

MAYO
CLINIC



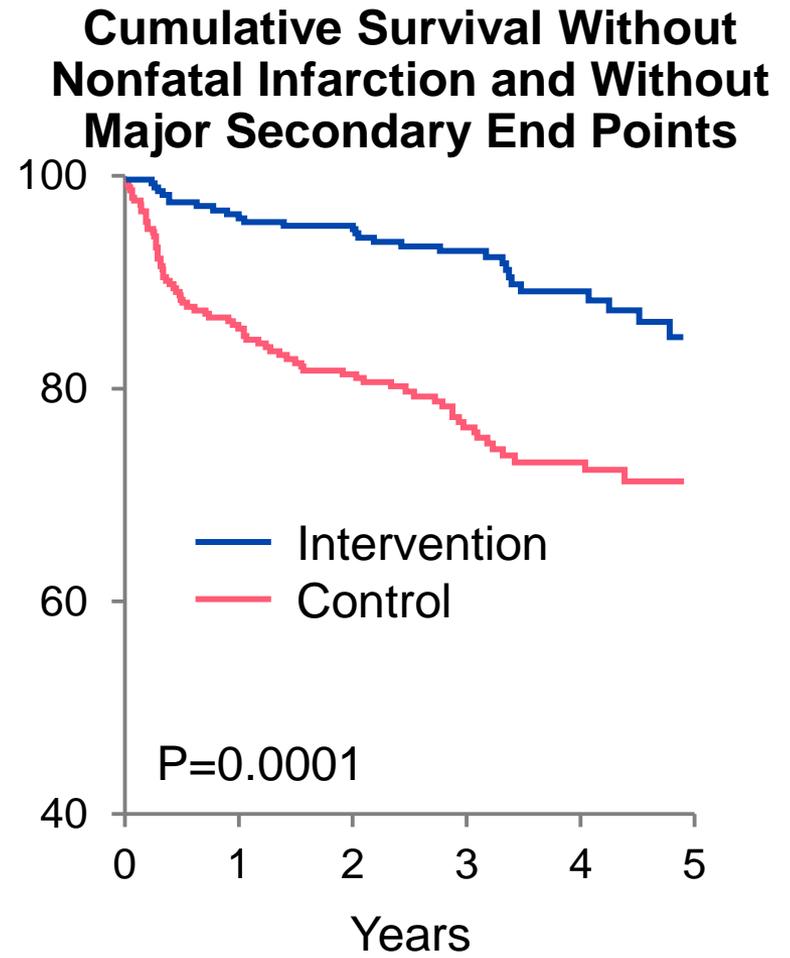
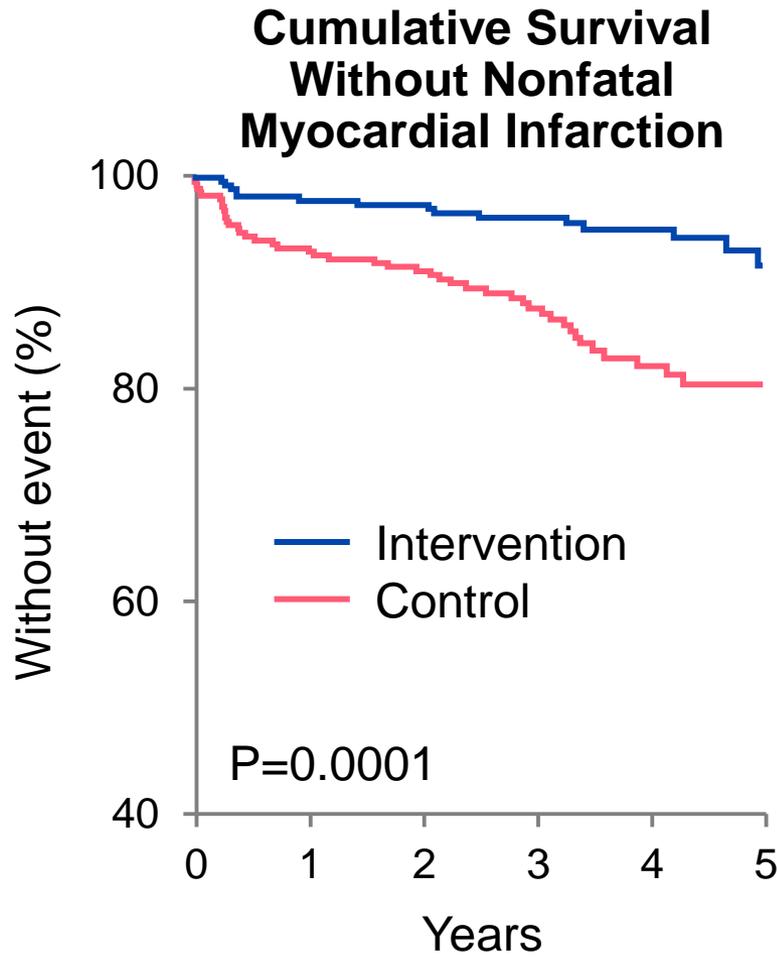
Food for the Healthy Heart

Amir Lerman, MD

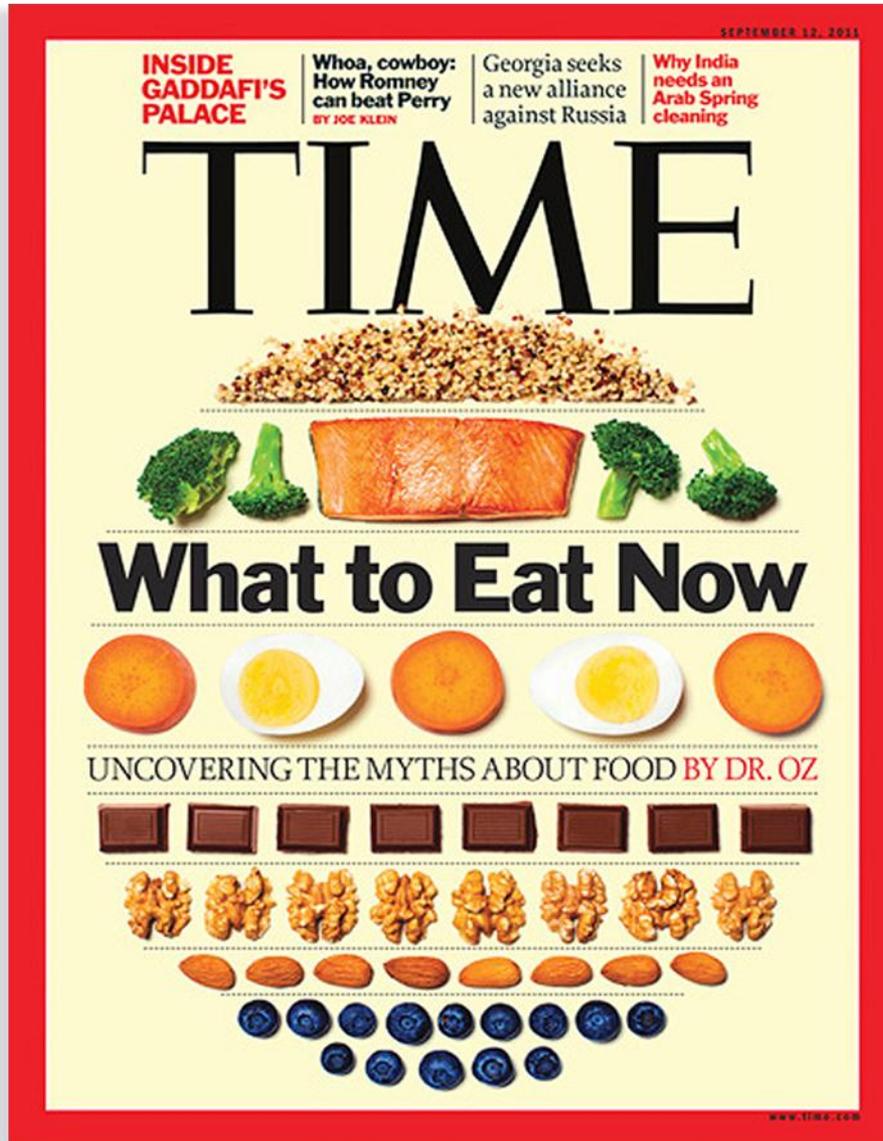
Professor of Medicine
Chair for Research
Cardiovascular Division
Mayo Clinic, Rochester, MN



New Intervention and CV Events in Patients Following Their First MI



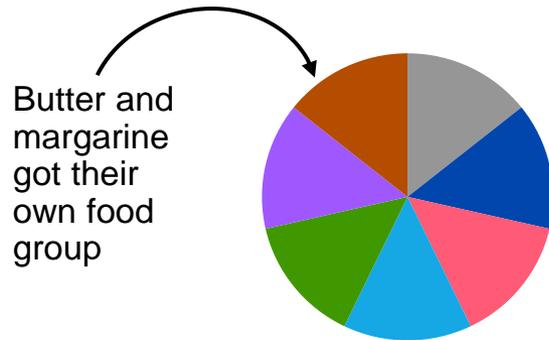
de Lorgeril M et al: *Circulation* 99:779,1999



The average American spends nearly 80 minutes per day eating, and/or deciding what to eat

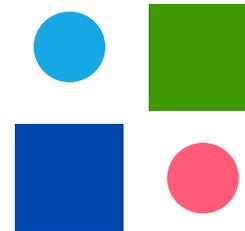
A Brief History of Dietary Guidelines

No Wonder We're Hungry for Clarity



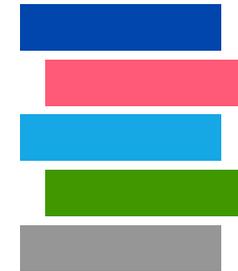
1940s

Good eating focused on choosing among the “basic seven” food groups



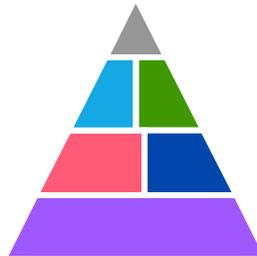
1956-1970s

A new guide touted “food for fitness” and trimmed the seven groups to four



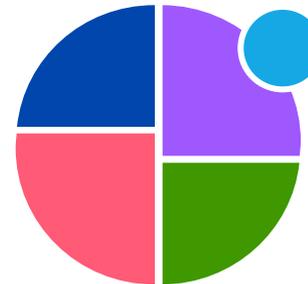
1979

A fifth group was added – along with a caution sign – for fats, sweets and alcohol



1992

The food pyramid emphasized how much of different foods to eat daily



2011

MyPlate uses a plate and cup to show daily portions (and shrinks the amount of grains)

- Fruit
- Vegetables
- Dairy
- Protein
- Grains
- Fat, sweets

Problem Statement(s)

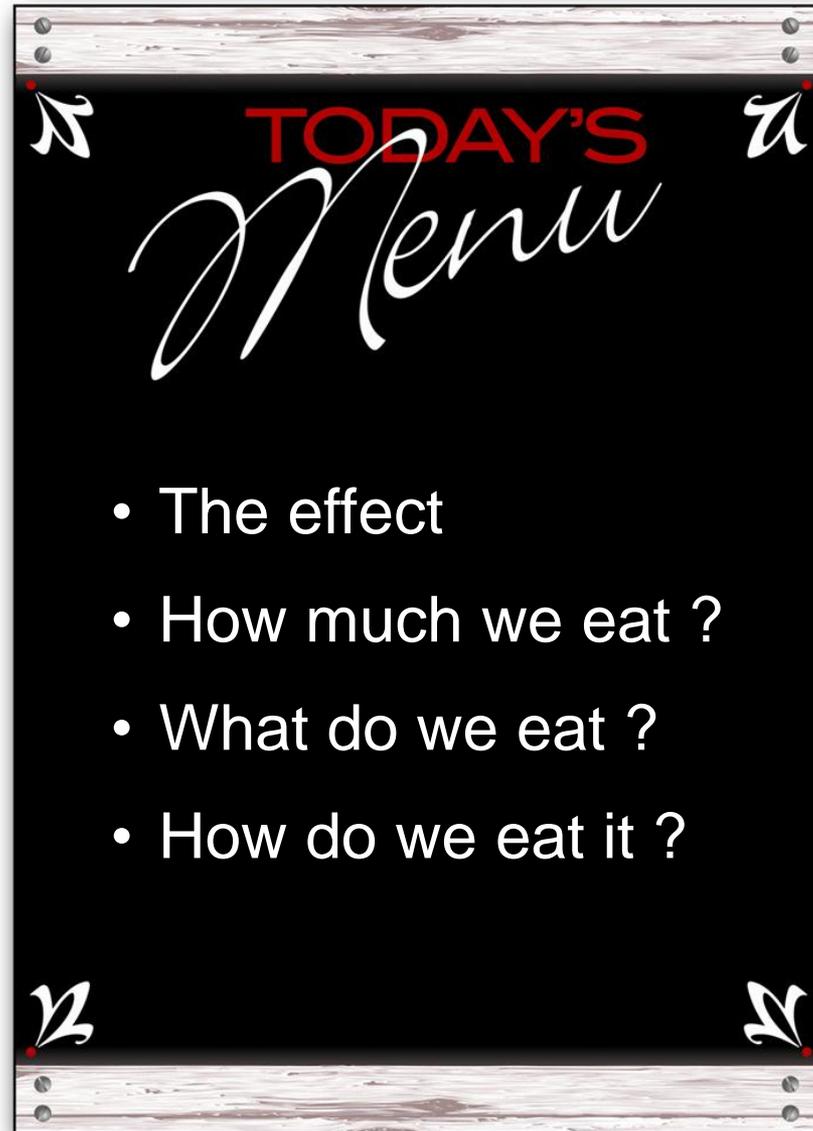
Discrepancy between epidemiological data and outcomes data

- Most data is retrospective or cohort in nature
- RCT data is difficult to accomplish in large numbers, well-controlled study and blinded

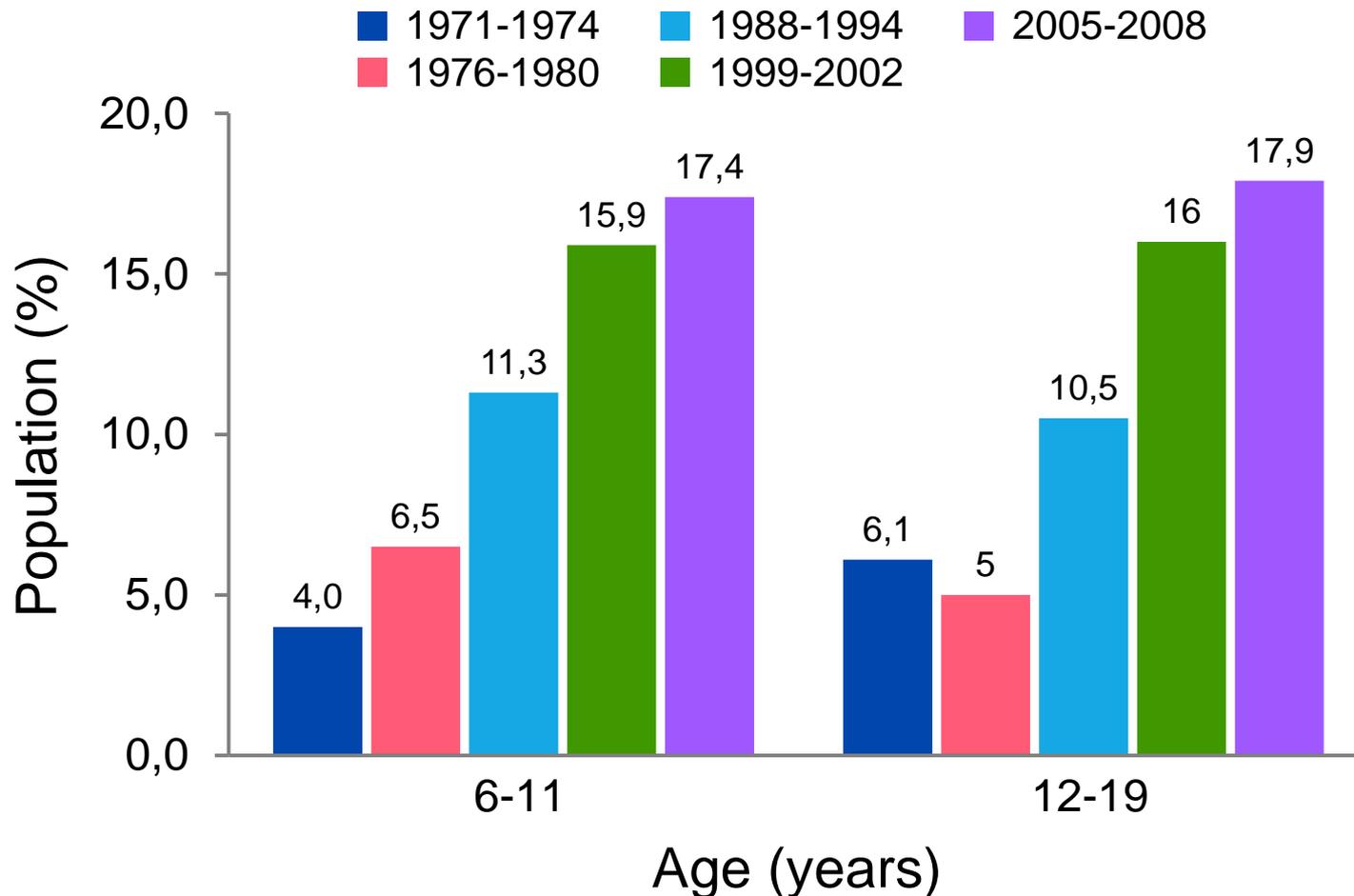
Discrepancy between studies examining “surrogate” CVD markers and studies measuring CVD outcomes

- Few studies have supported one single food as being overtly beneficial
- Difficulty in maintaining calorie neutral studies
- Most positive studies highlight “diets” as being beneficial without being to link mechanism to outcome

Food for Your Heart



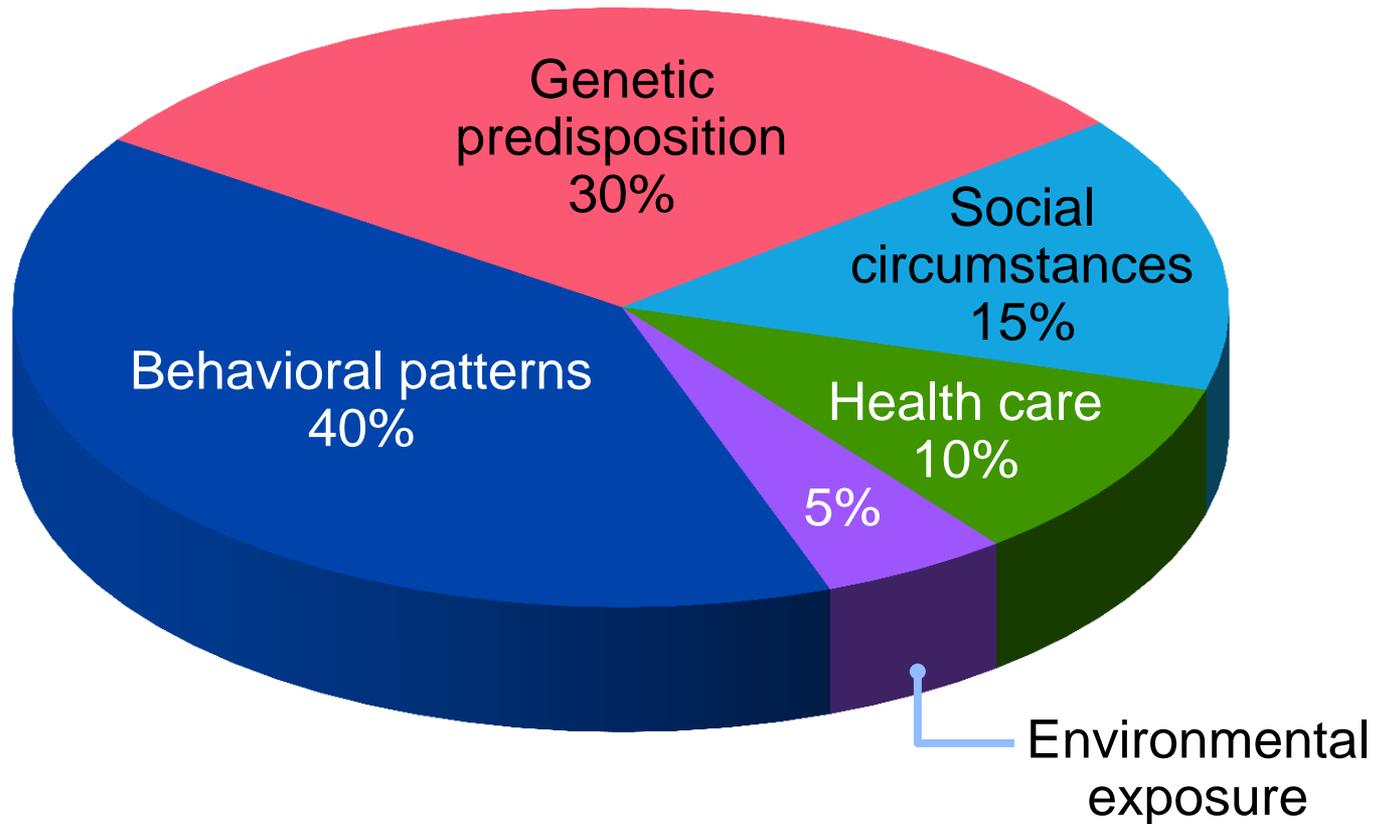
Trends in the Prevalence of Obesity Among U.S. Children and Adolescents by Age and Survey Year



