

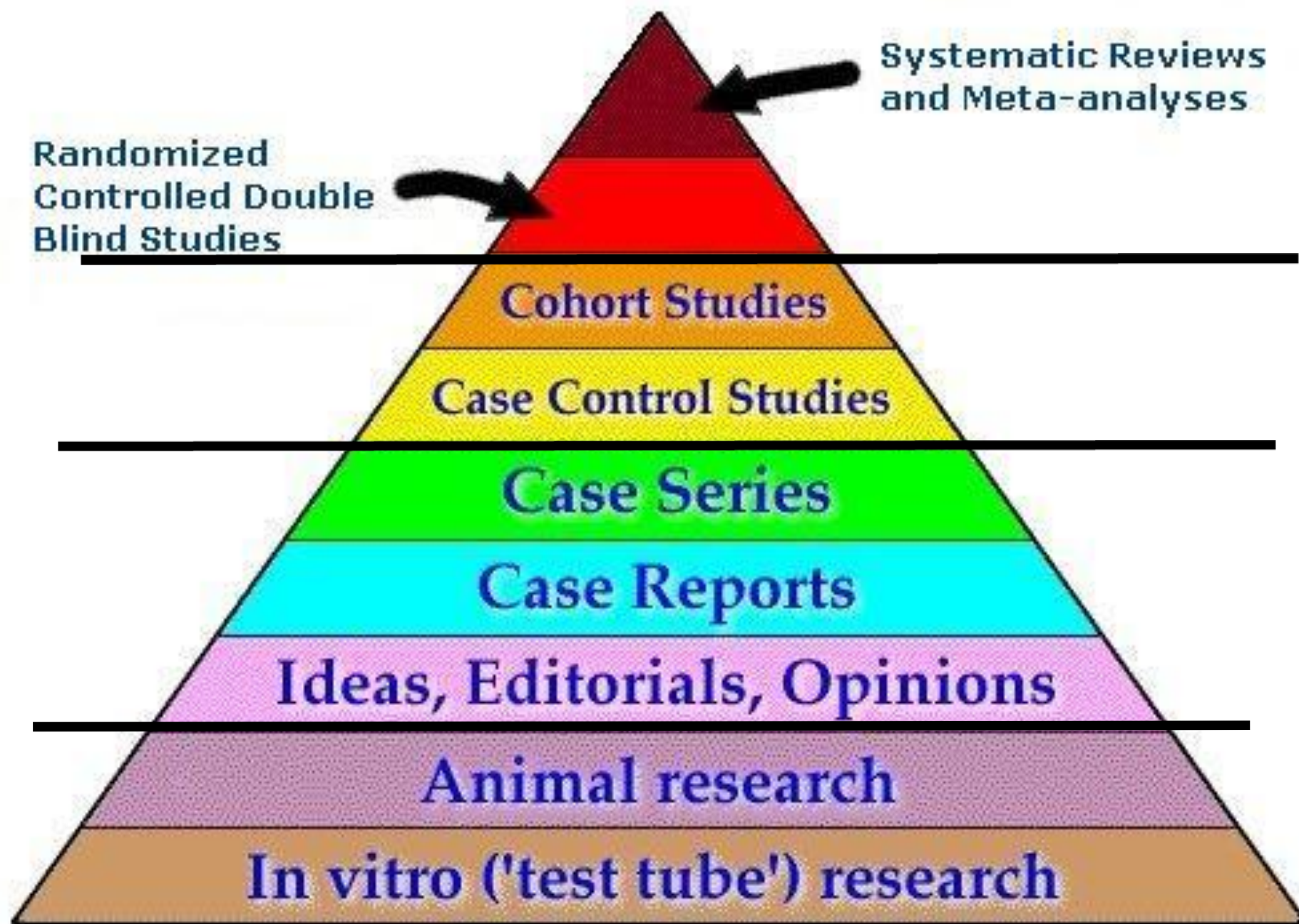


# Evidence-Based Evaluation of Benefits from Food Components

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# Disclosures

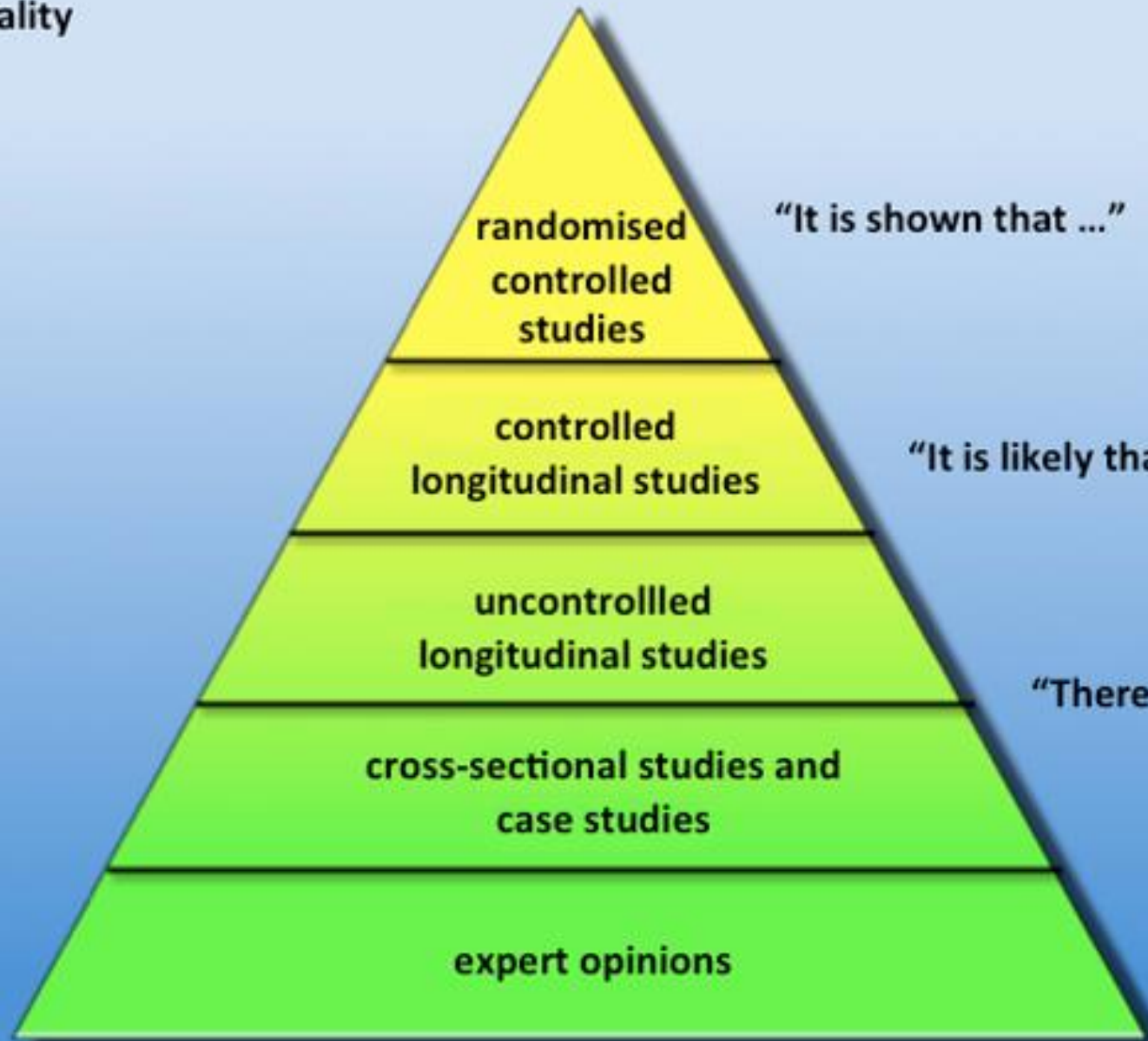
- No financial conflicts
- ACSH Board of Scientific Advisors
- AJCN Associate Editor



establish causality  
(bias --)



generate hypotheses  
(bias ++)



randomised  
controlled  
studies

“It is shown that ...”

controlled  
longitudinal studies

“It is likely that ...”

uncontrolled  
longitudinal studies

“There are signs that ...”

cross-sectional studies and  
case studies

expert opinions

“Experts are of the  
opinion that ...”

