

# The Vitamin D Pseudo-Controversy

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**Annual Meeting**  
**Massachusetts Academy of**  
**Dermatology**

Wentworth by the Sea, N.H.

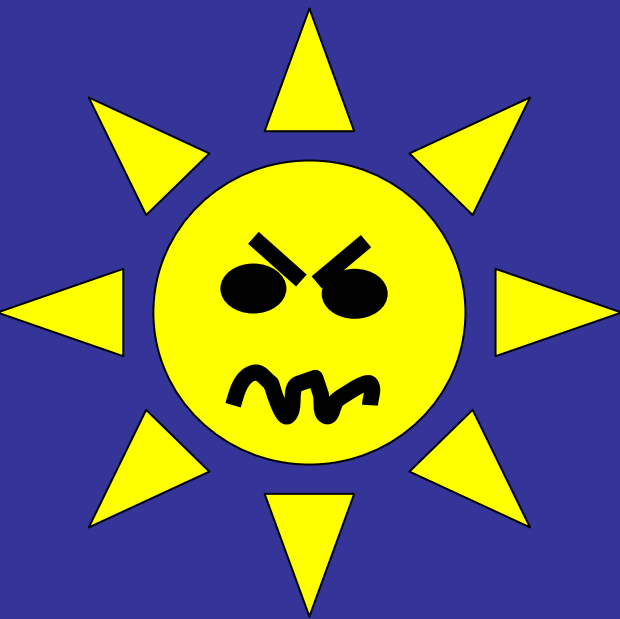
October 13, 2007

# The Pseudo-Controversy

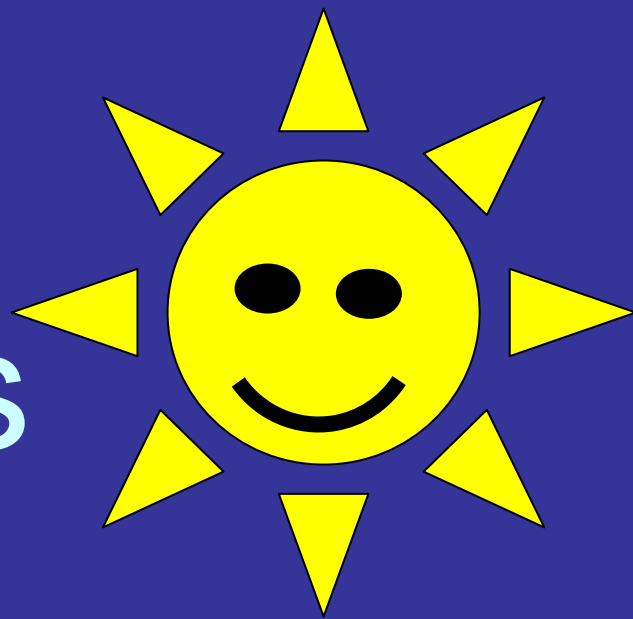
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Sunburn  
Skin Cancer  
Photoaging

Tanning  
Vitamin D  
Photosynthesis



VS



# The Pseudo-Controversy

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Should the public maximize vit D levels through intentional UV exposure in order to prevent cancer, hypertension, diabetes, multiple sclerosis ... ?

**Which is the lesser evil?**

**Skin cancer and photoaging or cancer of the colon, breast, prostate, and other organs in combination with the other listed diseases?**

# The Pseudo-Controversy is Irrational

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Ample vit D can be  
obtained from  
diet, supplements, and  
incidental sun exposure.

A supplement of 1000  
IU/day is safe and  
“sufficient” by even  
generous criteria.

# The Pseudo-Controversy is Irrational

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Cutaneous vit D photosynthesis is least efficient for population groups at highest risk of vit D deficiency

- Darkly pigmented individuals
- The elderly

The group most responsive to the “unprotected sun exposure” message is at lowest risk of vit D deficiency

- Healthy Caucasian teenagers

# **A Brief History of Sunshine Vitamin D**

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**(Early 1900's)**

- Vitamin D identified**
- UV shown to cure rickets  
and to improve cutaneous  
TB (lupus vulgaris)**
- Increasing popularity of  
sunbathing**