Roger et al: Circulation, 2012

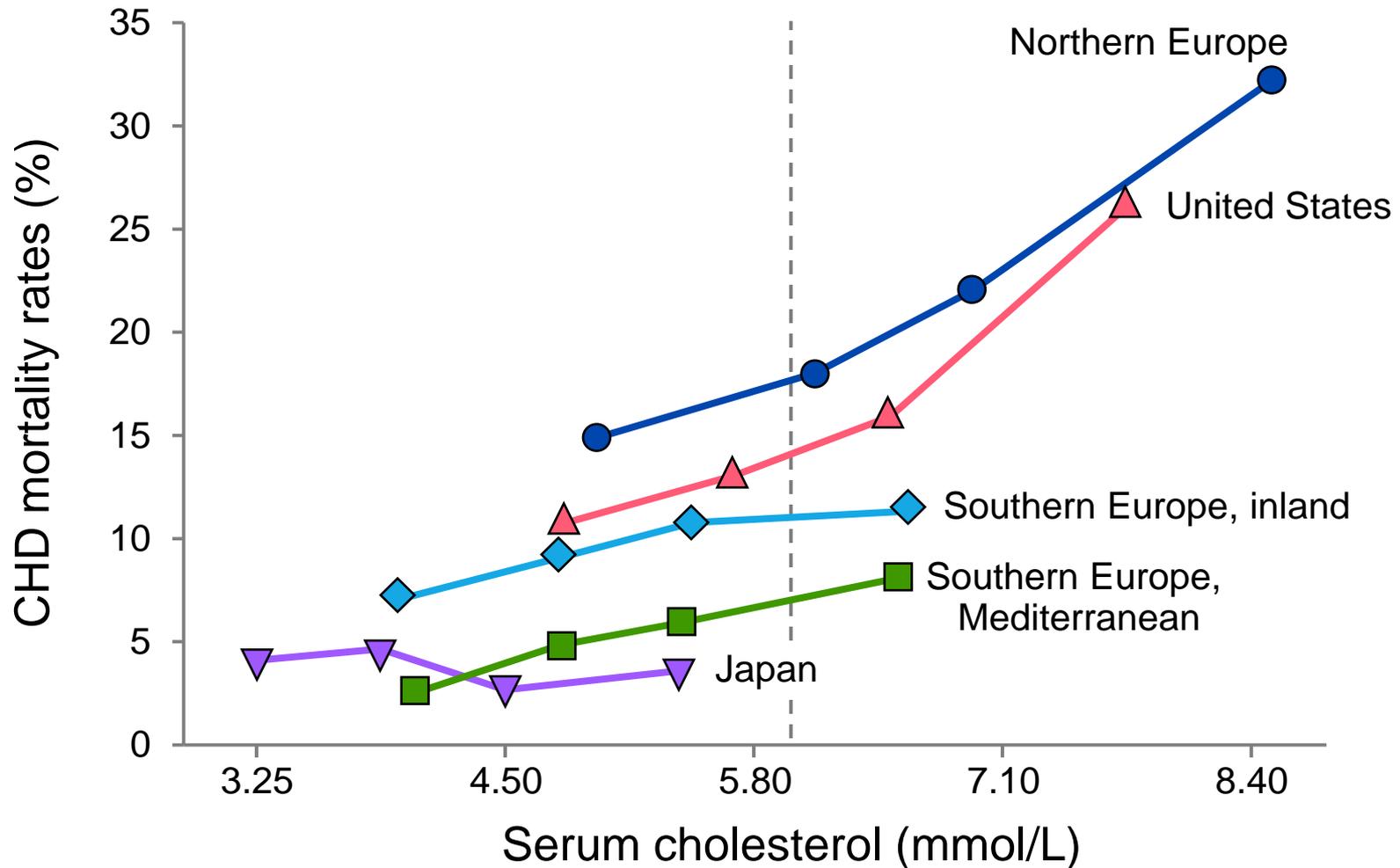
Determinants of Health and Their Contribution to Premature Death

Proportional Contribution to Premature Death



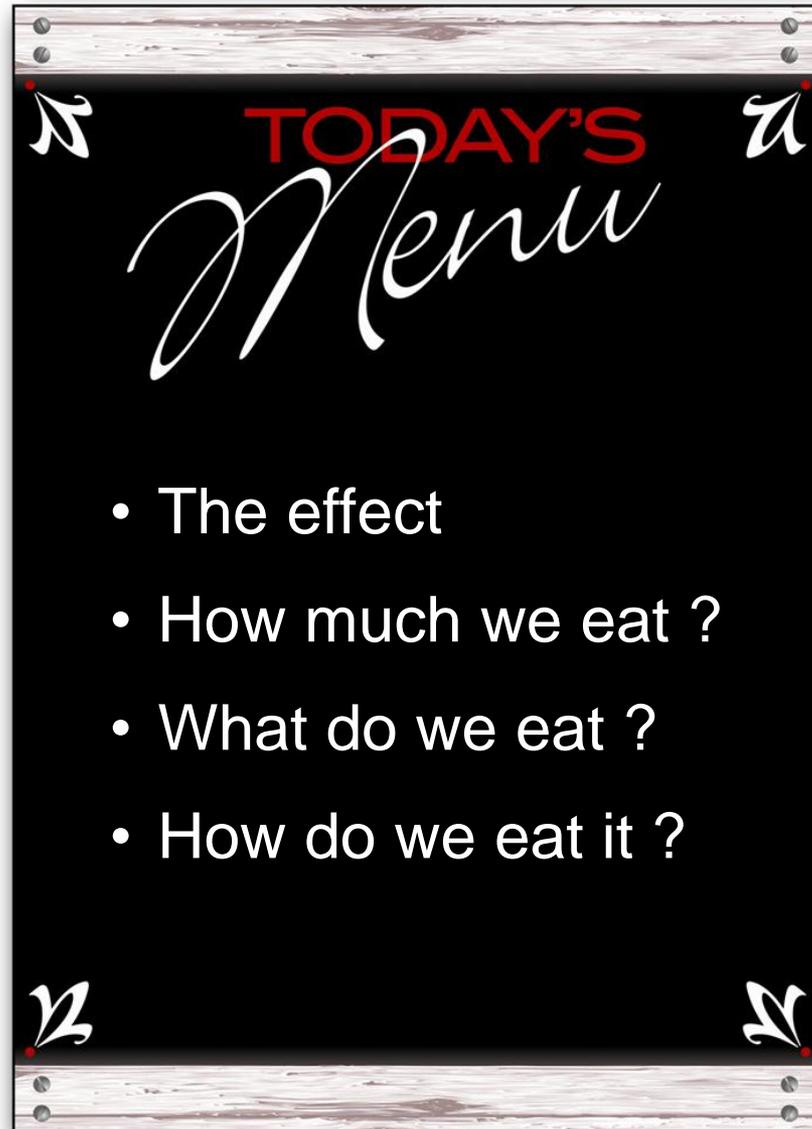
Schroeder SA: NEJM 357:1221, 2007

Coronary Heart Disease Mortality in the 7-Countries Study



De Lorgeril M: Current Opinion in Cardiology 15:364, 2000

Food for Your Heart



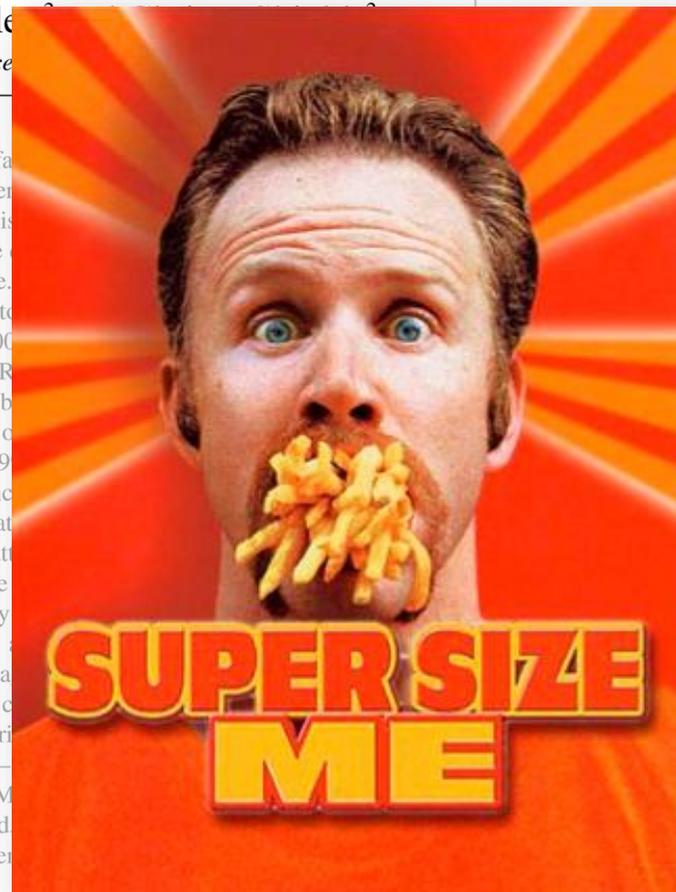
Research Article

THE ECOLOGY OF EATING: Smaller Portion Sizes in France Than in the United States Help Explain the French Paradox

Paul Rozin,¹ Kimberly Kabnick,¹ Erin Pete,¹ Claude Fischler

¹University of Pennsylvania and ²CNRS, Paris, France

- Two-thirds overweight (BMI >25)
- > 30% frankly obese (BMI >30)
- 30-40% metabolic syndrome
- 8-10% diabetic
- CHD mortality 2.6-3.0 higher



Restaurant Portion Sizes

Restaurant		No. of items sampled/no. larger in U.S.	Mean size ratio (U.S./France)	Range of ratios
In Paris	In Philadelphia			
Identical chains				
McDonald's	McDonald's	6/4	1.28	1.00-1.94
Hard Rock Café	Hard Rock Café	2/0	0.92	0.84-0.99
Pizza Hut	Pizza Hut	2/2	1.32	1.25-1.38
Häagen Dazs	Häagen Dazs	2/2	1.42	1.37-1.48
Comparable restaurants				
French: local bistro	French: local bistro	1/1	1.17	—
Quick	Burger King	5/4	1.36	0.73-1.81
Local Chinese	Local Chinese	6/4	1.72	0.87-2.78
Italian: Bistro Romain	Olive Garden	3/2	1.02	0.50-1.45
Crepes: local	Crepes: local	4/2	1.04	0.70-1.39
Local ice cream*	Local ice cream*	2/2	1.24	1.08-1.41
Pizza: local	Pizza: local	2/2	1.32	1.17-1.46

*Berthillon in Paris, Bassett's in Philadelphia
 Rozin P et al: Psych Sci 14:450, 2003

Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet

Iris Shai, R.D., Ph.D., Dan Schwarzfuchs, M.D., Yaakov Henkin, M.D., Danit R. Shahar, R.D., Ph.D., Shula Witkov, R.D., M.P.H., Ilana Greenberg, R.D., M.P.H., Rachel Golan, R.D., M.P.H., Drora Fraser, Ph.D., Arkady Bolotin, Ph.D., Hilel Vardi, M.Sc., Osnat Tangi-Rozental, B.A., Rachel Zuk-Ramot, R.N., Benjamin Sarusi, M.Sc., Dov Brickner, M.D., Ziva Schwartz, M.D., Einat Sheiner, M.D., Rachel Marko, M.Sc., Esther Katorza, M.Sc., Joachim Thiery, M.D., Georg Martin Fiedler, M.D., Matthias Blüher, M.D., Michael Stumvoll, M.D., and Meir J. Stampfer, M.D., Dr.P.H.,
for the Dietary Intervention Randomized Controlled Trial (DIRECT) Group

Background – It is currently unknown whether dietary weight loss interventions can induce regression of carotid atherosclerosis.

treatment groups). The low-carbohydrate group consumed the smallest amount of carbohydrates and the largest amounts of fat, protein, and cholesterol and had the highest percentage of participants with detectable urinary ketones ($P < 0.05$ for all comparisons among treatment groups). The mean weight loss was 2.9 kg for the low-fat group, 4.4 kg for the Mediterranean-diet group, and 4.7 kg for the low-carbohydrate group ($P < 0.001$ for the interaction between diet group and time); among the 272 participants who completed the intervention, the mean weight losses were 3.3 kg, 4.6 kg, and 5.5 kg, respectively. The relative reduction in the ratio of total cholesterol to high-density lipoprotein cholesterol was 20% in the low-carbohydrate group and 12% in the low-fat group ($P = 0.01$). Among the 36 subjects with diabetes, changes in fasting plasma glucose and insulin levels were more favorable among those assigned to the Mediterranean diet than among those assigned to the low-fat diet ($P < 0.001$ for the interaction among diabetes and Mediterranean diet and time with respect to fasting glucose levels).

CONCLUSIONS

Mediterranean and low-carbohydrate diets may be effective alternatives to low-fat diets. The more favorable effects on lipids (with the low-carbohydrate diet) and on glycemic control (with the Mediterranean diet) suggest that personal preferences and metabolic considerations might inform individualized tailoring of dietary interventions. (ClinicalTrials.gov number, NCT00160108.)

N ENGL J MED 359:3 WWW.NEJM.ORG JULY 17, 2008

The New England Journal of Medicine

Downloaded from nejm.org at MAYO CLINIC LIBRARY on October 7, 2011. For personal use only. No other uses without permission. Copyright © 2008 Massachusetts Medical Society. All rights reserved.

cine, Brigham and Women's Hospital and Harvard Medical School, and the Departments of Epidemiology and Nutrition, Harvard School of Public Health—all in Boston (M.J.S.). Address reprint requests to Dr. Shai at the S. Daniel Abraham International Center for Health and Nutrition, Department of Epidemiology and Health Systems Evaluation, Ben-Gurion University of the Negev, P.O. Box 653, Beer-Sheva 84105, Israel, or at irish@bgu.ac.il.

This article (10.1056/NEJMoa0708681) was updated on December 30, 2009, at NEJM.org.

N Engl J Med 2008;359:229-41.
Copyright © 2008 Massachusetts Medical Society.

229

Dietary Intervention to Reverse Carotid Atherosclerosis

Iris Shai, RD, PhD*; J. David Spence, MD*; Dan Schwarzfuchs, MD; Yaakov Henkin, MD; Grace Parraga, PhD; Assaf Rudich, MD, PhD; Aaron Fenster, PhD; Christiane Mallett, MSc; Noah Liel-Cohen, MD; Amir Tirosh, MD, PhD; Arkady Bolotin, PhD; Joachim Thiery, MD; Georg Martin Fiedler, MD; Matthias Blüher, MD; Michael Stumvoll, MD; Meir J. Stampfer, MD, DrPH; for the DIRECT Group

Background—It is currently unknown whether dietary weight loss interventions can induce regression of carotid atherosclerosis.

Methods and Results—In a 2-year Dietary Intervention Randomized Controlled Trial—Carotid (DIRECT-Carotid) study, participants were randomized to low-fat, Mediterranean, or low-carbohydrate diets and were followed for changes in carotid artery intima-media thickness, measured with standard B-mode ultrasound, and carotid vessel wall volume (VWV), measured with carotid 3D ultrasound. Of 140 complete images of participants (aged 51 years; body mass index, 30 kg/m²; 88% men), higher baseline carotid VWV was associated with increased intima-media thickness, age, male sex, baseline weight, blood

Clinical Trial Registration—<http://www.clinicaltrials.gov>. Unique Identifier: NCT00160108. (Circulation. 2010;121:1200-1208.)

Key Words: atherosclerosis ■ blood pressure ■ diet ■ imaging

Several recent studies suggest that lifestyle interventions can halt the progression of atherosclerosis,¹⁻³ whereas others show no effect.⁴ However, it is currently unknown whether dietary interventions can induce regression of carotid atherosclerosis, which could be detectable by B-mode and 3-dimensional ultrasound (3DUS).

Clinical Perspective on p 1208

Intima-media thickness (IMT) is a commonly used and direct assessment of early atherosclerosis and is generally considered a reliable surrogate end point of vascular outcomes.⁵ The average annual increase of IMT in untreated

Received May 11, 2009; accepted December 28, 2009.

From the S. Daniel Abraham Center for Health and Nutrition, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel (I.S., A.R., A.B.); Robarts Research Institute, University of Western Ontario, London, Ontario, Canada (J.D.S., G.P., A.F., C.M.); Nuclear Research Center Negev, Dimona, Israel (D.S.); Department of Cardiology, Soroka University Medical Center, Beer-Sheva, Israel (Y.H., N.L.-C.); Institute of Endocrinology, Sheba Medical Center, Tel-Hashomer, Israel (A.T.); Institute of Laboratory Medicine (J.T., G.M.F.) and Department of Medicine (M.B., M.S.), University of Leipzig, Leipzig, Germany; and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, and Departments of Epidemiology and Nutrition, Harvard School of Public Health, Boston, Mass (M.J.S.).

*The first 2 authors contributed equally to this work.

Guest Editor for this article was Paul W. Armstrong, MD.

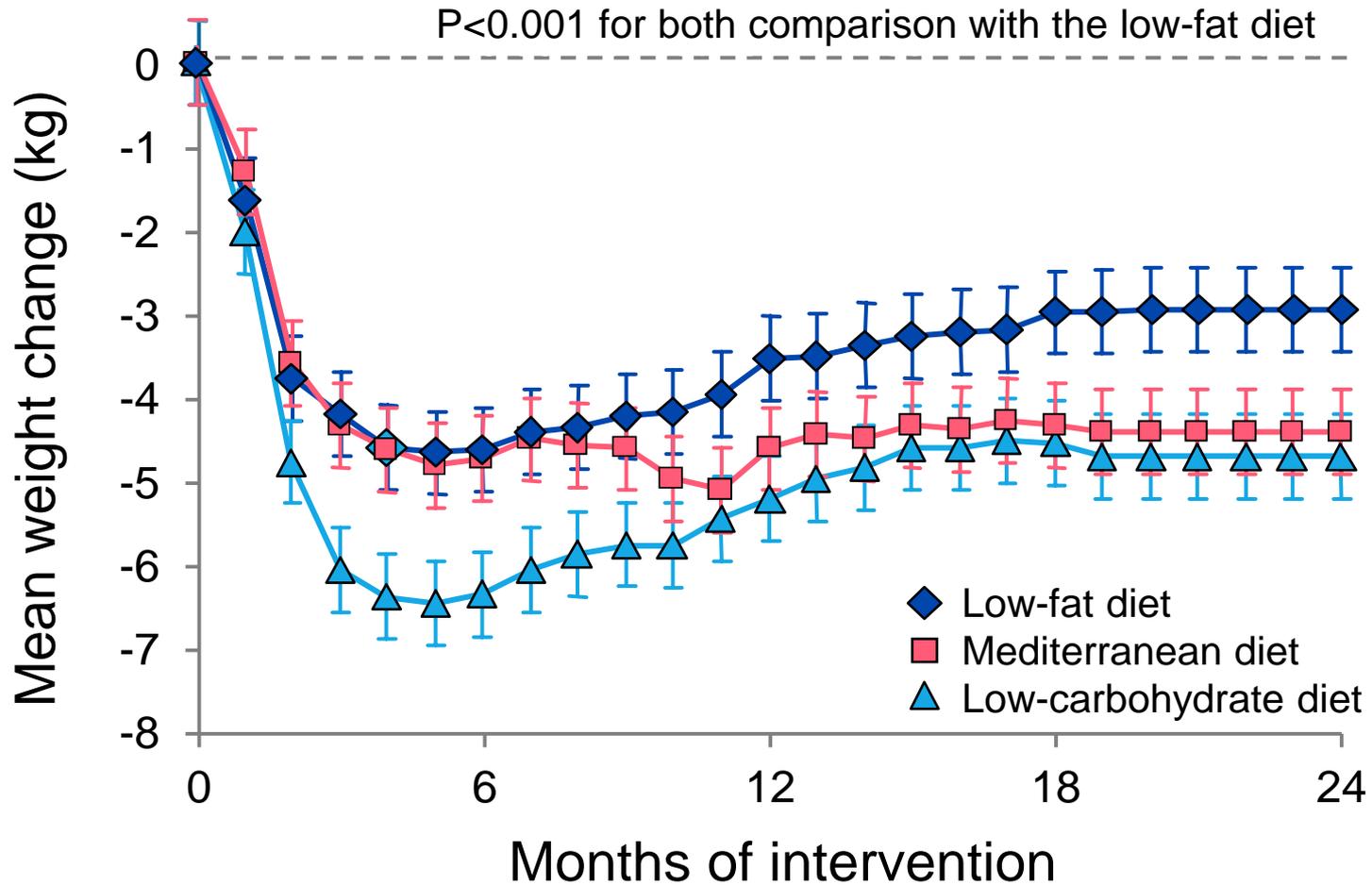
The online-only Data Supplement is available with this article at <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.109.879254/DC1>. Correspondence to Iris Shai, RD, PhD, The S. Daniel Abraham International Center for Health and Nutrition, Department of Epidemiology and Health Systems Evaluation, Ben-Gurion University of the Negev, PO Box 653, Beer-Sheva 84105, Israel. E-mail irish@bgu.ac.il

© 2010 American Heart Association, Inc.

