Vittle Virtues and Villainy

Edwin Cox, M.D.

Frontiers in Medicine
November 12, 2018

Victual verities

We must eat to live

- Food supplies fuel for the body's engine
- We require vitamins, minerals and other essential nutrients that come from food

We can choose what we eat

- Amazing variety of foods available
- Many combinations possible

Some foods can keep us especially healthy - virtuous

Other foods can poison and kill us - villainous

Choosing your diet

Enjoyment

Experience

Intuition

Advice of "experts"

Cost

Availability

Religion

Ease of preparation

Maximum health benefit

My approach

Maximize health benefits

Evidence-based

"Just the facts, Ma'am"

Rely solely on valid scientific studies

Where does the greatest danger lurk in our larder?

Is it the pesticides on our fruits and veggies, PCBs in fish, antibiotics and hormones in our meat, mercury in our fish, carbs, that we freak out about?

All scary, but actually, it's none of the above that threatens us most!

What foods provide the greatest benefit?

Is it fruits and veggies, yogurt, tofu, fish?

All good, but no, not really any of those is tip-top!

What to eat:
all you need to know

Regular physical activity

Base diet around nuts, whole grains, vegetables, fruits, beans, fish, poultry, olive oil, vegetable oils

Modest amounts of dairy, eggs

Sparing amounts of red meat, processed meats, sugary beverages, white potatoes, refined grains (white bread, rice, cereal, desserts)

Alcohol in small amounts if not otherwise excluded

Bottom line

Whole grains and nuts sustain health the most

- Surprising perhaps, because nuts are loaded with fat and whole grains are carbs

Red meat kills

- Big time, and it's not just the saturated fat

Fruits and vegetables are important, too

Everything else falls somewhere in between

Just the facts, Ma'am!

Gathering and evaluating the evidence

- Research studies

The purpose of studies is to infer causes

- For example, meat causes coronary heart disease or sugar shortens life span

Types of studies

- Basic research
- Randomized controlled trials
- Cohort (observational) studies

Basic research

Genomics

- Look for genes that are associated with diseases and susceptibility to exposures

Environmental factors

- Exposures correlated with disease causation and progression

Mechanisms of benefit or harm

- How do walnuts lower LDL-cholesterol?

Randomized controlled trials

Subjects allocated to different treatment arms by randomization

- Example: Half on Mediterranean diet, half on standard diet

Outcomes of treatment arms evaluated by statistical tests

Statistically significant results allow us to infer causality

Drawbacks with respect to nutritional epidemiology

- Long, expensive, intrusive
- Short-term studies inconclusive
- Rarely practical in nutritional research
- False positives and false negatives

Randomized Clinical Trials

Lyon Diet Heart Study (France)

- 300 subjects with existing heart disease (secondary prevention)
- Followup: 5 yrs

PREDIMED (Spain)

- 8000 subjects at risk for heart disease (primary prevention)
- Followup: 5 yrs

Both studied Mediterranean Diet

Both showed significant benefit in reducing coronary heart disease compared to control diet

Observational studies

Obtain a large sample of individuals with some well defined common attributes (nationality, occupation, age, etc)

Record age, weight, height, blood pressure, educational level, exercise level, blood tests

Obtain dietary history by food frequency questionnaire (FFQ), food diary, or 24 hr recall

Follow up to determine end points: death, cause of death, and/or onset of specific diseases

Food frequency questionnaire

BREADS (include use as toast and sandwiches)	Never or rarely	1-3 per month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day	Standard Serving Size	Standard	1/2 or less	1½ or more
White bread, rolls, buns, or French bread	○	○	○	○	○	○	○	○	○	2 slices or 1 bun/roll	○	○	○
Whole grain bread, rolls, buns, or oatmeal bread	○	○	○	○	○	○	○	○	○	2 slices or 1 bun/roll	○	○	○
Corn bread, Johnnycake	○	○	○	○	○	○	○	○	○	2 slices or pieces	○	○	○
Other breads, bagels, biscuits you eat? (*please write them in - use* CAPITAL *letters*):													
1. _____	○	○	○	○	○	○	○	○	○	2 slices or pieces	○	○	○

National Nutrition Database for Standard Reference

USDA Branded Food Products Database
Release v0.0 March, 2018

Full Report (All Nutrients) 45102292, BREAD, MADE WITH WHOLE GRAIN, UPC: 071301047179

Nutrient	Unit	Data points	Std. Error	2.0 SLICES 57g	1 Value Per100 g
Proximates					
Energy	kcal	--	--	150	263
Protein	g	--	--	5.00	8.77
Total lipid (fat)	g	--	--	2.00	3.51
Carbohydrate, by difference	g	--	--	28.00	49.12
Fiber, total dietary	g	--	--	2.0	3.5
Sugars, total	g	--	--	3.00	5.26
Minerals					
Calcium, Ca	mg	--	--	200	351
Iron, Fe	mg	--	--	1.58	2.77
Sodium, Na	mg	--	--	280	491
Vitamins					
Vitamin C, total ascorbic acid	mg	--	--	0.0	0.0
Thiamin	mg	--	--	0.000	0.000
Riboflavin	mg	--	--	0.136	0.239
Niacin	mg	--	--	1.754	3.077
Vitamin A, IU	IU	--	--	0	0
Lipids					
Fatty acids, total saturated	g	--	--	0.000	0.000
Fatty acids, total monounsaturated	g	--	--	0.000	0.000
Fatty acids, total polyunsaturated	g	--	--	0.502	0.880
Fatty acids, total trans	g	--	--	0.000	0.000
Cholesterol	mg	--	--	0	0

Observational study analysis

Evaluate outcomes with respect to the "risk factors" (demographic, personal and diet data) with statistical tests

- Example: Heart attack rate is higher in people eating more processed meat

Statistical significance indicates association between risk factors and outcome

Association does not prove causation

- *Achilles' heel* of observational studies
- Replication in different settings, plausible biological mechanisms can validate

Major observational studies

Nurses Health Study (NHS) 100K 30yrs

Health Professional Followup Study (HPFS) 50K 25yrs

Physicians' Health Study (PHS) 50K 25yrs

NIH-AARP Diet and Health Study (AARP) 500K 10yrs

European Prospective Investigation into Cancer and Nutrition (EPIC) 500K 18yrs

Adventist Health Study (AHS)

Health Survey for England (HSE)

Survival analysis

Area of statistical analysis

Duration of time until an event happens

- Death
- Onset of disease
- Relapse from remission
- Industrial - Failure of component

Developed for life insurance

- Rate individuals, set premiums
- Base predictions on risk factors (BP, smoking)

Survival analysis - example

Mortality in British physicians re: smoking

Conducted by UK epidemiologist Richard Doll

Study included 35,000 male British doctors

Study began 1948, last follow-up 2000

25,000 died, 5,000 remained alive, 4,000 withdrew

Cohort: Doctors aged 30-39

Doctors born 1921-1930: 7,385

1,713 never smoked up to age at entry

- 51 had died by age 50 (3.0%)
- Average annual mortality = 3.0%/15 yr = 0.2%/yr (2.0/1000/yr)

2,252 currently smoked at entry

- 158 had died by age 50 (7.0%)
- Average annual mortality = 7.0%/15 yr = 0.48%/yr (4.8/1000/yr)

3,420 former smokers

- Excluded from analysis

Mortality rates and ratios

Mortality rates

- Current smokers: 4.8/1000/yr
- Never smokers: 2.0/1000/yr

Mortality ratio (AKA relative risk, risk ratio)

- MR = RR = 4.8/2.0 = 2.4
- RR > 1: factor has adverse effect on mortality
- RR < 1: factor has beneficial effect on mortality
- RR = 1: factor has no effect on mortality

Interpretation

- "Current smokers at age 35 die 2.4 times as fast in the next 15 years compared to never-smokers"

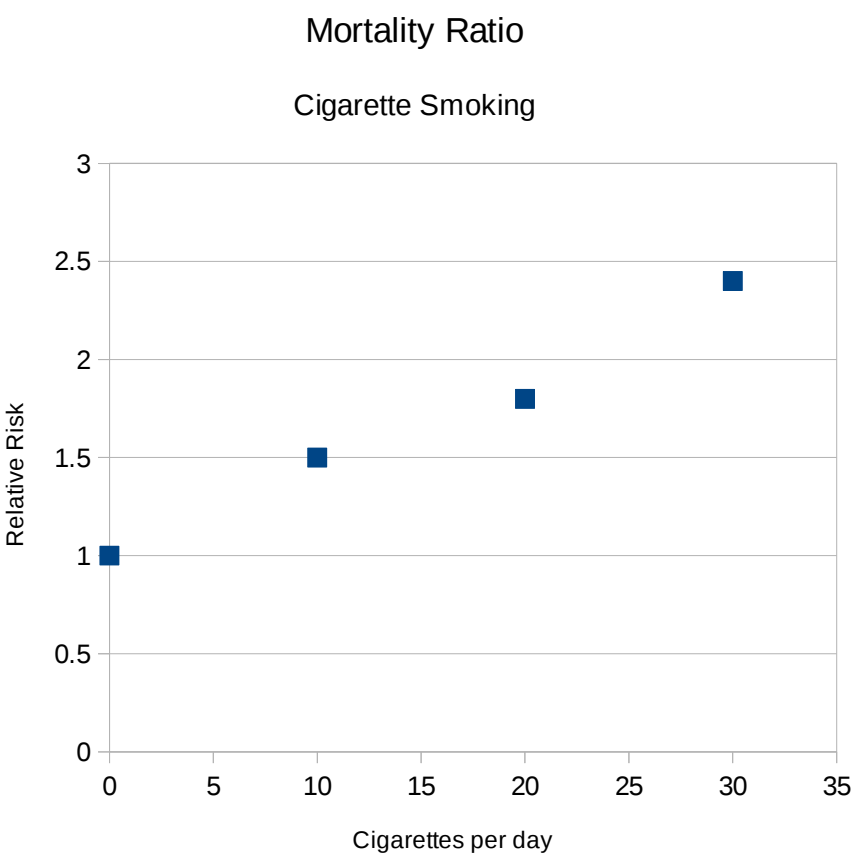
Dose-response: Smoking

Addressing the question: "Is smoking all-or-none, or does the harm increase with dose (number of cigarettes smoked per day)?"

