levels may or may not suggest a relationship to depression and other psychiatric symptoms potentially contributing to suicide. With a follow-up study evaluating diet changes and vitamin and mineral supplements provided over time.

I appreciate your addressing the preventative health of Alaskans.

With Kindest Regards,

Sharon Norton

Sharon Norton, RN

[Reference links attached.]

References links that support my response [sorry I did not have time to format them correctly].

Page 844 http://books.google.com/books?id=u-ohbTtxCeYC&pg=PA844&lpg=PA844&dq=vitamin+deficiency+and+depression+scientific+evidence&source=bl&ots=9fBDwji4xU&sig=Q8Su0TNEtpPOa3s6WUahWQmyj0Q&hl=en&ei=vFFOTYbeA42isQPL6onCg&sa=X&oi=book_result&ct=result&resnum=10&ved=0CGAQ6AEwCQ#v=onepage&q=vitamin%20deficiency%20and%20depression%20scientific%20evidence&f=true

Mayoclinic http://www.mayoclinic.com/health/vitamin-d/NS_patient-vitamind/DSECTION=evidence suggests among many other diagnoses that:
Seasonal affective disorder (SAD) is a form of depression that occurs during the winter months, possibly due to reduced exposure to sunlight. In one study, vitamin D was found to be better than light therapy in the treatment of SAD. Further studies are necessary to confirm these findings.

NYU Medical Center http://www.med.nyu.edu/content?ChunkIID=21566 Other micronutrients are also commonly deficient in elderly populations. A small study among nursing home residents found that low levels of the mineral selenium was associated with depression. Moreover, 8 weeks of mineral supplementation tended to improve the mood of the most seriously depressed patients with low selenium levels.

Science Direct: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WN2-4C0D0FP-YT&_user=10&_coverDate=02/28/1991&_rdoc=1&_fmt=high&_orig=search&_origin=search&_sort=d&_docanchor=&view=c&_searchStrId=1633643654&

Lance Armstrong Foundation: http://www.livestrong.com/article/309794-what-vitamin-mineral-deficiencies-cause-anxiety/

National Institute of Health: Vitamin D in fibromyalgia depression and anxiety
http://www.ncbi.nlm.nih.gov/pubmed/16850115

National Institute of Health: Vitamin D in over weight and obese:
http://www.ncbi.nlm.nih.gov/pubmed/18793245

National Institute of Health: Vitamin D and Women with Depression in the Winter
http://www.ncbi.nlm.nih.gov/pubmed/19616172

National Institute of Health: Vitamin D and Depression in Japanese
http://www.ncbi.nlm.nih.gov/pubmed/19690578

National Institute of Health: Vitamin D and Depression in Young Adults
http://www.ncbi.nlm.nih.gov/pubmed/21067618

Crystal Rogers

From: Rep. Paul Seaton
Sent: Tuesday, February 15, 2011 9:19 AM
To: Crystal Rogers
Subject: FW: thanks for HCR 5

From: Joy Lyon [mailto:jlyon@aeyc-sea.org]
Sent: Monday, February 14, 2011 6:21 PM
To: Rep. Paul Seaton
Subject: thanks for HCR 5

Dear Representative Seaton,

I just read the resolution on promotion of Vitamin D in Alaska, and I would like to personally thank you for your leadership in this area.
I told a group of pediatricians at a meeting today, and we are all so pleased that this important health issue is getting attention thanks to your resolution.
This is an example of a low or no-cost health care solution.

Thanks again, and if testimony on this is needed please let me know and I will be happy to help get the word out.

Joy Lyon, M.A.
Executive Director
AEYC Southeast Alaska
Main 907.789-1235 or 888-785-1235
Fax 907.789-1238
jlyon@aeyc-sea.org
www.aeyc-sea.org

www.threadalaska.org
connecting early care and education to Alaska

Crystal Rogers

From: Carole Baggerly [carole@grassrootshealth.org]
Sent: Wednesday, March 09, 2011 7:49 PM
To: Crystal Rogers
Cc: Heaney, Robert
Subject: Re: FW: Response to HCR 5--colon cancer + my comments

3/9/11
Crystal:
Re the colon cancer:
the Disease Incidence Chart has a Legend which states:
1. All percentages reference a common baseline of 25 ng/ml as shown on the chart
2. the x's in the bars indicate 'reasonable extrapolations' from the data but are beyond existing data.

On #1, the colon cancer item shows a 31% reduction *from 25 ng/ml* (not 50% from 12 ng/ml as in the paper). The reference point was changed to 25 ng/ml thus the % changed. There was a COMMON reference point of 25 ng/ml created so that all the papers could be compared to the same starting point.. all % are from 25 ng/ml.

#2, there are x's in the extension of the colon cancer line which represent what Dr. Garland considered a reasonable extrapolation of the the data to 42 ng/ml. At 42 ng/ml, there would be a 60% reduction in incidence compared with the baseline of 25 ng/ml.

I do not consider this erroneous or an omission but a different way of looking at the data.

Re the AADA letter, a few more of my own comments:
1. good to include the populations studied as noted in their pgh 1 on page 2
2. 'there are multiple studies that have suggested an inverse association between vitamin D intake and cancer.. etc....'
I would state that there are some very ambiguously analyzed data/methodologies that leave the conclusions open--certainly there is a need for more studies, but there are no well designed studies that I know of that show any negative associations with higher serum levels and cancer.
3. last page, agree that public AND physicians need to be educated about vitamin D... However, to encourage the individuals to consult with the physicians when the physicians are clearly also in need of education is a problem. (that is why we have developed the set of courses/videos that we have).

It is impressive that you have gotten their attention!!!! Congratulations. You're still on very solid ground.

Carole

Crystal Rogers wrote:
Hey Carole,

We just received a letter of opposition the day before the vitamin D hearing. Please let me know if you have any thoughts on this letter.

Is there anything written by Dr. Heaney about his Institute of Medicine's recommendations and what they did not take into consideration when creating their recommendations? The attached AAD letter says the IOM "released an exhaustive review of scientific literature," but was it Dr. Heaney's presentation, or your presentation that shows why the IOM was flawed in their review? I would be great to have this for the hearing tomorrow, which is 3:00--5:00 pm Alaska time.

Also, I am looking at the AAD's reference to the colorectal cancer; the chart prepared by you and Cedric Garland shows a 60% reduction in colorectal cancer with 42ng/ml, while the AAD's letter says is supposed to be a 50% reduction with 33ng/ml. I looked at the article abstract I found, and it appears the AAD's numbers match the article, but I honestly do not know if I am reading the article correctly.

For the article about Japanese school children, I don't understand the discrepancies between the AAD's letter and the Resolution's whereas statement.

Anything you have to add would be very helpful, especially if it will help clarify the IOM's recommendation due to what the vitamin D researchers are saying.

Thank you,

Crystal A. Rogers
Legislative Intern
Office of Representative Paul Seaton
Alaska State Legislature
(907) 465-6256

-----Original Message-----
From: Rep. Paul Seaton
Sent: Wednesday, March 09, 2011 4:44 PM
To: Crystal Rogers
Subject: FW: Response to HCR 5
Importance: High

-----Original Message-----
From: Kathryn Chandra [mailto:KChandra@aad.org]
Sent: Wednesday, March 09, 2011 2:18 PM
To: Rep. Wes Keller; Rep. Alan Dick; Rep. Bob Herron; Rep. Paul Seaton; Rep. Sharon Cissna; Rep. Bob Miller; Rep. Charisse Millett
Cc: jjordan@asmadocs.org
Subject: Response to HCR 5
Importance: High

Dear Representative Keller and Members of the House Health & Social Services Committee,

On behalf of the American Academy of Dermatology Association(AADA), attached is a letter which outlines several concerns with HCR 5. HCR 5 misrepresents several findings of the cited scientific literature, and as such endangers the health of Alaska's citizens by overemphasizing the role of vitamin D in disease prevention. The AADA would not want HCR 5 to be used as grounds to legitimize use of indoor tanning beds as a means for increasing vitamin D levels. We urge the committee to further review the scientific literature regarding vitamin D, and disease prevention before moving forward with a supplementation program aimed at specific, vulnerable segments of the population. Moreover, it is critical that the public be appropriately educated about vitamin D and be encouraged to consult their physician before taking any vitamin supplements.