Circulation is available at <http://circ.ahajournals.org>

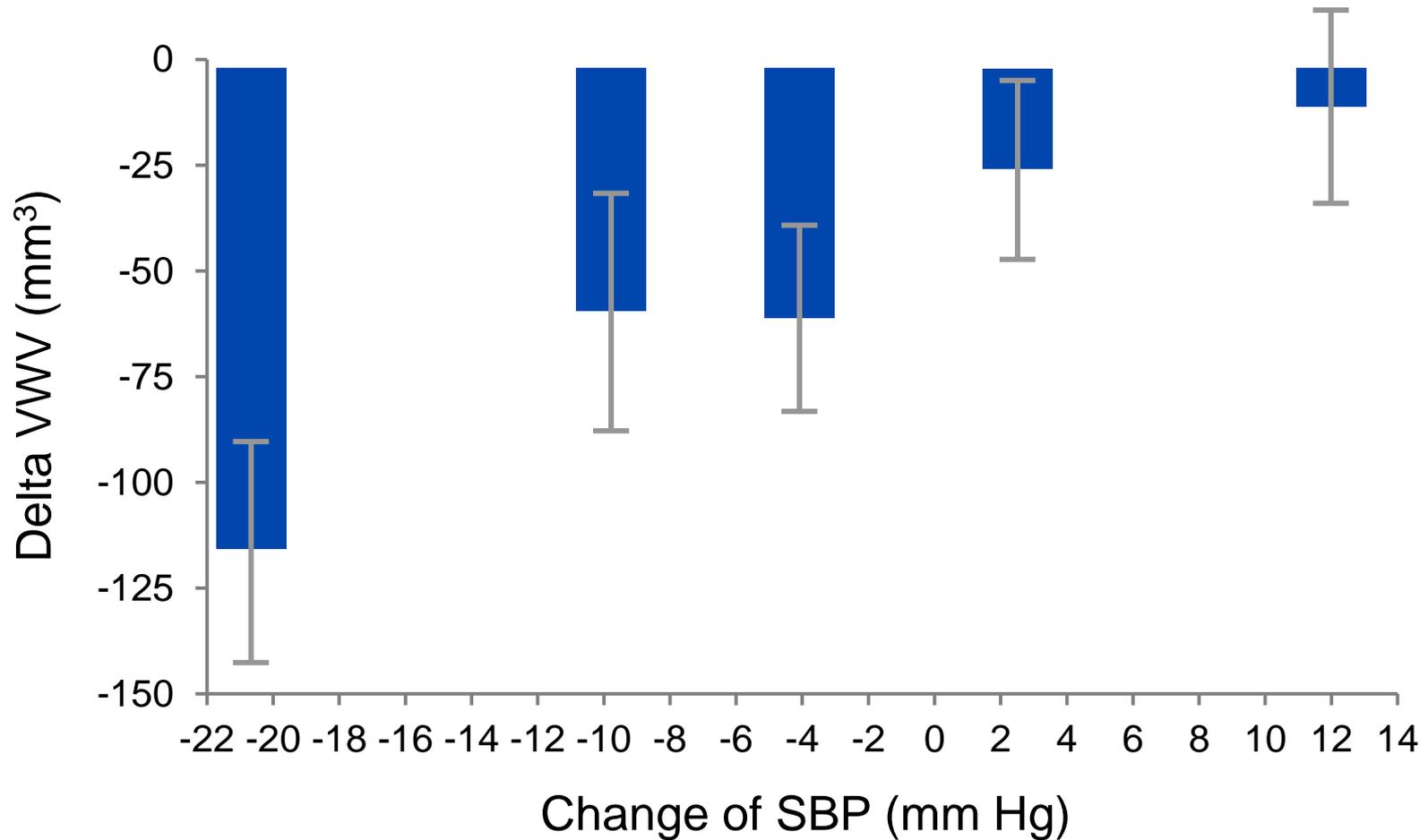
DOI: 10.1161/CIRCULATIONAHA.109.879254

Weight Changes During 2 Years According to Diet Group



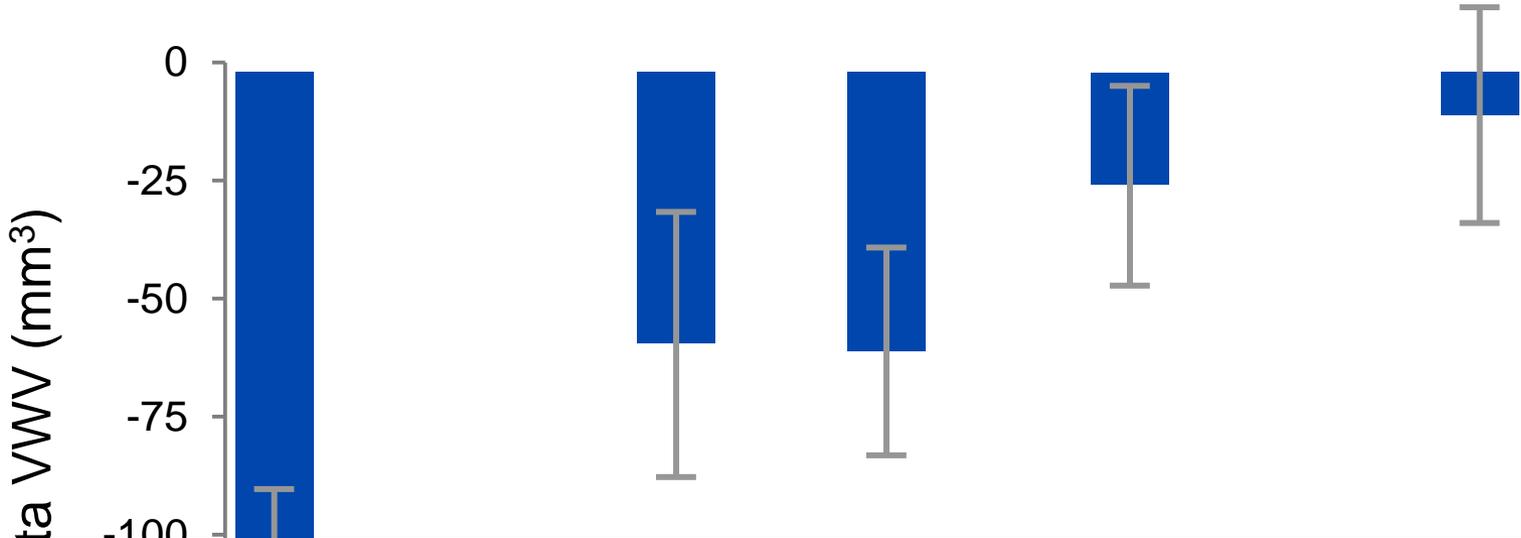
Shai et al: NEJM 359:3, 2008

2-Year Change in Carotid Vessel Wall Volume Across Quintiles of Change in Systolic Blood Pressure



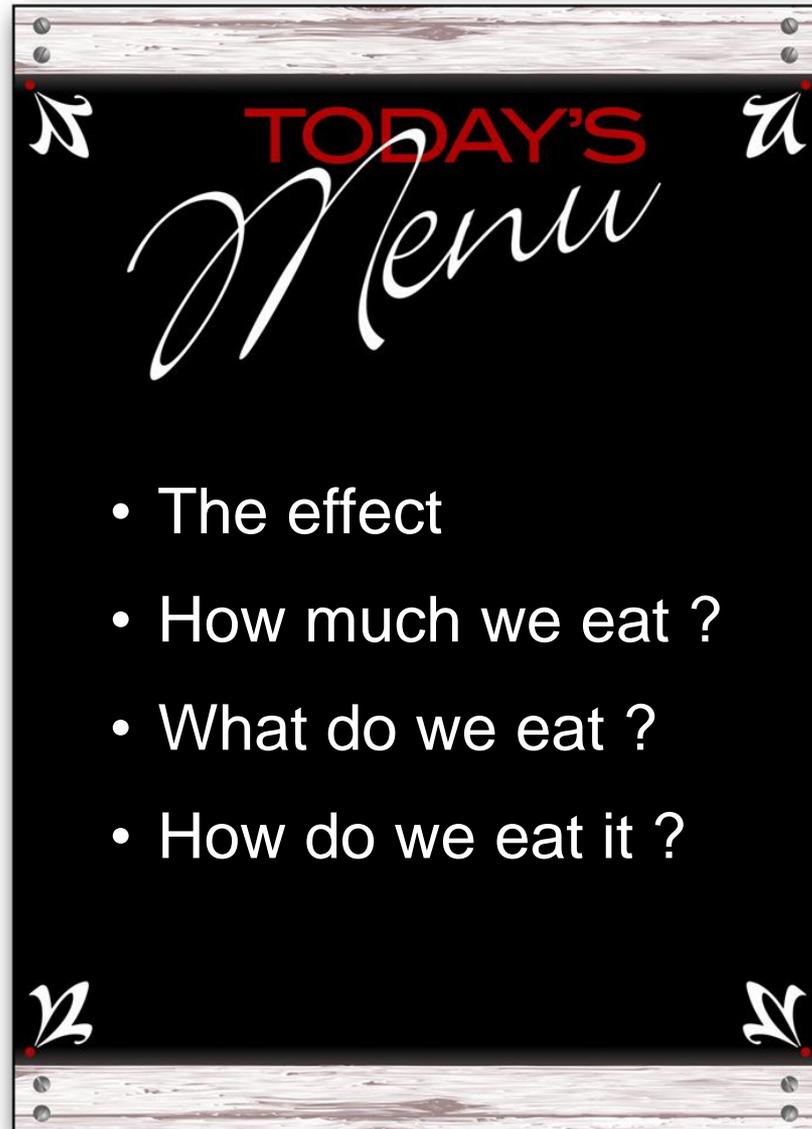
Shai et al: Circ 121:1200, 2010

2-Year Change in Carotid Vessel Wall Volume Across Quintiles of Change in Systolic Blood Pressure



Conclusions – Two-year weight loss diets can induce a significant regression of measurable carotid VWV. The effect is similar in low-fat, Mediterranean, or low-carbohydrate strategies and appears to be mediated mainly by the weight loss-induced decline in blood pressure

Food for Your Heart



Not All Calories Are Created Equal



Nuts vs French Fries



Take longer to chew

Contain fat and fiber that need more time to digest

Your stomach stays fuller, and you feel satisfied longer...

...so you eat less at your next meal

You lose

.057 lbs

Cooked starch is quickly broken down

Causes spike in sugar, or glucose in the bloodstream

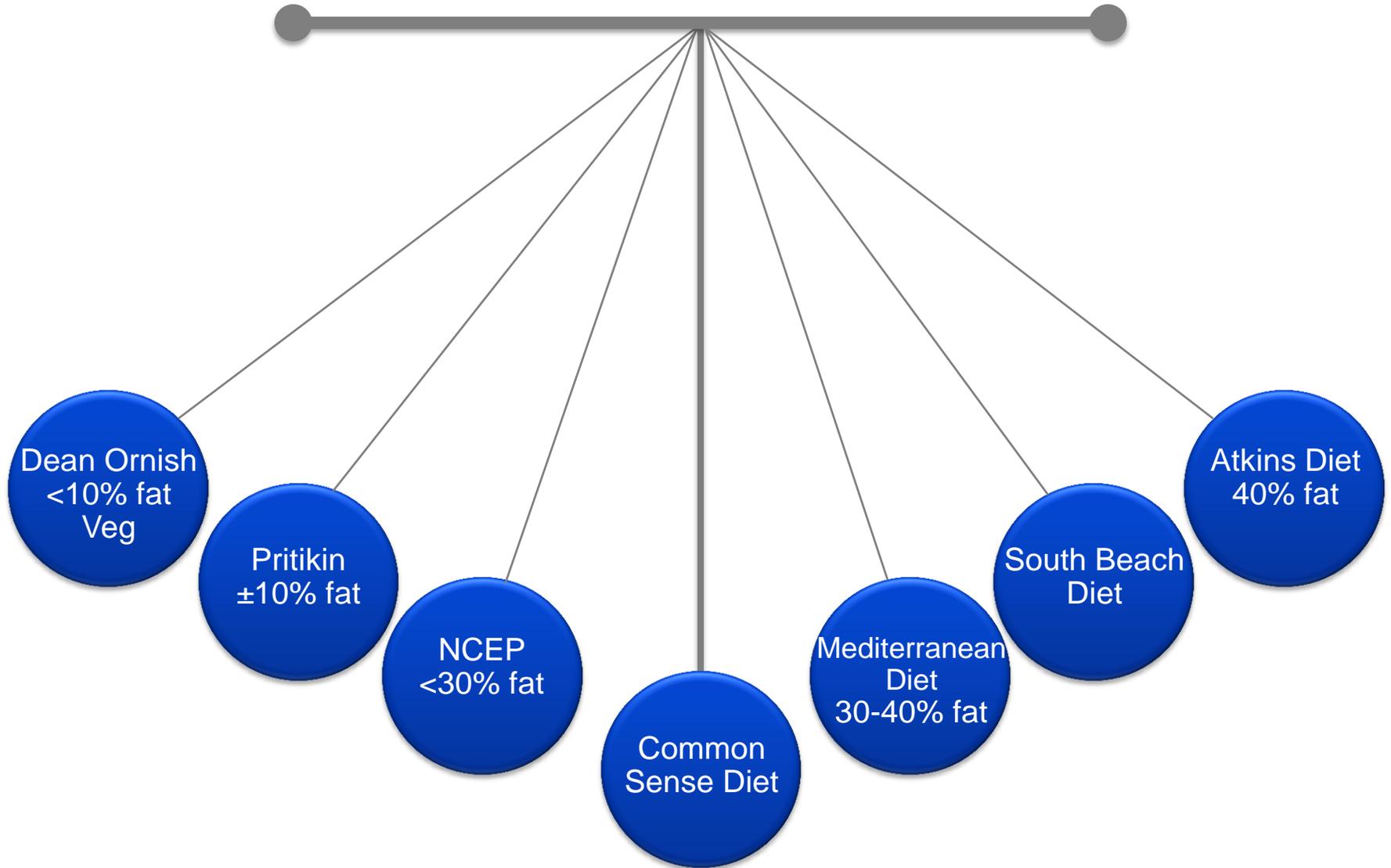
The body secretes insulin, leading to hunger signals...

...so you eat more at your next meal

You gain

3.35 lbs

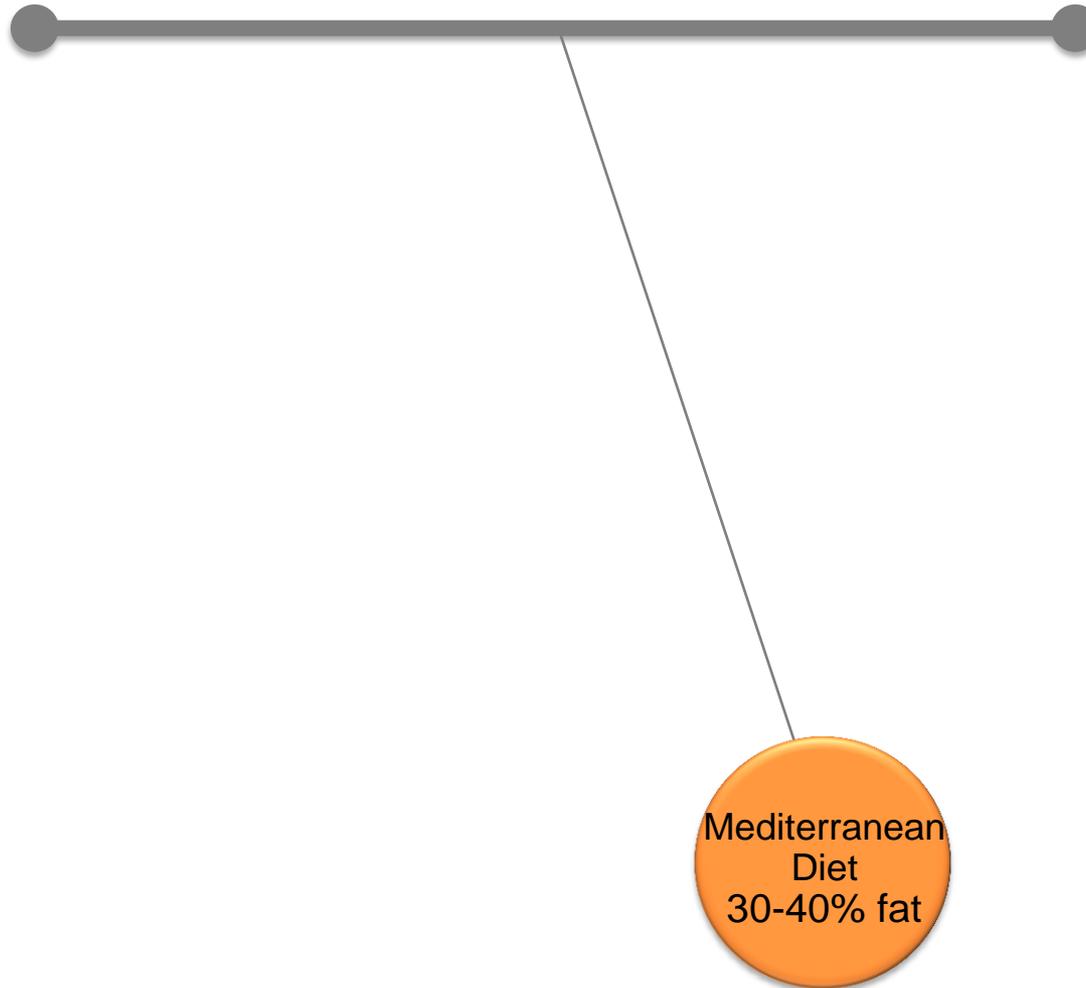
The Diet Pendulum



The Diet Pendulum



The Diet Pendulum



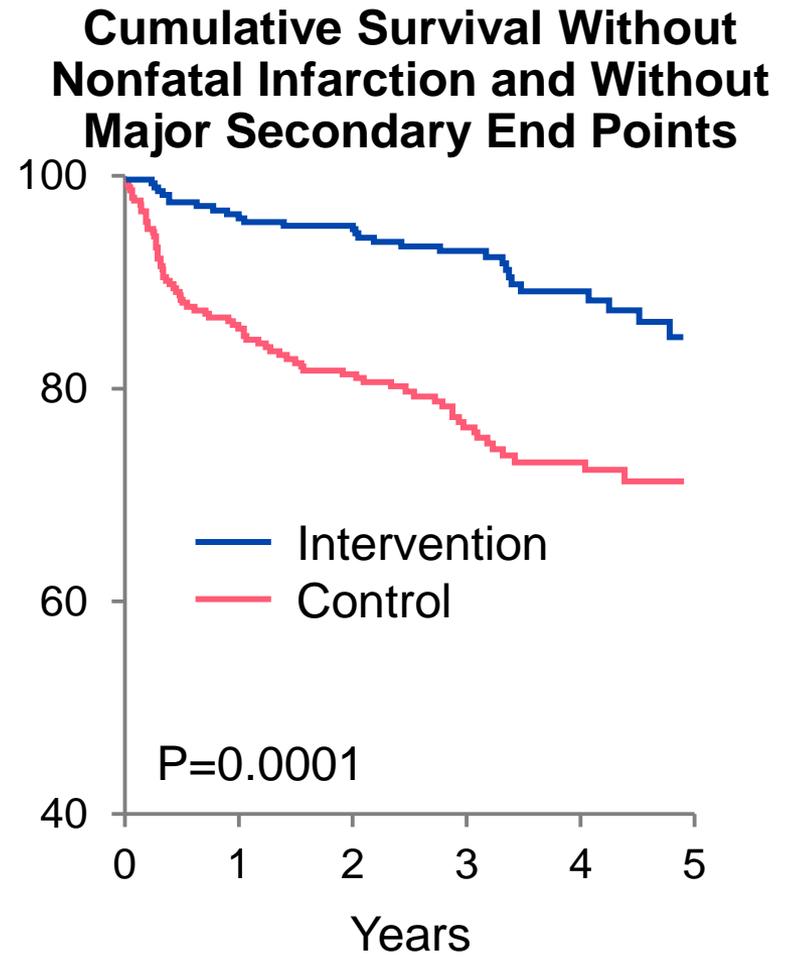
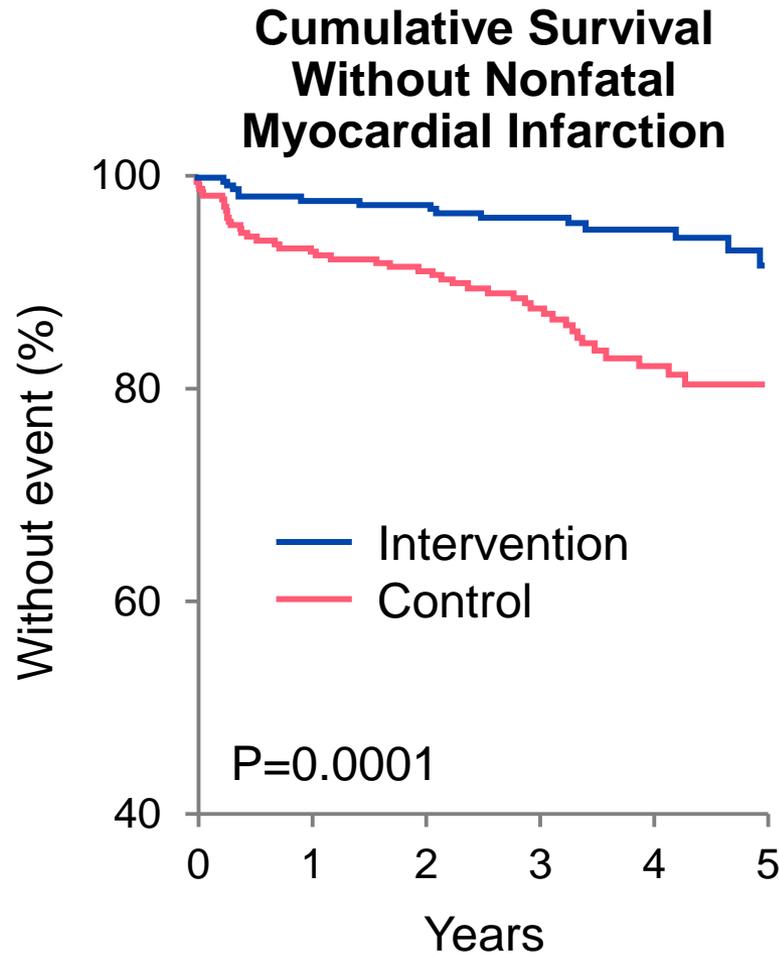
Lyon Diet Heart Study

605 men/women (302 treatment, 303 control)

- Diet – Mediterranean vs usual care
- Treatment – margarine, omega-3 FA (α linolenic acid)
 - ↓ total cardiac mortality 65%
 - ↓ sudden death 64%
(0% sudden death first 2 yrs)
- Lipids did not change
- Major benefit – omega-3 FA (α linolenic acid)
 - (+) better diet – ? wine

Ref: Lyon Heart Study, Circulation 1999;99:779-85

Mediterranean Diet and CV Events



de Lorgeril M et al: *Circulation* 99:779, 1999

Mediterranean Diet

Greece

- 22,000 adults – 20-86 years
- Follow-up 4 years
- Interviewed
 - What they ate and drank
 - Portion sizes
 - How often they ate
 - Smoking habits
- Measured – height, weight, waist circumference
- Rated – score of 0-9, how closely they followed traditional Mediterranean diet

N Engl J Med 2003;348:2599-2608

Mediterranean Diet

Greece

- A 2-point increase on diet adherence score
 - 25% ↓ death all cause
 - 33% ↓ heart disease death
 - 24% ↓ death from cancer
- Individual foods alone - no effect on risk ↓
(total diet)

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D., Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D., Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutiérrez, Ph.D., Miquel Fiol, M.D., Ph.D., José Lapetra, M.D., Ph.D., Rosa Maria Lamuela-Raventós, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D., Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D., José Alfredo Martínez, D.Pharm., M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D., for the PREDIMED Study Investigators*

- 7,447 persons at high risk of CV risk
- Randomized to 3 diets: A Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with mixed nuts, or a control diet (advice to reduce dietary fat)

causes). On the basis of the results of an interim analysis, the trial was stopped after a median follow-up of 4.8 years.

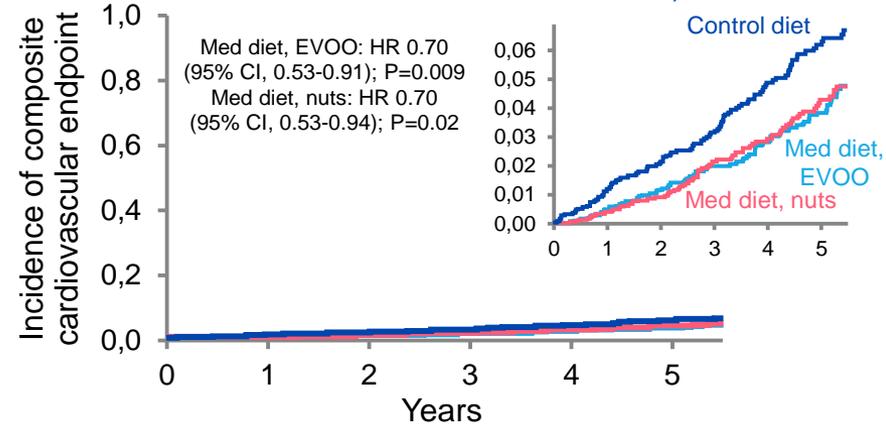
tributed equally to this article.

