

"Food is an important part of a balanced diet"

Fran Lebowitz

Nutrition and the Evidence Conundrum

What we know (very little) and what we will
likely never know (a lot) about nutrition

James McCormack, BSc(Pharm), Pharm D
Professor, Faculty of Pharmaceutical Sciences, UBC

*"Few things are more prey to fad and fashion
than alleged dietary influences on health"*

Geoff Watts - BMJ

Real Conflicts of Interest

I like food - there is very little else I actively wish to do three times a day

I have a sweet tooth

Chicken and beef are delicious but I don't eat them because of animal rights issues - but I do eat seafood

I think margarine tastes awful

Egg McMuffins (no meat) and Poutine (yes I know it has gravy in it) are delicious

For me any diet must include wine and chocolate



Why is a pharmacist talking about nutrition?

Pharmacists are not experts in nutrition - likely make errors with some “nutritiony” terms

Dieticians are experts in designing, implementing and monitoring nutritional care plans

Why is a pharmacist talking about nutrition?

WHERE I'M COMING FROM

In general, nutrition recommendations should be based on the best available evidence

Clinical trials are likely the “best” way to assess the health impact of dietary modifications

A dietitian is not necessarily an expert at looking at clinical trials

You need someone who is good at critically looking at evidence BUT there are some fundamental problems with the overall nutrition evidence base

Food Tribes:

Making up the rules as we go

Locavores - local food

Low Sodium Tribe

No-Gluten Tribe

The Vegan/Vegetarian Tribe

Paleolithic Tribe - Atkins with
Caveman Imagery

The Eliminators - Low Sugar/
Low Fat



Randy Shore - Vancouver Sun March 15 2014

When do we have debate about health issues?

the answer may be impossible to know
the best available evidence is tenuous
the potential difference in outcome is “small”
there is a belief about “a mechanism”
the stakes are high - pharmaceutical and
nutrition beliefs are very “marketable”

FOOD, especially with individual
nutrients, HAS ALL OF THESE

Cause and Effect



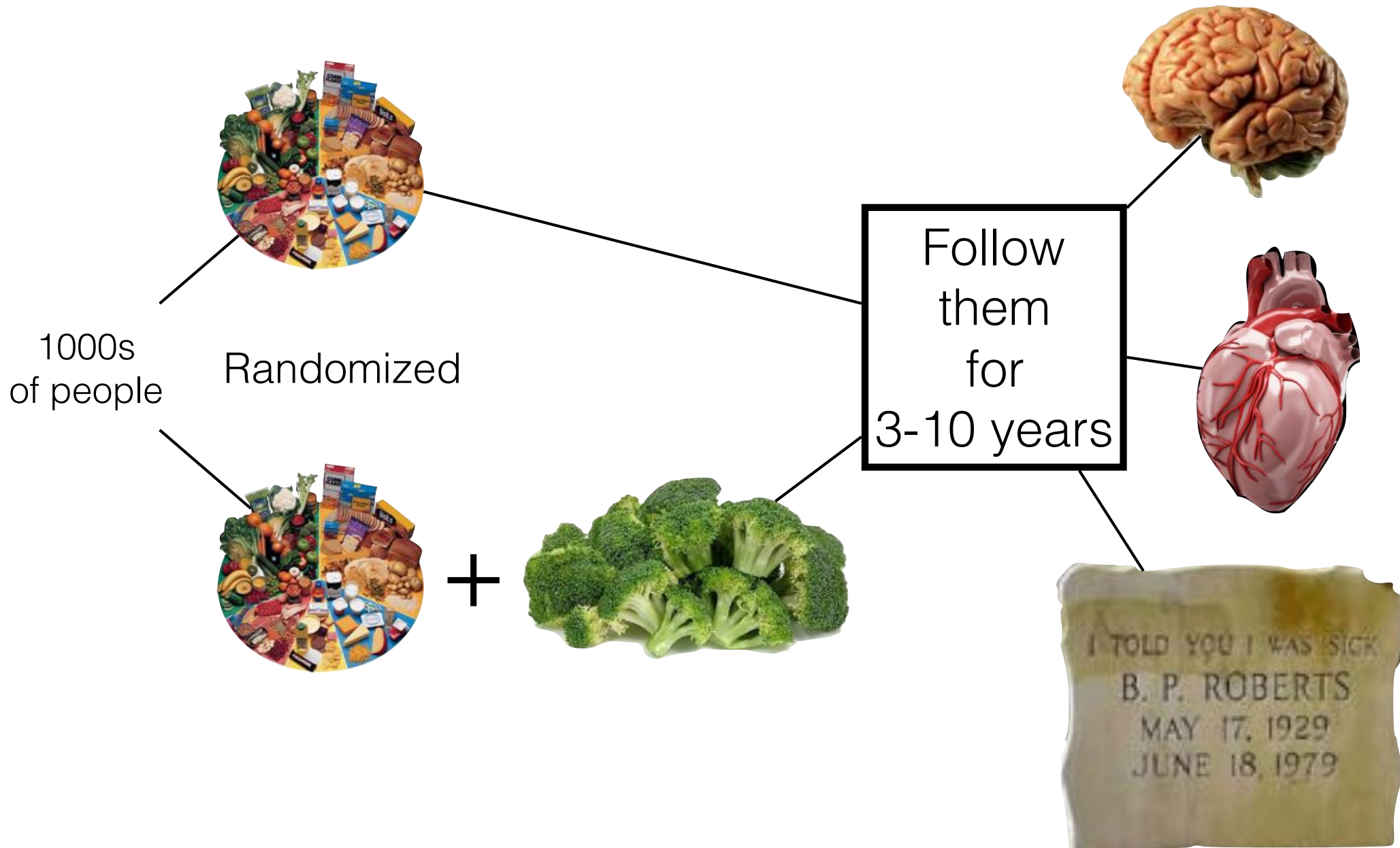
How do we
figure out
whether “food”
is healthy or
unhealthy?

****BIG** effects in nutrition have occurred
Vitamin deficiencies, Gross malnutrition etc**

How do we differentiate
association from causality?

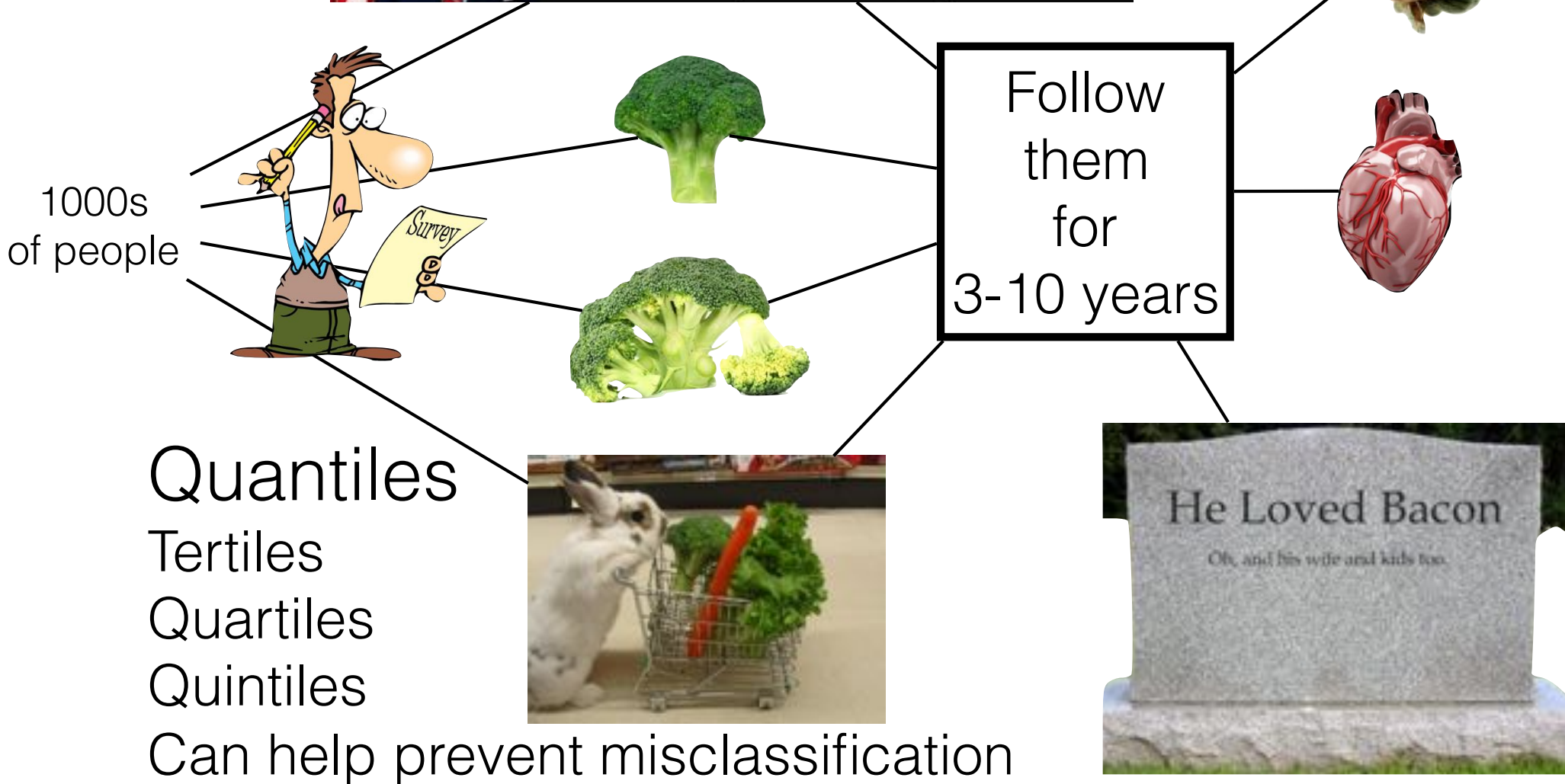
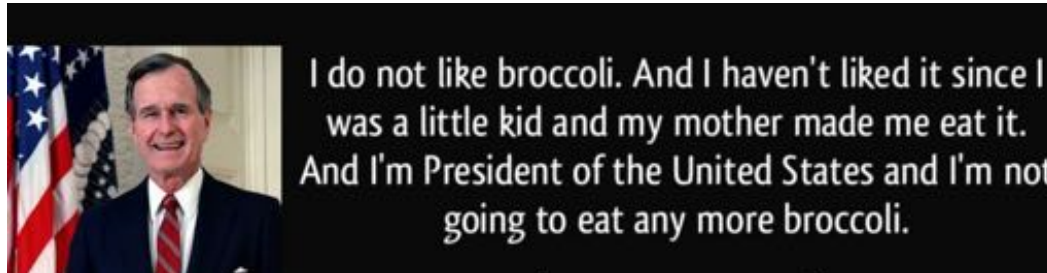
Then, how big is the effect?

The Best Way - RCTs - 10s



The OK way - Cohort Studies - 1000s

Prospective or retrospective



Nutritional cohort studies

EXAMPLES OF BIASES

Recall bias

Everybody is unblinded

EXAMPLES OF CONFOUNDING

When we see real differences but, there is a “third” cause

Coffee - does it cause lung cancer - smoking is a confounder

Beer preference is associated with less healthy dietary behaviour, especially compared with wine preference

Eating “healthy” - may be more physically active

Alcohol intake - may be more social, less stress

Nutritional studies

ALL STUDIES

PUBLICATION BIAS

Publish findings that are found to show differences or are controversial

REPORTING BIAS

Media flip-flopping - more likely to report “NEW or DIFFERENT” findings

Sugar Industry and Coronary Heart Disease Research

A Historical Analysis of Internal Industry Documents

Cristin E. Kearns, DDS, MBA; Laura A. Schmidt, PhD, MSW, MPH; Stanton A. Glantz, PhD

“Access to documents not meant for public consumption has provided the public health community unprecedented insight into industry motives, strategies, tactics, and data designed to protect companies from litigation and regulation.” and “Policymaking committees should consider giving less weight to food industry–funded studies”

HEALTH CARE POLICY AND LAW

Food Industry Funding of Nutrition Research

The Relevance of History for Current Debates

Marion Nestle, PhD, MPH

“ Today, it is almost impossible to keep up with the range of food companies sponsoring research—from makers of the most highly processed foods, drinks, and supplements to producers of dairy foods, meats, fruits, and nuts — typically yielding results favorable to the sponsor’s interests”

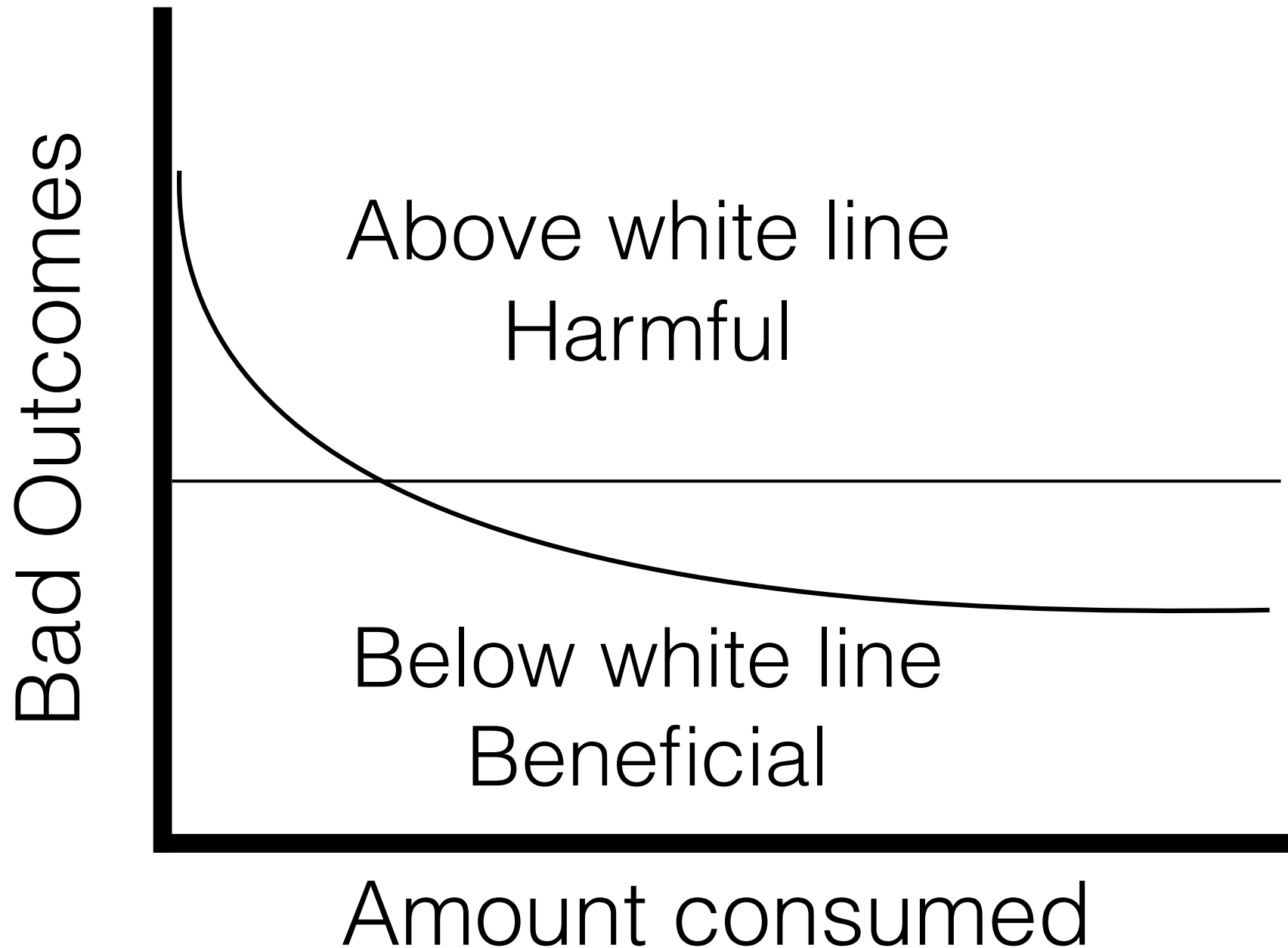
But despite all the limitations of observational studies, they will often be the best we have and will likely be the best we will ever have because RCTs may not be possible

U.S. Dietary Guidelines: An Evidence-Free Zone

Steven E. Nissen, MD

“a detailed review of the new guidelines confirms a disturbing reality: the nearly complete absence of high-quality randomized, controlled clinical trials (RCTs) studying meaningful clinical outcomes for dietary interventions. The report repeatedly makes recommendations based on observational studies and surrogate end points, failing to distinguish between recommendations based on expert consensus rather than high-quality RCTs. Unfortunately, the current and past U.S. dietary guidelines represent a nearly evidence-free zone”

Nutritional cohort studies



The Worst Way (to infer causality) - “Mechanisms” - 1000s

Assess the impact of nutrition on surrogate markers or get wedded to an hypothesis

insulin

glucose

lipids

weight

ketones

blood pressure

hormone balance

atherosclerosis

endothelial function

Eat what people ate 10,000+ years ago

What can we study?