# CHANEL



ASSOULINE

# UV Causes Skin Cancer in Mice

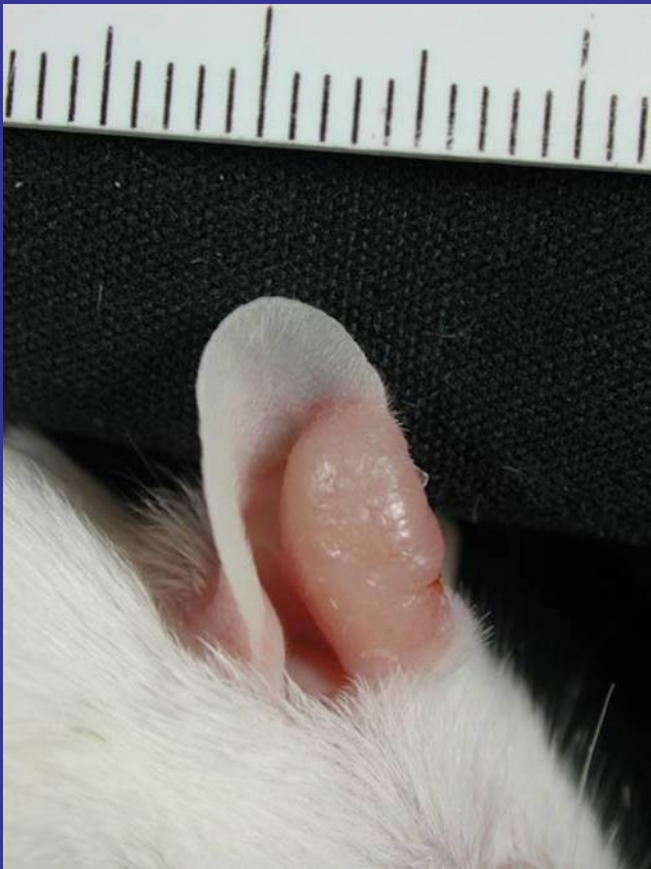
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**SCC in UV-irradiated  
hairless mouse**

**Goukassian et al. PNAS, 2004**

# UV Causes Skin Cancer in Mice



Amelanotic melanoma  
in UV-irradiated Tyr-H  
Ras/p19 KO mouse

Kannan et al. PNAS, 2004



BCC in UV-irradiated  
Ptch +/- mouse

Aszterbaum et al.  
Nature Med, 1999

# Faulty Repair of DNA Photoproducts Causes Xeroderma Pigmentosum

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**10 year old Japanese boy**

Courtesy of T. Maeda, M.D.

# Skin Cancer in 2007

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**Half of all human cancers**

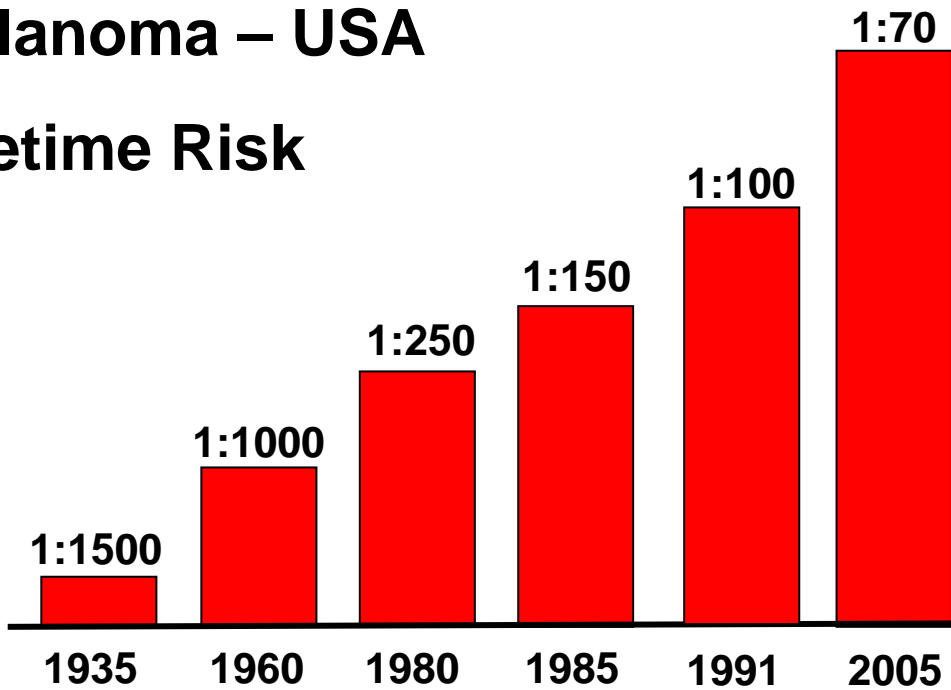
**In the US alone:**

- **Basal cell carcinoma**  
**>1,000,000 cases**
- **Squamous cell carcinoma**  
**>200,000 cases, 2,000 deaths**
- **Melanoma**  
**~90,000 cases, >8,000 deaths**