Thank you for the opportunity to provide written comments to the Committee in advance of the hearing on HCR 5 on Thursday, March 10, 2011.

Sincerely,

Kathryn Guccione Chandra, MA
Assistant Director, State Policy
American Academy of Dermatology Association
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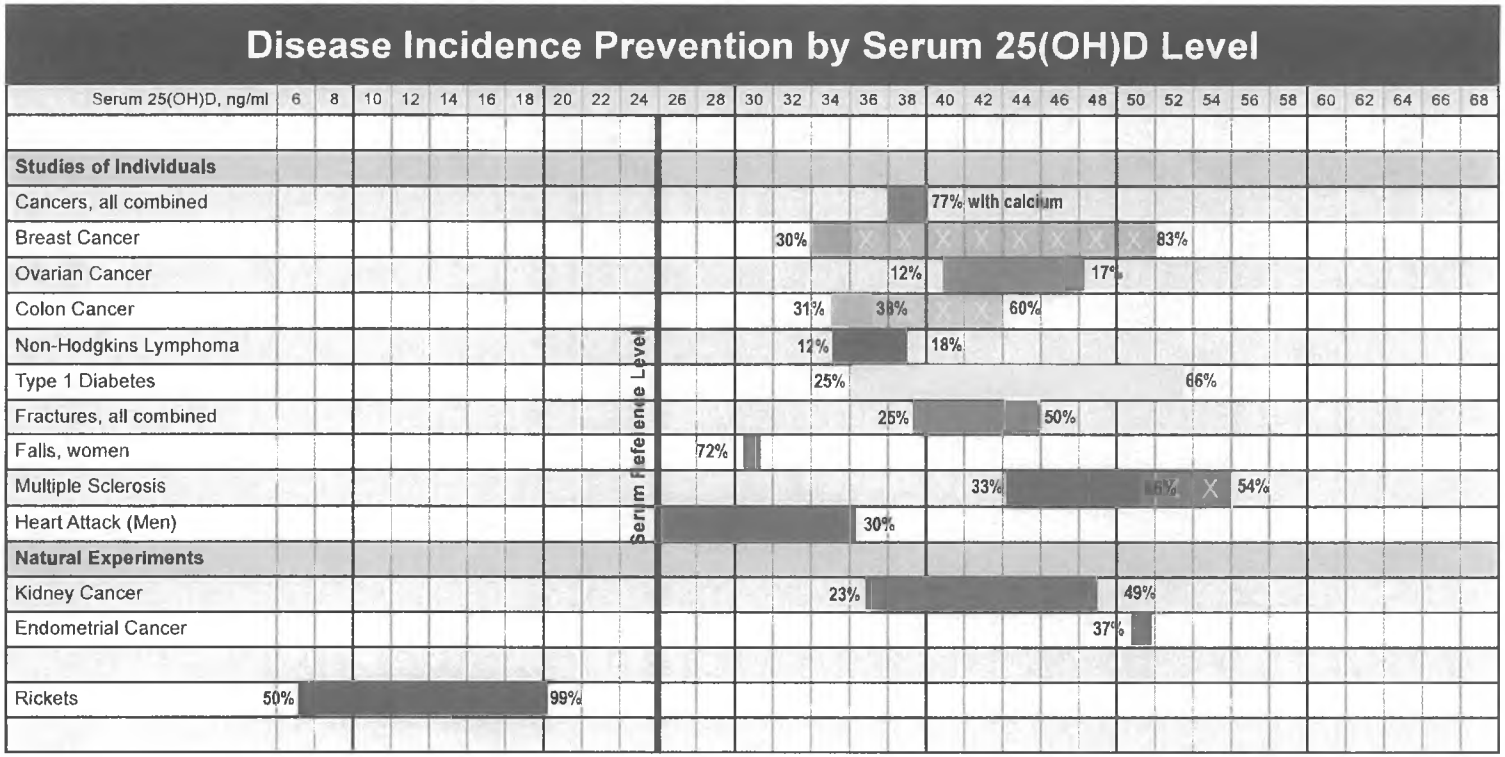

Chart prepared by: Garland CF, Baggerly CA

Legend:
All percentages reference a common baseline of 25 ng/ml as shown on the chart.
%'s reflect the disease prevention % at the beginning and ending of available data. Example: Breast cancer incidence is reduced by 30% when the serum level is 34 ng/ml vs the baseline of 25 ng/ml. There is an 83% reduction in incidence when the serum level is 50 ng/ml vs the baseline of 25 ng/ml.
The x's in the bars indicate 'reasonable extrapolations' from the data but are beyond existing data.

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Crystal Rogers

From: Pekula, Joyce M. [JOYCEPEKULA@creighton.edu]
Sent: Thursday, March 10, 2011 5:52 AM
To: Crystal Rogers
Cc: carole@grassrootshealth.org
Subject: IOM report
Attachments: JBMR RPH_MFH 2011.pdf; The IOM Report on Vitamin D Misleads eLetter Mar 4 2011.docx; Endocr Prac Holick_IOM_2011.pdf; Critical responses IOM report Feb 2011_Grant.docx

Crystal:

Dr. Heaney is traveling, and he asked me to get you this information.

The Academy of Dermatology has a position against tanning booths because of skin damage. So they oppose any effort which points out that we need more vitamin D than we are now getting, since they see that as an opening that would be exploited by the tanning industry. We take no position with respect to tanning and do not want to be caught in that crossfire. But we do insist that almost everybody needs more vitamin D than they are currently getting. And, incidentally, we note that getting your vitamin D through tanning is the expensive way.

I am attaching, at Dr. Heaney's instruction, four documents that may be helpful. First is his brief rebuttal of the IOM report in the Journal of Bone and Mineral Research; second is a necessarily even briefer rebuttal in the Journal of Clinical Endocrinology & Metabolism, in response to the official Journal publication in that same outlet; third is a rebuttal by Dr. Michael Holick published in Endocrine Practice which goes into much more detail about nonskeletal endpoints; and finally is a partial list of such rebuttals compiled by Dr. William Grant. You cannot get all of these, of course, by the time of the hearing. The list should help representative Seaton confirm that there is a lot of opposition to the IOM report, coming from a broad base of support within the vitamin D investigative community.

Regards,

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PERSPECTIVE

JBMR

Why the IOM Recommendations for Vitamin D Are Deficient

Robert P Heaney[1] and Michael F Holick[2]

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[2]Department of Medicine, Division of Endocrinology, Boston University Medical Center, Boston, MA, USA

ABSTRACT

The IOM recommendations for vitamin D fail in a major way on logic, on science, and on effective public health guidance. Moreover, by failing to use a physiological referent, the IOM approach constitutes precisely the wrong model for development of nutritional policy.

KEY WORDS: VITAMIN D; NUTRITIONAL POLICY; EVOLUTIONARY PHYSIOLOGY

Introduction

In the past two years, vitamin D supplement sales to consumers have increased by more than 100% per year.[1] Now, following publication of the report[2] on Dietary Reference Intakes (DRIs) for calcium and vitamin D by the Institute of Medicine (IOM), many physicians report that they are decreasing their vitamin D recommendations to patients. This change was explicitly proposed by members of the IOM panel in their various media statements. While a small fraction of consumers may well have all the vitamin D they need, on balance, we consider a general downward trend to be harmful to the health of the public.