Reference (comparison) is non-smokers

Cigarettes/day	0	1-14	15-24	>24
Mortality rate	19	29	35	45
Mortality ratio	1.0	1.5	1.8	2.4

Dose-response analysis: graphical



How does outcome (mortality, disease incidence) relate to level of exposure to factor?

- Is is a threshold (all-or-none) or a graded effect?

Smoking has a graded, direct (adverse) effect on mortality

Quantiles

Grouping subjects into equal-sized groups

- Halves – 2 groups
- Tertiles – 3 groups
- Quartiles – 4 groups
- Quintiles – 5 groups
- Deciles – 10 groups

Comparisons are made between each quantile and the reference group

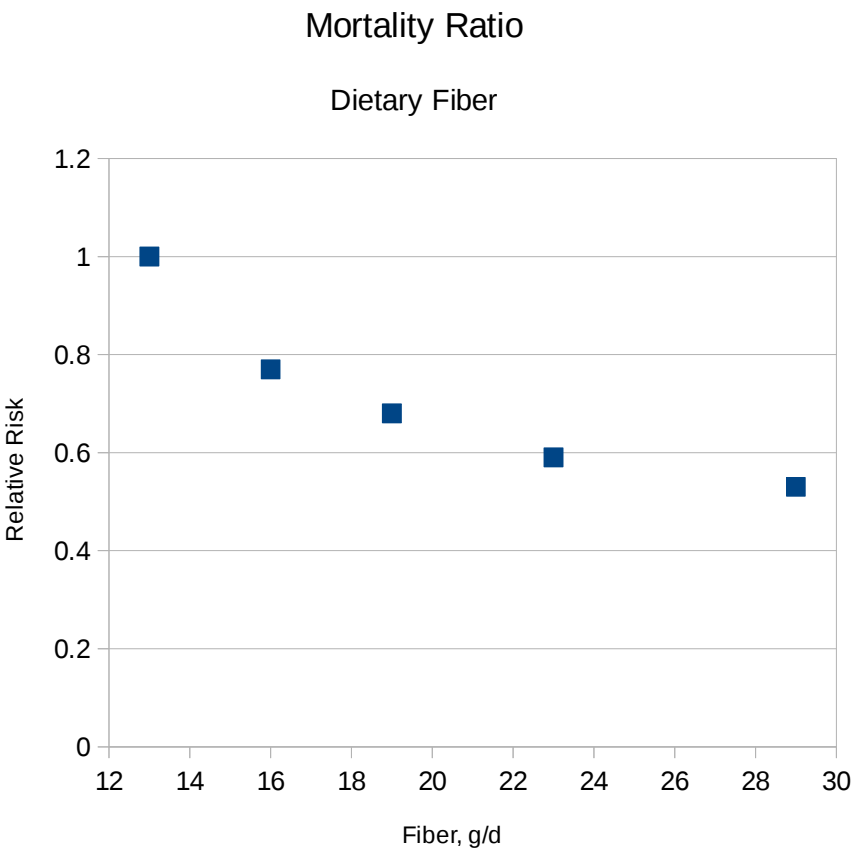
- In this example, subjects are groups in quintiles
- Reference group is quintile 1, the lowest fiber intake
- RR for each other group is its comparison to the first quintile

Dietary fiber and mortality					
Quintile	1	2	3	4	5
Fiber, g/d	13	16	19	23	29
RR	1.00	0.77	0.68	0.59	0.53

Dose-response analysis

How does outcome (mortality, disease incidence) relate to level of exposure to factor?

Dietary fiber has a graded, inverse (beneficial) effect on mortality



Mortality and dietary fiber

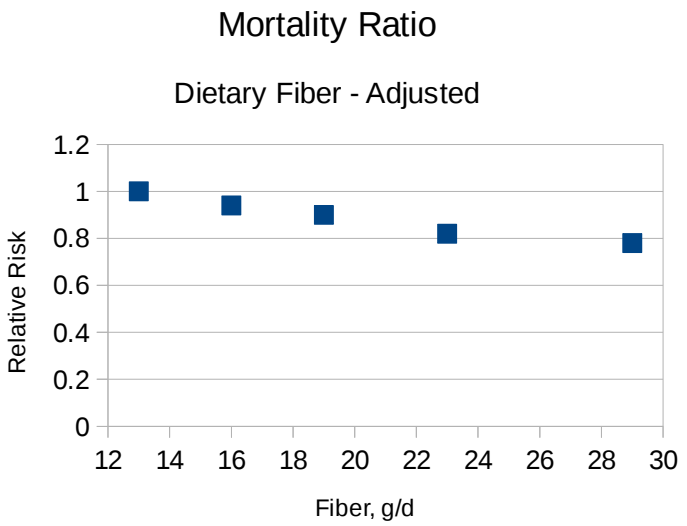
You can cut your mortality rate in half just by doubling your fiber intake?!?

But wait! Those eating less fiber are more likely to smoke cigarettes, are less likely to exercise, have higher body mass index, i.e., have additional risk factors

How do you take the effects of these co-factors into account?

- Multivariable statistical methods
- Proportional hazards survival analysis
- Multiple linear regression

Dose-response, adjusted for risk factors



Dietary fiber and mortality					
Quintile	1	2	3	4	5
Fiber, g/d	13	16	19	23	29
RR	1.00	0.77	0.68	0.59	0.53
Adjusted RR	1.00	0.94	0.90	0.82	0.78

Multiple regression analysis

Estimates effect of main factor after taking effects of other co-factors into account

Fiber effect falls from 47% reduction in mortality to 22% after accounting for co-factors

Causation vs. correlation

Regression analysis finds *associations* (correlation) between outcome and risk factors

Correlation does not prove causation

However, causation becomes more tenable when:

- A biologically plausible mechanism exists to support a cause-effect linkage
- Multiple studies replicate relationship
- Reverse causation is excluded

Lack of correlation does not disprove causation

A negative study does not establish the lack of an effect of a factor

Accurate measurement of intake levels is a gnarly problem in dietary studies

- Total sugar intake especially inaccurate
- Bias in measurements related to gender, BMI, other factors

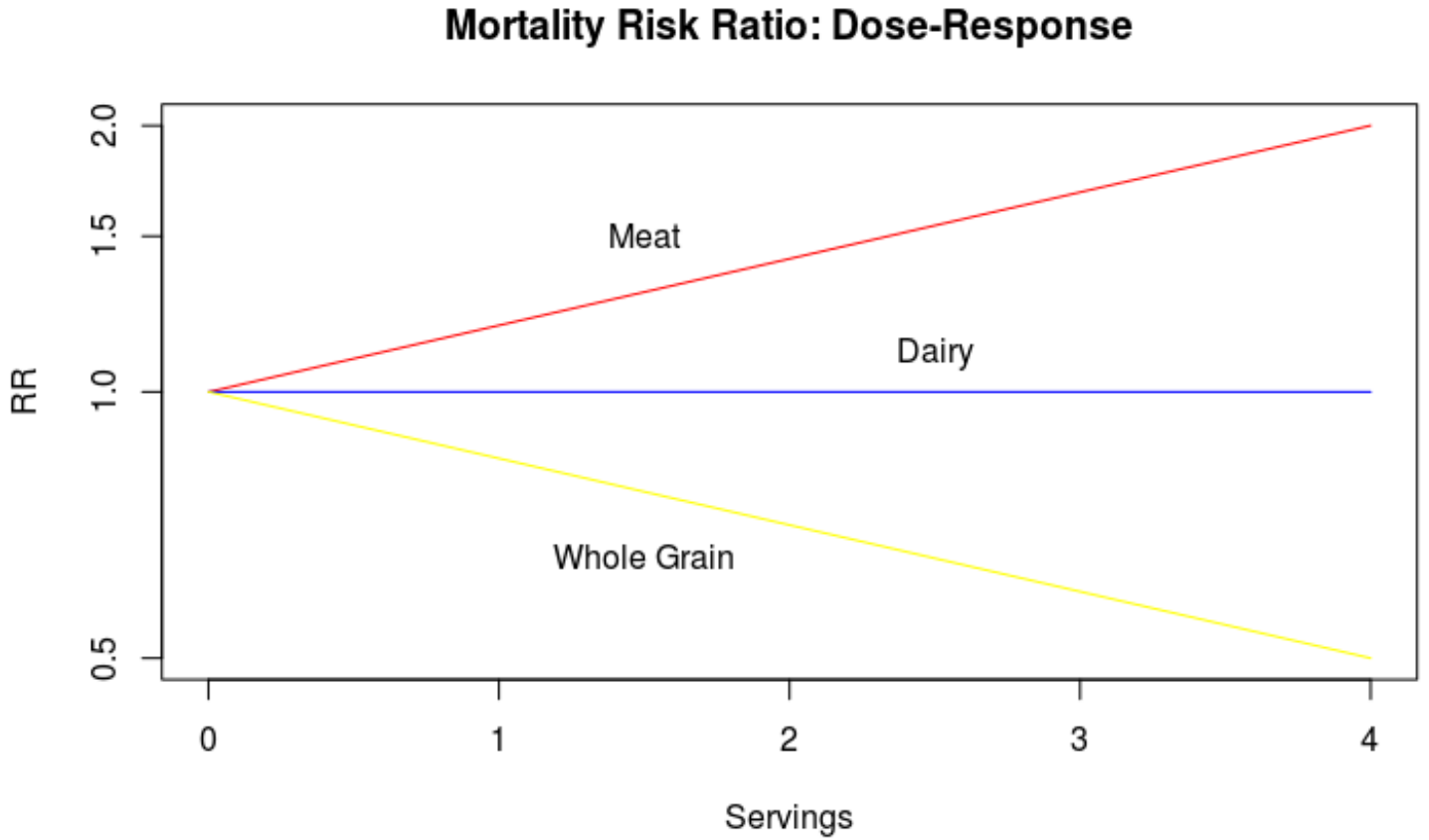
Mis-measurement drives relative risks toward the null (RR of 1.0, non-significant)