**30-fold ↑ risk since 1930's**

# Melanoma – USA

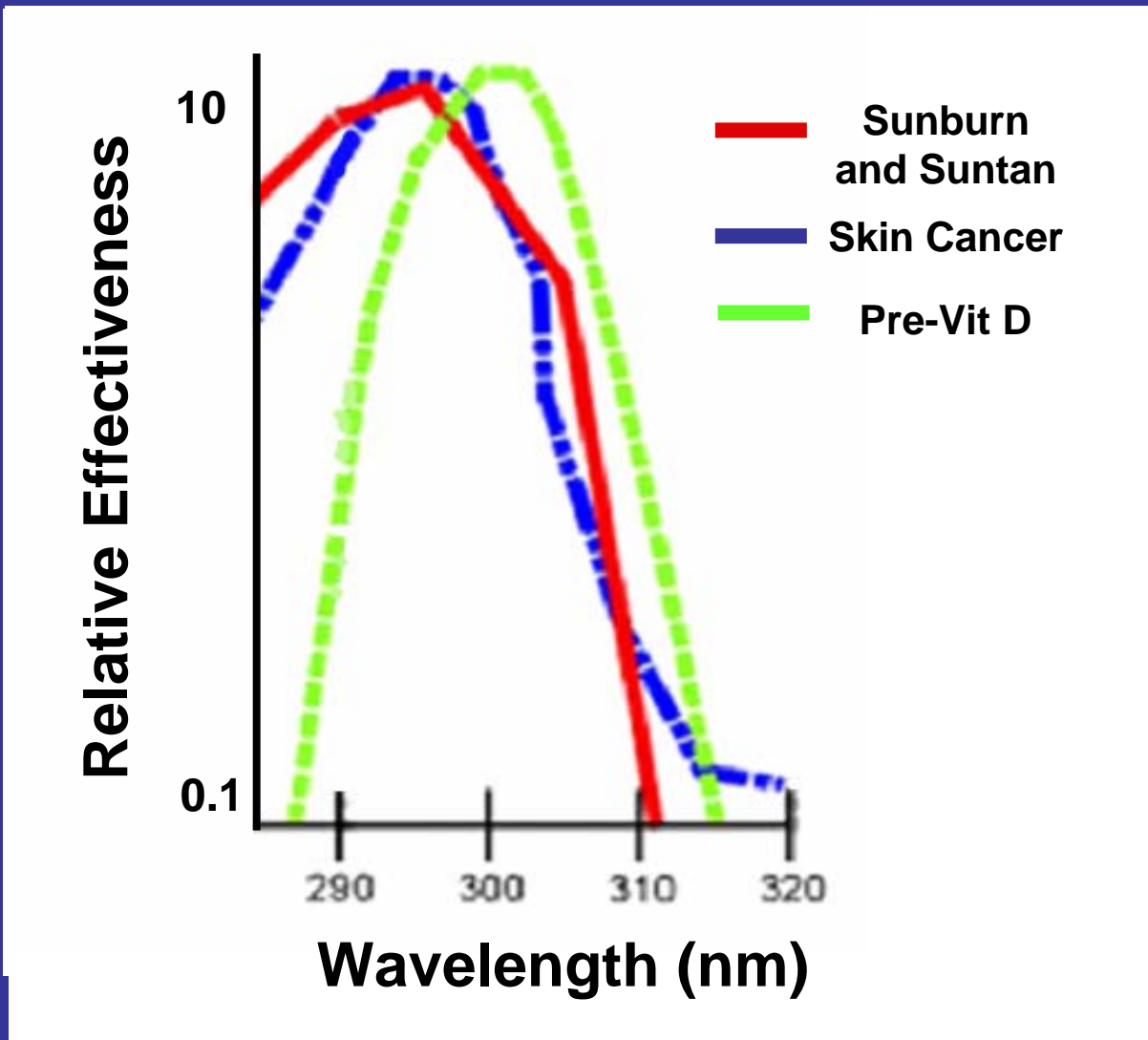
## Lifetime Risk



# **A Word About