Both the authors of this Perspective served as members of the panel that drafted the 1997 report of the IOM on the DRIs for calcium and vitamin D. That report was the first issued by the IOM under the then-new evidence-based guidelines for evaluating studies and making recommendations. We are thus familiar with the process and, most important, with vitamin D itself. On the basis of this experience, we respectfully dissent from many of the findings and recommendations in the current report, and we set forth here a small fraction of the reasons for that dissent.

The IOM report (and its presentation to the media) stressed that its recommendations for vitamin D were based primarily on the intake (and serum 25-hydroxyvitamin D concentration) needed to ensure skeletal health and that, in the panel's judgment, there was insufficient evidence to make any recommendations with respect to nonskeletal benefits, if any. Second, the report concluded that a serum level for 25-hydroxyvitamin D [25(OH)D] of 20 ng/mL was sufficient to ensure bone health. And third, the panel concluded that since the bulk of the American public had 25(OH)D values that were above 20 ng/mL, most individuals were getting all the vitamin D they needed and had no reason for further supplementation. These conclusions fail on three grounds: logic, science, and guidance.

First, logic. Since the panel, in its judgment, concluded that it did not know whether there might be nonskeletal benefits (or at what blood level they could be ensured), then it is patently incorrect to say that they know that people are getting enough. The most the panel could have said logically was, "Here's what you need for bone; most people get that much; we do not know whether more would confer possible nonskeletal benefits." That, at least, would have been an honest communication of the state of the issue as the panel apparently understands it. However, to state publicly that the general public does not need more goes well beyond what the panel admits it knows.

Second, science. The statement that skeletal health can be ensured at serum 25(OH)D levels of 20 ng/mL is simply incorrect. Without going into an exhaustive recital of all the evidence pointing to a skeletal need for higher levels, we cite here three illustrative observations that, in our collective judgment, indicate that instead of 20 ng/mL, a serum level of 30 ng/mL is closer to the bottom end of the acceptable range for skeletal health. First, there is the large randomized, controlled trial in the United Kingdom that raised serum 25(OH)D level from 21 to 29 ng/mL and produced a 33% reduction in all major osteoporotic fractures combined.[3] The fact that other trials, with less good compliance, failed to reproduce that effect does not negate the evidence of a well-conducted trial. Second, there are the many meta-analyses of Bischoff-Ferrari and colleagues[4,5] demonstrating that, taken overall, fracture reduction with vitamin D does not occur reproducibly below serum 25(OH)D

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For further discussion on this topic, please see Reid and Avenell (J Bone Miner Res. 2011;452–454. DOI: 10.1002/jbmr.327).

Journal of Bone and Mineral Research, Vol. 26, No. 3, March 2011, pp 455–457
DOI: 10.1002/jbmr.328

levels of 30 ng/mL and for some fractures even 40 ng/mL. Finally, there is the demonstration, in a large German autopsy series (strangely misinterpreted by the panel), that osteoid seam width—the histologic hallmark of vitamin D deficiency—does not reach fully normal values until serum 25(OH)D levels are above 30 ng/mL.[6] [N.B.: Of 33 patients with 25(OH)D values between 20 and 30 ng/mL, more than half (18) had elevated osteoid volume. A Recommended Daily Allowance (RDA), by definition, meets the need of 97.5% of the population.] In a closely related finding, investigators from South Australia[7] showed seasonal variation in osteoid seam width and mineral appositional rate, reflecting variations in serum 25(OH)D precisely within the 20 to 30 ng/mL range, that is, above the IOM panel's "adequate" level.

Additionally, there is an apparent inconsistency between the recommended intake (600 IU/day for all individuals up through age 70) and the bottom end of the acceptable 25(OH)D serum concentration range (let alone higher values). As virtually universal experience with vitamin D supplementation demonstrates, 600 IU/day, if the body's sole input of vitamin D, would not be enough to produce a value of even 10 ng/mL, let alone 20 ng/mL or above. There is a generally recognized "rule of thumb" to the effect that each additional 100 IU of vitamin D per day raises serum 25(OH)D concentration by approximately 1 ng/mL. That is, in fact, a "rounding up" for convenience of calculation. Several studies indicate that the response increment is closer to 0.7 ng/mL/100 IU.[8,9] Either way, 600 IU/day will not suffice without appreciable solar and dietary input. Furthermore, as is also widely recognized, 600 IU/day produces barely perceptible changes in individuals who are overweight or obese (now better than 50% of the US adult population). Hence the increase from the 1997 DRIs, while welcome, and certainly in the right direction, is simply inconsistent with current professional experience. It not only is inadequate, by itself, to meet even the panel's recommended serum levels, but this internal inconsistency detracts from the credibility of the whole report inasmuch as it flies in the face of the everyday experience of clinicians who recommend supplements to their patients and measure the resulting responses.

Finally, guidance. At already noted, the panel indicated that it was uncertain about extraskeletal benefits—benefits that might accrue at intakes above the new intake recommendations. At the same time, the panel raised the upper-level intake "TUIL" to 4000 IU/day. (The report acknowledges that intakes up to 10,000 IU/day are probably safe for everyone and applied an uncertainty factor[10] to that 10,000-IU figure to generate the 4000-IU TUIL. It is important to stress that the TUIL is not a limit but instead constitutes an assurance of safety for such an intake.) One should have thought that even a very simplistic game-theory approach would have led to a guidance statement such as the following: "We do not know whether taking more vitamin D than we are currently recommending will help you, but it could, and we can assure you that supplemental intakes up to at least 4000 IU/day are safe." Such a statement, couched, perhaps, in less straightforward language, nevertheless would provide guidance that both the public and governmental agencies could find useful. Instead, we now have only a confused public.

Beyond these errors and inconsistencies, though, serious as they are, lies a much deeper flaw in the approach taken by the panel, exemplified by a quote from one of the panel members to the *New York Times* at the time of release of the report.[11] The statement was simply that the "onus" (ie, burden of proof) fell on anyone who claimed benefits for intakes higher than the panel's current recommendations. This is an approach that is correct for drugs, which are foreign chemicals and which do carry an appropriately heavy requirement for proof. For drugs, the position of privilege is given to the placebo. And in the current IOM report, the privilege is given to a serum 25(OH)D level that is effectively the status quo. We judge that this is exactly backward for nutrients. The privilege instead must be given to the intake that prevailed during the evolution of human physiology, the intake to which, presumably, that physiology is fine-tuned. So far as can be judged from numerous studies documenting the magnitude of the effect of sun exposure,[12,13] the primitive intake would have been at least 4000 IU/day and probably two to three times that level, with corresponding serum 25(OH)D levels ranging from 40 to 80 ng/mL. The fact that primitive levels would have been higher than current IOM recommendations does not, of course, prove their necessity today. But such intakes should be given the presumption of correctness, and the burden of proof must be placed on those who propose that lower intakes (and lower serum levels) are without risk of preventable dysfunction or disease. The IOM, in its report, has utterly failed to recognize or meet that standard.

Finally, we commend the IOM panel for their concern about safety, certainly an appropriate posture for a body crafting public policy. However, the standards adopted by the panel for taking into evidence papers indicating possible risk were, we note, far lower than those the panel required to indicate benefit. Additionally, many of the purported risks were, on their face, implausible and inconsistent with the experience of population subgroups that routinely have serum levels in the range mentioned by the panel as possibly risky (eg, approximately 50 ng/mL). We note that one of the widely accepted Hill[14] criteria for acceptance of observational data is precisely biologic plausibility. Furthermore, we consider it highly implausible that serum levels such as prevailed during hominid evolution could carry more risk than benefit for the populations concerned. Had that been the case, one should have expected that natural selection would have eliminated those prone to such risks.