Biomarkers may be used to correct for bias and yield more accurate estimates of intake

- Urinary sugar excretion can be used to adjust for diet questionaire bias

Dose-response curve

Plotting mortality ratio vs. magnitude of the exposure

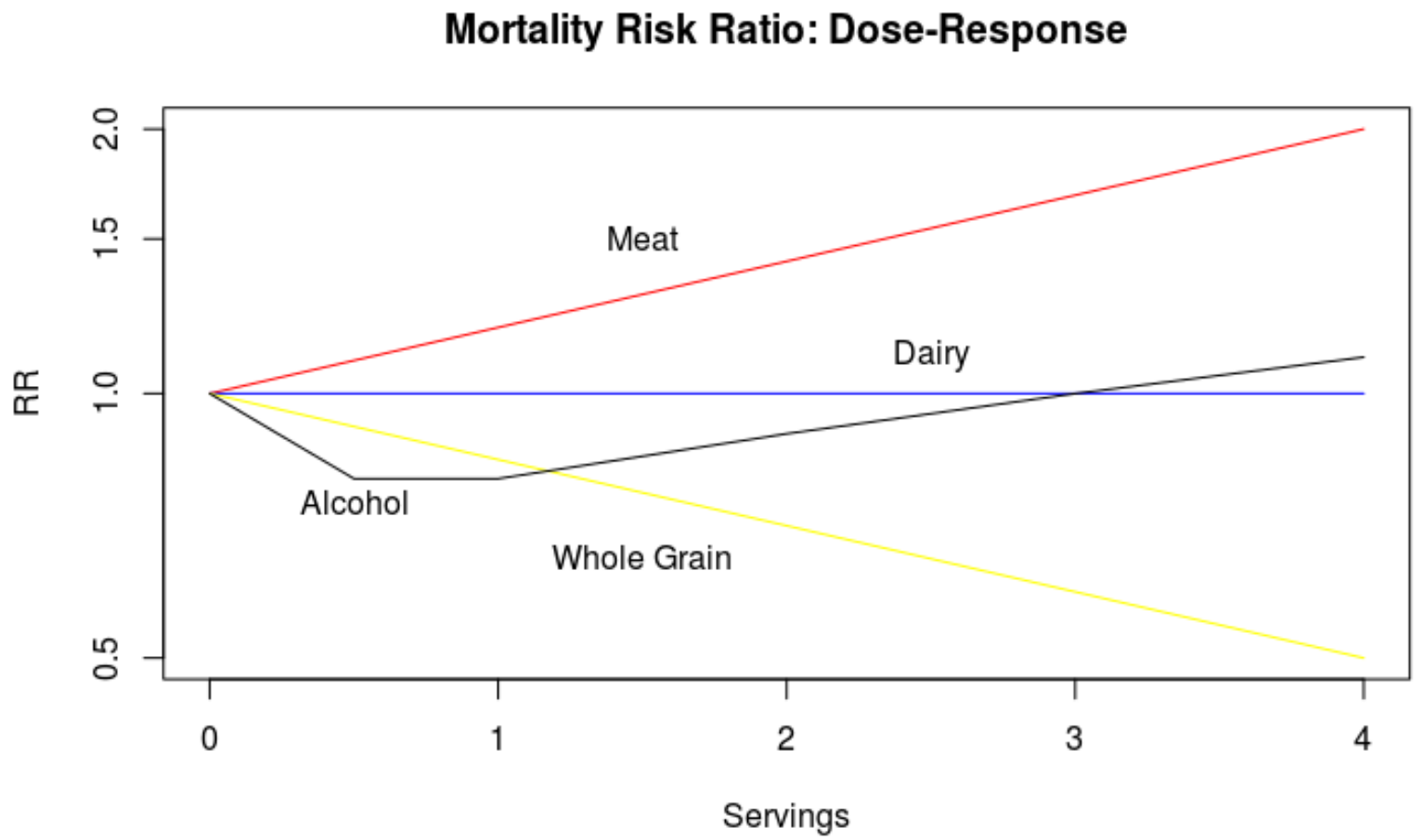


Dose-response curve

Rising D-R → higher risk of death; harmful

Falling D-R → lower risk of death; beneficial

U-shaped D-R → beneficial at low dose, but harm with increasing dose



Red meat kills!

NIH-AARP Diet & Health Study

Mortality from different causes associated with meat, heme iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study: population based cohort study

Arash Etemadi, Rashmi Sinha, Mary H Ward, Barry I Graubard, Maki Inoue-Choi, Sanford M Dawsey, Christian C Abnet

British Medical Journal, 2017

Meat & Mortality

NCI-AARP Diet & Health Study

- 1995 – Invitations sent to 3.5 million AARP members in six U.S. states
- 536,969 subjects (59% male, 41% female)
- Ages 50-71 at intake
- Predominantly white, more education than U.S. population, with fewer smokers, less fat and red meat, more fruits and vegetables consumed

NIH-AARP Study

Methods

- Prospective cohort – observational study
- FFQ 124 items, validated by 24 hr recall
- Meat intake categorized as total, processed, and unprocessed red meat
- White meat evaluated but will be presented separately
- 15 year follow-up with cause of death ascertainment
- Multivariate statistical analysis

NIH-AARP Meat and Mortality

Characteristics of NIH-AARP Diet and Health Study				
	Subjects	Deaths	Deaths CVD	Deaths Cancer
Males	316,505	84,848 (27%)		
Females	220,464	43,676 (20%)		
Total	536,969	128,524 (24%)	34,723	45,740

NIH-AARP Meat & Mortality

Table 1. All-cause Mortality vs. Daily Red Meat Consumption					
Quintile	1	2	3	4	5
Subjects	107,393	107,393	107,393	107,393	107,393
Red Meat consumed (oz/day)	0.6	1.5	2.2	3.1	4.7
Deaths expected	22,075	22,075	22,075	22,075	22,075
Deaths observed	22,075	23,765	25,532	27,321	29,831
Excess deaths (%)	0%	7.7%	16%	24%	35%

NIH-AARP Meat & Mortality

Subjects: 536,965

Deaths (observed): 128,524

Deaths (expected): 110,375

- Assuming all subjects ate little red meat

Excess deaths due to meat: 18,148 (16.4%)

Interpretation: 18,148 persons expected to be alive at the time of evaluation had died prematurely due to chronic meat toxicity

NHS - HPFS

Red Meat Consumption and Mortality: Results from Two Prospective Cohort Studies

An Pan, PhD, **Qi Sun, MD, ScD**, **Adam M. Bernstein, MD, ScD**, **Matthias B. Schulze, DrPH**, **JoAnn E. Manson, MD, DrPH**, **Meir J. Stampfer, MD, DrPH**, **Walter C. Willett, MD, DrPH**, and **Frank B. Hu, MD, PhD**

Departments of Nutrition (Drs Pan, Sun, Bernstein, Stampfer, Willett, and Hu) and Epidemiology (Drs Manson, Stampfer, Willett, and Hu), Harvard School of Public Health, Boston, Massachusetts; Channing Laboratory (Drs Sun, Stampfer, Willett, and Hu) and Division of Preventive Medicine (Dr Manson), Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts; Wellness Institute of the Cleveland Clinic (Dr Bernstein), Lyndhurst, Ohio; Department of Molecular Epidemiology (Dr Schulze), German Institute of Human Nutrition, Arthur-Scheunert-Allee 114-116 Nuthetal 14558, Germany

Archives of Internal Medicine, 2013

Meat & Mortality

Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS)

- 83,644 women & 37,698 men
- Studies begun in the 1980s, now with follow-up data approaching 30 years
- Homogeneous, well-educated populations with high rate of cooperation

NHS - HPFS

Methods

- Prospective cohort – observational
- FFQ 131-166 items
- Covariates: age, BMI, race, smoking, alcohol use, physical activity, multivitamin use, aspirin use, family history (diabetes, CVD), personal history (diabetes, hypertension, hypercholesterolemia)
- Follow-up: Up to 28 years
- Multivariate statistical analysis
- Serving
  - Unprocessed – 3 oz (85 g)
  - Processed – 15 g (bacon), 28 g (sandwich meat), 45 g (hot dog)