Photoaging**



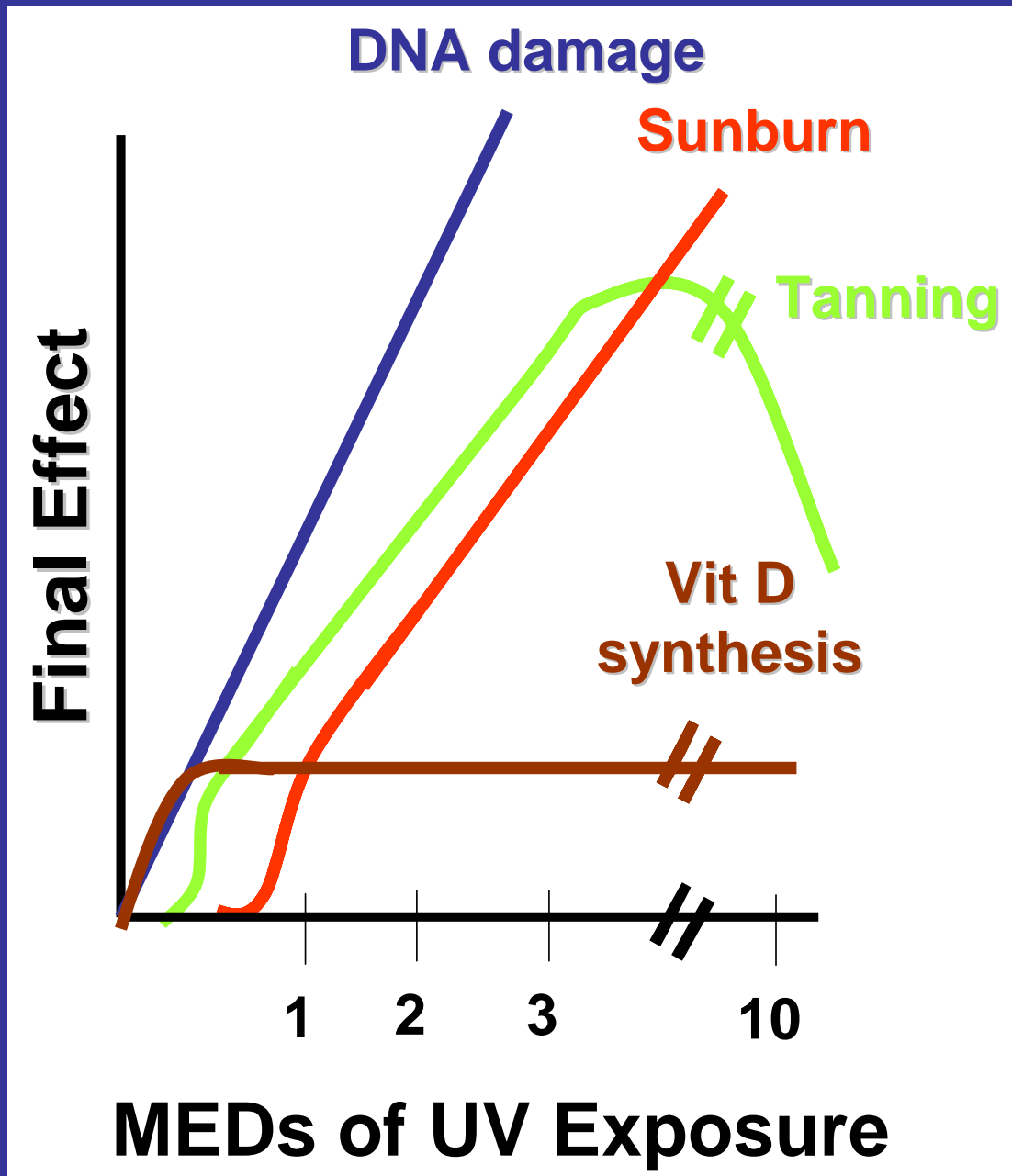
# UV Action Spectra in Human Skin



Wolpowitz & Gilchrest. JAAD, 2005.