Implausible results in human nutrition research

Definitive solutions won't come from another million observational papers or small randomized trials

John P A Ioannidis *professor of medicine, health research and policy, and statistics*

Stanford Prevention Research Center, Stanford, CA 94305, USA

BMJ 2013;347:f6698

Objectively speaking, we can't get definitive answers from more studies because they all have important biases, there are numerous confounders and evaluating surrogate markers is fraught with problems

Single Nutrients

“on the basis of dozens of randomized trials, single nutrients are unlikely to have relative risks less than 0.90 for major clinical outcomes ...”

“... most are greater than 0.95”

In other words, if differences exist they are
<10% and may be <5%

“Observational studies and even randomized trials of single nutrients

*seem hopeless,
with rare exceptions”*

BMJ 2013;347:f6698

Multiple Nutrients and Behaviours

“Larger effect sizes [ie. >10%] are more plausible for complex dietary patterns that sum the effects of multiple nutrients and behaviors”

PREDIMED, Lyon Diet Heart Study

Now, it is possible to *“identify nutrition related interventions that produce a 5-10% relative risk reduction in overall mortality in the general population”*

However, this would require
>10 times the sample size of PREDIMED
(n = 80,000 and 4,000 endpoints)

Risk of Smoking

The negative impact of smoking on CVD, cancer, lungs etc may be an order of magnitude larger than the effect of any single nutrient and possibly as big as, if not more, than overall nutrition

No RCTs because they are unethical

Decades to get to the “truth”

Dozens of cohort studies and mechanistic studies

Companies were able to convince people that smoking can't be concluded as a problem because of the confounders!!!

Sheer weight of evidence prevailed



The Process

Present the best available evidence I could find - MA or SR

Not doing a detailed critical appraisal - all RCTs and cohorts have design and implementation issues

If these “studies” I present have serious limitations then we are basically stuck with opinion that is not informed by evidence



You do not have to know
the details of every study
on these slides

Single Nutrients

and some little behaviours

Salt, breakfast, eggs, fiber,
coffee, daily servings, chocolate, alcohol

Does salt increase blood pressure and increase risk of cardiovascular disease?

The problem of the surrogate marker

Salt

Average Canadian daily
intake ~3000 mg/day

Health Canada

“This is more than double the
amount we need”

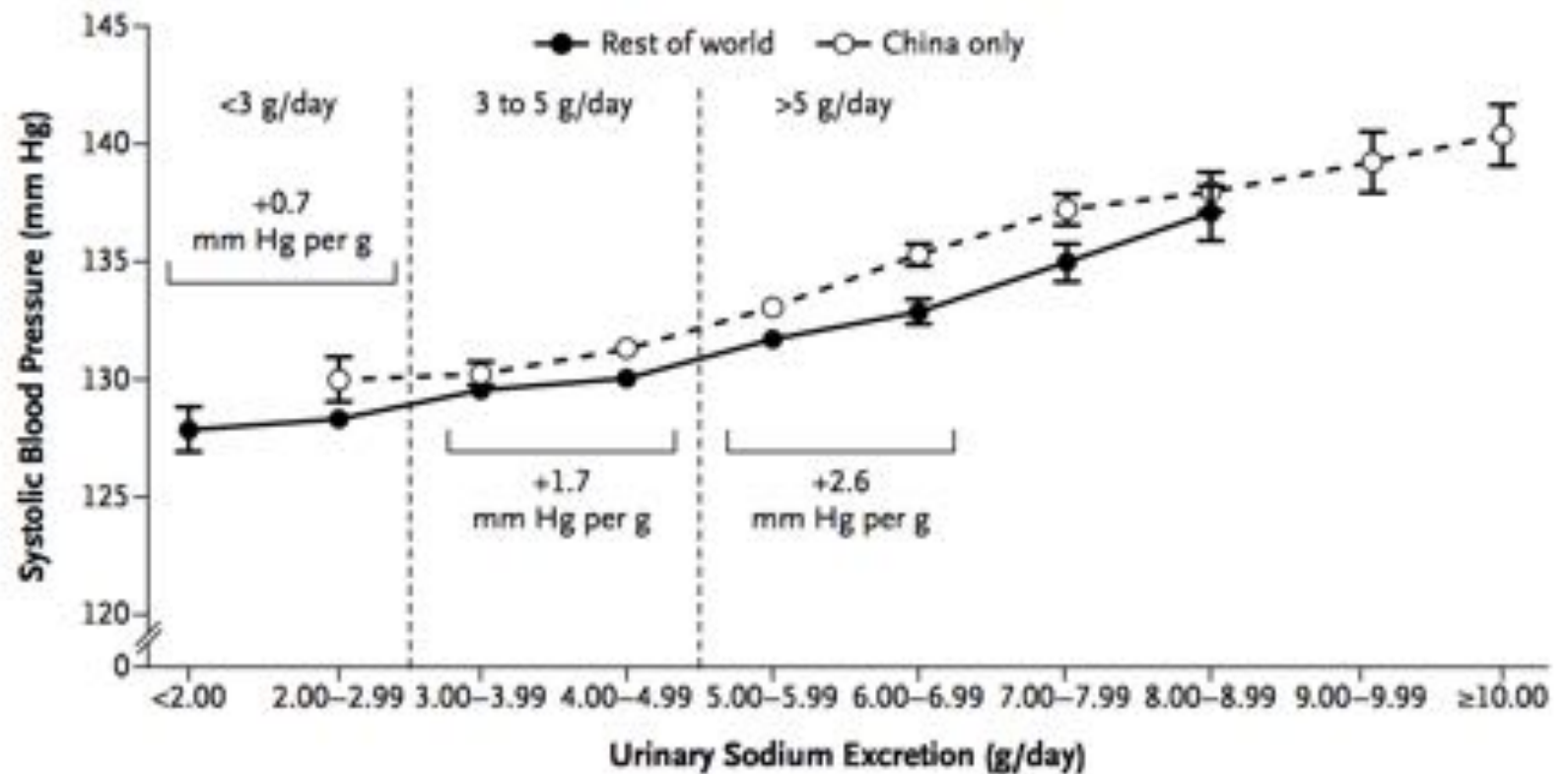
Aim for 1500 mg/day and
don't go over 2300 mg/day

BUT



Salt does (on average) increase BP

A



No. of Participants

China	1876	6,012	9,794	10,101	7177	4093	2035	1002	952
Other countries	1613	7384	15,101	16,015	10,810	5211	2048	992	

N Engl J Med 2014;371:601-11

Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials

“A modest reduction in salt intake for four or more weeks causes significant and, from a population viewpoint, important falls in blood pressure”

BMJ 2013;346:f1325 doi: 10.1136/bmj.f1325

Sodium Intake in Populations

Assessment of Evidence

Committee on the Consequences of Sodium Reduction in Populations
Food and Nutrition Board
Board on Population Health and Health Practice

Brian L. Strom, Ann L. Yaktine, and Maria Oria, *Editors*

Institute of Medicine - May 2013

“evidence from studies on direct health outcomes is inconsistent and insufficient to conclude that lowering sodium intakes below 2,300 mg per day either increases or decreases risk of CVD outcomes”

“the available evidence suggests that low sodium intakes may lead to higher risk of adverse events in mid- to late-stage CHF patients with reduced ejection fraction and who are receiving aggressive therapeutic regimens”

PURE study

Cohort - 101,945 people in 17 countries - 3.7 years
Association between CVD and sodium **excretion**

Rates of mortality and cardiovascular events, depending on grams of sodium excretion per day



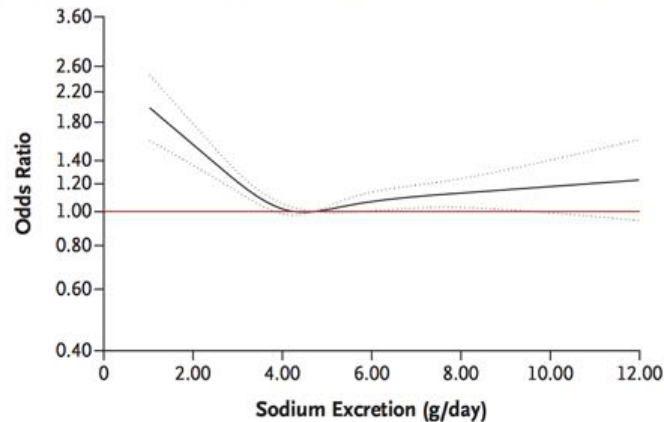
ABSOLUTE RISKS

N Engl J Med 2014;371:612-23

PURE study

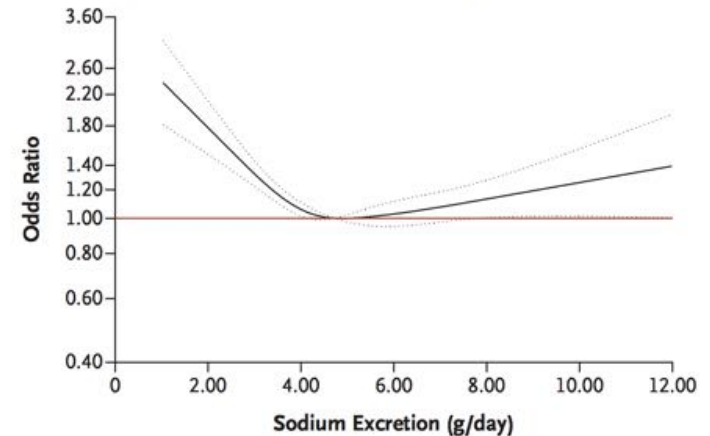
Cohort - 101,945 people in 17 countries - 3.7 years
Association between CVD and sodium **excretion**

A Estimated Sodium Excretion and Risk of Death or Cardiovascular Events



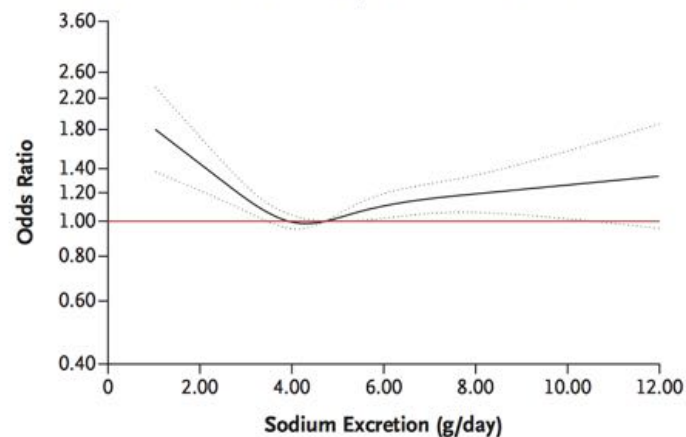
No. of Events	101	1,023	1,437	597	126	25
No. at Risk	1817	30,124	46,663	18,395	3885	756

B Estimated Sodium Excretion and Risk of Death from Any Cause



No. of Events	68	642	826	340	79	16
No. at Risk	1817	30,124	46,663	18,395	3885	756

C Estimated Sodium Excretion and Risk of Major Cardiovascular Events



No. of Events	57	602	869	369	75	13
No. at Risk	1817	30,124	46,663	18,395	3885	756

“These provocative findings beg for a randomized, controlled outcome trial to compare reduced sodium intake with usual diet. In the absence of such a trial, the results argue against reduction of dietary sodium as an isolated public health recommendation”

N Engl J Med 2014;371:677-9

Compared With Usual Sodium Intake, Low- and Excessive-Sodium Diets Are Associated With Increased Mortality: A Meta-Analysis

Usual daily sodium intake (115-215 mmol or 2,645-6,613 Na)

23 cohorts and 2 follow up RCTs

All cause mortality

HR 0.91 (0.82-0.99) in favour of usual vs low sodium

HR 1.16 (1.03-1.30) in favour of usual vs high sodium

Overall CVD

HR 0.90 (0.82-0.99) in favour of usual vs low sodium

HR 1.12 (1.02-1.24) in favour of usual vs high sodium

Reduced dietary salt for the prevention of cardiovascular disease (Review)

Adler AJ, Taylor F, Martin N, Gottlieb S, Taylor RS, Ebrahim S

“there is insufficient power to confirm clinically important effects of dietary advice and salt substitution on cardiovascular mortality in normotensive or hypertensive populations. Our estimates of the clinical benefits from advice to reduce dietary salt are imprecise, but are larger than would be predicted from the small blood pressure reductions achieved. Further well-powered studies would be needed to obtain more precise estimates. Our findings do not support individual dietary advice as a means of restricting salt intake”

CD009217-2014

The technical report on sodium intake and cardiovascular disease in low- and middle-income countries by the joint working group of the World Heart Federation, the European Society of Hypertension and the European Public Health Association

“Prospective cohort studies have identified the optimal range of sodium intake to reside in the moderate range (3–5 g/day), where the risk of cardiovascular disease and death is lowest. Therefore, there is consistent evidence from clinical trials and observational studies to support reducing sodium intake to less than 5 g/day in populations, but inconsistent evidence for further reductions below a moderate intake range (3–5 g/day).”

Does skipping breakfast
increase risk of obesity or
impact cognitive performance?

The problem of the cohort studies versus the RCT



FOOD

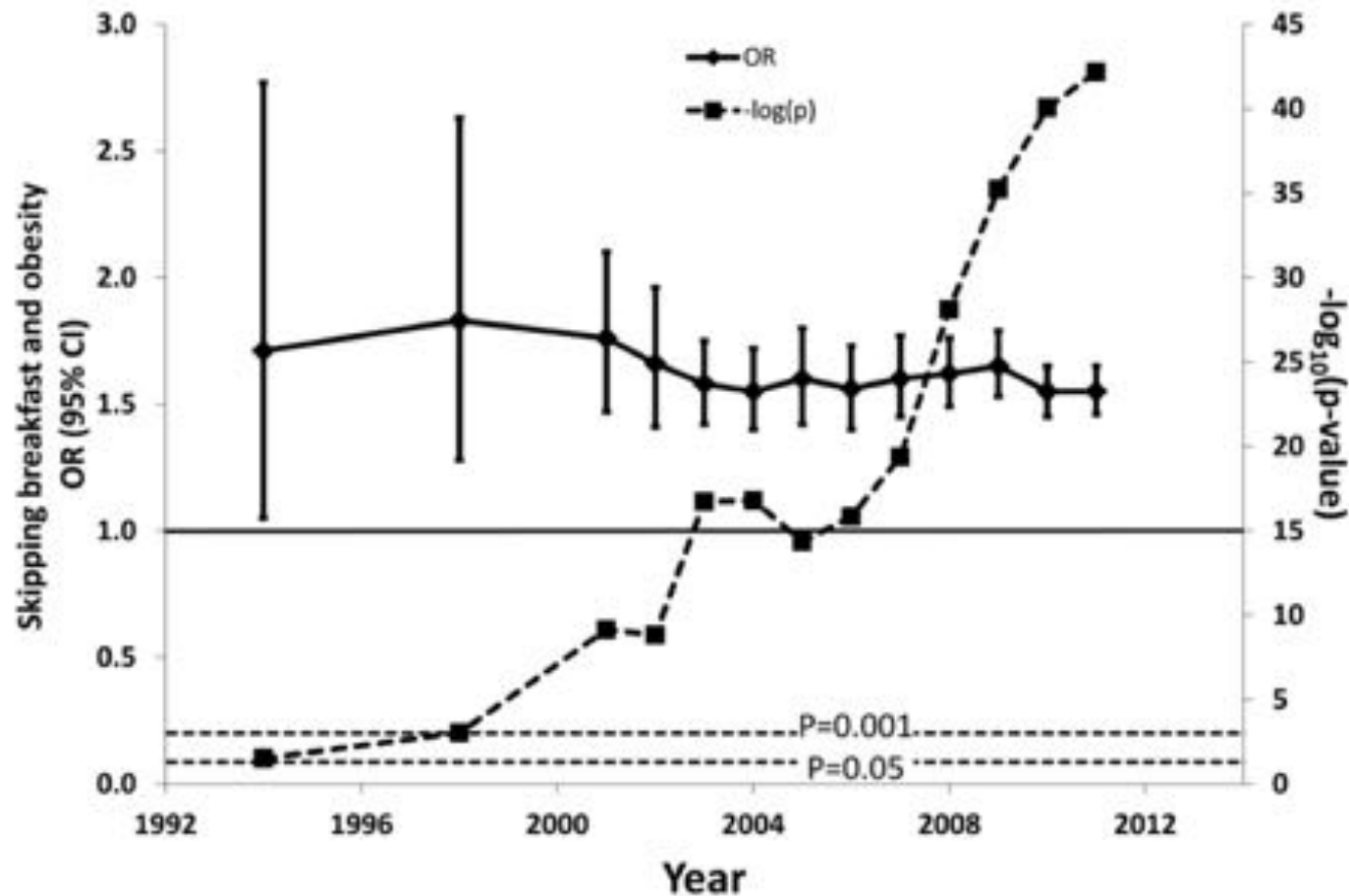
The New York Times Is Breakfast Overrated?

By GRETCHEN REYNOLDS

AUGUST 21, 2014 12:01 AM



58 studies - cross-sectional observational



But 5 of 8 RCTs - no difference

Am J Clin Nut 2013;98:1298-308

The effectiveness of breakfast recommendations on weight loss: a randomized controlled trial¹⁻³

16 weeks - 309 participants - 3 groups - control group, eat breakfast, skip breakfast

“A recommendation to eat or skip breakfast for weight loss was effective at changing self-reported breakfast eating habits (~93%), but contrary to widely espoused views this had no discernible effect on weight loss in free-living adults who were attempting to lose weight.”