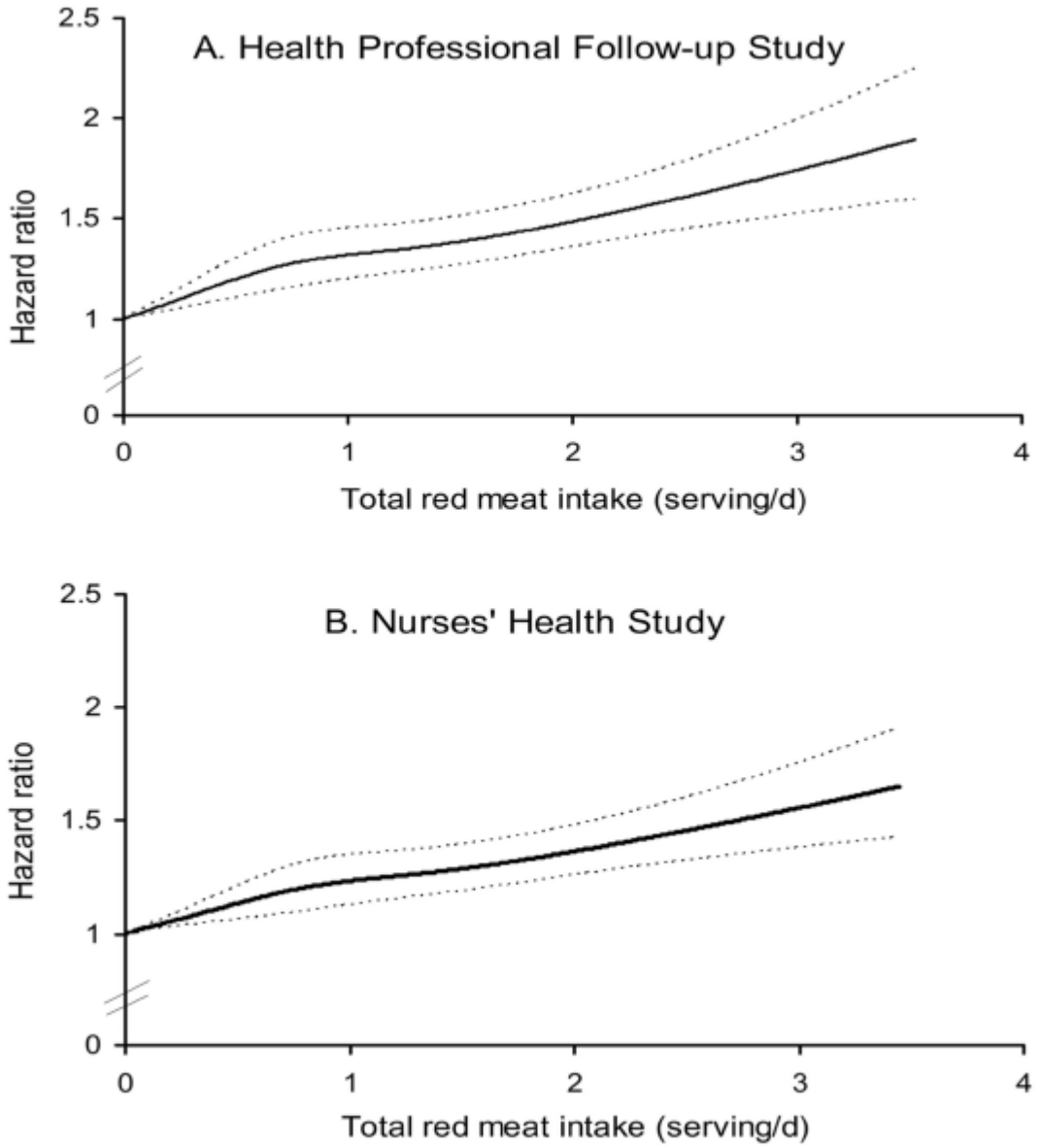


Figure 1. Dose-response relationship between red meat intake and risk of all-cause mortality in (A) Health Professionals Follow-up Study and (B) Nurses' Health Study

What about low-carb, meat-dominant diets?

The Atkins diet and similar weight-control programs rely heavily on meat

This approach may be safe and effective as a short-term strategy to preserve muscle mass while shedding excess fat

But…

A long-term maintenance diet based on red meat is risky business, based on best current evidence

Why is meat bad for us?

We have seen the "what"

Now tell us the "why"

Most powerful effect is on cardiovascular disease, due to atherosclerosis

ASCVD

Atherosclerotic cardiovascular disease

Risk factors identified for atherosclerosis

- Lipoprotein ("cholesterol") metabolism – higher LDL and triglycerides, lower HDL
- Hypertension
- Obesity
- Metabolic syndrome → diabetes

Yet, much of the disease risk remained unaccounted for by these factors

- Who's the perpetrator?
- It makes a great detective story!

Early Work – Meat & Health

Ancel Keys

- Nutrition researcher for U.S. Army during WWII
- Development of K-rations, studies of starvation
- Recognized epidemic of coronary heart disease in middle-class Americans in 1950s, and associated it with diet
- Focused on high saturated fat content of meats and dairy products as likely culprit; recommended moderation in consuming these

The "fat is bad" hypothesis

- The work of Keys and others was misinterpreted
  - Widespread impression that all fats contribute to CHD
  - Low-fat diets became the standard dietary recommendation from mid 1980s into the 2000s
  - Resulting promotion of carbohydrates as a substitute for fat in the diet led to epidemic of obesity, metabolic syndrome and diabetes
  - The specific role of meat consumption remained unclear
    - For example, the Atkins diet was a reaction, emphasizing carbohydrate restriction as a means to weight loss
    - Well-done studies to isolate the effect of specific parts of the diet were not available

The detective – Stan Hazen

Cleveland Clinic is a major heart disease referral center

- Project GeneBank started around 2000, aiming to advance knowledge of the causes, prevention and treatment of cardiovascular disease
- Goal of enrolling 10,000 subjects
- Blood samples obtained for studies

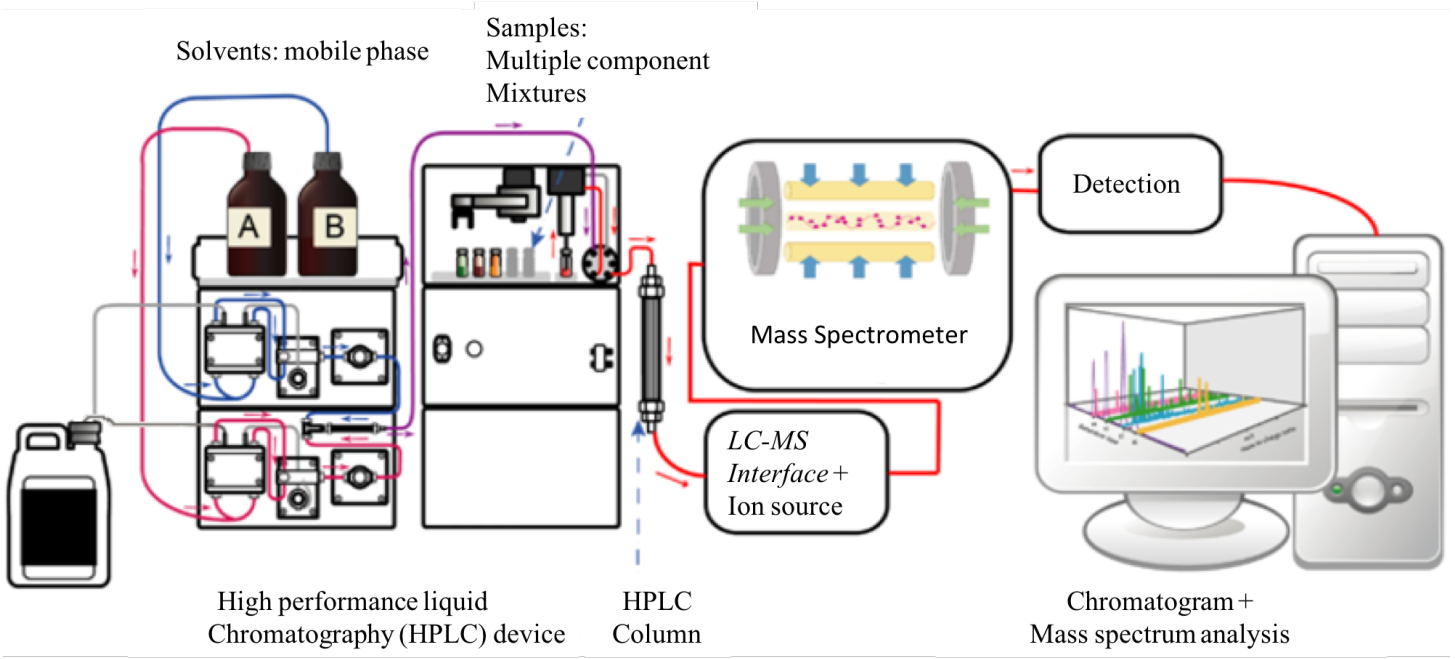
Stanley Hazen, M.D., Ph.D.

- Proposed looking for molecules in blood associated with ASCVD

Detective's high-tech tools

Liquid chromatography / mass spectrometry (LC/MS)

- Analytes separate in LC column by speed with which they flow in a solvent
- Each band of identical molecules characterized in MS by mass-to-charge ratio (m/z) → molecular weight & tentative ID



Hazen's approach

From GeneBank, randomly select 50 patients who had a major adverse cardiovascular event (MACE) and 50 unaffected controls within 3 years of accession

Patients and controls matched for age, sex

Assay blood with LC/MS

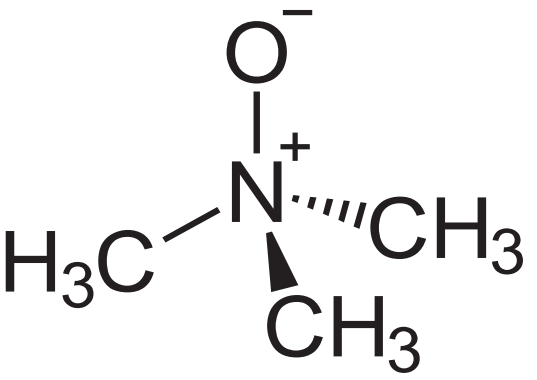
Molecules with higher concentration in patients vs. controls flagged for further study

Trimethylamine N-oxide (TMAO)

M/z 76 compound unequivocally ID'd as TMAO

TMAO is not in the typical human diet and plays no normal role in human metabolism

- What the heck is it doing there ??