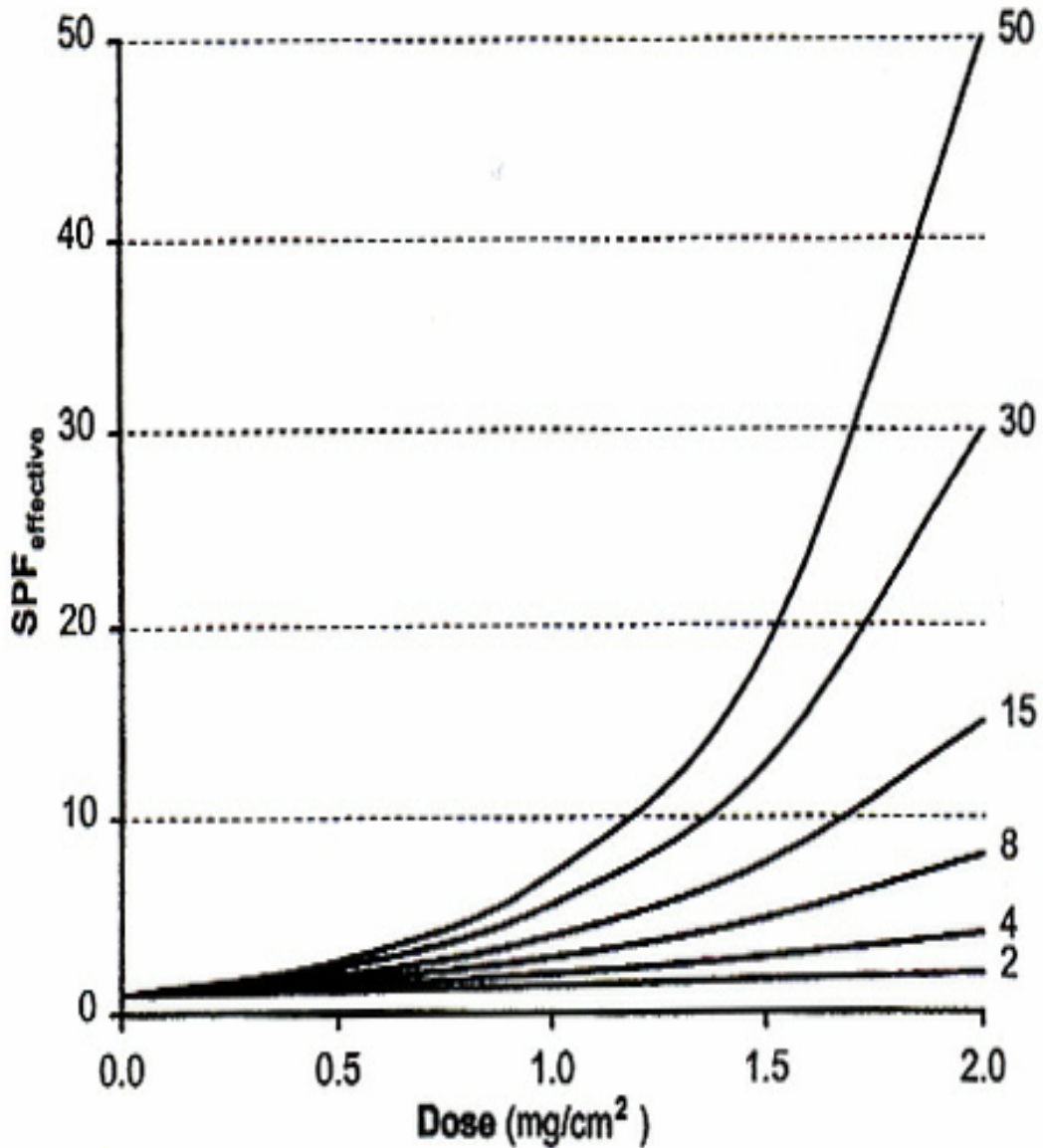
Adapted from Matsuoka et al. J Clin Endocrinol Metab, 1987; de Gruijl. Eur J Cancer, 1999; and Parrish et al. Photochem Photobiol; 1982

# Dose-Response Relationships for UV Effects



From: Gilchrest BA. Editorial / review in J. Steroid Biochem Mol Biol, 2007.

# Amount of Sunscreen Applied Affects SPF



Modified by Pinnell (JAAD, 2003) from Wulf et al

# The Real Controversy

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Does doubling an individual's "normal" serum 25(OH) vit D level (20-30 ng/ml  $\approx$  50-75 nmol/l), have health benefits?

- Fewer bone fractures?
- Fewer hip fractures?
- Fewer falls?
- Less cancer?
- Lower blood pressure?
- Less diabetes?

**The data are inconsistent, largely associational (not cause-and-effect) or extrapolated from very specific population groups.**

# Definitions of Vitamin D Terms

**Term**

**Conventional**

**New-Age**

## **Sufficient**

25(OH)D (ng/ml)     $\geq 15$  or 20     $>30$  or even  $>60$

PTH (pg/ml)                       $<65$                       Incapable of further reduction

Bone disease                      No                      No

## **Insufficient**

N/A

$<30$  or  $<60$

25(OH)D (ng/ml)                      Reduced by vitamin D supplementation even if  $\ll 65$

PTH (pg/ml)

Bone disease

Irrelevant\*

## **Deficient**

25(OH)D (ng/ml)     $<15$  or 20                      ?

PTH (pg/ml)                       $>65$                       ?

Bone disease                      Yes                      Yes

\* Statistically associated with higher rates of some diseases in some epidemiologic studies

# Is “Vitamin D Sufficiency” Desirable or Even Attainable?

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- Topic of great debate in endocrinology circles
- By New-Age definition, more than half of all northern Europeans and Americans do not have a “sufficient” 25(OH)D level
- There is no detectable individual health benefit to being vitamin D “sufficient” vs “insufficient.” All postulated benefits relate to statistical associations with disease rates (all low) in large populations with many possible confounding factors (ethnicity, lifestyle, etc).