# “Causal Language in Observational Studies of Obesity and Nutrition”

		Number of articles (% of 525)	Number with causal language, (%)	p value*
Journal	AJCN	142 (27.0%)	23 (16.2%)	<0.0001
	IJO	174 (33.1%)	41 (23.6%)	
	JON	70 (13.3%)	39 (55.7%)	
	OBS	139 (26.5%)	58 (41.7%)	
Study design	case control	18 (3.4%)	9 (50.0%)	0.0660**
	cohort	241 (45.9%)	73 (30.3%)	
	cross sectional	266 (50.7%)	79 (29.7%)	
Manuscript primary result p-value	'not significant' (>0.05)	69 (14.0%)	34 (49.3%)	0.0006
	'significant' (≤0.05)	423 (86.0%)	121 (28.6%)	
Industry funding source	no	419 (79.8%)	125 (29.8%)	0.6774
	not indicated	64 (12.2%)	21 (32.8%)	
	yes	42 (8.0%)	15 (35.7%)	

AJCN = *American Journal of Clinical Nutrition*; JON= *Journal of Nutrition*; OBS = *Obesity*; IJO = *International Journal of Obesity*.

\*Chi-square comparison of number with causal language.

\*\* Fisher's exact test, p < 0.05 considered significant difference.

# Limitations of Human Nutrition Studies

- RCTs are rare for chronic disease and results have been null
- Observational studies dominate
- Most rely on potentially biased self-reports
- FFQs are semi-quantitative
  - “Validation” is simply correlation against 24-hr recall
  - Not valid for energy or protein – A Schatzkin et al, Int J Epidemiol, 2003
  - When nutrients are divided by invalid energy, no correct conclusion possible
  - Is this why diet patterns are replacing nutrients in health epidemiology?
- Baseline intake does not predict long-term diet
- Variability in nutrient content of foods is ignored

# GRADE

- Grading of Recommendations Assessment, Development and Evaluation
- GH Guyatt et al, GRADE: an emerging consensus on rating quality of evidence and strength of recommendations, BMJ 2008;336:924 and four other papers at same time; several since then.
  - Clear separation between quality of evidence and strength of recommendations
  - Explicit criteria for upgrading and downgrading quality of evidence ratings
  - RCTs begin as high quality and observational studies as low quality
- [www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)

# Rating the certainty of evidence for a causal association according to GRADE guidance

Certainty of the evidence is rated for each outcome, across studies

Randomized controlled trials with a high rating, observational studies with a low rating

Rating is then modified downward:

✓ Study limitations

✓ Imprecision

✓ Inconsistency of results

✓ Publication bias likely

Rating is then modified upward:

✓ Large magnitude of effect

✓ Dose response is observed

✓ Confounders likely minimize the effect

Final rating for each outcome is 'high', 'moderate', or 'low'



# Traditional DRIs vs. DRIs for Chronic Disease





Traditional DRIs	Chronic Disease DRIs
DRIs for essential nutrients are needed because their deficiencies and toxicities:	Are not warranted unless <u>sufficient evidence</u> exists because:
a) will affect everyone, if intake is inadequate	a) risk to acquire CDs varies by individual
b) are caused by one nutrient	b) chronic diseases are often related to many risk factors (genetic, environmental)
c) are prevented by nutritional interventions	c) nutritional interventions will only partly ameliorate the risk of CD

