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Martin Juneau M.D., M.Ps., FRCP(C)
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Préface de Pierre Lavoie
TRÉCARRÉ

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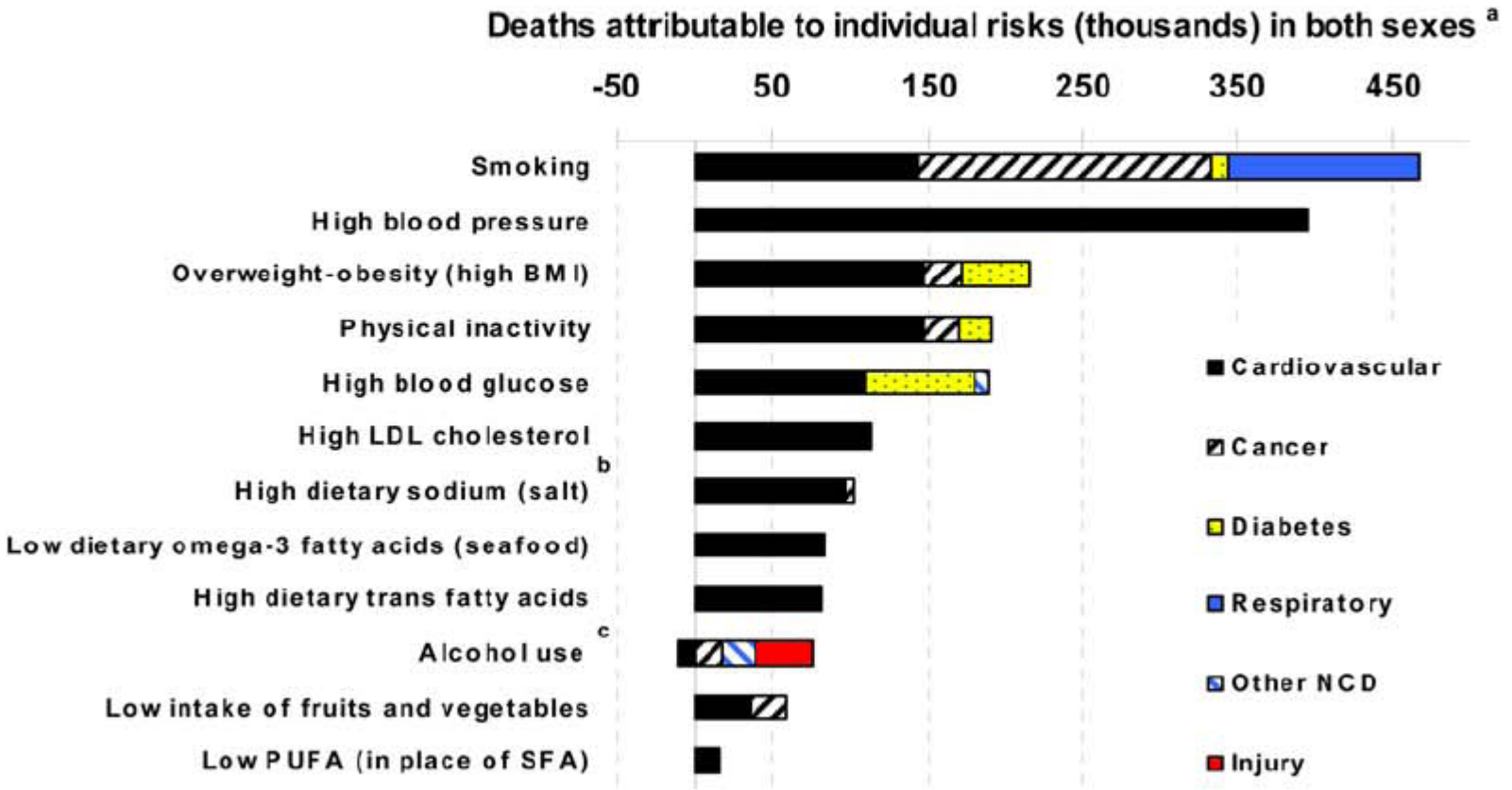
Mortality Effects of Risk Facto



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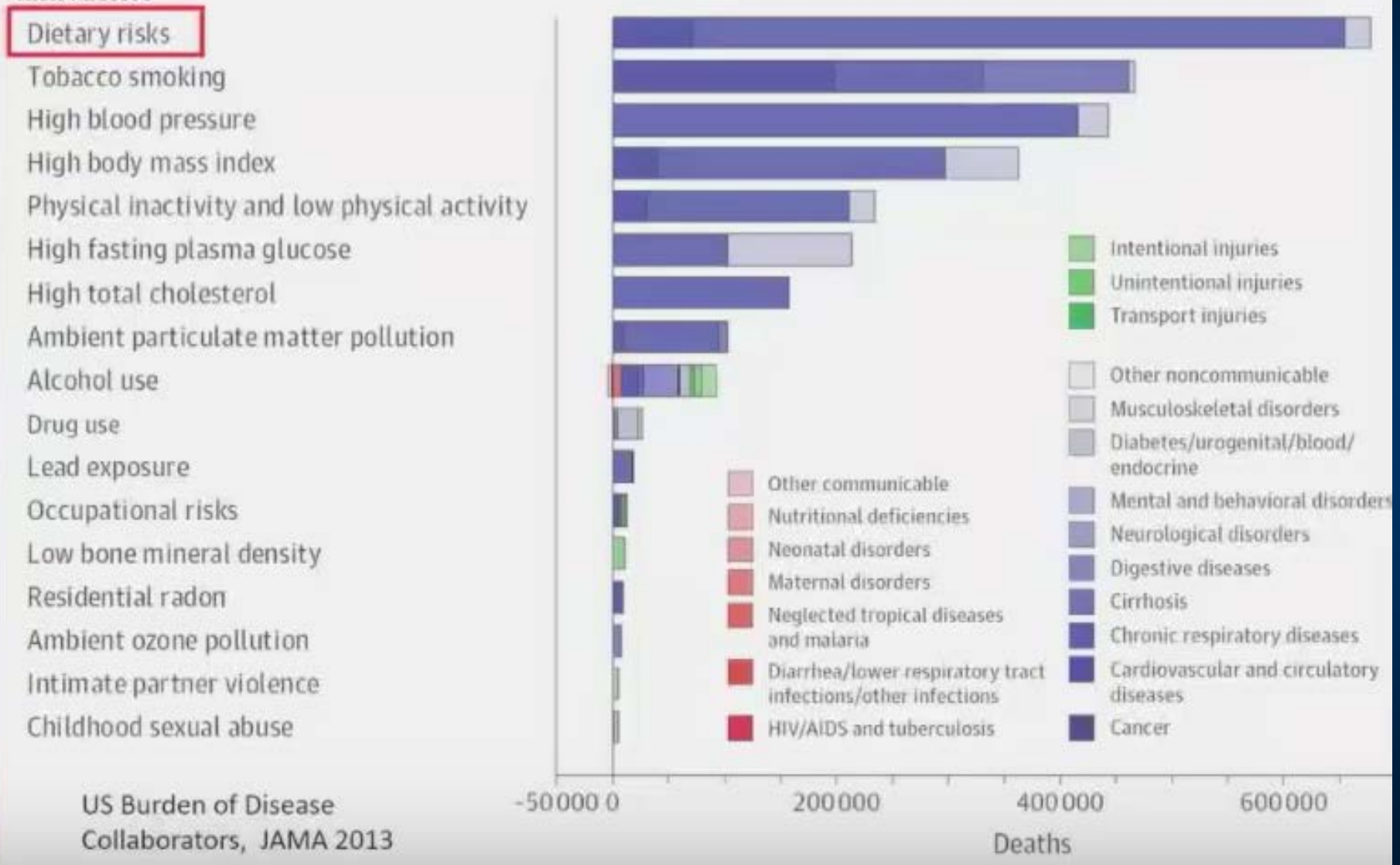

US Burden of Disease Collaborators, JAMA 2013

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QUARTERLY FOCUS ISSUE: HEART RHYTHM DISORDERS

Metabolic Syndrome and Risk of Acute Myocardial Infarction

A Case-Control Study of 26,903 Subjects From 52 Countries

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Hamilton, Ontario, Canada; Bangkok, Thailand; and Gaborone, Botswana

Objectives This study examines the risk of acute myocardial infarction (MI) conferred by the metabolic syndrome (MS) and its individual factors in multiple ethnic populations.

Background The risk of the MS on MI has not been well characterized, especially in multiple ethnic groups.

Methods Participants in the INTERHEART study (n = 26,903) involving 52 countries were classified using the World Health Organization (WHO) and International Diabetes Federation (IDF) criteria for MS, and their odds ratios (ORs) for MI were compared with the individual MS component factors.

Results The MS is associated with an increased risk of MI, both using the WHO (OR: 2.69; 95% confidence interval [CI]: 2.45 to 2.95) and IDF (OR: 2.20; 95% CI: 2.03 to 2.38) definitions, with corresponding population attributable risks of 14.5% (95% CI: 12.7% to 16.3%) and 16.8% (95% CI: 14.8% to 18.8%), respectively. The associations are directionally similar across all regions and ethnic groups. Using the WHO definition, the association with MI by the MS is similar to that of diabetes mellitus (OR: 2.72; 95% CI: 2.53 to 2.92) and hypertension (OR: 2.60; 95% CI: 2.46 to 2.76), and significantly stronger than that of the other component risk factors. The clustering of ≥3 risk factors with subthreshold values is associated with an increased risk of MI (OR: 1.50; 95% CI: 1.24 to 1.81) compared with having component factors with "normal" values. The IDF definition showed similar results.

Conclusions In this large-scale, multi-ethnic, international investigation, the risk of MS on MI is generally comparable to that conferred by some, but not all, of its component risk factors. The characterization of risk factors, especially continuous variables, as dichotomous will underestimate risk and decrease the magnitude of association between MS and MI. (J Am Coll Cardiol 2010;55:2390–8) © 2010 by the American College of Cardiology Foundation

The common clustering of metabolic abnormalities including abdominal obesity, elevated glucose, abnormal lipids, and elevated blood pressure has been extensively referred to in the medical literature as the "metabolic syndrome" (MS) (1,2). The presence of MS is associated with an increased risk of coronary heart disease (3–5), with limited evidence that this risk is greater than that conferred by its constituent components (6). The value of classifying subjects with MS has recently been called into question as the definition of MS is arbitrary (7,8), and the American Diabetes Association and the European Association for the Study of Diabetes have called for an aggressive research agenda to bring clarity to this debate (8). In this large-scale, multi-ethnic, international investigation, the objectives are to: 1) determine the risk of acute myocardial infarction (MI) among patients with MS defined using existing criteria; 2) assess if

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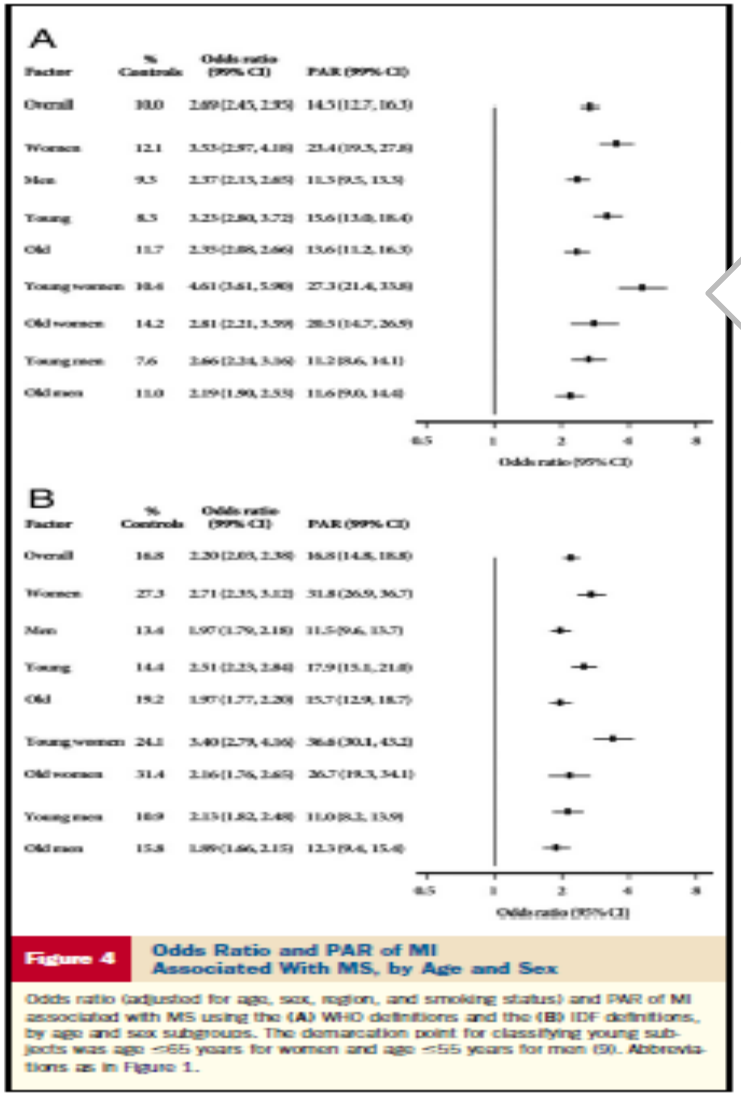

Figure 4 **Odds Ratio and PAR of MI Associated With MS, by Age and Sex**

Odds ratio (adjusted for age, sex, region, and smoking status) and PAR of MI associated with MS using the (**A**) WHO definitions and the (**B**) IDF definitions, by age and sex subgroups. The demarcation point for classifying young subjects was age ≤65 years for women and age ≤55 years for men (9). Abbreviations as in Figure 1.

suggest that the risk associated with MS is not greater than the sum of its component factors.

The MS refers to a cluster of risk factors which when present together is believed to confer an increased risk of cardiovascular disease (1,2). Subjects with MS have a higher cardiovascular disease risk than do subjects without the

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Circulation

ORIGINAL RESEARCH ARTICLE

Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population

BACKGROUND: Americans have a shorter life expectancy compared with residents of almost all other high-income countries. We aim to estimate the impact of lifestyle factors on premature mortality and life expectancy in the US population.

METHODS: Using data from the Nurses' Health Study (1980–2014; n=78 865) and the Health Professionals Follow-up Study (1986–2014, n=44 354), we defined 5 low-risk lifestyle factors as never smoking, body mass index of 18.5 to 24.9 kg/m^2, ≥30 min/d of moderate to vigorous physical activity, moderate alcohol intake, and a high diet quality score (upper 40%), and estimated hazard ratios for the association of total lifestyle score (0–5 scale) with mortality. We used data from the NHANES (National Health and Nutrition Examination Surveys; 2013–2014) to estimate the distribution of the lifestyle score and the US Centers for Disease Control and Prevention WONDER database to derive the age-specific death rates of Americans. We applied the life table method to estimate life expectancy by levels of the lifestyle score.

RESULTS: During up to 34 years of follow-up, we documented 42 167 deaths. The multivariable-adjusted hazard ratios for mortality in adults with 5 compared with zero low-risk factors were 0.26 (95% confidence interval [CI], 0.22–0.31) for all-cause mortality, 0.35 (95% CI, 0.27–0.45) for cancer mortality, and 0.18 (95% CI, 0.12–0.26) for cardiovascular disease mortality. The population-attributable risk of nonadherence to 5 low-risk factors was 60.7% (95% CI, 53.6–66.7) for all-cause mortality, 51.7% (95% CI, 37.1–62.9) for cancer mortality, and 71.7% (95% CI, 58.1–81.0) for cardiovascular disease mortality. We estimated that the life expectancy at age 50 years was 29.0 years (95% CI, 28.3–29.8) for women and 25.5 years (95% CI, 24.7–26.2) for men who adopted zero low-risk lifestyle factors. In contrast, for those who adopted all 5 low-risk factors, we projected a life expectancy at age 50 years of 43.1 years (95% CI, 41.3–44.9) for women and 37.6 years (95% CI, 35.8–39.4) for men. The projected life expectancy at age 50 years was on average 14.0 years (95% CI, 11.8–16.2) longer among female Americans with 5 low-risk factors compared with those with zero low-risk factors; for men, the difference was 12.2 years (95% CI, 10.1–14.2).

CONCLUSIONS: Adopting a healthy lifestyle could substantially reduce premature mortality and prolong life expectancy in US adults.

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*Drs Li and Pan contributed equally.

Key Words: healthy lifestyle ■ life expectancy ■ mortality, premature

Sources of Funding, see page XXX

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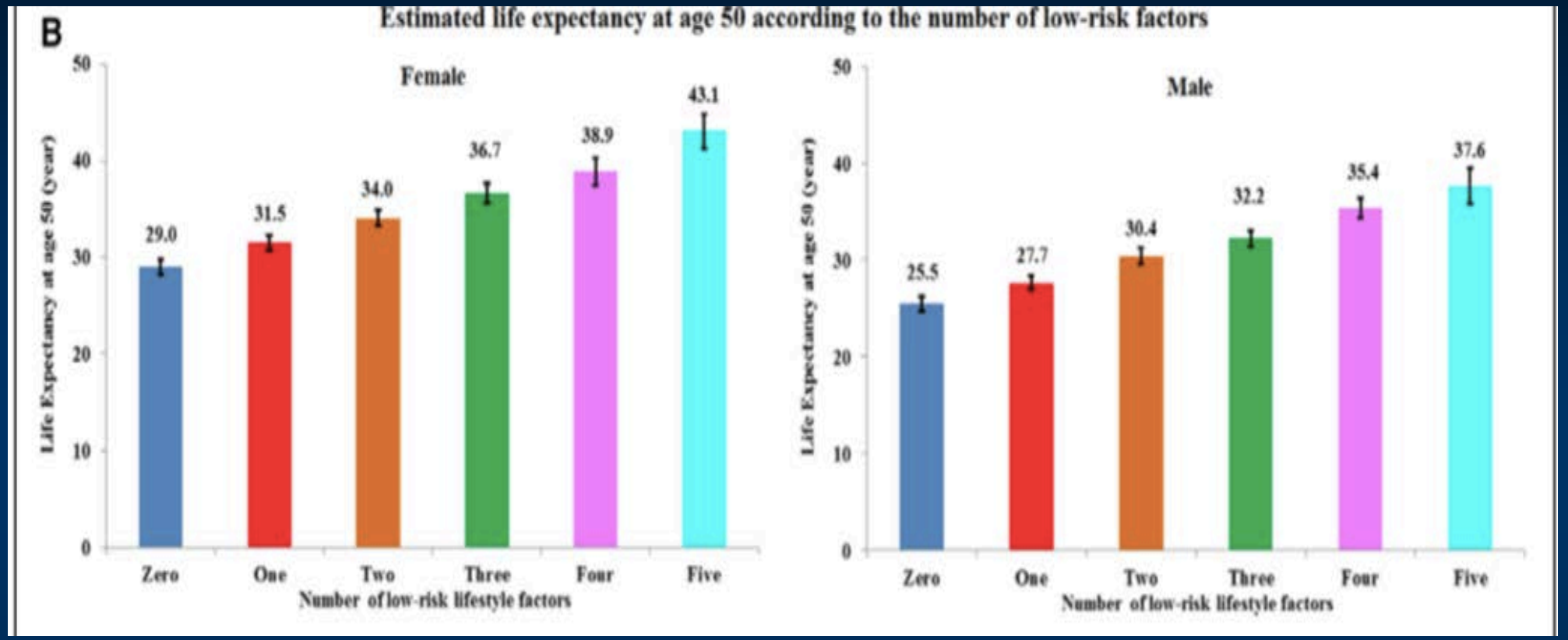
B
Estimated life expectancy at age 50 according to the number of low-risk factors
Female
Life Expectancy at age 50 (year)
50
40
30
20
10
0
29.0
31.5
34.0
36.7
38.9
43.1
Zero
One
Two
Three
Four
Five
Number of low-risk lifestyle factors
Male
Life Expectancy at age 50 (year)
50
40
30
20
10
0
25.5
27.7
30.4
32.2
35.4
37.6
Zero
One
Two
Three
Four
Five
Number of low-risk lifestyle factors

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ORIGINAL INVESTIGATIONS

Low-Risk Diet and Lifestyle Habits in the Primary Prevention of Myocardial Infarction in Men

A Population-Based Prospective Cohort Study

Agneta Åkesson, PhD, Susanna C. Larsson, PhD, Andrea Discacciati, MSc, Alicja Wolk, DMSc

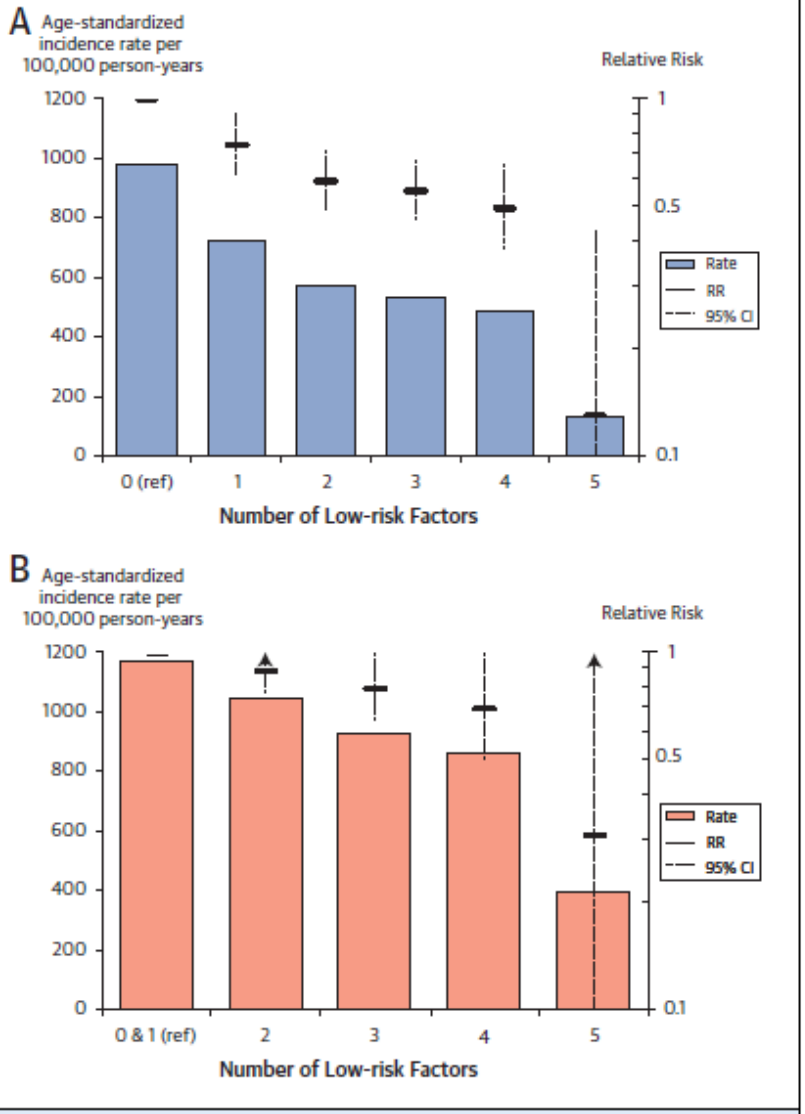

FIGURE 1 **MI Incidence for the Addition of Any Low-Risk Behavior**

Age-standardized incidence rates and multivariable-adjusted relative risks of MI for the addition of any single low-risk factor compared with the high-risk group for men without hypertension and high cholesterol (n = 20,721), p for trend < 0.001 **(A)**, and men with hypertension and high cholesterol (n = 7,139), p for trend = 0.002 (3 and 4 statistically

OPEN ACCESS Freely available online PLoS MEDICINE

Combined Impact of Health Behaviours and Mortality in Men and Women: The EPIC-Norfolk Prospective Population Study

Kay-Tee Khaw[1]*, Nicholas Wareham[2], Sheila Bingham[3], Ailsa Welch[1], Robert Luben[1], Nicholas Day[1]

1 Department of Public Health and Primary Care, Institute of Public Health, University of Cambridge School of Clinical Medicine, Cambridge, United Kingdom, 2 Medical Research Council, Epidemiology Unit, Cambridge, United Kingdom, 3 Medical Research Council, Dunn Nutrition Unit, Cambridge, United Kingdom

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Competing Interests: The authors have declared that no competing interests exist.

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Abbreviations: CI, confidence interval; ICD, International Classification of Disease; RR, relative risk

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ABSTRACT

Background

There is overwhelming evidence that behavioural factors influence health, but their combined impact on the general population is less well documented. We aimed to quantify the potential combined impact of four health behaviours on mortality in men and women living in the general community.

Methods and Findings

We examined the prospective relationship between lifestyle and mortality in a prospective population study of 20,244 men and women aged 45–79 y with no known cardiovascular disease or cancer at baseline survey in 1993–1997, living in the general community in the United Kingdom, and followed up to 2006. Participants scored one point for each health behaviour: current non-smoking, not physically inactive, moderate alcohol intake (1–14 units a week) and plasma vitamin C >50 mmol/l indicating fruit and vegetable intake of at least five servings a day, for a total score ranging from zero to four. After an average 11 y follow-up, the age-, sex-, body mass–, and social class–adjusted relative risks (95% confidence intervals) for all-cause mortality(1,987 deaths) for men and women who had three, two, one, and zero compared to four health behaviours were respectively, 1.39 (1.21–1.60), 1.95 (1.70–2.25), 2.52 (2.13–3.00), and 4.04 (2.95–5.54) $p < 0.001$ trend. The relationships were consistent in subgroups stratified by sex, age, body mass index, and social class, and after excluding deaths within 2 y. The trends were strongest for cardiovascular causes. The mortality risk for those with four compared to zero health behaviours was equivalent to being 14 y younger in chronological age.

Conclusions

Four health behaviours combined predict a 4-fold difference in total mortality in men and women, with an estimated impact equivalent to 14 y in chronological age.

The Editors' Summary of this article follows the references.

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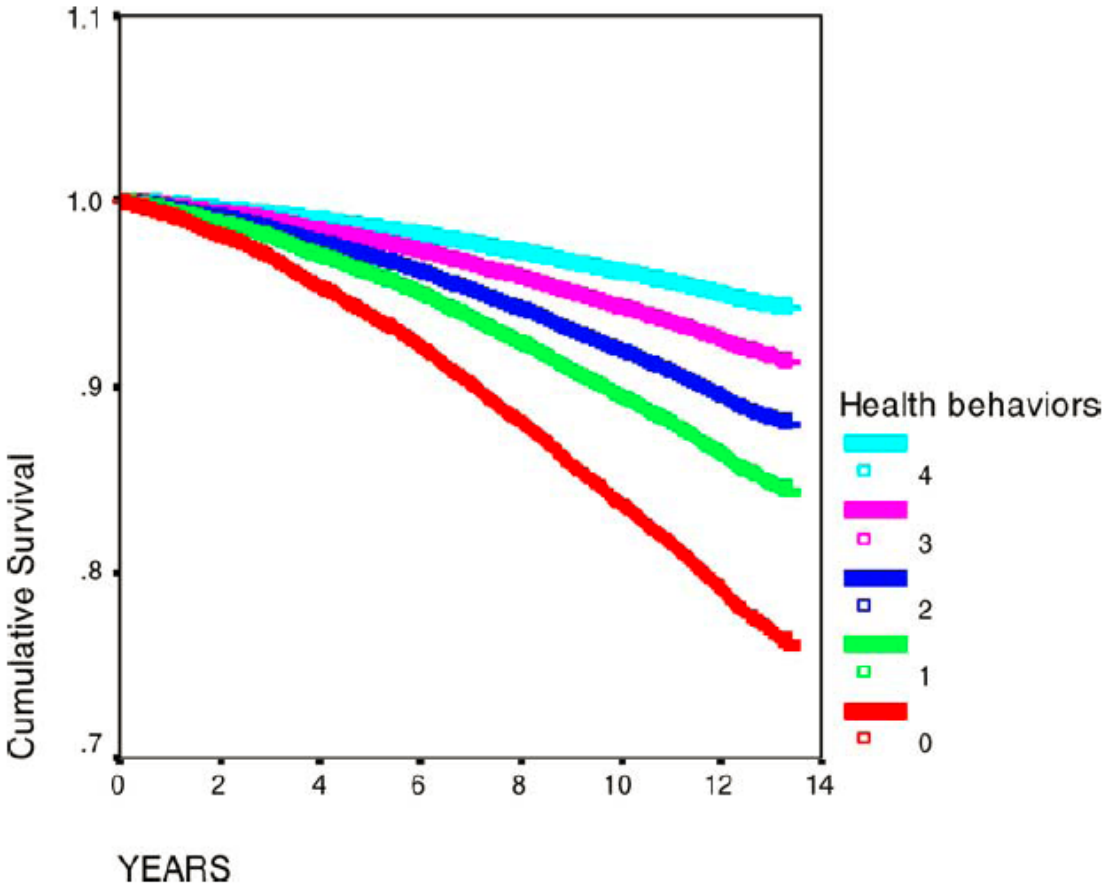

Figure 1. Survival Function According to Number of Health Behaviours in Men and Women Aged 45–79 Years without Known Cardiovascular Disease or Cancer, Adjusted for Age, Sex, Body Mass Index and Social Class, EPIC-Norfolk 1993–2006

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EDITORIAL COMMENT

The Promise of Lifestyle for Cardiovascular Health

Time for Implementation*

Dariush Mozaffarian, MD, DrPH

and of abdominal obesity to 4 in 5 MIs. These findings highlight the primacy of healthy lifestyle. For both individual patients and populations, lifestyle goals should not be formulated solely for control of weight or blood pressure, cholesterol, and glucose levels. Although lifestyle has major benefits on these physiological factors, a healthier diet, greater activity, and nonsmoking influence numerous other pathways of risk and produce substantial additional benefits for cardiovascular and noncardiovascular health (5). For example, in the present investigation among >20,000 Swedish men, the combination of a healthier diet

an end and instead recognizing the relevance of lifestyle as a primary target for health. It is time for medical educators, clinicians, health administrators, and insurance providers to follow suit by designing and implementing a comprehensive, ambitious agenda to incorporate measures of and targets for dietary quality, physical activity, smoking, and central obesity into every aspect of the health system (9). Patients should enter their doctor's office and not simply ask "How are my blood pressure, cholesterol, and glucose levels?" but also ask "How are my dietary habits, physical activity level, smoking, and waist measurement?"

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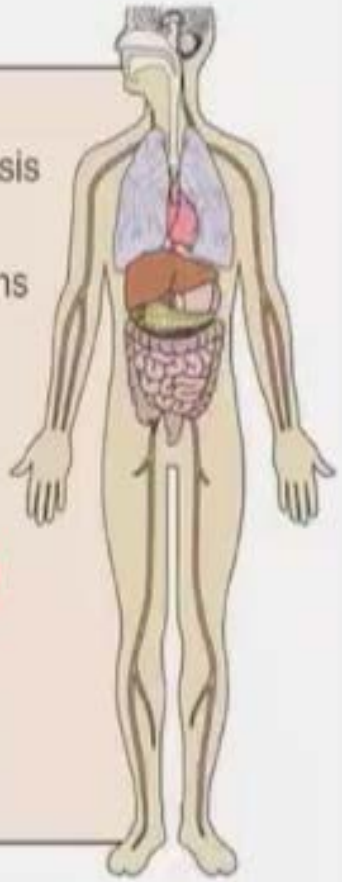
Diet & Health: Modern Science

Refined grains, starches, sugars
Fruits, vegetables, nuts
Whole grains, legumes
Yogurt, cheese, milk
Fish, shellfish
Processed meats, red meats
Vegetable oils, specific fatty acids
Coffee, tea, alcohol
Sugary beverages, juice
Minerals, antioxidants, phytochemicals
Food-based dietary patterns
Food processing, preparation methods

Blood pressure
Glucose-insulin homeostasis
Liver fat synthesis
Blood lipids, apolipoproteins
Endothelial function
Systemic inflammation
Brain reward, craving
Gut microbiome
Satiety, hunger, obesity
Adipocyte function
Cardiac function
Thrombosis, coagluation
Vasular adhesion



Mozaffarian D, Circulation 2016

Original Investigation

Different Time Trends of Caloric and Fat Intake Between Statin Users and Nonusers Among US Adults

Gluttony in the Time of Statins?

Takehiro Sugiyama, MD, MSHS; Yusuke Tsugawa, MD, MPH; Chi-Hong Tseng, PhD; Yasuki Kobayashi, MD, PhD; Martin F. Shapiro, MD, PhD

IMPORTANCE Both dietary modification and use of statins can lower blood cholesterol. The increase in caloric intake among the general population is reported to have plateaued in the last decade, but no study has examined the relationship between the time trends of caloric intake and statin use.

OBJECTIVE To examine the difference in the temporal trends of caloric and fat intake between statin users and nonusers among US adults.

DESIGN, SETTING, AND PARTICIPANTS A repeated cross-sectional study in a nationally representative sample of 27 886 US adults, 20 years or older, from the National Health and Nutrition Examination Survey, 1999 through 2010.

EXPOSURES Statin use.

MAIN OUTCOMES AND MEASURES Caloric and fat intake measured through 24-hour dietary recall. Generalized linear models with interaction term between survey cycle and statin use were constructed to investigate the time trends of dietary intake for statin users and nonusers after adjustment for possible confounders. We calculated model-adjusted caloric and fat intake using these models and examined if the time trends differed by statin use. Body mass index (BMI) changes were also compared between statin users and nonusers.