# Half of Hawaiian Surfer-Dudes Can Be Classified as Having “Vitamin D Insufficiency”!!!

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Binkley et al J Clin Endocrinol Metab, 2007

- Convenience sample: 93 healthy adults from University of Hawaii and nearby skate board shop, avg. age 24 years, avg. BMI 23.6 kg/m<sup>2</sup>
- Self-reported minimum sun exposure of 15 hr (avg. 29 hr) weekly for past 3 months
- 40% never used sunscreen, group averaged 22.4 hr/week of unprotected sun exposure
- Group mean 25(OH)D = 31.6 ng/ml (max 62 ng/ml)
- 51% fell below a “vitamin D sufficiency” cutoff of 30 ng/ml

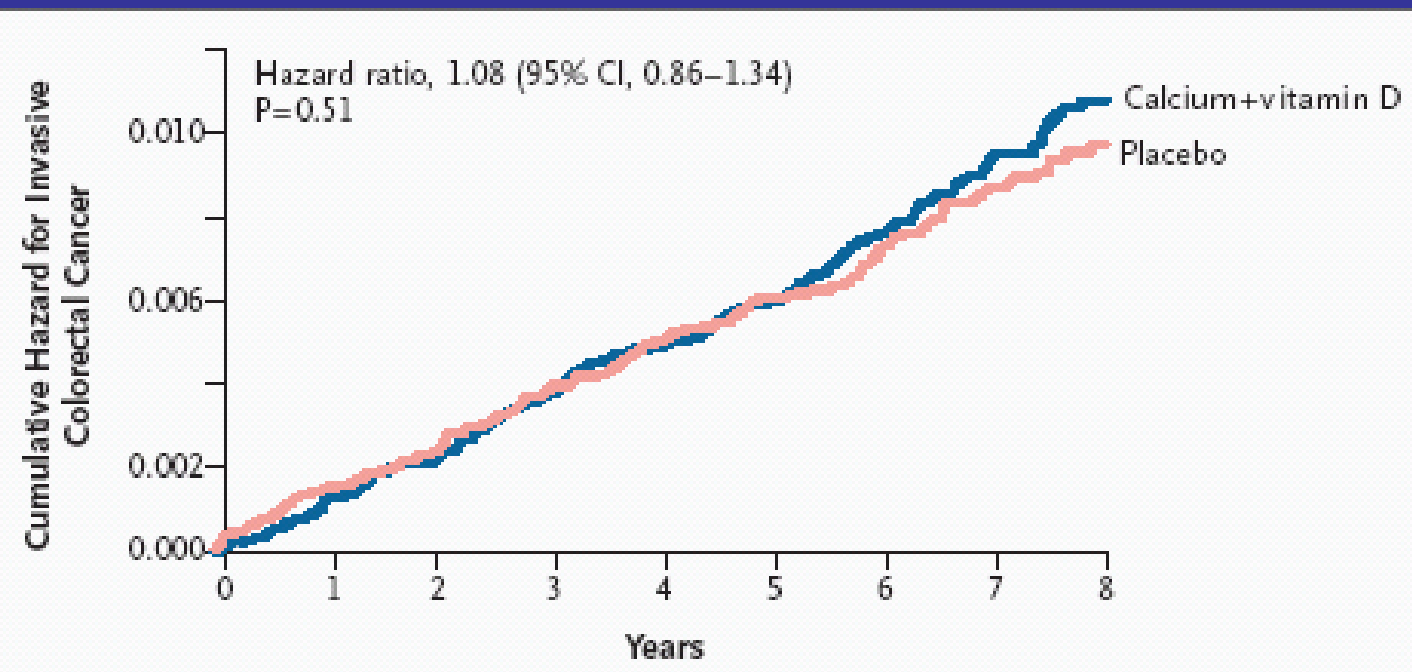
# Vitamin D and Colorectal Cancer

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- Widely publicized epidemiologic studies linking high cancer risk with “low” vit D levels or indirectly with low sun exposure
- Other epidemiologic studies with inverse or no association, but not publicized
- Prospective randomized placebo-controlled  $\geq 7$  year trial of  $>36,000$  older women: no relationship of cancer incidence or mortality with sun exposure or use of supplements