# Association Between Dietary Factors and Mortality From Heart Disease, Stroke, and Type 2 Diabetes in the United States

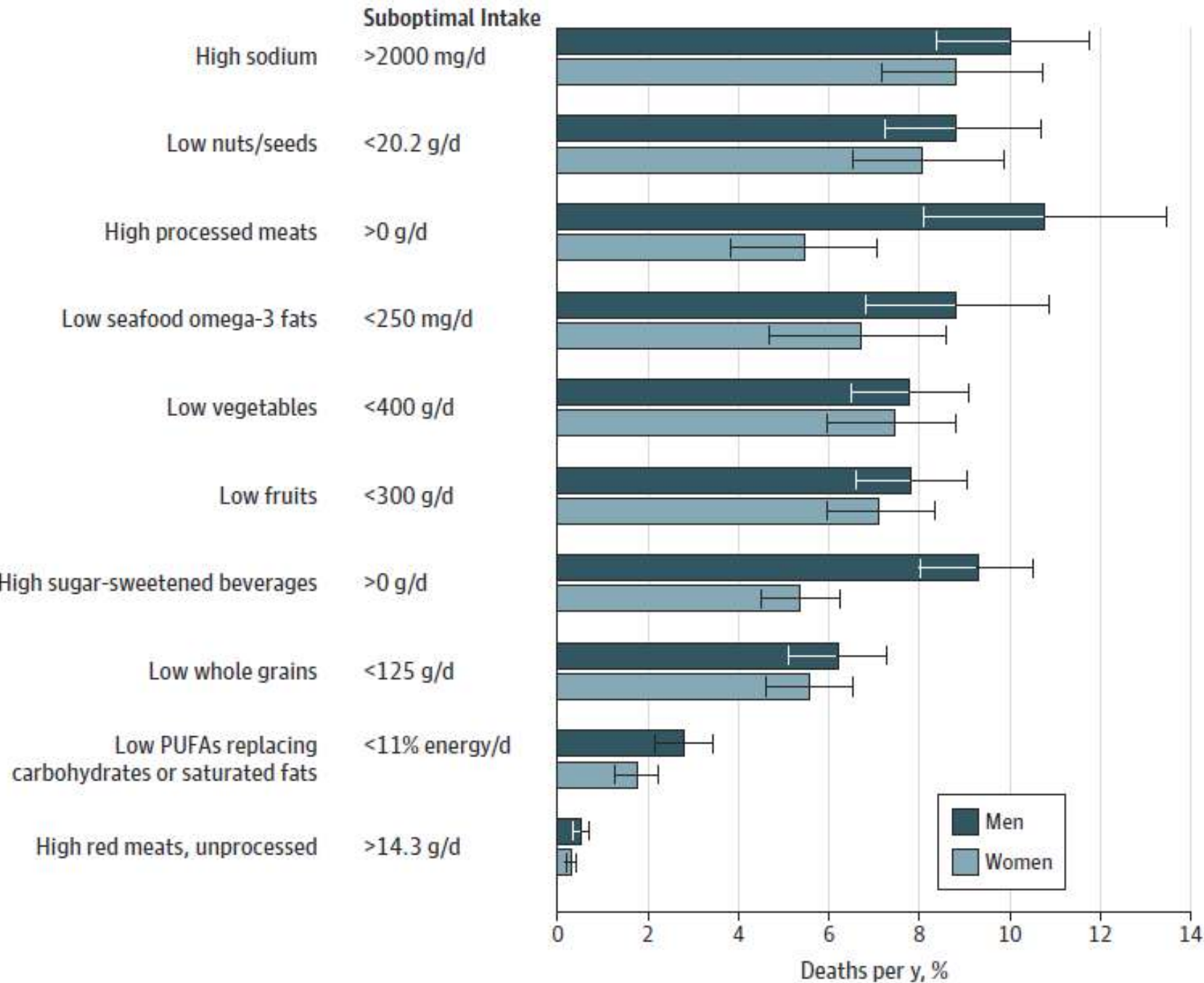
Renata Micha, RD, PhD; Jose L. Peñalvo, PhD; Frederick Cudhea, PhD; Fumiaki Imamura, PhD; Colin D. Rehm, PhD; Dariush Mozaffarian, MD, DrPH

**IMPORTANCE** In the United States, national associations of individual dietary factors with specific cardiometabolic diseases are not well established.

**OBJECTIVE** To estimate associations of intake of 10 specific dietary factors with mortality due to heart disease, stroke, and type 2 diabetes (cardiometabolic mortality) among US adults.

-  [Editorial page 908](#)
-  [JAMA Report Video](#)
-  [Supplemental content](#)
-  [CME Quiz at   
jamanetworkcme.com](#)

Proportional cardiometabolic mortality attributable to dietary habits in the United States in 2012



Cumulatively, 45% of deaths associated with suboptimal intake in abstract but this figure claims those deaths are attributable to dietary habits

# “Attributing Death to Diet. Precision Counts”

- Assumption that exposure-outcome relationship is causal
  - Strong evidence from randomized trials not available
  - Confounding bias could be substantial
- Are the 10 factors the right set?
  - Not included: trans fat, sugar, potassium
- How dietary factors are interrelated and modified by each other
  - Unreasonable to assume factors are all additive to affect 70% of deaths
- “The findings reported by Micha et al appear correct
  - But the reduction could be 30% to 70%.”

