

**IUNS 21<sup>st</sup> International Congress of Nutrition  
Functional Foods and Bioactive Compounds (Track 6 #144/3127)  
Framing the Issues: Is there a role for dietary/food supplements in  
nutrition and health? (Symposium144/88)**

**17 October 2017 - Buenos Aires**

**Dietary/Food Supplements in Health Promotion:  
Illustrations of the Benefits and Risks of Research**

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## Conflict of Interest Disclosure

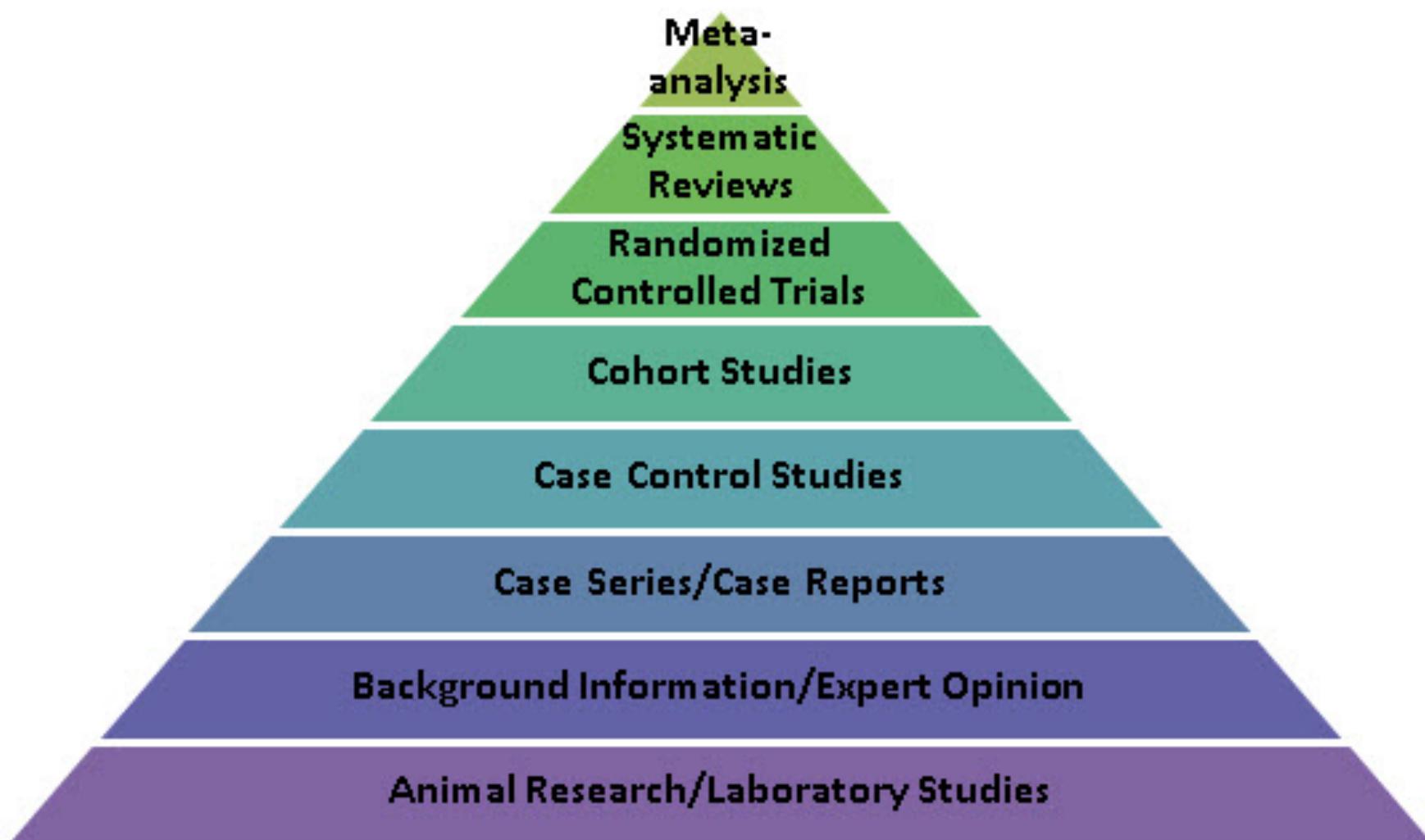
**I wish to declare a potential conflict of interest,  
and that I have received partial support from the  
International Alliance of Dietary/Food Supplement  
Associations for partial travel and per diem expenses  
to attend this conference.**