Am J Clin Nutr 2014;100:507–13

The causal role of breakfast in energy balance and health: a randomized controlled trial in lean adults¹⁻⁴

33 participants - 6 weeks - breakfast group/
fasting group - looked at energy balance,
glycemic response, body mass

breakfast group - increased energy intake
BUT a similar increase in activity

no difference in body mass or adiposity

The effect of breakfast composition and energy contribution on cognitive and academic performance: a systematic review¹⁻³

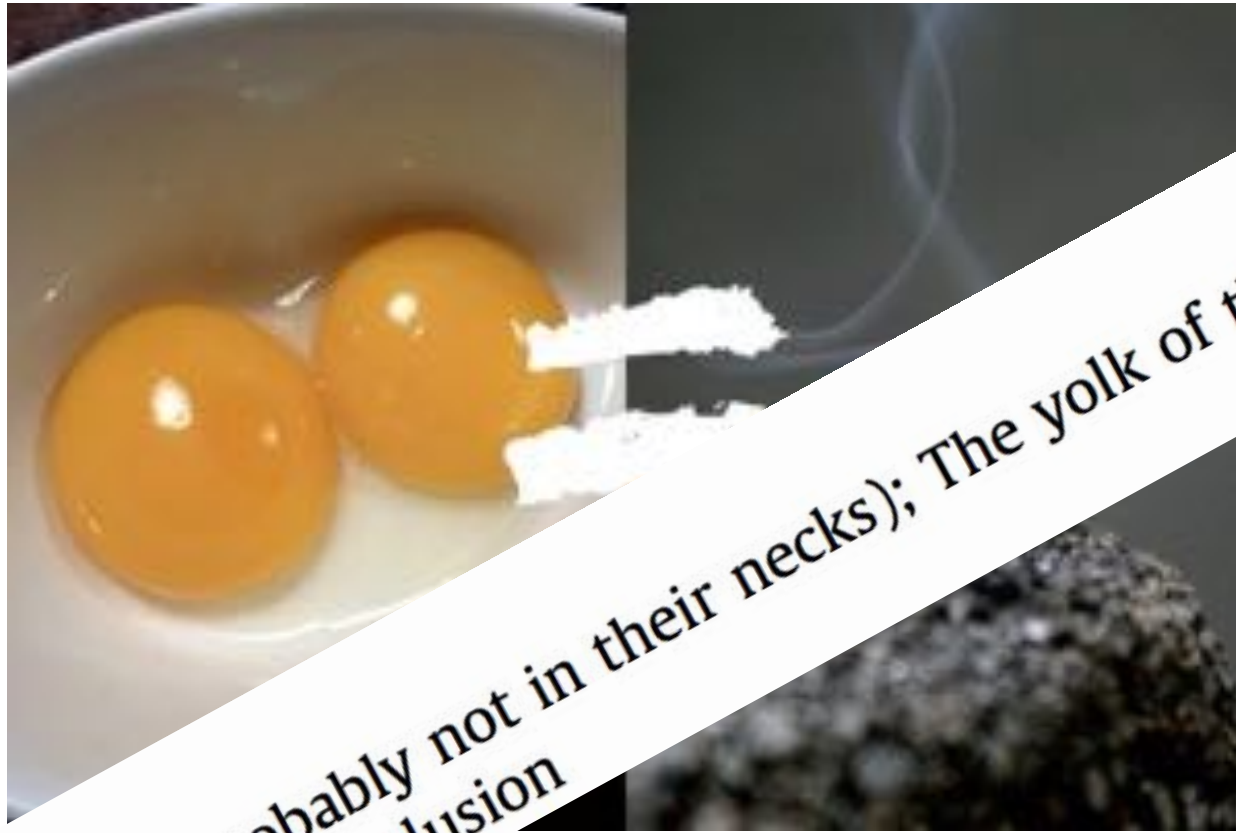
15 studies

“there was insufficient quantity and consistency among the studies to draw firm conclusions on the relation between the amount of energy intake at breakfast and breakfast composition and cognitive and academic performance”

Do eggs increase the risk
of coronary heart
disease?

The problem of mechanisms and surrogate markers

2012



Letter to the Editor

“Egg on their faces (probably not in their necks); The yolk of the tenuous cholesterol-to-plaque conclusion

almost as bad as smoking”

“breakfast is trying to murder you”

“do egg yolks and smoking have in common”

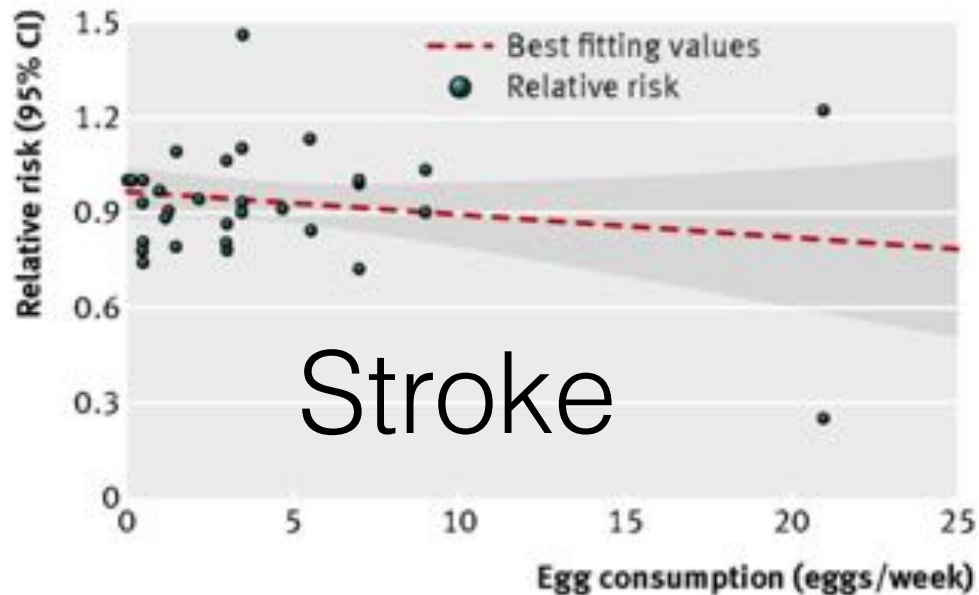
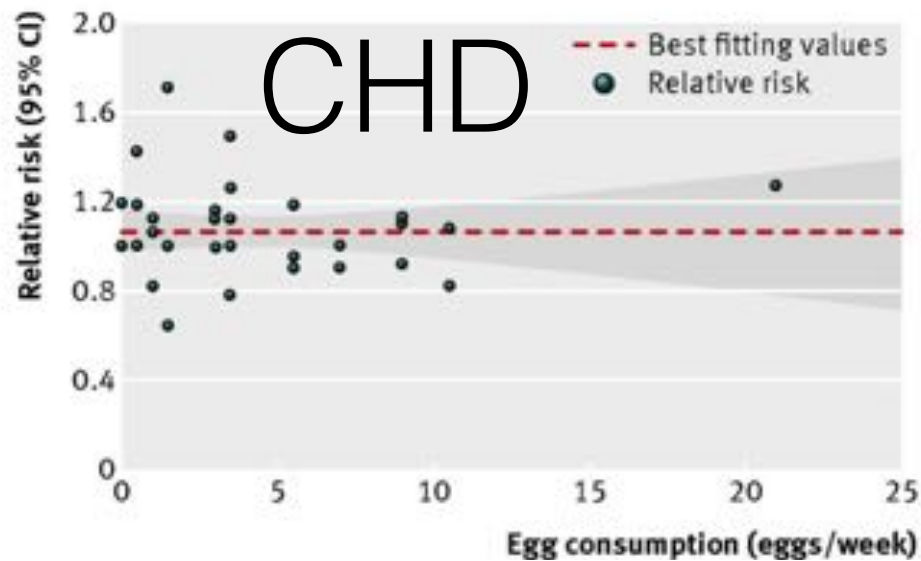
Atherosclerosis 2012;224:469-73

Egg consumption and risk of coronary heart disease and stroke: dose-response meta-analysis of prospective cohort studies

8 articles - 17 reports - 9 for CHD, 8 for stroke

3,081,269 person years and 5847 incident cases for CHD; 4,148,095 person years and 7579 incident cases for stroke

Risk for every additional egg eaten/day
CHD 0.99 (0.85-1.15), Stroke 0.91 (0.81-1.02)



Another systematic review
and meta-analysis supports
these data

overall CVD 0.97 (0.86, 1.09)

Am J Clin Nutr doi: 10.3945/ajcn.112.051318

Does increasing fiber
decrease the risk of
cardiovascular disease?

The problem of the size of the difference

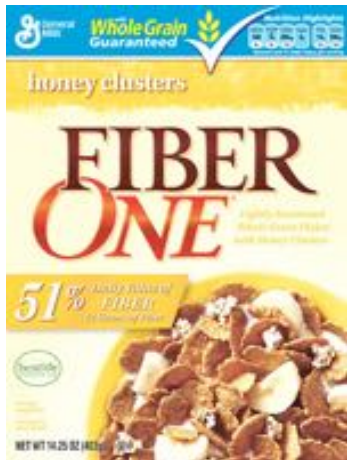
ORIGINAL INVESTIGATION

Dietary Fiber and Risk of Coronary Heart Disease

A Pooled Analysis of Cohort Studies

Mark A. Pereira, PhD; Eilis O'Reilly, MSc; Katarina Augustsson, PhD; Gary E. Fraser, MBChB, PhD;
Uri Goldbourt, PhD; Berit L. Heitmann, PhD; Goran Hallmans, MD, PhD; Paul Knekt, PhD;
Simin Liu, MD, ScD; Pirjo Pietinen, DSc; Donna Spiegelman, ScD; June Stevens, MS, PhD; Jarmo Virtamo, MD;
Walter C. Willett, MD; Alberto Ascherio, MD

Arch Intern Med 2004;164:370-6



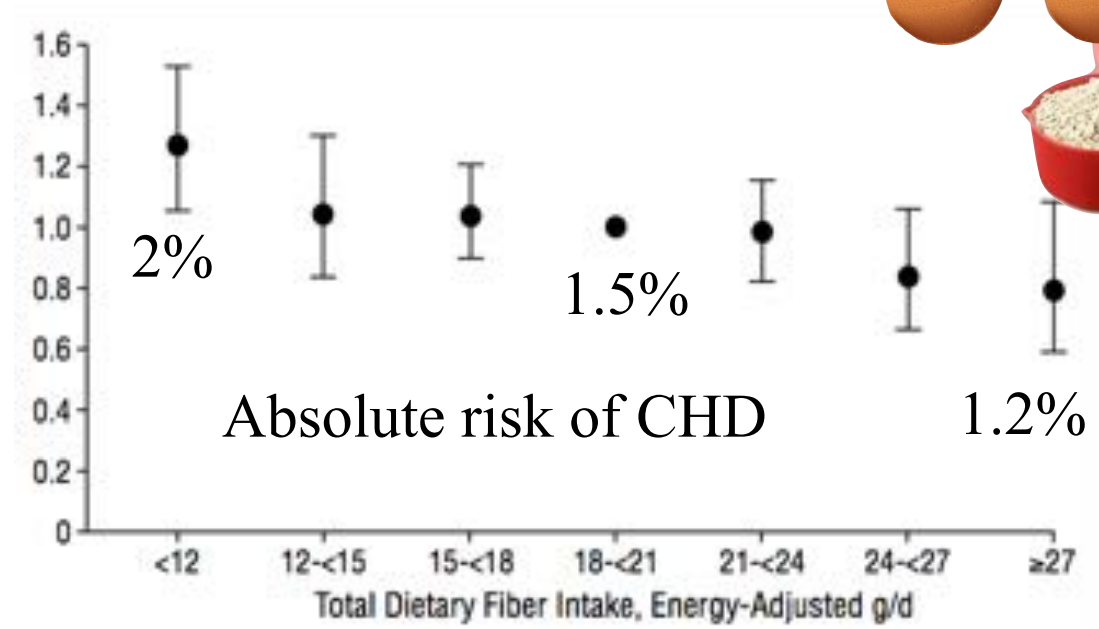
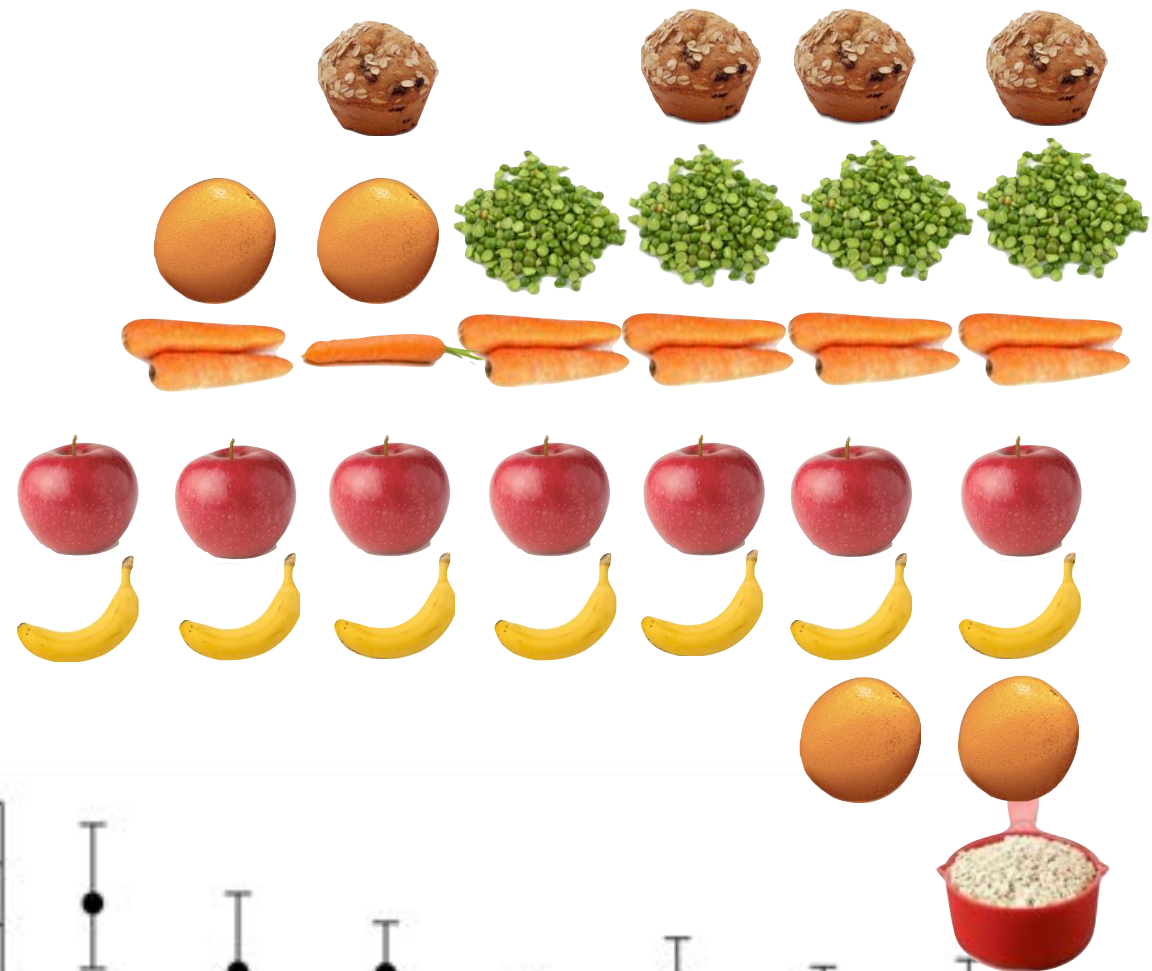
10 prospective cohorts - 6-10 years
336,244 - avg age ~ 50-55
5,249 events



for each 10g/day increment of dietary fiber
CHD was reduced by 14% CI (4-22)