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

Thomas R. Frieden, M.D., M.P.H.

**A** CORE PRINCIPLE OF GOOD PUBLIC HEALTH PRACTICE IS TO BASE ALL policy decisions on the highest-quality scientific data, openly and objectively derived.<sup>1</sup> Determining whether data meet these conditions is difficult; uncertainty can lead to inaction by clinicians and public health decision makers. Although randomized, controlled trials (RCTs) 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.<sup>2-8</sup> In this article, I describe the use of RCTs and alternative (and sometimes superior) data sources from the vantage point of public health, illustrate key limitations of RCTs, and suggest ways to improve the use of multiple data sources for health decision making.

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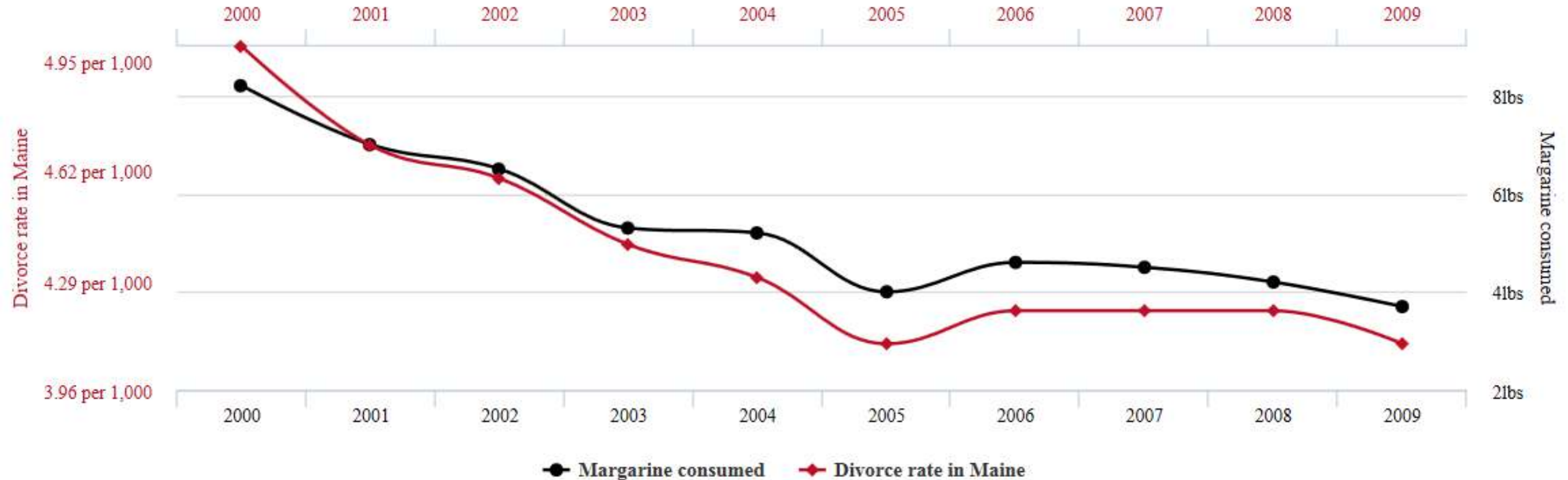
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# Divorce rate in Maine

correlates with

## Per capita consumption of margarine

Correlation: 99.26% ( $r=0.992558$ )



tylervigen.com

# Red Meat: 7 of 14 cohort studies Processed Meat: 12 of 18 cohort studies

## Carcinogenicity of consumption of red and processed meat

In October, 2015, 22 scientists from ten countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to evaluate the carcinogenicity of the consumption of red meat and processed meat. These assessments will be published in volume 114 of the IARC Monographs.<sup>1</sup>

Red meat refers to unprocessed mammalian muscle meat—for example, beef, veal, pork, lamb, mutton, horse, or goat meat—including minced or frozen meat; it is usually consumed cooked

more than 200 g per person per day.<sup>4</sup> Less information is available on the consumption of processed meat.