In this Perspective, we have deliberately avoided a mind-numbing laundry list of the vast number of factual inaccuracies and misinterpretations in the report. We are informed that there is a request, through the Freedom of Information Act, to obtain the external review comments submitted to the IOM in response to a prepublication draft. When those materials become available, those interested can review the many problems with the IOM report in detail. For now, our recommendation to the American public is that the IOM report should be taken with a grain of salt (another nutrient the IOM finds risky).

Disclosures

Both authors state that they have no conflicts of interest.

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The IOM Report on Vitamin D Misleads

4 March 2011

Robert P. Heaney, M.D.
Creighton University,
William B. Grant,
Michael F. Holick,
Michael Amling

Send letter to journal:
Re: The IOM Report on Vitamin D Misleads

Email Robert P. Heaney, et al.

The Commentary by Ross et al. (1), concerning the recent calcium and vitamin D recommendations of the Institute of Medicine (IOM) has the potential to be substantially misleading. First, the title ("What clinicians need to know") is incorrect. The focus of all recommendations from the Food and Nutrition Board is, as the text of the article states, "normal healthy persons". Those recommendations have no applicability for patients with disease, or for physicians attempting to prevent disease in at-risk populations. That distinction is something clinicians need to know.

The Commentary also gives no hint of the substantial dissent which the recommendations have evoked from the vitamin D investigative community. The draft report had been submitted to external experts, and it is to be presumed that their findings were made available to the panel. While the details of these reviews are shrouded behind a pledge of secrecy, it is clear from the published comments of several of them that the review uncovered errors both factual and strategic/analytic. Some acknowledgement of this dissent would have been useful. One infers that there must also have been dissent within the panel itself, as one of its members was a co-author of Canadian guidelines (2) which specifically recommended cholecalciferol intakes approximately three times higher than the IOM. Thus, rather than being a settled issue, clinicians need to know that the IOM recommendations do not represent a consensus.

There is not room here to recount the many factual errors in the IOM report, some described elsewhere (3,4). But two in particular are, we judge, suggestive of how the panel approached evidence. In a study by one of us (MA), describing the relation of osteoid volume to vitamin D status (5), it was shown that serum 25(OH)D $\geq$ 30 ng/mL was necessary to ensure that there was no residue of osteomalacia. Specifically there were no instances of osteoid volume (OV/BV) above 1% for 25(OH)D > 32 ng/mL. Nevertheless the IOM panel accepted 20 ng/mL as the lower bound of normal, despite the fact that approximately half of the individuals between 20 and 32 had OV/BV values above 1% (and ranging up to 4.5%).

In another instance, the panel attempted to discredit on methodologic grounds the results of one of us (RPH), showing that calcium absorption efficiency was not fully normalized below 30-32 ng/mL (6,7). This was despite the fact that the method used was the gold standard in Europe and its results in this context had been confirmed by others. In both instances, there seemed to have been an effort to discredit or distort studies that were incompatible with the panel's proposed 20

ng/mL lower bound for normal vitamin D status.

Finally, in their conclusion, Ross et al. call for more randomized controlled trials. This is such a part of the conventional wisdom that it would seem to be entirely reasonable. Instead it dodges the panel's responsibility to deal with the available evidence. Most of the "needed" randomized trials are simply unfeasible (8), as they would require low intake contrast groups with serum 25(OH)D levels below even the IOM's already low recommendation. Such trials would be unethical. Since they cannot be done, this purported "need" leaves critical nutritional policy issues in a kind of permanent limbo.

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the nutritional context. [Appendix: Amplification on certain of the points discussed in the paper (online only).] Nutr Rev 68:478-484

6/30

Commentary

VITAMIN D
(OW)

THE D-BATABLE INSTITUTE OF MEDICINE REPORT: A D-LIGHTFUL PERSPECTIVE

Michael F. Holick, PhD, MD

Abbreviations:
IOM = Institute of Medicine;
25(OH)D = 25-hydroxyvitamin D

During the past decade, several thousand articles have been written about the health benefits of vitamin D and sun exposure (1-4). Being born or living at lower latitudes and being exposed to more sunlight reduces the risk of type 1 diabetes mellitus, multiple sclerosis, hypertension, and dying of cancer. Numerous studies have reported an inverse association with vitamin D status, ie, lower serum 25-hydroxyvitamin D (25[OH]D) levels are associated with increased risk for cancers of the breast, prostate, and colon among others; type 2 diabetes mellitus; cardiovascular disease; multiple sclerosis; rheumatoid arthritis; osteoarthritis; preeclampsia; cesarean delivery; depression; Alzheimer disease; infectious diseases; and neurocognitive dysfunction (1-5). However, because these studies were association and observational studies, they were dismissed by the recent Institute of Medicine (IOM) report on dietary reference intakes (6) as not qualifying as a high enough level of evidence to confirm the beneficial effect of vitamin D on these nonskeletal-related health outcomes.

Submitted for publication January 11, 2011
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To put this into perspective, the adage a picture is worth 1000 words can also be applied to digesting the more than 700 pages of documentation in the IOM report (6), represented with Figures 1 and 2. The committee focused on the role of vitamin D and bone health and reviewed studies on parathyroid hormone plateaus. They concluded that discrepancies at the level parathyroid hormone plateaued could be due in part to differences in populations studied and statistical methods used. In postmenopausal women, parathyroid hormone levels continued to decrease until a blood 25(OH)D concentration of approximately 30 ng/mL was reached and there was no further decline in the prevalence of secondary hyperparathyroidism (7) (Fig. 1A and 1B). The committee recognized the work of Priemel et al (8) who examined 675 iliac crest biopsy specimens from male and female German patients (401 males, mean age of 58.2 years, and 270 females, mean age of 68.2 years) for structural and histomorphometric parameters including osteoid indices. Priemel et al (8) could not establish a minimum 25(OH)D concentration that was inevitably associated with mineralization defects and did not find pathologic accumulation of osteoid in any patient with circulating 25(OH)D concentrations above 30 ng/mL. They concluded a minimum 25(OH)D threshold of 30 ng/mL along with adequate calcium intake was necessary for maintaining skeletal health. The IOM Committee, however, concluded from the same study that a 25(OH)D concentration of 20 ng/mL was adequate to prevent osteomalacia in at least 97.5% of the population (6).

The IOM report (6) reviewed the literature regarding vitamin D intake in women of childbearing age and concluded that being pregnant or lactating did not increase their need for their vitamin D intake above what was recommended for a woman of the same age, ie, 600 IU of vitamin D daily despite what others have reported (9). However, as noted in Figure 1C, of 40 mostly black pregnant women who were documented to be ingesting a prenatal vitamin (400 IU vitamin D_2) and drinking on average 2 glasses of milk (200 IU of vitamin D) a day, thus consuming approximately 600 IU of vitamin D a day, at the time that they gave