This article was published on February 25,

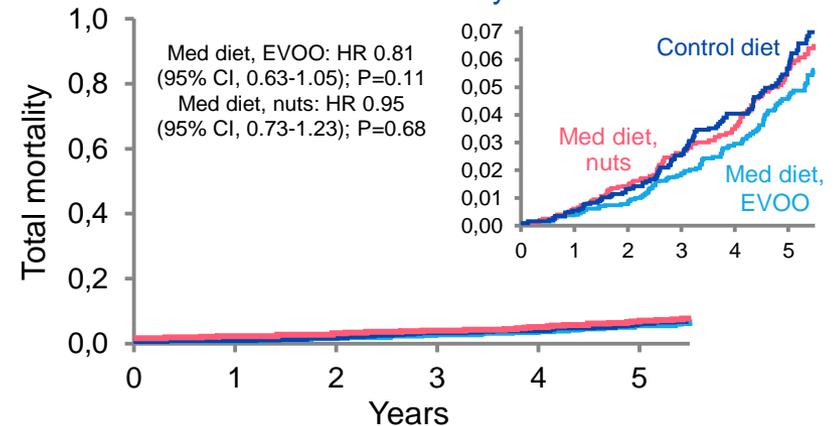
Conclusions: Among persons at high cardiovascular risk, a Mediterranean diet supplemented with extra-virgin olive oil or nuts reduced the incidence of major cardiovascular events

Kaplan-Meier Estimates of the Incidence of Outcome Events in Total Study Population

Primary Endpoint (Acute MI, Stroke or Death from CV Causes)

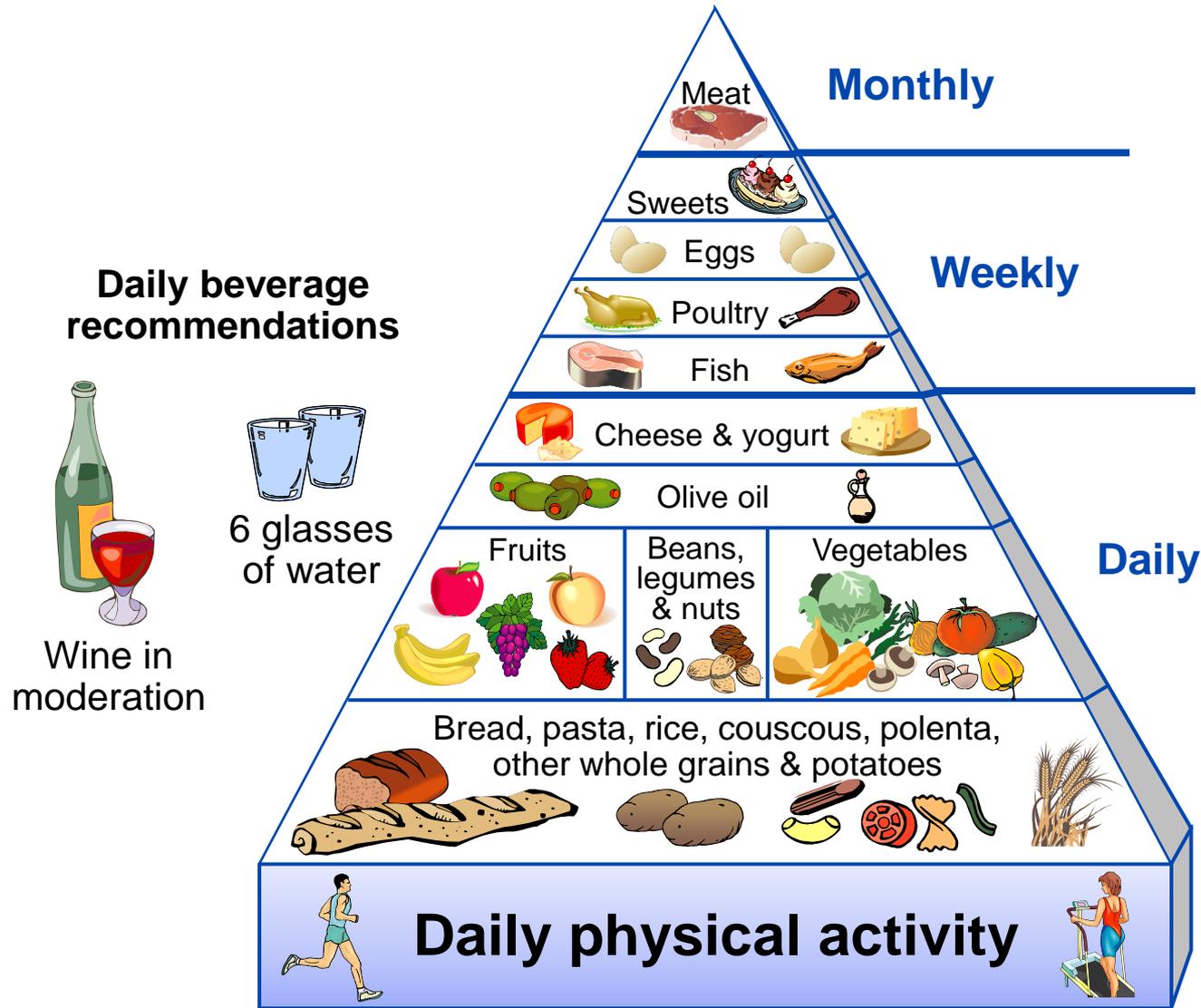


Total Mortality



Estruch et al: NEJM, 2013

The Traditional Healthy Mediterranean Diet Pyramid

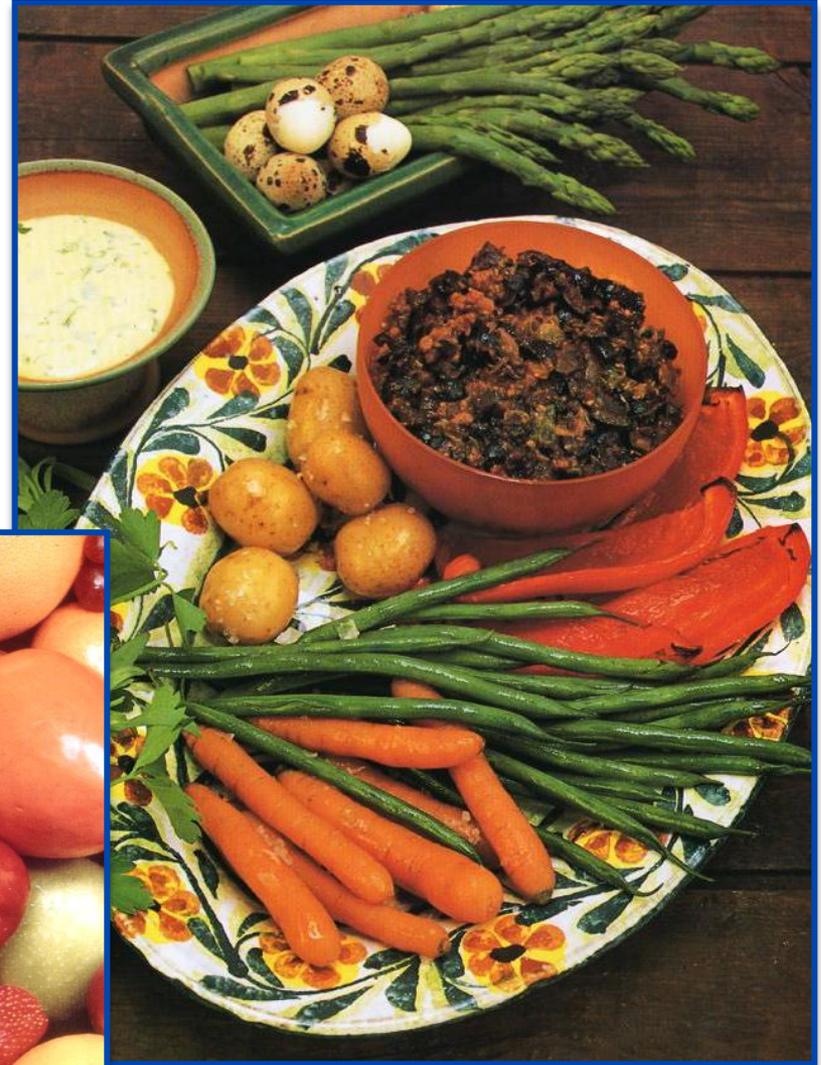


2000 Oldways Preservation & Exchange Trust

Mediterranean Diet – Health Effects

Vegetables and fruits

- High in phytochemicals
- Low in calories
- Associated with low risk of CHD*



*Ann Intern Med 134:1106, 2001

The Human Microbiome Projects




Science & Space

Home | NewsFeed | U.S. | Politics | World | Business | Tech | Health | Science

Home | Environment | Energy | Going Green | Space | Animals | Photos



HEALTH

You Are Your Bacteria: How the Gut Microbiome Influences Health

The bacteria in our gut already plays an important role in digestion. But new studies indicate that our bacteria could play a major role in whether or not we become obese

22 86 2 17

Like Share

Subscribe to the Newsletter

Text size Print Forward

Comments

22 Share 30 Read Later

"AN AMAZING RESULT WITH POSSIBLY ENORMOUS IMPLICATIONS FOR THE TREATMENT AND EVEN PREVENTION OF THE GREATEST PUBLIC HEALTH ISSUE OF OUR TIME"

Microbiome breakthrough: Gut flora implicated in metabolic disorders



By Nathan Gray+
29-Aug-2013

Post a comment



The diversity and richness of bacteria in our gut may have a direct impact our risks of developing metabolic conditions including heart disease and type 2 diabetes, according to the new MetaHIT data.

Related tags: Microbiota, Gut health, Obesity

Related topics: Probiotics, Phood, Research, Probiotics and prebiotics, Cardiovascular health, Diabetes, Gut health, Immune system

There is a distinct link between the composition of our gut bacteria and incidence of obesity related conditions including heart disease and diabetes, according to new data from the MetaHIT project.

The new findings, published in *Nature*, find a link between the 'richness' of bacterial species in our gut and susceptibility to metabolic

RELATED NEWS:
Probiotic yogurt does not

it for
it
Scientists think that gut microbiome could be linked to obesity and other disorders.

ids
ia
useful and nutritious
r recently that new genomic
idy of our gut microbiome,
people is extremely
f the inhabitants of our guts
tabolic disorders and others
e others stay thin.

Email Print
Share Comment

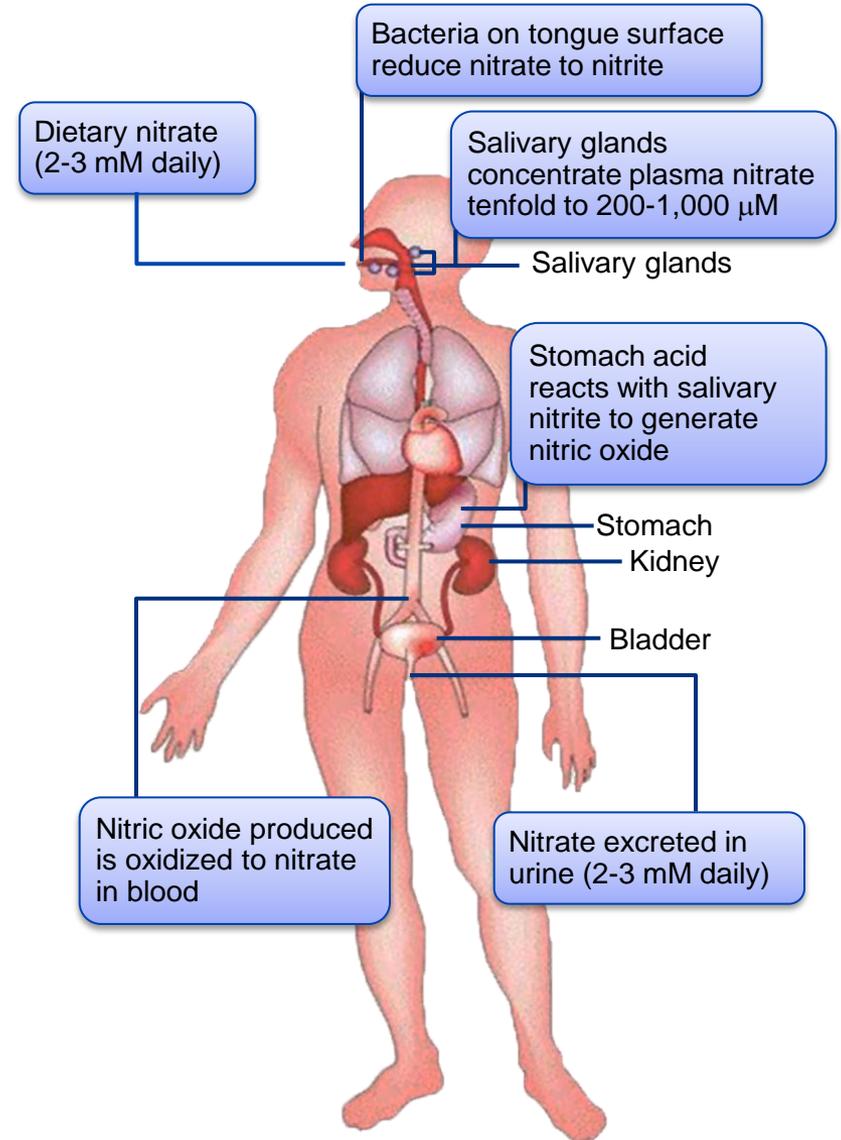
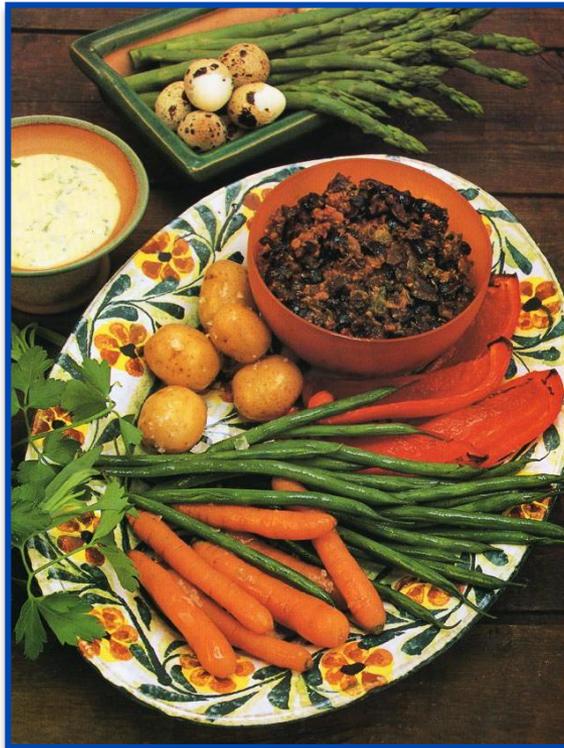
Follow @TIME

he microbiome is difficult. When a person or a mouse with a
nfluencing the gut flora or are the gut flora contributing to the
acteria by changing the way we eat? While researchers have probed
d have come up with some fascinating answers—for instance, you
s from an obese mouse, suggesting that at least in mice, gut flora
sired for answers that could be applicable to real life. A pair of
can consortia devoted to the study of the gut microbiome, add new



Mediterranean Diet – Health Effects

Vegetables, the main dietary source of nitrate, account for 60–80% of the daily nitrate intake



*Ann Intern Med 134:1106, 2001

ONLINE FIRST

Vegetarian Dietary Patterns and Mortality in Adventist Health Study 2

Michael J. Orlich, MD; Pramil N Singh, DrPH; Joan Sabaté, MD, DrPH; Karen Jaceldo-Siegl, DrPH; Jing Fan, MS; Synnove Knutsen, MD, PhD; W. Lawrence Beeson, DrPH; Gary E. Fraser, MBChB, PhD

Design: Prospective cohort study; mortality analysis by Cox proportional hazards regression, controlling for important demographic and lifestyle confounders.

Participants: A total of 96 469 Seventh-day Adventist men and women recruited between 2002 and 2007, from which an analytic sample of 73 308 participants remained after exclusions.

... and endocrine mortality. Associations in men were larger and more often significant than were those in women.

Participants: A total of 96 469 men and women recruited between 2002 and 2007, from which an analytic sample of 73 308 participants remained after exclusions.

... previous studies have identified dietary factors associated with mortality. Those found to correlate with

See Invited Commentary

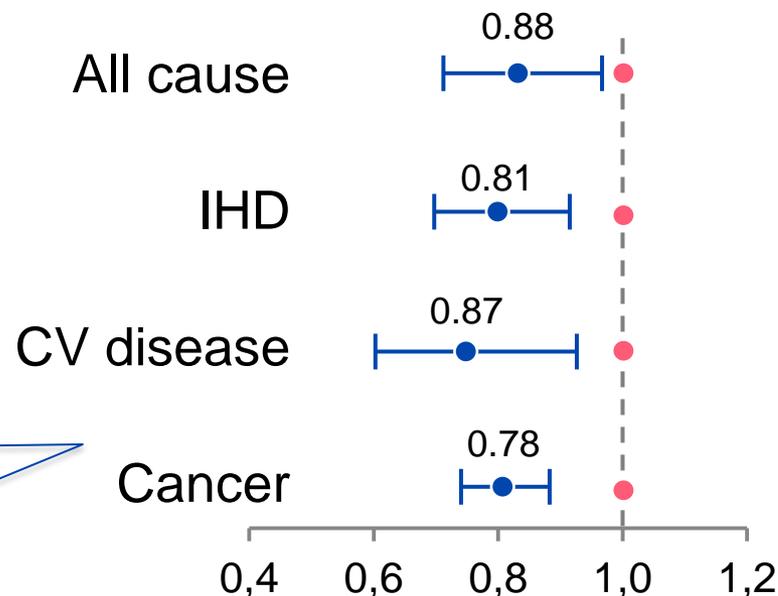
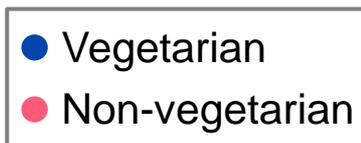
Results: There were 2570 deaths among 73 308 participants during a mean follow up time of 5.79 years.

©2013 American Medical Association. All rights reserved.

Conclusions and Relevance: Vegetarian diets are associated with lower all-cause mortality and with some reductions in cause-specific mortality.

Comparison of Vegetarian With Nonvegetarian Dietary Patterns With Respect to All-Cause and Cause-Specific Mortality From a Cox Proportional Hazards Regression Model Among Participants in Adventist Health Study 2, 2002-2009

Characteristics



Mediterranean Diet – Health Effects

Olive oil

- Monounsaturated fat
- Lowers total and LDL cholesterol
- Doesn't lower HDL cholesterol
- Resistant to oxidation
- Associated with reduced risk of CHD



*Ann Intern Med 134:1106, 2001

Olive oil consumption, plasma oleic acid, and stroke incidence

The Three-City Study

Objective – To determine whether high olive oil consumption, and high plasma oleic acid as an indirect biological marker of olive oil intake, are associated with lower incidence of stroke in older subjects

Samieri, Equipe Epidémiologie de la Nutrition et des Comportements Alimentaires, INSERM, U897, Université Bordeaux 2, ISPED case 11, 146 rue Léo-Saignat, F-33076

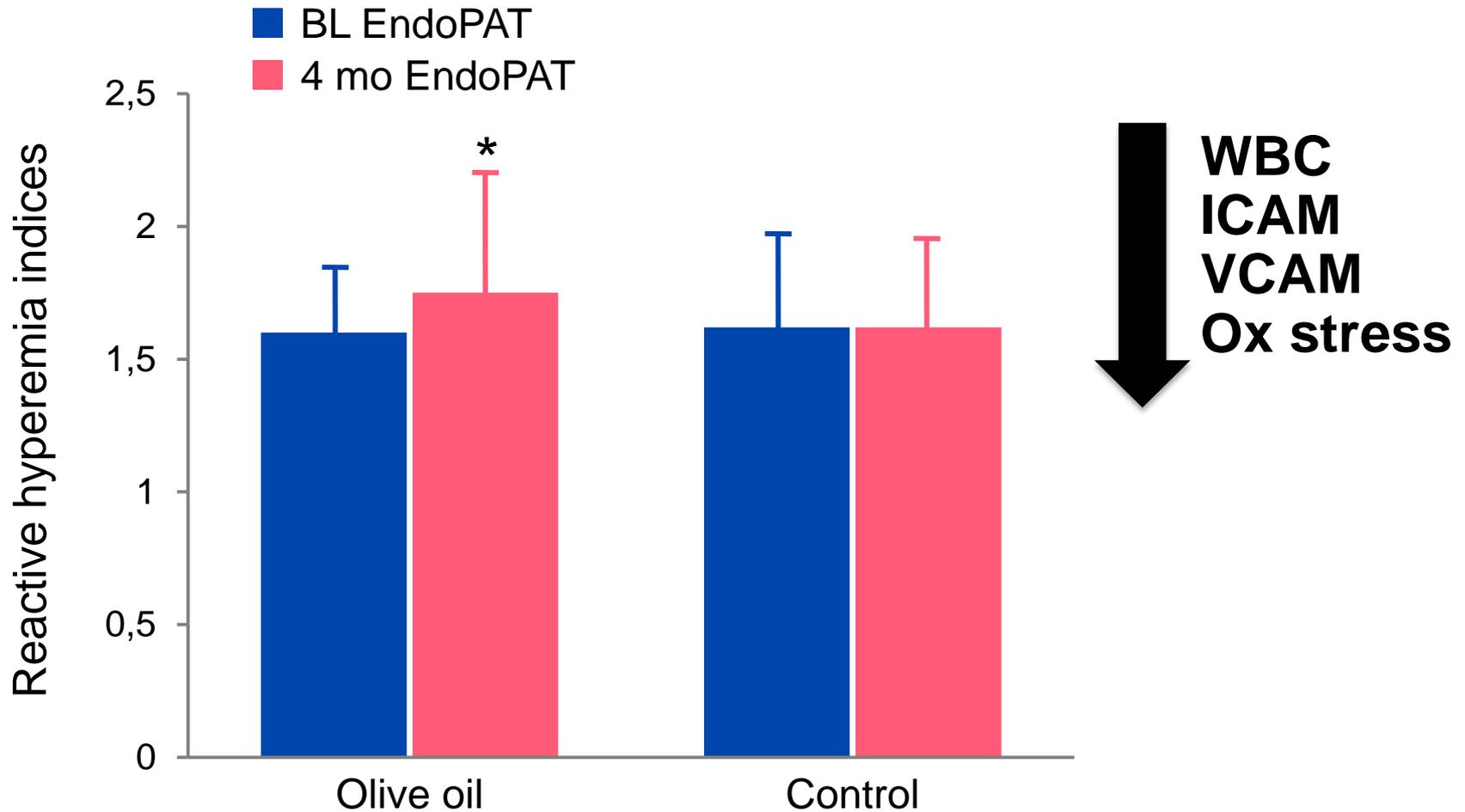
6%–63%, $p = 0.03$) lower risk of stroke. In the secondary sample, 27 incident strokes occurred. After full adjustment, higher plasma oleic acid was associated with lower stroke incidence (p for trend = 0.03). Compared to those in the first tertile, participants in the third tertile of plasma oleic acid had a 73% (95% confidence interval 10%–92%, $p = 0.03$) reduction of stroke risk.