RESULTS In the 1999-2000 period, the caloric intake was significantly less for statin users compared with nonusers (2000 vs 2179 kcal/d; $P = .007$). The difference between the groups became smaller as time went by, and there was no statistical difference after the 2005-2006 period. Among statin users, caloric intake in the 2009-2010 period was 9.6% higher (95% CI, 1.8-18.1; $P = .02$) than that in the 1999-2000 period. In contrast, no significant change was observed among nonusers during the same study period. Statin users also consumed significantly less fat in the 1999-2000 period (71.7 vs 81.2 g/d; $P = .003$). Fat intake increased 14.4% among statin users (95% CI, 3.8-26.1; $P = .007$) while not changing significantly among nonusers. Also, BMI increased more among statin users (+1.3) than among nonusers (+0.4) in the adjusted model ($P = .02$).

CONCLUSIONS AND RELEVANCE Caloric and fat intake have increased among statin users over time, which was not true for nonusers. The increase in BMI was faster for statin users than for nonusers. Efforts aimed at dietary control among statin users may be becoming less intensive. The importance of dietary composition may need to be reemphasized for statin users.

Editor's Note page 1046

Supplemental content at jamainternalmedicine.com

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Table 3. Model-Adjusted[a] Relative Changes in Caloric and Fat Intake Among US Adults by Statin Use, 1999-2010

Characteristic	Change From 1999-2000 to 2009-2010, % (95% CI)		*P* Value for Difference in Trends[b]
	Statin User	Statin Nonuser	
Caloric Intake			
1999-2000	0 [Reference]	0 [Reference]	.001
2001-2002	1.7 (−5.6 to 9.5)	0.8 (−2.0 to 3.6)	
2003-2004	6.0 (−1.2 to 13.7)	1.7 (−1.0 to 4.5)	
2005-2006	7.1 (0.2 to 14.8)	0.1 (−3.2 to 3.6)	
2007-2008	4.4 (−3.4 to 12.8)	−2.0 (−5.2 to 1.3)	
2009-2010	9.6 (1.8 to 18.1)	−1.9 (−4.6 to 0.9)	
Fat Intake			
1999-2000	0 [Reference]	0 [Reference]	<.001
2001-2002	2.8 (−6.9 to 13.6)	1.8 (−1.4 to 5.1)	
2003-2004	10.9 (−0.1 to 23.0)	3.8 (0.5 to 7.2)	
2005-2006	14.2 (3.9 to 25.4)	2.5 (−1.8 to 6.9)	
2007-2008	12.1 (1.6 to 23.6)	−0.2 (−4.0 to 3.8)	
2009-2010	14.4 (3.8 to 26.1)	−2.3 (−5.6 to 1.1)	

[a] Adjusted for age category, sex, race and ethnicity, educational attainment, and diabetes diagnosis.

[b] Significance of interaction terms between survey cycle (continuous) and statin use (binary).

Original Investigation

Statins and Physical Activity in Older Men
The Osteoporotic Fractures in Men Study

David S. H. Lee, PharmD, PhD; Sheila Markwardt, BS; Leah Goeres, PharmD; Christine G. Lee, MD; Elizabeth Eckstrom, MD, MPH; Craig Williams, PharmD; Rongwei Fu, PhD; Eric Orwoll, MD; Peggy M. Cawthon, PhD; Marcia L. Stefanick, PhD; Dawn Mackey, PhD; Douglas C. Bauer, MD; Carrie M. Nielson, PhD

IMPORTANCE Muscle pain, fatigue, and weakness are common adverse effects of statin medications and may decrease physical activity in older men.

OBJECTIVE To determine whether statin use is associated with physical activity, longitudinally and cross-sectionally.

DESIGN, SETTING, AND PARTICIPANTS Men participating in the Osteoporotic Fractures in Men Study (N = 5994), a multicenter prospective cohort study of community-living men 65 years and older, enrolled between March 2000 and April 2002. Follow-up was conducted through 2009.

EXPOSURES Statin use as determined by an inventory of medications (taken within the last 30 days). In cross-sectional analyses (n = 4137), statin use categories were users and nonusers. In longitudinal analyses (n = 3039), categories were prevalent users (baseline use and throughout the study), new users (initiated use during the study), and nonusers (never used).

MAIN OUTCOMES AND MEASURES Self-reported physical activity at baseline and 2 follow-up visits using the Physical Activity Scale for the Elderly (PASE). At the third visit, an accelerometer measured metabolic equivalents (METs [kilocalories per kilogram per hour]) and minutes of moderate activity (METs ≥3.0), vigorous activity (METs ≥6.0), and sedentary behavior (METs ≤1.5).

RESULTS At baseline, 989 men (24%) were users and 3148 (76%) were nonusers. The adjusted difference in baseline PASE between users and nonusers was −5.8 points (95% CI, −10.9 to −0.7 points). A total of 3039 men met the inclusion criteria for longitudinal analysis: 727 (24%) prevalent users, 845 (28%) new users, and 1467 (48%) nonusers. PASE score declined by a mean (95% CI) of 2.5 (2.0 to 3.0) points per year for nonusers and 2.8 (2.1 to 3.5) points per year for prevalent users, a nonstatistical difference (0.3 [−0.5 to 1.0] points). For new users, annual PASE score declined at a faster rate than nonusers (difference of 0.9 [95% CI, 0.1 to 1.7] points). A total of 3071 men had adequate accelerometry data, 1542 (50%) were statin users. Statin users expended less METs (0.03 [95% CI, 0.02-0.04] METs less) and engaged in less moderate physical activity (5.4 [95% CI, 1.9-8.8] fewer minutes per day), less vigorous activity (0.6 [95% CI, 0.1-1.1] fewer minutes per day), and more sedentary behavior (7.6 [95% CI, 2.6-12.4] greater minutes per day).

CONCLUSIONS AND RELEVANCE Statin use was associated with modestly lower physical activity among community-living men, even after accounting for medical history and other potentially confounding factors. The clinical significance of these findings deserves further investigation.

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Invited Commentary

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FOCUS ISSUE: CARDIOMETABOLIC RISK

Statin Treatment

Simvastatin Impairs Exercise Training Adaptations

Catherine R. Mikus, PhD,* Leryn J. Boyle, MSc,† Sarah J. Borengasser, PhD,‡ Douglas J. Oberlin, MSc,† Scott P. Naples, MSc,† Justin Fletcher, MSc,† Grace M. Meers, BSc,§ Meghan Ruebel, MA,‖ M. Harold Laughlin, PhD,¶ Kevin C. Dellsperger, MD, PhD,§ Paul J. Fadel, PhD,# John P. Thyfault, PhD†‡**

Durham, North Carolina; Columbia, Missouri; and Little Rock, Arkansas

Objectives This study sought to determine if simvastatin impairs exercise training adaptations.

Background Statins are commonly prescribed in combination with therapeutic lifestyle changes, including exercise, to reduce cardiovascular disease risk in patients with metabolic syndrome. Statin use has been linked to skeletal muscle myopathy and impaired mitochondrial function, but it is unclear whether statin use alters adaptations to exercise training.

Methods This study examined the effects of simvastatin on changes in cardiorespiratory fitness and skeletal muscle mitochondrial content in response to aerobic exercise training. Sedentary overweight or obese adults with at least 2 metabolic syndrome risk factors (defined according to National Cholesterol Education Panel Adult Treatment Panel III criteria) were randomized to 12 weeks of aerobic exercise training or to exercise in combination with simvastatin (40 mg/day). The primary outcomes were cardiorespiratory fitness and skeletal muscle (vastus lateralis) mitochondrial content (citrate synthase enzyme activity).

Results Thirty-seven participants (exercise plus statins: $n = 18$; exercise only: $n = 19$) completed the study. Cardiorespiratory fitness increased by 10% ($p < 0.05$) in response to exercise training alone, but was blunted by the addition of simvastatin resulting in only a 1.5% increase ($p < 0.005$ for group by time interaction). Similarly, skeletal muscle citrate synthase activity increased by 13% in the exercise-only group ($p < 0.05$), but decreased by 4.5% in the simvastatin-plus-exercise group ($p < 0.05$ for group-by-time interaction).

Conclusions Simvastatin attenuates increases in cardiorespiratory fitness and skeletal muscle mitochondrial content when combined with exercise training in overweight or obese patients at risk of the metabolic syndrome. (Exercise, Statins, and the Metabolic Syndrome; NCT01700530) (J Am Coll Cardiol 2013;62:709–14) © 2013 by the American College of Cardiology Foundation

MJ

JACC Vol. 62, No. 8, 2013
August 20, 2013:709–14

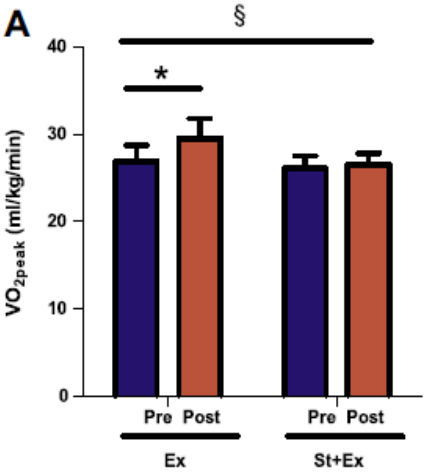


Figure 1 Cardiorespiratory Fitness

(A) Peak oxygen consumption (Vo_2peak) before (Pre) and after (Post) 12 weeks of supervised aerobic exercise training (Ex) or combination exercise-plus-statin therapy (St+Ex). **(B)** Vo_2peak presented as within-group change (Δ) from baseline. Data are expressed as mean ± SE. *$p < 0.005$ for within-group change from baseline. §$p < 0.005$ for between-group difference in change from baseline.

MJ

had any problems taking the medication. In addition, cholesterol was uniformly lowered in the statin group providing evidence that mediation adherence was more than adequate.

Effects of intervention on anthropometric outcomes. At 12 weeks, body weight decreased significantly in the exercise group ($p < 0.01$ for change within group) but not the exercise-plus-statin group ($p < 0.01$ for between-group difference in change from baseline) (Table 1). Similarly, there was a significant decrease in fat mass in the exercise group ($p < 0.05$). In the exercise-plus-statin group, the decrease in fat mass approached significance ($p = 0.056$). Lean body mass increased significantly in the exercise-plus-statin group only ($p < 0.05$ for with-in group change from baseline; $p < 0.05$ for difference in between-group change from baseline). BMI was not changed in either group.

Effects of intervention on lipid profiles. Lipid profiles are shown in Table 1. Total cholesterol decreased by 29% ($p < 0.001$ for within-group change from baseline), and LDL-C decreased by 38% ($p < 0.001$) in the exercise-plus-statin group. There were no significant changes in total cholesterol or LDL-C in the exercise group ($p < 0.001$ for between-group differences in change from baseline). High-density lipoprotein cholesterol did not change significantly in either group.

Effects of intervention on cardiorespiratory fitness. Simvastatin significantly attenuated increases in cardiorespiratory fitness (Vo_2peak, expressed as milliliters of oxygen consumed per kilogram of body weight per minute), in response to the exercise training program ($p < 0.005$ for between-group difference in change from baseline) (Fig. 1A). Cardiorespiratory fitness, increased by 10% in response to exercise training alone ($p < 0.005$ for change from baseline) but did not increase significantly in the group assigned to combined exercise-plus-statin therapy (Fig. 1B).


INESSS
LE SAVOIR PREND FORME
JUIN 2017
AVIS
Statines, hypolipémiants et diminution du risque cardiovasculaire
Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)
Québec

avec hypertension.

Tableau 4 NST et NST ajusté selon la persistance à une statine pendant 5 ans en prévention primaire pour prévenir un premier événement coronarien, mortel et non mortel, calculés par l'INESSS

Événement coronarien fatal ou non par catégorie de risque CV	Taux incidence MCC Témoins (N/p-a)	Rapport de cote[1]	NST[2] Eq. 5-ans[3]	Persistance[4] au traitement	NST ajusté selon la persistance[5] Eq. 5-ans[3]
Hypercholestérolémie sans comorbidité CV	0,0037 215/57576	0,54 (0,43-0,68)	117 (94 - 167)	81 % (moyenne pondérée)	146 (117 - 211)
Hypercholestérolémie avec comorbidités CV	0,0144 358/24868	0,70 (0,60-0,82)	46 (34 - 78)	74 % (moyenne pondérée)	53 (39 - 88)

CV = cardiovasculaire; NST = nombre de sujets à traiter; NS : résultats statistiquement non significatifs; p-a : personne-année.

[1] Les rapports de cote et les intervalles de confiance à 95 % proviennent de la table méta-analyse

[2] NST calculé selon la formule: (1 / [Taux d'incidence chez les témoins – (taux d'incidence chez les témoins x rapport de cote)]) / 5

[3] NST et NST ajusté selon la persistance ajustés pour un équivalent 5 ans (durée médiane de suivi pour toutes les études).

[4] Persistance moyenne au traitement par statine déclarée dans les études, pondérée par le nombre de personnes-années dans le sous-groupe.

[5] NST ajusté selon la persistance = NST x (% persistance au traitement/65 %).
Le 65 % est le taux de persistance moyen provenant d'une cohorte suivis de 2010 à 2015 via la base de données nationale de l'assurance médicaments du Québec [INESSS, 2017].

Association of Diet, Exercise, and Smoking Modification With Risk of Early Cardiovascular Events After Acute Coronary Syndromes

Clara K. Chow, MBBS, FRACP, PhD; Sanjit Jolly, MD, MSc, FRCPC;
Purnima Rao-Melacini, MSc; Keith A.A. Fox, BSc (Hons), MB, ChB, FRCP, FESC, FMedSci;
Sonia S. Anand, MD, PhD, FRCPc; Salim Yusuf, DPhil, FRCPC, FRSC

Background—Although preventive drug therapy is a priority after acute coronary syndrome, less is known about adherence to behavioral recommendations. The aim of this study was to examine the influence of adherence to behavioral recommendations in the short term on risk of cardiovascular events.

Methods and Results—The study population included 18 809 patients from 41 countries enrolled in the Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS) 5 randomized clinical trial. At the 30-day follow-up, patients

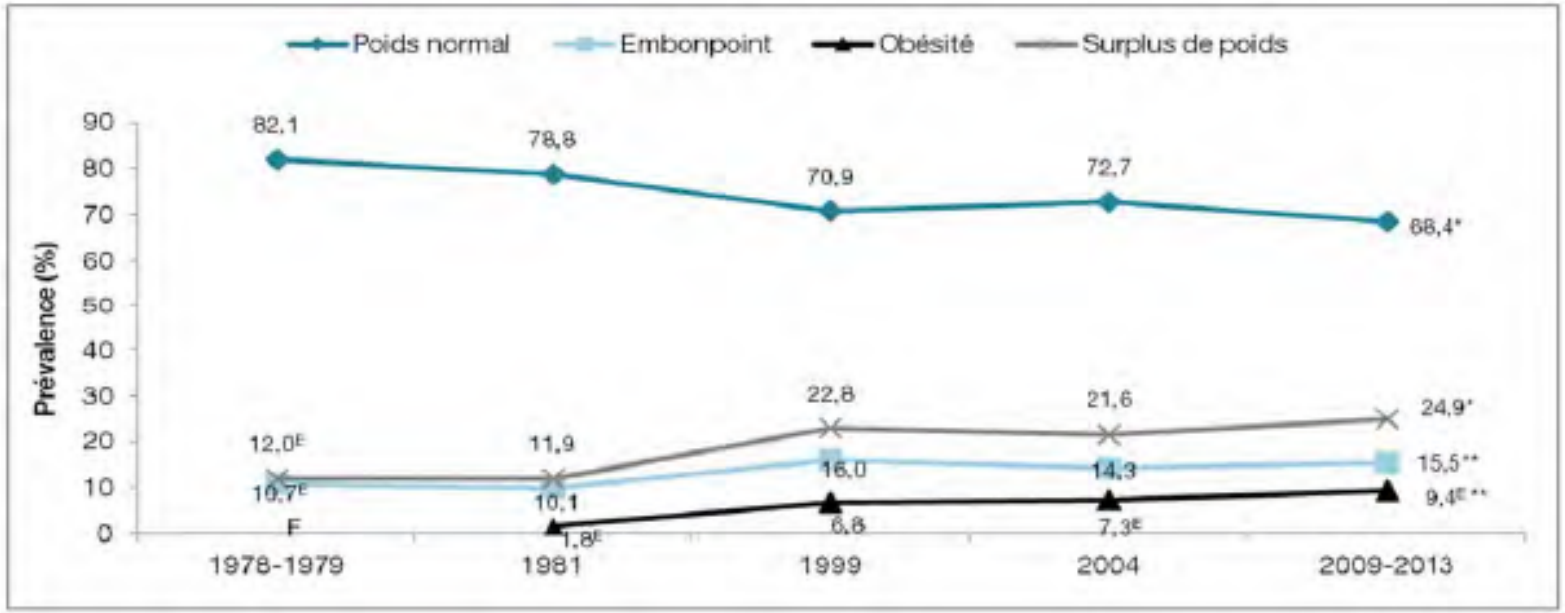
(*Circulation*. 2010;121:750-758.

Table 6. Relationship Between Diet/Exercise Modification and Repeat Cardiovascular Events in Patients With ACS

	Risk of MI		Risk of Stroke		Risk of Death		Risk of Death/MI/Stroke	
Category	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
No diet/exercise	Reference		Reference		Reference		Reference	
Diet only	0.93 (0.74–1.16)	0.5137	0.84 (0.54–1.31)	0.4357	0.91 (0.73–1.13)	0.3986	0.91 (0.77–1.07)	0.2605
Exercise only	0.78 (0.56–1.1)	0.1547	0.94 (0.52–1.68)	0.8256	0.61 (0.42–0.88)	0.0091	0.69 (0.54–0.89)	0.0037
Both diet and exercise	0.52 (0.40–0.69)	<0.0001	0.46 (0.26–0.82)	0.0079	0.45 (0.33–0.60)	<0.0001	0.46 (0.38–0.57)	<0.0001

Models were adjusted for age; sex; region; history of hypertension, diabetes, and prior MI; body mass index; creatinine; PCI/CABG before 30 days; and use of β-blockers, statins, antiplatelets, and ACE/ARB drugs at 30 days.

Figure 2 Statut pondéral chez les jeunes québécois âgés de 6 à 17 ans, Québec, 1978-1979, 1981[a], 1999[b], 2004 et 2009-2013



Source des données : Statistique Canada, fichiers maîtres de l'ESC 1978-1979, l'ESCC-2.2, 2004, l'ECMS cycles 2 et 3 fusionnés 2009-2013. Institut de la statistique du Québec, fichier maître de l'ESSEA – volet nutrition 1999. Fichier de microdonnées de l'ECPC 1981.
Analyses statistiques : INSPQ, 2015.

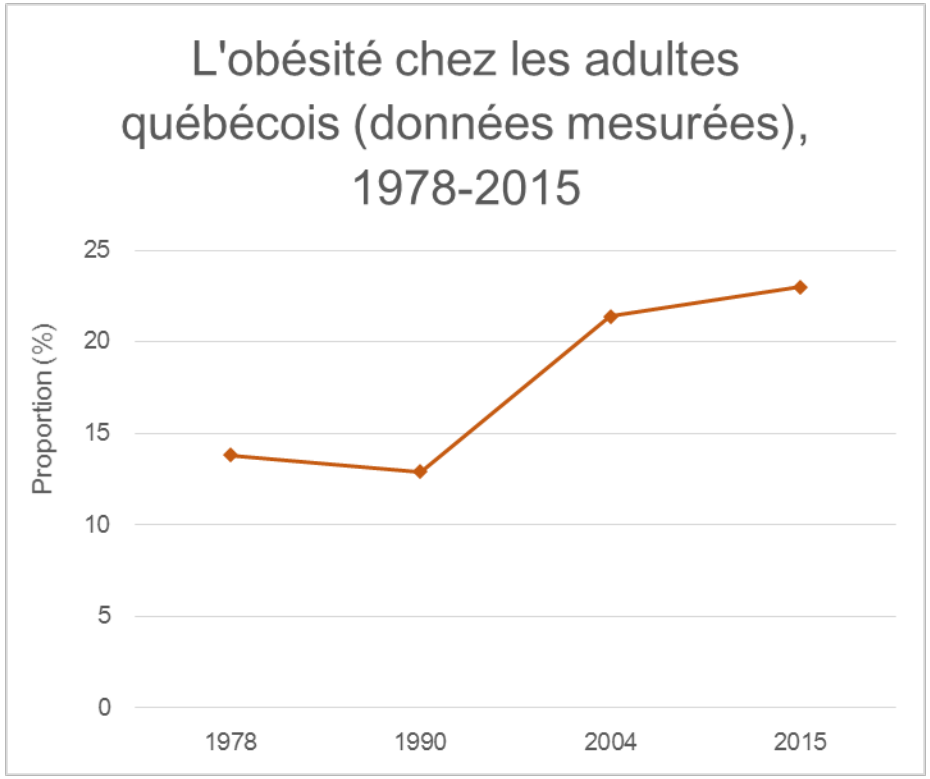
[a] La population ciblée dans l'ECPC de 1981 était les Canadiens de 7 à 69 ans, les résultats présentés sont représentatifs des jeunes québécois âgés de 7 à 17 ans en l'absence des 6-17 ans.

[b] La population ciblée dans l'ESSEA – volet nutrition de 1999 était les jeunes québécois âgés de 6 à 16 ans, les résultats présentés sont représentatifs des jeunes québécois âgés de 6 à 16 ans en l'absence des 6-17 ans.

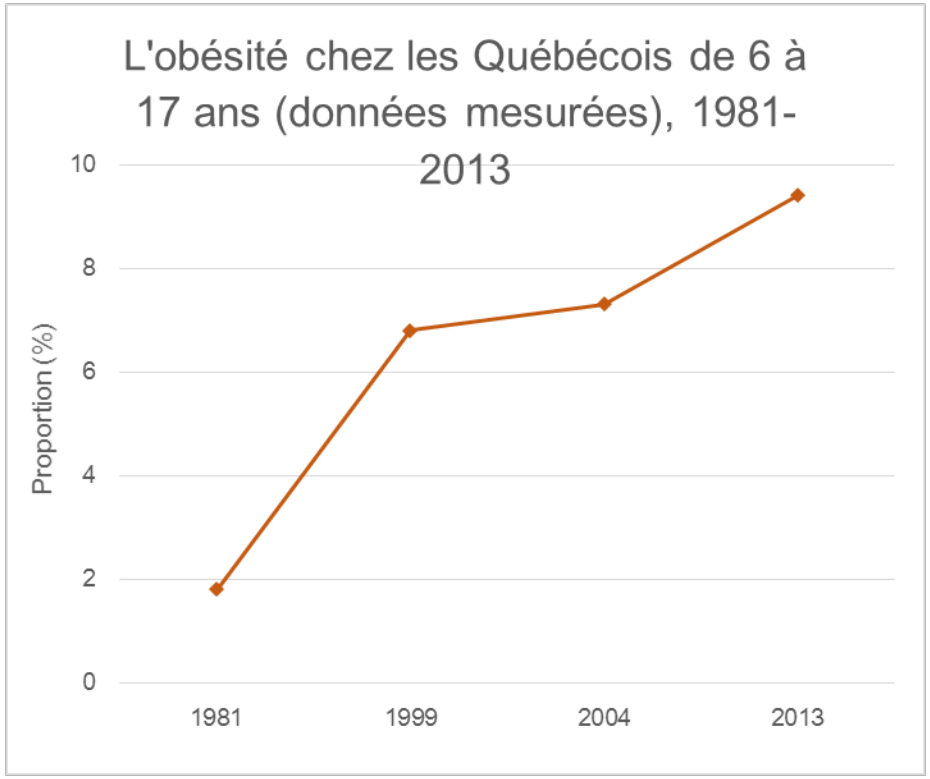
E CV compris entre 16,6 % et 33,3 % (interpréter avec prudence).

F CV supérieur à 33,3 % (donnée non diffusée).

* Valeur significativement différente de l'estimation de l'ESC 1978-1979. ** Valeur significativement différente de l'estimation de l'ECPC 1981 pour les 7-17 ans.



- **La montée de l'obésité au Québec**
- 1978:13,8% des adultes au Québec sont obèses
- 2015: 23% des adultes au Québec sont obèses



- **L'obésité augmente aussi chez les enfants et les adolescents**
- 1981: 1,8% des 6 à 17 ans au Québec sont obèses
- 2009-2013: 9,4% des 6 à 17 ans au Québec sont obèses

Original Investigation

Added Sugar Intake and Cardiovascular Diseases Mortality Among US Adults

Quanhe Yang, PhD; Zefeng Zhang, MD, PhD; Edward W. Gregg, PhD; W. Dana Flanders, MD, ScD; Robert Merritt, MA; Frank B. Hu, MD, PhD

IMPORTANCE Epidemiologic studies have suggested that higher intake of added sugar is associated with cardiovascular disease (CVD) risk factors. Few prospective studies have examined the association of added sugar intake with CVD mortality.

OBJECTIVE To examine time trends of added sugar consumption as percentage of daily calories in the United States and investigate the association of this consumption with CVD mortality.

DESIGN, SETTING, AND PARTICIPANTS National Health and Nutrition Examination Survey (NHANES, 1988-1994 [III], 1999-2004, and 2005-2010 [n = 31 147]) for the time trend analysis and NHANES III Linked Mortality cohort (1988-2006 [n = 11 733]), a prospective cohort of a nationally representative sample of US adults for the association study.

Invited Commentary

Supplemental content at jamainternalmedicine.com

Table 3. Adjusted HR of CVD Mortality Comparing Percentage of Calories From Added Sugar Greater Than or Equal to 10% or 25% With Less Than 10%[a]

Characteristic	Midvalue of Usual Percentage of Calories From Added Sugar[b]			*P* Value[c]
	5.0%	17.5%	28.7%	
Range (0-100)/usual percentage, %	0 to <10.0	10.0 to <25.0	≥25.0	
HR (95% CI)				
Adjusted only for age, sex, race/ethnicity	1 [Ref]	1.39 (1.20 to 1.62)	3.55 (2.00 to 6.29)	<.001
Fully adjusted[d]	1 [Ref]	1.30 (1.09 to 1.55)	2.75 (1.40 to 5.42)	.004

Abbreviations: CVD, cardiovascular disease; HR, hazard ratio; Ref, reference.

calories from added sugar and CVD mortality based on the Satterthwaite

F test, all tests are 2 tailed.

JAMA Internal Medicine | Special Communication

Sugar Industry and Coronary Heart Disease Research
A Historical Analysis of Internal Industry Documents

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

Early warning signals of the coronary heart disease (CHD) risk of sugar (sucrose) emerged in the 1950s. We examined Sugar Research Foundation (SRF) internal documents, historical reports, and statements relevant to early debates about the dietary causes of CHD and assembled findings chronologically into a narrative case study. The SRF sponsored its first CHD research project in 1965, a literature review published in the *New England Journal of Medicine*, which singled out fat and cholesterol as the dietary causes of CHD and downplayed evidence that sucrose consumption was also a risk factor. The SRF set the review's objective, contributed articles for inclusion, and received drafts. The SRF's funding and role was not disclosed. Together with other recent analyses of sugar industry documents, our findings suggest the industry sponsored a research program in the 1960s and 1970s that successfully cast doubt about the hazards of sucrose while promoting fat as the dietary culprit in CHD. Policymaking committees should consider giving less weight to food industry–funded studies and include mechanistic and animal studies as well as studies appraising the effect of added sugars on multiple CHD biomarkers and disease development.

JAMA Intern Med. doi:10.1001/jamainternmed.2016.5394
Published online September 12, 2016.

Invited Commentary
Author Audio Interview
Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Stanton A. Glantz, PhD, UCSF Center for Tobacco Control Research and Education, 530 Parnassus Ave, Ste 366, San Francisco, CA 94143-1390 (glantz@medicine.ucsf.edu).

In the 1950s, disproportionately high rates of coronary heart disease (CHD) mortality in American men led to studies of the role of dietary factors, including cholesterol, phytosterols, excessive calories, amino acids, fats, carbohydrates, vitamins, and minerals in influencing CHD risk.[1] By the 1960s, 2 prominent physiologists were championing divergent causal hypotheses of CHD[2,3]: John Yudkin identified added sugars as the primary agent, while Ancel Keys identified total fat, saturated fat, and dietary cholesterol. However, by the 1980s, few scientists believed that added sugars played a significant role in CHD, and the first *1980 Dietary Guidelines for Americans*[4] focused on reducing total fat, saturated fat, and dietary cholesterol for CHD prevention.

Although the contribution of dietary sugars to CHD is still debated, what is clear is that the sugar industry, led by the Sugar Association, the sucrose industry's Washington, DC–based trade association,[5] steadfastly denies that there is a relationship between added sugar consumption and CVD risk.[6,7] This Special Communication uses internal sugar industry documents to describe how the industry sought to influence the scientific debate over the dietary causes of CHD in the 1950s and 1960s, a debate still reverberating in 2016.

Methods

The Sugar Association evolved from the Sugar Research Foundation (SRF), founded in 1943.[8] We located correspondence between the SRF and Roger Adams, a professor who served on the SRF's scientific advisory board (SAB) between 1959 and 1971, in the University of Illinois Archives[9] (319 documents totaling 1551 pages). We located correspondence between the SRF and D. Mark Hegsted, professor of nutrition at the Harvard School of Public Health and codirector of the SRF's first CHD research project from 1965 to 1966,[10] in the Harvard Medical Library[11] (27 documents totaling 31 pages).

We collected additional SRF materials through a WorldCat search including annual reports, symposium proceedings, and internal reviews of research. We reviewed historical reports and statements contextualizing scientific debates in the 1950s and 1960s on dietary factors causally related to CHD published by the National Academy of Sciences–National Research Council (NAS-NRC), US Public Health Service, the American Heart Association (AHA), and American Medical Association (AMA). Findings were assembled chronologically into a narrative case study.

Results

SRF's Interest in Promoting a Low-Fat Diet to Prevent CHD

Sugar Research Foundation president Henry Hass's 1954 speech, "What's New in Sugar Research,"[12] to the American Society of Sugar Beet Technologists identified a strategic opportunity for the sugar industry: increase sugar's market share by getting Americans to eat a lower-fat diet: "Leading nutritionists are pointing out the chemical connection between [American's] high-fat diet and the formation of cholesterol which partly plugs our arteries and capillaries, restricts the flow of blood, and causes high blood pressure and heart trouble... if you put [the middle-aged man] on a low-fat diet, it takes just five days for the blood cholesterol to get down to where it should be... If the carbohydrate industries were to recapture this 20

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Invited Commentary

HEALTH CARE POLICY AND LAW

Food Industry Funding of Nutrition Research

The Relevance of History for Current Debates

Marion Nestle, PhD, MPH

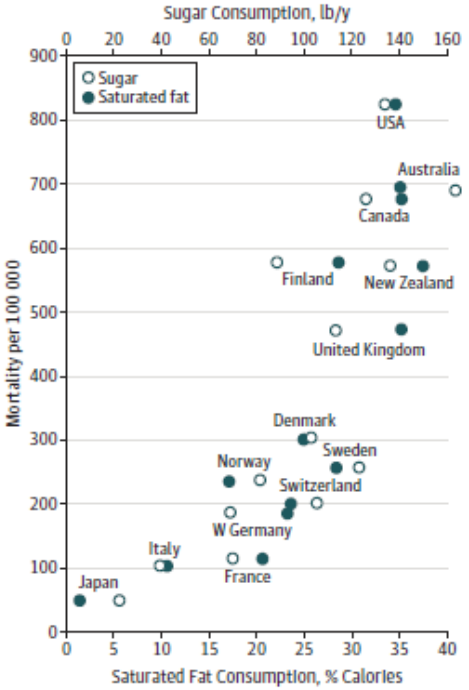
Industry-sponsored nutrition research, like that of research sponsored by the tobacco, chemical, and pharmaceutical industries, almost invariably produces results that confirm the benefits or lack of harm of the sponsor's products, even when independently sponsored research comes to opposite conclusions.[1] Although considerable evidence demonstrates that those industries deliberately influenced the design, results, and interpretation of the studies they paid for,[2] much less is known about the influence of food-company sponsorship on nutrition research. Typically, the disclosure statements of sponsored nutrition studies state that the funder had no role in their design, conduct, interpretation, writing, or publication. Without a "smoking gun" it is difficult to prove otherwise.