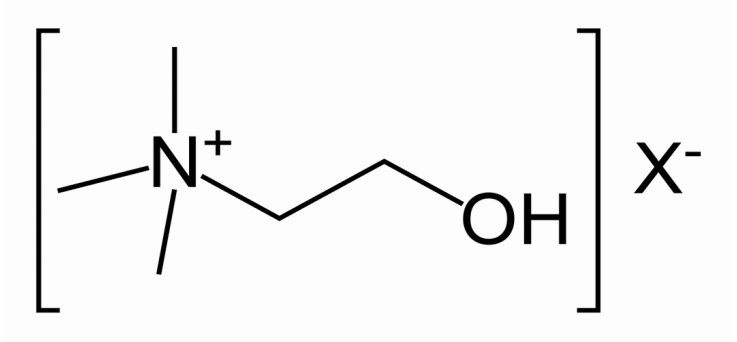
Trimethylamine N-oxide (TMAO)

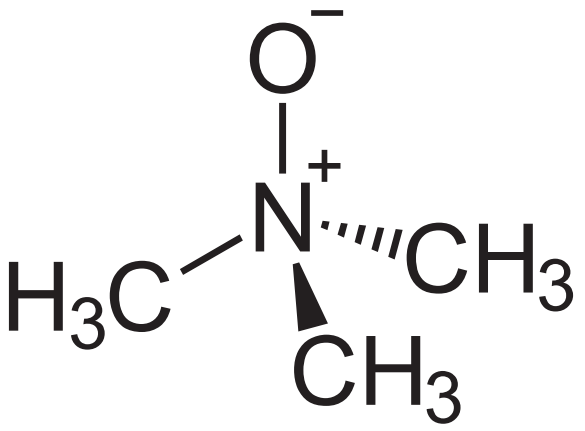
Important compound in deep-sea fish

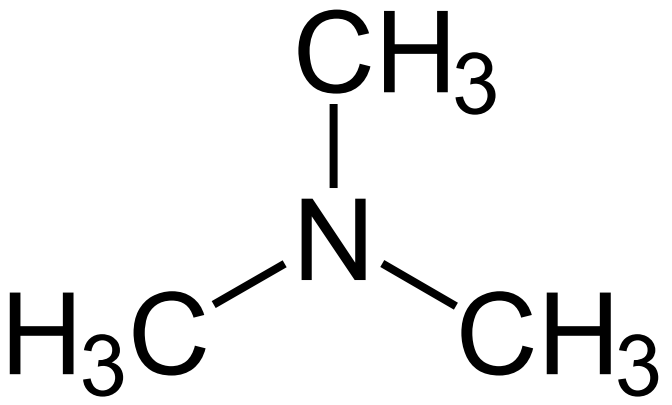
- Stabilizes protein molecules against effects of pressure and osmolarity

Found in other animals, and its metabolism is known

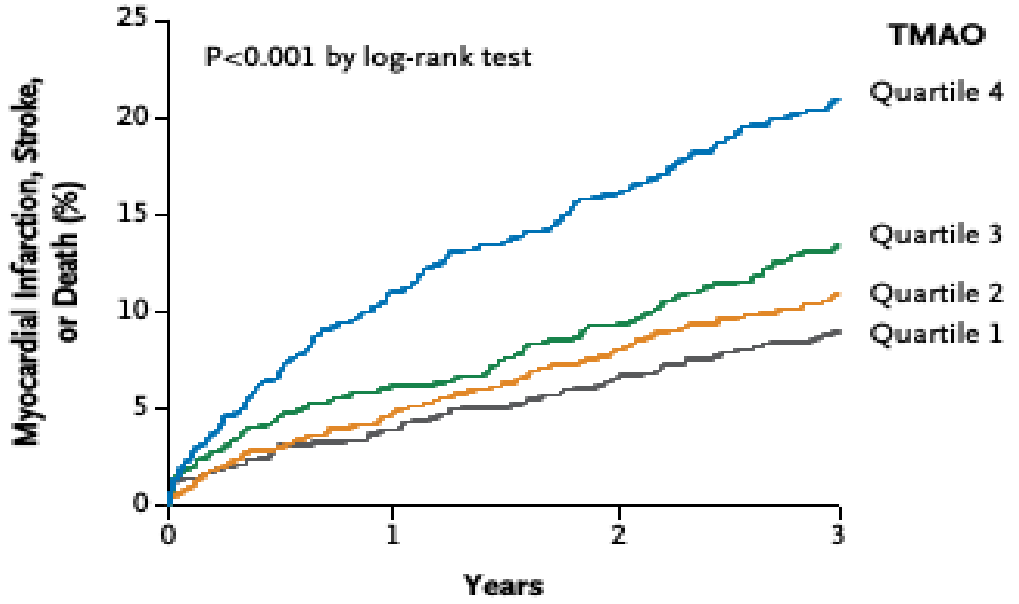
- It's a metabolic product of choline, by way of trimethylamine







ASCVD events and TMAO



No. at Risk				
Quartile 1	1001	933	869	827
Quartile 2	998	940	884	843
Quartile 3	1003	938	888	835
Quartile 4	1005	913	849	791

Figure 2. Kaplan–Meier Estimates of Major Adverse Cardiovascular Events, According to the Quartile of TMAO Level.

Data are shown for 4007 participants in the clinical-outcomes study. The P value is for all comparisons.

Of mice and men and TMAO

Give TMAO to ASCVD-prone mice (APM) → accelerated atherosclerosis (AAS)

APM fed choline or carnitine have TMAO in blood → AAS

Germ-free APM, or those given antibiotics, + choline or carnitine → No AAS!

Humans fed choline or carnitine increase blood TMAO levels

Humans fed choline or carnitine + antibiotics do not increase TMAO

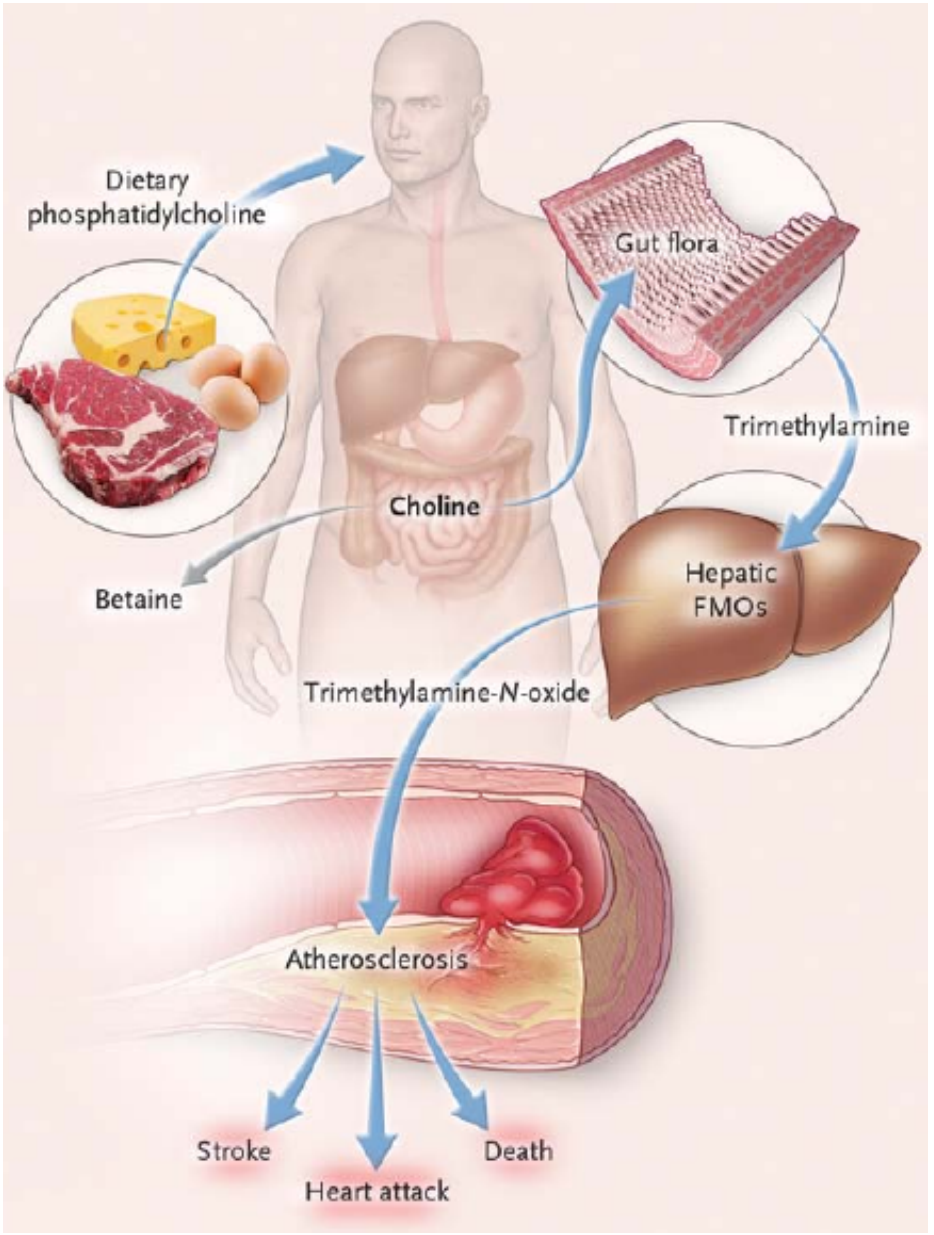
Humans with elevated blood TMAO levels have increased ASCVD events

TMAO & ASCVD

Interpretation

- Choline or carnitine in diet is converted to TMAO by action of gut bacteria (mice and humans)
- Bacterial production of TMAO is suppressed by antibiotics (or absent in germ-free mice)
- TMAO in atherosclerosis-prone mice speeds up atherosclerosis
- Humans likely undergo the same reactions as mice upon exposure to sufficient amounts of dietary choline and carnitine

TMAO & ASCVD



Three step process

- Choline and related molecules in food (carnitine, lecithin) transformed by intestinal bacteria to TMA
- TMA absorbed and transformed by liver enzyme to TMAO
- TMAO promotes AS by interfering with cholesterol disposal