***Knowing is not enough;  
we must apply  
Willing is not enough;  
we must do.***

**- Johann Wolfgang von Goethe  
(1749-1832)**

# Hierarchy of Evidence-based Nutrition



# The Misuse of Meta-analysis in Nutrition Research

***Nutrition science presents special challenges for meta-analyses. When individual studies vary substantially in their populations and methods, a meta-analysis may be less useful than a single (or small number of) well-conducted investigation(s). Meta-analyses, particularly involving diet, influence health policy, carry considerable weight in the media and in public perception, and have the potential to do harm.***

# Evidence for Health Decision Making — Beyond Randomized, Controlled Trials

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*Although randomized controlled trials have long been presumed to be the ideal source for data on the effects of treatment, other methods of obtaining evidence for decisive action are receiving increased interest, prompting new approaches to leverage the strengths and overcome the limitations of different data sources.*

*Elevating RCTs at the expense of other potentially highly valuable source of data is counterproductive.*

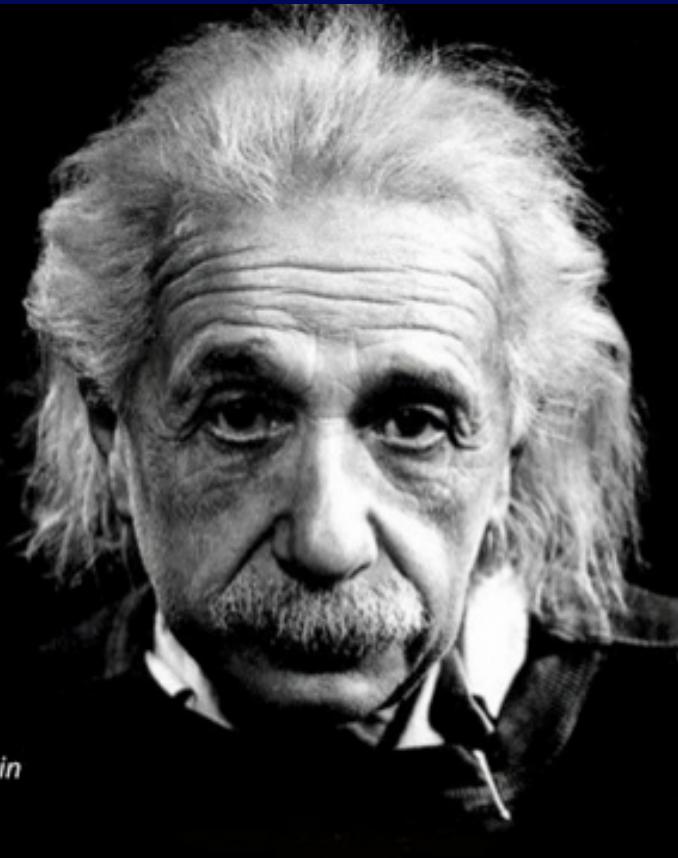
# Evidence-based Nutrition Practice-based Evidence Evidence Informed Policy

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**What approach is best  
for the question being asked?**

"If I had an hour to solve a problem and my life depended on the solution, I would spend the first 55 minutes determining the proper question to ask, for once I know the proper question, I could solve the problem in less than 5 minutes."