Author Audio Interview

Related article

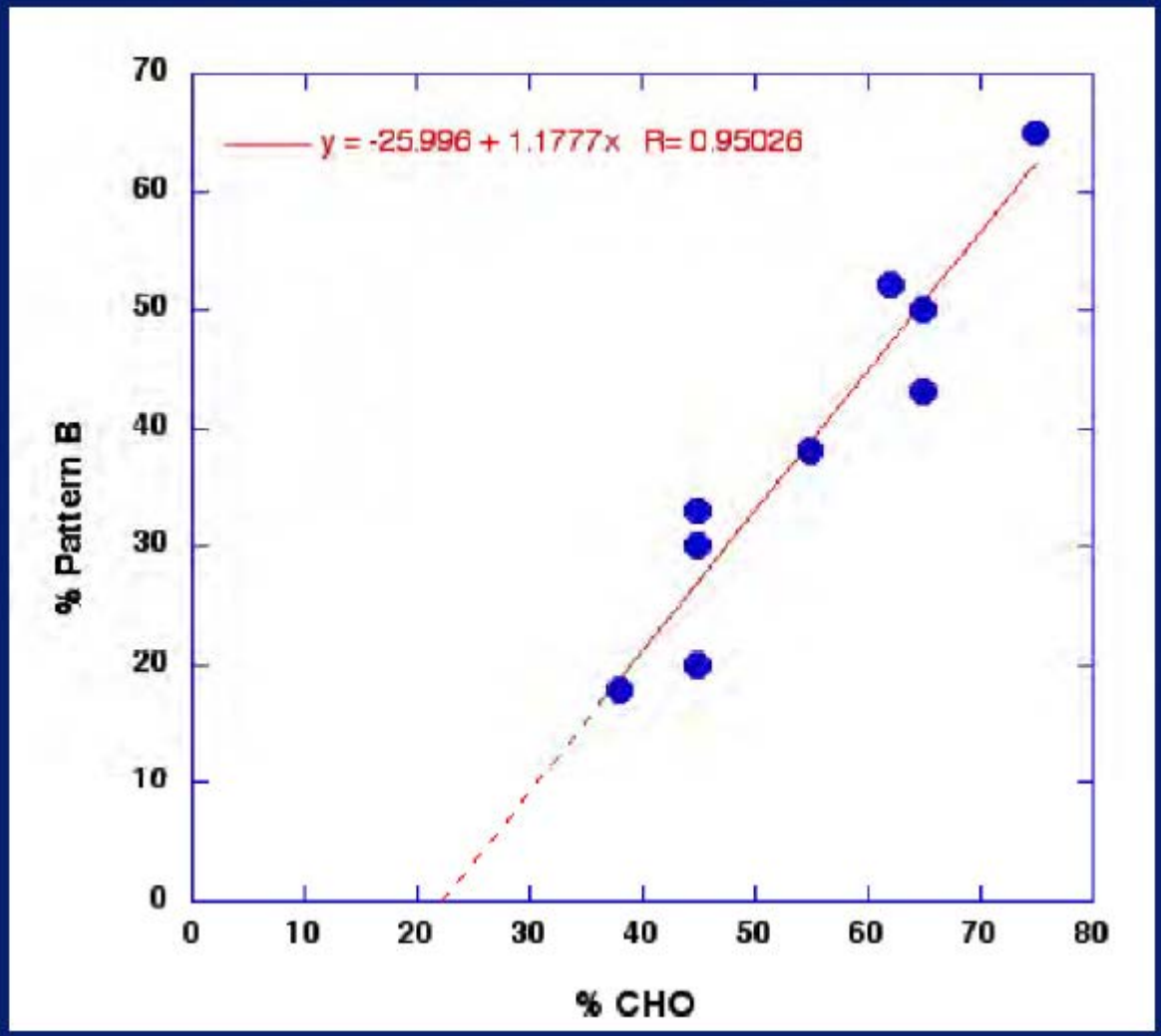
In this issue of *JAMA Internal Medicine*, Kearns and colleagues[3] report on having found a smoking gun. From a deep dive into archival documents from the 1950s and 1960s, they have produced compelling evidence that a sugar trade association not only paid for but also initiated and influenced research expressly to exonerate sugar as a major risk factor for coronary heart disease (CHD). Although studies at that time indicated a relationship between high-sugar diets and CHD risk, the sugar association preferred scientists and policymakers to focus on the role of dietary fat and cholesterol. The association paid the equivalent of more than $48 000 in today's dollars to 3 nutrition professors, at Harvard no less, to

Figure. Close Epidemiological Correlations Between Sugar and Saturated Fat "Consumption" and Mortality in 14 Countries



Adapted from the article by McGandy et al[4] and used with permission. Courtesy of Domingo Piñero, PhD.

LDL particle size is responsive to dietary CHO



Krauss, J Nutr 131:340S, 2001

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
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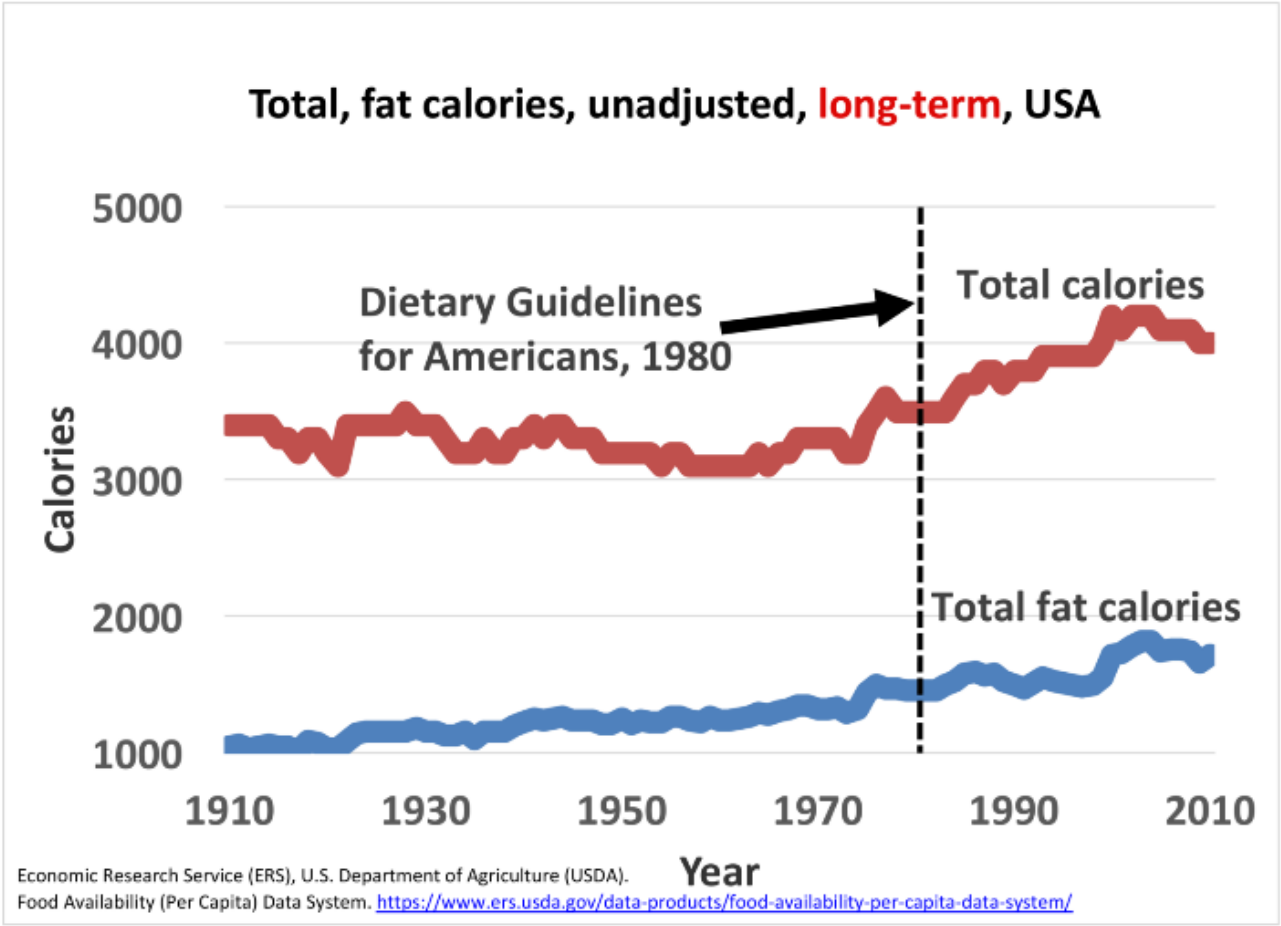
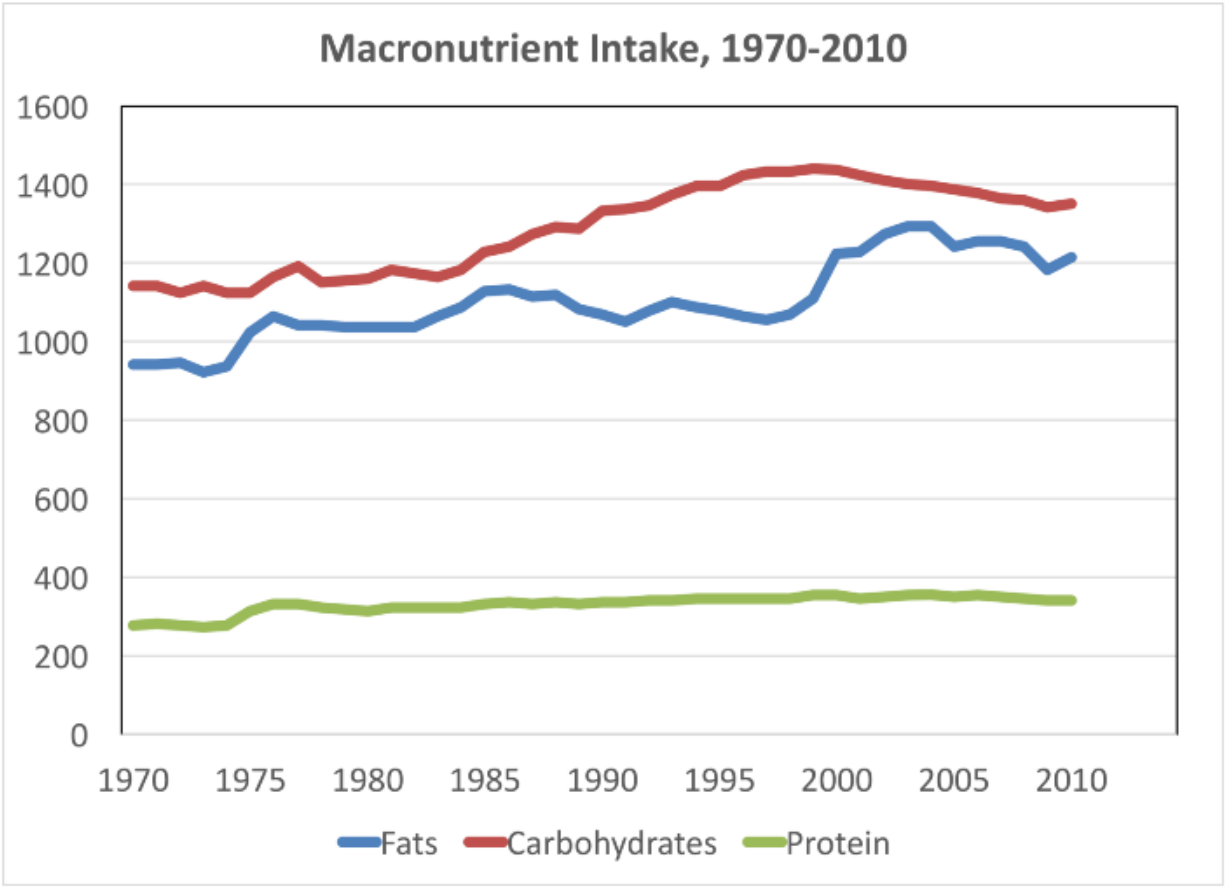
Dietary Sugars Intake and Cardiovascular Health: A Scientific Statement From the American Heart Association

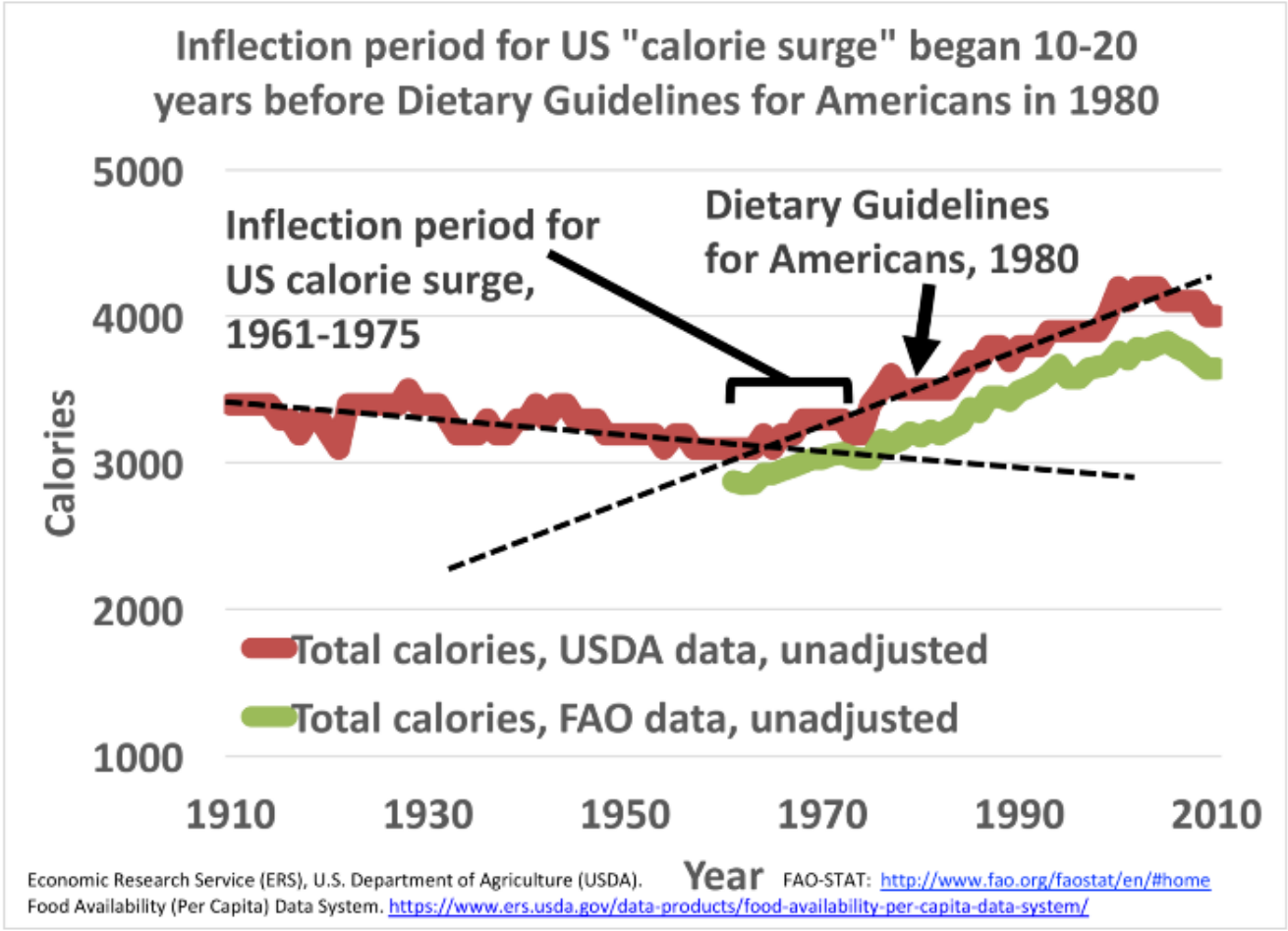
Rachel K. Johnson, Lawrence J. Appel, Michael Brands, Barbara V. Howard, Michael Lefevre, Robert H. Lustig, Frank Sacks, Lyn M. Steffen, Judith Wylie-Rosett and on behalf of the American Heart Association Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism and the Council on Epidemiology and Prevention

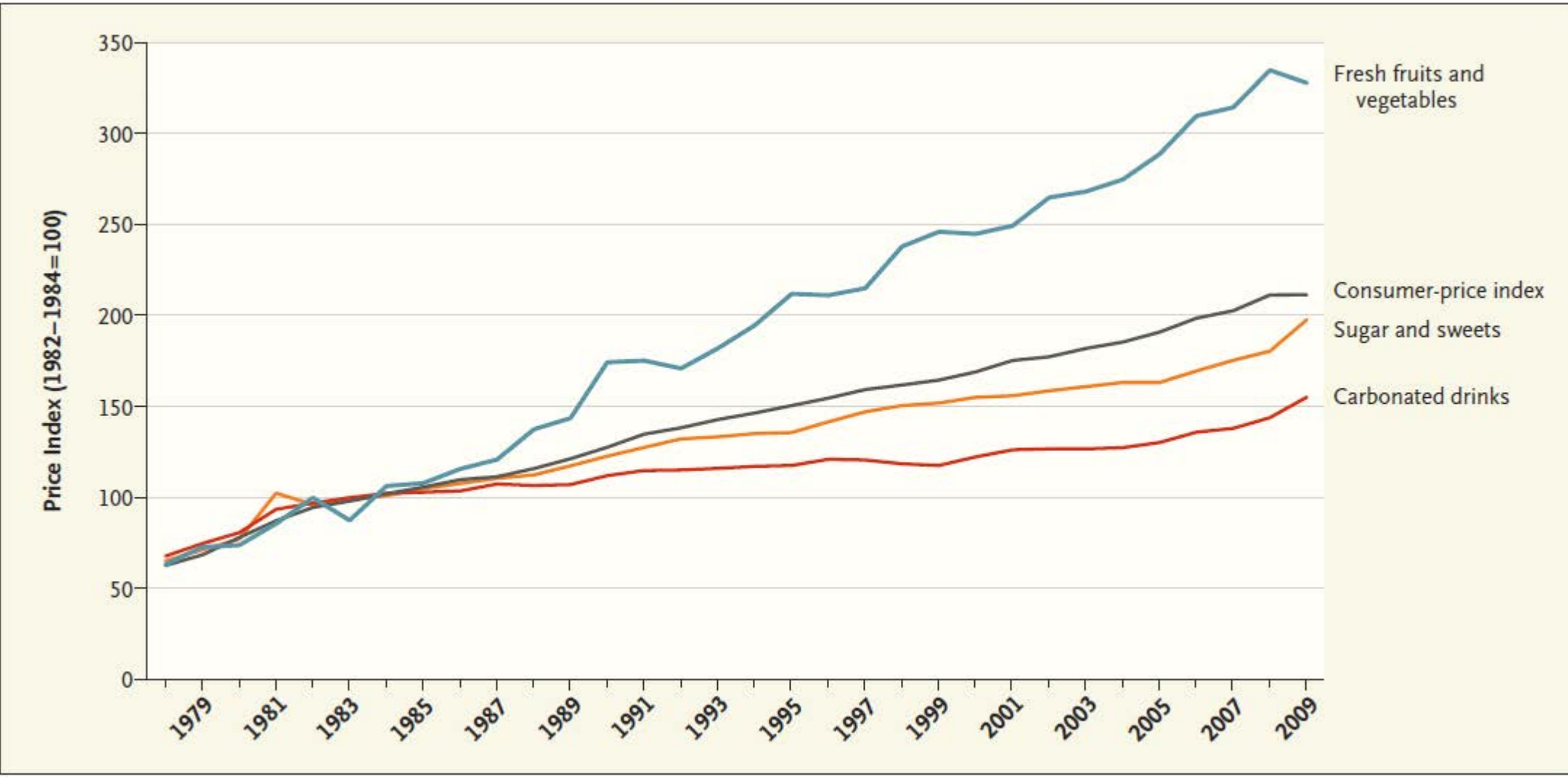
Circulation 2009;120;1011-1020; originally published online Aug 24, 2009;


Total, fat calories, unadjusted, long-term, USA
5000
4000
3000
2000
1000
Calories
Dietary Guidelines
for Americans, 1980
Total calories
Total fat calories
1910
1930
1950
1970
1990
2010
Year
Economic Research Service (ERS), U.S. Department of Agriculture (USDA).
Food Availability (Per Capita) Data System. https://www.ers.usda.gov/data-products/food-availability-per-capita-data-system/



Fat increasing, as carbohydrates decrease and obesity increases.


Inflection period for US "calorie surge" began 10-20 years before Dietary Guidelines for Americans in 1980
5000
4000
3000
2000
1000
Calories
Inflection period for US calorie surge, 1961-1975
Dietary Guidelines for Americans, 1980
Total calories, USDA data, unadjusted
Total calories, FAO data, unadjusted
1910
1930
1950
1970
1990
2010
Year
Economic Research Service (ERS), U.S. Department of Agriculture (USDA). Food Availability (Per Capita) Data System. https://www.ers.usda.gov/data-products/food-availability-per-capita-data-system/
FAO-STAT: http://www.fao.org/faostat/en/#home



Relative Price Changes for Fresh Fruits and Vegetables, Sugars and Sweets, and Carbonated Drinks, 1978–2009.

"There's no question that sedentary lifestyles have caused the obesity crisis to get out of control."

- Indra Nooyi, CEO PepsiCo

"active balanced lifestyle" Coca-Cola

"balanced active lifestyle"

"a balanced and healthy lifestyle" General Mills

"a balanced lifestyle" PEPSICO

"a balanced diet and lifestyle" Unilever

"a well-balanced lifestyle" MARS incorporated

"a balanced lifestyle" Nestlé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runjumpthrow
HERSHEY / Athletics Canada

Français

Athletics Canada Announces Expansion of Run Jump Throw Program through Partnership with The Hershey Company

Athletics Canada announced today a new five-year partnership with The Hershey Company that aims to get children excited about physical activity.

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Coca-Cola
Coca-Cola
Coca-Cola
386


CardioSmart
American College of Cardiology
Search
FOR CAREGIVERS
FOR CLINICIANS
FOR EMPLOYERS
Heart Conditions
Drugs & Treatments
Heart Basics
Healthy Living
Connect With Others
News & Events
My Dashboard
News & Events
Aug 09, 2013
Coca-Cola Family Field Day
Members of the CardioSmart team will be in Atlanta on Aug. 17 to help promote an active lifestyle and provide tips on heart health.
Aug 17, 2013, 8:00 AM - 1:00 PM
The World Of Coca-Cola at Pemberton Place: 121 Baker St NW, Atlanta, GA 30313
Coca-Cola family field day
+ Enlarge
CardioSmart is participating in Coca-Cola Family Field Day, which looks to inspire families and teens to rediscover the joy of being active to create long-term healthy habits. The day is filled with fun, light-hearted competition where teams of four complete six field day events striving for the best overall time to win an exciting grand prize. Events will be slightly challenging while also being humorous (there's a tricycle race!) Other activities during the field day include:
* Health & Wellness Expo where attendees can pick up heart healthy information and great CardioSmart giveaways
* Kids Zone
* Coca-Cola Open Happiness Truck
* Coca-Cola Recycling Truck
For more information and to register for the event, visit Coca-Cola's Family Field Day page.
Not a member?
Join CardioSmart Now
Earn CardioSmart Points
10 Points Per Day
Track Your Activity
Earn CardioSmart Points for logging your daily activity.
Calculate Your Heart Disease Risk
TXT
CardioSmart
PREVENT

- **La présence accrue de la restauration rapide**
- 1972: La première franchise McDonald ouvre au Québec
- 2014: Plus de 8000 établissements de restauration rapides au Québec
- Pour en savoir plus sur la restauration rapide et le gain de poids

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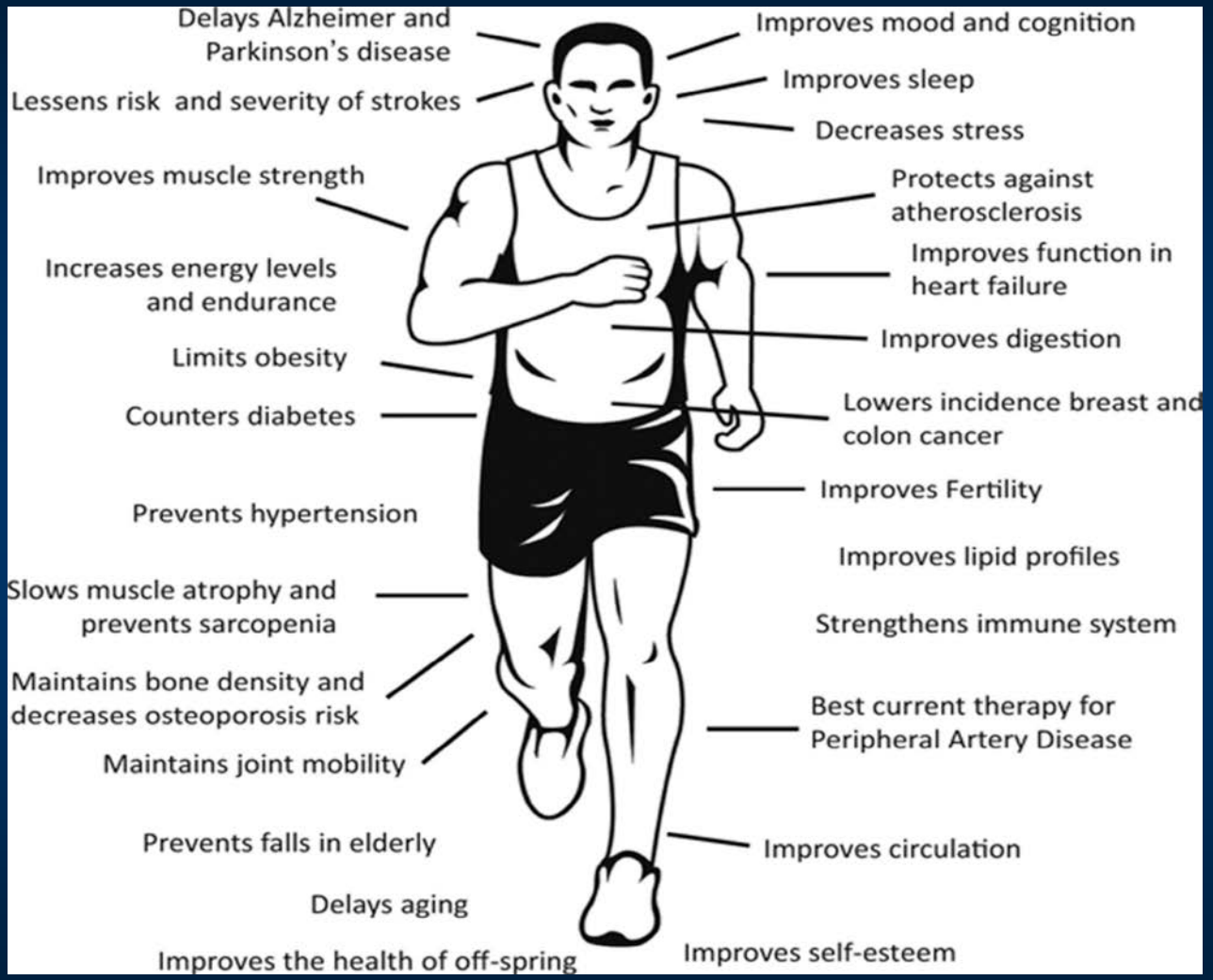
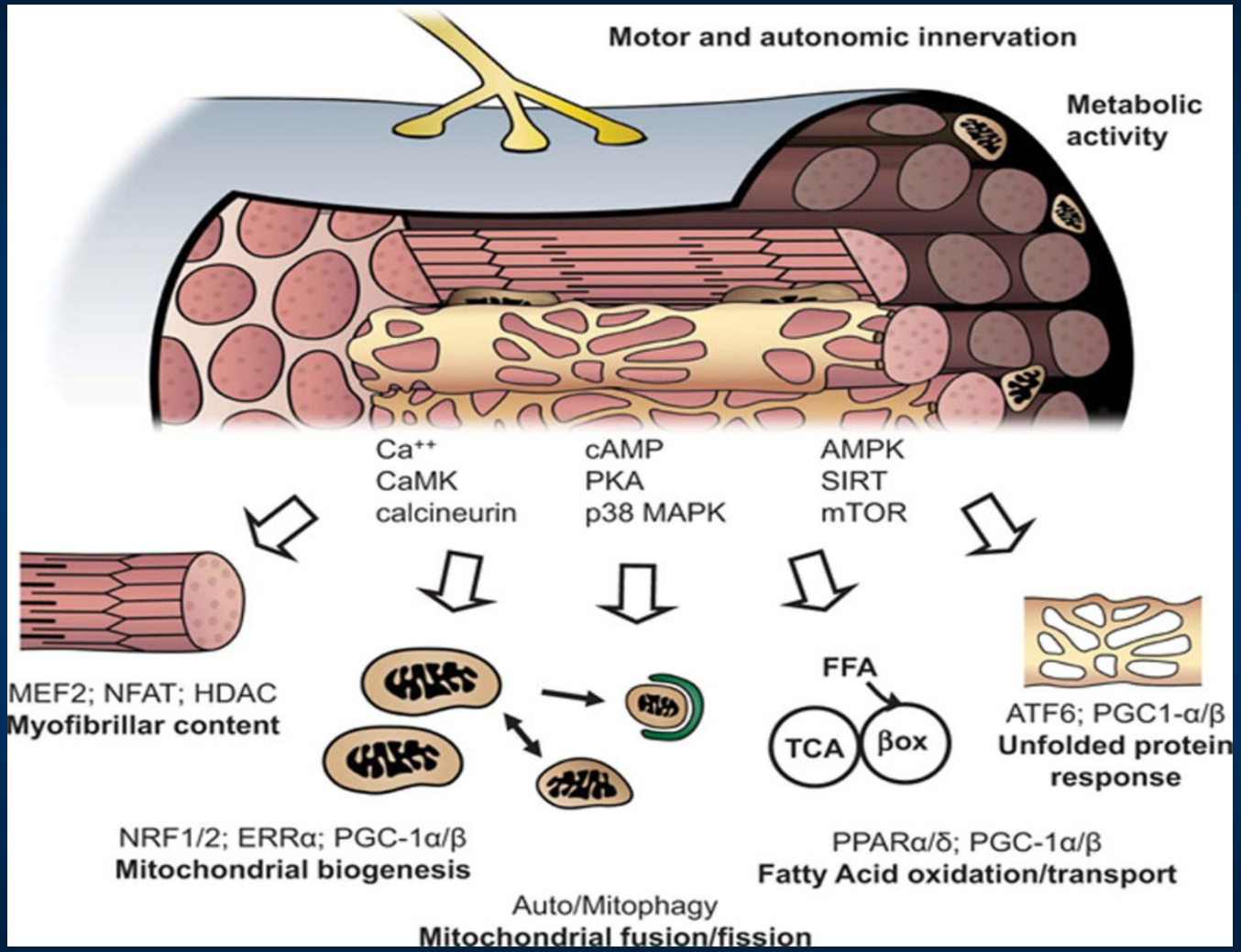
The many long-term benefits of regular endurance exercise.



Rowe G et al. Circulation 2014;129:798-810

MJ

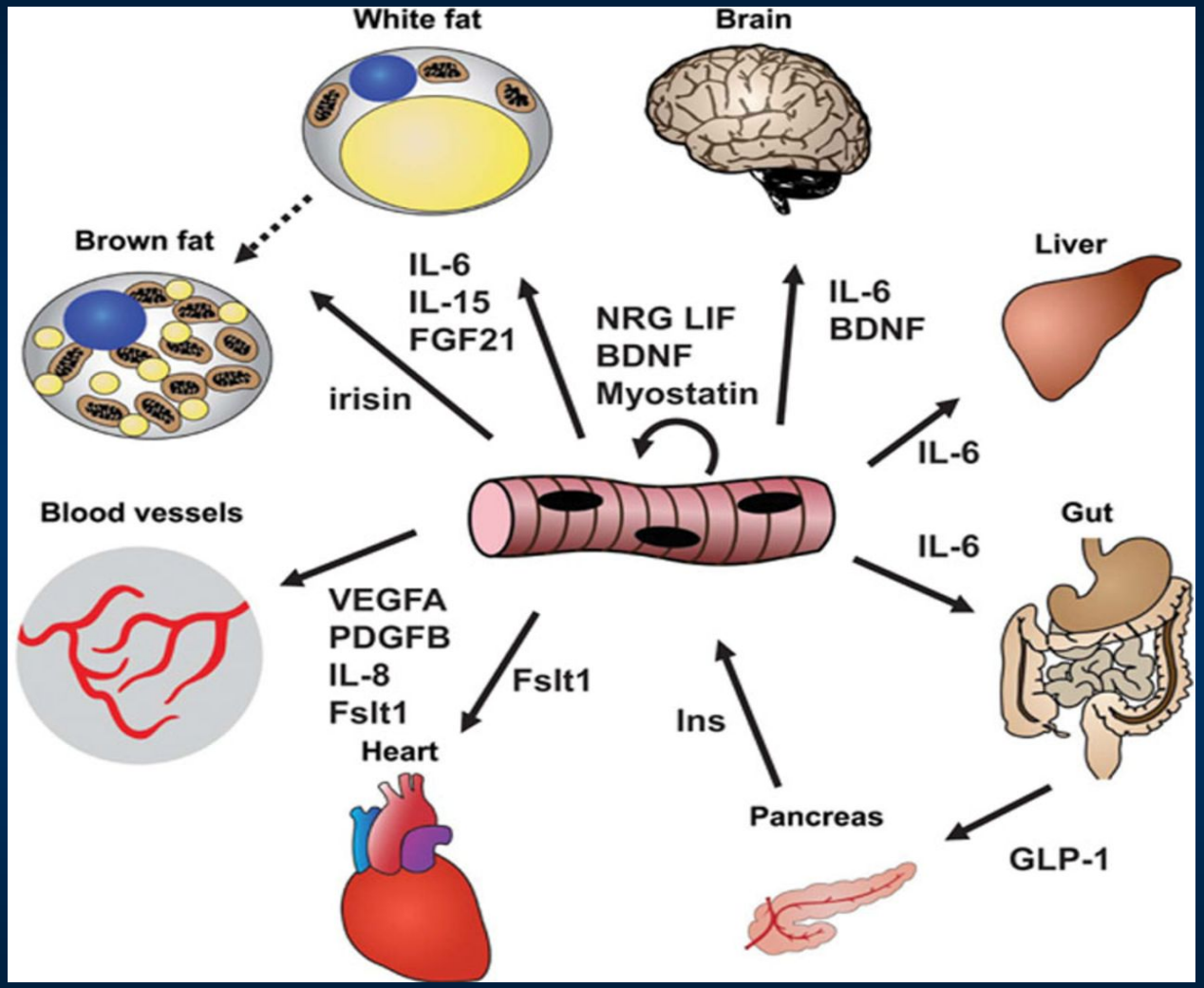
Modular signaling pathways that underpin muscular adaptations to endurance exercise.