The Working Group assessed more than 800 epidemiological studies that investigated the association of cancer with consumption of red meat or processed meat in many countries, from several continents, with diverse ethnicities and diets. For the evaluation, the greatest weight was given to prospective cohort studies done in the general population. High quality

day of red meat and an 18% increase (95% CI 1.10–1.28) per 50 g per day of processed meat.<sup>12</sup>

Data were also available for more than 15 other types of cancer. Positive associations were seen in cohort studies and population-based case-control studies between consumption of red meat and cancers of the pancreas and the prostate (mainly advanced prostate cancer), and between consumption of processed



*Lancet Oncol* 2015

Published Online

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[http://dx.doi.org/10.1016/](http://dx.doi.org/10.1016/S1470-2045(15)00444-1)

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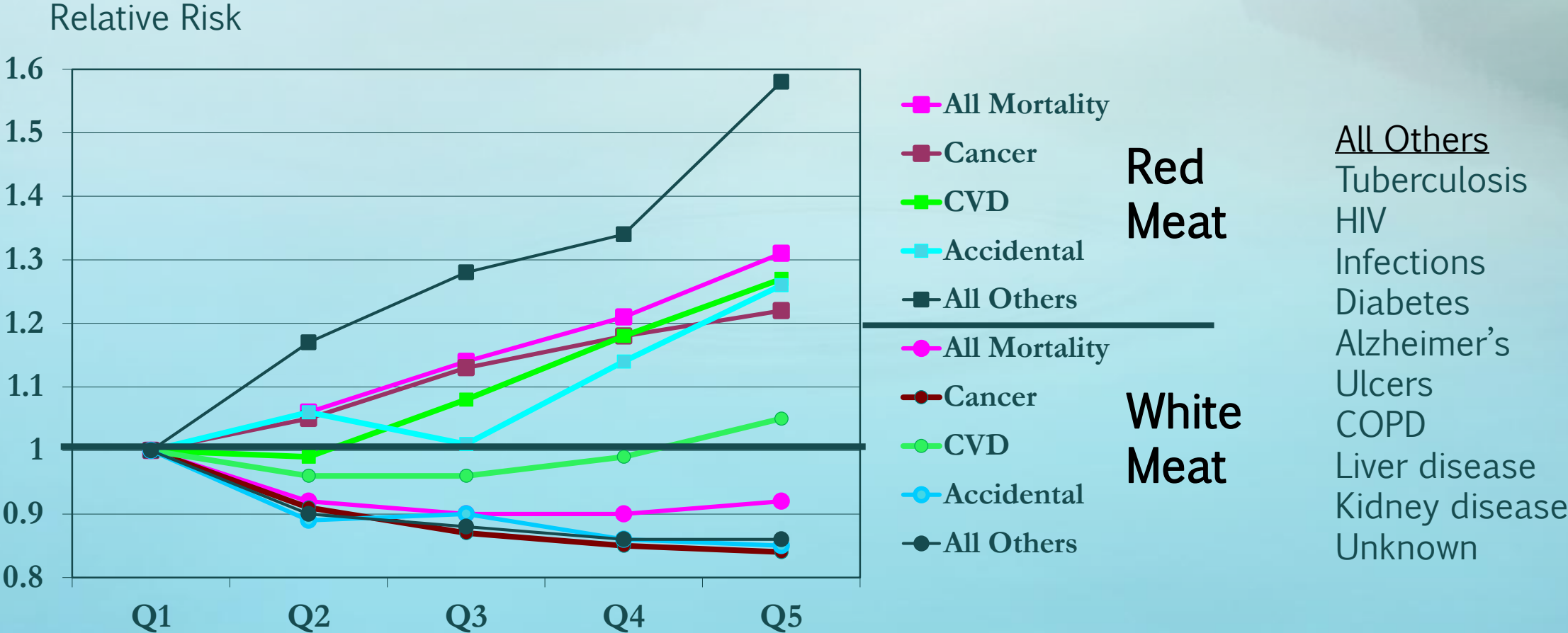
Monograph with all data was to be published by IARC sometime in 2016

# Risk of Colon Cancer Associated with Meat Consumption

- **Absolute Risk**
  - Lifetime risk of colon cancer among vegetarians – 4.5%
  - Lifetime risk of colon cancer among people who eat two ounces of processed meat every day – 5.3%
- **IARC Identified hazard, not degree of risk**
  - **Statistical significance in human studies was determined by RR!!**
  - No systematic literature search
  - Quality of individual studies was not evaluated
  - No meta-analysis – Lancet Oncology summary cited a 2011 meta-analysis by one member not mentioned at working group meeting
  - Virtually no review of epidemiology studies by rest of working group