Product	Quantity	Carnitine
Beef steak	100 g	95 mg
Ground beef	100 g	94 mg
Pork	100 g	27.7 mg
Bacon	100 g	23.3 mg
Tempeh	100 g	19.5 mg
Cod fish	100 g	5.6 mg
Chicken breast	100 g	3.9 mg
American cheese	100 g	3.7 mg
Ice cream	100 ml	3.7 mg
Whole milk	100 ml	3.3 mg
Avocado	one medium	2 mg[20]
Cottage cheese	100 g	1.1 mg
Whole-wheat bread	100 g	0.36 mg
Asparagus	100 g	0.195 mg
White bread	100 g	0.147 mg
Macaroni	100 g	0.126 mg
Peanut butter	100 g	0.083 mg
Rice (cooked)	100 g	0.0449 mg
Eggs	100 g	0.0121 mg
Orange juice	100 ml	0.0019 mg

White meat and mortality

Relative Risk of mortality per 20 g per 1,000 kcal per day increase in meat			
	All-cause	CVD	Cancer
Total white meat	0.92	0.92	0.93
Unprocessed white meat	0.92	0.92	0.94
Processed white meat	0.95	0.96*	0.92

$P < 0.001$, except * NS

NIH-AARP Meat and Mortality Study

Wrap on meat

We are engulfed in an epidemic of chronic red meat poisoning that we are scarcely aware of

Meat toxicity could be responsible for more than 10% excess all-cause mortality, much of it from ASCVD

Mechanism for toxicity yet to be fully proven

- TMAO from carnitine could be a major contributor

Bottom line on meat

There is no nutritional requirement for meat

- Plant-sourced protein is fully adequate, as long as care is taken to get all essential amino acid

White meat (poultry) has no associated health threats that have been reported

- Except for rare bacterial contamination of raw product

Red meat (beef, pork) kills!

- Multiple high-quality studies are now in agreement, that excess mortality is highly associated with dietary red meat
- Processed meats (bacon, lunch meats, hot dogs, etc) are especially lethal

Consider reducing your red meat to a couple of servings per week

Why haven't we heard this?

If red meat is so dangerous, why haven't the health authorities and the media informed us?

1) The definitive data are hot off the press

- Published in 2017

2) Unclear why the media has missed it

- Too complicated, not sexy enough

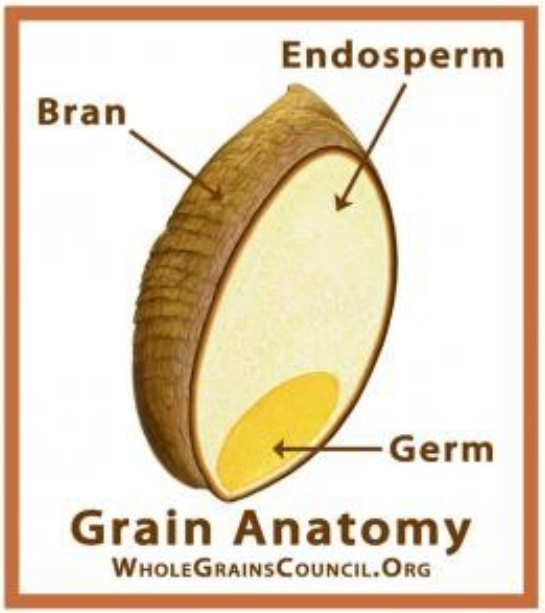
3) Meat industry infiltrates USDA and other committees that generate guidelines

4) Some think it is "old news" → saturated fats

- WRONG!

Virtuous vittles

Nuts and whole grains: They do a body good!



Nuts and whole grains

Botanically similarities

- Seeds – the procreational part of the plant
- DNA, enzymes, protective coat and fuel supply for germination

Differences

- Grains use starches for fuel supply
- Nuts use fats for fuel supply

Fiber is a key component of both

- But what is fiber? It's a carbohydrate...

What are carbohydrates?

Chemical definition

- Compounds made up of single sugars, small clusters of sugars, or large chains of sugars

Nutritional definition

- Sugars
- Starches
- Fiber

Dietary definition

- The main ingredient of many plant-based foods, especially grains, fruits and vegetables
- Absent from animal-based foods other than dairy, which may have lactose

Fiber: Residual Carbohydrates

Oligo- and polysaccharides that cannot be digested pass into the colon, referred to as "fiber"

- Misnomer, since many are small molecules and not literally strands of material implied by the name

In the colon, bacteria consume some of them

- Important, beneficial byproducts are produced

The remainder passes into the stool unchanged

Types of dietary fiber

- Insoluble fiber
  - Cellulose, hemicellulose, lignins, others
  - Passes out of colon intact, binds bile salts, adds bulk to stool
- Soluble fiber
  - Feedstock for intestinal micro-organisms ("gut microbiome")
  - Products of fermentation include many compounds that are beneficial to the colon and body: short-chain fatty acids providing energy, immune signaling, psychoactive compounds

Soluble fiber

- Fructans (polymers of fructose)
  - Inulin (chickory, Jerusalem artichoke, many others)
  - Fructose oligosaccharides (FOS)
- Pectin (polymers of glucuronic acid)
  - Apples, citrus peels
- Raffinose (trisaccharide galactose-glucose-fructose)
  - Legumes, leafy vegetables
  - Bacteria digest, produce gas
  - Alpha-galactosidase (Beano) splits to galactose and sucrose
- Alginic acids
  - Algae

Sources of dietary fiber

- Whole grains
  - Wheat, barley, quinoa, rice, corn, aramanth, ...
  - Fiber is in the bran, the hull of the kernel
  - Processed grains have the fiber removed
- Fruits
- Vegetables
- Pulses (AKA legumes, beans)
- Nuts
- Seeds

Fiber ca. 1960's knowledge

- Useful for treating constipation, irritable bowel, and similar intestinal problems
- Adjunct for lowering cholesterol level by removing bile salts before they recirculate
- Psyllium seed (Metamucil) was the main preparation recommended; inulin, dextran
- Fruits and vegetables contain substantial amounts of fiber, and we know they are good for us
- Fiber slows intestinal absorption, reducing glucose spikes and resulting insulin spikes
- Beans are "good for the heart", but are hard to digest and bring on undesirable side effects ("the musical fruit")

Fiber ca. 2016 knowledge

- Fiber feeds our gut microbiome
  - The human "meta-organism": human + microbiome
  - Gut microbiome considered by some to be an endocrine organ
  - Food for our microbiome given the name "prebiotics"
- The quality of what we feed our microbiome is a key determinant of how well it functions on our behalf
  - More about the microbiome and its functions next semester

Fiber & mortality: NIH-AARP

Dietary fiber intake and mortality in the NIH-AARP Diet and Health Study

Yikyung Park, Sc.D[1], **Amy F. Subar, Ph.D.**[2], **Albert Hollenbeck, Ph.D**[3], and **Arthur Schatzkin, MD**[1]

[1]Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD

[2]Division of Cancer Control and Population Sciences, National Cancer Institute, Rockville, MD

[3]AARP, Washington, DC

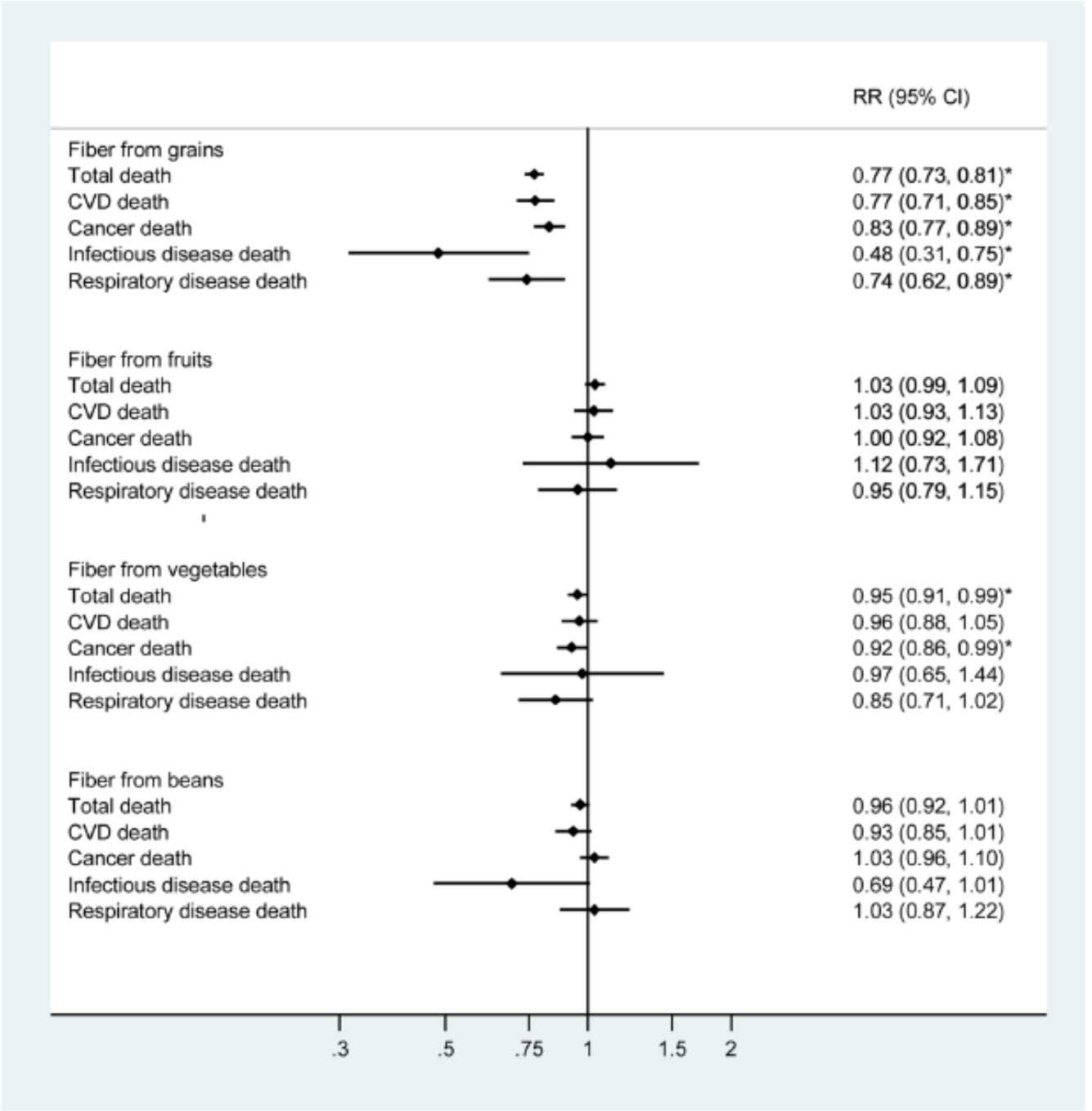
Park et al Arch Int Med 2011

Table 2

Relative risks and 95% confidence intervals of total death for quintiles of dietary fiber intake in men and