Rowe G et al. Circulation 2014;129:798-810

MJ

Muscle as an endocrine organ.



Rowe G et al. Circulation 2014;129:798-810

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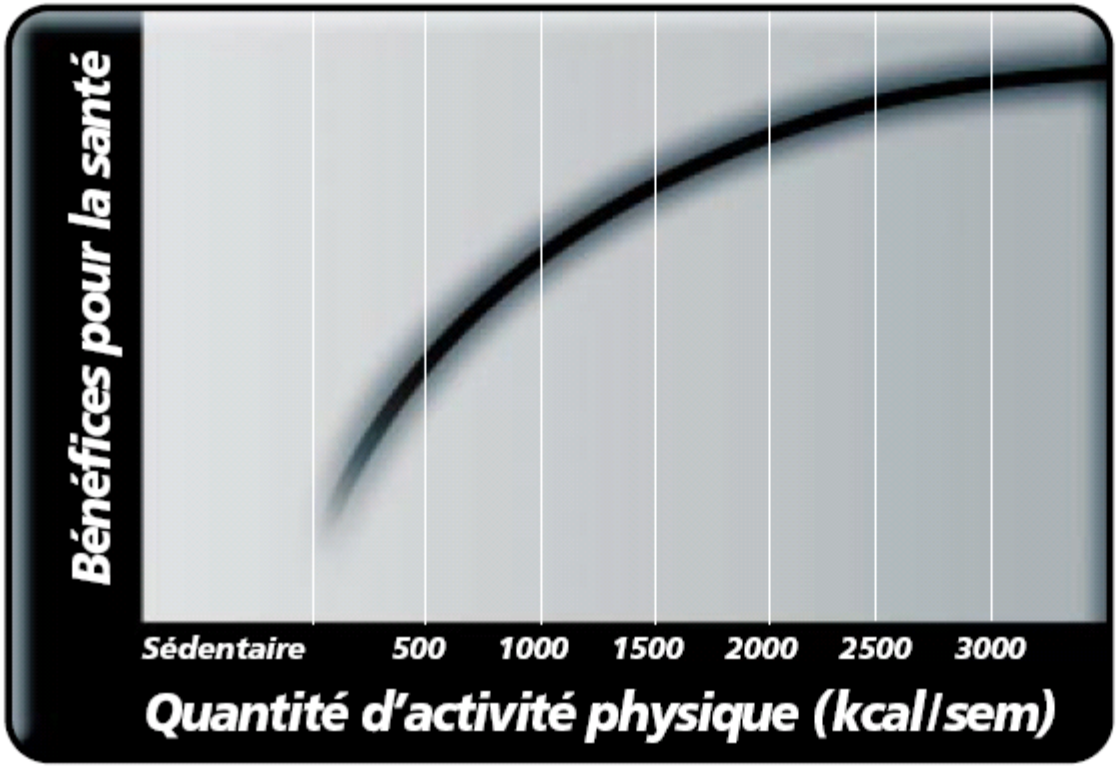
Figure II

Relation « quantité-bénéfices » illustrant le lien entre la dépense hebdomadaire d'énergie et les bénéfices attendus pour la santé chez les personnes sédentaires



Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study

Chi Pang Wen, Jackson Pui Man Wai*, Min Kuang Tsai, Yi Chen Yang, Ting Yuan David Cheng, Meng-Chih Lee, Hui Ting Chan, Chwen Keng Tsao, Shan Pou Tsai, Xifeng Wu*

Summary

Background The health benefits of leisure-time physical activity are well known, but whether less exercise than the recommended 150 min a week can have life expectancy benefits is unclear. We assessed the health benefits of a range of volumes of physical activity in a Taiwanese population.

Methods In this prospective cohort study, 416 175 individuals (199 265 men and 216 910 women) participated in a standard medical screening programme in Taiwan between 1996 and 2008, with an average follow-up of 8·05 years

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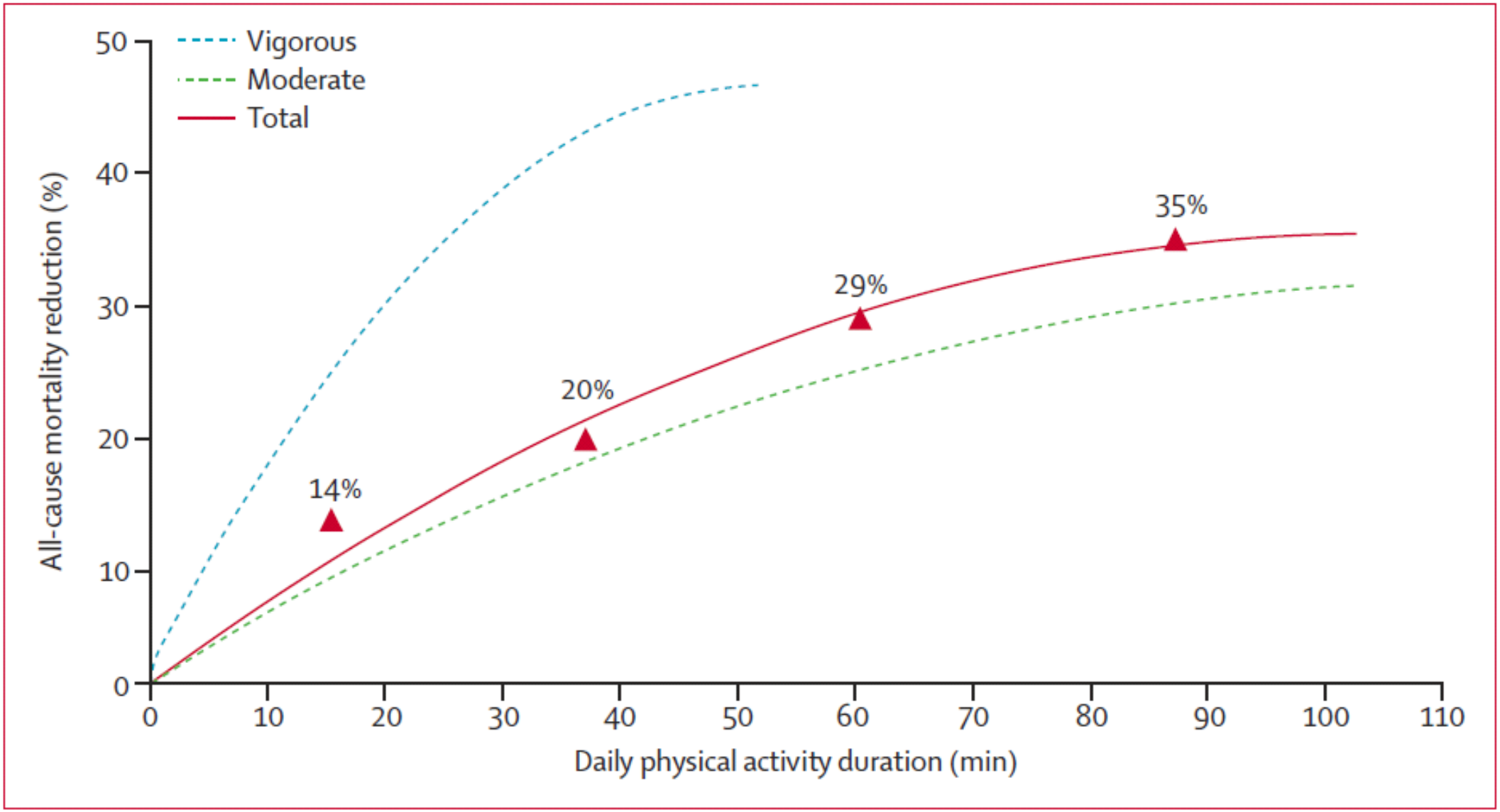
See Online/Comment DOI:10.1016/S0140-6736(11)61029-5


Vigorous
Moderate
Total
All-cause mortality reduction (%)
50
40
30
20
10
0
14%
20%
29%
35%
0
10
20
30
40
50
60
70
80
90
100
110
Daily physical activity duration (min)

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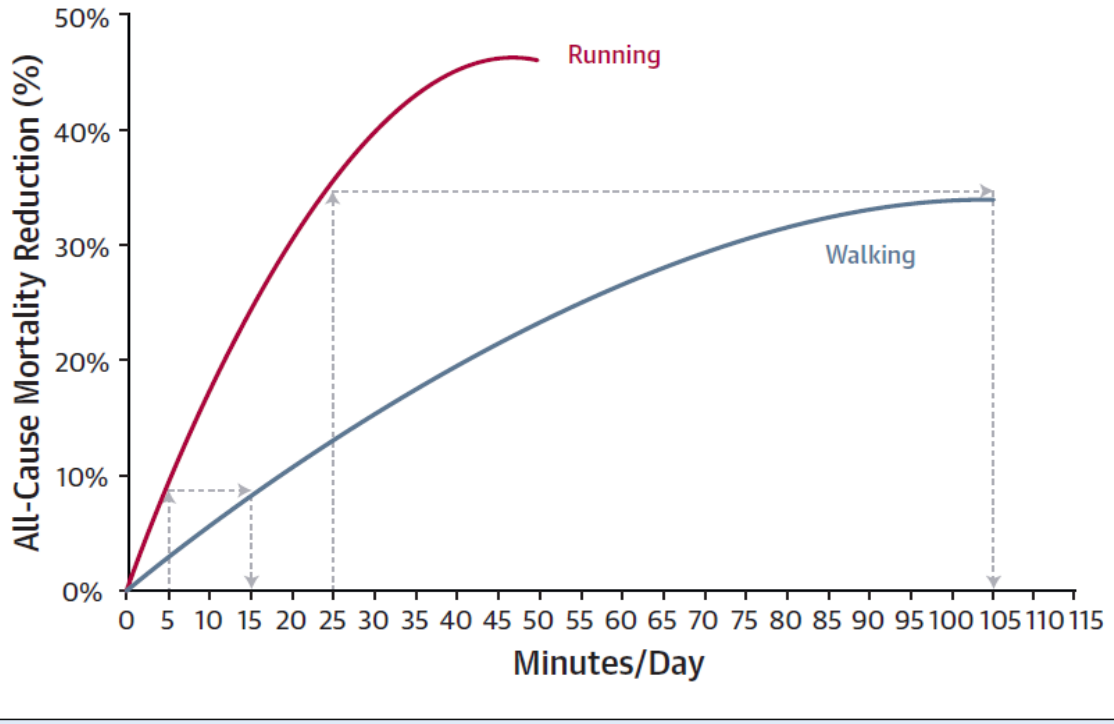

FIGURE 1 Comparison of Benefits Between Walking and Running

A 5-min run generates the same benefits as a 15-min walk, and a 25-min run is equivalent to a 105-min walk.

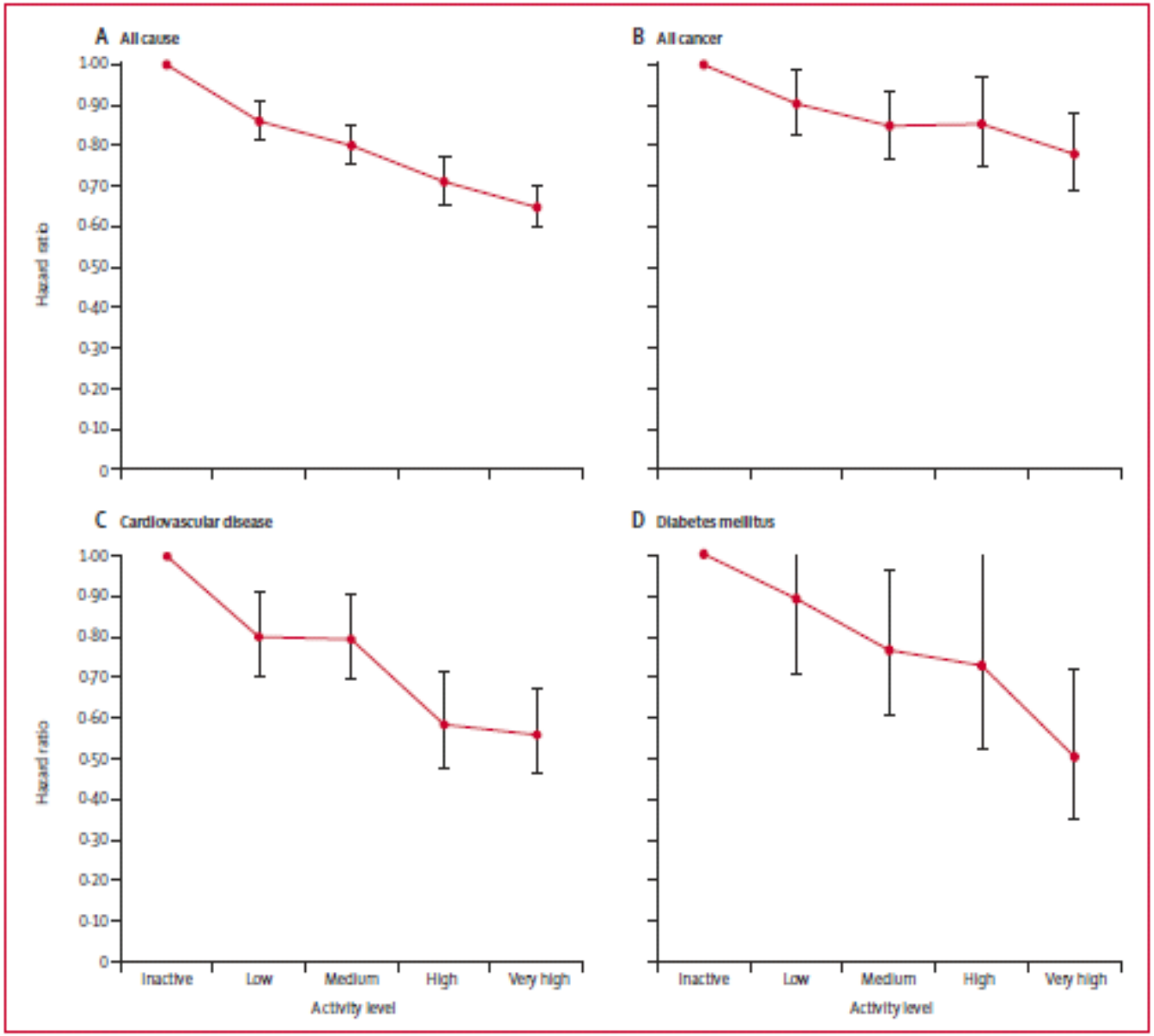

Figure 1: Relation between physical activity volume and mortality reduction compared with individuals in the inactive group
Bars show 95% CIs.

The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study

Scott A Lear, Weihong Hu, Sumathy Rangarajan, Danijela Gasevic, Darryl Leong, Romaina Iqbal, Amparo Casanova, Sumathi Swaminathan, R M Anjana, Rajesh Kumar, Annika Rosengren, Li Wei, Wang Yang, Wang Chuangshi, Liu Huaxing, Sanjeev Nair, Rafael Diaz, Hany Swidon, Rajeev Gupta, Noushin Mohammadifard, Patricio Lopez-Jaramillo, Aytekin Oguz, Katarzyna Zatonska, Pamela Seron, Alvaro Avezum, Paul Poirier, Koon Teo, Salim Yusuf

Summary

Background Physical activity has a protective effect against cardiovascular disease (CVD) in high-income countries, where physical activity is mainly recreational, but it is not known if this is also observed in lower-income countries, where physical activity is mainly non-recreational. We examined whether different amounts and types of physical activity are associated with lower mortality and CVD in countries at different economic levels.

Methods In this prospective cohort study, we recruited participants from 17 countries (Canada, Sweden, United Arab Emirates, Argentina, Brazil, Chile, Poland, Turkey, Malaysia, South Africa, China, Colombia, Iran, Bangladesh, India, Pakistan, and Zimbabwe). Within each country, urban and rural areas in and around selected cities and towns were identified to reflect the geographical diversity. Within these communities, we invited individuals aged between 35 and 70 years who intended to live at their current address for at least another 4 years. Total physical activity was assessed using the International Physical Activity Questionnaire (IPQA). Participants with pre-existing CVD were excluded from the analyses. Mortality and CVD were recorded during a mean of 6·9 years of follow-up. Primary clinical outcomes during follow-up were mortality plus major CVD (CVD mortality, incident myocardial infarction, stroke, or heart failure), either as a composite or separately. The effects of physical activity on mortality and CVD were adjusted for sociodemographic factors and other risk factors taking into account household, community, and country clustering.

Findings Between Jan 1, 2003, and Dec 31, 2010, 168916 participants were enrolled, of whom 141945 completed the IPAQ. Analyses were limited to the 130 843 participants without pre-existing CVD. Compared with low physical activity (<600 metabolic equivalents [MET]× minutes per week or <150 minutes per week of moderate intensity physical activity), moderate (600–3000 MET× minutes or 150–750 minutes per week) and high physical activity (>3000 MET× minutes or >750 minutes per week) were associated with graded reduction in mortality (hazard ratio 0·80, 95% CI 0·74–0·87 and 0·65, 0·60–0·71; p<0·0001 for trend), and major CVD (0·86, 0·78–0·93; p<0·001 for trend). Higher physical activity was associated with lower risk of CVD and mortality in high-income, middle-income, and low-income countries. The adjusted population attributable fraction for not meeting the physical activity guidelines was 8·0% for mortality and 4·6% for major CVD, and for not meeting high physical activity was 13·0% for mortality and 9·5% for major CVD. Both recreational and non-recreational physical activity were associated with benefits.

Interpretation Higher recreational and non-recreational physical activity was associated with a lower risk of mortality and CVD events in individuals from low-income, middle-income, and high-income countries. Increasing physical activity is a simple, widely applicable, low cost global strategy that could reduce deaths and CVD in middle age.

Funding Population Health Research Institute, the Canadian Institutes of Health Research, Heart and Stroke Foundation of Ontario, Ontario SPOR Support Unit, Ontario Ministry of Health and Long-Term Care, AstraZeneca, Sanofi-Aventis, Boehringer Ingelheim, Servier, GSK, Novartis, King Pharma, and national and local organisations in participating countries that are listed at the end of the Article.

Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide[1] and a major economic global burden.[2] Despite reductions in CVD mortality in high-income countries, global CVD mortality increased by 41% between 1990 and 2013, largely driven by rises in low-income and lower-middle-income countries.[3] Indeed, 70% of global CVD deaths come from low-income and middle-income countries, where it is the commonest cause of death.[4,5] 23% of the world's population is estimated to be insufficiently active[6] and WHO has recommended a decrease in insufficient physical activity of 10% (of the aforementioned 23%) by 2020.[7]

Many studies from high-income countries have reported significant inverse associations of physical activity with mortality and CVD morbidity,[8] but such data from low-

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Faculty of Health Sciences, Simon Fraser University, Burnaby and Division of Cardiology, Providence Health Care, Vancouver, BC, Canada (S A Lear PhD); Population Health Research Institute, Hamilton Health Sciences & McMaster University, Hamilton, ON, Canada (W Hu MSc, S Rangarajan MSc, D Leong PhD, A Casanova PhD, K Teo MB, S Yusuf DPhil); Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK (D Gasevic PhD); Department of Community Health Sciences and Medicine, Aga Khan University, Karachi, Pakistan (R Iqbal PhD); St John's Research Institute, St John's National Academy of Health Sciences, Bangalore, India (S Swaminathan PhD); Madras Diabetes Research Foundation, Chennai, India (R M Anjana PhD); School of Public Health, Postgraduate Institute of Medical Education & Research, Chandigarh, India (R Kumar MD); Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden (A Rosengren MD); Medical Research & Biometrics Center, National Center for Cardiovascular Diseases, Fu Wai Hospital, Beijing, China (L Wei PhD, W Yang MSc, W Chuangshi MM); Center for Disease Control & Prevention, Mengla County, Xishuangbanna Prefecture,

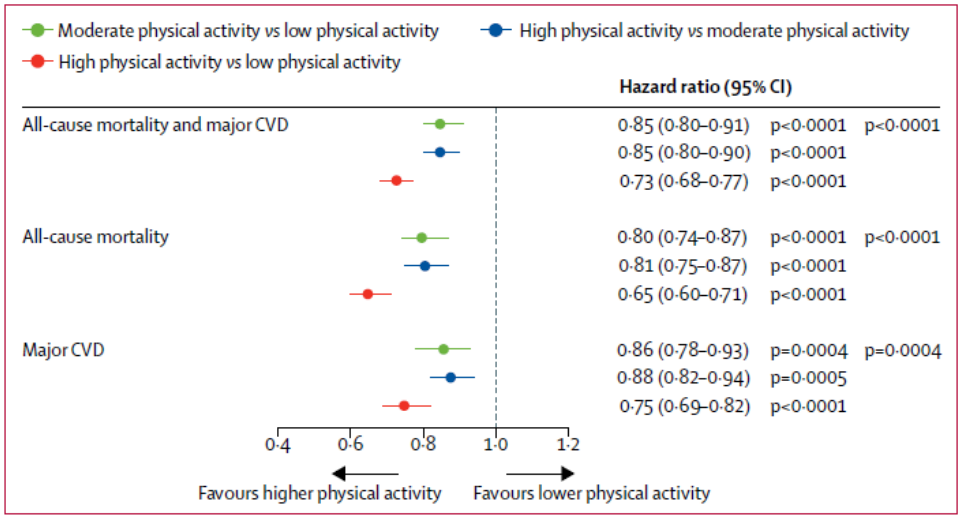


***Figure 1*: Hazard ratios and 95% CI for all-cause mortality and major CVD, all-cause mortality, or major CVD by level of physical activity**

Data adjusted for age, sex, education, country income level, urban or rural residency, family history of CVD, and smoking status; taking into account household, community, and country clustering. There were 3155 events for all-cause mortality and major CVD, 2041 events for all-cause mortality, and 1723 events for major CVD. The p values of the first column show the significance of each comparison. p values of the second column show the significance of the overall effect of physical activity. Low physical activity=<600 MET × min per week. Moderate physical activity=600–3000 MET × min per week. High physical activity=>3000 MET × min per week. CVD=cardiovascular disease. Major CVD=CVD mortality plus incident myocardial infarction, stroke, or heart failure. MET=metabolic equivalents.

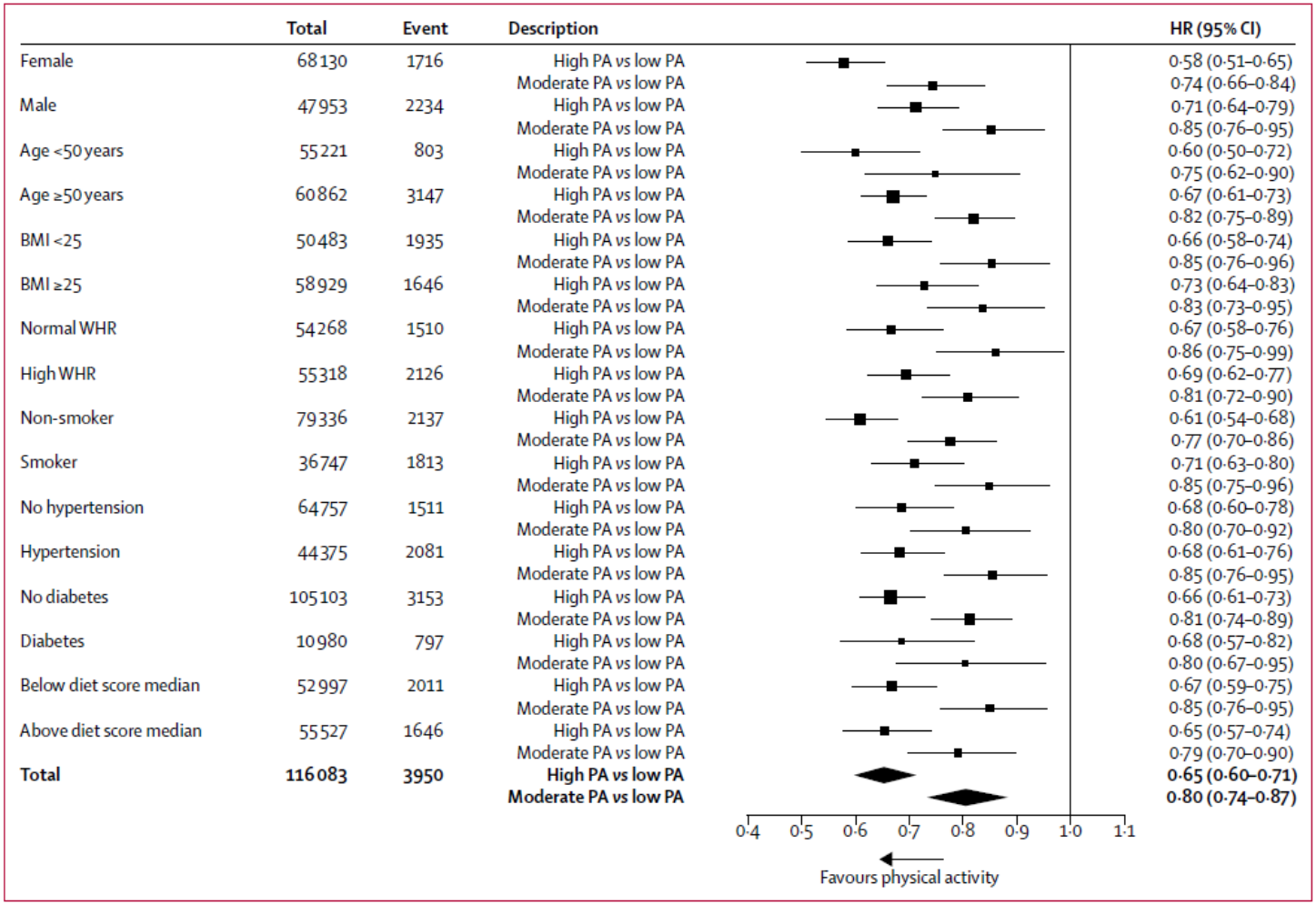
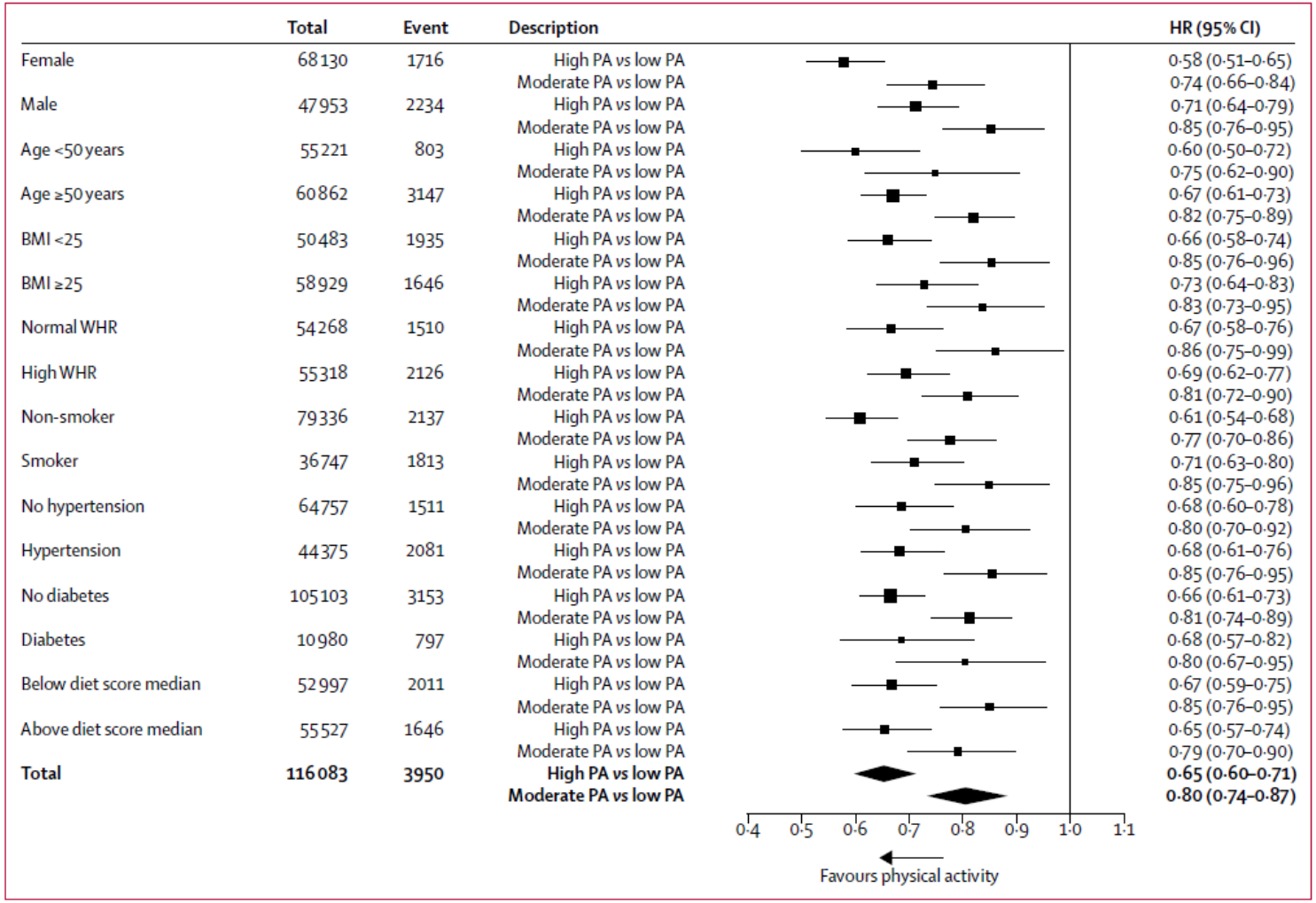


Figure 2: **Hazard ratios and 95% CI of total physical activity for mortality**

Adjusted for age, sex, education, country income level, urban or rural residency, family history of cardiovascular disease, and smoking status taking into account household, community, and country clustering. Based on data for 115 436 participants with complete data. Low physical activity (<600 MET × min per week) is the reference group. Moderate physical activity=600–3000 MET × min per week. High physical activity=>3000 MET × min per week. PA=physical activity. HR=hazard ratio. MET=metabolic equivalents. BMI=body-mass index. WHR=waist-to-hip ratio (high WHR was defined as above 0·85 for women and girls and above 0·9 for men and boys).