Baseline olive oil use	HR (95% CI)	P
No use	Ref	–
Moderate use (cooking or dressing)	0.80 (0.53-1.20)	0.28
Intensive use (both cooking and dressing)	0.59 (0.37-0.94)	0.03

Conclusions – These results suggest a protective role for high olive oil consumption on the risk of stroke in older subjects. *Neurology*®2011;77:1-1

quant components, including phenolic compounds found in high olive oil intake

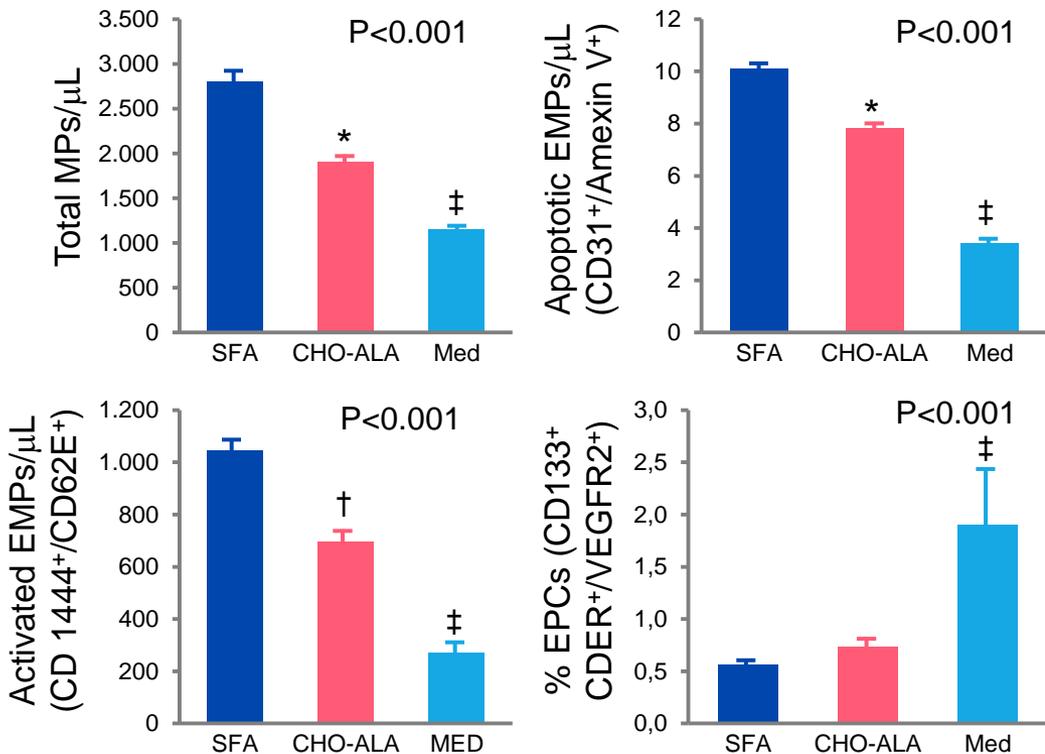
Olive Oil Improves Endothelial Function



Widmer & Lerman E J Nut 2012

Mediterranean Diet Reduces Endothelial Damage and Improves the Regenerative Capacity of Endothelium

- 20 healthy elderly
- 3 diets randomized crossover
- Each diet for 4 weeks
- Saturated FA diet
- High carbohydrate
- Mediterranean diet



Conclusion: Consumption of the Med Diet induces a reduction in endothelial damage and dysfunction, which is associated with an improvement in the regenerative capacity of the endothelium

Mediterranean Diet – Health Effects

- Fish and shellfish – omega-3 fatty acids
 - Anti-arrhythmic effect
 - Antithrombotic effect
 - Lowers triglycerides
 - Lowers blood pressure
 - Anti-inflammatory effect
- Associated with reduced risk of CHD and sudden death (DART* and GISSI-Prevenzione** trials)



*Lancet 16:1450,1989; **Lancet 354:447, 1999

Fish and Omega-3 Fatty Acid Intake

Secondary Prevention Trial

GISSI – Prevenzione Trial

- 11,324 pts (mainly men) post-MI
- 1 g fish oil omega-3/day - 2 yrs
 - ↓ 20% all-cause mortality
 - ↓ 45% sudden death

Ref JAMA 2002;287(14):1815-21

Trans Fat Consumption and Aggression

Beatrice A. Golomb^{1,2*}, Marcella A. Evans^{1†}, Halbert L. White³, Joel E. Dimsdale⁴

¹ Department of Medicine, University of California San Diego, San Diego, California, United States of America, ² Department of Family and Preventive Medicine, University of California San Diego, San Diego, California, United States of America, ³ Department of Economics, University of California San Diego, California, United States of America, ⁴ Department of Psychiatry, University of California San Diego, California, United States of America

Dietary trans fatty acids (dTFA) are primarily synthetic compounds that have been introduced only recently. dTFA inhibit production of omega-3 fatty acids, which experimentally have been shown to reduce aggression.

Received August 19, 2011; Accepted January 22, 2012; Published March 5, 2012
Copyright: © 2012 Golomb et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Funding: This research was supported by a grant from the National Institutes of Health (NHLBI RO1 HL63055-05). The funder had no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.
Competing Interests: The authors have declared that no competing interests exist.
 * E-mail: bgolomb@ucsd.edu

This study provides the first evidence linking dTFA with behavioral irritability and aggression.

outcomes have been previously reported [21–23]. Due to the range of their deleterious biological effects, including inhibition by dTFA of n3FA production (by inhibition of delta-6 desaturase activity) [24,25], we theorized that dTFA may be associated with greater aggression and irritability. diabetes, cardiovascular disease, HIV, or cancer were excluded [26]. The study protocol was approved by the University of California, San Diego Human Research Protections Program. All subjects gave written informed consent.

Aggression Measure	
Variable	Mean
OASMa	2.50±4.72
Conflict Tactics Scale	1.08±1.70
Life history of aggression	10.1±6.93
Impatience	1.87±2.12
Irritability	1.30±1.83



Intestinal Microbial Metabolism of Phosphatidylcholine and Cardiovascular Risk

Pathways Linking Dietary Phosphatidylcholine, Intestinal Microbiota, and Incident Adverse Cardiovascular Events

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812

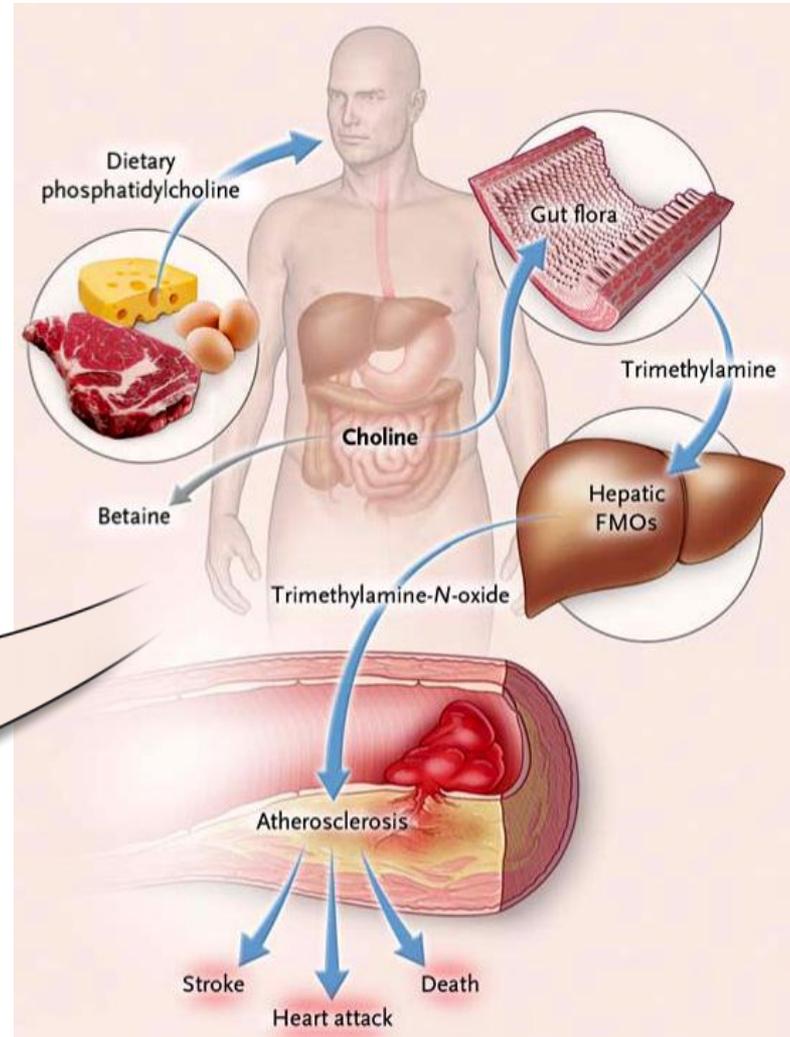
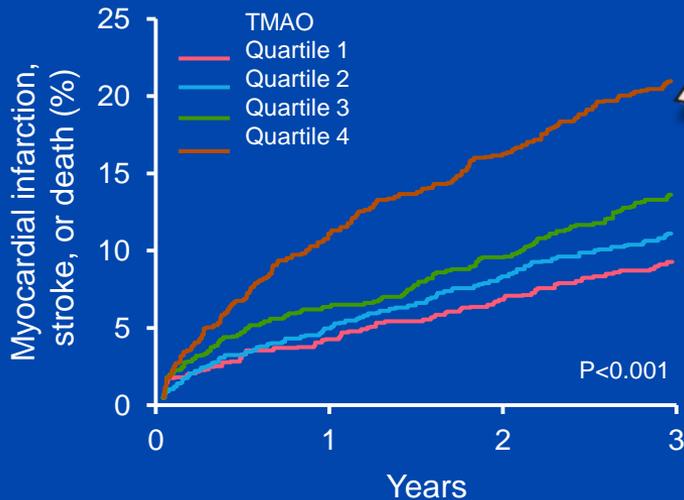
APRIL 25, 2013

VOL. 368 NO. 17

Intestinal Microbial Metabolism of Phosphatidylcholine and Cardiovascular Risk

W.H. Wilson Tang, M.D., Zeneng Wang, Ph.D., Bruce S. Levison, Ph.D., Robert A. Koeth, B.S., Earl B. Britt, M.D., Xiaoming Fu, M.S., Yuping Wu, Ph.D., and Stanley L. Hazen, M.D., Ph.D.

Kaplan-Meier Estimates of Major Adverse Cardiovascular Events, According to the Quartile of TMAO Level – 4,007 Participants

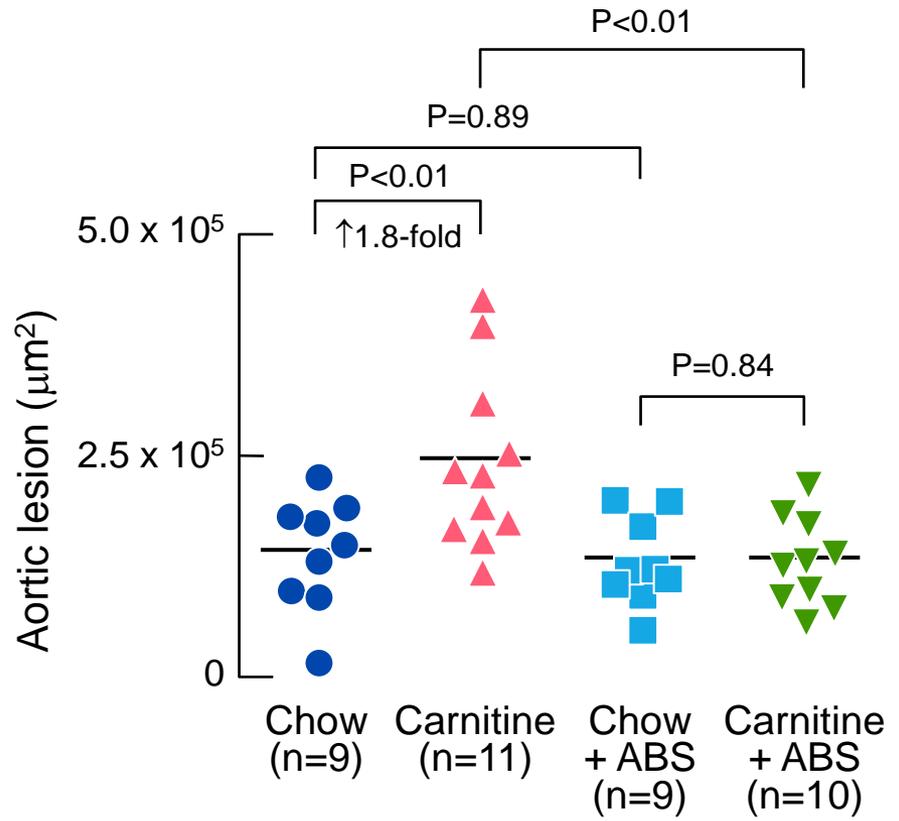
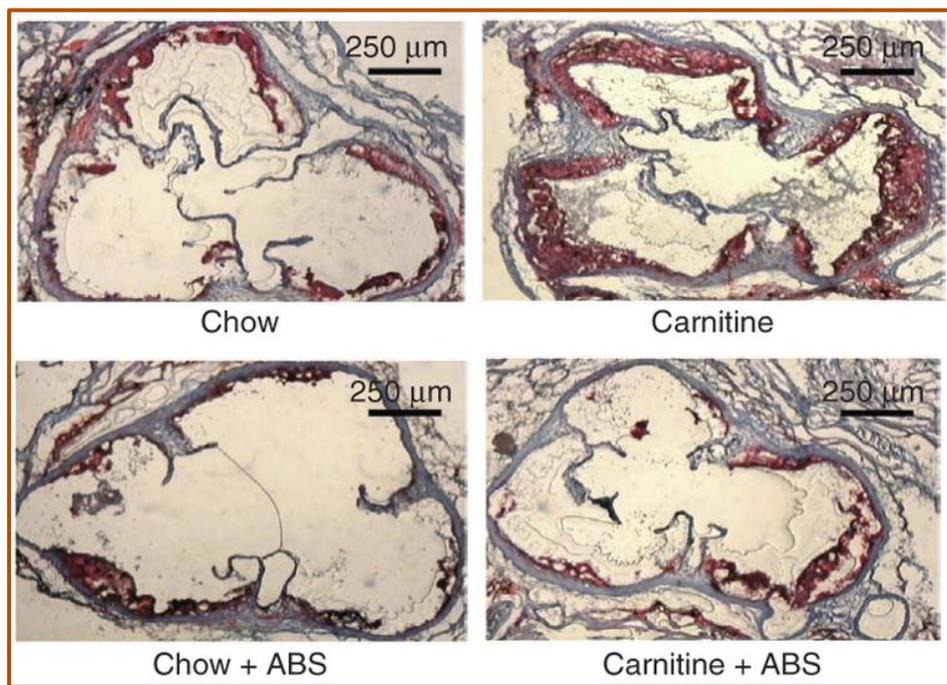


The microbiota metabolizes dietary L-carnitine and choline to form TMA and TMAO. TMAO affects cholesterol and sterol metabolism in macrophages, liver and intestine

Dietary L-Carnitine Accelerates Atherosclerosis and Inhibits Reverse Cholesterol Transport in a Microbiota Dependent Fashion in Apoe KO Mice

Red O-Stained

Plaque Area

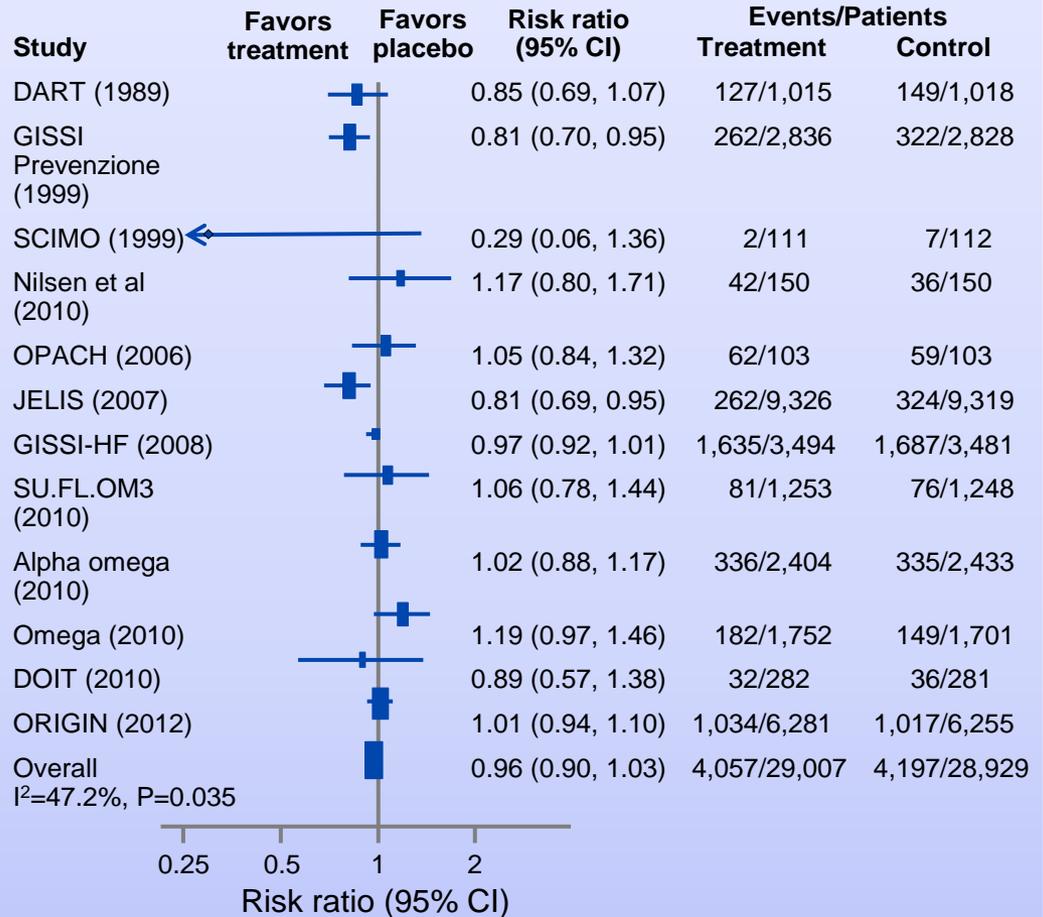


Omega 3 Fatty Acids and Cardiovascular Outcomes
Systematic Review and Meta-Analysis

Sradha Kotwal, BHB, MBChB, FRACP; Min Jun, BSc (Hons), MSc; David Sullivan, MBE
Vlado Perkovic, MBBS, PhD, FRACP; Bruce Neal, MBChB, PhD, FRACP

- We assessed the effects of ω -3 FA on cardiovascular and other important clinical outcomes
- 20 studies including 63,030 participants were included
- Adverse events were more common in the treatment group than the placebo group (RR=1.18; 95% CI; 1.02-1.37; P=0.03), predominantly because of an excess of gastrointestinal side effects

Effect of ω -3 Fatty Acids on Composite Cardiovascular Outcomes

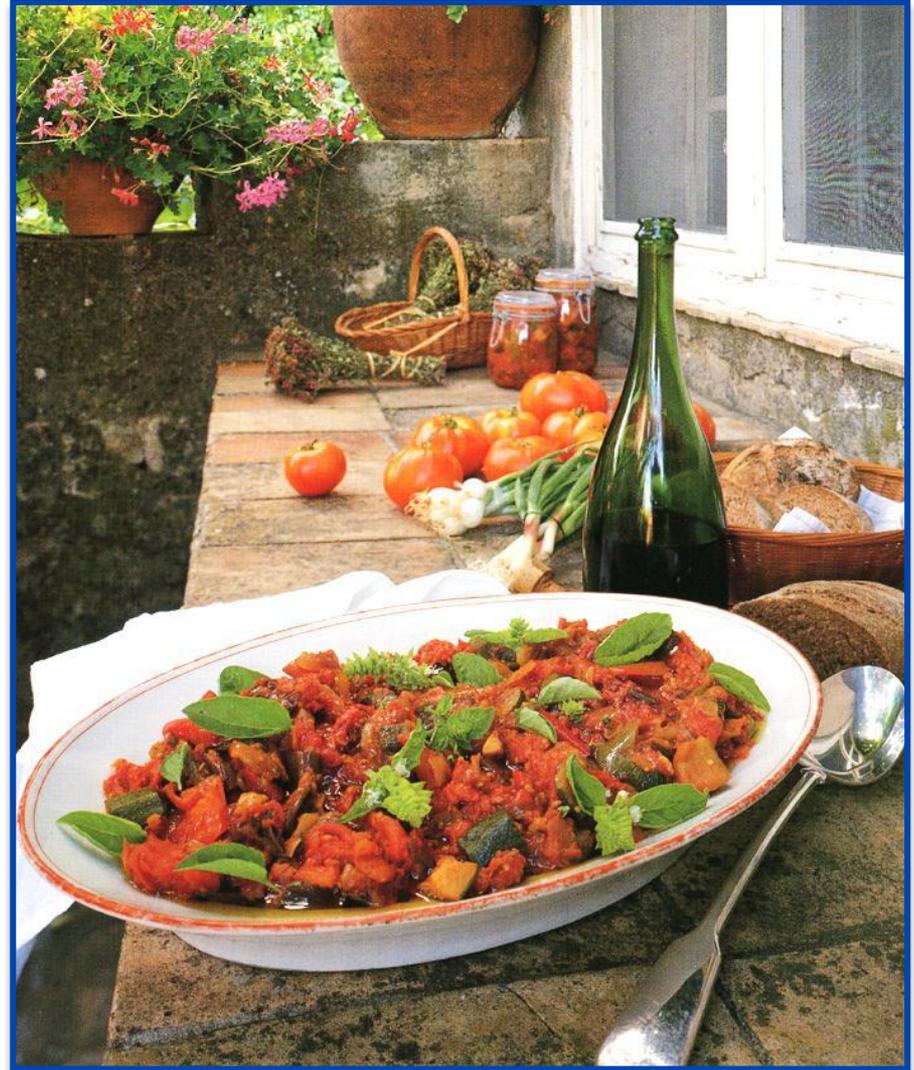


Weights are from random effects analysis

Mediterranean Diet – Health Effects

Wine

- Raises HDLc
- Inhibits platelet aggregation
- High in phenolic antioxidants
- Alcohol associated with reduced risk of CHD