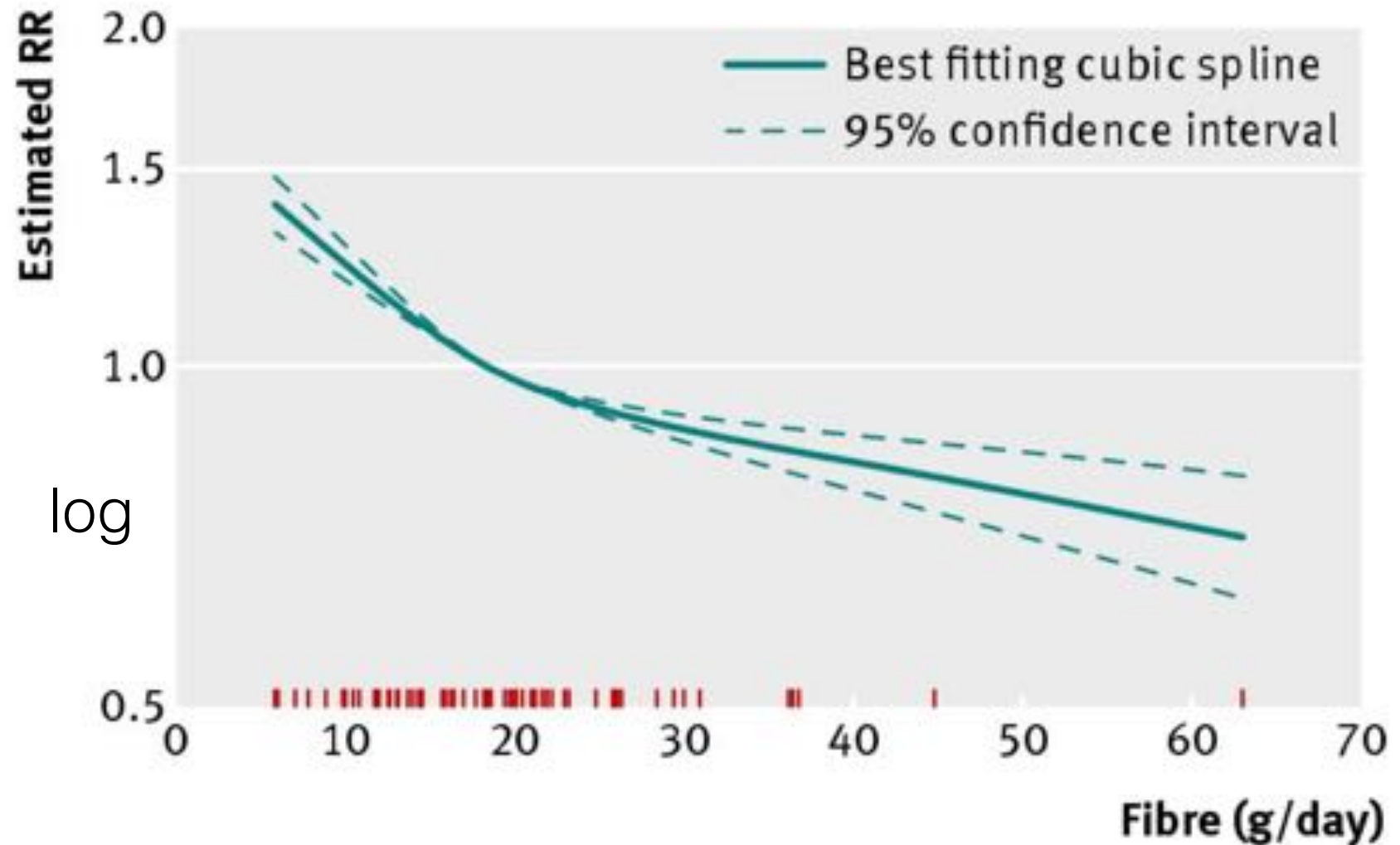
55 y/o
 increase fiber
 from
 none to a lot
 for 5-10 years
 1 in 125 would
 not die from
 CHD



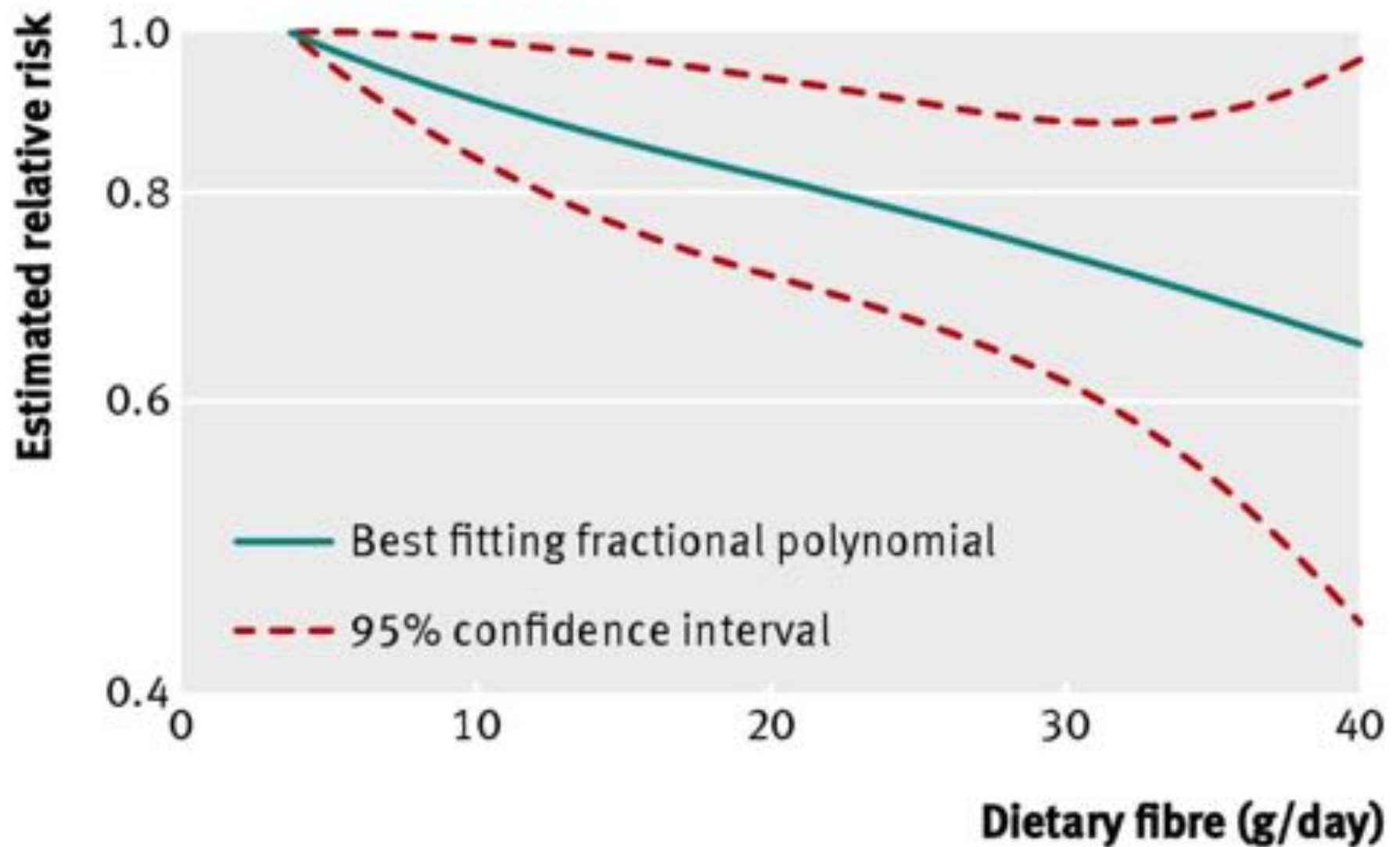
Relative risk of death from coronary heart disease by category of total dietary fiber intake. The relative risks are adjusted for the same variables as table 3. Error bars indicate 95% confidence intervals.



Fibre and risk of cardiovascular disease



Fibre and risk of colorectal cancer

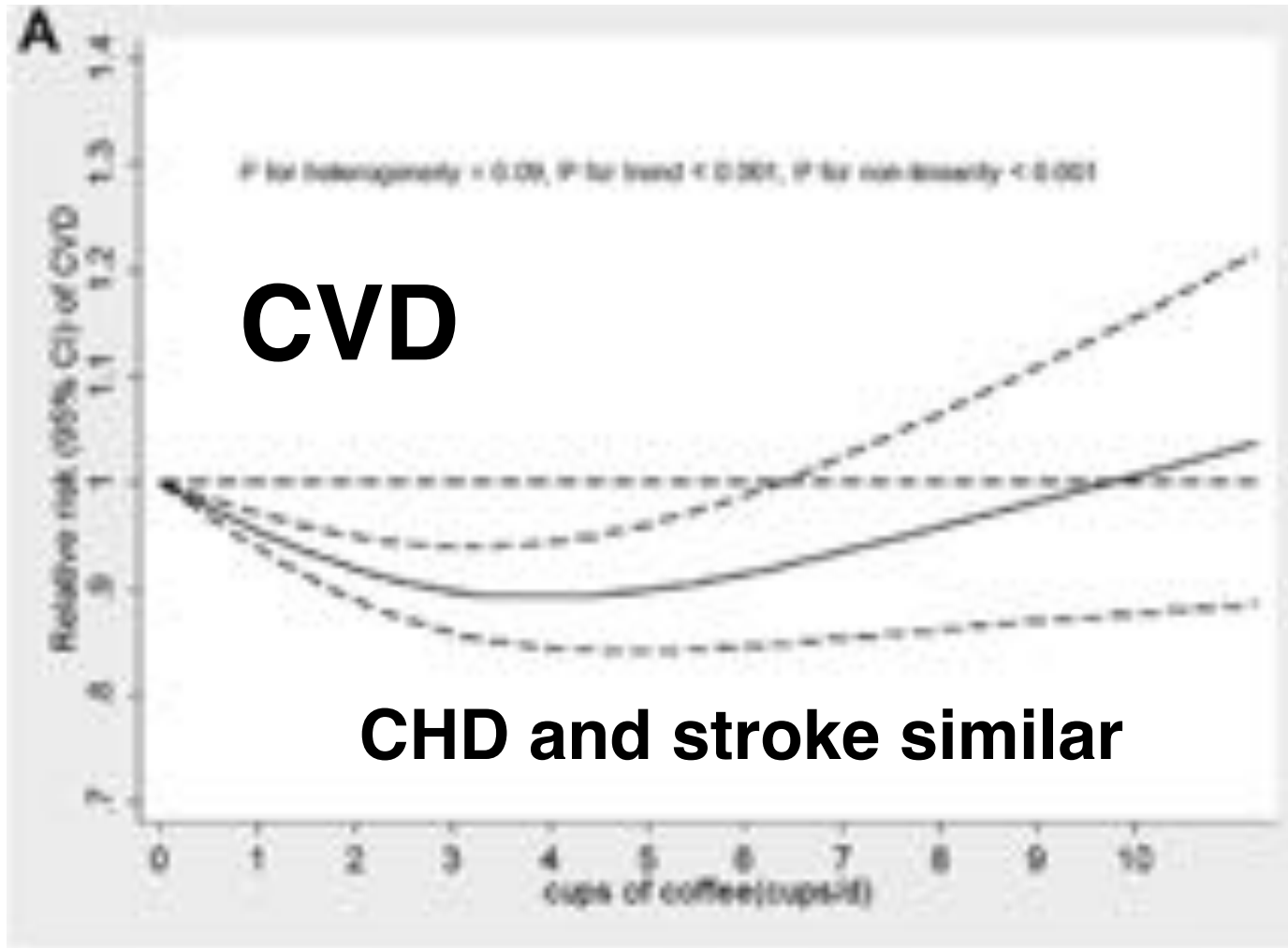


BMJ 2011;343:d6617 doi: 10.1136/bmj.d6617

Does coffee increase cardiovascular risk?

The problem of “I like coffee”

Thirty-six prospective cohort studies
1,279,804 participants, 36,352 CVD cases



“the lowest CVD
risk at 3 to 5
cups per day of
coffee
consumption,
and heavy
coffee
consumption
was not
associated with
CVD risk”

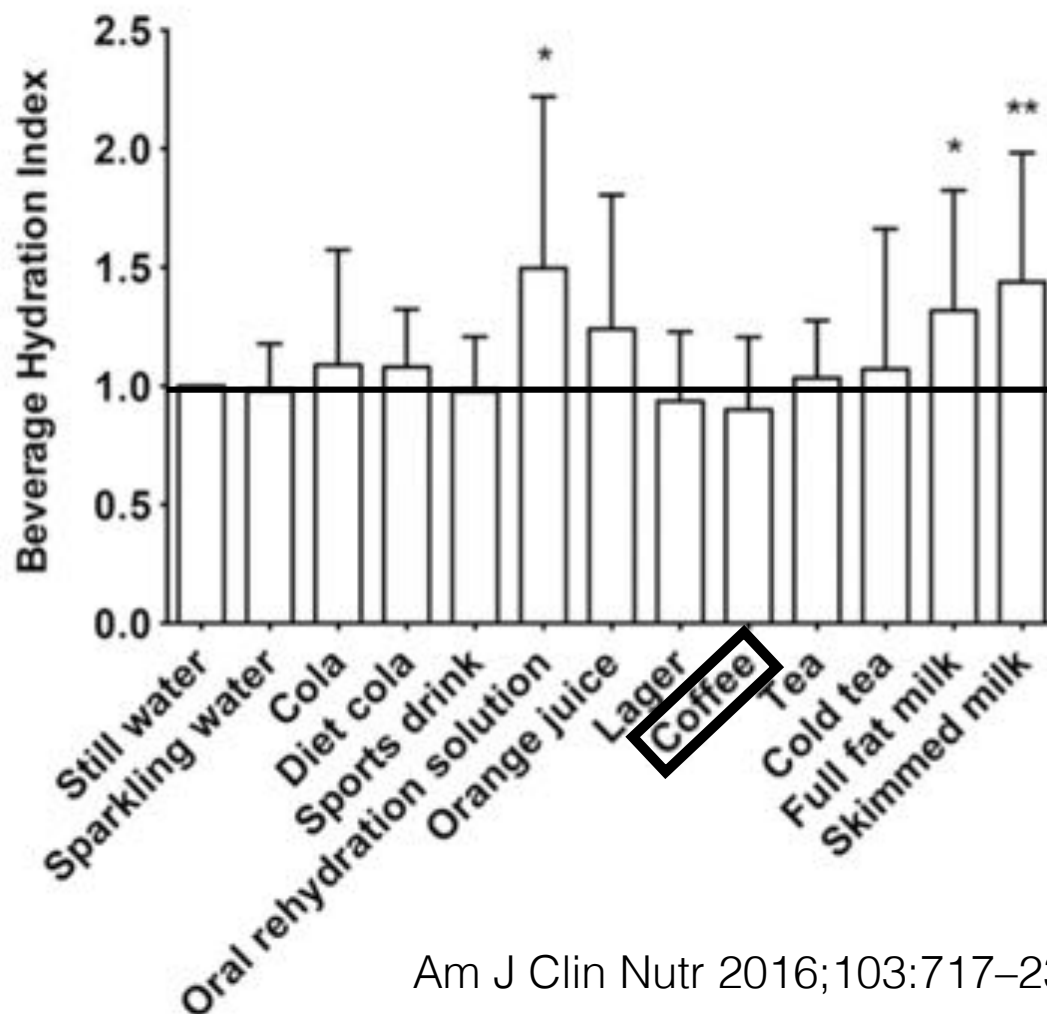
Circulation
2014;129:643–59

“coffee intake is inversely related to all
cause and, probably, CVD mortality”

Eur J Epidemiol
2013;28:527–39

Beverage hydration index

13 different commonly consumed drinks on urine output and fluid balance
when ingested in a hydrated state - 72 males



Am J Clin Nutr 2016;103:717-23

How many daily servings
of fruits and vegetables a
day do we need?

The problem of inappropriate conclusions and reporting

theguardian

News Sport Comment Culture Business Money Life & style

News Society Health

Five a day will do, larger study of fruit and veg intake suggests

Chinese and American researchers settle on lower number than seven-a-day recommendation of English study

5 a day

The Telegraph

Home News World Sport Finance Comment Culture Travel Life Women Fashion Lu
Women Men Motoring Health Property Gardening Food History Relationships Ex
Health News Health Advice Diet and Fitness Wellbeing Expat Health Pets Health Brita

HOME > HEALTH > HEALTH NEWS

A five a day diet of fruit and vegetables is best – more is pointless study finds

Five five portions of fruit and vegetables per day and no more cuts your risk of dying early, a study has found, contradicting recent findings suggesting optimum number may be seven servings.