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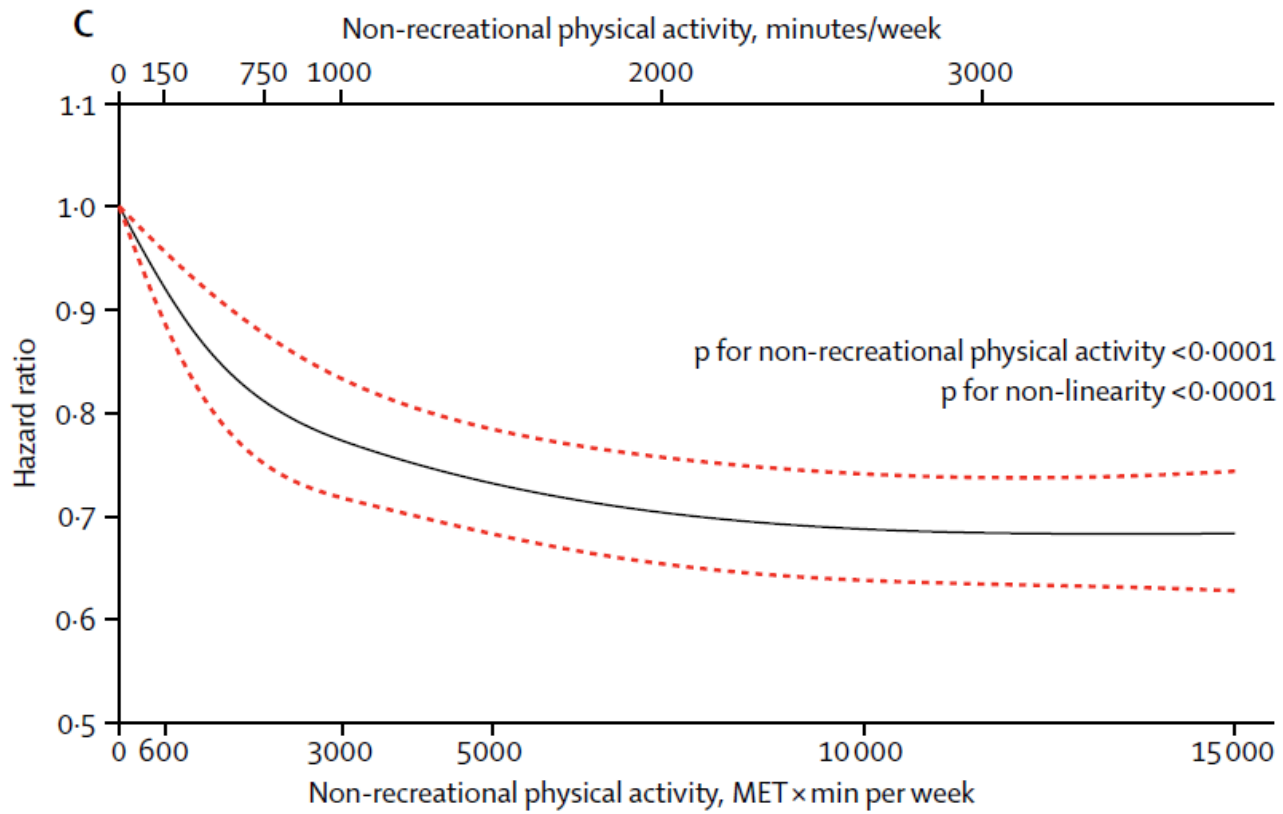
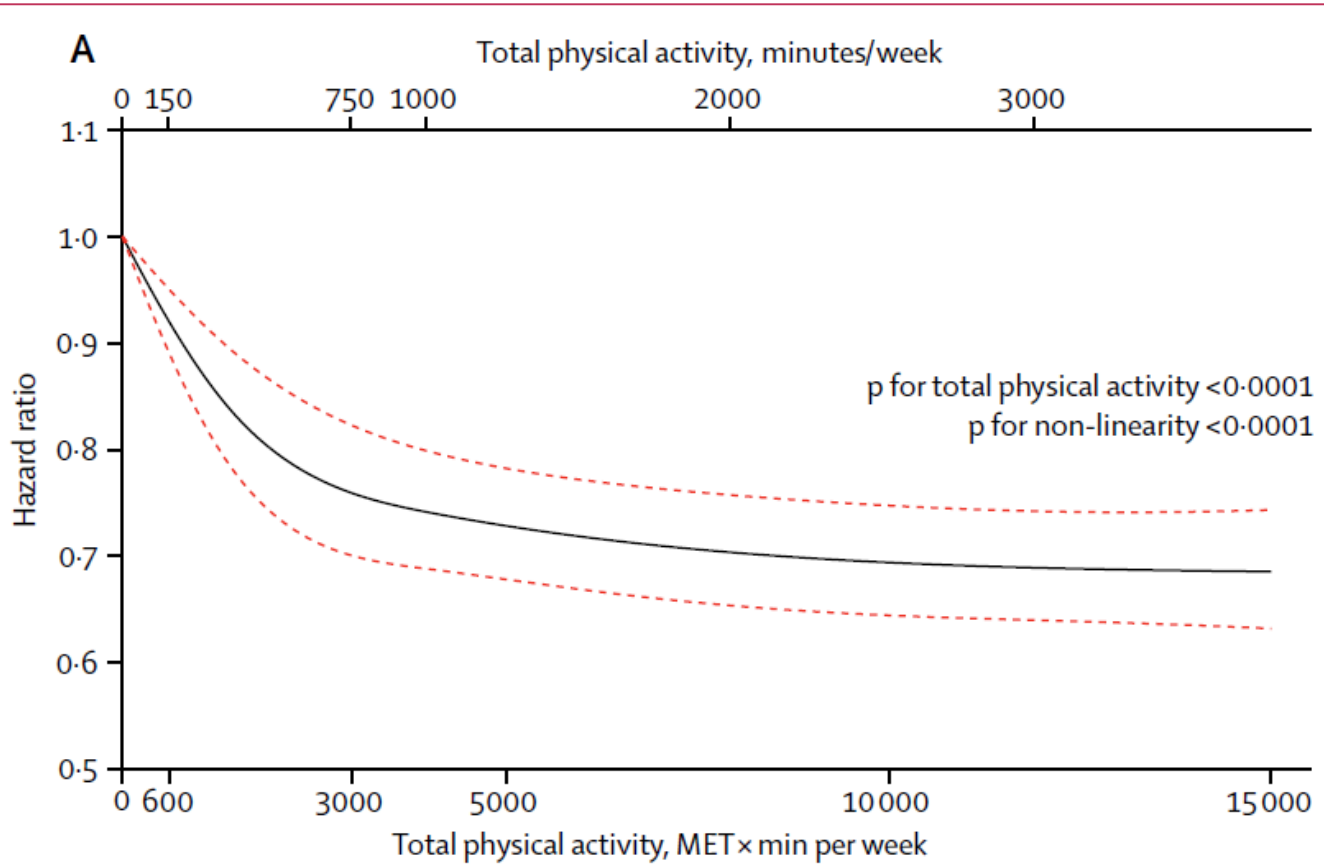


Interval (MET × min per week)	0–600	600–3000	3000–5000	5000–10 000	10 000–15 000	>15 000
	27 968	47 964	15 571	17 547	7597	6020
Total Number of events	2384	2964	873	1077	459	419



Interval (MET × min per week)	0–600	600–3000	3000–5000	5000–10 000	10 000–15 000	>15 000
Total	21 690	46 409	18 781	20 801	8566	6420
Number of events	1941	3007	1028	1247	507	446

The New England
Journal of Medicine

VOLUME 346 MARCH 14, 2002 NUMBER 11

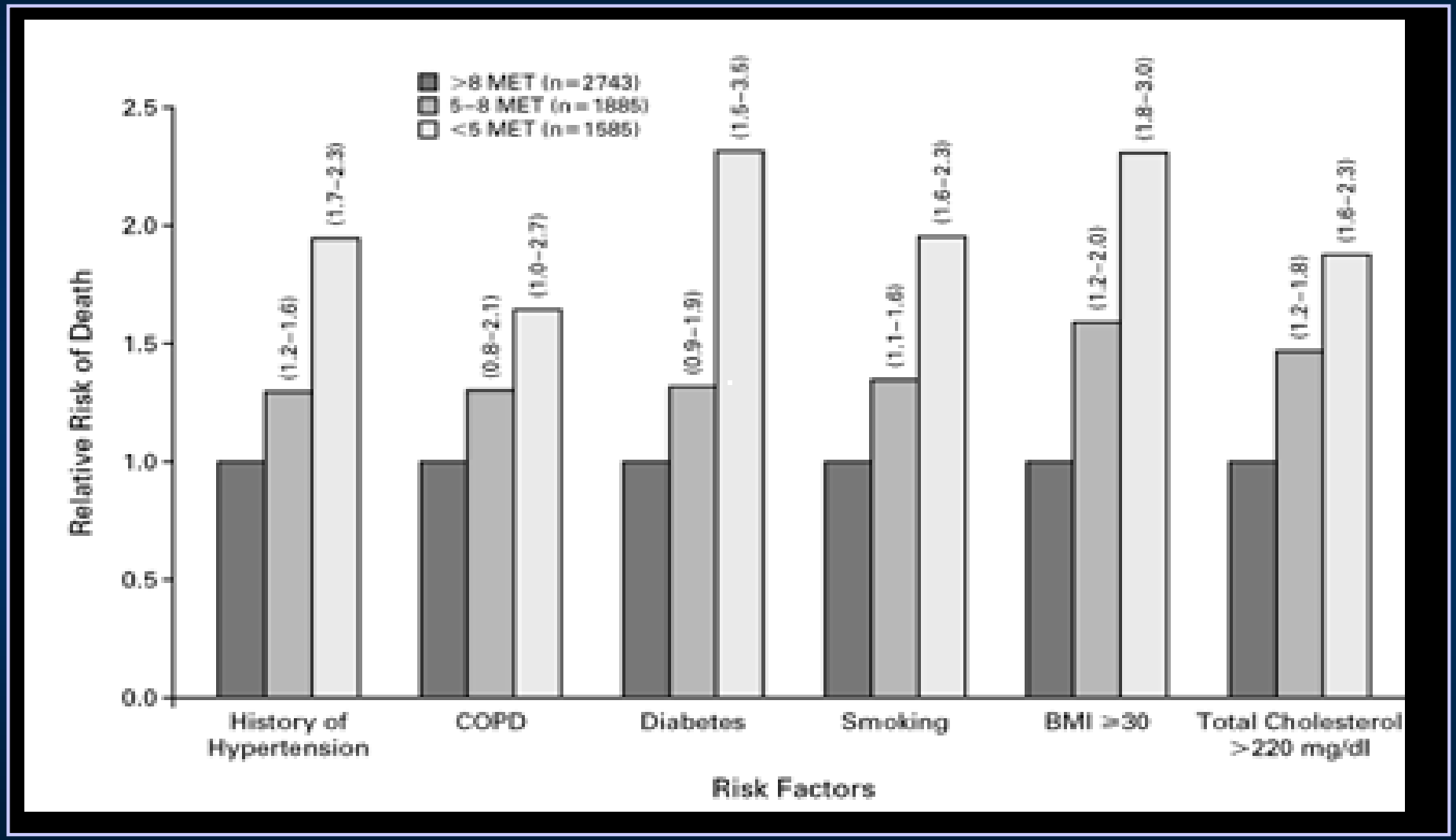
EXERCISE CAPACITY AND MORTALITY AMONG MEN REFERRED FOR EXERCISE TESTING

JONATHAN MYERS, PH.D., MANISH PRAKASH, M.D., VICTOR FROELICHER, M.D., DAT DO, M.D., SARA PARTINGTON, B.SC., AND J. EDWIN ATWOOD, M.D.

ABSTRACT

Background Exercise capacity is known to be an important prognostic factor in patients with cardiovascular disease, but it is uncertain whether it predicts mortality equally well among healthy persons. There is also uncertainty regarding the predictive power of

DURING the past two decades, exercise capacity and activity status have become well-established predictors of cardiovascular and overall mortality.[1,2] The fact that exercise capacity is a strong and independent predictor of outcomes supports the value of the exercise test as a clin-


>8 MET (n=2743)
5–8 MET (n=1885)
<5 MET (n=1585)
Relative Risk of Death
2.5
2.0
1.5
1.0
0.5
0.0
(1.2–1.6)
(1.7–2.3)
(0.8–2.1)
(1.0–2.7)
(0.9–1.9)
(1.5–3.5)
(1.1–1.6)
(1.6–2.3)
(1.2–2.0)
(1.8–3.0)
(1.2–1.8)
(1.6–2.3)
History of Hypertension
COPD
Diabetes
Smoking
BMI ≥30
Total Cholesterol >220 mg/dl
Risk Factors

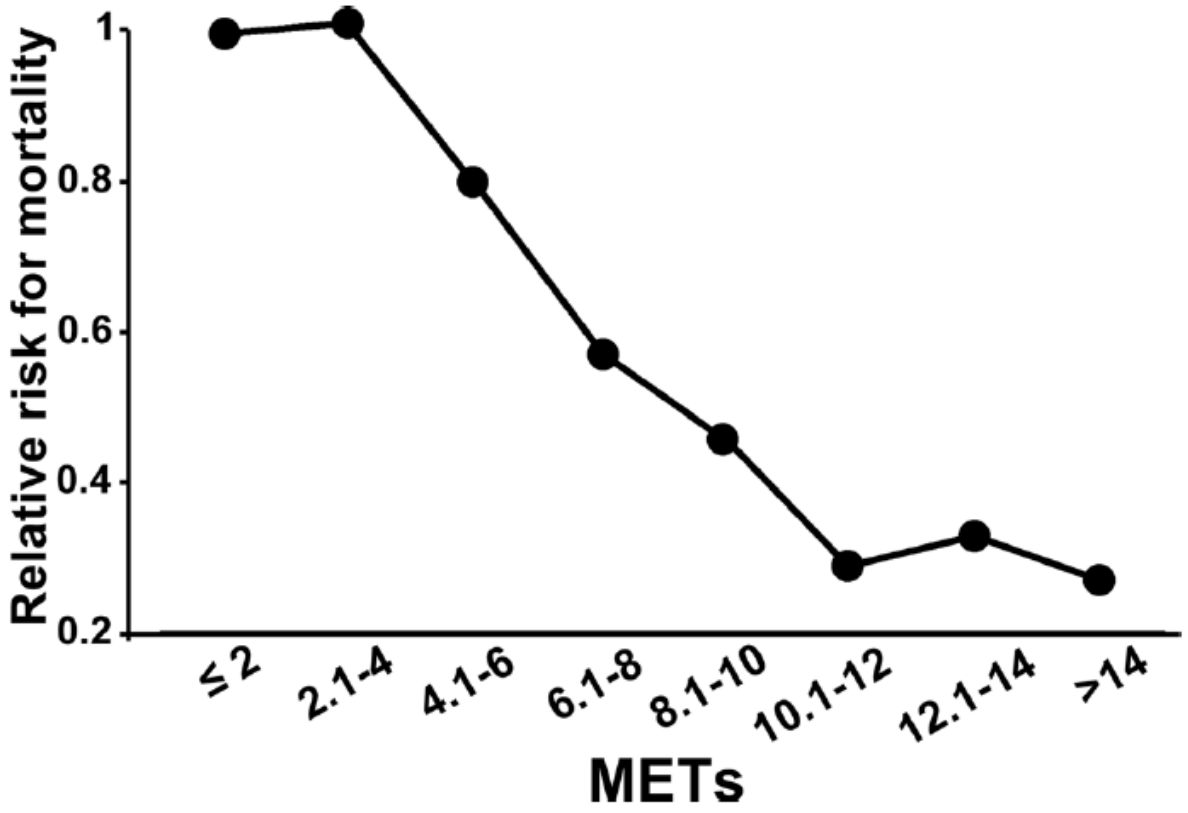
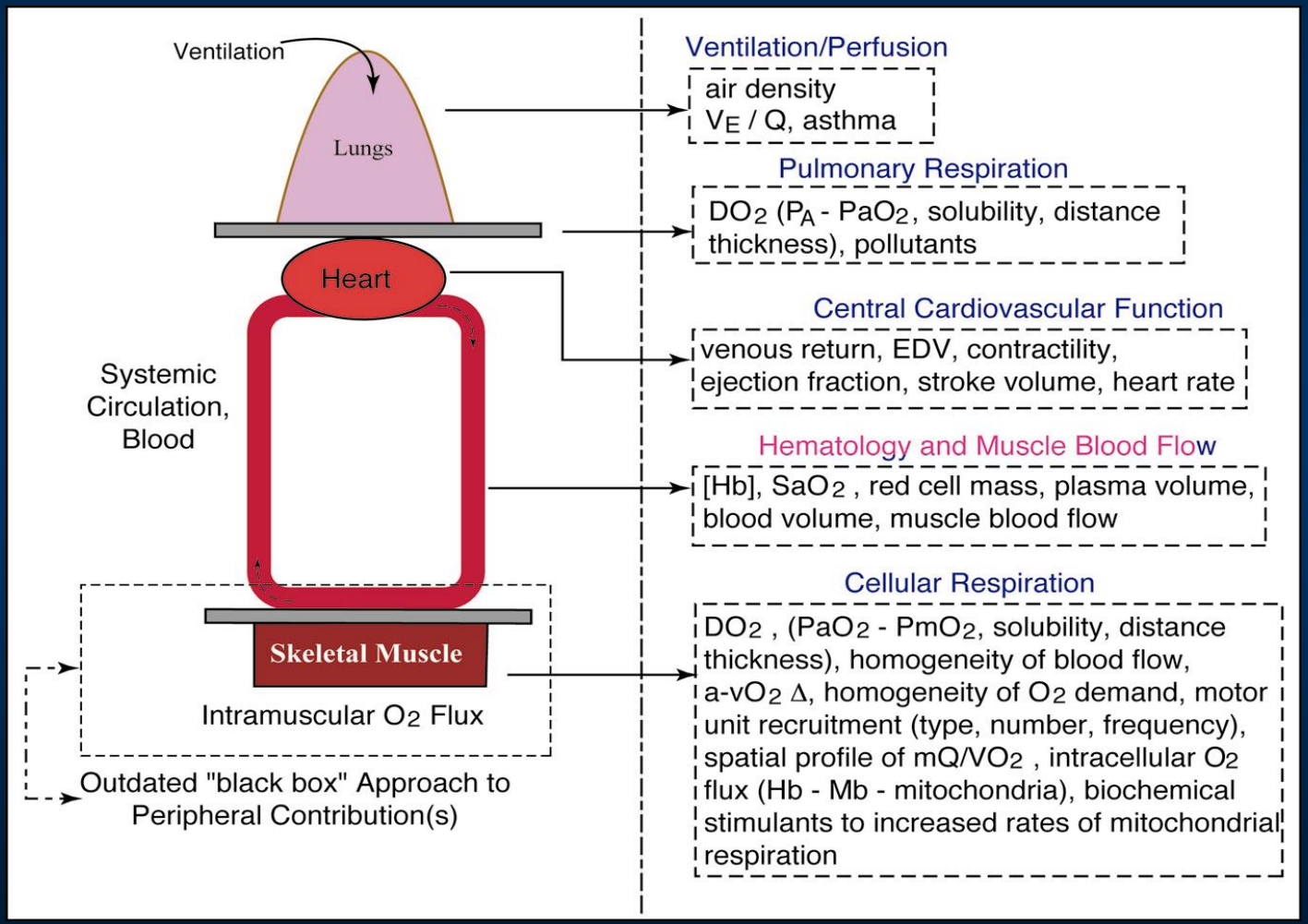


Figure 7 Mortality risk at different exercise capacities. Significant reductions in mortality do not occur less than 4 metabolic equivalents of resting metabolism (METs), become less at approximately 4 to 6 METs and an asymptote occurring at approximately 10 METs in 15,000 US veterans of wars. [Reproduced, with permission, from reference (277,279)].

Limitations de la capacité maximale:



(Wasserman et al 2005, Robergs 2001, ATS/ACCP Statement CPET 2003)

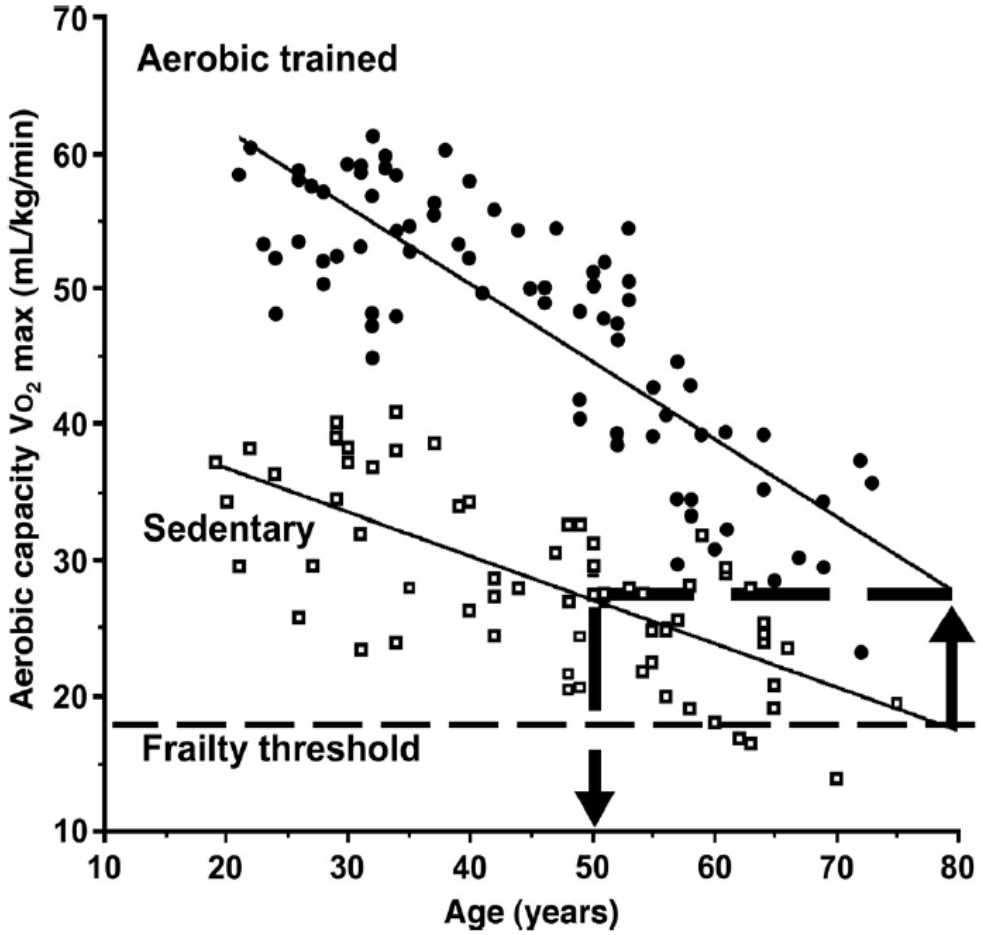


Figure 4 Best-fit linear lines are shown for aerobic capacities of two cross-sectional groups (aerobic trained and sedentary) as a function of their increasing chronological age. At the chronological age of 80 years, a horizontal line is extended from the endurance-trained line to the left where it intersects the sedentary line at age 50 years. Subjects were women who had been aerobically trained for at least 2 years with road-racing competition (closed circles) versus women who were sedentary (open squares) who performed no regular exercise and had body mass indexes (BMIs) more than 35 kg/m^2 (aerobic-trained

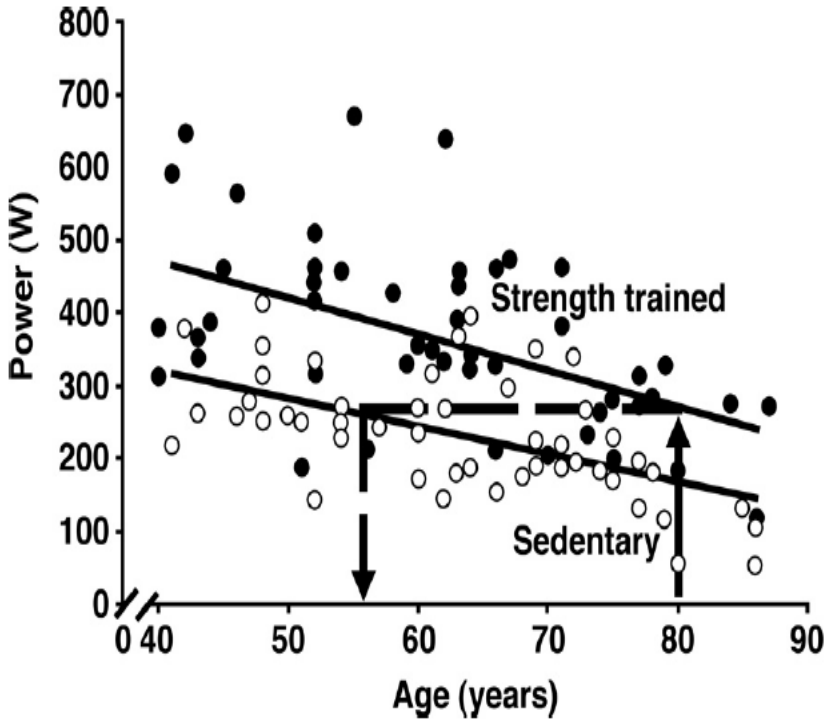


Figure 6 Best-fit linear lines are shown for power of two cross-sectional groups (strength trained and sedentary) as a function of their increasing chronological age. At the chronological age of 80 years, a horizontal line is extended from the power-trained line to the left where it intersects the sedentary line at age 56 years. The cross-sectional strength-trained subjects are shown in closed circles and sedentary in open circles. [Reproduced, with permission, from reference (401)].

Measuring and Monitoring Success in Compressing Morbidity

James F. Fries, MD

The Compression of Morbidity paradigm, introduced in 1980, maintains that if the average age at first infirmity, disability, or other morbidity is postponed and if this postponement is greater than increases in life expectancy, then cumulative lifetime morbidity will decrease—compressed between a later onset and the time of death. The National Long-Term Care Survey, the National Health Interview Survey, and other data now document declining disability trends beginning in 1982 and accelerating more recently. The decline is about 2% per year, contrasted with a decline in mortality rates of about 1% per year, thereby documenting compression of morbidity in the United States at the population level. Longitudinal studies now link good health risk status with long-term reductions in cumulative lifetime disability; persons with few behavioral health risks have only one-fourth the disability of those who have more risk factors, and the onset of disability is postponed from 7 to 12 years, far more than any increases in longevity in the groups. Randomized, controlled trials of health enhancement programs in elderly populations show reduction in health risks, improved health status, and decreased medical care utilization. Health policy initiatives now being undertaken have promise of increasing and consolidating health gains for the elderly.

Ann Intern Med. 2003;139:455-459. www.annals.org

For author affiliation, see end of text.

The Compression of Morbidity paradigm, which was presented as an hypothesis in 1980 (1), noted that most illness was chronic and occurred in later life and postulated that the lifetime burden of illness could be reduced if the onset of chronic illness could be postponed and if this postponement could be greater than increases in life expectancy. Figure 1 illustrates this concept. Estimated present lifetime morbidity is portrayed with three possible future scenarios: life extension, shift-to-the-right, and compression of morbidity. The lines represent the length of life, and the shaded triangles depict lifetime morbidity. Two arrows are shown for each scenario: The left arrow represents the median age at onset of chronic morbidity

been rising with the emergence of chronic illnesses, but it could be argued that this period was ending with declining incidences of major chronic illnesses, such as cardiovascular disease (1).

The Compression paradigm focuses attention on the quality of life over its quantity and considers morbidity as a lifetime cumulative area-under-the-curve concept rather than just a cross-sectional particular point of time, such as a specific age. It suggests that the national burden of illness may be reduced by postponing the onset of infirmity. Thus, the national illness burden that is increasing because of the growing number of elderly persons in the population may be offset, at least in part, by a lower average illness

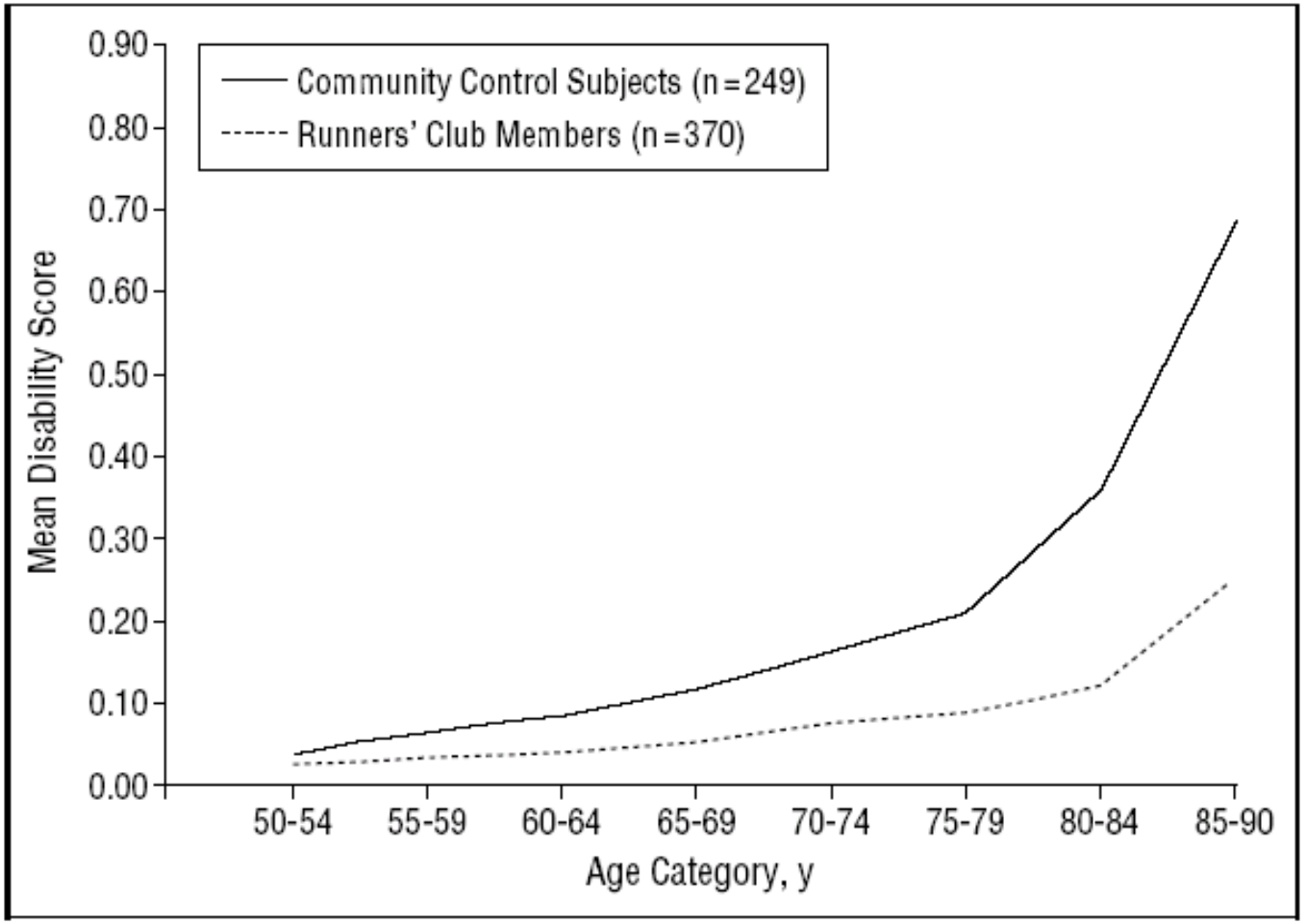


Figure 4. Mean disability scores by age category (at the 1997 questionnaire) and runner status. Subjects contributed one mean disability score to each age group when more than one score was available.

OTTAWA-GATINEAU, le 28 juillet 2011 – Aujourd'hui, le Conseil de la radiodiffusion et des télécommunications canadiennes (CRTC) a publié son *Rapport de surveillance sur les communications*, lequel offre une vue d'ensemble des industries canadiennes de la

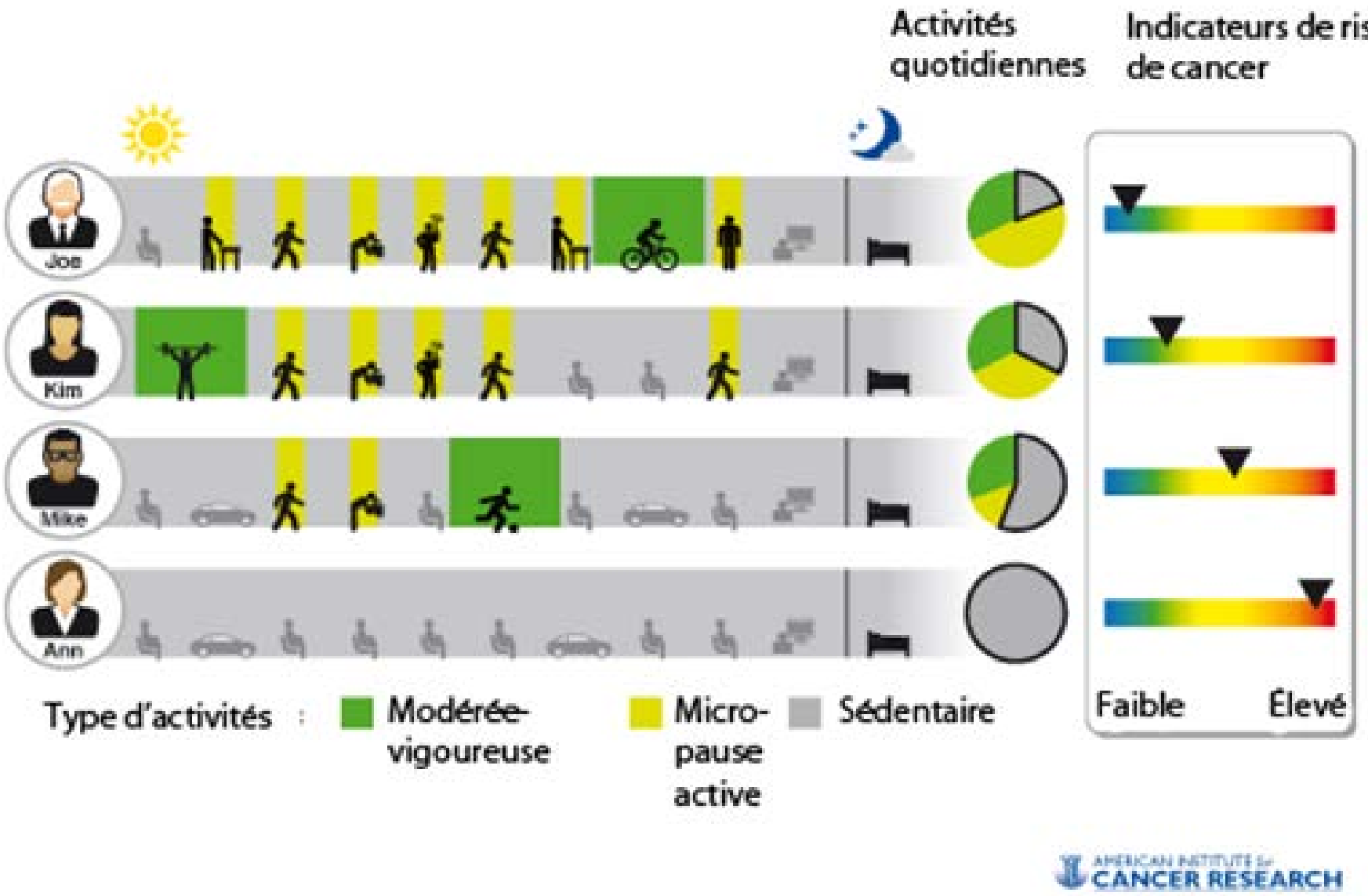
Relationship of Sedentary Behavior and Physical Activity to Incident Cardiovascular Disease

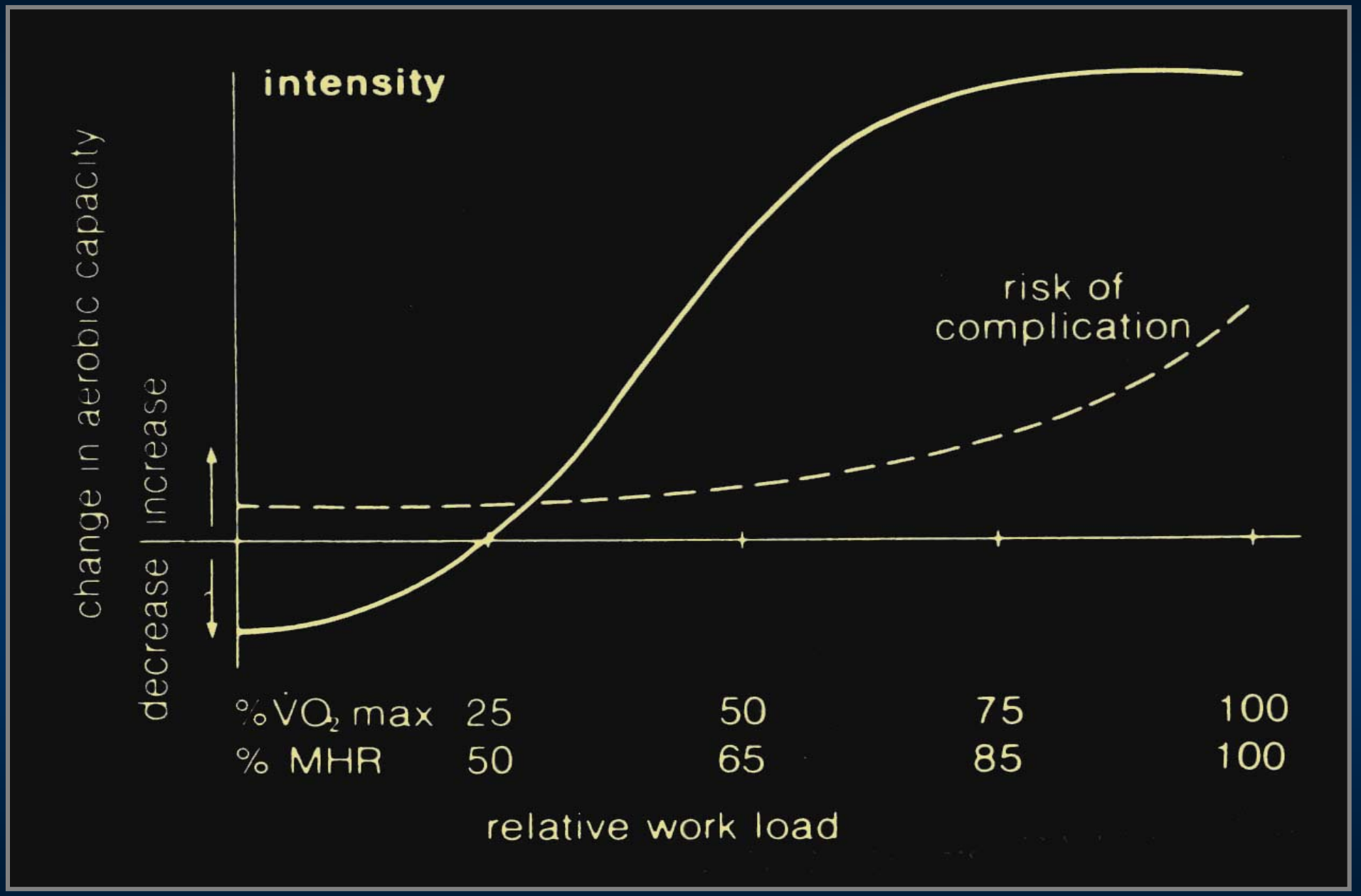
Results From the Women's Health Initiative

Andrea K. Chomistek, ScD,* JoAnn E. Manson, MD, DrPH,† Marcia L. Stefanick, PhD,‡
Bing Lu, MD, DrPH,† Megan Sands-Lincoln, PhD,§ Scott B. Going, PhD,‖ Lorena Garcia, PhD,¶
Matthew A. Allison, MD,# Stacy T. Sims, PhD,‡ Michael J. LaMonte, PhD,**
Karen C. Johnson, MD,†† Charles B. Eaton, MD‡‡§§

Boston, Massachusetts; Stanford, Davis, and San Diego California; Philadelphia, Pennsylvania; Tucson, Arizona; Buffalo, New York; Memphis, Tennessee; and Providence and Pawtucket, Rhode Island

Objectives The aim of this study was to examine the independent and joint associations of sitting time and physical activity with risk of incident cardiovascular disease (CVD).