*Ann Intern Med 134:1106, 2001

QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Alcohol Consumption and Mortality in Patients With Cardiovascular Disease

A Meta-Analysis

Simona Costanzo, ScD, Augusto Di Castelnuovo, ScD, Maria Benedetta Donati, MD, PhD, Licia Iacoviello, MD, PhD, Giovanni de Gaetano, MD, PhD
 Campobasso, Italy

QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Alcohol Consumption and Cardiovascular Mortality Among U.S. Adults, 1987 to 2002

Kenneth J. Mukamal, MD, MPH, MA,* Chiung M. Chen, MA,† Sowmya R. Rao, PhD,‡
 Rosalind A. Breslow, PhD¶

Boston, Massachusetts; and Rockville, Maryland

- Objectives** The aim of this study was to determine the association of alcohol consumption and cardiovascular mortality in the U.S. population.
- Background** Alcohol consumption has been associated with a lower risk of cardiovascular disease in cohort studies, but this association has not been prospectively examined in large, detailed, representative samples of the U.S. population.
- Methods** We analyzed 9 iterations of the National Health Interview Survey, an annual survey of a nationally representative sample of U.S. adults between 1987 and 2000. Exposures of interest included usual volume, frequency, and quantity of alcohol consumption and binge drinking. Mortality was ascertained through linkage to the National Death Index through 2002. Relative risks were derived from random-effects meta-analyses of weighted, multivariable-adjusted hazard ratios for cardiovascular mortality from individual survey administrations.
- Results** Light and moderate volumes of alcohol consumption were inversely associated with cardiovascular mortality. Compared with lifetime abstainers, summary relative risks were 0.95 (95% confidence interval [CI]: 0.88 to 1.02) among lifetime infrequent drinkers, 1.02 (95% CI: 0.94 to 1.11) among former drinkers, 0.69 (95% CI: 0.59 to 0.82) among light drinkers, 0.62 (95% CI: 0.50 to 0.77) among moderate drinkers, and 0.95 (95% CI: 0.82 to 1.10) among heavy drinkers. The magnitude of lower risk was similar in subgroups of sex, age, or baseline health status. There was no simple relation of drinking pattern with risk, but risk was consistently higher among those who consumed ≥ 3 compared with 2 drinks/drinking day.
- Conclusions** In 9 nationally representative samples of U.S. adults, light and moderate alcohol consumption were inversely associated with CVD mortality, even when compared with lifetime abstainers, but consumption above recommended limits was not. (J Am Coll Cardiol 2010;55:1328-35) © 2010 by the American College of Cardiology Foundation

Alcohol consumption has been consistently associated with a lower risk of cardiovascular disease (CVD) in epidemiological studies (1,2), an association attributed in great part to the increase in high-density lipoprotein cholesterol (HDL-C) caused by alcohol consumption (3). However, a number of uncertainties about the association of alcohol consumption and CVD remain, punctuated by

the absence of a long-term randomized controlled trial on CVD events with which to confirm the results of observational studies. These uncertainties include potentially diverse effects on coronary heart disease (CHD) and stroke (4), inclusion of former or occasional drinkers with long-term abstainers as a referent category (5), generalizability to the adult U.S. population (6), and the importance of

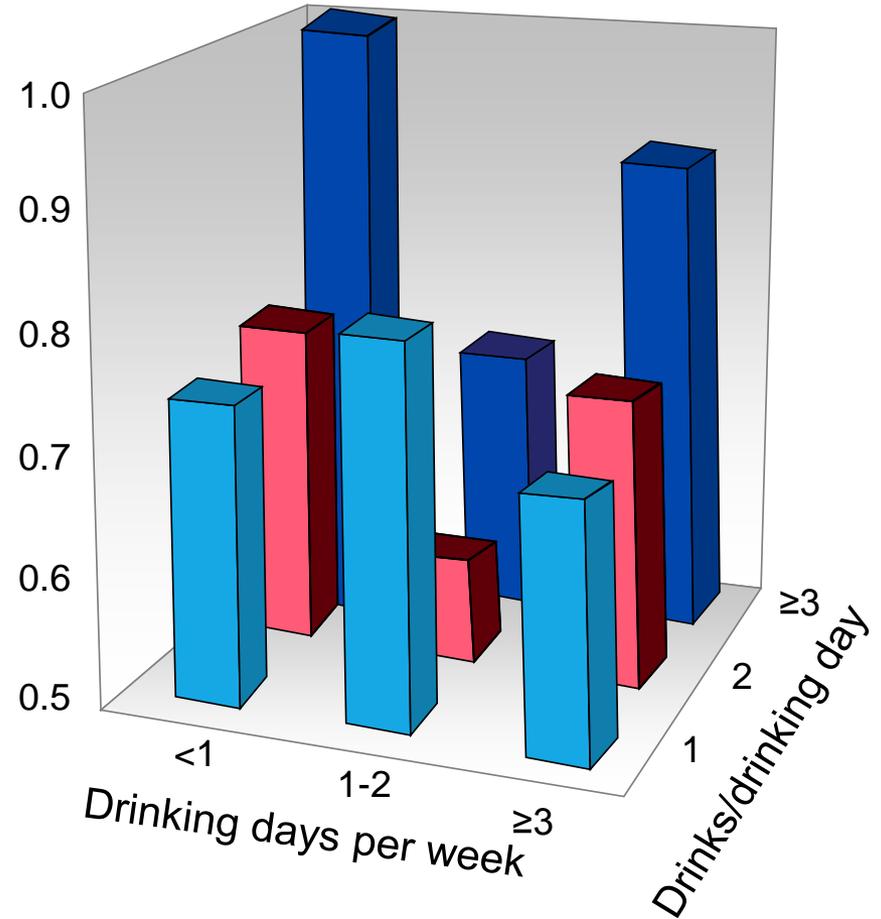
See page 1336

drinking patterns in modifying the association (7). Measures of overall volume of alcohol consumption obscure the relative contributions of drinking frequency (how often alcohol is consumed), drinking quantity (how much alcohol is typically consumed on those days), and binge drinking (episodes of 5 or more drinks in a day); and their individual contributions to CVD risk have not been thoroughly investigated.

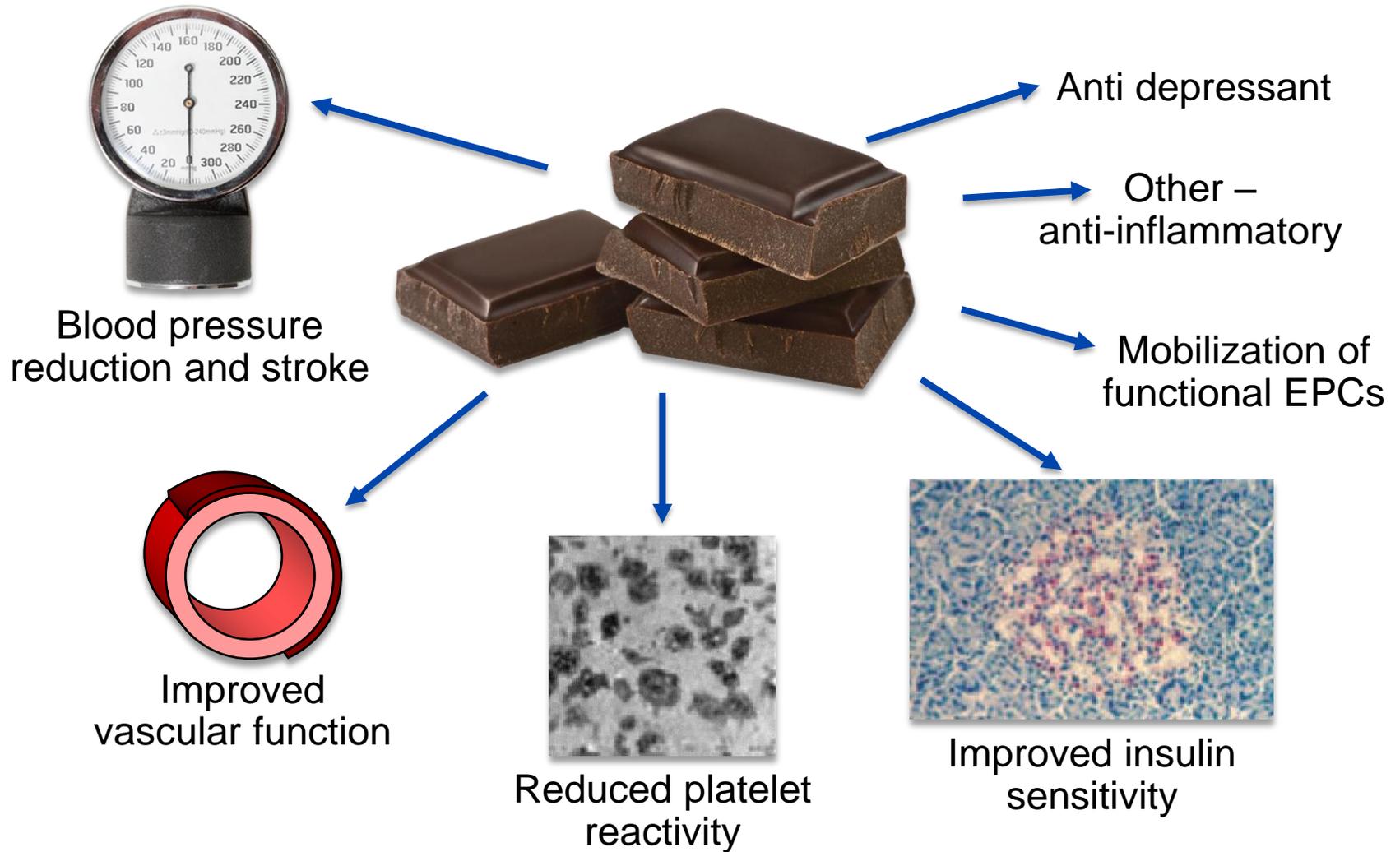
To evaluate the associations of alcohol consumption and drinking patterns with CVD, cerebrovascular, and

From the *Division of General Medicine and Primary Care, Beth Israel Deaconess Medical Center, Boston, Massachusetts; KCSR Incorporated, Arlington, Virginia; †Biostatistics Center and Institute for Health Policy, Massachusetts General Hospital, Boston, Massachusetts; and the ‡Division of Epidemiology and Prevention Research, National Institute on Alcohol Abuse and Alcoholism, Rockville, Maryland. Computer programming and statistical support were provided through the Alcohol Epidemiologic Data System funded by contracts N0AA32807 and HHSN267200800023C from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The NIAAA reviewed and approved this report before submission. The findings and conclusions in this report are those of the authors and not necessarily those of the agency. Dr. Rao has received funding from GE Corporate Healthcare. Manuscript received August 4, 2009; revised manuscript received September 16, 2009; accepted October 14, 2009.

HR for CVD Mortality



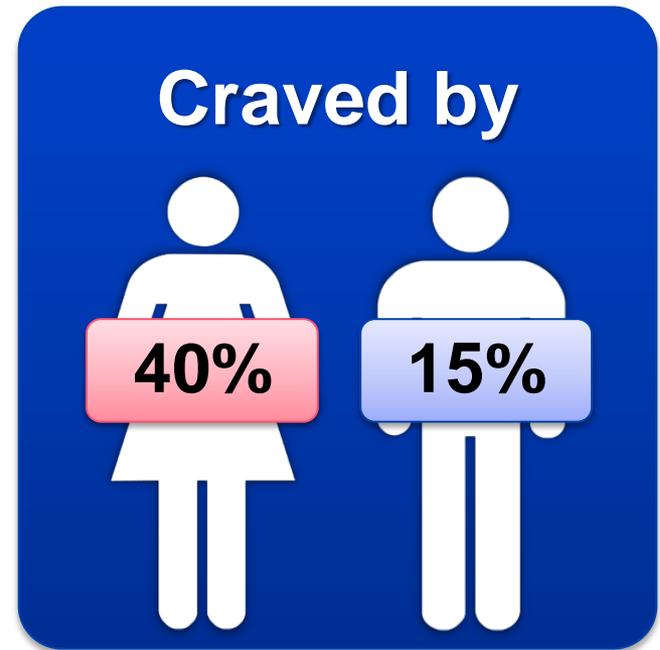
Dessert – Health-Relevant Effect of Chocolate



Modified from Corti et al: *Circ*, 2009

Chocolate

- Consistently the No. 1 most craved food
- Contains mood-altering chemicals including phenylethylamine (rises naturally when people are in love)
- Also has theobromine (a mild stimulant), tyramine and tryptophan (antidepressant precursors that create a sense of calm)



OCCASIONAL NOTES

Chocolate Consumption, Cognitive Function, and Nobel Laureates

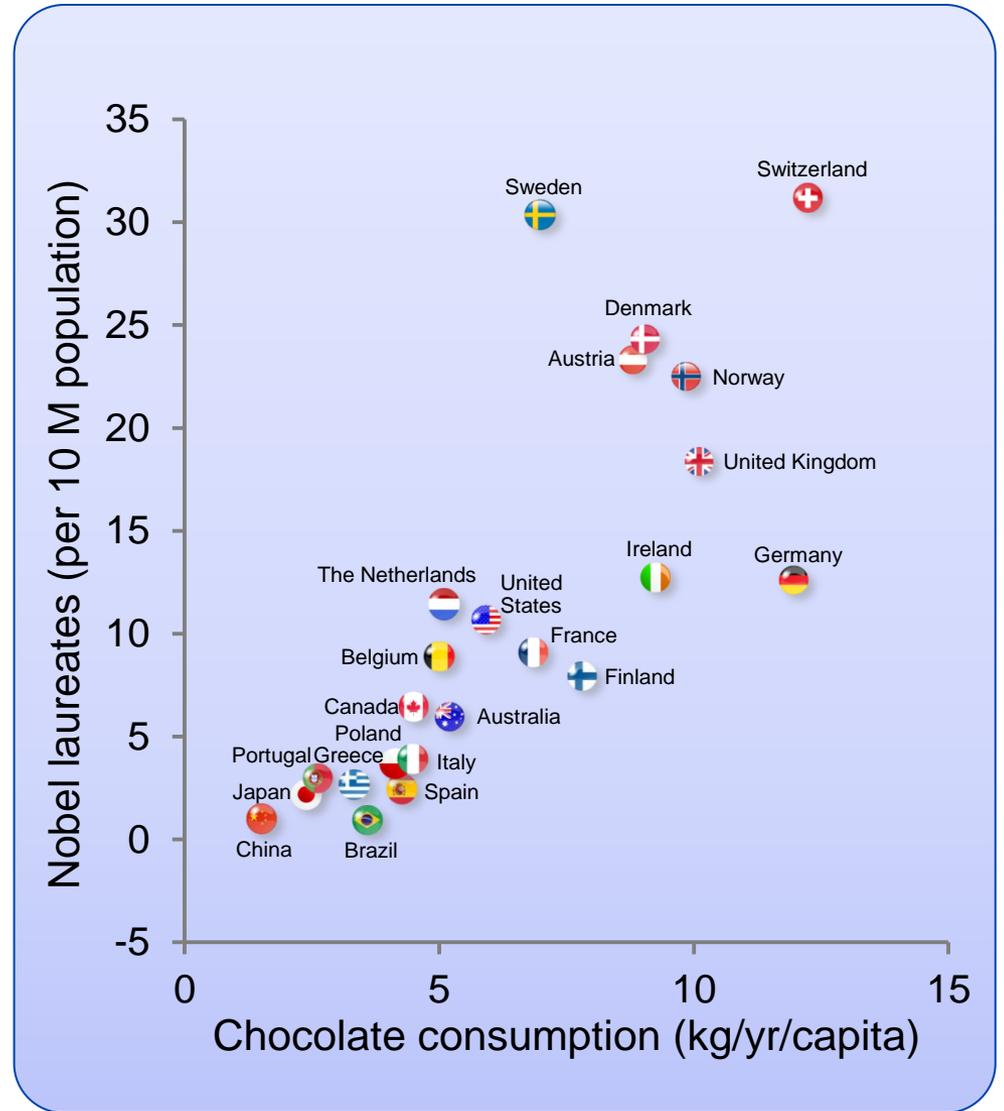
Franz H. Messerli, M.D.

Dietary flavonoids, abundant in plant-based foods, have been shown to improve cognitive function. Specifically, a reduction in the risk of dementia, enhanced performance on some cognitive tests, and improved cognitive function in elderly patients with mild impairment have been associated with a regular intake of flavonoids.^{1,2} A subclass of flavonoids called flavanols, which are widely present in cocoa, green tea, red wine, and some fruits, seems to be effective in slowing down or even reversing the reductions in cognitive performance that occur with aging. Dietary flavanols have also been shown to improve endothelial function and to lower blood pressure by causing vasodilation in the peripheral vasculature and in the brain.^{3,4} Improved cognitive performance with the administration of a cocoa polyphenolic

cause the population of a country is substantially higher than its number of Nobel laureates, the numbers had to be multiplied by 10 million. Thus, the numbers must be read as the number of Nobel laureates for every 10 million persons in a given country.

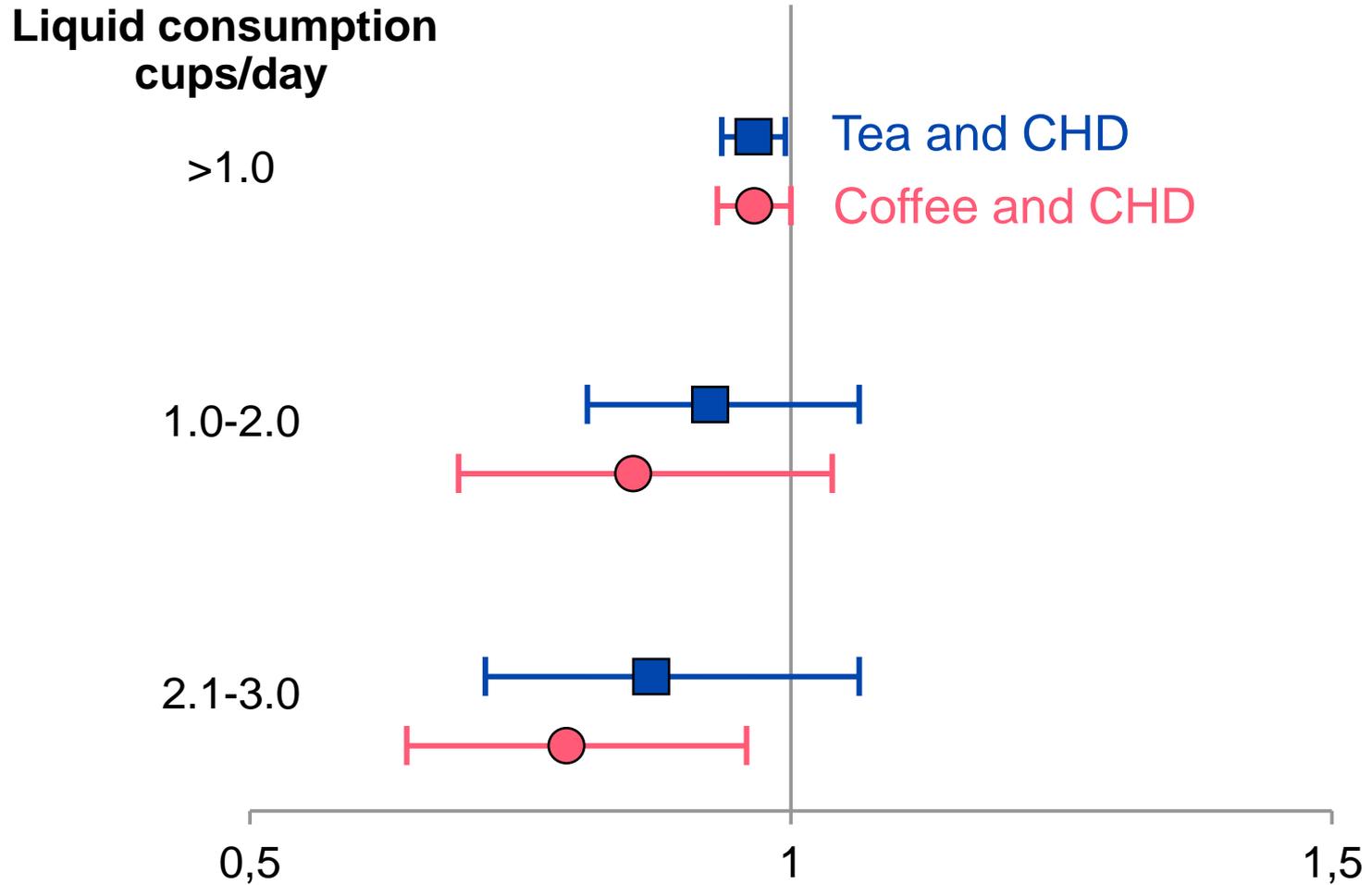
All Nobel Prizes that were awarded through October 10, 2011, were included. Data on per capita yearly chocolate consumption in 22 countries was obtained from Chocosuisse (www.chocosuisse.ch/web/chocosuisse/en/home), Theobroma-cacao (www.theobroma-cacao.de/wissen/wirtschaft/international/konsum), and Caobisco (www.caobisco.com/page.asp?p=213). Data were available from 2011 for 1 country (Switzerland), from 2010 for 15 countries, from 2004 for 5 countries, and from 2002 for 1 coun-

Conclusion – Chocolate consumption enhances cognitive function, which is a sine qua non for winning the Nobel Prize, and it closely correlates with the number of Nobel laureates in each country