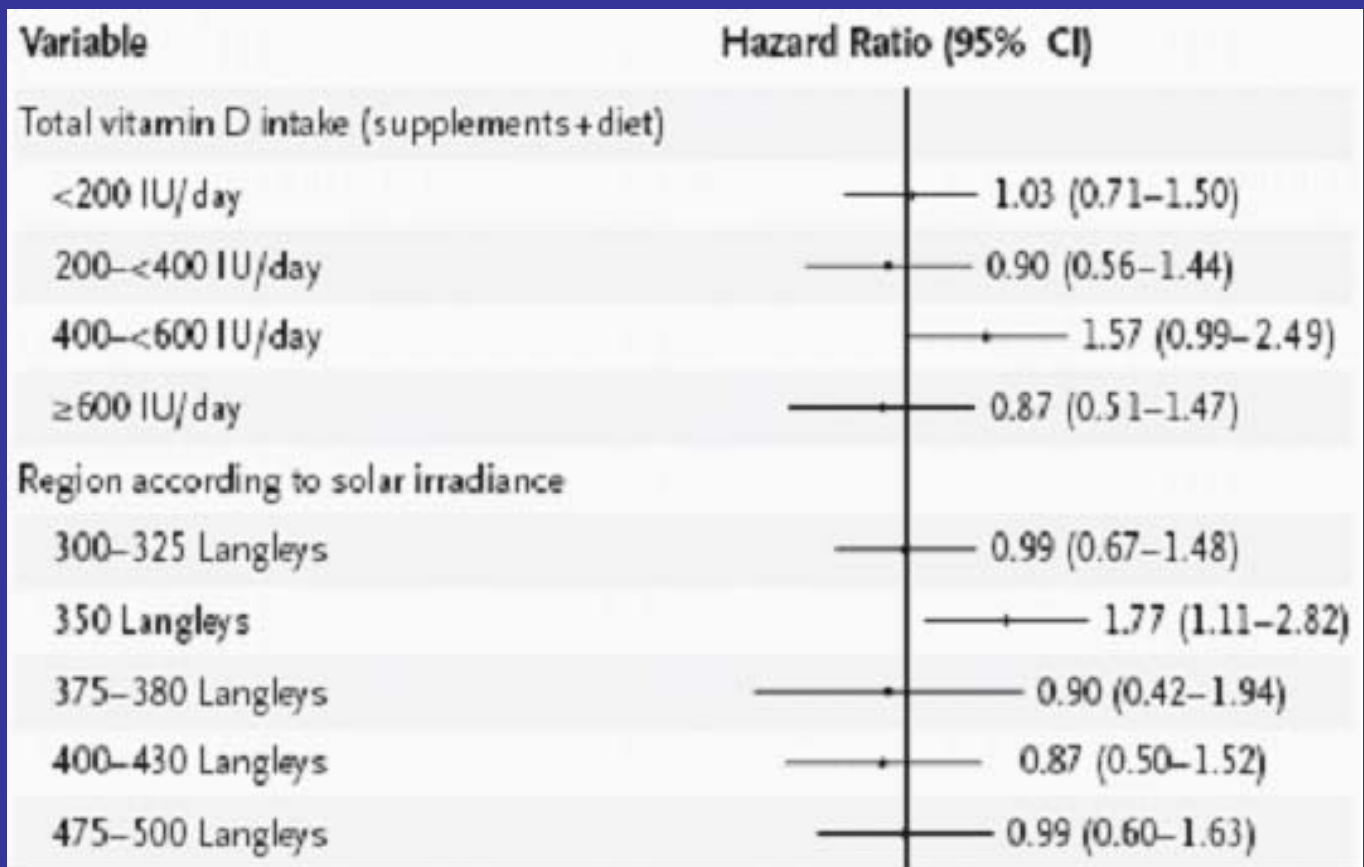
# Effect of Supplemental Calcium Plus Vitamin D on Risk of Colorectal Cancer (Kaplan-Meier Estimates)

N= 36,282 randomized subjects



From: Wactawski-Wende et al.  
N Engl J Med, 2006.

# Effect of Supplemental Ca Plus Vit D and Environmental Sun Intensity on Risk of Colorectal Cancer



From: Wactawski-Wende et al.  
N Engl J Med, 2006.

# A Real Life Scenario

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Suppose a fair-skinned teenager wants to maximize vit D photosynthesis in order to avoid colon cancer at age 60.



Assume the MED dose is 15 minutes of sun exposure and maximum pre-vit D production is achieved in 5 minutes.

# A Real Life Scenario

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Now, assume an SPF 30 sunscreen is applied once as  $1 \text{ mg/cm}^2$  (actual SPF 5) before a 30 minute exposure.