Activités quotidiennes
Indicateurs de risque de cancer
Joe
Kim
Mike
Ann
Faible
Élevé
Type d'activités :
Modérée-vigoureuse
Micro-pause active
Sédentaire
AMERICAN INSTITUTE for CANCER RESEARCH


intensity
change in aerobic capacity
increase
decrease
risk of
complication
%VO2 max 25 50 75 100
% MHR 50 65 85 100
relative work load

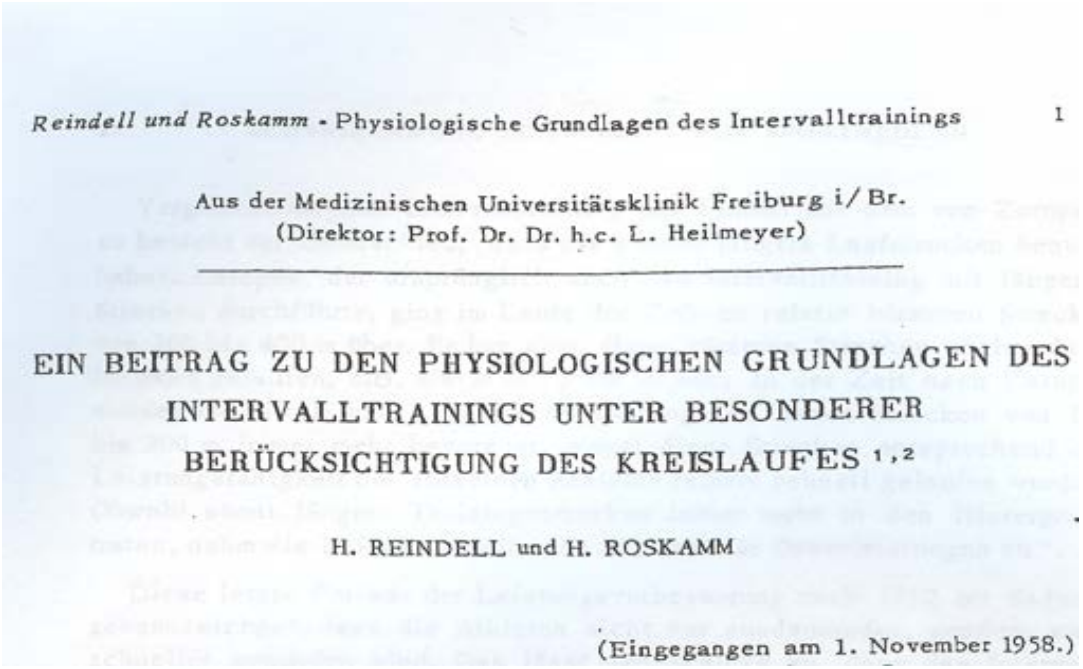
MJ

ECHELLE DE BORG

Perception de la fatigue

	6
TRES TRES FACILE	7
	8
TRES FACILE	9
	10
ASSEZ FACILE	11
	12
UN PEU DIFFICILE	13
	14
DIFFICILE	15
	16
TRES DIFFICILE	17
	18
TRES TRES DIFFICILE	19
	20

EXERCICE INTERMITTENT : HISTORIQUE



Reindell und Roskamm - Physiologische Grundlagen des Intervalltrainings 1

Aus der Medizinischen Universitätsklinik Freiburg i/ Br.
(Direktor: Prof. Dr. Dr. h.c. L. Heilmeyer)

EIN BEITRAG ZU DEN PHYSIOLOGISCHEN GRUNDLAGEN DES INTERVALLTRAININGS UNTER BESONDERER BERÜCKSICHTIGUNG DES KREISLAUFES [1,2]

H. REINDELL und H. ROSKAMM

(Eingegangen am 1. November 1958.)

Reindell (1950's)

Emile Zatopek (1952)

Astrand et coll.

Intermittent muscular work.

Acta Physiol Scand 1960 ; 48 : 448-453

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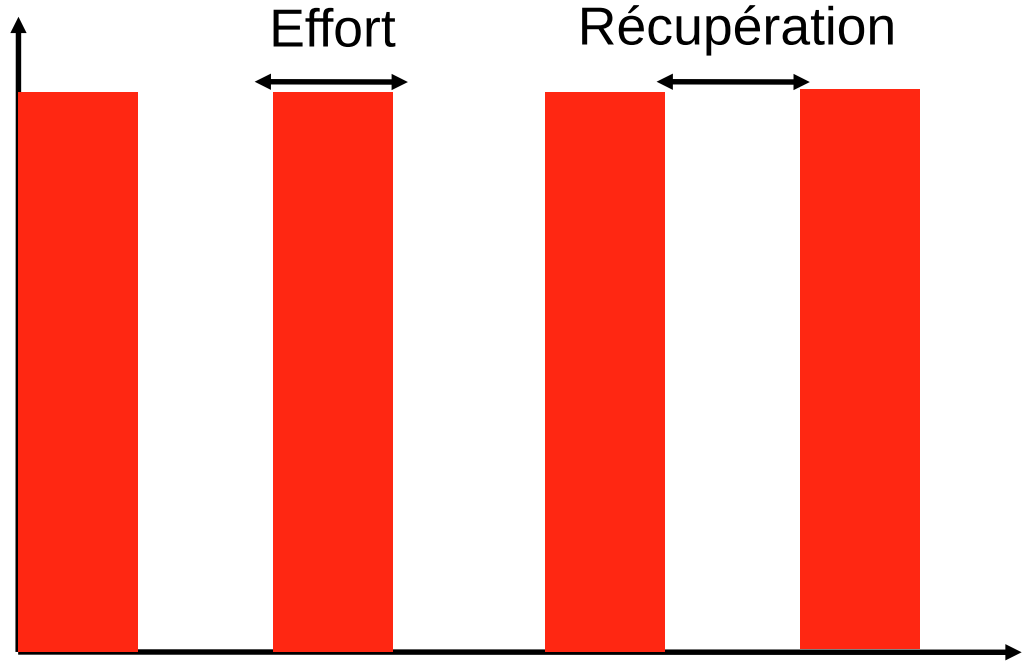
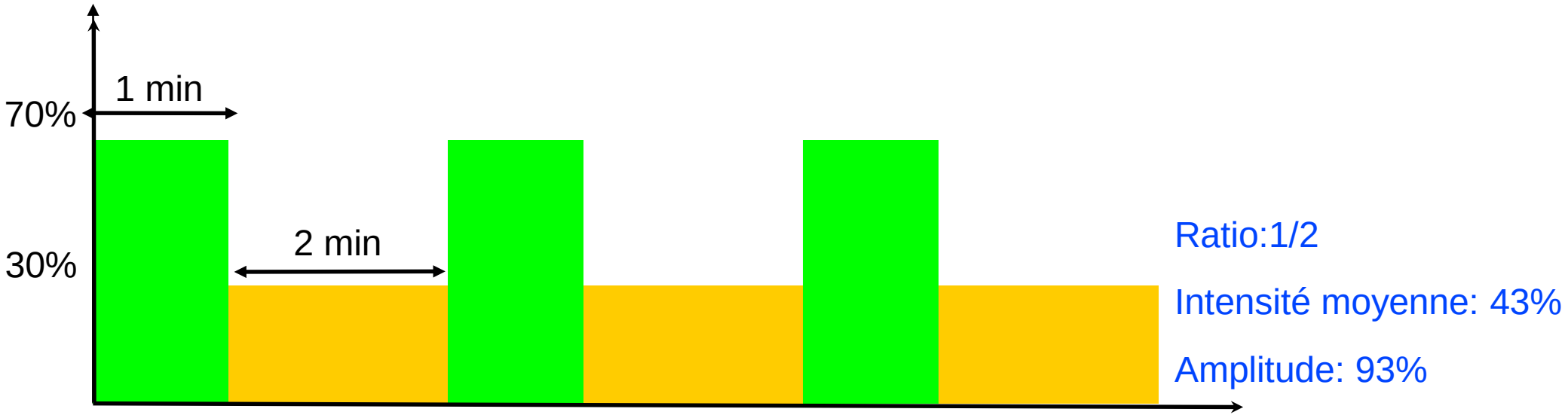
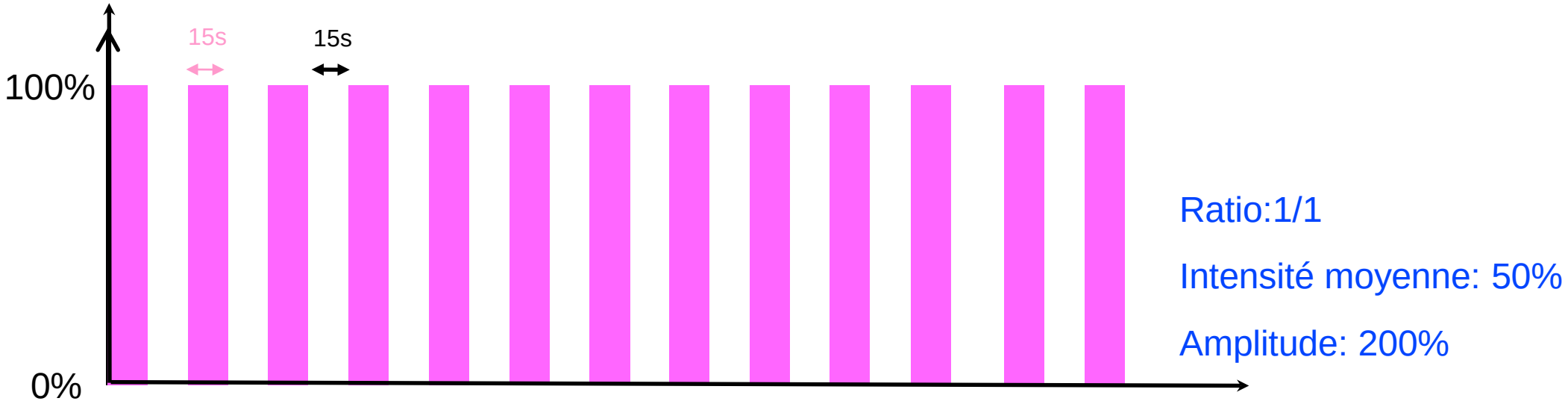


Intermittent



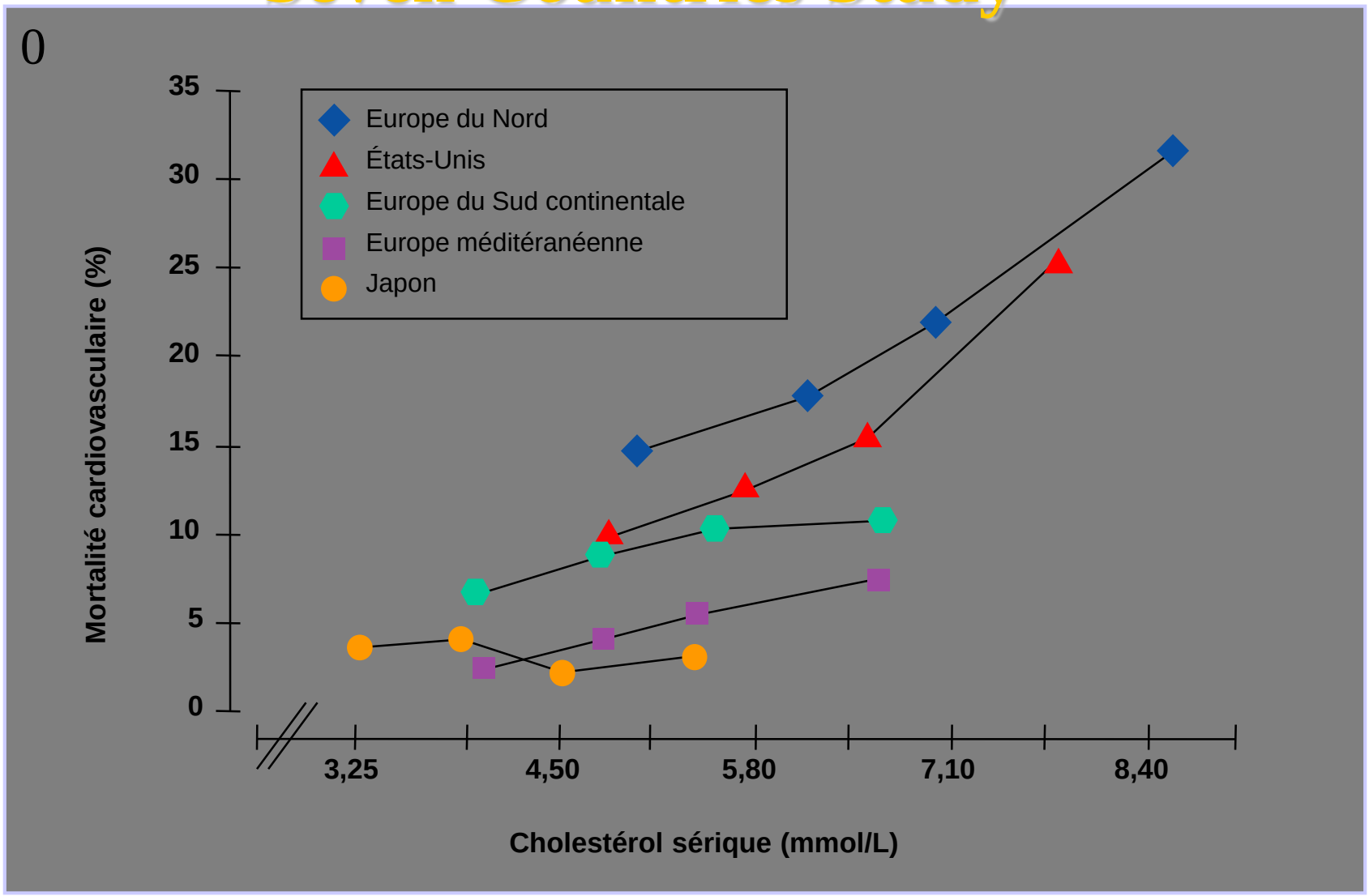


Saltin et al. 1960

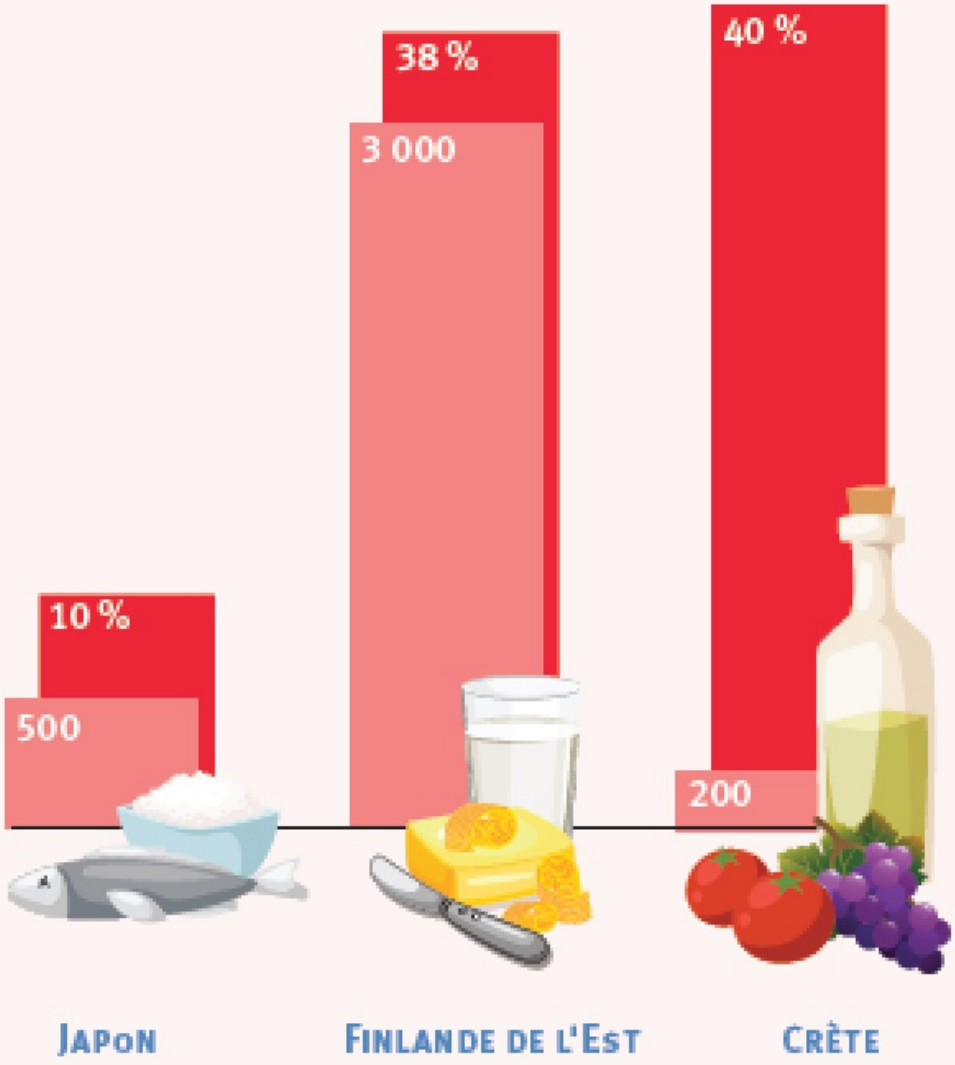
MJ

Mortalité cardiovasculaire sur 25 ans

Seven Countries Study



BIEN CHOISIR SES GRAS POUR PRÉVENIR LES MALADIES CARDIOVASCULAIRES



Même si 6 % des gras de l'alimentation des Finlandais et des Crétois est similaire, c'est la qualité des gras (huile d'olive, noix, etc.) qui explique la faible incidence de maladies cardiovasculaires en Crète.

Pourcentage de calories provenant des gras

Incidence de maladie coronarienne dans une population de 10 000 hommes sur une période de 10 ans

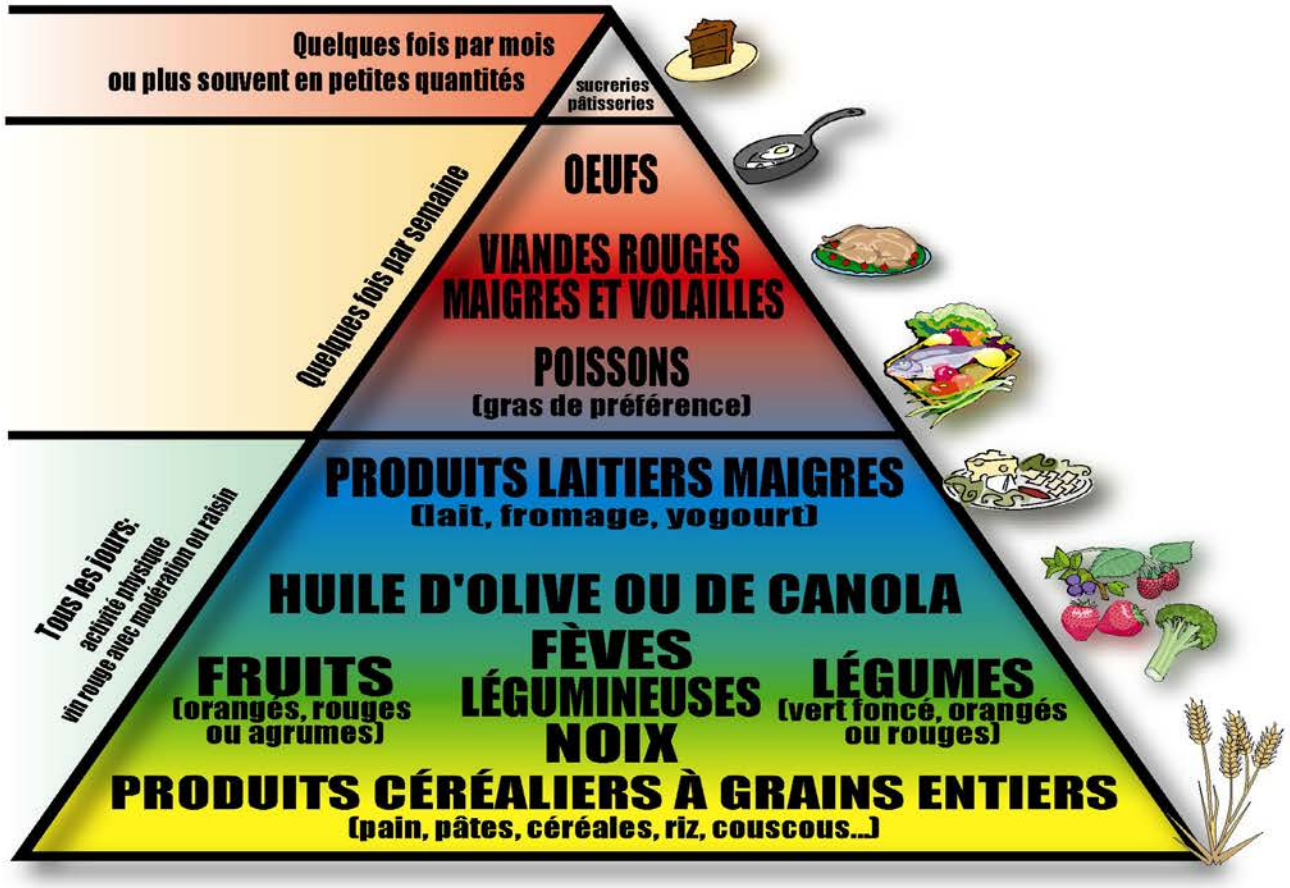
FIGURE 29

D'après Stampfer et Willett (2006)

MJ

Alimentation Méditerranéenne Modifiée

ÉPIC

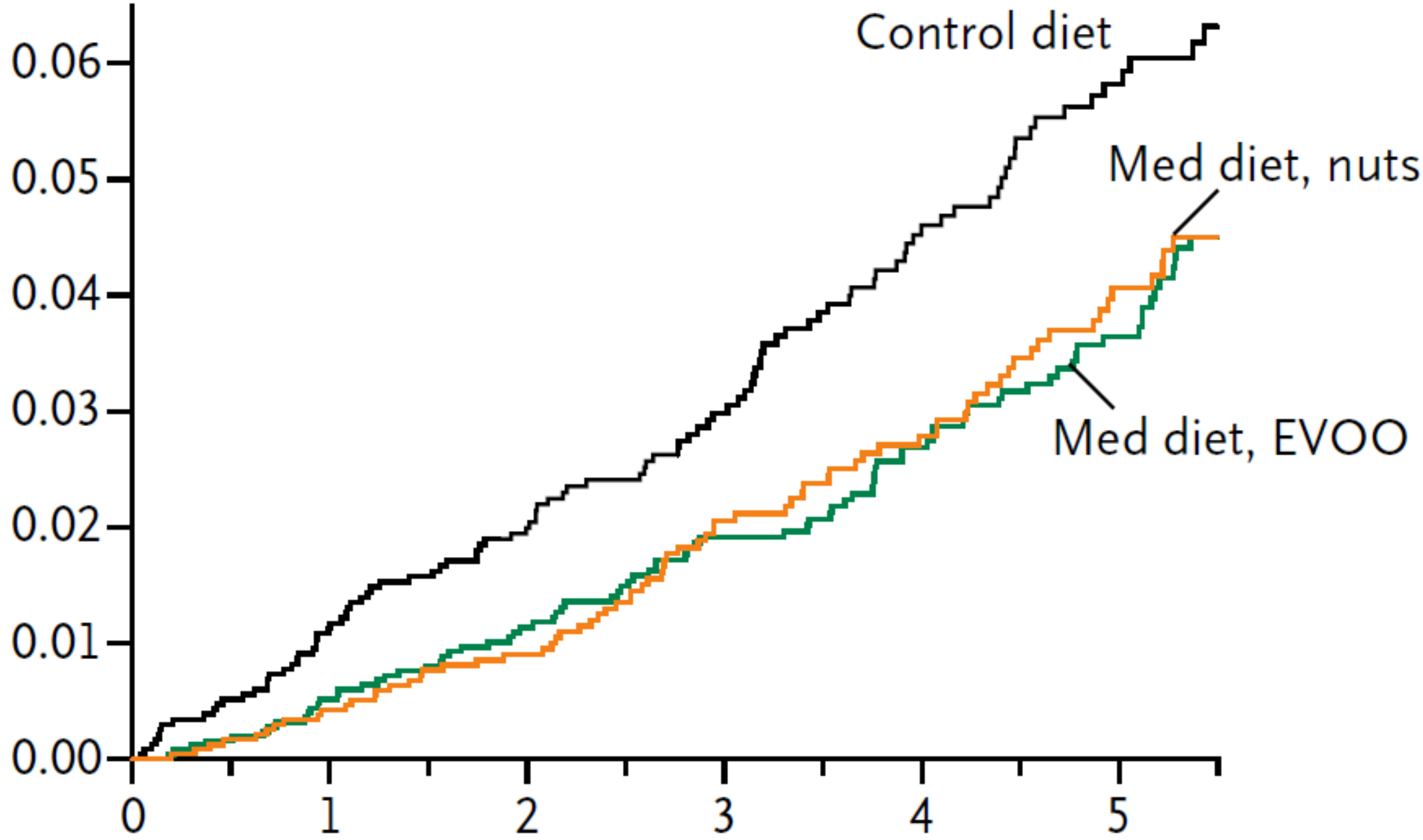


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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-Raventos, 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*


Control diet
Med diet, nuts
Med diet, EVOO
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
1
2
3
4
5

Original Investigation

Mediterranean Diet and Invasive Breast Cancer Risk Among Women at High Cardiovascular Risk in the PREDIMED Trial
A Randomized Clinical Trial

Estefanía Toledo, MD, MPH, PhD; Jordi Salas-Salvadó, MD, PhD; Carolina Donat-Vargas, PharmD; Pilar Buil-Cosiales, MD, PhD; Ramón Estruch, MD, PhD; Emilio Ros, MD, PhD; Dolores Corella, DPharm, PhD; Montserrat Fitó, PhD; Frank B. Hu, MD, PhD; Fernando Arós, MD, PhD; Enrique Gómez-Gracia, MD, PhD; Dora Romaguera, MSc, PhD; Manuel Ortega-Calvo, MD; Lluis Serra-Majem, MD, PhD; Xavier Pintó, MD, PhD; Helmut Schröder, PhD; Josep Basora, MD, PhD; José Vicente Sorlí, MD, PhD; Mònica Bulló, BSc, PhD; Merce Serra-Mir, RD; Miguel A. Martínez-González, MD

IMPORTANCE Breast cancer is the leading cause of female cancer burden, and its incidence has increased by more than 20% worldwide since 2008. Some observational studies have suggested that the Mediterranean diet may reduce the risk of breast cancer.

OBJECTIVE To evaluate the effect of 2 interventions with Mediterranean diet vs the advice to follow a low-fat diet (control) on breast cancer incidence.

DESIGN, SETTING, AND PARTICIPANTS The PREDIMED study is a 1:1:1 randomized, single-blind, controlled field trial conducted at primary health care centers in Spain. From 2003 to 2009, 4282 women aged 60 to 80 years and at high cardiovascular disease risk were recruited after invitation by their primary care physicians.

INTERVENTIONS Participants were randomly allocated to 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).

MAIN OUTCOMES AND MEASURES Breast cancer incidence was a prespecified secondary outcome of the trial for women without a prior history of breast cancer (n = 4152).

RESULTS After a median follow-up of 4.8 years, we identified 35 confirmed incident cases of breast cancer. Observed rates (per 1000 person-years) were 1.1 for the Mediterranean diet with extra-virgin olive oil group, 1.8 for the Mediterranean diet with nuts group, and 2.9 for the control group. The multivariable-adjusted hazard ratios vs the control group were 0.32 (95% CI, 0.13-0.79) for the Mediterranean diet with extra-virgin olive oil group and 0.59 (95% CI, 0.26-1.35) for the Mediterranean diet with nuts group. In analyses with yearly cumulative updated dietary exposures, the hazard ratio for each additional 5% of calories from extra-virgin olive oil was 0.72 (95% CI, 0.57-0.90).

CONCLUSIONS AND RELEVANCE This is the first randomized trial finding an effect of a long-term dietary intervention on breast cancer incidence. Our results suggest a beneficial effect of a Mediterranean diet supplemented with extra-virgin olive oil in the primary prevention of breast cancer. These results come from a secondary analysis of a previous trial and are based on few incident cases and, therefore, need to be confirmed in longer-term and larger studies.