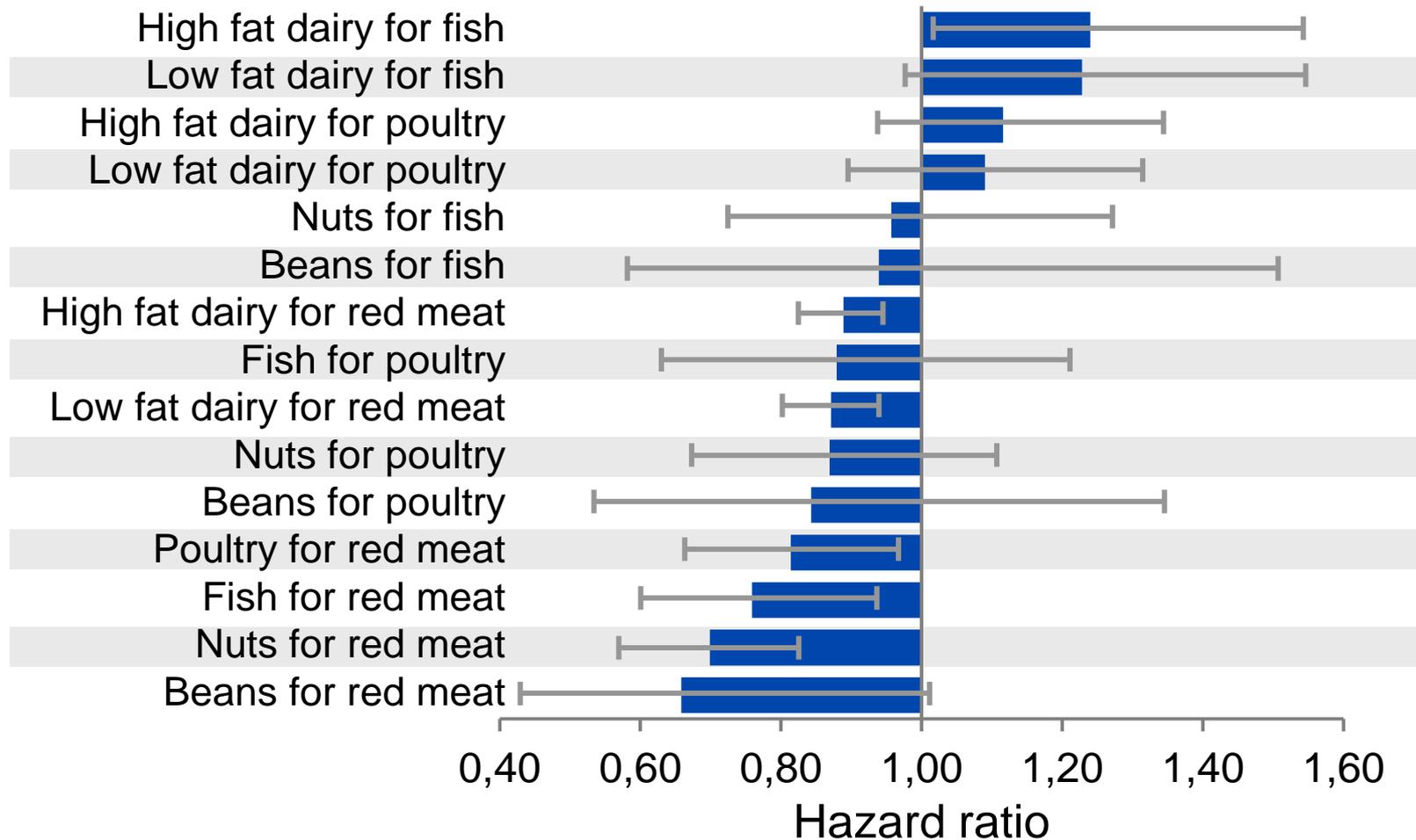


Messerli: NEJM October 11, 2012

Coffee or Tea Consumption and CHD

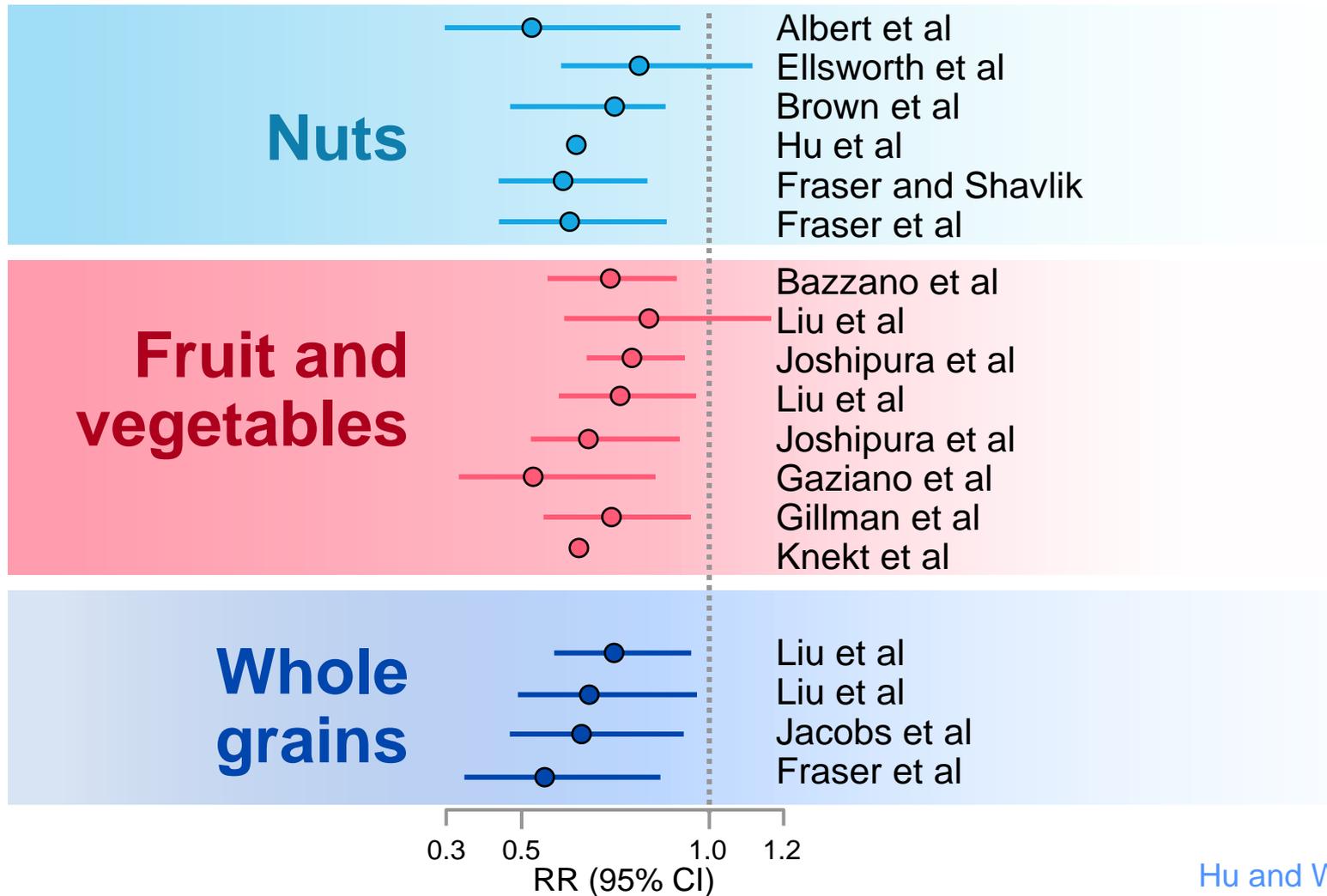


RRs and 95% CIs for CHD Associated With Replacement of a Major Dietary Protein Source With Another



Bernstein et al, Circ

Prospective Cohort Studies of Cardiovascular Disease and Consumption of Nuts, Fruits and Vegetables or Whole Grains



Hu and Willett:
JAMA 288(20):2569, 2002

How Do We Know if a Diet is Good for Your Heart?

Improved vascular function

- Improved reactive hyperemia indices
- Reduced inflammation
- Improved platelet function
- Enhanced NO utilization & availability

Reduced blood pressure

- Improved vascular function
- Reduced inflammation
- Reduced ROS
- Enhanced NO utilization

Weight reduction

- Reduces ROS, lipid profiles, & BP
- Improves exercise capacity

**Improved
Cardiovascular
Health Reduced CVD
Morbidity and Mortality**

Reduced oxidative stress

- Reduces LDL-oxidation
- Improves anti-oxidant capacity
- Reduced ROS
- Reduced isoprostanes

Improved lipid profiles

- Reduced LDL-c, TG & TC
- Increases HDL-c
- Reduces LDL-oxidation

Effect of Ingredients of Polymeal in Reducing Risk of CVD

Ingredients	Reduction in risk of CVD (%) (95% CI)	Source
Wine (150 mL/day)	32 (23-41)	DiCastelnuovo, 2002 (MA)
Fish (114 g x 4w)	14 (8-19)	Whelton, 2004 (MA)
Dark chocolate (100 g/d)	21 (14-27)	Taubert, 2003 (RCT)
Fruit/vegetables (400 g/d)	21 (14-27)	John, 2002 (RCT)
Garlic (2.7 g/d)	25 (21-27)	Ackerman, 2001 (MA)
Almonds (68 g/d) (RCT)	12.5 (10.5-13.5)	Jenkins, Sabate 2002, 2003
Combined effect	76 (63-84)	

MA = meta-analysis; RCT = randomized controlled trial

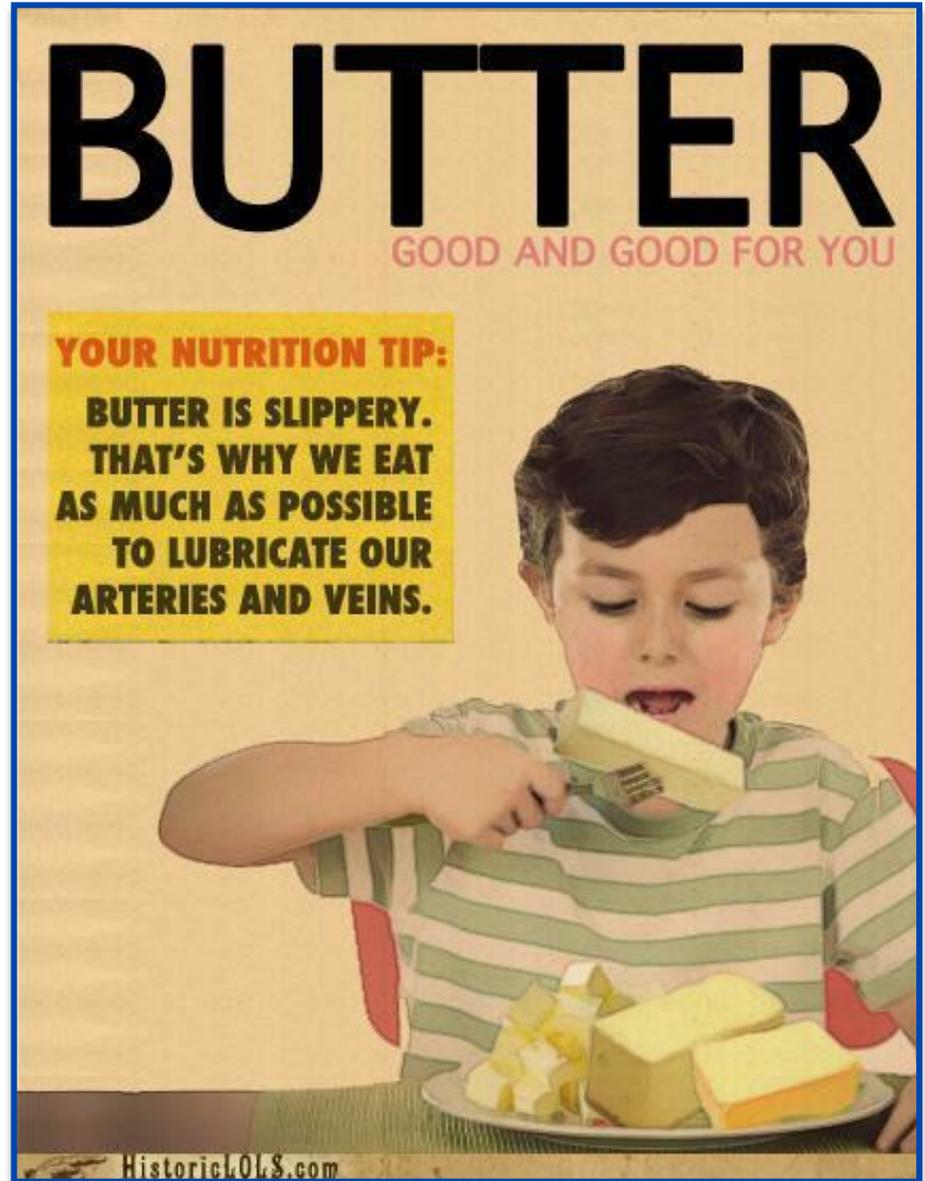
OH Franco et al., BMJ 2004; 329:1447

Polypill - NJ Wald et al., BMJ 2003; 326:1419

Statin, ASA, Folic Acid, BP (ACE-I, β -blocker, Thiazide) - **% Reduction 85%**

Food for Your Heart Menu

- The effect
- How much we eat?
- What do we eat?
- Types of diets
 - Epidemiology data
 - Prospective studies
 - Myths



Food for Your Heart



special report

Chicken Soup Inhibits Neutrophil Chemotaxis *In Vitro**

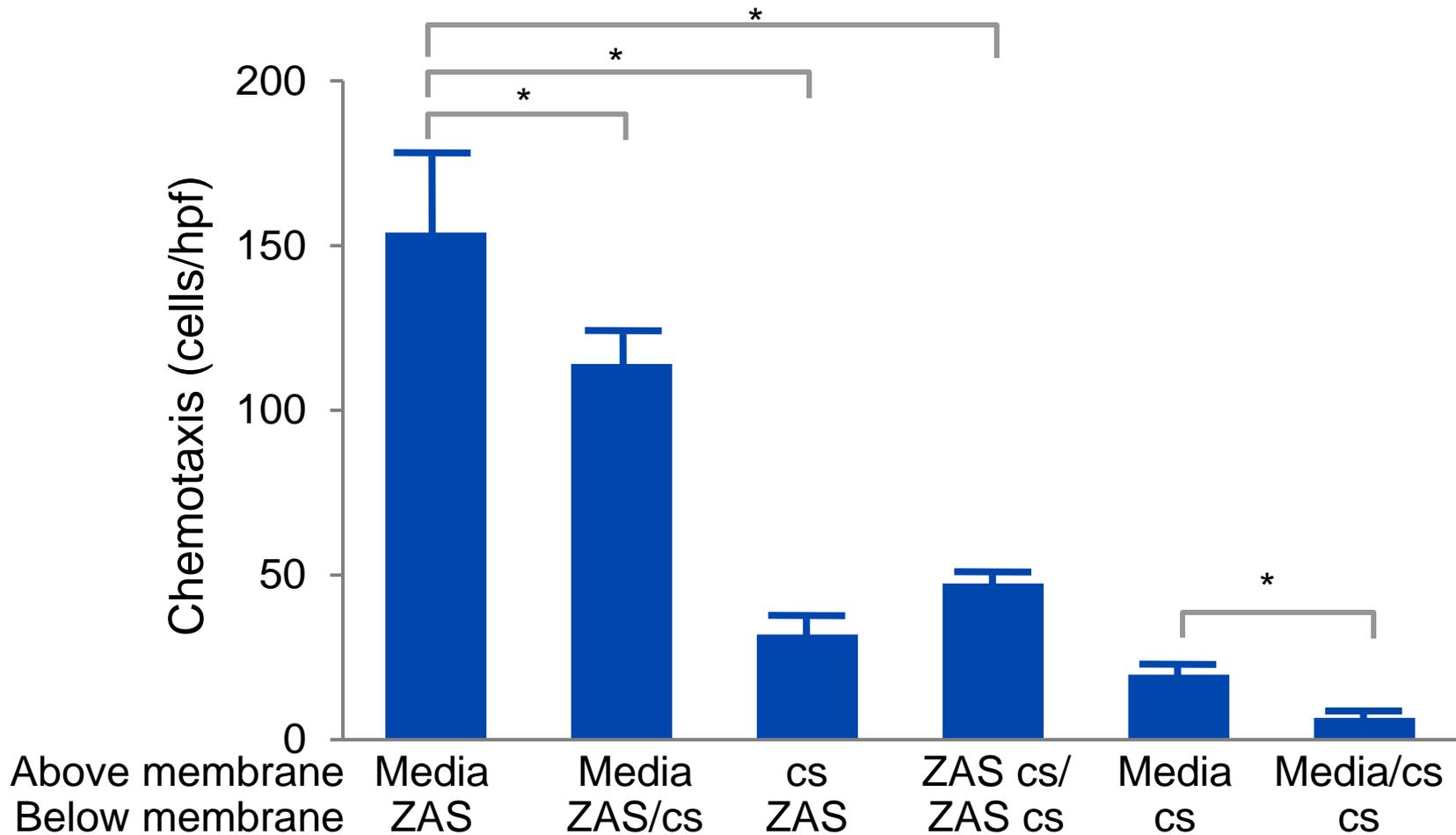
Menu

- The effect
- How much we eat?
- What do we eat?
- Types of diets
 - Epidemiology data
 - Prospective studies
 - Myth: Chicken soup...

Key words: chicken soup; neutrophil chemotaxis

Abbreviations: fMLP = fMet-Leu-Phe; HBSS = Hank's balanced salt solution; ZAS = zymosan-activated serum

Inhibition of Neutrophil Chemotaxis by Chicken Soup



Rennard et al: Chest 118:1150, 2000
P<0.05

Food for Your Heart

Menu

- The effect
- How much we eat ?
- What do we eat ?
- Types of diets
 - Epidemiology data
 - Prospective studies
 - Myth: Organic food

The New York Times **Environment**

WORLD | U.S. | N.Y. / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION

ENVIRONMENT | SPACE & COSMOS

What could happen to the stock market if Republicans take
If you have a \$500,000 portfolio, you should download the latest report by *Forbes* on what we think may happen in the 2012 elections and why. This must-read report includes use in your portfolio right now. Don't miss it! [Click Here to Download Your Report](#)

Stanford Scientists Cast Doubt on Advantages of Organic Meat and Produce



Jim Wilson/The New York Times

Conventional strawberries in Watsonville, California. Researchers say organic foods are no more nutritious and no less likely to be contaminated.

By **KENNETH CHANG**

Food for Your Heart Menu

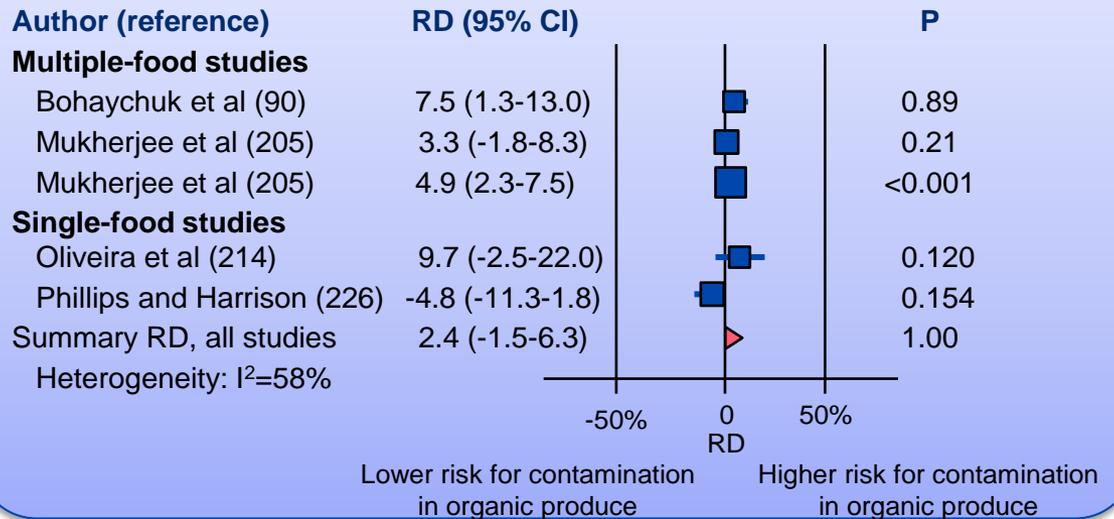
- The effect
- How much we eat?
- What do we eat?
- Types of diets
 - Epidemiology data
 - Prospective studies
 - Myth: Organic food

Are Organic Foods Safer or Healthier Than Conventional Alternatives?

A Systematic Review

Crystal Smith-Spangler, MD, MS; Margaret L. Brandeau, PhD; Grace E. Hunter, BA; J. Clay Bavinger, BA; Maren Pearson, BS; Paul J. Eschbach; Vandana Sundaram, MPH; Hau Liu, MD, MS, MBA, MPH; Patricia Schirmer, MD; Christopher Stave, MLS; Ingram Olkin, PhD; and Dena M. Bravata, MD, MS

RD of detecting *Escherichia coli* in organic and conventional fruits, vegetables, and grains



Stanford Scientists Cast Doubt on Advantages of Organic Meat and Produce



Prospective Study of Breakfast Eating and Incident Coronary Heart Disease in a Cohort of Male US Health Professionals

Epidemiology and Prevention

Prospective Study of Breakfast Eating and Incident Coronary Heart Disease in a Cohort of Male US Health Professionals

Leah E. Cahill, PhD; Stephanie E. Chiuve, ScD; Rania A. Mekary, PhD; Majken K. Jensen, PhD; Alan J. Flint, MD, DrPh; Frank B. Hu, MD, PhD; Eric B. Rimm, ScD

Background—Among adults, skipping meals is associated with excess body weight, hypertension, insulin resistance, and elevated fasting lipid concentrations. However, it remains unknown whether specific eating habits regardless of dietary composition influence coronary heart disease (CHD) risk. The objective of this study was to prospectively examine eating habits and risk of CHD.

- 26,902 men ages 45-82 years – free of CV disease
- 16 years follow-up

Although it is commonly stated that breakfast is the most important meal of the day, no evidence-based recommendations exist for adults in terms of eating habits (the frequency and or timing of meals, snacks, and caloric beverages). The 2010 Dietary Guidelines for Americans recommend breakfast for children but make no recommendation for adults, stating “behaviors have been studied, such as snacking and frequency of eating, but there is currently not enough evidence to support a specific recommendation for these behaviors.”¹

Clinical Perspective on p 343

Results from the 2002 National Health and Nutrition Examination Survey (NHANES) suggest that snacking and skipping breakfast are common practices among American adults, with 18% skipping breakfast and 86% snacking each day.² The Nationwide Food Consumption Survey 1965 to 1991 reported that breakfast consumption is down from 86% (1965) to 75% (1991).³ This trend may have adverse

consequences at a population level because results from short-duration trials, preliminary cross-sectional studies, and small prospective studies report that eating habits such as skipping meals have been positively associated with several cardio-metabolic health outcomes, including overweight⁴ and weight gain,⁵ dyslipidemia,^{6,7} blood pressure,⁸ insulin sensitivity,^{6,7} and diabetes mellitus.⁹ However, to the best of our knowledge, no human studies of eating habits and coronary heart disease (CHD) have been published. The objective of our study was to prospectively determine whether eating habits, including skipping breakfast, are related to an increased risk of CHD.