**Result:** No sunburn, an 80% reduction in photodamage, and maximum vit D synthesis.

**Result without sunscreen:** A painful sunburn, substantial photodamage, and the same vit D synthesis.

**...but all this is irrelevant to the value of sun protection.**

- **If you believe you or your patients would benefit from a higher serum 25(OH) vit D level, recommend a supplement and/or vit D-enriched foods.**
- **If you believe it would be sound public health policy to increase the RDA for vit D and/or the standard multivitamin dose or the number of enriched foods, work with professional societies to achieve these goals.**

# Why is There a Pseudo-Controversy?

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- The sun protection message is old (and wimpy).
- People, especially teenagers, want to sunbathe and tan.
- Sunbathing and making one's own vitamin D have a back-to-nature holistic appeal.
- The indoor tanning industry knows it's good for business.

# The Indoor Tanning Industry

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- **\$5 B annual revenues in U.S.**
- **50,000 facilities in U.S. with 28 M customers/year (>1 M visits/day)**
- **>70% of users are Caucasian women aged 16-49 years**
- **>50% of all teenaged girls in some regions of the U.S.**
- **Large lobbying effort fighting proposed restrictive regulations**
- **Health benefits of vit D photo-synthesis is the best argument**



**Roadside advertisement in Ontario.**

**U.S. state legislatures are bombarded with selected epidemiologic studies that support a cancer prevention effect of high 25(OH)D levels.**

# **The Appeal of “Natural” Solutions**

## **Versus**

## **The Problems of Civilization**

- **Humans evolved as relatively hairless and darkly pigmented beings in a highly insolated tropical subsistence environment.**
- **Humans migrated away from the equator to far less insolated climates and evolved to be lighter skinned.**
- **Cities were built, societies became industrialized.**
- **Airplanes, social inversions, and get-away packages were invented.**

# Consequences of Geographic Mobility

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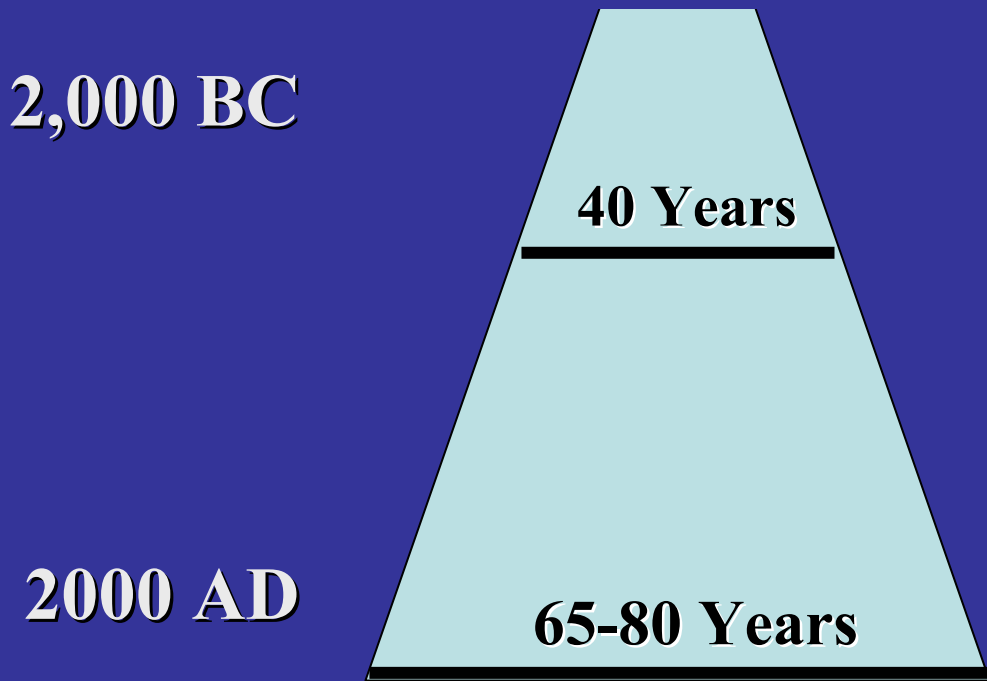
Dark-skinned people largely indoors in poorly insulated places

→ Childhood rickets among inner city ethnic minorities

Fair-skinned people often outdoors in highly insulated places

→ A 1 in 3 lifetime risk of skin cancer for Caucasians

# Life expectancy



In a primitive society with a life expectancy of 40 years, rickets is a problem but skin cancer and photoaging are not.

# In the 21<sup>st</sup> Century...

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- The average lifespan in the U.S. is nearly 80 years.
- If you are **fair-skinned**, you will benefit enormously from regular lifelong safe sun practices.
- While wearing a high SPF sunscreen in season, you will probably maximize your vit D photosynthesis during incidental sun exposure.
- Daily oral vit D supplementation can completely compensate for lack of cutaneous photosynthesis.