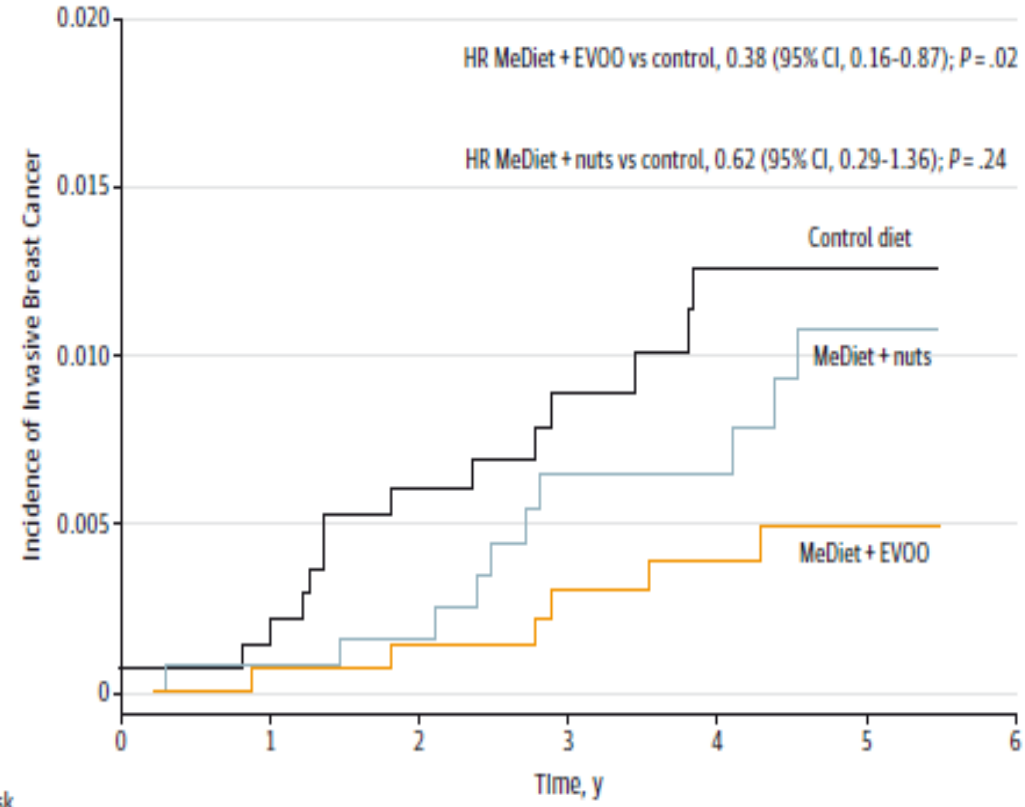
Editor's Note

Supplemental content at jamainternalmedicine.com

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The PREDIMED (Prevención con Dieta Mediterránea)

Figure 1. Incidence of Invasive Breast Cancer, According to the Intervention Group



No. at risk

MeDiet + EVOO	1476	1463	1369	1184	1013	785
MeDiet + nuts	1285	1271	1117	879	741	532
Control diet	1391	1353	1209	940	759	573

Hazard ratios were obtained from Cox regression models.
EVOO indicates extra-virgin olive oil;
HR, hazard ratio;
MeDiet, Mediterranean diet.

Mediterranean Diet, Traditional Risk Factors, and the Rate of Cardiovascular Complications After Myocardial Infarction

Final Report of the Lyon Diet Heart Study

Michel de Lorgeril, MD; Patricia Salen, BSc; Jean-Louis Martin, PhD; Isabelle Monjaud, BSc; Jacques Delaye, MD; Nicole Mamelle, PhD

Background—The Lyon Diet Heart Study is a randomized secondary prevention trial aimed at testing whether a Mediterranean-type diet may reduce the rate of recurrence after a first myocardial infarction. An intermediate analysis showed a striking protective effect after 27 months of follow-up. This report presents results of an extended follow-up (with a mean of 46 months per patient) and deals with the relationships of dietary patterns and traditional risk factors with recurrence.

Methods and Results—Three composite outcomes (COs) combining either cardiac death and nonfatal myocardial infarction (CO 1), or the preceding plus major secondary end points (unstable angina, stroke, heart failure, pulmonary or peripheral embolism) (CO 2), or the preceding plus minor events requiring hospital admission (CO 3) were studied. In the Mediterranean diet group, CO 1 was reduced (14 events versus 44 in the prudent Western-type diet group, $P=0.0001$), as were CO 2 (27 events versus 90, $P=0.0001$) and CO 3 (95 events versus 180, $P=0.0002$). Adjusted risk ratios ranged from 0.28 to 0.53. Among the traditional risk factors, total cholesterol (1 mmol/L being associated with an increased risk of 18% to 28%), systolic blood pressure (1 mm Hg being associated with an increased risk of 1% to 2%), leukocyte count (adjusted risk ratios ranging from 1.64 to 2.86 with count $>9\times10^9$/L), female sex (adjusted risk ratios, 0.27 to 0.46), and aspirin use (adjusted risk ratios, 0.59 to 0.82) were each significantly and independently associated with recurrence.

Conclusions—The protective effect of the Mediterranean dietary pattern was maintained up to 4 years after the first infarction, confirming previous intermediate analyses. Major traditional risk factors, such as high blood cholesterol and blood pressure, were shown to be independent and joint predictors of recurrence, indicating that the Mediterranean dietary pattern did not alter, at least qualitatively, the usual relationships between major risk factors and recurrence. Thus, a comprehensive strategy to decrease cardiovascular morbidity and mortality should include primarily a cardioprotective diet. It should be associated with other (pharmacological?) means aimed at reducing modifiable risk factors. Further trials combining the 2 approaches are warranted. **(*Circulation*. 1999;99:779-785.)**

Key Words: diet ■ trials ■ coronary disease ■ myocardial infarction

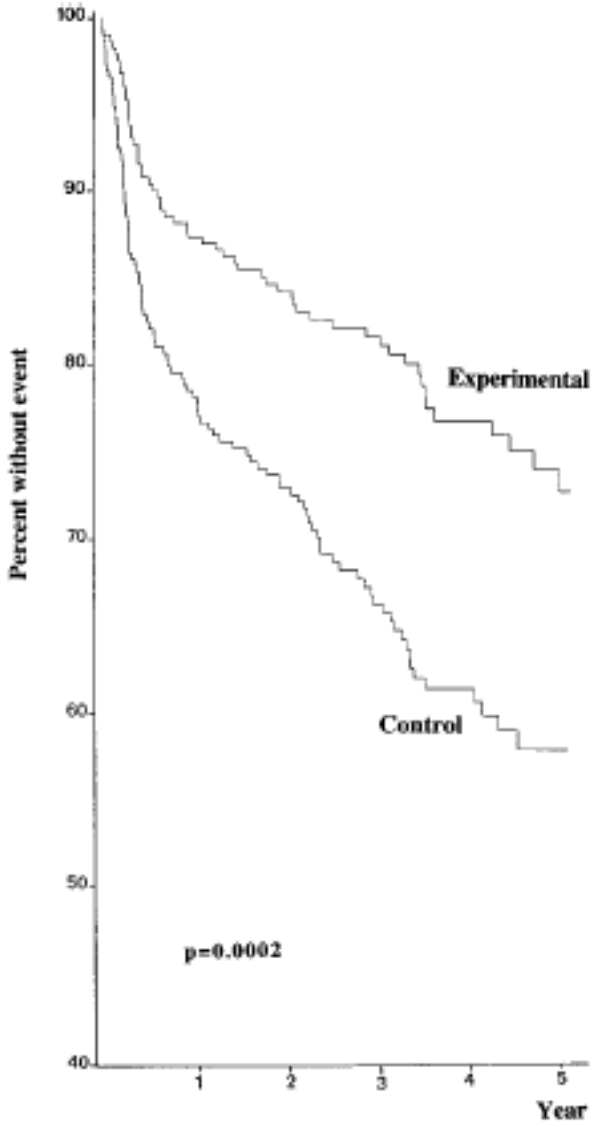


Figure 3. Cumulative survival without nonfatal infarction, without major secondary end points, and without minor secondary end points (CO 3).

TABLE 2. Main Risk Factors and Selected Biological Parameters Recorded on the Final Visit

	Control (n=204)	Experimental (n=219)
Body mass index, kg/m²	26.9 (3.4)	26.3 (3.7)
Systolic blood pressure, mm Hg	128 (16)	128 (17)
Diastolic blood pressure, mm Hg	79 (10)	78 (11)
Total cholesterol, mmol/L	6.18 (1.04)	6.20 (1.06)
Triglycerides, mmol/L	1.75 (0.83)	1.94 (0.85)
HDL-cholesterol, mmol/L	1.28 (0.34)	1.29 (0.34)
LDL-cholesterol, mmol/L	4.23 (0.98)	4.17 (0.93)
Lipoprotein (a), g/L	0.35 (0.49)	0.33 (0.35)
Albumin, g/L	47.10 (2.88)	47.28 (3.07)
Glycated hemoglobin, %	4.61 (1.23)	4.66 (1.52)
Creatinine, μmol/L	116 (20)	115 (21)
Uric acid, μmol/L	348 (81)	338 (87)
Leukocyte count, $\times 10^9$/L	6.00 (1.69)	5.99 (1.68)
Current smokers, %	17.9	18.3
Medication, %		
Anticoagulant agents	16.1	11.4
Antiplatelet agents	69.7	75.8
β-Blocking agents	47.3	47.5
Calcium channel blockers	28.4	25.6
ACE inhibitors	17.4	18.3
Lipid-lowering drugs	34.0	26.5

Values are mean (SD).

cholesterol, blood pressure, leukocyte count, and aspirin use). With regard to the effect of 18:3(ω-3) on CO 2 and CO 3, the associations were borderline nonsignificant ($P=0.08$ and $P=0.12$).

Évènements Étude de Lyon

- Mortalité CV:
- 19/204 = 9.3% 6/219=2.7% Diff absolue 6.6%

- Infarctus non fatal:
- 25/204= 12.2 % 8/219= 3.6% Diff absolue 8.6%

- Mortalité toutes causes:
- 24/204= 11.7% 14/219= 6.4% Diff absolue 5.3%

- DIFFÉRENCES RELATIVES: 71%, 70%, 45%

TABLE 3. Daily Nutrient Intake Recorded on the Final Visit in 83 Control and 144 Experimental Nonselected Consecutive Patients

	Control	Experimental	*P*
Total calories	2088 (490)	1947 (468)	0.033
% calories			
Total lipids	33.6 (7.80)	30.4 (7.00)	0.002
Saturated fats	11.7 (3.90)	8.0 (3.70)	0.0001
Polyunsaturated fats	6.10 (2.90)	4.60 (1.70)	0.0001
18:1(ω-9) (oleic)	10.8 (4.10)	12.9 (3.20)	0.0001
18:2(ω-6) (linoleic)	5.30 (2.80)	3.60 (1.20)	0.0001
18:3(ω-3) (linolenic)	0.29 (0.19)	0.84 (0.46)	0.0001
Alcohol	5.98 (6.90)	5.83 (5.80)	0.80
Proteins, g	16.6 (3.80)	16.2 (3.10)	0.30
Fiber, g	15.5 (6.80)	18.6 (8.10)	0.004
Cholesterol, mg	312 (180)	203 (145)	0.0001

Values are mean (SD).

Original Investigation

Association of Specific Dietary Fats With Total and Cause-Specific Mortality

Dong D. Wang, MD, MSc; Yanping Li, PhD; Stephanie E. Chiuve, ScD; Meir J. Stampfer, MD, DrPH; JoAnn E. Manson, MD, DrPH; Eric B. Rimm, ScD; Walter C. Willett, MD, DrPH; Frank B. Hu, MD, PhD

IMPORTANCE Previous studies have shown distinct associations between specific dietary fat and cardiovascular disease. However, evidence on specific dietary fat and mortality remains limited and inconsistent.

OBJECTIVE To examine the associations of specific dietary fats with total and cause-specific mortality in 2 large ongoing cohort studies.

DESIGN, SETTING, AND PARTICIPANTS This cohort study investigated 83 349 women from the Nurses' Health Study (July 1, 1980, to June 30, 2012) and 42 884 men from the Health Professionals Follow-up Study (February 1, 1986, to January 31, 2012) who were free of cardiovascular disease, cancer, and types 1 and 2 diabetes at baseline. Dietary fat intake was assessed at baseline and updated every 2 to 4 years. Information on mortality was obtained from systematic searches of the vital records of states and the National Death Index, supplemented by reports from family members or postal authorities. Data were analyzed from September 18, 2014, to March 27, 2016.

MAIN OUTCOMES AND MEASURES Total and cause-specific mortality.

RESULTS During 3 439 954 person-years of follow-up, 33 304 deaths were documented. After adjustment for known and suspected risk factors, dietary total fat compared with total carbohydrates was inversely associated with total mortality (hazard ratio [HR] comparing extreme quintiles, 0.84; 95% CI, 0.81-0.88; $P < .001$ for trend). The HRs of total mortality comparing extreme quintiles of specific dietary fats were 1.08 (95% CI, 1.03-1.14) for saturated fat, 0.81 (95% CI, 0.78-0.84) for polyunsaturated fatty acid (PUFA), 0.89 (95% CI, 0.84-0.94) for monounsaturated fatty acid (MUFA), and 1.13 (95% CI, 1.07-1.18) for *trans*-fat ($P < .001$ for trend for all). Replacing 5% of energy from saturated fats with equivalent energy from PUFA and MUFA was associated with estimated reductions in total mortality of 27% (HR, 0.73; 95% CI, 0.70-0.77) and 13% (HR, 0.87; 95% CI, 0.82-0.93), respectively. The HR for total mortality comparing extreme quintiles of ω-6 PUFA intake was 0.85 (95% CI, 0.81-0.89; $P < .001$ for trend). Intake of ω-6 PUFA, especially linoleic acid, was inversely associated with mortality owing to most major causes, whereas marine ω-3 PUFA intake was associated with a modestly lower total mortality (HR comparing extreme quintiles, 0.96; 95% CI, 0.93-1.00; $P = .002$ for trend).

CONCLUSIONS AND RELEVANCE Different types of dietary fats have divergent associations with total and cause-specific mortality. These findings support current dietary recommendations to replace saturated fat and *trans*-fat with unsaturated fats.

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Related article

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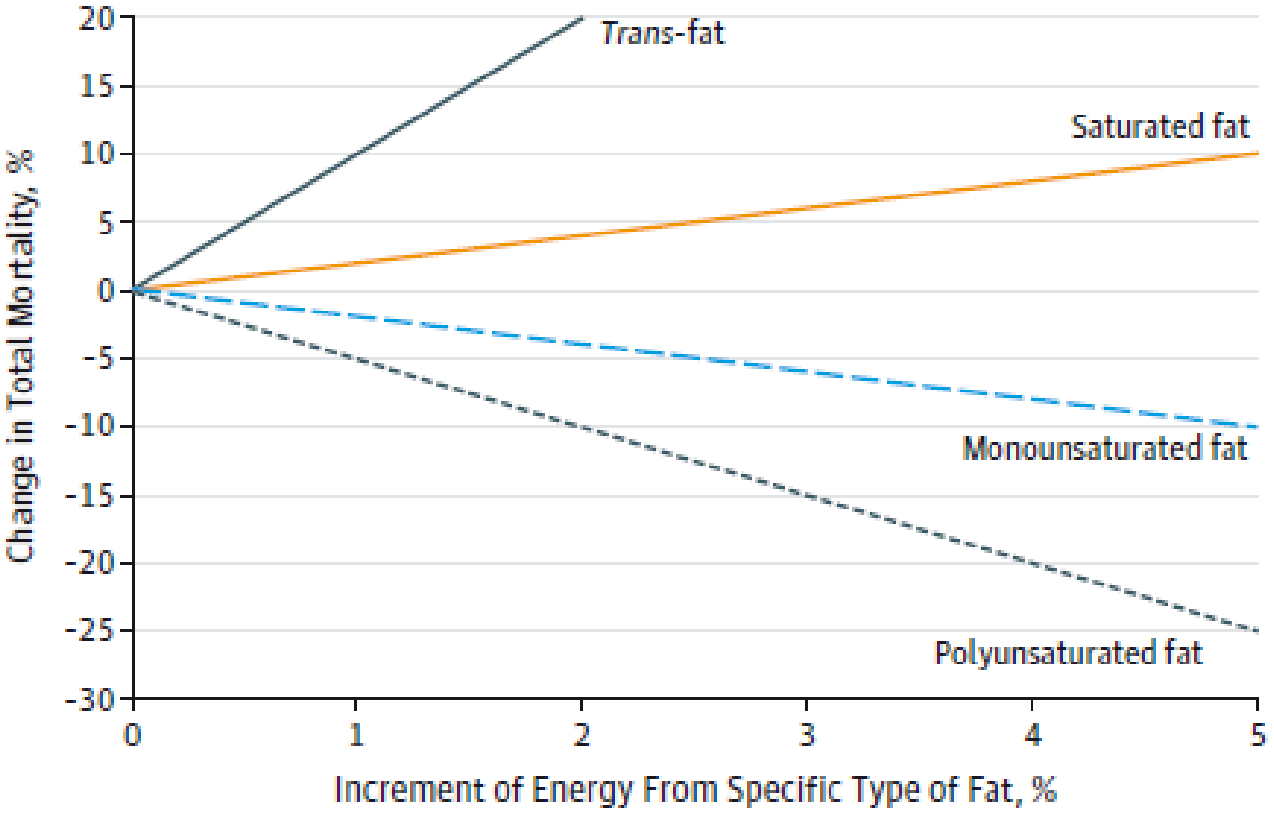
Association of Dietary Fats and Total and Cause-Specific Mortality

Figure 1. Change in Total Mortality Associated With Increases in the Percentage of Energy From Specific Types of Fat



LES MATIÈRES GRASSES DE L'ALIMENTATION

Gras et acides gras

Gras saturés
Gras animal, beurre, saindoux, huiles tropicales

Gras insaturés

Gras « trans »
Huiles hydrogénées shortening, margarines

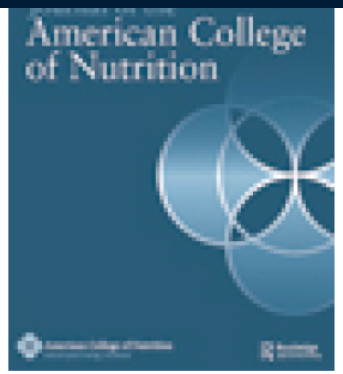
Gras polyinsaturés

Acides gras oméga-6
Huiles végétales (maïs, tournesol...)
Pro-inflammatoires
Procancéreux

Acides gras oméga-3
Sardine, maquereau, saumon, graines de lin, soja, noix
Anti-inflammatoires
Anticancéreux

Gras mono-insaturés

Acides gras oméga-9
Huiles d'olive, de canola, avocats, amandes



Journal of the American College of Nutrition

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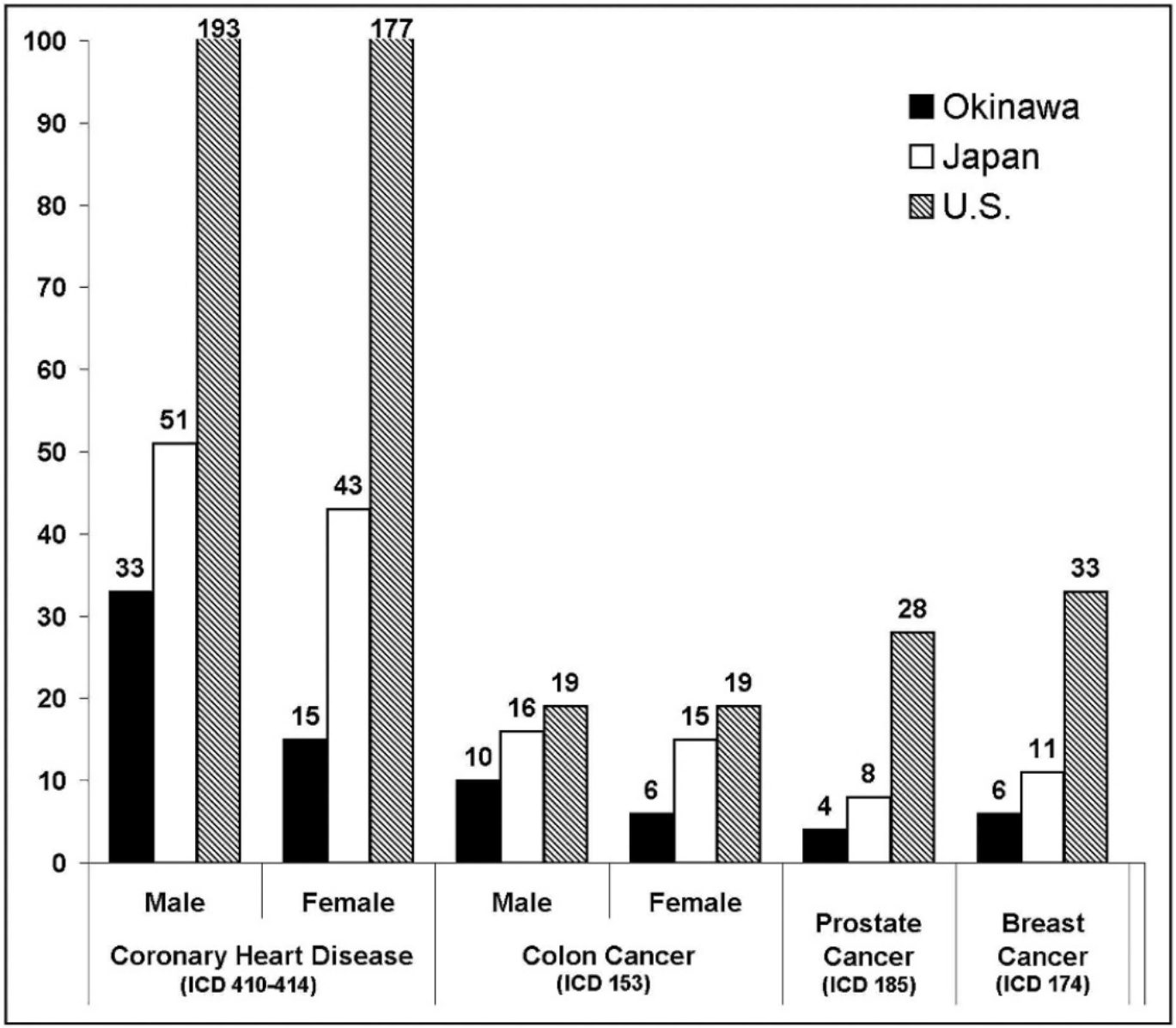
The Okinawan Diet: Health Implications of a Low-Calorie, Nutrient-Dense, Antioxidant-Rich Dietary Pattern Low in Glycemic Load

D. Craig Willcox PhD, Bradley J. Willcox MD, Hidemi Todoriki PhD & Makoto Suzuki MD, PhD



. Mortality rates from coronary heart disease and cancers in Okinawans, Japanese, and Americans [1].

Journal of the American Col

ISSN: 0731-5724 (Print) 1541-1087 (Online) Journal h

The Okinawan Diet: Health
Calorie, Nutrient-Dense, A
Pattern Low in Glycemic Lo

D. Craig Willcox PhD, Bradley J. Willcox M
Suzuki MD, PhD

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of Nutrition, 28:sup4, 500S-516S, DOI: 10.1080/07

JAMA Internal Medicine | Original Investigation

Association of Animal and Plant Protein Intake With All-Cause and Cause-Specific Mortality

Mingyang Song, MD, ScD; Teresa T. Fung, ScD; Frank B. Hu, MD, PhD; Walter C. Willett, MD, DrPH; Valter D. Longo, PhD; Andrew T. Chan, MD, MPH; Edward L. Giovannucci, MD, ScD

IMPORTANCE Defining what represents a macronutritionally balanced diet remains an open question and a high priority in nutrition research. Although the amount of protein may have specific effects, from a broader dietary perspective, the choice of protein sources will inevitably influence other components of diet and may be a critical determinant for the health outcome.

OBJECTIVE To examine the associations of animal and plant protein intake with the risk for mortality.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study of US health care professionals included 131 342 participants from the Nurses' Health Study (1980 to end of follow-up on June 1, 2012) and Health Professionals Follow-up Study (1986 to end of follow-up on January 31, 2012). Animal and plant protein intake was assessed by regularly updated validated food frequency questionnaires. Data were analyzed from June 20, 2014, to January 18, 2016.

MAIN OUTCOMES AND MEASURES Hazard ratios (HRs) for all-cause and cause-specific mortality.

RESULTS Of the 131 342 participants, 85 013 were women (64.7%) and 46 329 were men (35.3%) (mean [SD] age, 49 [9] years). The median protein intake, as assessed by percentage of energy, was 14% for animal protein (5th-95th percentile, 9%-22%) and 4% for plant protein (5th-95th percentile, 2%-6%). After adjusting for major lifestyle and dietary risk factors, animal protein intake was not associated with all-cause mortality (HR, 1.02 per 10% energy increment; 95% CI, 0.98-1.05; *P* for trend = .33) but was associated with higher cardiovascular mortality (HR, 1.08 per 10% energy increment; 95% CI, 1.01-1.16; *P* for trend = .04). Plant protein was associated with lower all-cause mortality (HR, 0.90 per 3% energy increment; 95% CI, 0.86-0.95; *P* for trend < .001) and cardiovascular mortality (HR, 0.88 per 3% energy increment; 95% CI, 0.80-0.97; *P* for trend = .007). These associations were confined to participants with at least 1 unhealthy lifestyle factor based on smoking, heavy alcohol intake, overweight or obesity, and physical inactivity, but not evident among those without any of these risk factors. Replacing animal protein of various origins with plant protein was associated with lower mortality. In particular, the HRs for all-cause mortality were 0.66 (95% CI, 0.59-0.75) when 3% of energy from plant protein was substituted for an equivalent amount of protein from processed red meat, 0.88 (95% CI, 0.84-0.92) from unprocessed red meat, and 0.81 (95% CI, 0.75-0.88) from egg.

CONCLUSIONS AND RELEVANCE High animal protein intake was positively associated with cardiovascular mortality and high plant protein intake was inversely associated with all-cause and cardiovascular mortality, especially among individuals with at least 1 lifestyle risk factor. Substitution of plant protein for animal protein, especially that from processed red meat, was associated with lower mortality, suggesting the importance of protein source.

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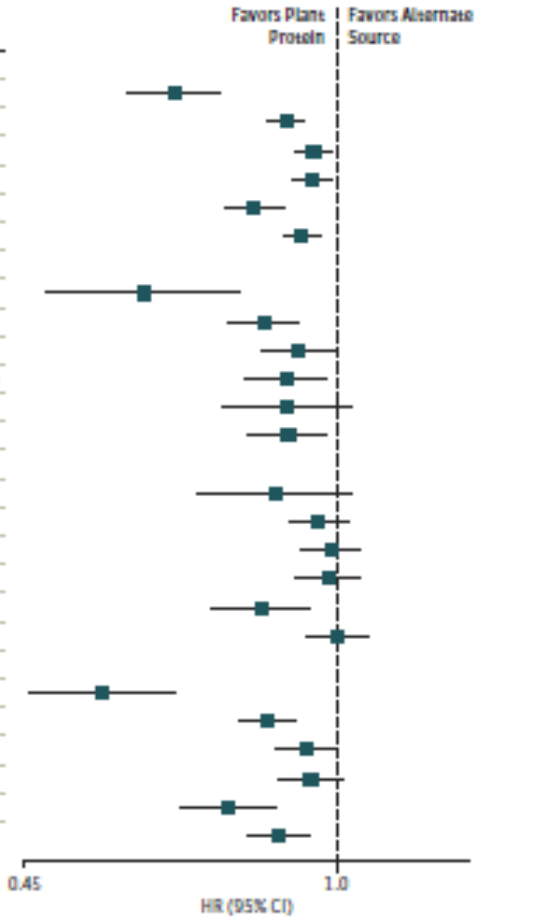
MJ

Figure. Risk for Mortality Associated With Replacement of 3% Energy From Various Animal Protein Sources With Plant Protein

Animal Protein Source by Cause of Death	HR (95% CI)
All cause	
Processed red meat	0.66 (0.59-0.75)
Unprocessed red meat	0.88 (0.84-0.92)
Poultry	0.94 (0.90-0.99)
Fish	0.94 (0.89-0.99)
Egg	0.81 (0.75-0.88)
Dairy	0.92 (0.87-0.96)
CVD	
Processed red meat	0.61 (0.48-0.78)
Unprocessed red meat	0.83 (0.76-0.91)
Poultry	0.91 (0.83-1.00)
Fish	0.88 (0.80- 0.97)
Egg	0.88 (0.75-1.04)
Dairy	0.89 (0.80-0.98)
Cancer	
Processed red meat	0.86 (0.71-1.04)
Unprocessed red meat	0.96 (0.89-1.03)
Poultry	0.99 (0.91-1.06)
Fish	0.98 (0.91-1.06)
Egg	0.83 (0.73-0.93)
Dairy	1.00 (0.93-1.09)
Other	
Processed red meat	0.55 (0.46-0.67)
Unprocessed red meat	0.84 (0.78-0.90)
Poultry	0.93 (0.86-1.00)
Fish	0.94 (0.87-1.01)
Egg	0.76 (0.67-0.86)
Dairy	0.86 (0.80-0.93)



Protein intake from plant sources and from all the animal food items considered were included in the multivariable model that was also adjusted for total caloric intake and percentage of energy from saturated fat, polyunsaturated fat, monounsaturated fat, and trans-fat (all continuous), multivitamin use (yes or no), smoking status (never, past, or current [1-14, and ≥15 cigarettes/d]), pack-years of smoking (in women, ≤15, 16-25, 26-45, and ≥46; in men, <10, 11-24, 25-44, and ≥45), body mass index (calculated as weight in kilograms divided by height in meters squared; <23.0, 23.0-24.9, 25.0-26.9, 27.0-29.9, 30.0-34.9, and ≥35), physical activity (quintiles), alcohol consumption (in women, 0, 0.1-5.0, 5.1-15.0, and >15.0 g/d; in men, 0, 0.1-10.0, 10.1-20.0, and >20.0 g/d), history of hypertension diagnosis (yes or no), glycemic index (in quintiles), and intake of whole grains, total fiber, fruits, and vegetables (all in quintiles).
CVD indicates cardiovascular disease; HR, hazard ratio. Error bars indicate 95% CIs.

Articles

Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study

Kay-Tee Khaw, Sheila Bingham, Ailsa Welch, Robert Luben, Nicholas Wareham, Suzy Oakes, Nicholas Day

Summary

Background Ascorbic acid (vitamin C) might be protective for several chronic diseases. However, findings from prospective studies that relate ascorbic acid to cardiovascular disease or cancer are not consistent. We aimed to assess the relation between plasma ascorbic acid and subsequent mortality due to all causes, cardiovascular disease, ischaemic heart disease, and cancer.

Methods We prospectively examined for 4 years the relation between plasma ascorbic acid concentrations and mortality due to all causes, and to cardiovascular disease, ischaemic heart disease, and cancer in 19 496 men and women aged 45–79 years. We recruited individuals by post using age-sex registers of general practices. Participants completed a health and lifestyle questionnaire and were examined at a clinic visit. They were followed-up for causes of death for about 4 years. Individuals were divided into sex-specific quintiles of plasma ascorbic acid. We used the Cox proportional hazard model to determine the effect of ascorbic acid and other risk factors on mortality.

Findings Plasma ascorbic acid concentration was inversely related to mortality from all-causes, and from cardiovascular disease, and ischaemic heart disease in men and women. Risk of mortality in the top ascorbic acid quintile was about half the risk in the lowest quintile ($p<0·0001$). The relation with mortality was continuous through the whole distribution of ascorbic acid concentrations. 20 μmol/L rise in plasma ascorbic acid concentration, equivalent to about 50 g per day increase in fruit and vegetable intake, was associated with about a 20% reduction in risk of all-cause mortality ($p<0·0001$), independent of age, systolic blood pressure, blood cholesterol, cigarette smoking habit, diabetes, and supplement use. Ascorbic acid was inversely related to cancer mortality in men but not women.

Interpretation Small increases in fruit and vegetable intake of about one serving daily has encouraging prospects for possible prevention of disease.

Lancet 2001; **357:** 657–63

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Introduction

The role of antioxidants in chronic diseases such as cardiovascular disease and cancer is controversial. Evidence from prospective studies suggests that a high dietary intake of antioxidants is protective for cardiovascular disease and cancer, although findings have not been consistent and trial data have not been conclusive.[1–7] Ascorbic acid (vitamin C) plays a part in many biological processes, including free radical scavenging, collagen and hormone synthesis, haemostasis, and protection of lipid membranes which might affect chronic disease risk.[8–11] Investigators in some prospective studies have shown a significant inverse relation between ascorbic acid and cancer or cardiovascular disease, but the protective concentration and the potential size of the relation have varied between these studies. Results of some studies show only increased risk of mortality or cardiovascular disease at very low concentrations,[12] but no effect within the usual population range; conversely, those of others indicate only reduced risk in individuals with high concentrations or those who take supplements.[12] Findings from trials on the effect of supplementation have shown no change in mortality, but these trials have been generally small and of short duration.[14,15] Most studies have been in men or with data for men and women pooled. Data for women alone are more inconsistent than data on men.[13]

We present data from a prospective population study examining the relation between plasma ascorbic acid and subsequent mortality due to all causes, cardiovascular disease, ischaemic heart disease, and cancer in men and women.