# Meat Intake and Mortality NIH-AARP Study



71,000 deaths in 500,000 people DM Klurfeld, Meat Sci 109:86 (2015)  
 adapted from R Sinha et al, Arch Intern Med 169:562 (2009)

# RCTs and Colon Cancer

- **Polyp Prevention Trial**

- ~950 subjects/group with polyp removed, 3 yr follow-up
- Low meat diet high in F/V, whole grains, legumes
- A Schatzkin et al, NEJM 342:1149-1152, 2000
- RR of recurrence – **1.00** (95% CI, 0.90-1.12)

- **Women's Health Initiative**

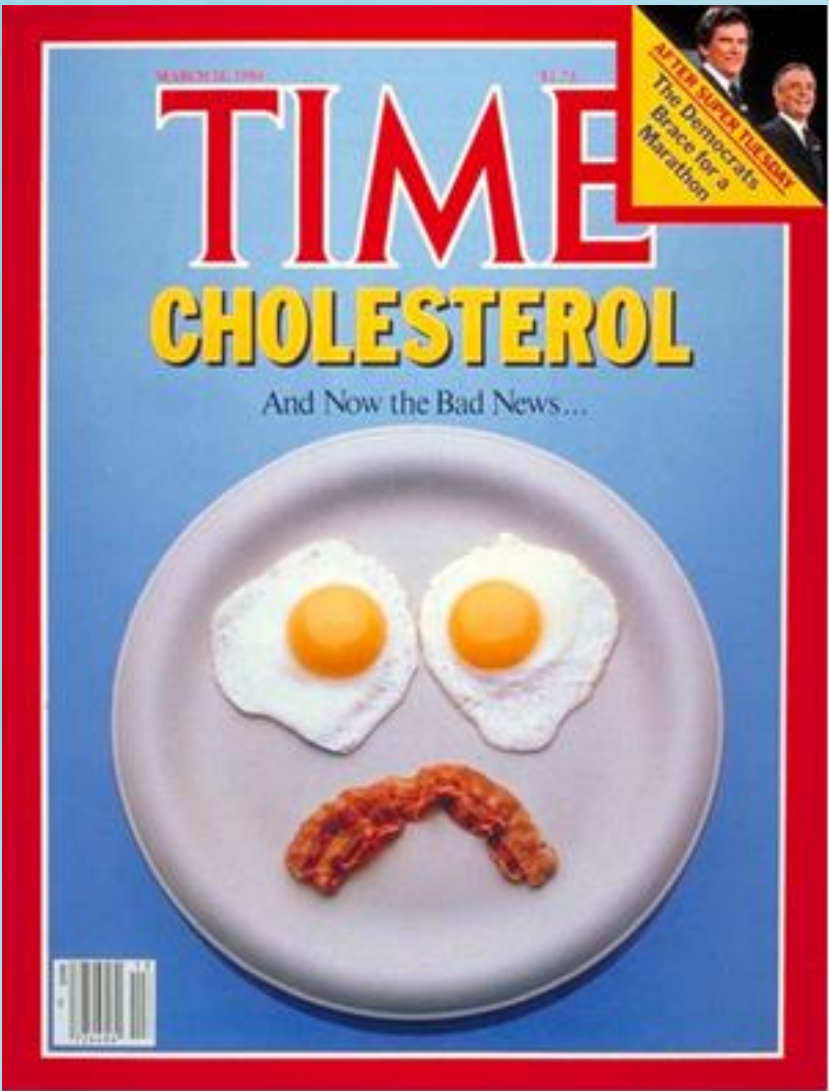
- 19,500 on low fat, low meat diet; 29,000 on usual diet for up to 9 yr
- SA Beresford et al, JAMA 295:643-654, 2006
- RR of colon cancer – **1.08** (95% CI, 0.90-1.29)