Methods

Study Population

The Health Professionals Follow-up Study (HPFS) is an ongoing prospective study of 51 529 male health professionals (dentists, veterinarians, pharmacists, optometrists, osteopaths, and podiatrists) 40 to 75 years of age at enrollment in 1986. Approximately 97% of

Received September 20, 2012; accepted May 23, 2013.

From the Departments of Nutrition (L.E.C., S.E.C., R.A.M., M.K.J., A.J.F., F.B.H., E.B.R.) and Epidemiology (F.B.H., E.B.R.), Harvard School of Public Health, Boston, MA; and Division of Preventive Medicine (S.E.C.) and Channing Division of Network Medicine (F.B.H., E.B.R.), Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.

Guest Editor for this article was Robert H. Eckel, MD.

The online-only Data Supplement is available with this article at <http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIRCULATIONAHA.113.001474/-/DC1>.

Correspondence to Leah E. Cahill, PhD, Harvard School of Public Health, 655 Huntington Ave, Bldg II, Room 349, Boston, MA 02115. E-mail leahc@hsph.harvard.edu

© 2013 American Heart Association, Inc.

Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.113.001474

Downloaded from <http://circ.ahajournals.org> at MAYO CLINIC on September 3, 2013

Eating Breakfast and Multivariate RR of CHD With 95% CIs

	Breakfast		P
	Yes	No	
Cases (n)	1,356	171	
Person-years	338,074	49,880	
Age-adjusted model: RR (95% CI)	1.00 (Referent)	1.33 (1.13-1.57)	0.0008
Diet factors	1.00 (Referent)	1.38 (1.15-1.66)	0.0006
Demographic factors	1.00 (Referent)	1.29 (1.07-1.55)	0.007
Activity factors	1.00 (Referent)	1.27 (1.06-1.53)	0.01

Conclusions – Eating breakfast was associated with significantly lower CHD risk in this cohort of male health professionals (Circulation. 2013;128:337-343.)

Cahill et al: Circ 128:337, 2013

The Role of Dietary Supplements

**\$28
Billion**

Estimated amount that Americans spent on dietary supplements last year, according to

0

Number of times since 1994 that the

EDITION: INTERNATIONAL | U.S. | MÉXICO | ARABIC

TV: CNNi | CNN en Español

Set edition preference



Home

Video

World

U.S.

Africa

Asia

Europe

Latin America

Middle East

Business

World Sport

FDA warns one brand of vitamin B supplement contains dangerous steroids

By David Simpson, for CNN

July 31, 2013 -- Updated 1659 GMT (0059 HKT)

Multivitamins in the Prevention of Cardiovascular Disease in Men

The Physicians' Health Study II Randomized Controlled Trial

Howard D. Sesso, ScD, MPH

William G. Christen, ScD

Vadim Bubec, PhD

Joanne P. Smith, BA

Jean MacFadyen, BA

Miriam Schwartz, MD

John A. ... MD, PhD

Context Although multivitamins are used to prevent vitamin and mineral deficiency, there is a perception that multivitamins may prevent cardiovascular disease (CVD). Observational studies have shown inconsistent associations between regular multivitamin use and CVD, with no long-term clinical trials of multivitamin use.

Objective To determine whether long-term multivitamin supplementation decreases the risk of major cardiovascular events among men.

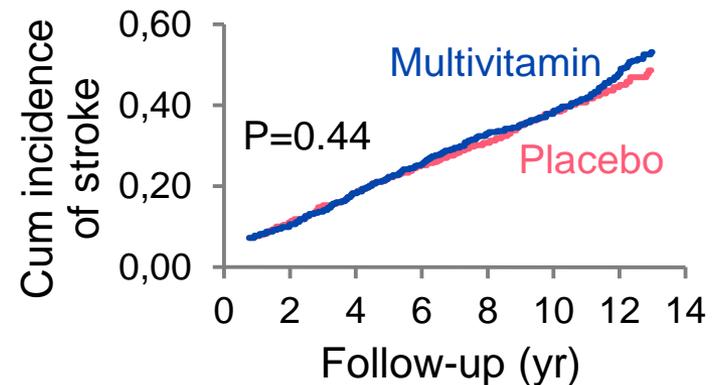
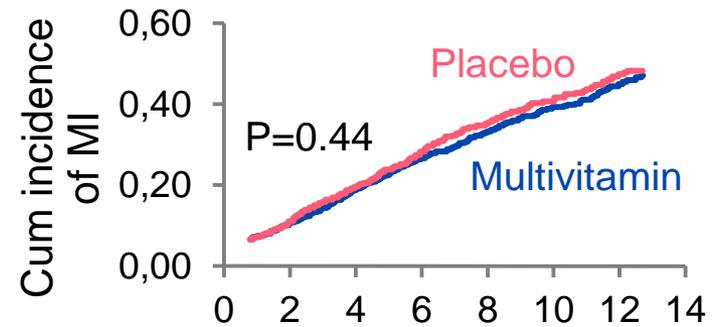
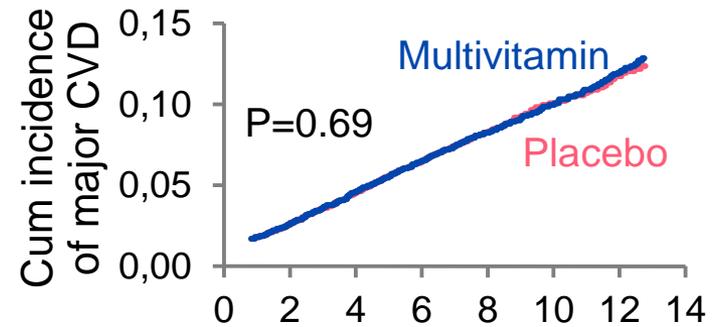
Design, Setting, and Participants The Physicians' Health Study II, a randomized, double-blind, placebo-controlled trial of a common daily multivitamin, began in 1997 and followed 14,641 men through June 1, 2011.

Objective

To determine whether long-term multivitamin supplements decreases the risk of major cardiovascular events among men

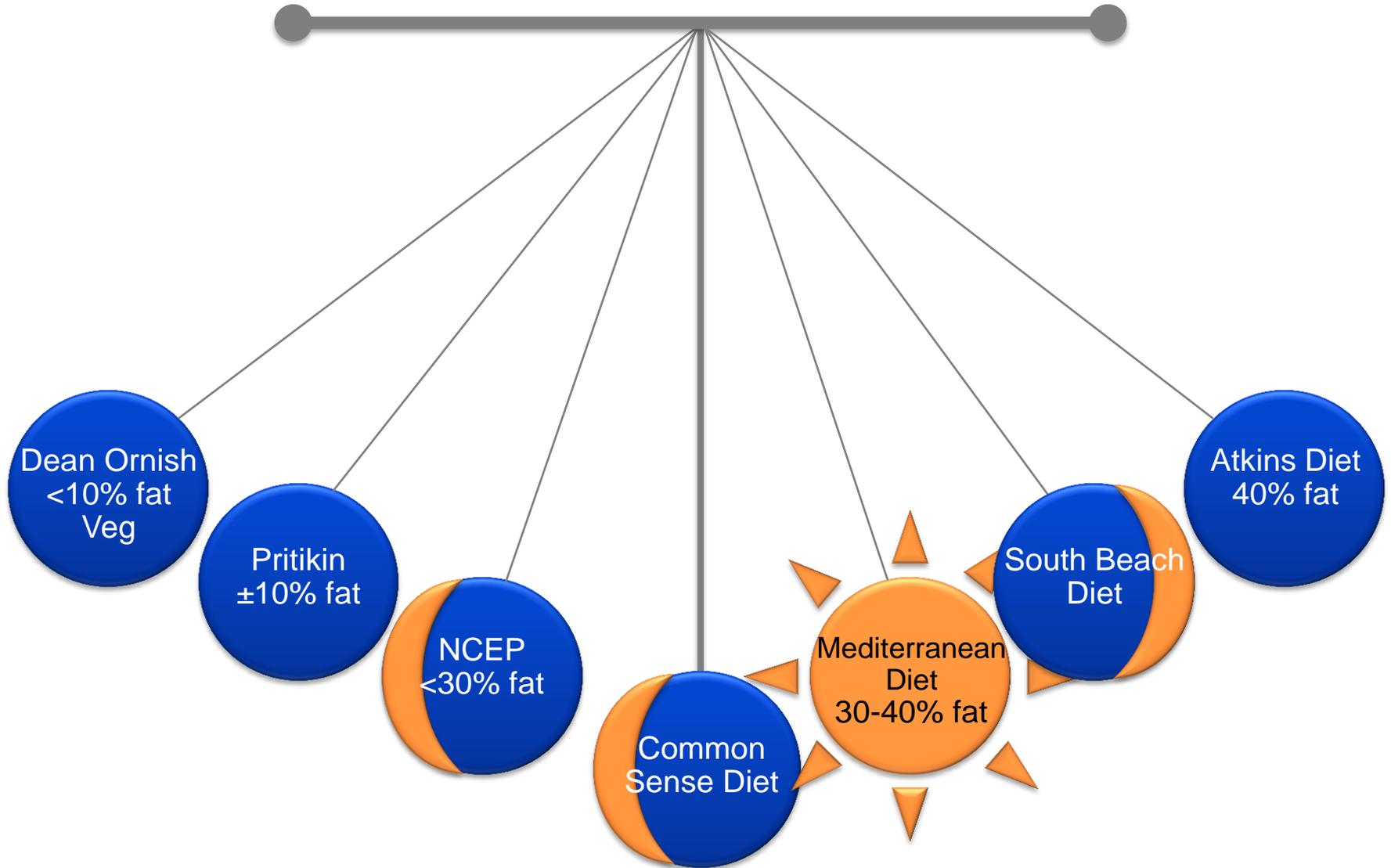
Design, Setting, and Participants

The Physicians' Health Study II, randomized, double-blind, placebo-controlled trial of a common daily multivitamin, began in 1997 with continued treatment and follow-up through June 1, 2011. A total of 14,641 male U.S. physicians initially aged 50 years or older (mean 64.3 [SD, 9.2] years), including 754 men with a history of CVD at randomization were enrolled.

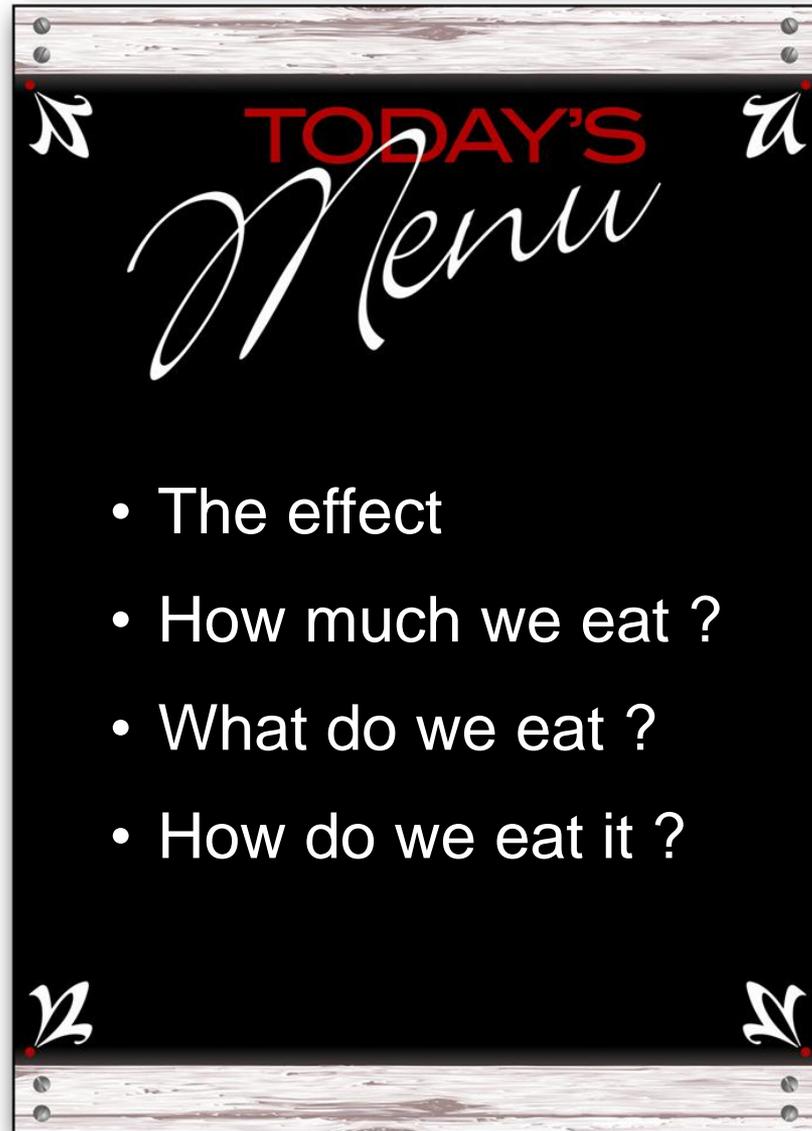


Sesso HD et al: JAMA 308(17): 1751, 2012

The Diet Pendulum



Food for Your Heart



Television Viewing Time and Mortality

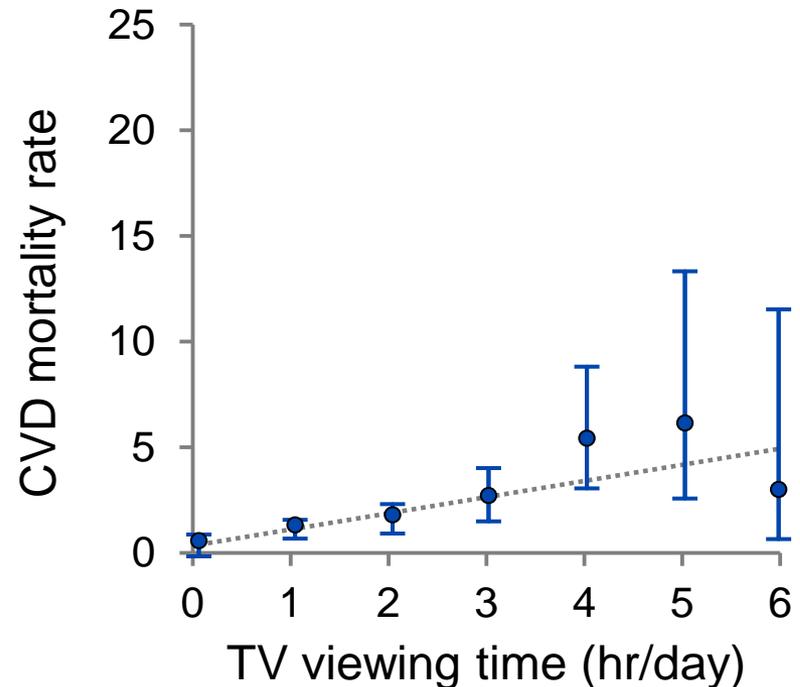
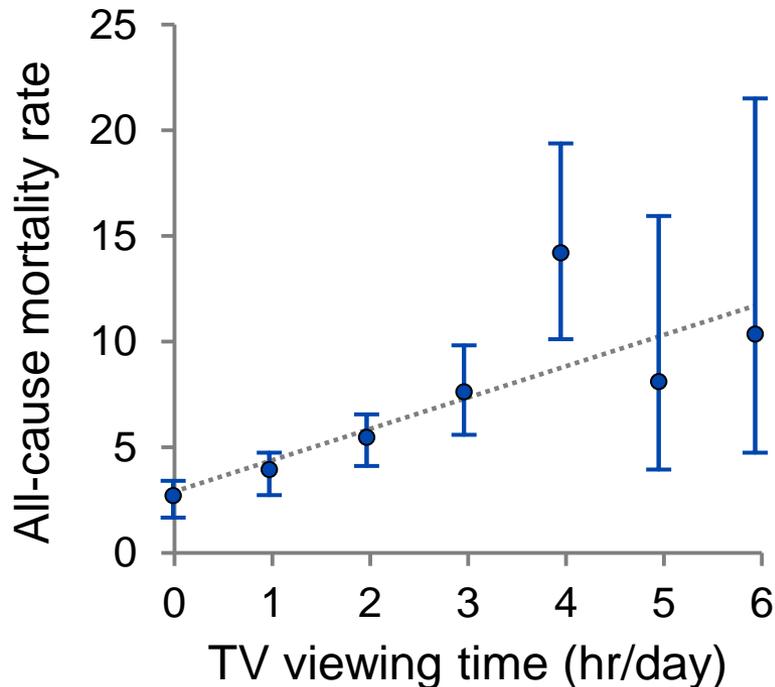
The Australian Diabetes, Obesity and Lifestyle Study (AusDiab)

D.W. Dunstan, PhD; E.L.M. Barr, PhD; G.N. Healy, PhD; J. Salmon, PhD; J.E. Shaw, MD;
B. Balkau, PhD; D.J. Magliano, PhD; A.J. Cameron, PhD; P.Z. Zimmet, PhD; N. Owen, PhD

Background—Television viewing time, the predominant leisure-time sedentary behavior, is associated with biomarkers of cardiometabolic risk, but its relationship with mortality has not been studied. We examined the associations of prolonged television viewing time with all-cause, cardiovascular disease (CVD), cancer, and non-CVD/noncancer mortality in

Background We examined the associations of prolonged television viewing time with all-cause, cardiovascular disease (CVD), cancer, and non-CVD/noncancer mortality in Australian adults.

CI, 1.00 to 3.25). The associations with both cancer mortality and non-CVD/noncancer mortality were not significant.
Conclusions—Television viewing time was associated with increased risk of all-cause and CVD mortality. In addition to



Dunstan et al: Circ 121:384, 2010



*Family Values
Traditional Spirit
Since 1912*

Roseto, PA



Roseto, IT

©2010 Google - Map data ©2010 Europa Technologies.



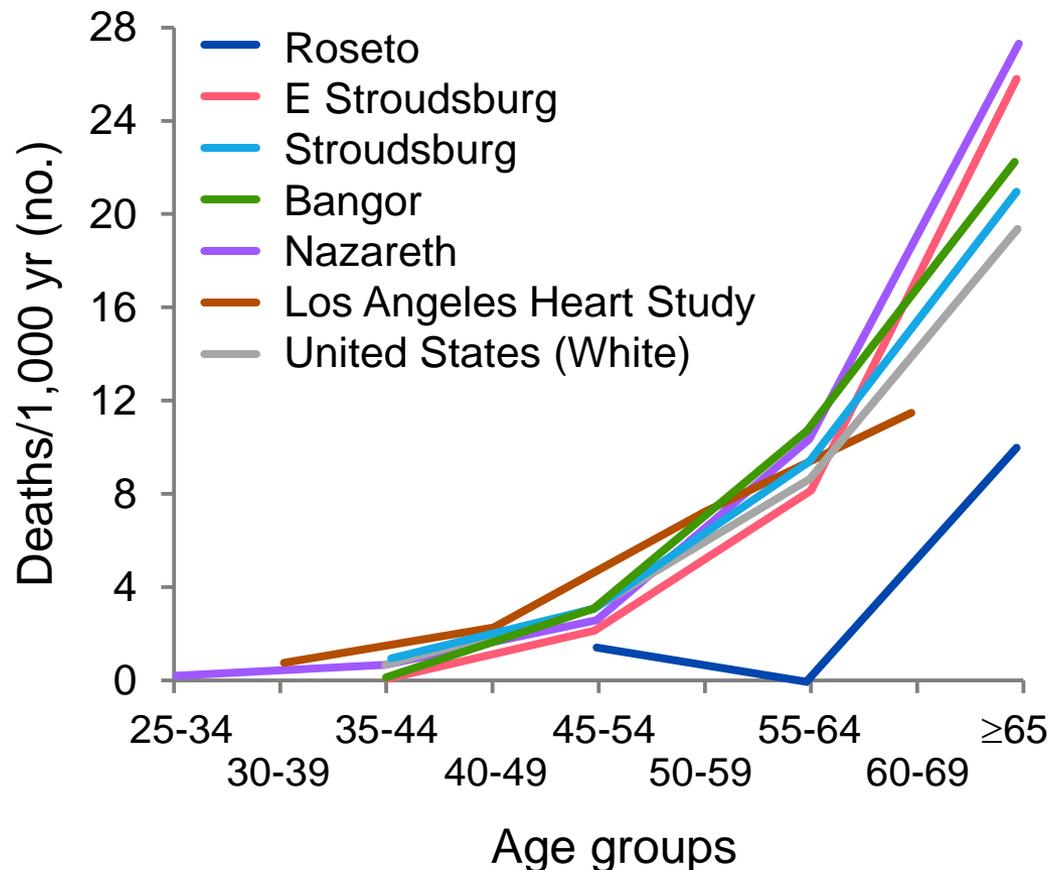
Comparison of Death Rates from Coronary Heart Disease in Males

Predictors of Myocardial Infarction Over a Span of 30 Years in Roseto, Pennsylvania

STEWART WOLF

Abstract—Predictors of myocardial infarction with or without survival were sought in a 30-year study of Roseto, Pennsylvania, a nearly exclusively Italian community of approximately 1,600, compared to the immediately adjacent town of Bangor with a population of approximately 5,000. At the start of the study the death rate from myocardial infarction among men in Roseto was less than half that in Bangor despite an equal prevalence of the usual risk factors, mainly smoking and diet. The communities were followed prospectively for 30 years during a striking social change in Roseto toward less family and community cohesion and more commitment to individual goals and adherence to materialistic values. During this period the prevalence of and mortality from myocardial infarction increased sharply to equal the situation in Bangor. The predictive values of measurements made of Rosetans during individual examinations in 1962-63 were tested against the outcome in 1990. Those who experienced fatal myocardial infarction and those who had a well documented infarction and survived were matched with and compared to controls. Although subjects with cholesterol concentration above 200 were twice as likely to experience myocardial infarction as those with concentrations below 200, less than 20% of those whose cholesterol concentration was above 200 experienced any evidence of myocardial infarction over the nearly 30-year period. Moreover, there were no significant differences between the coronary patients, with or without survival, and their sex, age, and cholesterol matched controls; nor were smoking, evidence of hypertension, diabetes, or obesity predictive of significant differences between the two groups. These data lead to the inference that while those with the conventional risk factors are more likely to develop myocardial infarction than are those without the risk factors, an even larger proportion of the population may have the risk factors and not succumb to myocardial infarction over a period of nearly three decades.

grative Physiological and Behavioral Science, July-September, 1992, Vol. 27, No. 3, 246-257



Wolf S: Physiological & Behavioral Science 27(3): 246, 1992

Bon Appetite



Food for Your Heart



TODAY'S
Menu

Drink(s)	Red wine, 1-2 servings
Appetizer	Nuts, salad, olives, fish
Salad	Yes, with oil- based dressing
Main course	Fish, veggies, whole-grain pasta
Dessert	Dark chocolate
Drink	Green tea