EXPRESS

Home of
the Daily and
Sunday Express

Forget the five-a-day servings of fruit and veg... now you need seven to be healthy

7+ a day

BBC

NEWS HEALTH

Seven-a-day fruit and veg 'saves lives'

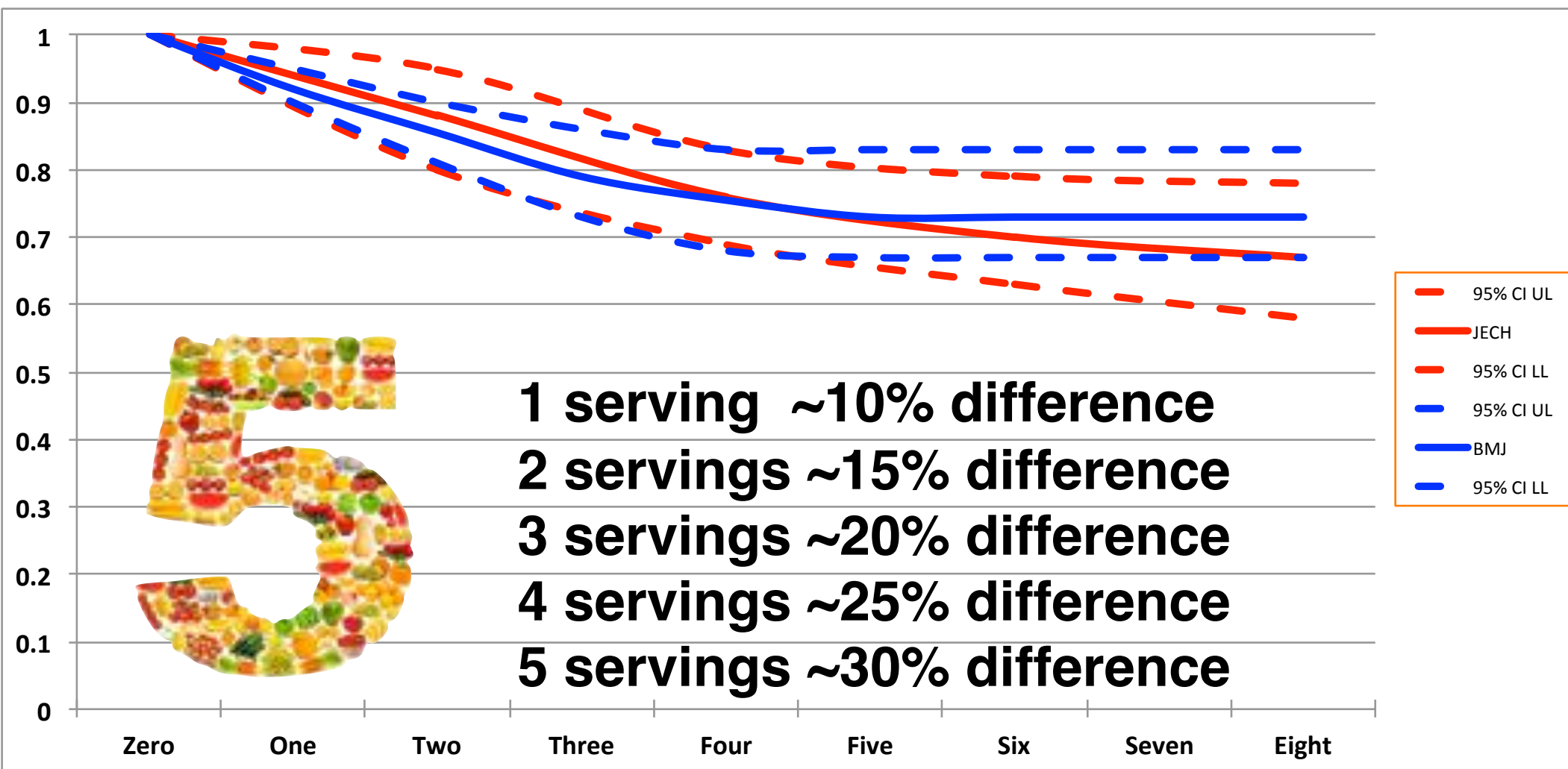
Fruit and vegetable consumption and all-cause, cancer and CVD mortality: analysis of Health Survey for England data

J Epidemiol Community Health - March 2014

Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies

BMJ - June 2014

Numbers of servings a day vs total mortality



Cancer mortality - no difference observed

PURE study

Fruit, vegetable, and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study

135,000 individuals, seven geographical regions - 7.4 years

“Benefits appear to be maximum for both non-cardiovascular mortality and total mortality at three to four servings per day”

August 29, 2017 <http://dx.doi.org/10.1016/>

“Drink at least eight glasses of water a day.” Really?
Is there scientific evidence for “8 × 8”?

“Despite an extensive search of the literature and many personal inquiries and discussions with nutritionists and colleagues, I have found no scientific reports concluding that we all must drink at least eight glasses of water a day. On the contrary, there are publications that state the opposite”

Am J Physiol Regul Integr Comp Physiol 2002;283: R993–R1004

Does alcohol or red wine
decrease the risk of
cardiovascular disease

The problem of “I like wine”

The cardioprotective association of average alcohol consumption and ischaemic heart disease: a systematic review and meta-analysis

44 observational studies

38,627 IHD events (mortality or morbidity) among 957,684 participants

20 grams

~ Pint (550 mL) of beer/cider

~ 1/4 (200 mL) bottle of wine

~ Double (70 mL) spirits (vodka, whisky, rum, gin)

Addiction 2012;107:1246–60

Ischemic heart disease

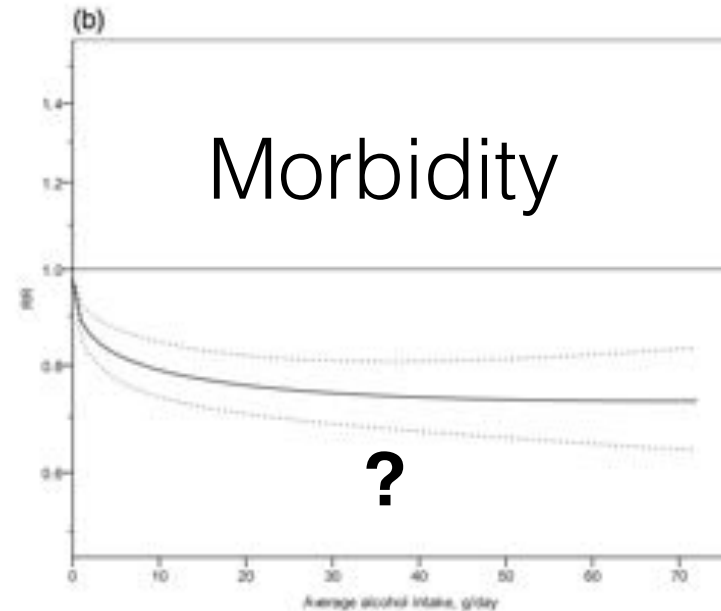
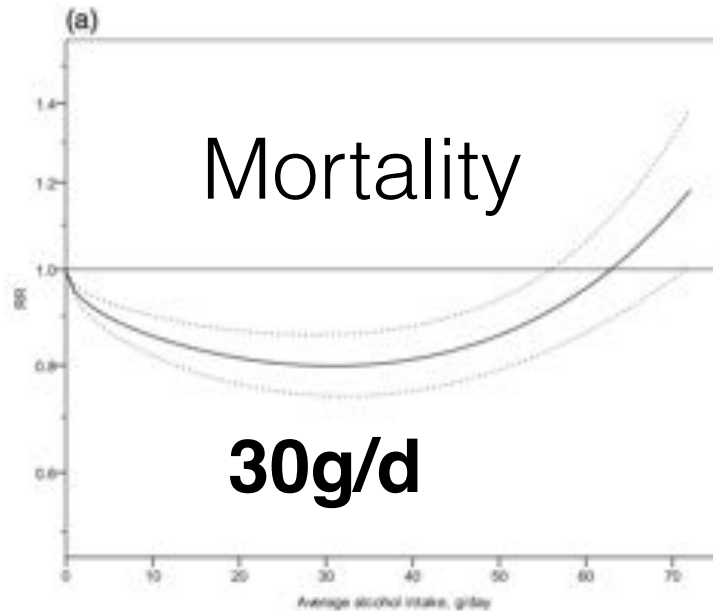
20 grams

~ Pint (550 mL) of beer/cider

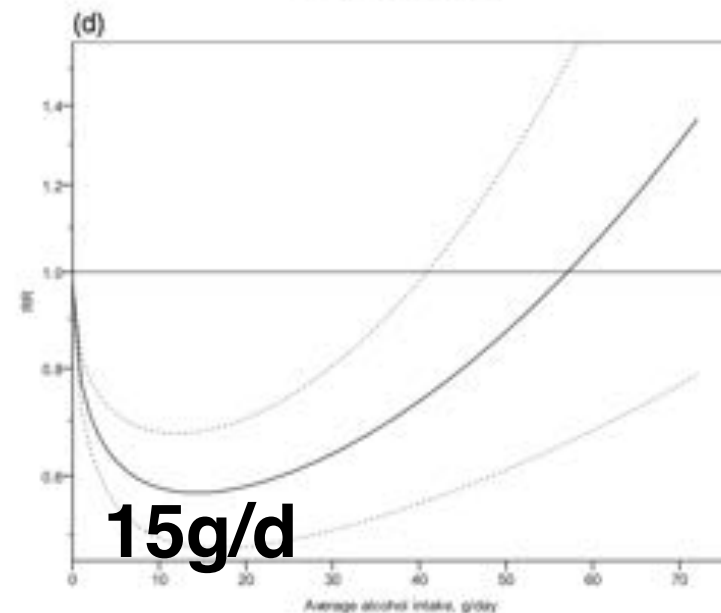
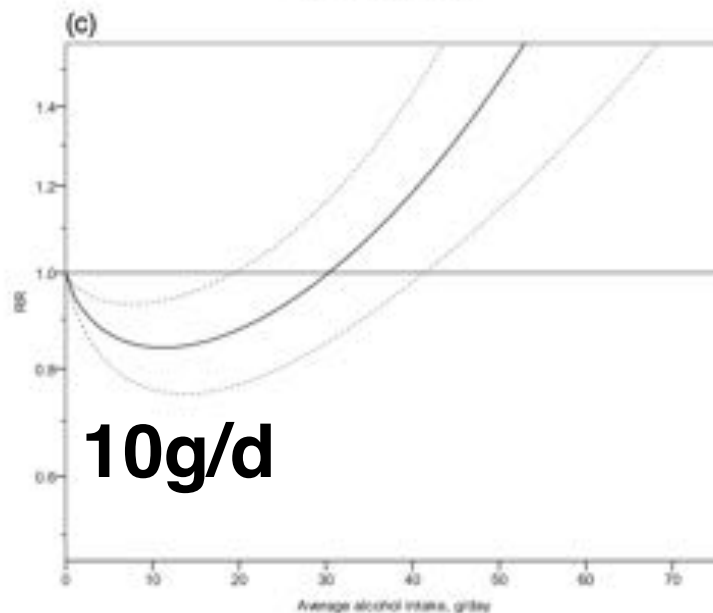
~ 1/4 (200 mL) bottle of wine

~ Double (70 mL) spirits

Men



Women



Other meta-analyses - cardiovascular disease

Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis

“Dose-response analysis revealed that the lowest risk of coronary heart disease mortality occurred with 1–2 drinks a day, but for stroke mortality it occurred with ≤ 1 drink per day.”

BMJ 2011;342:d671

Alcohol consumption, drinking patterns, and ischemic heart disease: a narrative review of meta-analyses and a systematic review and meta-analysis of the impact of heavy drinking occasions on risk for moderate drinkers

“Epidemiological evidence for a beneficial effect of low alcohol consumption without heavy drinking episodes is strong, corroborated by experimental evidence. However, episodic and chronic heavy drinking do not provide any beneficial effect on IHD”

BMC Medicine 2014;12:182

Overall Mortality

All cause mortality and the case for age specific alcohol consumption guidelines: pooled analyses of up to 10 population based cohorts

“Beneficial associations between low intensity alcohol consumption and all cause mortality may in part be attributable to inappropriate selection of a referent group and weak adjustment for confounders.”

BMJ 2015;350:h384 doi: 10.1136/bmj.h384

Do “Moderate” Drinkers Have Reduced Mortality Risk? A Systematic Review and Meta-Analysis of Alcohol Consumption and All-Cause Mortality

“Meta-analyses adjusting for these factors find that low-volume alcohol consumption (1.3 to 25g/day) has no net mortality benefit compared with lifetime abstinence or occasional drinking.”

J Stud Alcohol Drugs 2016;77:185–98

Does chocolate decrease the risk of cardiovascular disease

The problem of “I like chocolate”

Chocolate consumption and cardiometabolic disorders: systematic review and meta-analysis

7 observational studies - 114,009 participants

“highest levels of chocolate consumption were associated with a 37% reduction in cardiovascular disease and a 29% reduction in stroke compared with the lowest levels”

definition of “highest level” varied

BMJ 2011;343:d4488 doi: 10.1136/bmj.d4488

Chocolate consumption and risk of myocardial infarction: a prospective study and meta-analysis

“Chocolate consumption is associated with lower risk of MI and ischaemic heart disease”

Heart 2016 doi:10.1136/heartjnl-2015-309203

Multiple Nutrients and Behaviours



The Journal of Nutrition
Nutrient Requirements and Optimal Nutrition

Americans Do Not Meet Federal Dietary Recommendations¹

“nearly the entire U.S. population consumes a diet that is not on par with recommendations”

Is this a problem with the population, the guidelines or both?

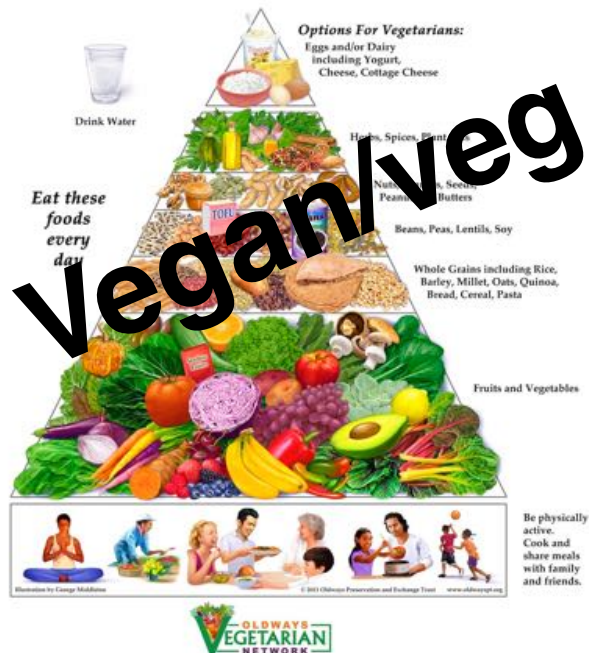
J Nutr 2010;140:1832–38

The DASH Food Pyramid



OLDWAYS Vegetarian & Vegan Diet Pyramid

Putting More Plants on Your Plate



THE ATKINS LIFESTYLE FOOD GUIDE PYRAMID™



The Traditional Healthy Mediterranean Diet Pyramid



“currently there is insufficient material to give a proper definition of what the Mediterranean diet is or was in terms of well defined chemical compounds or even in terms of foods.... The all embracing term 'Mediterranean diet' should not be used in scientific literature....”

Eur J Clin Nutr 1989;43:13–29

Original Article

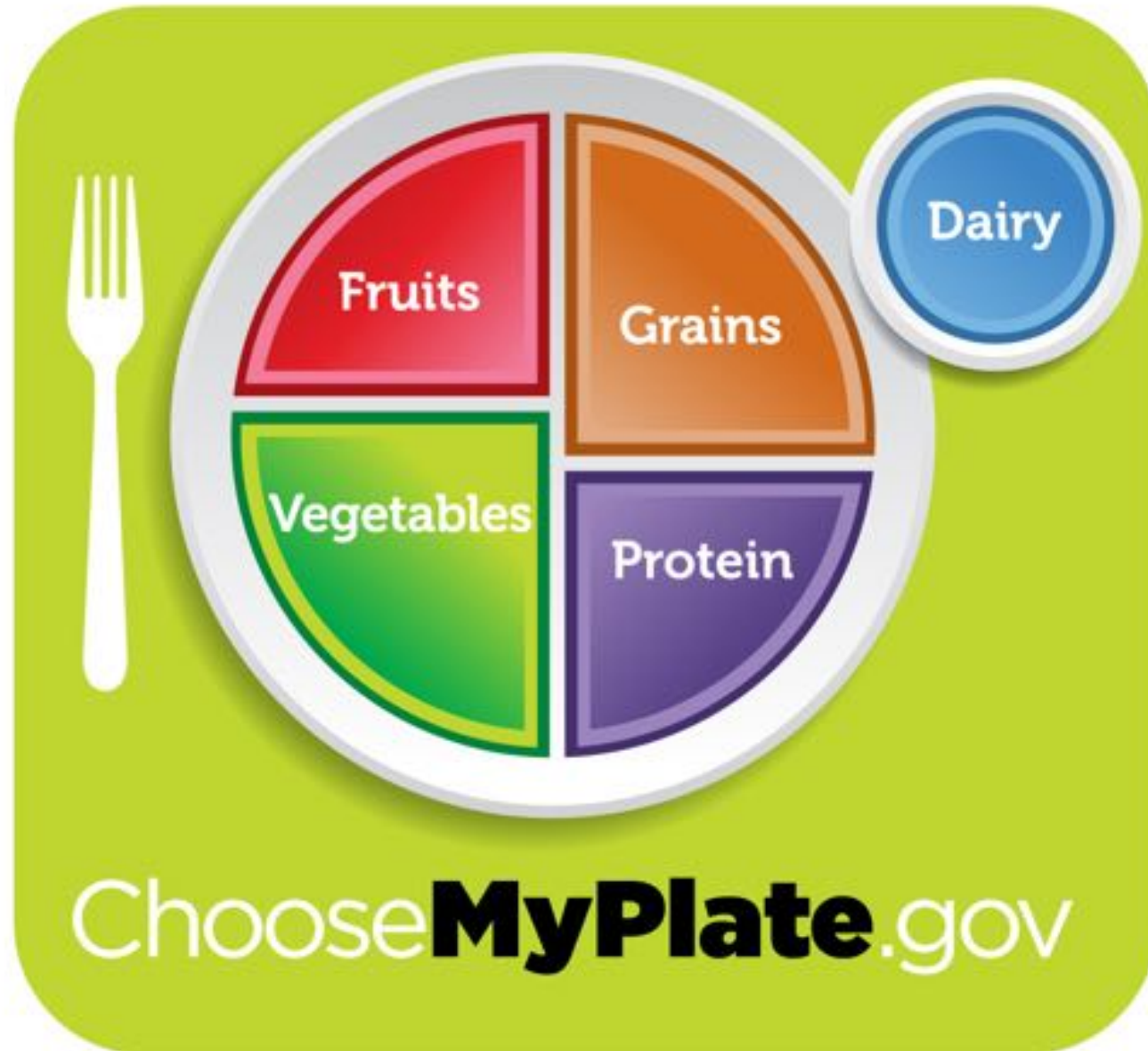
There are many Mediterranean diets

Ann Noah MSc and Arthur Stewart Truswell MD, DSc

Canada's Food Guide



USDA



Diets: Different but equal?