# When is a carcinogen not a carcinogen?

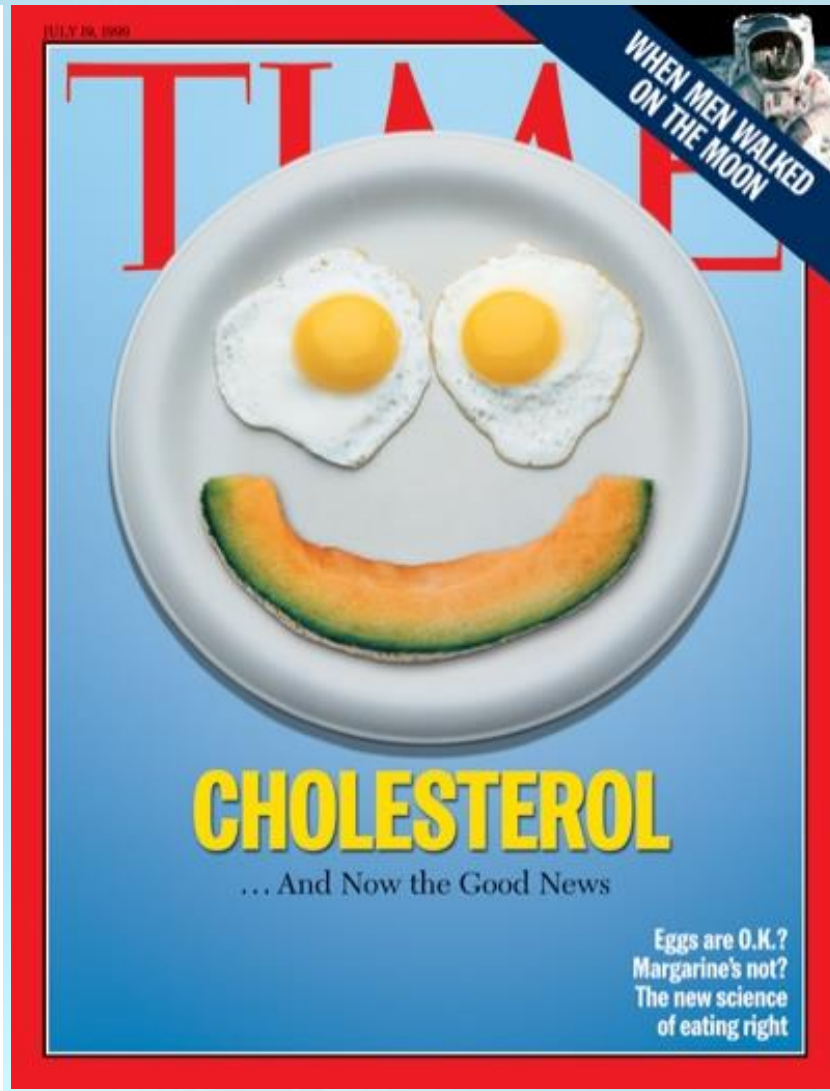
*Lancet Oncology editorial, June 2016*

A month rarely passes by without something being declared unhealthy or carcinogenic. Often, the WHO International Agency for Research on Cancer (IARC) is at the centre of such pronouncements and is duly rounded on to explain the consequences. IARC, however, is not the only agency with responsibility for determining carcinogenicity of products, compounds, or lifestyles,

These latest disputes regarding carcinogen classification highlight the problem of determining reliable findings when data are equivocal and where there are vested interests. They also highlight the difficulties of translating carcinogenicity research into appropriate health policies and recommendations for risk management. Furthermore, there is an equally clear need for a standardised, internationally agreed methodology for carcinogen assessment, alongside ways of presenting results that are easily understood and accepted by all interested parties. Until these objectives are met, carcinogen definition and regulation will continue to be the poor relation to other cancer preventative measures. ■ *The Lancet Oncology*



1984



1999



2014

# Key Takeaways

- Nutrition research will not earn the same respect as other hard science fields until we accept the same rigorous standards for reaching conclusions
- Grading of nutrition recommendations should be done with existing processes like systematic reviews, meta-analyses and GRADE
- Uncertainty factors point to the need for precision nutrition; targeting based on differences in genome, proteome, epigenome, metabolome, microbiome ...
  - Personalized nutrition sounds great but likely overpromises
  - One-size-fits-all approach is likely to fade away



**Evidence**

**27**

**Implementation**

**590**