*- Albert Einstein*



# Critical Elements in Research Designs

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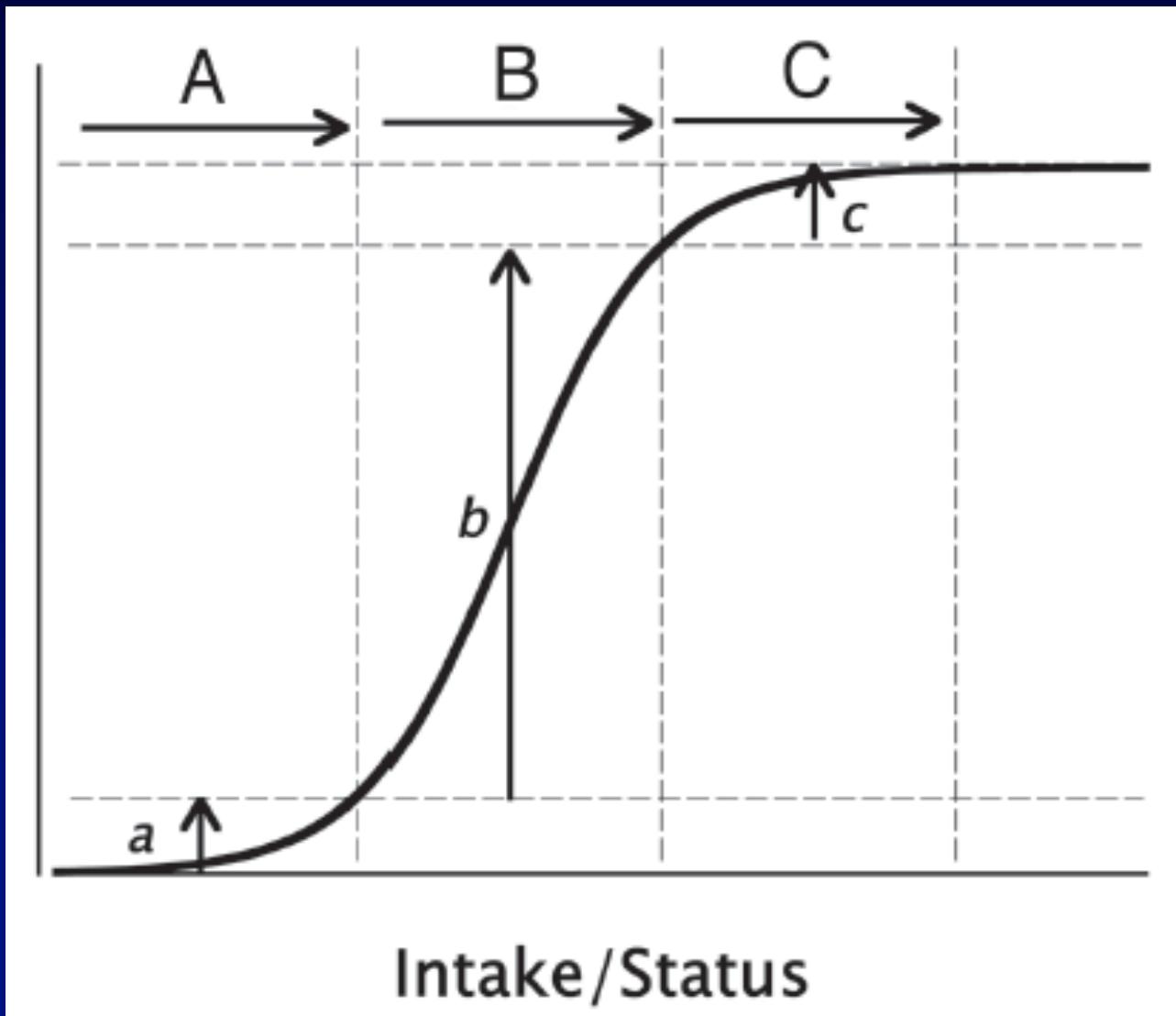
- Cohort Considerations

- Health status (phenotype, genotype)
- Baseline nutrient intake and status
- Susceptibility to outcome
- Synergies with non-intervention nutrients
- Environment (cultural, economic, social)

- Intervention Considerations

- Selection of nutrient(s), food(s) or diet(s)
- Selection of form(s) and dose(s)
- Duration and follow-up periods
- Assessment of compliance