RCT (2 yrs, 3 arms)

322 pts - Age 52, 86% male, BMI 31 (mean)

Weight CHANGE (kg)	Low fat	Medit	Low carb
24 months	-2.9	*-4.4	*-4.7

N Engl J Med 2008;359:229-41

Systematic Review - “The results suggested that the proportion of macronutrients in the diet was not important in predicting changes in weight”

Food & Nutrition Research 2012;56:19103

Low Carbohydrate versus Isoenergetic Balanced Diets for Reducing Weight and Cardiovascular Risk: A Systematic Review and Meta-Analysis

“This review, including 19 RCTs with 3,209 participants showed there is probably little or no difference in changes in weight and cardiovascular and diabetes risk factors with low CHO (high fat or protein) weight loss diets compared to isoenergetic balanced weight loss diets.”

No stat differences but “seemed” to favour low CHO
but even if real - 1 kg difference

PLOS ONE 2014;9:e100652

Comparison of Weight Loss Among Named Diet Programs in Overweight and Obese Adults

A Meta-analysis

48 RCTs - Atkins, Ornish, ZONE, LEARN, Jenny Craig, Nutrisystem, Weight Watchers, South Beach, Rosemary Conley, Slimming World, Volumetrics, Biggest Loser

“evidence of low to moderate quality showed that both low-carbohydrate and low-fat diets were associated with an estimated 8-kg weight loss at 6-month follow-up compared with no diet”

“although there are statistically significant differences between some of the named diets, these differences are small (~1.5kg) and likely to be unimportant to many seeking to lose weight”

Are there
differences in
cardiovascular
outcomes in
people
randomized to
different diets?



Mediterranean diet in secondary prevention of coronary heart disease - Lyon Diet Heart Study

27 months - 605 patients <age 60 with a previous MI in the last 6 months - 90% male

one group advised in a one-hour session (with a couple of follow ups) to adopt a diet of more bread, more root vegetables, more fish, less beef, lamb and pork (replaced with poultry), no day without fruit; and butter and cream replaced with margarine - also used rapeseed, and olive oils in salad

Results

Weight, cholesterol, lipoproteins and blood pressure **were not statistically different** between groups

Mediterranean diet in secondary prevention of coronary heart disease

	Total mortality (%)	Cardiovascular deaths (%)	Non-fatal MI's (%)	Total primary endpoints (%)
Dietary intervention	3.5	1.0	1.7	2.6
No dietary intervention	6.6	5.3	5.6	10.9
Relative risk reduction	47	81	NSS	76
Absolute risk reduction	3.1	4.3		8.3
Number needed to treat	32	23		12

Lancet 1994;343:1454-9

Women's Health Initiative Randomized Controlled Dietary Modification Trial - “low fat”

48,835 postmenopausal women (62 y/o) - 4% prev CVD - 8.1 years

1) lower fat intake to 20% of their total calories, and to eat five or more fruit/vegetable servings and six or more grain servings a day

2) asked not to make any dietary changes

led to ~10% reduction in energy from fat and one more serving a day of vegetables/fruit

no statistical difference in CHD, CVD, stroke, breast cancer, colorectal cancer

JAMA 2006;295:629-642, 643-54, 655-66

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet PREDIMED - 4 years, 67 y/o, 58% male, 48% T2DM

	Total mortality (%)	Myocardial infarction, stroke, and death from cardiovascular causes (%)	MI (%)	Stroke (%)
Control “Low fat”	4.7	4.4	1.6	2.4
Mediterranean diet** - EVOO - 1 liter/week	4.6	3.8*	1.5	1.9*
Mediterranean diet** - NUTS (30 gm of mixed nuts per day)	4.7	3.4*	1.3	1.3*

**increased weekly servings of fish (by 0.3 servings)
and legumes (by 0.4 servings)

* statistical different from control
N Engl J Med 2013; 368:1279-90

Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis

25 observational studies

both nuts (approx 24%) and legumes (approx 14%) reduced total IHD - but no impact on stroke

Amer J Clin Nutr 2014;100:278-88

Reduced or modified dietary fat for preventing cardiovascular disease (Review)

36 hard (non-surrogate) outcomes were reported

1 outcome showed a statistically significant difference in combined cardiovascular events 0.86 (0.77-0.96)

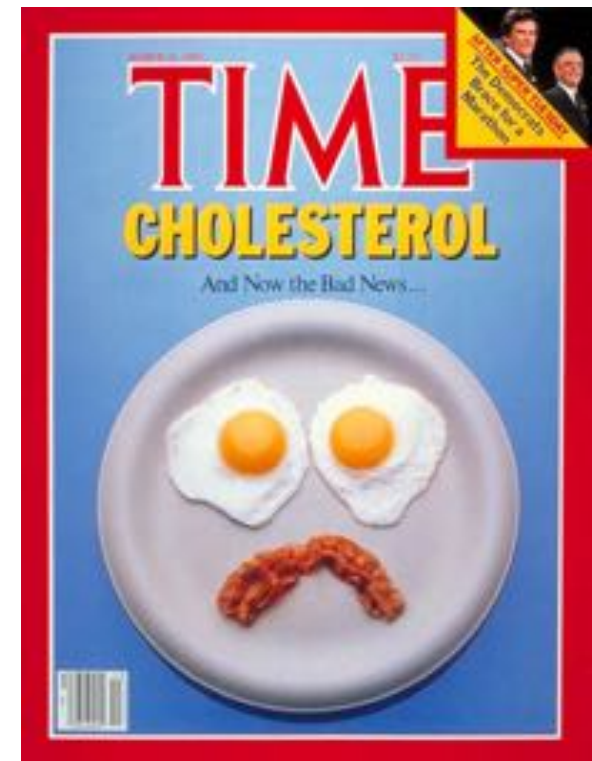
If true - 1% absolute reduction in risk



Fats/ cholesterol

January
1961

March
1984



September
1999

June
2014



Science Base Chapter:

*Food and Nutrient Intakes,
and Health:
Current Status and Trends*

Subcommittee 1

health.gov

- Cholesterol is not considered a nutrient of concern for overconsumption.

**HOWEVER, THE FINAL REPORT
RELEASED IN JANUARY 2016 STATES
“individuals should eat as little cholesterol
as possible”**

Food and Nutrient Intakes, and Health: Current Status and Trends

News

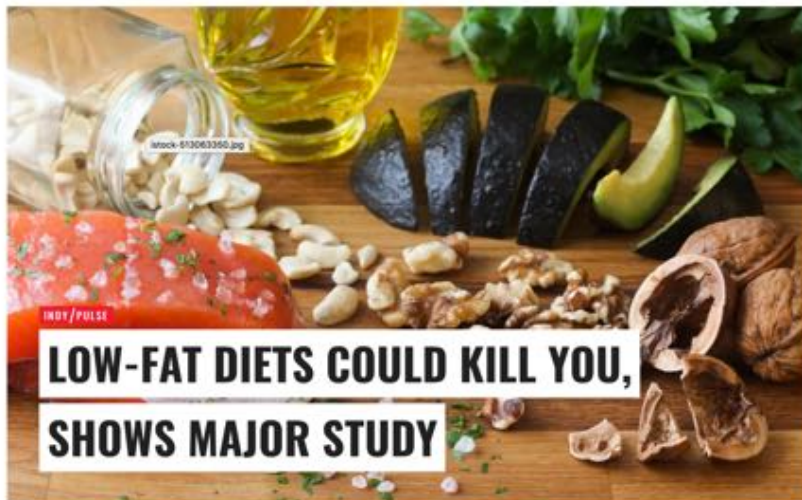
Low-fat diet could kill you, major study shows



48 Comments



★★★★★ 246 Amazon.com customer reviews
 "I have lots of headphones, and this is by far the best one."



HEALTH

Huge new study casts doubt on conventional wisdom about fat and carbs

By PATRICK SKERRETT @PSkerrett / AUGUST 29, 2017



SEAN GALLUP/GETTY IMAGES

Meeting Coverage > ESC

ESC: Huge Diet Study Shows Carbs, Not Fats Are the Problem

— But PURE also challenges belief that more is better for fruits and vegetables

by Larry Husten, CardioBrief

August 29, 2017

ADVERTISEMENT

A Key

Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study

50 y/o (M40%, F60%) over 7.4 years -
looked at the impact of % energy from
macronutrients

Looked at quintiles

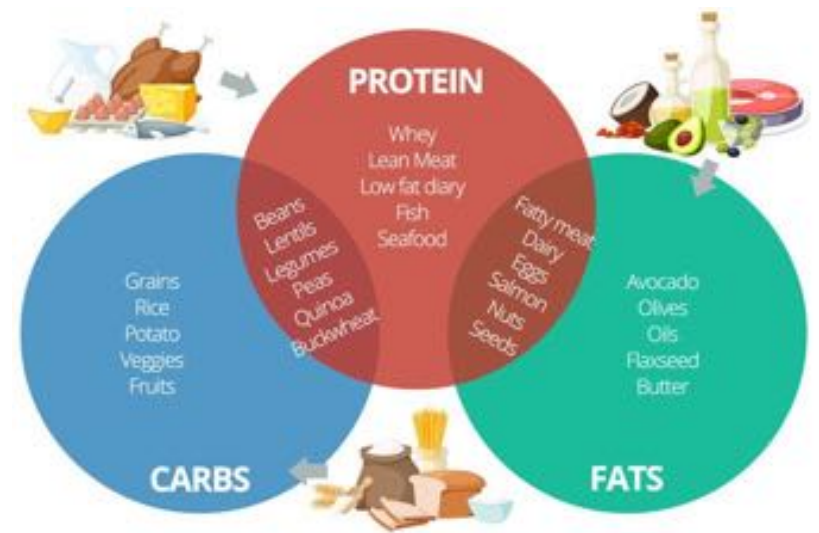
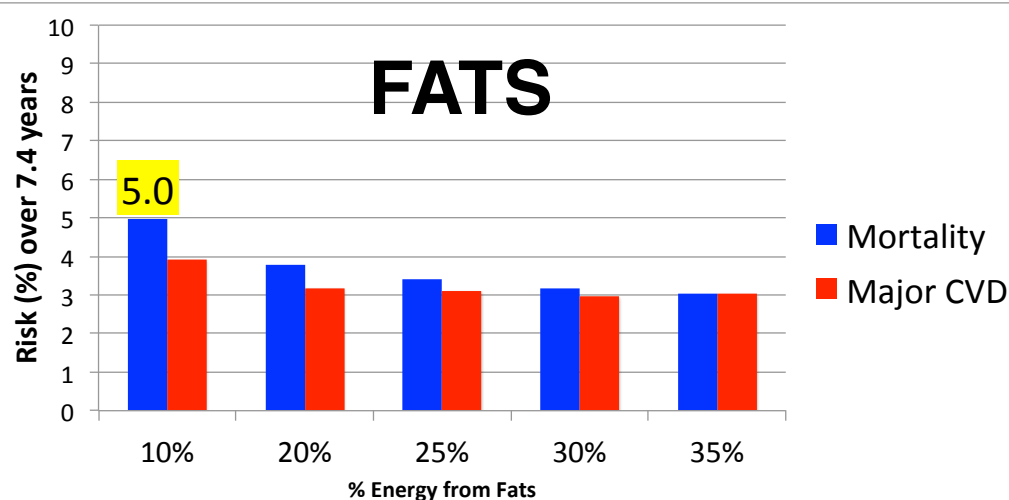
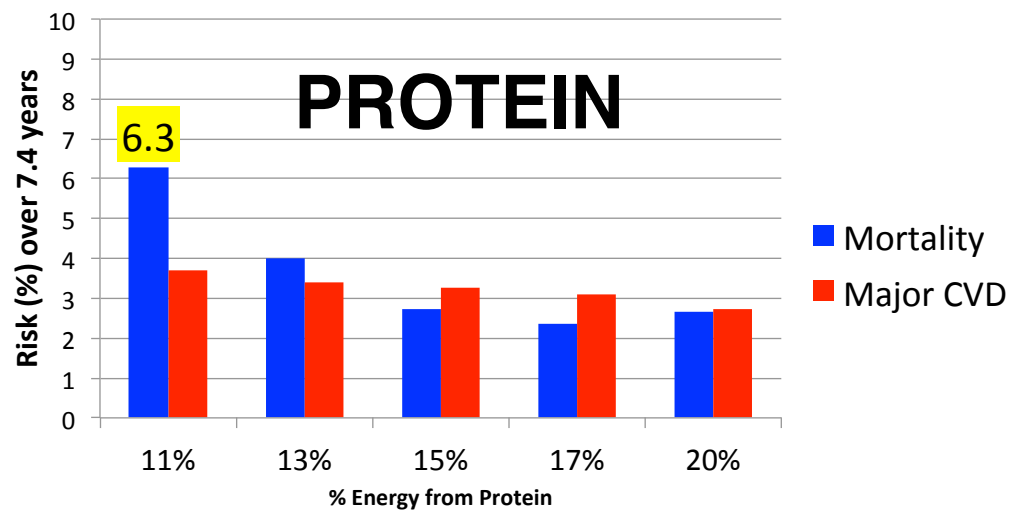
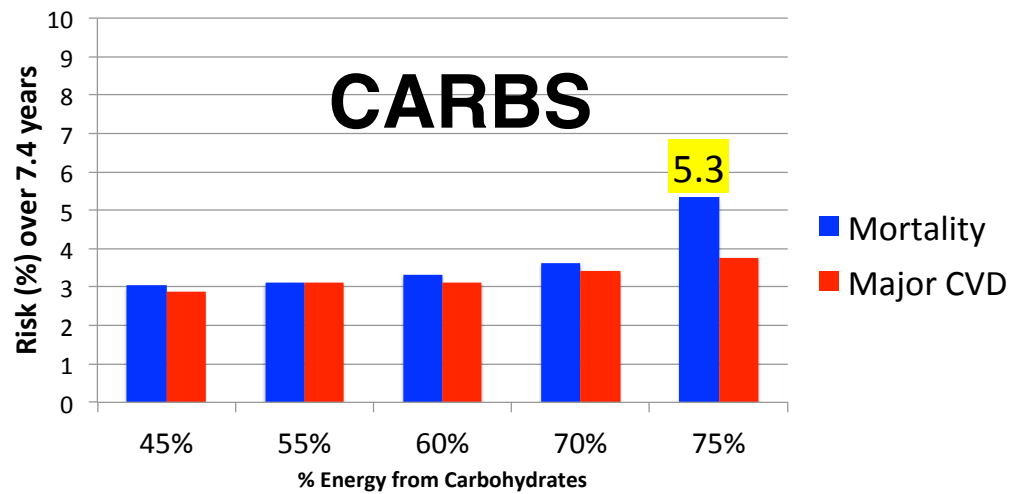
Carbs from 45-75%

Fats from 10-35%

Protein from 10-20%

Lancet Aug 29/2017

Risk(%) of mortality and CVD over 7.4y based on % energy from macronutrients



Lancet Aug 29/2017

50 y/o (M40%, F60%) over 7.4 years

FINDINGS

CVD - Macronutrient % intake made no difference on overall CVD

Mortality

a) No harm as long as carbs < 70%, and fat and protein > 10%-15%

b) If eat > 70% carbs or < 10-15% protein or fat for 7.5 years

1-2% will die prematurely but 99-98% won't

	Type	Carb (%)	Protein (%)	Total Fat (%)
Atkins	High Fat and Protein	6 ?	35 ?	59 ?
Protein Power		9 ?	37 ?	54 ?
South Beach		28 ?	33 ?	39 ?
Mediterranean	High Fat and Carb	40 ?	17	43 ?
Sugar Blasters	High Protein	40 ?	28 ?	32
The Zone		40 ?	28 ?	32
Dash Diet	Balanced	55	18	27
ADA	Moderate High Carb	60	20	20
Anderson		63	16	21
Mayo Clinic		66	27 ?	13
Pritikin	High Carb	73 X	18	9 X
Ornish		74 X	18	7 X

X = harm ? = not studied

Do saturated fats
increase the risk of
cardiovascular disease

The problem of a theory gone completely haywire

Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review and meta-analysis

“Dietary recommendations were introduced for 220 million US and 56 million UK citizens by 1983, in the absence of supporting evidence from RCTs.”

Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease¹⁻⁵

Requested RR for extreme quantiles of saturated fat intake

1.07 (0.96-1.19) for CHD

0.81 (0.62-1.05) for stroke

1.00 (0.89-1.11) for CVD

“A meta-analysis of prospective epidemiologic studies showed that there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD.”