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P trend
Men (median intake, g/day)	12.6	16.4	19.4	22.9	29.4	
Death (n)	5278	4292	3898	3453	3205	
Mortality rate[a]	1391	1081	957	824	747	
Age-adjusted	1.00	0.77 (0.74–0.81)	0.68 (0.66–0.71)	0.59 (0.56–0.61)	0.53 (0.51–0.56)	<0.001
Multivariate I[b]	1.00	0.90 (0.86–0.93)	0.86 (0.82–0.89)	0.78 (0.75–0.82)	0.75 (0.72–0.79)	<0.001
Multivariate II[c]	1.00	0.94 (0.90–0.98)	0.90 (0.86–0.94)	0.82 (0.78–0.87)	0.78 (0.73–0.82)	<0.001
Smoking status[d]						
Never smokers (n=3877)[e]	1.00	0.96 (0.86–1.08)	0.96 (0.86–1.08)	0.84 (0.74–0.95)	0.81 (0.71–0.93)	<0.001
Former smokers (n=10777)	1.00	0.91 (0.86–0.97)	0.87 (0.82–0.93)	0.81 (0.76–0.87)	0.76 (0.70–0.82)	<0.001
Current smokers (n=4502)	1.00	0.99 (0.91–1.07)	0.96 (0.88–1.06)	0.85 (0.76–0.95)	0.82 (0.70–0.95)	0.003
Body mass index[f]						
<25 (n=6307)	1.00	1.00 (0.93–1.08)	0.95 (0.87–1.03)	0.86 (0.78–0.94)	0.82 (0.74–0.92)	<0.001
25–<30 (n=8961)	1.00	0.93 (0.87–0.99)	0.92 (0.86–0.99)	0.82 (0.76–0.89)	0.79 (0.72–0.86)	<0.001
≥30 (n=4148)	1.00	0.86 (0.78–0.94)	0.79 (0.71–0.87)	0.78 (0.70–0.87)	0.74 (0.65–0.84)	<0.001

A. men



* P-trend <0.05

Nut consumption & mortality

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Association of Nut Consumption with Total and Cause-Specific Mortality

Ying Bao, M.D., Sc.D., Jiali Han, Ph.D., Frank B. Hu, M.D., Ph.D., Edward L. Giovannucci, M.D., Sc.D., Meir J. Stampfer, M.D., Dr.P.H., Walter C. Willett, M.D., Dr.P.H., and Charles S. Fuchs, M.D., M.P.H.

- Bao et al – NEJM - 2013

Nut Consumption & mortality

- Prospective cohort studies begun in 1980s
  - Nurses' Health Study 76,000 women
  - Health Professionals Follow-up Study 42,000 men
  - 27,000 deaths for analysis
  - 30 year follow-up
  - Excluded: pre-existing cancer, heart disease or stroke; incomplete data

All-cause mortality relative risk vs. nut consumption

	Nuts: Servings per Week					
	0	<1	1	2-4	5-6	7+
RR Unadjusted	1.00	0.72	0.68	0.62	0.65	0.67
RR Adjusted	1.00	0.93	0.89	0.87	0.85	0.80

- Increasing nut consumption was strongly associated with lower all-cause mortality
  - 33% reduction for habitual consumption vs. never
- However, some of this was accounted for by healthier life habits (e.g., less smoking, more exercise)
- Even after adjusting for these risk factors, those consuming the most nuts had a 20% lower mortality than those never consuming nuts

Nut Consumption & Mortality

- Heart disease
  - 26% reduction in death rate
  - Men = women
  - Peanuts = tree nuts
- Cancer
  - 9% reduction in death rate
  - Tree nuts > peanuts

NIH-AARP
Whole Grain & Mortality

Huang *et al. BMC Medicine* (2015) 13:59
DOI 10.1186/s12916-015-0294-7

BMC Medicine

RESEARCH ARTICLE Open Access

Consumption of whole grains and cereal fiber and total and cause-specific mortality: prospective analysis of 367,442 individuals

Tao Huang[1], Min Xu[1], Albert Lee[2], Susan Cho[3] and Lu Qi[1,4*]

NIH-AARP WG & Mortality

	Unadjusted		Adjusted	
	Relative risk	% change	Relative risk	% change
All causes	0.61	-39	0.83	-17
Cardiovascular	0.60	-40	0.83	-17
Cancer	0.61	-39	0.85	-15
Diabetes	0.37	-63	0.52	-48*
Respiratory	0.45	-55	0.89	-11*
Infection	0.57	-43	0.77	-23*
Other	0.72	-28	0.86	-14*

Mortality for quintile 5 (highest) vs. quintile 1 (lowest) level of **whole grain** consumption

P<0.0001, except * 0.02<p<0.0009

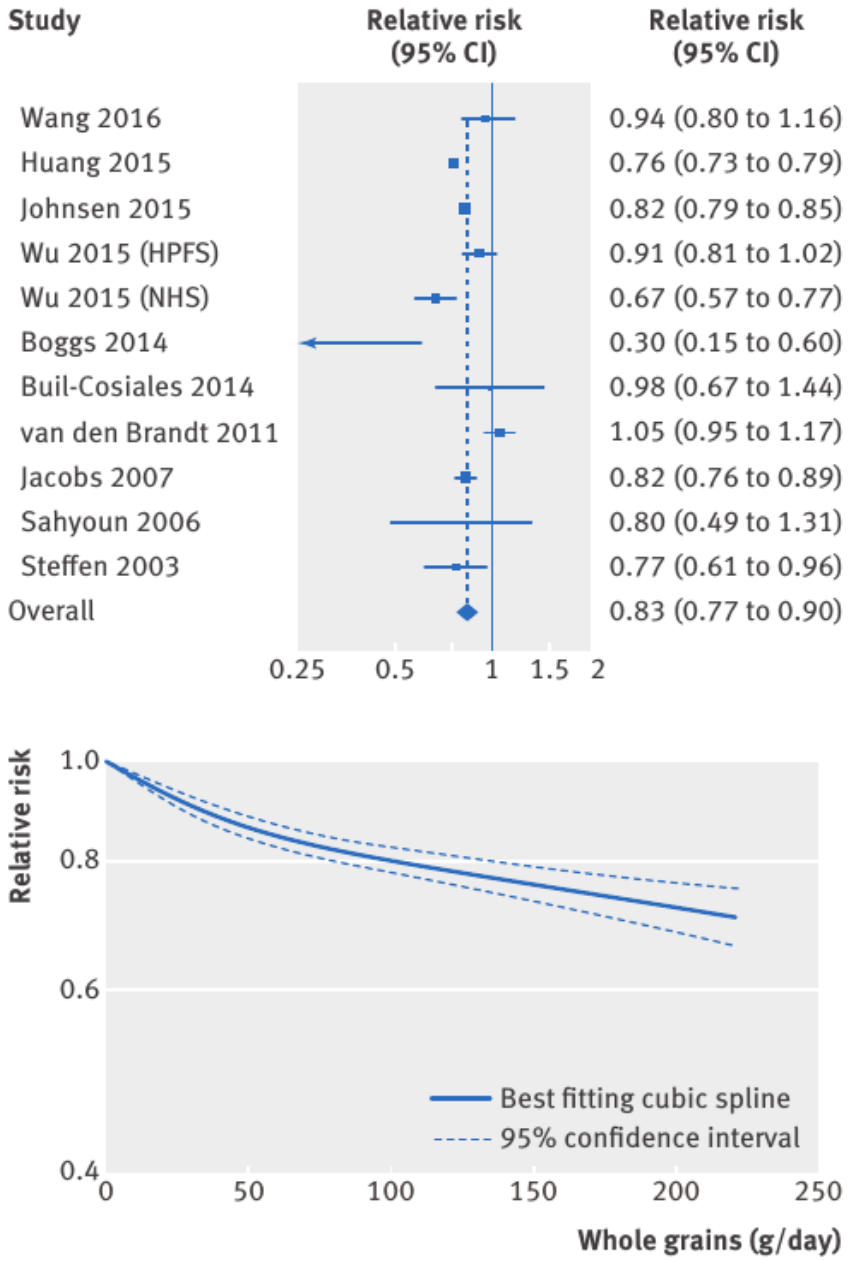


Fig 6 | Forest plot for consumption of whole grains (per 90 g/day) and risk of all cause mortality, with graph illustrating non-linear response