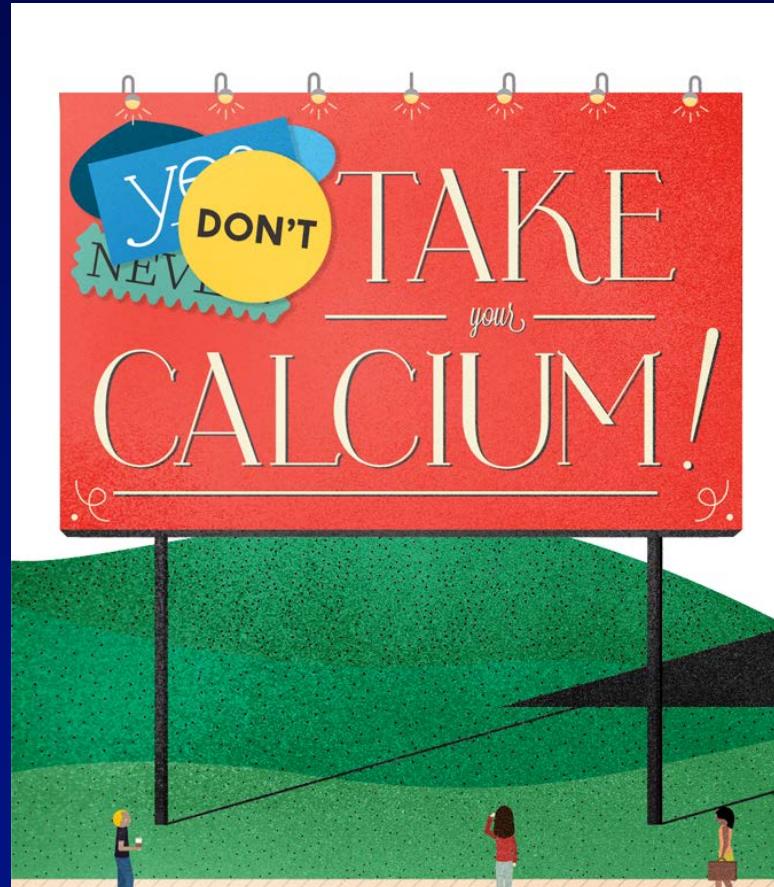
# Implications of Nutrient Threshold Dose-Response Characteristics



# Vitamin D and Calcium Supplementation Do Not Prevent Fractures in Adults: Meta-analysis

## USPSTF Recommendation Statement

*...current is insufficient to assess the balance of the benefits and harms of combined vitamin D and calcium supplementation for the primary prevention of fractures in premenopausal women or in men.*



# Vitamin D and Calcium Supplementation Do Not Reduce Hip Fractures in Women *Women's Health Initiative*

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## RCT

- n, 36,282
- age, 50-79 y
- F/U, 7 y



- 2000 mg Ca + 400 IU vit D<sub>3</sub> or placebo
- Ca intake was 1135 and 2000 mg/d in the placebo and supplement groups; HR=0.88 (95% CI: 0.72-1.08)
- 56% of the cohort took Ca + vit D before RCT

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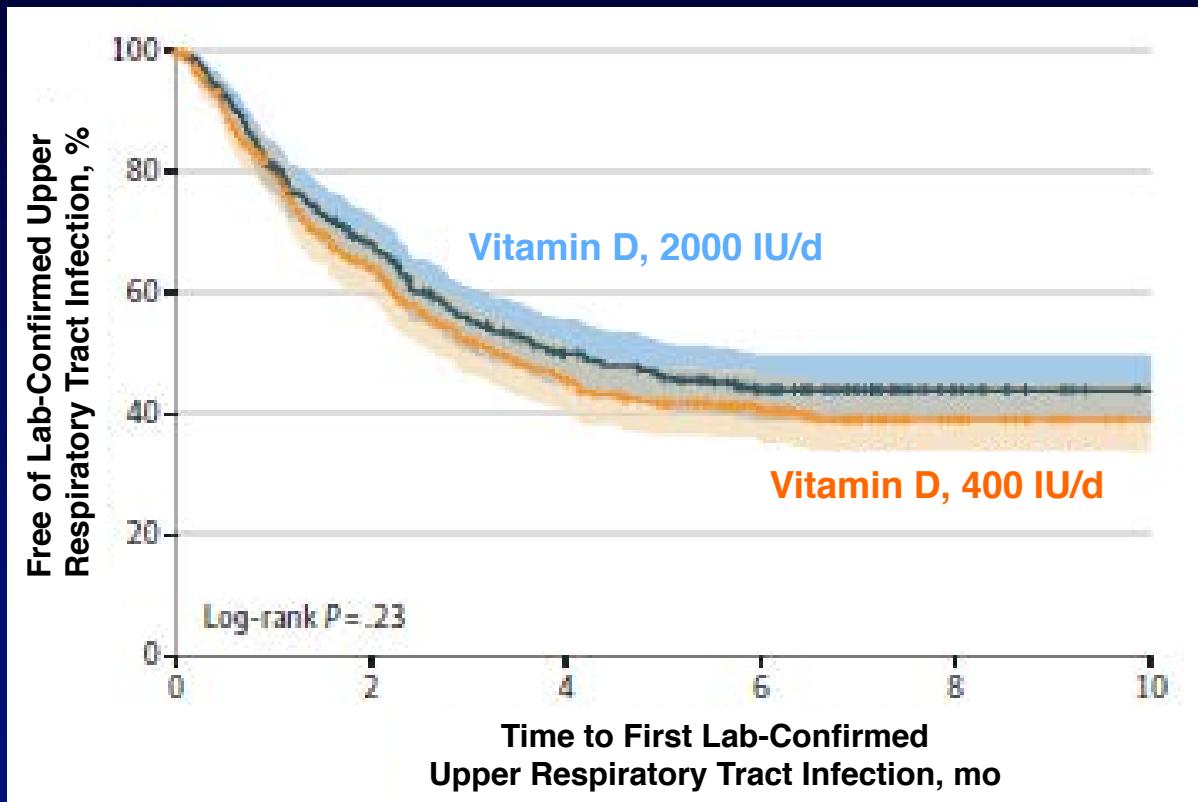
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- 56% of the cohort took Ca + vit D before RCT
- Among the women not taking calcium or vitamin D supplements at baseline; HR=0.62 (95% CI: 0.38-1.00)