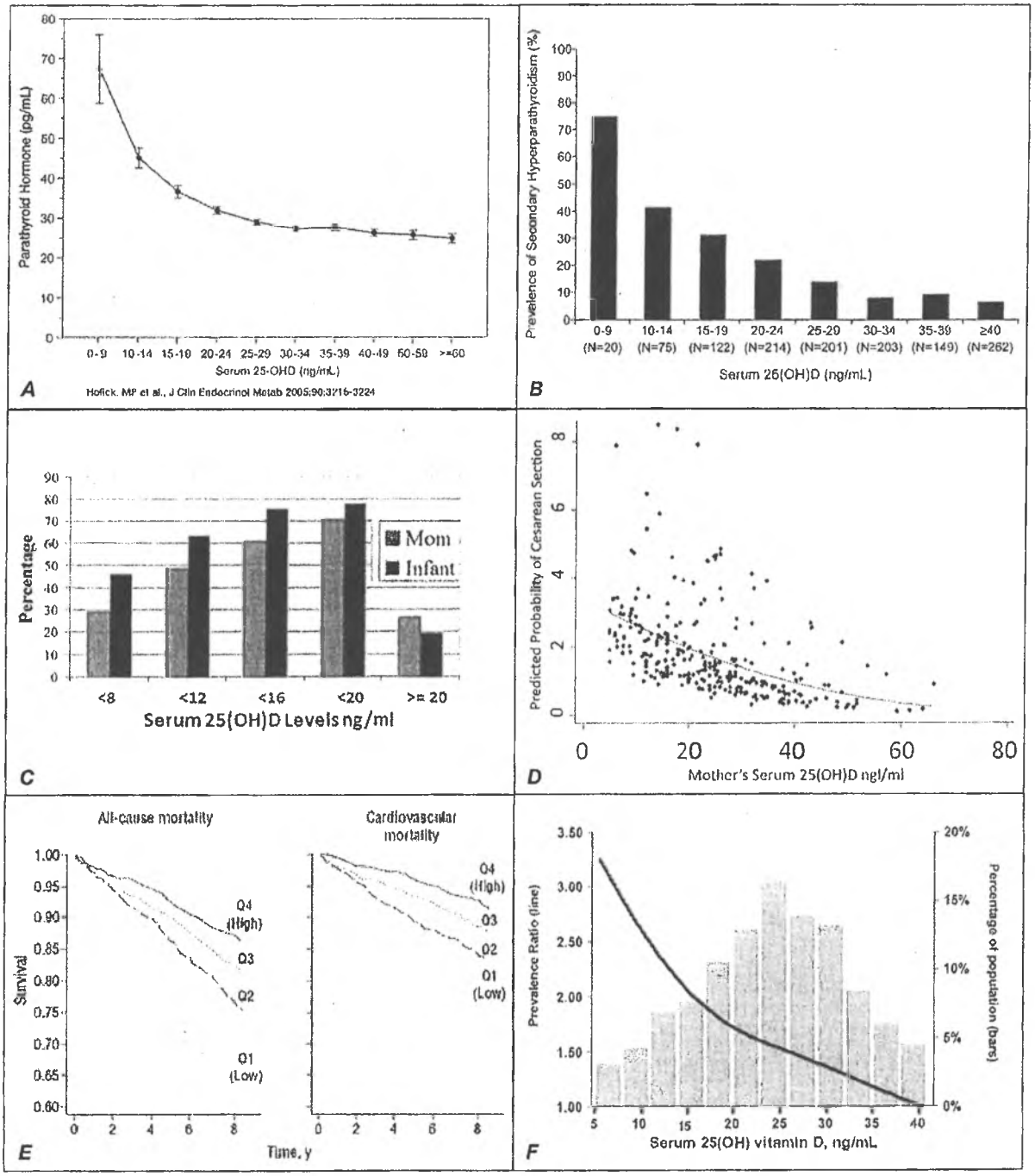

Fig. 1. ***Panel A***. Mean (±standard error) serum parathyroid hormone (PTH) by serum 25-hydroxyvitamin D (25[OH]D) subgroups. Participants' PTH concentrations relative to serum 25(OH)D concentrations sorted by subgroups delineated by predefined cutoffs for analyses of 25(OH)D inadequacy. Serum PTH values begin to increase with 25(OH)D concentrations less than 29.8 ng/mL. Adapted from *J Clin Endocrinol Metab*, 90:3215-3224, Holick MF, Siris ES, Binkley N, et al, Prevalence of vitamin D inadequacy among postmenopausal North American women receiving osteoporosis therapy, Copyright (2005), with permission from The Endocrine Society. ***Panel B***. Percentage of subjects with secondary hyperparathyroidism by 25(OH)D level. The percentage of subjects with secondary hyperparathyroidism (parathyroid hormone greater than 40 pg/mL) sorted by subgroups with serum 25(OH)D concentrations delineated by predefined cutoffs for analyses of 25(OH)D inadequacy. Adapted from *J Clin Endocrinol Metab*, 90:3215-3224, Holick MF, Siris ES, Binkley N, et al, Prevalence of vitamin D inadequacy among postmenopausal North American women receiving osteoporosis therapy,

Fig. 1 Legend ***(Continued)***

Copyright (2005), with permission from The Endocrine Society. ***Panel C.*** The percentages of mostly black women and their neonates with serum 25(OH)D concentrations below predefined cut-off values of <8, <12, <16, <20, and ≥20 ng/mL. At the time of birth, the pregnant women were documented to be ingesting a prenatal vitamin (400 IU vitamin D_2) and drinking on average 2 glasses of milk (200 IU of vitamin D) a day, thus consuming approximately 600 IU of vitamin D a day. Adapted from *Clin Pediatr (Phila)*, 46:42-44, Lee JM, Smith JR, Philipp BL, Chen TC, Mathieu J, Holick MF, Vitamin D deficiency in a healthy group of mothers and newborn infants, Copyright (2007), with permission from Sage Publications. ***Panel D.*** Blood concentrations of 25(OH)D in 253 pregnant women, demonstrating an association between the mother's increased 25(OH)D levels and decreased predicted probability of having a cesarean vs vaginal delivery, with a quadratically fit line. Adapted from *J Clin Endocrinol Metab*, 94:940-945, Merewood A, Mehta SD, Chen TC, Bauchner H, Holick MF, Association between vitamin D deficiency and primary cesarean section, Copyright (2009), with permission from The Endocrine Society. ***Panel E.*** Kaplan-Meier plots of all-cause and cardiovascular mortality in the 25(OH)D quartiles (Q). Log-rank test indicated a significant difference across all 25(OH)D quartiles (P<.001). Multivariate-adjusted hazard ratios for patients in the lower 2 25(OH)D quartiles (median, 7.6 and 13.3 ng/mL) were higher for all-cause mortality (hazard ratio, 2.08; 95% confidence interval, 1.60-2.70; and hazard ratio, 1.53; 95% confidence interval, 1.17-2.01; respectively) and for cardiovascular mortality (hazard ratio, 2.22; 95% confidence interval, 1.57-3.13; and hazard ratio, 1.82; 95% confidence interval, 1.29-2.58; respectively) compared with patients in the highest 25(OH) D quartile (median, 28.4 ng/mL). Adapted from *Arch Intern Med*, 168:1340-1349, Dobnig H, Pilz S, Scharnagl H, et al, Independent association of low serum 25-hydroxyvitamin D and 1,25-dihyroxyvitamin D levels with all-cause and cardiovascular mortality, Copyright (2008), with permission from the American Medical Association. All rights reserved. ***Panel F.*** Multivariable adjusted prevalence ratio of peripheral artery disease associated with serum 25(OH)D levels between 5 and 40 ng/mL. Adapted from *Arterioscler Thromb Vasc Biol*, 28:1179-1185, Melamed ML, Muntner P, Michos ED, et al, Serum 25-hydroxyvitamin D levels and the prevalence of peripheral arterial disease: Results from NHANES 2001 to 2004, Copyright (2008), with permission from Wolters Kluwer Health.

birth, 76% were vitamin D deficient as defined by the IOM cutoff of less than 20 ng/mL. Eighty-one percent of their newborns were vitamin D deficient according to this same cutoff (10). The IOM report focused on vitamin D's effect on musculoskeletal health and fall reduction, especially in adults older than 70 years (6), but disregarded vitamin D's effect on muscle function in pregnant women at the time of birthing. Figure 1D shows blood concentrations of 25(OH)D in 253 pregnant women, demonstrating an association between a mother's increased 25(OH)D levels and decreased predicted probability of having a cesarean vs vaginal delivery (11).