Am J Clin Nutr 2010;91:535–46

Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk

A Systematic Review and Meta-analysis

32 observational studies (512,420 participants) of fatty acids from dietary intake

17 observational studies (25,721 participants) of fatty acid biomarkers

27 randomized controlled trials (105,085 participants) of fatty acid supplementation

Compared tertiles

Ann Intern Med 2014;160:398-406

Monounsaturated fat

Polyunsaturated fat

- Olive oil
 - Canola oil
 - Sunflower oil
 - Peanut oil
 - Sesame oil
 - Avocados
 - Olives
 - Nuts (almonds, peanuts, macadamia nuts, hazelnuts, pecans, cashews)
 - Peanut butter
- COHORT
9 studies - CHD
1.00 (0.91-1.10)

- Soybean oil ω -6 FA
 - Corn oil ω -6 FA
 - Safflower oil ω -6 FA
 - Walnuts ω -3 FA
 - Sunflower, sesame, and pumpkin seeds ω -6 FA
 - Flaxseed ω -3 FA
 - Fatty fish (salmon, tuna, mackerel, herring, trout, sardines) ω -3 FA
 - Soymilk ω -6 FA
 - Tofu ω -3 FA
- COHORT
 ω -6
8 studies - CHD
0.98 (0.90-1.06)
- COHORT
 ω -3 short chain
Plant oils
7 studies - CHD
0.99 (0.86-1.14)
- COHORT
 ω -3 long chain
Marine Oils
16 studies - CHD
0.87 (0.78-0.97)

Saturated fat

Trans fat

- High-fat cuts of meat (beef, lamb, pork)
 - Chicken with the skin
 - Whole-fat dairy products (milk and cream)
 - Butter
 - Cheese
 - Ice cream
 - Palm and coconut oil
 - Lard
- COHORT
20 studies - CHD
1.03 (0.98-1.07)

- Commercially-baked pastries, cookies, doughnuts, muffins, cakes, pizza dough
 - Packaged snack foods (crackers, microwave popcorn, chips)
 - Stick margarine
 - Vegetable shortening
 - Fried foods (French fries, fried chicken, chicken nuggets, breaded fish)
 - Candy bars
- COHORT
5 studies - CHD
1.16 (1.06-1.27)

Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies

Saturated fat intake

all cause mortality (0.99, 95% CI 0.91 to 1.09)

CVD mortality (0.97, 0.84 to 1.12)

total CHD (1.06, 0.95 to 1.17)

ischemic stroke (1.02, 0.90 to 1.15)

type 2 diabetes (0.95, 0.88 to 1.03)

Total trans fat intake

all cause mortality (1.34, 1.16 to 1.56)

CHD mortality (1.28, 1.09 to 1.50)

total CHD (1.21, 1.10 to 1.33)

ischemic stroke (1.07, 0.88 to 1.28)

type 2 diabetes (1.10, 0.95 to 1.27)

Industrial, but not ruminant, trans fats

CHD mortality (1.18 (1.04 to 1.33) v 1.01 (0.71 to 1.43))

CHD (1.42 (1.05 to 1.92) v 0.93 (0.73 to 1.18))

“Saturated fats are not associated with all cause mortality, CVD, CHD, ischemic stroke, or type 2 diabetes, but the evidence is heterogeneous with methodological limitations. Trans fats are associated with all cause mortality, total CHD, and CHD mortality, probably because of higher levels of intake of industrial trans fats than ruminant trans fats.”

“Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats”

Ann Intern Med 2014;160:398-406

“The present systematic review [secondary prevention] provides no evidence (moderate quality evidence) for the beneficial effects of reduced/modified fat diets in the secondary prevention of coronary heart disease”

BMJ Open 2014;4:e004487 doi:10.1136/bmjopen-2013-004487

Dietary fat guidelines have no evidence base: where next for public health nutritional advice?

Zoë Harcombe

“Dietary fat guidelines have prevailed for almost 40 years.

The evidence base at the time of their introduction has been examined for the first time and found lacking.

Evidence currently available provides no additional support. Public health opinion differed when the guidelines were introduced. Opposition to the guidelines is becoming more strident. Substantial increases in diet-related illness over the past four decades, particularly obesity and type 2 diabetes, indicate that a review of dietary advice is warranted.”

PURE study

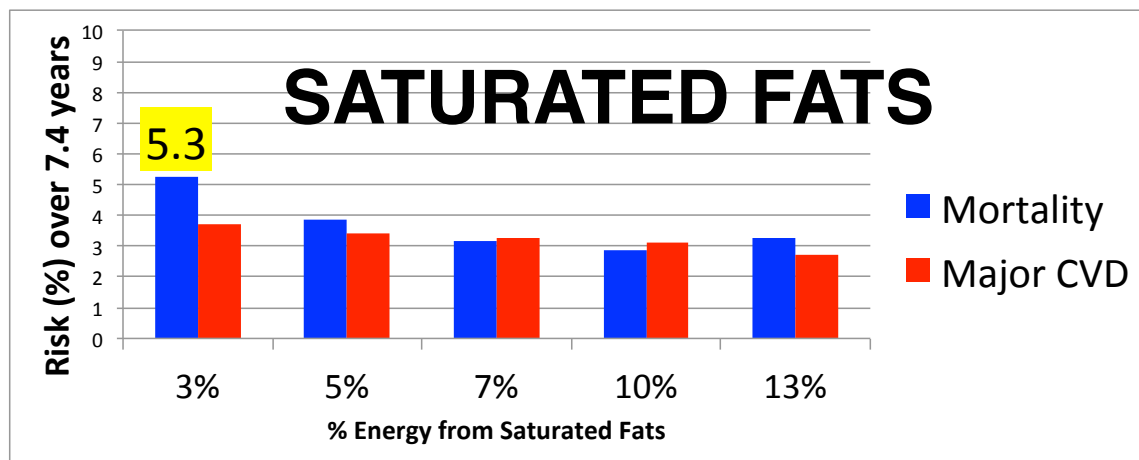
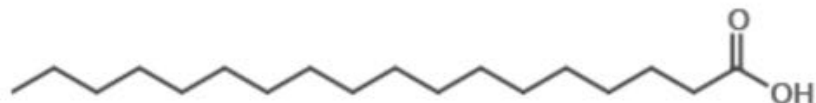
Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study

135,000 individuals, seven geographical regions - 7.4 years

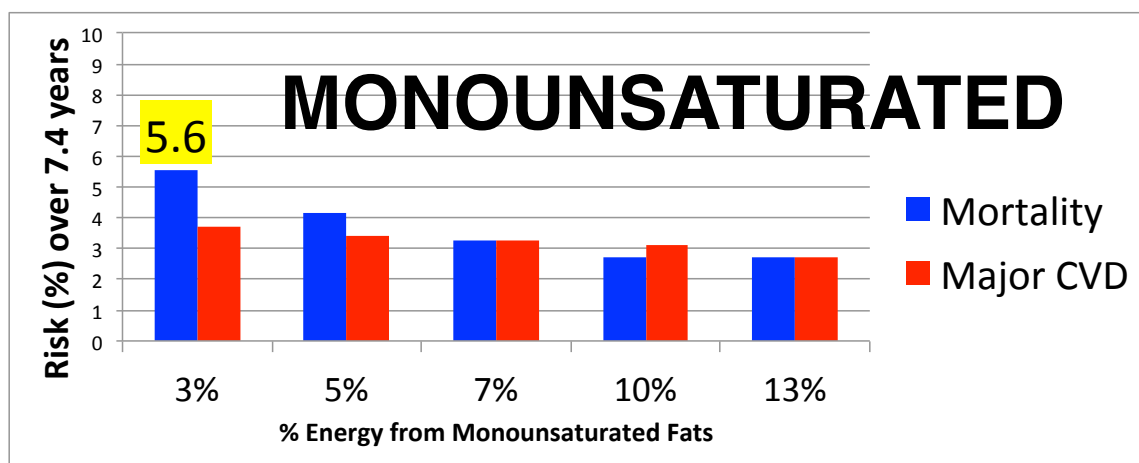
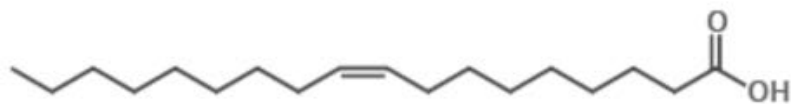
“Global dietary guidelines
should be reconsidered in light
of these findings”

August 29, 2017 <http://dx.doi.org/10.1016>

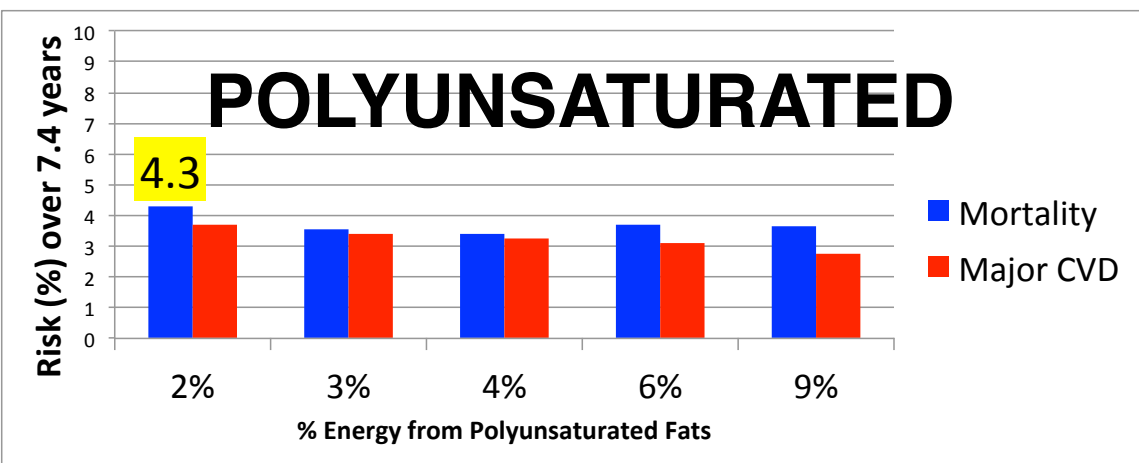
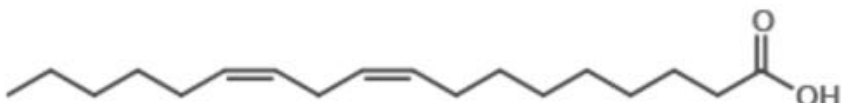
SATURATED FATS



MONOUNSATURATED FATS



POLYUNSATURATED FATS





Recovered Data

Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis

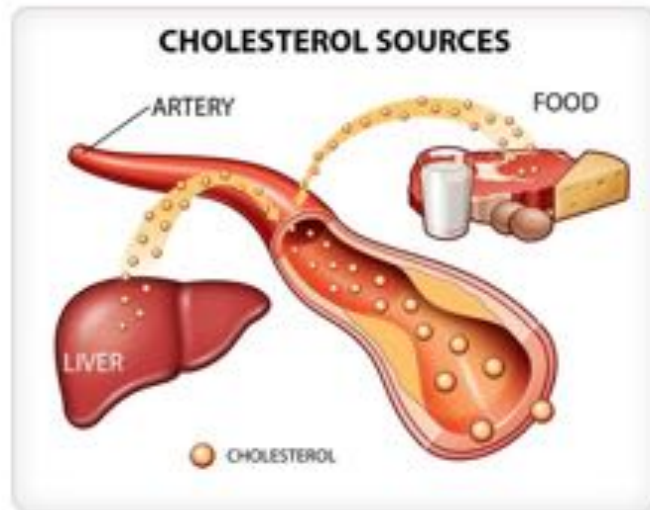
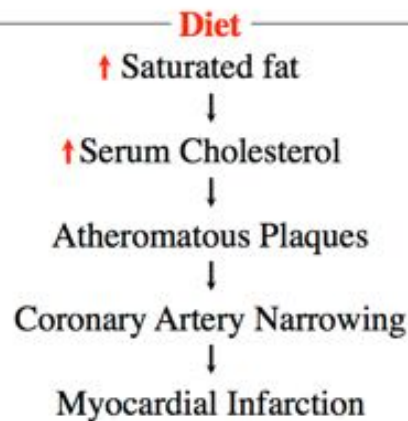
2013

Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73)

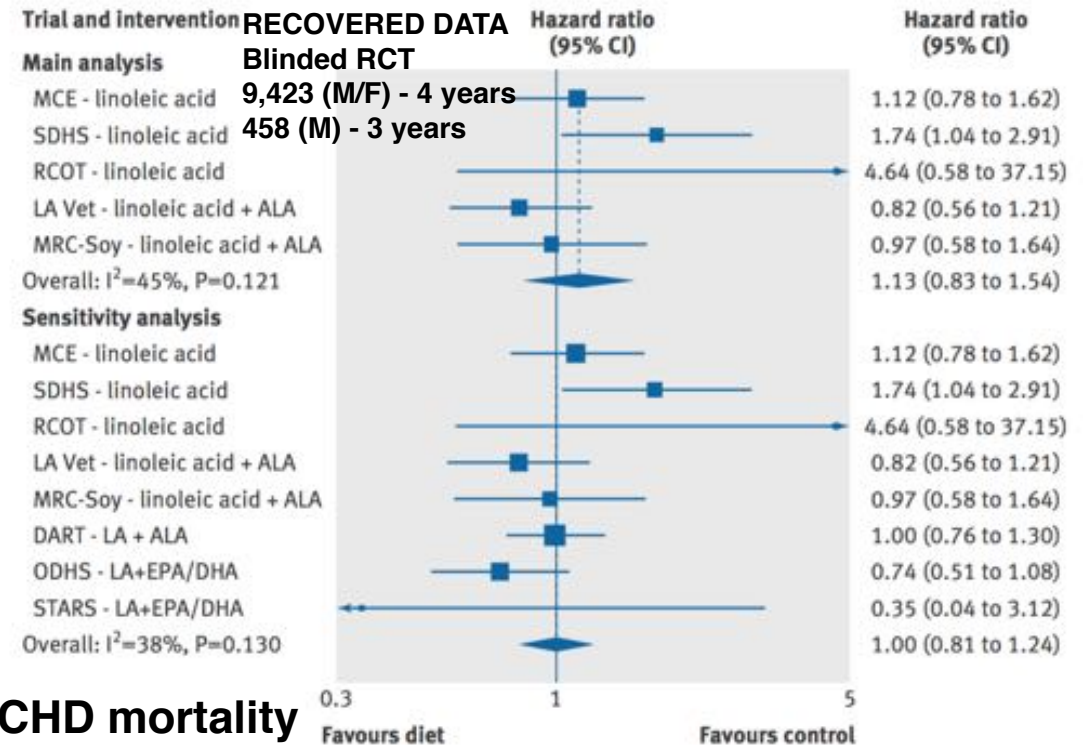
2016

CHD mortality

Classic Diet-Heart Hypothesis



Randomized controlled trials of replacing saturated fat with vegetable oil rich in linoleic acid (corn oil)



“the totality of evidence no longer provides support for the traditional diet-heart hypothesis”

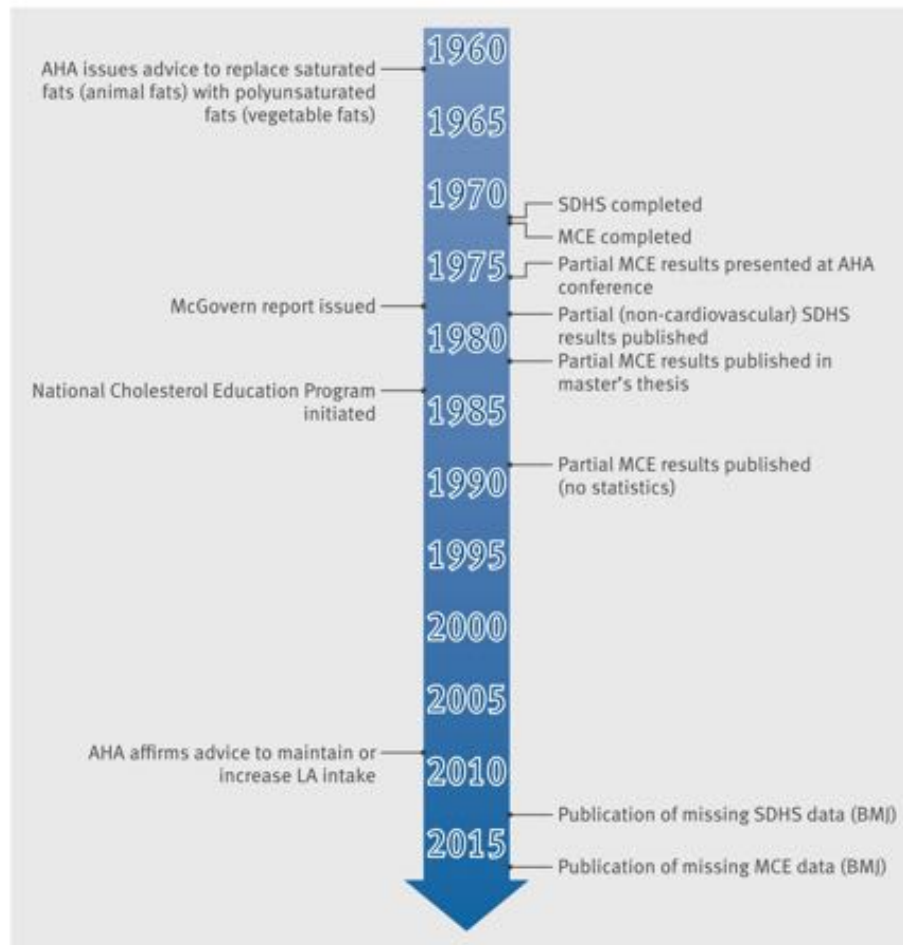


Fig 10 | Diet-heart timeline: key research and policy events. SDHS=Sydney Diet heart Study; MCE=Minnesota Coronary Experiment; AHA=American Heart Association; LA=linoleic acid

“The history of the traditional diet-heart hypothesis suggests that nutrition research could be improved by not overemphasizing intermediate biomarkers; cautious interpretation of non-randomized studies; and ensuring timely and complete publication of all randomized controlled trials. Given the limitations of current evidence, the best approach might be one of humility, highlighting limitations of current knowledge and setting a high bar for advising intakes beyond what can be provided by natural diets.”

Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review and meta-analysis

“Dietary recommendations were introduced for 220 million US and 56 million UK citizens by 1983, in the absence of supporting evidence from RCTs.”

Does red meat consumption
increase the risk of
cardiovascular disease?

The problem of different types of meat

Red and Processed Meat Consumption and Risk of Incident Coronary Heart Disease, Stroke, and Diabetes Mellitus

A Systematic Review and Meta-Analysis

20 studies - 1,218,380 individuals and 23,889 CHD, 2,280 stroke, and 10,797 diabetes mellitus cases

Red meat - unprocessed meat from beef, hamburgers, lamb, pork, or game and excluding poultry, fish, or eggs

Processed meat - meat preserved by smoking, curing, or salting or addition of chemical preservatives, such as bacon, salami, sausages, hot dogs, or processed deli or luncheon meats, and excluding fish or eggs

Relative risk	Red meat (per 100g serving/day)	Processed meat (per 50g serving/day)
CHD	1.00 (0.81-1.23)	1.42 (1.07-1.89)
Stroke	1.17 (0.40-3.43)	1.14 (0.94-1.39)

Systematic Reviews and Meta- and Pooled Analyses

Red Meat and Processed Meat Consumption and All-Cause Mortality: A Meta-Analysis

Nine prospective studies

1,330,352 individuals and 137,376 deaths

Relative risk of all-cause mortality (highest vs lowest intake)

Unprocessed red meat 1.10 (0.98, 1.22)

Processed meat 1.23 (1.17, 1.28)

Does added sugar consumption
increase the risk of obesity or
cardiovascular disease?

The potential problem of a new theory and
the size of the differences

Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies

Adults

Reduced intake of dietary sugars was associated with a decrease in body weight - 0.80 kg (0.39-1.21)

Increased sugars intake was associated with a weight increase - 0.75 kg (0.30 -1.19)

Isoenergetic exchange of dietary sugars with other carbohydrates showed no change in body weight - 0.04 kg (–0.04 to 0.13)

Children

Sugar sweetened beverages - one year follow-up in prospective studies - odds ratio for being overweight or obese was 1.55 (1.32 to 1.82) - highest intake compared with the lowest intake

Epidemiology and Prevention

Sweetened Beverage Consumption, Incident Coronary Heart Disease, and Biomarkers of Risk in Men

Compared never drink vs 2 servings (12oz)/month vs 2/week vs 7/week

Only 7 servings/week showed a difference in CHD - roughly 20%

Circulation 2012;125:1735-41

Only 7 servings/week showed a difference in CVD mortality - roughly 30%

JAMA Intern Med 2014;174:516-24

Added Sugar Intake and Cardiovascular Diseases Mortality Among US Adults

DEFINITION OF ADDED SUGARS

all sugars used in processed or prepared foods, such as sugar-sweetened beverages, grain-based desserts, fruit drinks, dairy desserts, candy, ready-to-eat cereals, and yeast breads, BUT NOT naturally occurring sugar, such as in fruits and fruit juices

FREE SUGARS = ADDED SUGARS + honey, syrups, or fruit juice

JAMA Intern Med 2014;174:516-24

Do Sugar-Sweetened Beverages Cause Obesity and Diabetes? Industry and the Manufacture of Scientific Controversy

“We established that experimental studies that have financial conflicts with the SSB industry (25 of 26 studies) are much more likely than independently funded ones (1 of 34 studies) to find no relationship between SSB consumption and metabolic outcomes.”

Ann Int Med 2016;165:895-7

The Scientific Basis of Guideline Recommendations on Sugar Intake

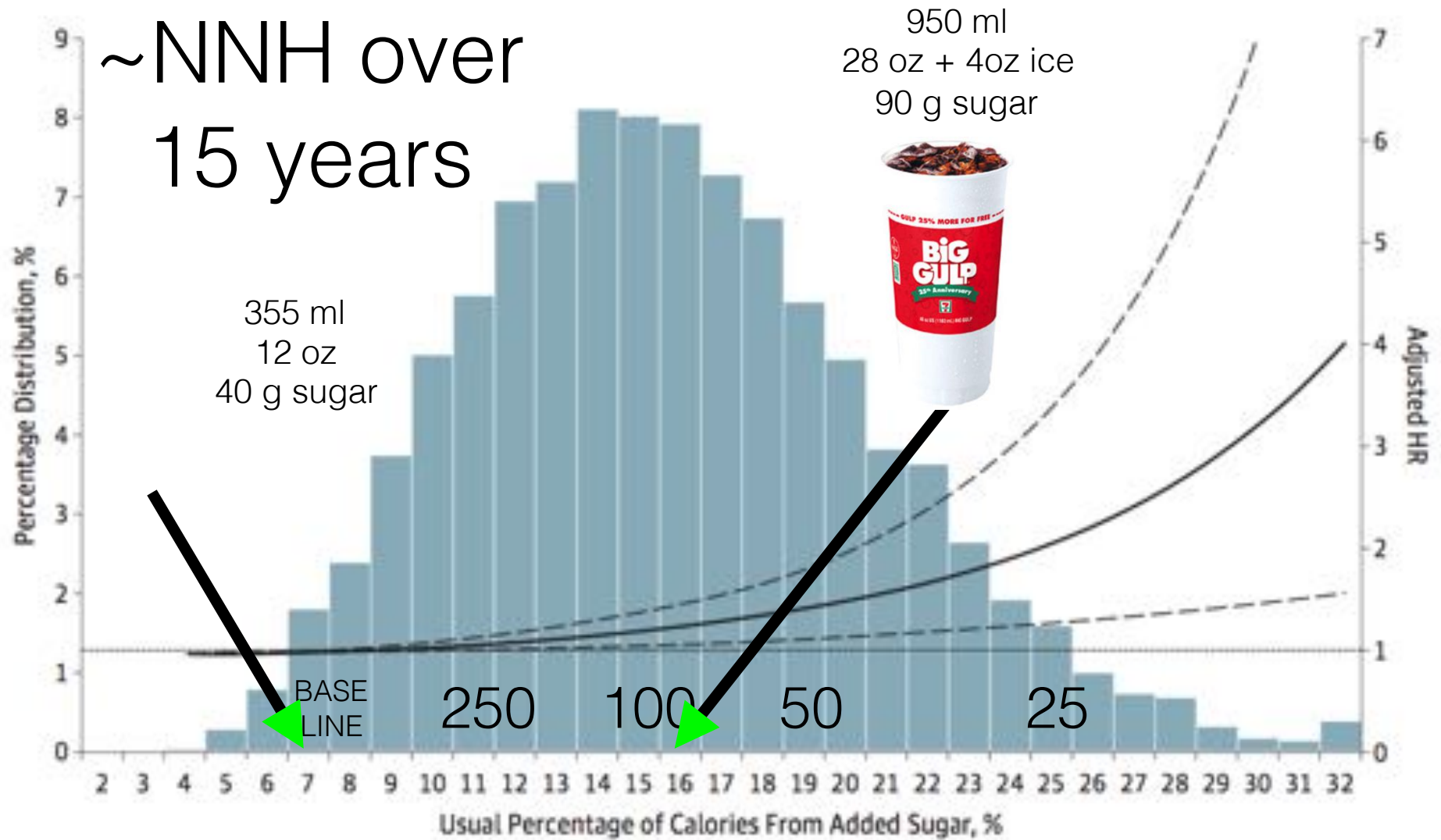
A Systematic Review

Jennifer Erickson, RD*; Behnam Sadeghirad, PharmD, MPH*; Lyubov Lytvyn, MSc; Joanne Slavin, PhD, RD; and Bradley C. Johnston, PhD

“Guidelines on dietary sugar do not meet criteria for trustworthy recommendations and are based on low-quality evidence. Public health officials (when promulgating these recommendations) and their public audience (when considering dietary behavior) should be aware of these limitations.”

BUT - authors had lots of COIs

Figure 1. Adjusted Hazard Ratio (HR) of the Usual Percentage of Calories From Added Sugar for Cardiovascular Disease Mortality Among US Adults 20 Years or Older: National Health and Nutrition Examination Survey Linked Mortality Files, 1988-2006



Can We Say What Diet Is Best for Health?

“There have been no rigorous, long-term studies comparing contenders for best diet laurels using methodology that precludes bias and confounding, and for many reasons such studies are unlikely”

“In medicine in particular, the illusion that science can provide some objective answer that applies to everyone -- how much salt to eat, how and how often to screen for cancer, even whom to treat with cholesterol-lowering drugs, and so on -- is a special danger.”

Wall Street Journal, 19 Aug 2014

What is the answer?

Teasing out the benefits and harms of things we eat is
EXTREMELY complicated

SINGLE NUTRIENTS

Not enough robust data to ascribe causality

Some interesting associations - eggs, salt, coffee, alcohol

MULTIPLE NUTRIENTS AND BEHAVIOURS

Issues of RCTs and Cohorts - bias and confounding -
answer may be unknowable

How to best lose weight is very individual - low carb/higher
fat/protein maybe somewhat better? - is the difference
important?

Overall nutrition is hugely personal and emotional

Bad Outcomes

“There are no bad foods;
only bad diets”

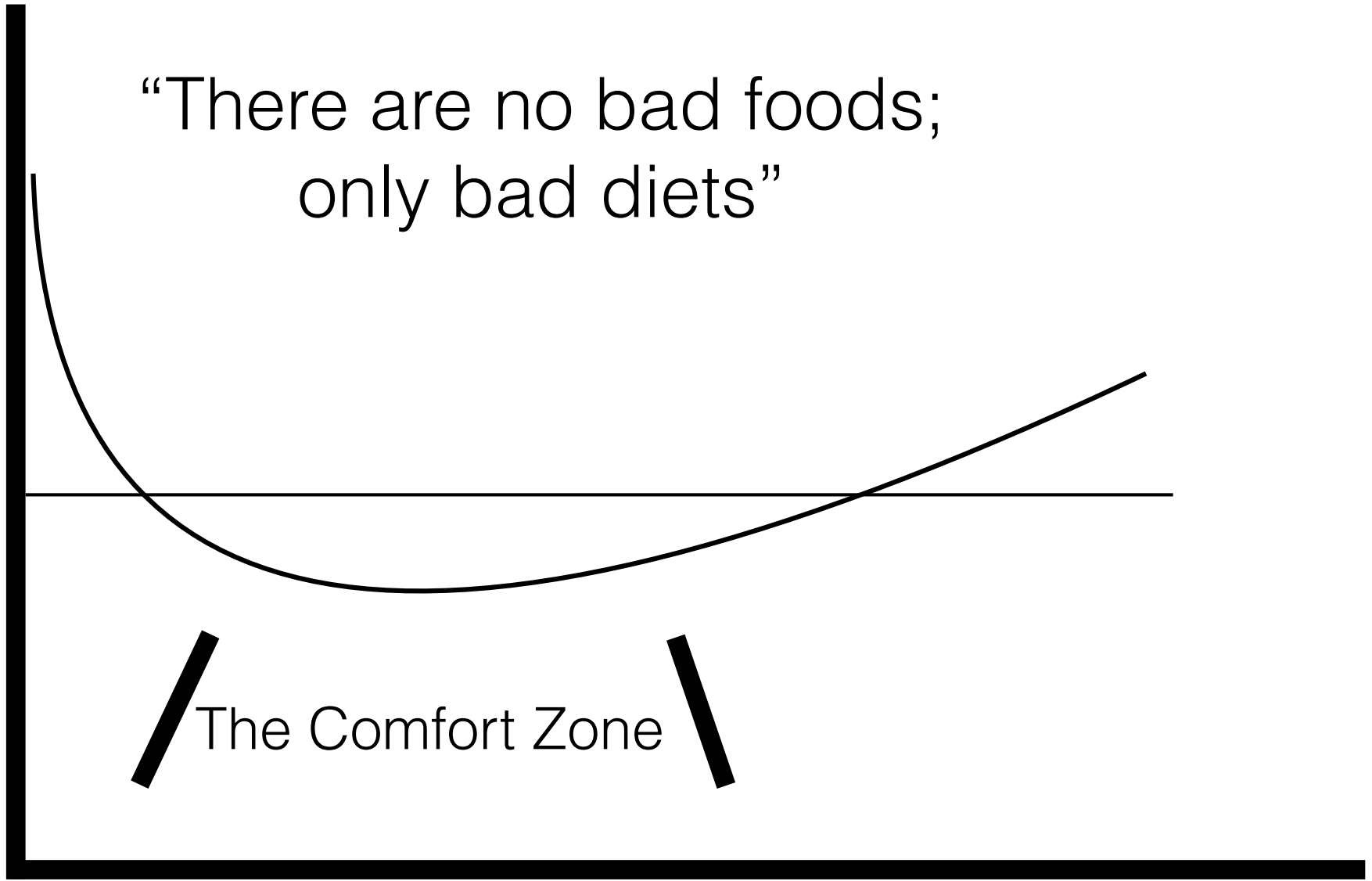
The Comfort Zone

Nothing

Moderation

Way to !@#\$\$% much

Food Ingestion



Organic Foods

Organic food has increased approximately 10 fold in the last 10-15 years

Typically costs - 20-40% more??

Systematic review - all studies on the health nutritional and safety of organic and conventional food

Their conclusions

“The published literature lacks strong evidence that organic foods are significantly more nutritious than conventional foods.

Consumption of organic foods may reduce exposure to pesticide residues and antibiotic-resistant bacteria.”

Ann Intern Med 2012

237 studies

17 health outcomes, 223 nutritional and contaminant levels

Health outcomes

3 looked at clinical outcomes – wheezing allergic symptoms – no differences

Rest looked at vitamin and lipid level type of outcomes – no differences

No studies looking at pesticide levels in humans

Nutritional and contaminant levels - Vitamin C, beta carotene, potassium, calcium, phosphorus, magnesium, iron, protein, fiber, total flavonoids, total phenols

Vitamins - No difference

Nutrients – significantly higher phosphorus and total phenols (have antioxidant effect), organic milk contained more omega 3 fatty acids

Pesticide residues – 7% organic and 38% of conventional samples – but no difference when looking at maximum allowed limits – meat, poultry, eggs and milk not studied

Bacterial contamination - E. coli overall around 6-7% - no difference – looked at animal products – 1/3 to 2/3 were contaminated - 33% higher resistance

Can We Say What Diet Is Best for Health?

“There have been no rigorous, long-term studies comparing contenders for best diet laurels using methodology that precludes bias and confounding, and for many reasons such studies are unlikely”

What is the answer?

Teasing out the benefits and harms of things we eat is EXTREMELY complicated

SINGLE NUTRIENTS

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Some interesting associations - eggs, salt, coffee, alcohol

MULTIPLE NUTRIENTS AND BEHAVIOURS

Issues of RCTs and Cohorts - bias and confounding - answer may be unknowable

How to best lose weight is very individual - low carb/higher fat/protein maybe somewhat better? - is the difference important?

Overall nutrition is hugely personal and emotional

The % of macronutrients, as long as it is well balanced, seems to not make much, if any difference to important outcomes

1. ENJOY EATING

Differences in outcomes are typically found from “extremes” and are “small”

The Mediterranean diet (whatever it is) seems reasonable - also CFG/USDA ~DASH

Eat in moderation/moderation/moderation

Avoid “highly” processed food - within reason

You can easily justify some red meat, butter etc

Eggs, coffee, salt, and alcohol in moderation seem fine if not even healthy

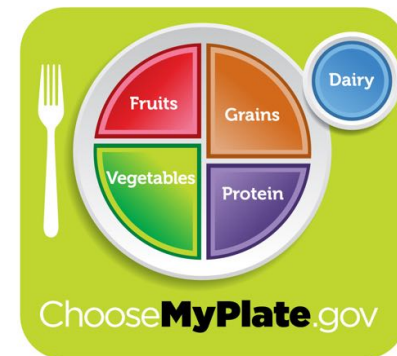
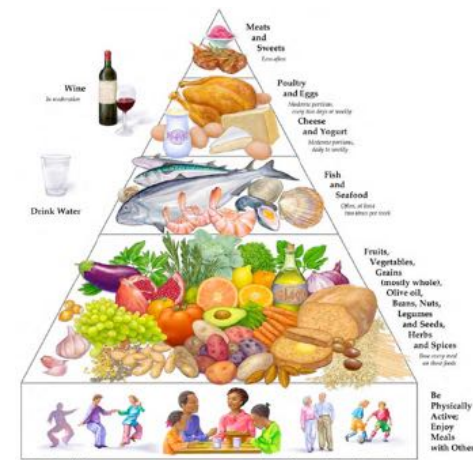
8. Saturated fats - OK - trans-fat?

Added sugars at the high end seem to increase risk

“Big Gulps”- really what is the point of them?

It is VERY unlikely a single “nutrient” would have an important effect

Animal rights/environmental issues are a whole other topic



The M&M's Diet



Mediterranean



Moderation

*"The secret of life is to eat what you like and
let the food fight it out inside"*

Mark Twain