# Vitamin D for Upper Respiratory Tract Infections

## *Vitamin D Outcomes and Interventions in Toddlers (DO IT)*

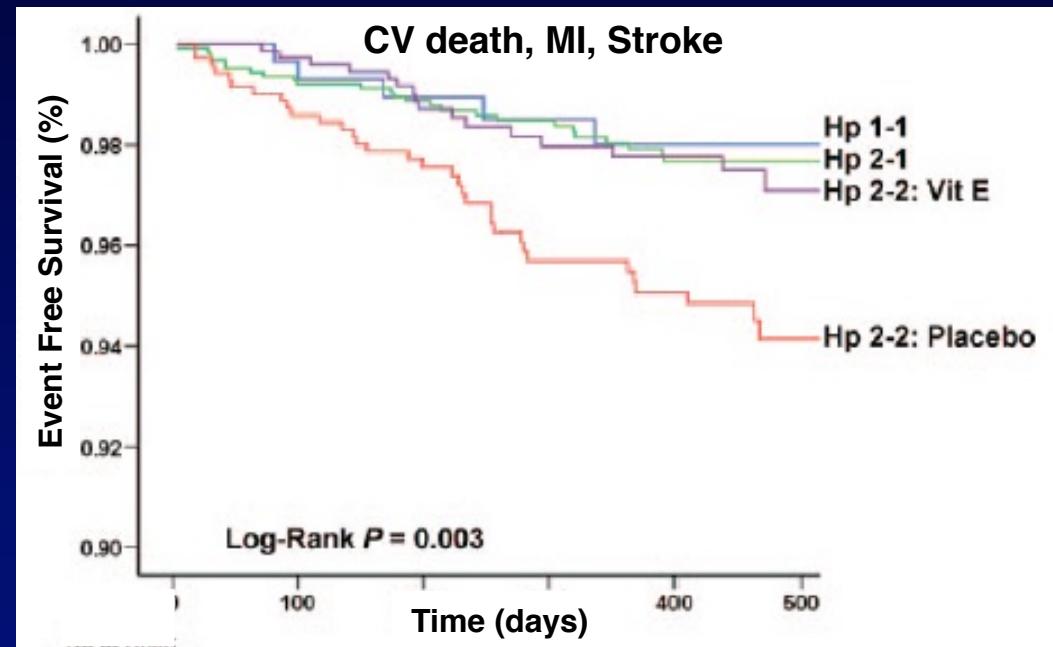
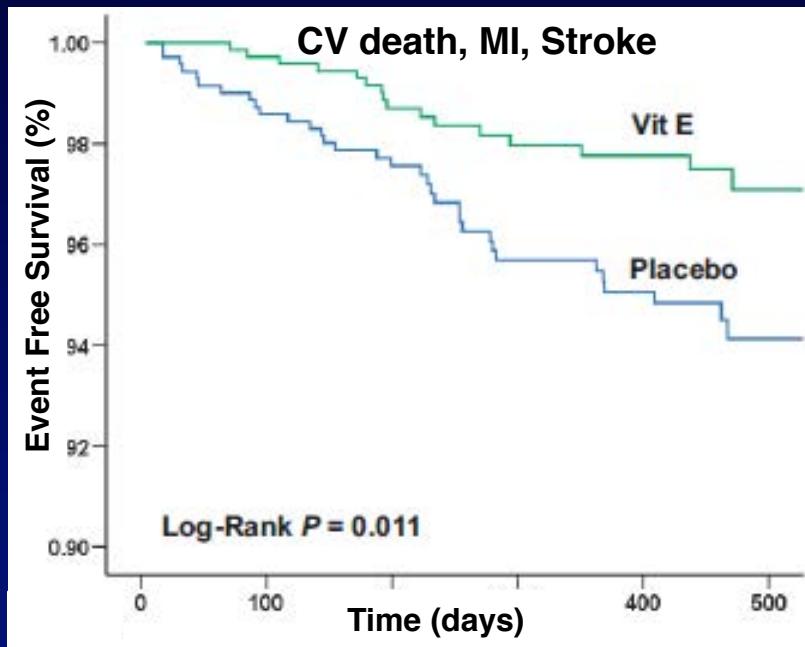
### RCT