The association of vitamin D deficiency with a 50% increased risk of myocardial infarction (12) and more than 100% increased chance of dying of the event (13) (Fig. 1E) was also dismissed as not being supported by randomized clinical trials (6). The IOM did note that 25(OH)D concentrations lower than 15 ng/mL were associated with increased risk of mortality and that some, but not all, studies observed that increasing the blood 25(OH)D concentration above 30 ng/mL was associated with increased mortality (6), including the report by Melamed et al (14). The major cause for mortality was cardiovascular disease. However, Melamed et al concluded that there was a lower risk of mortality for 25(OH)D concentrations of 30 to 49 ng/mL and concentrations greater than 50 ng/mL were associated with a higher risk of mortality in women, but not in men. The same authors also reported a strong inverse association with peripheral vascular disease and serum 25(OH) D levels (15) (Fig. 1F). This observation is supported by the findings of a randomized controlled trial conducted by Dong et al (16). In 49 normotensive black boys and girls aged 16.3 ± 1.5 years who received 2000 IU of vitamin D_3 daily for 4 months, Dong and colleagues reported a significant increase in plasma 25(OH)D levels from 11 ng/mL to 34 ng/mL and a reduction in arterial wall stiffness, a prelude to hypertension and atherosclerotic deposition, as determined by carotid-radial pulse wave velocity. No effect was observed in the children who received 400 IU of vitamin D_3 daily and increased their blood 25(OH)D concentration from 11 ng/mL to 24 ng/mL. This mirrors the observation that serum 25(OH)D levels less than 30 ng/mL are strongly associated with hypertension and metabolic syndrome in adolescents (17).

It has been estimated that more than 70% of children aged 6 to 11 years in the United States have a blood 25(OH) D concentration less than 30 ng/mL (18). Infectious diseases have enormous health implications globally, not only increasing risk of morbidity, but also mortality. Urashima et al (19) reported a multicenter, double-blind, placebo controlled, parallel-group trial to assess the effect of supplementing school children aged 6 to 15 years with 1200 IU of vitamin D_3 daily from December through March on the incidence of seasonal influenza A infection (diagnosed with influenza antigen testing and nasopharyngeal swab specimen analysis). They observed a 42% relative risk reduction in the children who received 1200 IU of vitamin D daily for 4 months. Furthermore, those children who took 1200 IU of vitamin D daily and who had a previous diagnosis of asthma had a relative risk reduction of 93% for having an asthma attack compared with the children taking placebo. This observation is supported by a study of 1024 children with a history of mild-to-moderate persistent asthma who were vitamin D insufficient and had a one and a half times higher odds ratio for any hospitalization or emergency department visit (20). Serial concentrations of

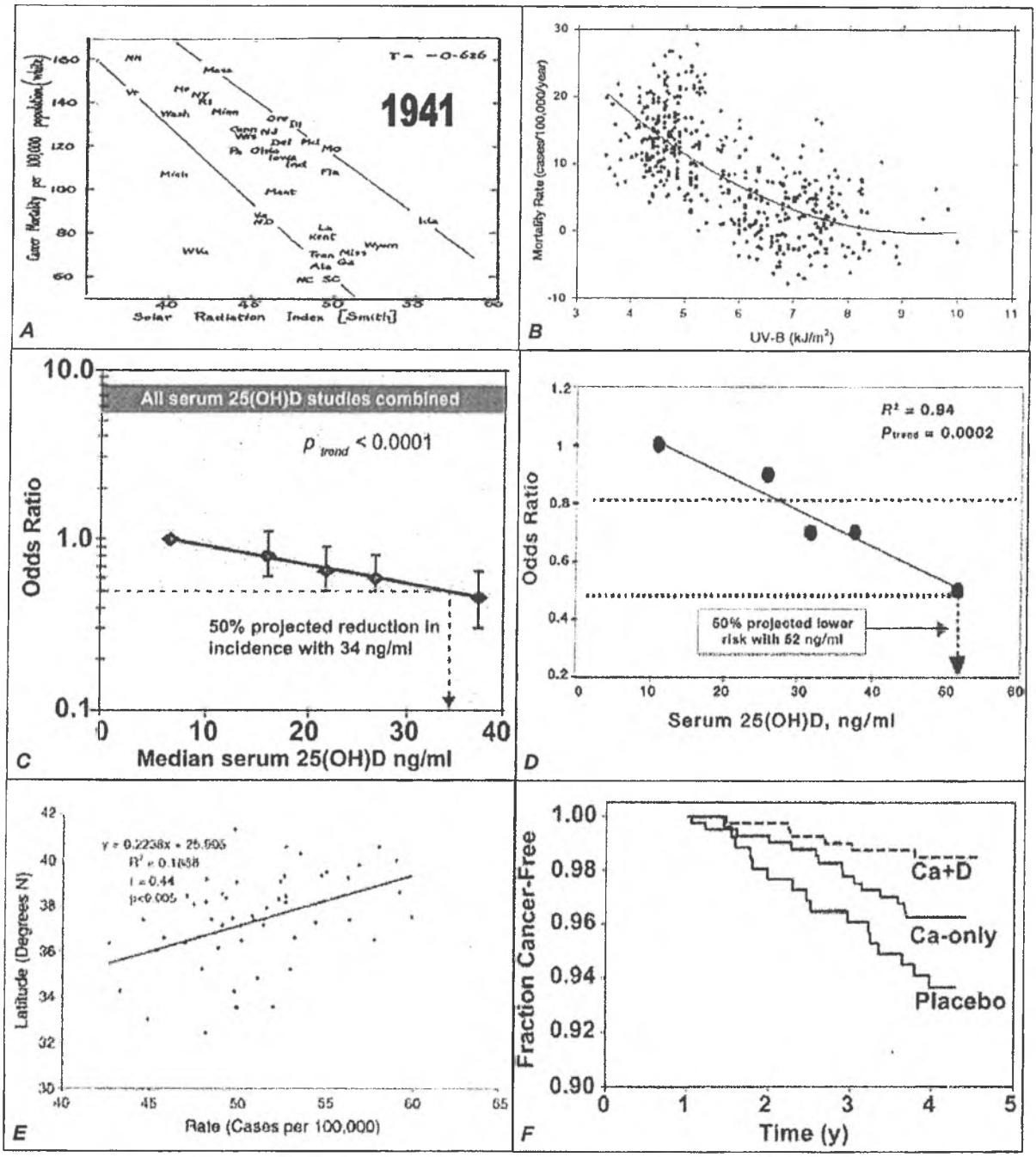

Fig. 2. ***Panel A***. Cancer mortality per 100000 population (white) and solar radiation index. Adapted and reprinted from *Cancer Res*, 1:191-195, Apperly FL, The relation of solar radiation to cancer mortality in North America, Copyright (1941), with permission from the American Association for Cancer Research. ***Panel B***. Mortality rate of cancer cases compared with solar UV-B index. Reprinted from *Cancer*, 94:1867-1875, Grant WB, An estimate of premature cancer mortality in the U.S. due to inadequate doses of solar ultraviolet-B radiation, Copyright (2002), with permission from John Wiley and Sons. ***Panel C***. Dosage-response gradient for colorectal cancer according to serum 25-hydroxyvitamin D (25[OH]D) concentration of 5 studies combined. The 5 points are the odds ratios for each quintile of 25(OH)D on the basis of the combined data from the 5 studies. Reprinted from *Am J Prev Med*, 32:210-216, Gorham ED, Garland CF, Garland FC, et al, Optimal vitamin D status for colorectal cancer prevention: A quantitative meta analysis, Copyright (2007), with permission from Elsevier. ***Panel D***. Dose-response gradient of breast cancer risk according to serum 25(OH)D concentration, pooled analysis. Reprinted from *J Steroid Biochem Mol Biol*, 103:708-711, Garland CF, Gorham ED, Mohr SB, et al, Vitamin D and prevention of breast