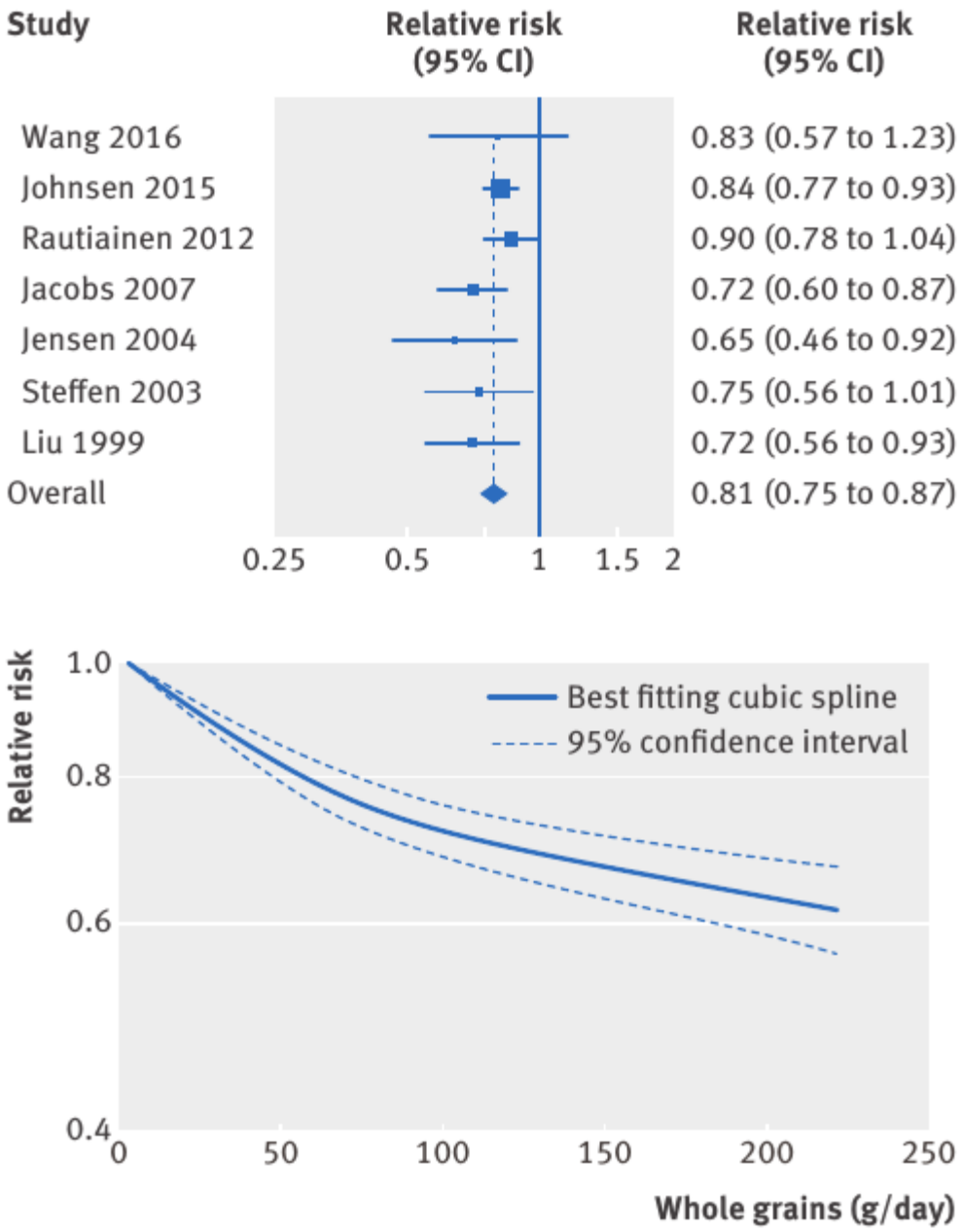


Fig 2 | Forest plot for consumption of whole grains (per 90 g/day) and risk of coronary heart disease, with graph illustrating non-linear response

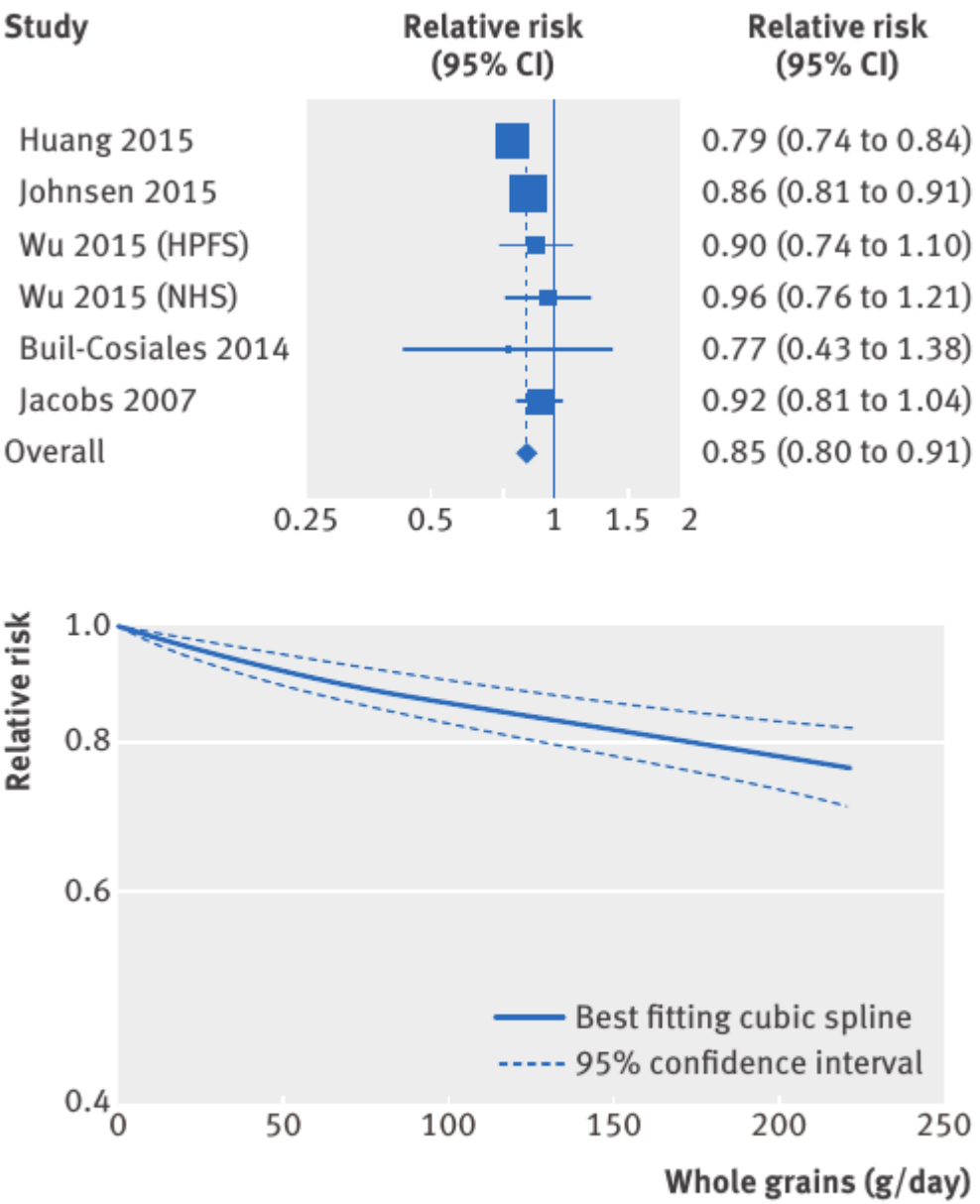


Fig 5 | Forest plot for consumption of whole grains (per 90 g/day) and risk of total cancer, with graph illustrating non-linear response

Finding Whole Grain Foods

THE BASIC STAMP

THE 100% STAMP

Fiber Rule of 10%

We get about 1000 calories / day from carbs (50% of 2000 Kcal)

That's 250 g of carbs (1000 g / 4 cal per g)

We're aiming for 25 g of fiber / day

25/250 is 10%

If we eat carbs where fiber is 10% or more of total carbs, we will get 25 g of fiber / day

- White pasta has 2 g fiber, 40 g total carb per serving → 5% fiber
- Whole grain pasta has 5 g fiber, 40 g carb per serving → 12.5% fiber
- Whole grain pasta contributes a good share, white pasta not so much

Data needed is on Nutrition Facts label on package

Plant foods to eat regularly

Nuts

- ½ to 1 oz a day
- Tree nuts and peanuts both fine

Whole grains

- Whole grain breakfast cereals (bran)
- Whole grain bread
- Whole grain pasta
- Brown rice
- 5 servings a day

Vegetable oils

- Olive oil
- Salad dressings (full fat)
- Casseroles based on vegetable oils

Fiber

- 30+ g/d
- Nutrition Facts label
  - Products with 1+ g fiber for every 10 g total carbs

Fruits and vegetables

- 3+ servings a day of each
- 6 servings a day combined
- Avoid fruit sugar "bombs"
  - Fruits juices
  - Canned, frozen fruits with sugar pack

Legumes

- Beans
- Hummus

Plant foods to eat sparingly

One serving a day **total**

Refined carbohydrates

- White bread, rolls, biscuits, crackers
- White rice
- White pasta
- Desserts: cakes, cookies, pies, donuts

Starches

- White potatoes

Sugar

- Beverages
- Candy
- Desserts
- Added and natural sugar

Animal foods OK to eat regularly

Poultry

- Main every-day meat
- Chicken
- Turkey

Fish

- 2 servings a week
- Oily deep-sea fish (omega-3)

Dairy

- Cheese
- Yogurt

Animal foods to eat sparingly

Red meat

- Once a week for main course
- As a condiment – small portions to add flavor and interest
- Beef, pork, lamb
- Processed more potent – smaller servings

Eggs

- Twice a week

Dairy

- Milk, for cereal and with tea or coffee

Other lifestyle influences

Alcohol

- Possible benefit of a small daily drink (5 oz wine, 12 oz beer, 1.5 oz liquor)
- Non-drinkers should not start drinking "for health's sake"
- Increasing consumption invites serious health and other problems

Exercise

- Substantial health benefit accompanies regular moderate physical activity
- Even 20 minutes a day of steady walking is useful
- Benefit increases with increasing level of activity

Harvard Food Pyramid

More information

Web site for my OLLI at Duke class:

http://olli-what-to-eat-and-why.weebly.com

Web site for OLLI courses:

http://learnmore.duke.edu/OLLI