- n, 703
- age, 1-5 y
- F/U, 10 mo



Dose (IU)	Serum 25-OH vitamin D, ng/mL	
	Baseline	Termination
400	35.9	36.9
2000	36.8	48.7

# Vitamin E Reduces Cardiovascular Events in Type 2 Diabetics with Haptoglobin 2-2 Genotype



## RCT

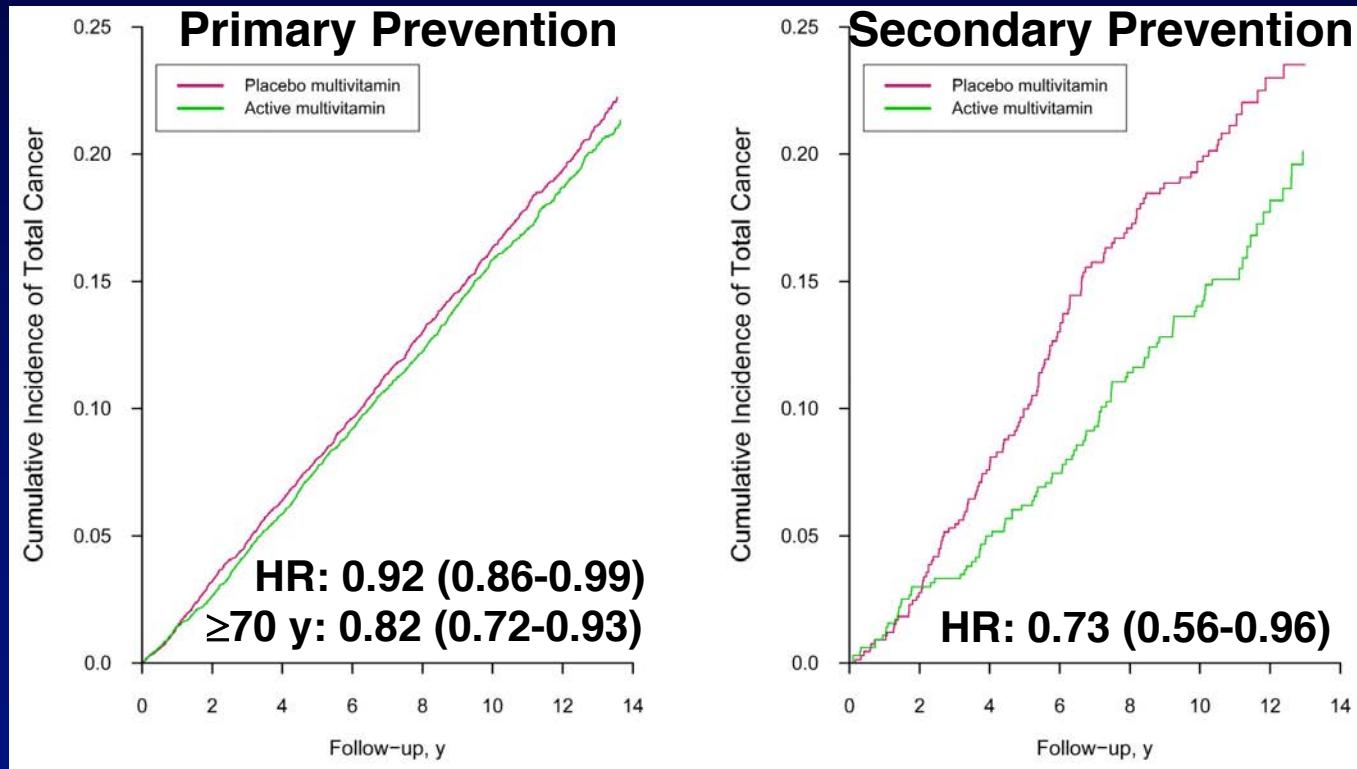
- n, 1434
- age,  $\geq 55$  y
- F/U, 18 mo