Fig. 2 Legend ***(Continued)***

cancer: Pooled analysis, Copyright (2007), with permission from Elsevier. ***Panel E.*** Latitude vs the number of adults diagnosed with colon cancer independent of race in the state of California. The R^2 value is a measure of how well the data fit the linear regression. The larger the value, the better the fit. Pearson correlation coefficient (r) calculated for the rate of colon cancer vs latitude, independent of race was measured to be $r = 0.44$ ($P<.005$), demonstrating a significant positive linear relationship. The strongest possible value is 1.0 and no correlation measured as 0. Reprinted from *J Steroid Biochem Mol Biol*, 97:111-120, Spina C, Tangpricha V, Yao M, et al, Colon cancer and solar ultraviolet B radiation and prevention and treatment of colon cancer in mice with vitamin D and its Gemini analogs, Copyright (2005), with permission from Elsevier. ***Panel F.*** Kaplan-Meier survival curves (ie, free of cancer) for the 3 treatment groups randomly assigned in the cohort of women who were free of cancer at 1 year of intervention (n = 1085). Sample sizes are 266 for the placebo group, 416 for the calcium-only (Ca-only) group, and 403 for the calcium plus vitamin D (Ca+D) group. The survival at study end for the Ca+D group is significantly higher than that for the placebo group, by logistic regression. (Reproduced with permission from Dr. Robert Heaney, 2007.)

25(OH)D in 198 healthy adults revealed that a concentration of 38 ng/mL or higher reduced the risk of developing acute viral respiratory tract infections and numbers of days ill 2-fold (21).

The IOM assessed the effect of UV-B exposure and vitamin D status on cancer risk and mortality on the basis of several large studies, including those from the Agency for Healthcare Research and Quality in the United States and Canada and the Women's Health Initiative. As a whole, the studies are not supportive of a role for vitamin D with or without calcium in reducing cancer risk (6,22-24). These conclusions are eerily similar to how the scientific and medical communities responded to what Sniadecki in 1822 and Palm in 1889 reported regarding their observations on the effect of latitude and sun exposure on the incidence of rickets (25). They had concluded that the incidence of rickets increased in the inner cities because of lack of sun exposure and that rickets was also was associated with living at higher latitudes. It was inconceivable during the 19th century that exposure to sunlight on the skin would have any beneficial effect on bone health, and these observations were quickly dismissed without further study; thus, rickets continued to be a devastating consequence of living in sun-deprived environments. It was only later in the 1920s when Hess and Unger exposed children to UV-B radiation and sunlight when it was finally accepted that this was a "definite and dependable cure of rickets" (26). Hoffman (27) was the first to appreciate that living in cities and higher latitudes between 1908 and 1912 was associated with increased cancer mortality. In the 1930s, Peller and Stephenson analyzed cancer incidence in a population with increased exposure to solar UV radiation—the United States Navy—and reported the rate of skin cancer in the US Navy was 8 times higher than in the civilian population, but that the total number of deaths resulting from other cancers was 60% less (28). In 1941, Apperly demonstrated a significant correlation between reduced cancer mortality in adults who lived in the south compared with those living in the northeast (29) (Fig. 2A). In the 1980s and 1990s, Garland et al (30), and then later many other investigators (31-35), began reporting on epidemiologic studies that evaluated the correlation between cancer, sun exposure, and cutaneous production of vitamin D. They demonstrated a strong negative correlation between latitude, sun exposure, and vitamin D status and the risk of many cancers including colon, breast, ovarian, and prostate (Figs. 2C and 2D). Grant (36) reported an inverse relationship with cancer mortality in both men (Fig. 2B) and women and exposure to solar UV-B radiation. Grant calculated that over a span of 24 years (between 1970 and 1994) a total of 566400 Americans died prematurely of 1 of the 13 cancers because of inadequate exposure to solar UV-B radiation. Even in California where there is a wide range of latitudes, the incidence of colon cancer was significantly affected by living at a higher latitude and was associated with decreased solar UV-B exposure. An overall increase in occurrence of colon cancer was observed by 7.5% to 10.5% per degree latitude independent of race (Fig. 2E) (37). The IOM countered with the Agency for Healthcare Research and Quality reports (6,22,23) and made special note that the Women's Health Initiative trial examined the effect of combined supplementation of vitamin D and calcium (400 IU of vitamin D in 1000 mg of elemental calcium), and that over an average of 7 years follow-up, no significant trend towards risk reduction for cancer mortality was observed in postmenopausal women (24). However, what the IOM and Agency for Healthcare Research and Quality did not note was that many of the studies that were reviewed, including the Women's Health Initiative, stated that more than 50% of the participants admitted not taking the calcium and vitamin D on a daily basis and blood levels of 25(OH)D were often not measured at baseline and/or at study end. The authors of the Women's Health Initiative acknowledged that the 400 IU of vitamin D was inadequate to raise the blood level of 25(OH)D above 30 ng/mL, which is what most studies (31-33) have suggested is required to reduce cancer risk. Virtually all of the subjects in the Women's Health Initiative study were vitamin D insufficient, ie, 25(OH)D less than 30 ng/mL, both at the beginning and end of the 7-year trial. Of great interest, and what should have been considered an important finding from this study, was that women in the lowest quartile of 25(OH)D levels (less than 12 ng/mL) had an incidence of colorectal cancer that was 253% higher than the incidence

in women who had a baseline 25(OH)D level in the highest quartile (serum 25[OH]D of ≥24 ng/mL) (38). Lappe et al (39) reported a 60% reduction in all cancers in postmenopausal women who ingested 1100 IU of vitamin D and 1000 mg of elemental calcium daily for 4 years (Fig. 2F). They even accounted for the possibility that some cancers were developing during the first year; when they considered this, they showed a 77% reduction after only 3 years of enhanced vitamin D and calcium intake.

The IOM committee did a careful and thoughtful analysis of the vitamin D literature and recognized that the IOM's 1997 recommendations for adequate vitamin D intakes (40) were woefully inadequate and recommended a 3-fold increase in the vitamin D intake for most children and adults. They recognized that vitamin D is not as toxic as once thought and substantially raised the upper limit from 2000 IU to 4000 IU for children older than 12 years and all adults and noted that 10000 IU is the dosage considered to have no observed adverse effect. They also concluded that the definition of vitamin D deficiency defined in the 1997 report as a 25(OH)D concentration less than 10 ng/mL was also in need of an upward adjustment to at least less than 20 ng/mL. Thus, they appreciated what many experts had been reporting for the past decade: a vitamin D intake of 200 IU daily put both children and adults at high risk for vitamin D deficiency and all of its health consequences (1-5). The IOM committee disregarded association studies and mainly relied on randomized controlled trials for the recommendations. Yet, curiously, there are few if any randomized controlled trials that have demonstrated that 600 IU of vitamin D daily for either children or adults up to the age of 70 years will maintain their blood 25(OH)D concentration above 20 ng/mL. Six hundred IU of vitamin D daily in the absence of any sun exposure will not maintain blood 25(OH)D levels even at 20 ng/mL. This is demonstrated by the fact that people of color have much lower blood levels of 25(OH)D than white persons (18,41,42); the main reason is due to the sunscreening of their skin melanin content in reducing vitamin D synthesis (43). Humans, and in fact most vertebrates, have always depended on sun exposure for most if not all of their vitamin D requirement, and this source of vitamin D should not be dismissed as inconsequential (1,6). It is well known that excessive exposure to sunlight increases risk of nonmelanoma skin cancer, which is easy to detect and easy to treat. Melanoma, the most deadly form of skin cancer, occurs on the least sun-exposed areas, and occupational and environmental sun exposure reduces risk for this highly invasive cancer (44). Thus, it is not unreasonable to consider sensible sun exposure as a good source of vitamin D (34,35,43).