# Multivitamins Reduce the Risk of Total Cancer

## *Physicians' Health Study II*

### RCT

- **n, 14,641**
- **age,  $\geq 50$  y**
- **F/U, 13.3 y**



# Is It Too Soon to Tell Men That Vitamins Prevent Cancer?

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*The PHS II study was a well-done, large-scale, blinded, randomized clinical trial with objective verification of cancer outcomes.*

*...the biological plausibility of the study hypothesis – that a multivitamin would be protective in a well-nourished population – is limited. This matters, because the chance that the study finding of a protective effect is true is intrinsically related (by Bayes theorem) to the plausibility of the hypothesis.*

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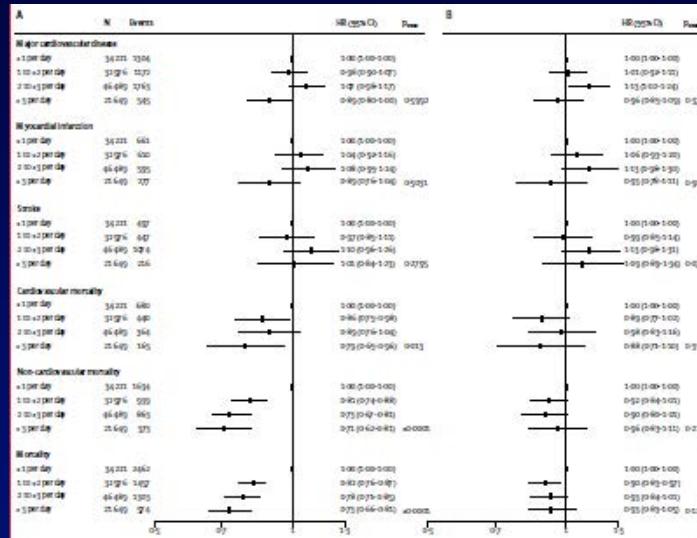
*...before drawing a definitive conclusion from this study that daily multivitamins reduce the risk of cancer in men, physicians and other readers must be convinced that the observed treatment effect is real and thus is likely to be reproduced in future experience, rather than a random event that is unlikely to recur.*

# Guidelines for Fruits and Vegetables Are Too High

## *Prospective Urban Rural Epidemiology (PURE)*

### Prospective cohort study

- n, 135,335
- age, 35-70 y
- F/U, 7.4 y



Our findings that even three servings per day (375 g/day) show similar benefit against the risk of non-cardiovascular and total mortality as higher intakes indicates that optimal health benefits can be achieved with a more modest level of consumption, an approach that is likely to be more affordable in poor countries.

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Argentina, Bangladesh, Brazil, Canada, Chile, China, Colombia, India, Iran, Malaysia, Pakistan, Palestine, Poland, South Africa, Sweden, Turkey, United Arab Emirates, Zimbabwe

Our findings that even three servings per day (375 g/day) show similar benefit against the risk of non-cardiovascular and total mortality as higher intakes indicates that optimal health benefits can be achieved with a more modest level of consumption, an approach that is likely to be more affordable in poor countries.

# Is There Evidence for Botanical Ingredients in Dietary/Food Supplements?

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## Curcumin (*Curcuma longa*)

- **total citations, 6942**
- **human intervention studies, 78**
- **meta-analyses, 11**
- **randomized controlled trials, 29**



## Green tea (*Camellia sinensis*) extracts

- **total citations, 3642**
- **human intervention studies, 77**
- **meta-analyses, 42**
- **randomized controlled trials, 23**



## Ashwagandha (*Withania somnifera*)

- **total citations, 477**
- **human intervention studies, 7**
- **randomized controlled trials, 10**



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Willing is not enough;  
we must do.***

**- Johann Wolfgang von Goethe  
(1749-1832)**

A portrait painting of Voltaire, an 18th-century French Enlightenment writer, historian, and philosopher. He is shown from the chest up, wearing a dark green velvet jacket over a white cravat and a red waistcoat. His hair is powdered and powdered. He has a slight smile and is looking slightly to the right.

*Le mieux est  
l'ennemi du bien*

The perfect is  
the enemy of the good

- Voltaire (François-Marie Arouet)  
1694-1778