As more randomized controlled trials report on the nonskeletal health benefits of vitamin D, the recommendation will likely be to increase vitamin D intake to at least 1000 IU of vitamin D daily for children and 2000 IU of vitamin D daily for adults (43). There is no downside to increasing vitamin D intake, just as there is no downside to considering a serum level of 25(OH)D of 21 to 29 ng/mL as being vitamin D insufficient and 30 to 100 ng/mL as being sufficient (1-5,33-35,45). Because vitamin D toxicity is a very rare occurrence and is not observed until the blood 25(OH)D concentration is greater than 150 ng/mL (1), maintaining a concentration up to 100 ng/mL is considered safe. The fact that the IOM recognized the wide variability in the 25(OH)D assay is all the more reason that to guarantee vitamin D sufficiency (with the exception of patients with granulomatous disorders), children and adults should maintain a blood 25(OH)D concentration of 30 ng/mL or higher, not only to maximize bone health, but also to reduce risk of infectious diseases, autoimmune diseases, type 2 diabetes, cancers, and cardiovascular disease.

One has to wonder whether during Copernicus's time, if an Agency for Astronomical Research and Quality (AARQ) had reviewed all of the astronomical observations by the experts and included Copernicus's and Galileo's observations, would they have concluded that the world was round? We know what happened to them when they voiced their opinions and published their observational studies proposing that the world was round. How many more randomized controlled astronomical trials (RCATs) would have been needed for AARQ to conclude that the world was round, as Copernicus and Galileo proclaimed?

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DISCLOSURE

The author has no multiplicity of interest to disclose.

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March 9, 2011

The Honorable Wes Keller
Chair, House Health & Social Services Committee
Alaska Capitol, Room 427
Juneau, Alaska 99801

Dear Representative Keller,

As a board-certified dermatologist practicing in Anchorage, I am writing to share concerns with HCR 5 and point out several inaccuracies in the cited data regarding vitamin D. I strongly believe the resolved statements in HCR 5 endanger the health of Alaska's citizens by overemphasizing the role of vitamin D in disease prevention. As a physician, my utmost concern is quality patient care and patient safety. It is critical that patients, particularly those who are at-risk for vitamin D deficiency, seek a medical evaluation prior to beginning a vitamin D supplementation regime. As noted in a 2010 study published by the Institute of Medicine (IOM), determining appropriate vitamin D intake is complicated and requires medical judgment and supervision.

I would like to point out specific omissions (**noted in bold**) in the cited data in HCR 5, which erroneously make the case for substantial vitamin D supplementation:

- A 2007 article published in the American Journal of Clinical Nutrition reported that a study that compared cancer rates of a group ***of post menopausal women*** taking 1100 IU of vitamin D supplements in combination with calcium to cancer rates of a group taking a placebo found the risk of developing any cancer after four years was 60 percent lower in the group taking vitamin D supplements *(page 1, line 16 – page 2, lines 1-4);*
- A 2007 article published in the American Journal of Preventative Medicine reported that a study found blood serum levels of vitamin D of at least 33 ng/ml ***to be associated with a 50 percent lower risk of colorectal cancer incidence*** compared with blood serum levels of vitamin D of less than 12 ng/ml *(page 2, lines 9-12)*;
- A 2001 study published in the Lancet found that children in Finland who received 2,000 IU a day of vitamin D for the first year of life 78 percent reduced risk of type 1 diabetes ***over the ensuing 31 years*** compared to children receiving 400 IU a day of vitamin D *(page 2, lines 23-26)*;
- The Centers for Disease Control and Prevention report that influenza vaccine effectiveness varies greatly ***based on the age and immunocompetence of the vaccine recipient and the degree of similarity between the viruses in the vaccine and those in circulation*** *(page 3, line 22-23)*;
- A 2010 article published in the American Journal of Clinical Nutrition reported that a study of a group of Japanese school children who received ***1200 IU*** of vitamin D ***had a decreased incidence of influenza compared to children receiving placebo. The reduction was more prominent in specific subgroups of children who had not been taking other vitamin D supplements and who started nursery school after age 3*** *(page 3, lines 27-30)****; and***
- A 2010 article in The Lancet reported that the risk of multiple sclerosis increases with latitude ***and with low blood serum levels of vitamin D*** *(page 4, lines 3-4).*

The key information missing from the above whereas clauses misrepresent the scientific data regarding vitamin D health benefits by neglecting to include critical information on the populations involved in the studies and the intent of the research. While there are epidemiologic studies that show a statistical relationship between lower vitamin D levels and a higher incidence of some of these diseases, there are also multiple studies that have suggested an inverse association between vitamin D intake and cancer. There is some evidence that too much vitamin D may be harmful.

Vitamin D should be obtained through a healthy diet which includes drinking milk, eating foods which are good sources of vitamin D, and taking vitamin supplements. Intentional exposure to ultraviolet light from indoor tanning beds or the outdoor sun to produce optimum levels of vitamin D is not recommended, as ultraviolet (UV) radiation exposure is associated with increased risk of skin cancer and melanoma.

> **FURTHER RESOLVED** that the Alaska State Legislature urges the Department of Health and Social Services to provide vitamin D supplements to the elderly to prevent bone loss, falls, fractures, and other age-related health problems;

Calcium and vitamin D are two essential nutrients in bone health. Vitamin D supplements taken orally (according to the Institute of Medicine recommended dosage) along with calcium can prevent bone loss, falls and fractures in the elderly.

> **FURTHER RESOLVED** that the Alaska State Legislature urges the Department of Health and Social Services to investigate substituting vitamin D supplementation for influenza vaccination as a less costly method for preventing influenza;

Studies have not conclusively demonstrated than vitamin D supplements will prevent infectious diseases. Vigorous vaccination practices and healthy living conditions will lower the rates of preventable infectious diseases and also reduce morbidity and mortality. HCR 5 would endanger patients by replacing a proven method of disease prevention with a vitamin supplementation program which has not been tested to protect the general population from infectious disease, such as influenza.

> **FURTHER RESOLVED** that the Alaska State Legislature urges the Department of Health and Social Services to provide vitamin D supplements to pregnant women and infants to prevent pregnancy complications, preterm births, type 1 diabetes, and rickets.

As a physician who treats patients on a daily basis with skin cancer, including melanoma, I have seen first-hand the impact of the use of indoor tanning beds and an increase in diagnoses particularly in young women. This is a devastating disease for patients and their families, and I would urge you to take precaution in promoting vitamin D intake in a way that would increase use of indoor tanning beds. It is critical that the public be appropriately educated about vitamin D and be encouraged to consult their physician before taking any vitamin supplements. Finally, Alaskans should be educated about the dangers of ultraviolet radiation (UV). As stated previously, UV radiation from the sun and indoor tanning beds is associated with a significant increased risk in the development of skin cancer and melanoma. The public should be educated about proper sun protection and urged to avoid UV exposure from indoor tanning devices.

Thank you for the opportunity to provide written comments on HCR 5. For further information, please contact me at (907) 646-8500.

Sincerely,

Peter Ehrnstrom, MD, FAAD
3841 Piper Street, Suite T4-020
Anchorage, Alaska 99508

March 9, 2011

The Honorable Wes Keller
Chair, House Health & Social Services Committee
Alaska Capitol, Room 427
Juneau, Alaska 99801

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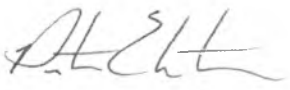

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