Methods

Participants

The individuals in this analysis were part of EPIC-Norfolk, a prospective population study of 30 466 men and women aged between 45 and 79 years, resident in Norfolk, UK, who completed a baseline questionnaire survey, and of whom 25 663 attended a clinic visit.[16] They were recruited from age-sex registers of general practices in Norfolk as part of a nine-country collaborative study (EPIC, European Prospective Investigation into Cancer and Nutrition) designed to investigate dietary and other determinants of cancer. We obtained additional data for the EPIC-Norfolk cohort to enable the assessment of chronic disease determinants. Eligible participants were recruited by post. Because we requested individuals to provide detailed dietary, biological and other health data, and to be followed up over a few years, we had about a 45% response rate, so participants were not a random population sample. Nevertheless, they were closely similar to UK population samples with respect to many characteristics, including anthropometry, blood pressure, and lipids, but with a lower proportion of smokers.[16]

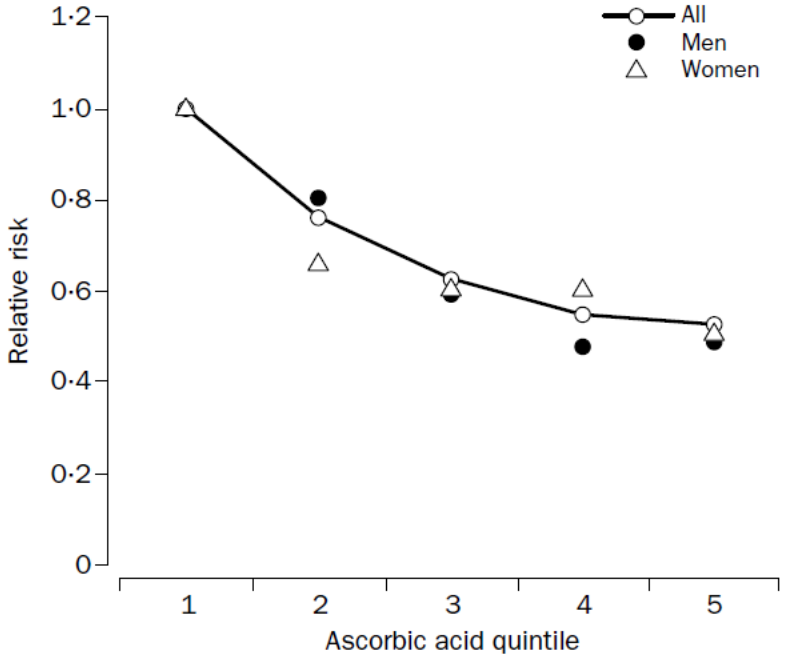

Figure 1: **Relative risk of total mortality by quintile of plasma ascorbic acid**
Age-adjusted and sex adjusted Cox regression model for relative risk, including a quadratic term for ascorbic-acid.

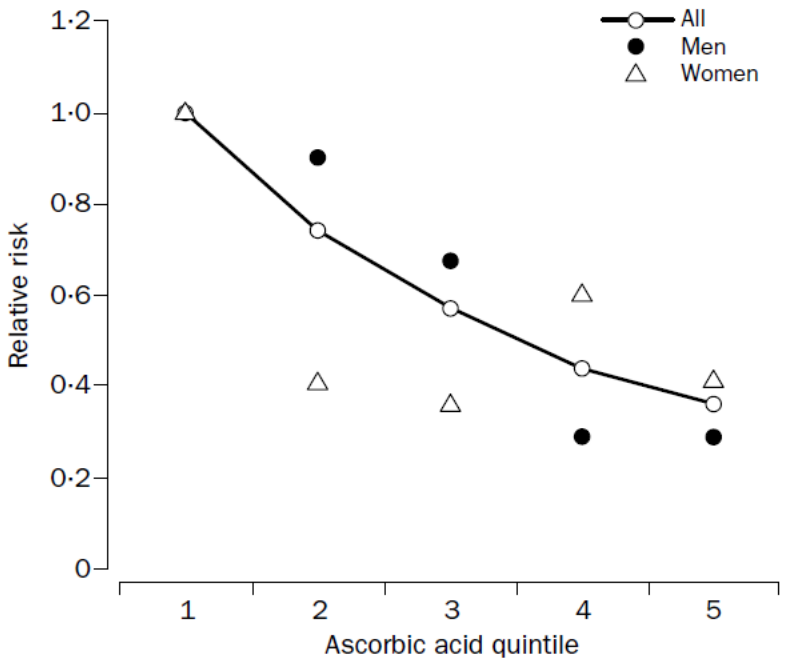

Figure 2: **Relative risk for cardiovascular disease mortality by quintile of plasma ascorbic acid**
Age-adjusted and sex-adjusted Cox regression model for relative risk, including a quadratic term for ascorbic acid.

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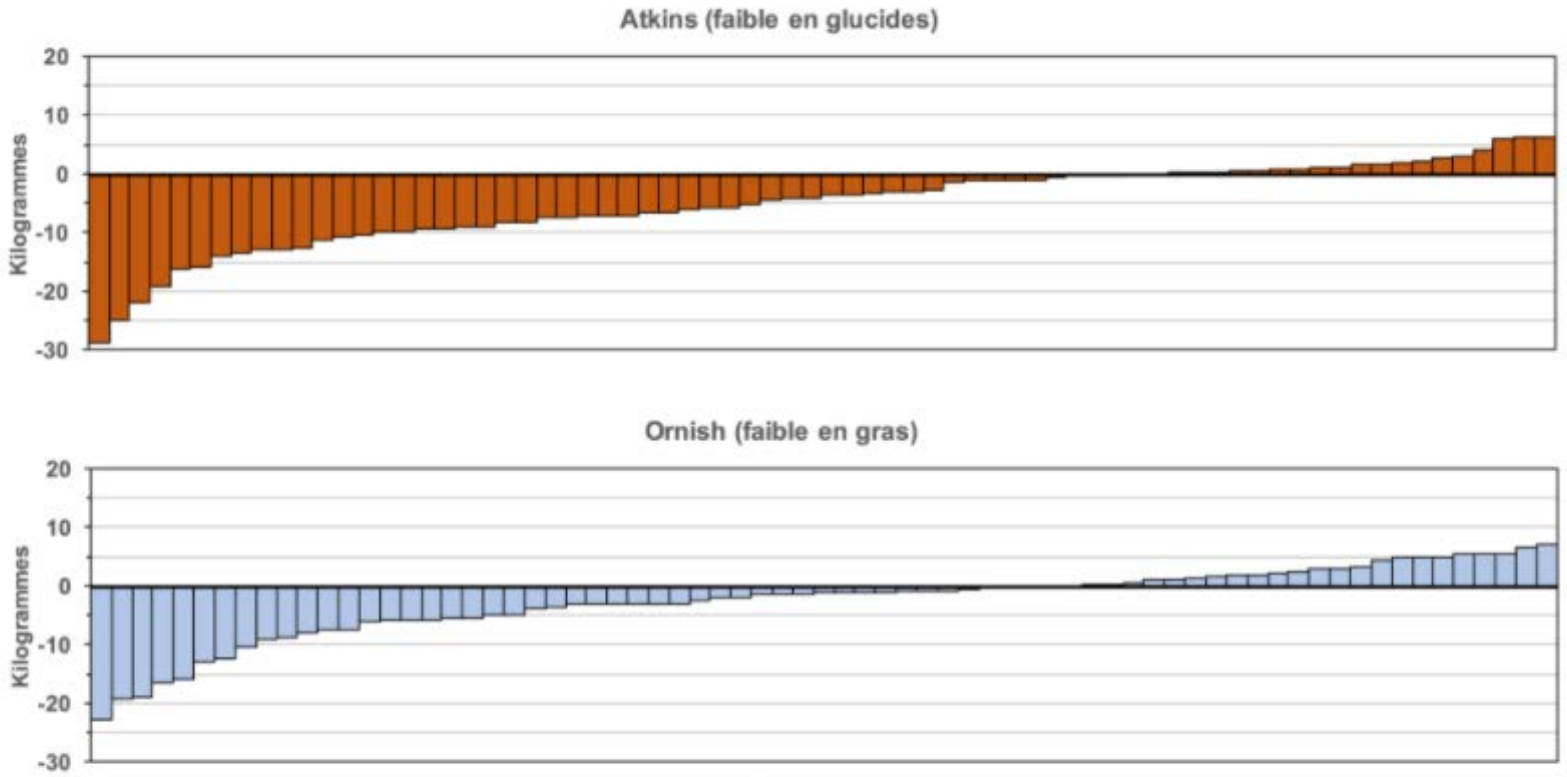

Figure 2. Distribution des variations de poids pour chacun des participants d'une étude comparant l'efficacité de régimes faibles en glucides (Atkins) ou en gras (Ornish). Adapté de Gardner (2012).

JAMA | Original Investigation

Effect of Low-Fat vs Low-Carbohydrate Diet on 12-Month Weight Loss in Overweight Adults and the Association With Genotype Pattern or Insulin Secretion

The DIETFITS Randomized Clinical Trial

Christopher D. Gardner, PhD; John F. Trepanowski, PhD; Liana C. Del Gobbo, PhD; Michelle E. Hauser, MD; Joseph Rigdon, PhD; John P. A. Ioannidis, MD, DSc; Manisha Desai, PhD; Abby C. King, PhD

IMPORTANCE Dietary modification remains key to successful weight loss. Yet, no one dietary strategy is consistently superior to others for the general population. Previous research suggests genotype or insulin-glucose dynamics may modify the effects of diets.

OBJECTIVE To determine the effect of a healthy low-fat (HLF) diet vs a healthy low-carbohydrate (HLC) diet on weight change and if genotype pattern or insulin secretion are related to the dietary effects on weight loss.

DESIGN, SETTING, AND PARTICIPANTS The Diet Intervention Examining The Factors Interacting with Treatment Success (DIETFITS) randomized clinical trial included 609 adults aged 18 to 50 years without diabetes with a body mass index between 28 and 40. The trial enrollment was from January 29, 2013, through April 14, 2015; the date of final follow-up was May 16, 2016. Participants were randomized to the 12-month HLF or HLC diet. The study also tested whether 3 single-nucleotide polymorphism multilocus genotype responsiveness patterns or insulin secretion (INS-30; blood concentration of insulin 30 minutes after a glucose challenge) were associated with weight loss.

INTERVENTIONS Health educators delivered the behavior modification intervention to HLF (n = 305) and HLC (n = 304) participants via 22 diet-specific small group sessions administered over 12 months. The sessions focused on ways to achieve the lowest fat or carbohydrate intake that could be maintained long-term and emphasized diet quality.

MAIN OUTCOMES AND MEASURES Primary outcome was 12-month weight change and determination of whether there were significant interactions among diet type and genotype pattern, diet and insulin secretion, and diet and weight loss.

RESULTS Among 609 participants randomized (mean age, 40 [SD, 7] years; 57% women; mean body mass index, 33 [SD, 3]; 244 [40%] had a low-fat genotype; 180 [30%] had a low-carbohydrate genotype; mean baseline INS-30, 93 μIU/mL), 481 (79%) completed the trial. In the HLF vs HLC diets, respectively, the mean 12-month macronutrient distributions were 48% vs 30% for carbohydrates, 29% vs 45% for fat, and 21% vs 23% for protein. Weight change at 12 months was −5.3 kg for the HLF diet vs −6.0 kg for the HLC diet (mean between-group difference, 0.7 kg [95% CI, −0.2 to 1.6 kg]). There was no significant diet-genotype pattern interaction (P = .20) or diet-insulin secretion (INS-30) interaction (P = .47) with 12-month weight loss. There were 18 adverse events or serious adverse events that were evenly distributed across the 2 diet groups.

CONCLUSIONS AND RELEVANCE In this 12-month weight loss diet study, there was no significant difference in weight change between a healthy low-fat diet vs a healthy low-carbohydrate diet, and neither genotype pattern nor baseline insulin secretion was associated with the dietary effects on weight loss. In the context of these 2 common weight loss diet approaches, neither of the 2 hypothesized predisposing factors was helpful in identifying which diet was better for whom.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01826591

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Supplemental content

CME Quiz at jamanetwork.com/learning and **CME Questions** page 715

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Table 3. 12-Month Change Estimates for Anthropometric Variables by Diet

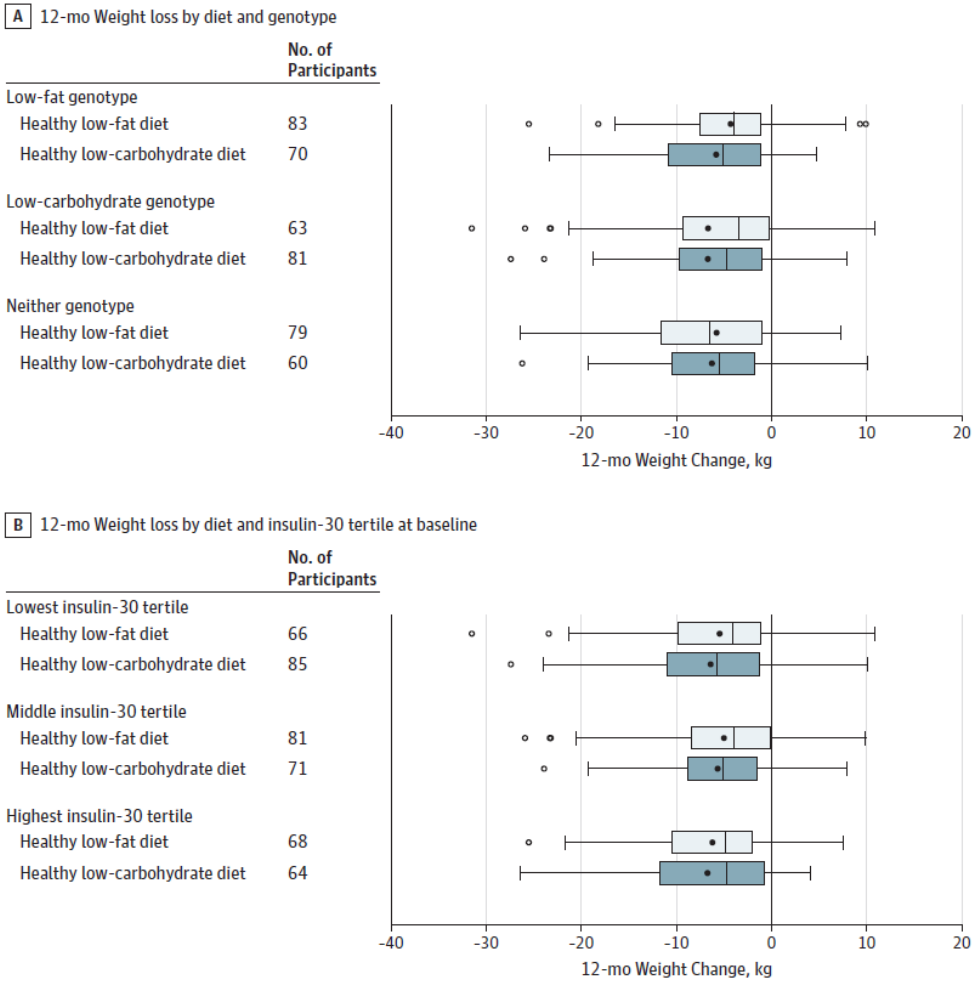
	12-mo Change Estimate (95% CI)[a]		
	Healthy Low-Fat Diet (n = 305)	Healthy Low-Carbohydrate Diet (n = 304)	Between-Group Difference (95% CI)[b]
Weight, kg	−5.29 (−5.93 to −4.65)	−5.99 (−6.63 to −5.35)	0.70 (−0.21 to 1.60)
Body mass index[c]	−1.75 (−1.97 to −1.52)	−2.07 (−2.30 to −1.85)	0.33 (0.01 to 0.64)
Body fat %[d]	−1.97 (−2.38 to −1.56)	−2.15 (−2.54 to −1.75)	0.18 (−0.40 to 0.75)
Waist circumference, cm	−3.74 (−4.64 to −2.84)	−4.41 (−5.31 to −3.51)	0.67 (−0.60 to 1.94)
Lipid level, mmol/L			
High-density lipoprotein cholesterol	0.40 (−0.37 to 1.18)	2.64 (1.87 to 3.41)	−2.24 (−3.33 to −1.15)
Low-density lipoprotein cholesterol	−2.12 (−4.70 to 0.47)	3.62 (1.04 to 6.19)	−5.74 (−9.38 to −2.09)
Triglycerides	−9.95 (−17.46 to −2.44)	−28.20 (−35.67 to −20.72)	18.25 (7.65 to 28.84)
Blood pressure, mm Hg			
Systolic	−3.18 (−4.33 to −2.03)	−3.72 (−4.86 to −2.58)	0.54 (−1.07 to 2.16)
Diastolic	−1.94 (−2.65 to −1.22)	−2.64 (−3.34 to −1.93)	0.70 (−0.31 to 1.71)
Fasting glucose, mg/dL	−3.67 (−4.90 to −2.44)	−2.10 (−3.32 to −0.87)	−1.58 (−3.31 to 0.16)
Fasting insulin, μIU/mL	−2.64 (−3.79 to −1.49)	−2.33 (−3.48 to −1.19)	−0.31 (−1.93 to 1.31)
Insulin-30, μIU/mL[e]	−15.38 (−21.13 to −9.62)	−11.48 (−17.18 to −5.78)	−3.90 (−12.00 to 4.20)
Metabolic syndrome, No. (%)[f]			
Had metabolic syndrome at baseline but not at 12 mo	36 (11.8)	36 (11.8)	
Had metabolic syndrome at baseline and 12 mo	39 (12.8)	36 (11.8)	
Did not have metabolic syndrome at baseline or 12 mo	128 (42.0)	137 (45.1)	
Did not have metabolic syndrome at baseline but had metabolic syndrome at 12 mo	13 (4.3)	11 (3.6)	
Respiratory exchange ratio[g]	−0.008 (−0.018 to 0.002)	−0.027 (−0.037 to −0.018)	0.020 (0.006 to 0.033)
Resting energy expenditure, kcal[g]	−66.45 (−96.65 to −36.26)	−76.93 (−106.68 to −47.19)	10.48 (−31.91 to 52.87)
Energy expenditure, kcal/kg/d	0.55 (0.20 to 0.90)	0.49 (0.13 to 0.84)	0.06 (−0.44 to 0.56)

SI conversion factors: To convert glucose to mmol/L, multiply by 0.0555; high-density and low-density lipoprotein cholesterol to mg/dL, divide by 0.0259; insulin to pmol/L, multiply by 6.945; triglycerides to mg/dL, divide by 0.0113.

and 123 in the healthy low-carbohydrate diet group. This was due to a combination of dropout and not having any data for cohort 1.

[e] Indicates the blood concentration of insulin at the 30-minute time point of an oral glucose tolerance test.

Figure 2. Interaction Among Diet and Genotype and Diet and Insulin-30 Tertile at Baseline and 12-Month Weight Loss



The black solid circle indicates the mean, the left and right borders of the box mark the first and third quartiles, the black vertical line indicates the median, the error bars indicate the 5th and 95th percentiles, and the hollow circles indicate the individuals whose values were outside the 5th or 95th percentiles. The No. of participants reflect data for the individuals who had weight data at these 2 genotype patterns. By design, as described in the initial National Institutes of Health grant application, those individuals with neither of the main 2 genotype patterns were not included in the main analyses. There were 39 participants who had compromised or missing DNA.

B, Three-way interaction term among diet, insulin, and the 12-month time

Ten Years of Life

Is It a Matter of Choice?

Gary E. Fraser, MB, ChB, PhD; David J. Shavlik, MSPH

Background: Relative risk estimates suggest that effective implementation of behaviors commonly advocated in preventive medicine should increase life expectancy, although there is little direct evidence.

Objective: To test the hypothesis that choices regarding diet, exercise, and smoking influence life expectancy.

Methods: A total of 34 192 California Seventh-Day Adventists (75% of those eligible) were enrolled in a cohort and followed up from 1976 to 1988. A mailed questionnaire provided dietary and other exposure information at study baseline. Mortality for all subjects was ascertained by matching to state death tapes and the National Death Index.

Results: California Adventists have higher life expectancies at the age of 30 years than other white Californians by 7.28 years (95% confidence interval, 6.59-7.97 years) in men and by 4.42 years (95% confidence interval, 3.96-4.88 years) in women, giving them perhaps the highest life expectancy of any formally described population. Commonly observed combinations of diet, exercise, body mass index, past smoking habits, and hormone replacement therapy (in women) can account for differences of up to 10 years of life expectancy among Adventists. A comparison of life expectancy when these factors take high-risk compared with low-risk values shows independent effects that vary between 1.06 and 2.74 years for different variables. The effect of each variable is assessed with all others at either medium- or high-risk levels.

Conclusions: Choices regarding diet, exercise, cigarette smoking, body weight, and hormone replacement therapy, in combination, appear to change life expectancy by many years. The longevity experience of Adventists probably demonstrates the beneficial effects of more optimal behaviors.

Arch Intern Med. 2001;161:1645-1652

Table 5. Expected Length of Life at Birth and at the Age of 65 Years: California Adventists Compared With International Populations

	Length of Life, y			
	Men		Women	
Country (Year)	At Birth	At Age 65 y	At Birth	At Age 65 y
Australia (1990)	73.9	15.2	80.0	19.0
Canada (1985-1987)	73.0	14.9	79.7	19.1
Denmark (1989-1990)	72.0	14.1	77.7	17.9
Finland (1989)	70.9	13.8	78.9	17.7
Iceland (1989-1990)	75.7	16.1	80.3	19.3
Japan (1990)	75.9	16.2	81.8	19.9
New Zealand (1987-1989)	71.6	14.1	77.6	17.8
Norway (1990)	73.4	14.6	79.8	18.6
United Kingdom (1985-1987)	71.9	13.4	77.6	17.3
United States (1990)	73.0	14.9	79.7	19.1
California Adventists (1980-1988)*	78.5	19.1	82.3	21.6
Vegetarians	80.2	20.3	84.8	22.6

*Hazards for those aged 0 to 29 years are those from California State data, as data for these ages are not available for Adventists. Non-Adventist data are taken from international longevity comparisons (1992).[22]

Non-Profit Produces First-Ever Agreement on Overall Principles of Healthy Eating

PR Newswire – BOSTON, MA (November 19, 2015)

agreement. Scientific co-chairs Dr. Walter Willett, Nutrition Chair of the Harvard School of Public Health and Dr. David Katz, Founding Director of the Yale Prevention Research Center, led the group in a two-day debate dissecting scientific studies and comparing diets to arrive at a clear outline of what healthy eating entails, agreeing on standards and sources of evidence, and the need to base judgments on the weight of evidence.

"The foods that define a healthy diet include abundant fruits, vegetables, nuts, whole grains, legumes and minimal amounts of refined starch, sugar and red meat, especially keeping processed red meat intake low. When you put it all together, that's a lot of common ground."

EN RÉSUMÉ

EAT FOOD,
MOSTLY PLANTS,
NOT TOO MUCH.

M Pollan

MEDICAL SCIENCE

Can lifestyle changes reverse coronary heart disease?

The Lifestyle Heart Trial

DEAN ORNISH SHIRLEY E. BROWN LARRY W. SCHERWITZ
JAMES H. BILLINGS WILLIAM T. ARMSTRONG THOMAS A. PORTS
SANDRA M. MCLANAHAN RICHARD L. KIRKEEIDE
RICHARD J. BRAND K. LANCE GOULD

In a prospective, randomised, controlled trial to determine whether comprehensive lifestyle changes affect coronary atherosclerosis after 1 year, 28 patients were assigned to an experimental group (low-fat vegetarian diet, stopping smoking, stress management training, and moderate exercise) and 20 to a usual-care control group. 195 coronary artery lesions were analysed by quantitative coronary angiography. The average percentage diameter stenosis regressed from 40·0 (SD 16·9)% to 37·8 (16·5)% in the experimental group yet progressed from 42·7 (15·5)% to 46·1 (18·5)% in the control group. When only lesions greater than 50% stenosed were analysed, the average percentage diameter stenosis regressed from 61·1 (8·8)% to 55·8 (11·0)% in the experimental group and progressed from 61·7 (9·5)% to 64·4 (16·3)% in the control group. Overall, 82% of experimental-group patients had an average change towards regression. Comprehensive lifestyle changes may be able to bring about regression of even severe coronary atherosclerosis after only 1 year, without use of lipid-lowering drugs.

Lancet 1990; **336**: 129-33.

Introduction

The Lifestyle Heart Trial is the first randomised, controlled clinical trial to determine whether patients outside hospital can be motivated to make and sustain comprehensive lifestyle changes and, if so, whether regression of coronary atherosclerosis can occur as a result of lifestyle changes alone. Over twenty clinical trials are being carried out to determine whether the progression of coronary atherosclerosis can be modified; in all of these, cholesterol-lowering drugs, plasmapheresis, or partial ileal bypass surgery are the primary interventions.[1]

We carried out trials in 1977 and 1980 to assess the short-term effects of lifestyle changes on coronary heart disease with non-invasive endpoint measures (improvements in cardiac risk factors, functional status, myocardial perfusion,[2] and left ventricular function[3]). However, the subjects of those studies were not living in the community during the trial, and we did not use angiography to assess changes in coronary atherosclerosis.

Patients and methods

Patients with angiographically documented coronary artery disease were randomly assigned to an experimental group or to a usual-care control group. Experimental-group patients were prescribed a lifestyle programme that included a low-fat vegetarian diet, moderate aerobic exercise, stress management training, stopping smoking, and group support. Control-group patients were not asked to make lifestyle changes, although they were free to do so. Progression or regression of coronary artery lesions was assessed in both groups by quantitative coronary angiography at baseline and after about a year.

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Intensive Lifestyle Changes for Reversal of Coronary Heart Disease

Dean Ornish, MD; Larry W. Scherwitz, PhD; James H. Billings, PhD, MPH; K. Lance Gould, MD; Terri A. Merritt, MS; Stephen Sparler, MA; William T. Armstrong, MD; Thomas A. Ports, MD; Richard L. Kirkeeide, PhD; Charissa Hogeboom, PhD; Richard J. Brand, PhD

Context.—The Lifestyle Heart Trial demonstrated that intensive lifestyle changes may lead to regression of coronary atherosclerosis after 1 year.

Objectives.—To determine the feasibility of patients to sustain intensive lifestyle changes for a total of 5 years and the effects of these lifestyle changes (without lipid-lowering drugs) on coronary heart disease.

Design.—Randomized controlled trial conducted from 1986 to 1992 using a randomized invitational design.

Patients.—Forty-eight patients with moderate to severe coronary heart disease were randomized to an intensive lifestyle change group or to a usual-care control group, and 35 completed the 5-year follow-up quantitative coronary arteriography.

Setting.—Two tertiary care university medical centers.

Intervention.—Intensive lifestyle changes (10% fat whole foods vegetarian diet, aerobic exercise, stress management training, smoking cessation, group psychosocial support) for 5 years.

Main Outcome Measures.—Adherence to intensive lifestyle changes, changes in coronary artery percent diameter stenosis, and cardiac events.

Results.—Experimental group patients (20 [71%] of 28 patients completed 5-year follow-up) made and maintained comprehensive lifestyle changes for 5 years, whereas control group patients (15 [75%] of 20 patients completed 5-year follow-up) made more moderate changes. In the experimental group, the average percent diameter stenosis at baseline decreased 1.75 absolute percentage points after 1 year (a 4.5% relative improvement) and by 3.1 absolute percentage points after 5 years (a 7.9% relative improvement). In contrast, the average percent diameter stenosis in the control group increased by 2.3 percentage points after 1 year (a 5.4% relative worsening) and by 11.8 percentage points after 5 years (a 27.7% relative worsening) ($P = .001$ between groups. Twenty-five cardiac events occurred in 28 experimental group patients vs 45 events in 20 control group patients during the 5-year follow-up (risk ratio for any event for the control group, 2.47 [95% confidence interval, 1.48-4.20]).

Conclusions.—More regression of coronary atherosclerosis occurred after 5 years than after 1 year in the experimental group. In contrast, in the control group, coronary atherosclerosis continued to progress and more than twice as many cardiac events occurred.

JAMA. 1998;280:2001-2007

From the Department of Medicine (Dr Ornish), and the Division of Cardiology (Dr Armstrong), California Pacific Medical Center, San Francisco; the Department of Medicine (Dr Ornish), the Division of Cardiology, Cardiac Catheterization Laboratory, Cardiovascular Research Institute (Dr Ports), and the Division of Biostatistics (Drs Brand and Hogeboom), School of Medicine, University of California, San Francisco; the Division of Cardiology, University of Texas Medical School, Houston (Drs Gould and Kirkeeide); and the Preventive Medicine Research Institute, Sausalito, Calif (Drs Ornish Scherwitz, and Billings, Mr Sparler, and Ms Merritt).

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THE LIFESTYLE Heart Trial was the first randomized clinical trial to investigate whether ambulatory patients could be motivated to make and sustain comprehensive lifestyle changes and, if so, whether the progression of coronary atherosclerosis could be stopped or reversed without using lipid-lowering drugs as measured by computer-assisted quantitative coronary arteriography. This study derived from earlier studies that used noninvasive measures.[1,2]

After 1 year, we found that experimental group participants were able to make and maintain intensive lifestyle changes and had a 37.2% reduction in low-density lipoprotein (LDL) cholesterol levels and a 91% reduction in the frequency of anginal episodes.[3] Average percent diameter stenosis regressed from 40.0% at baseline to 37.8% 1 year later, a change that was correlated with the degree of lifestyle change. In contrast, patients in the usual-care control group made more moderate changes in lifestyle, reduced LDL cholesterol levels by 6%, and had a 165% increase in the frequency of reported anginal episodes. Average percent diameter stenosis progressed from 42.7% to 46.1%.

Given these encouraging findings, we extended the study for an additional 4 years to determine (1) the feasibility of patients sustaining intensive changes in diet and lifestyle for a much longer time, and (2) the effects of these changes on risk factors, coronary atherosclerosis, myocardial perfusion, and cardiac events after 4 additional years.

METHODS

The design, recruitment, and study population were previously described.[3-5] In brief, we recruited men and women

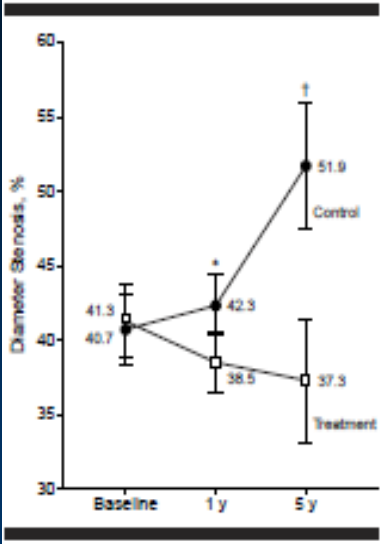

Figure 1.—Mean percentage diameter stenosis in treatment and control groups at baseline, 1 year, and 5 years. Error bars represent SEM; asterisk, $P = .02$ by between-group 2-tailed test; dagger, $P = .001$ by between-group 2-tailed test.

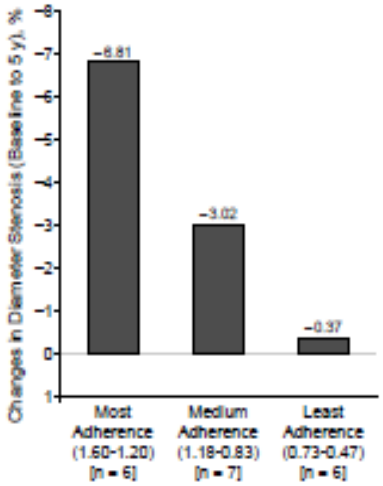

Figure 2.—Changes in percentage diameter stenosis by 5-year adherence tertiles for the experimental group.

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The authors reported no potential conflict of interest relevant to this article.

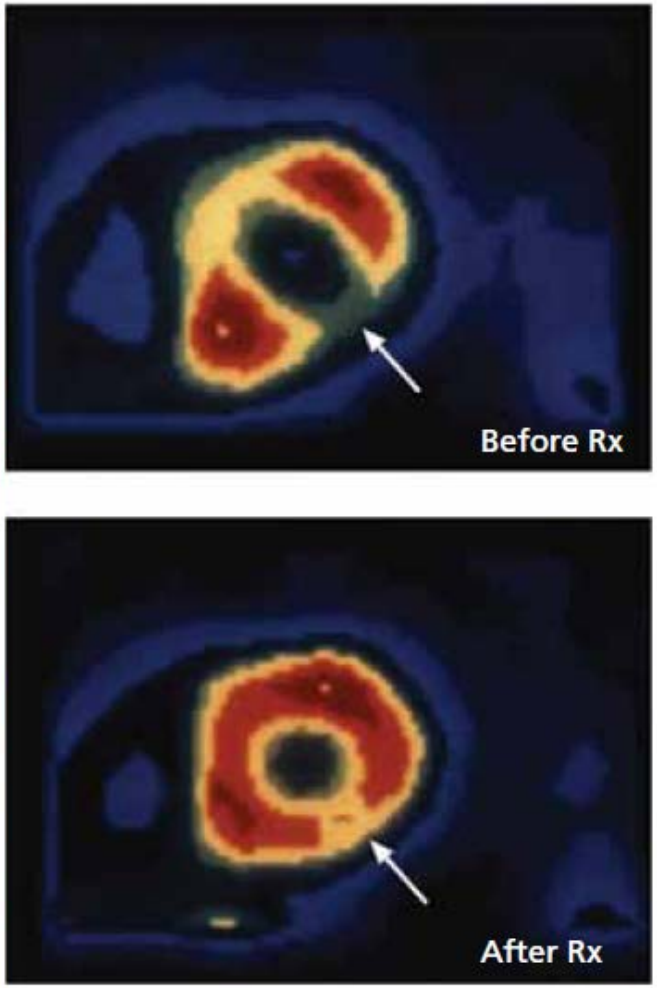
ORIGINAL RESEARCH

A way to reverse CAD?

Though current medical and surgical treatments manage coronary artery disease, they do little to prevent or stop it. Nutritional intervention, as shown in our study and others, has halted and even reversed CAD.

FIGURE 1

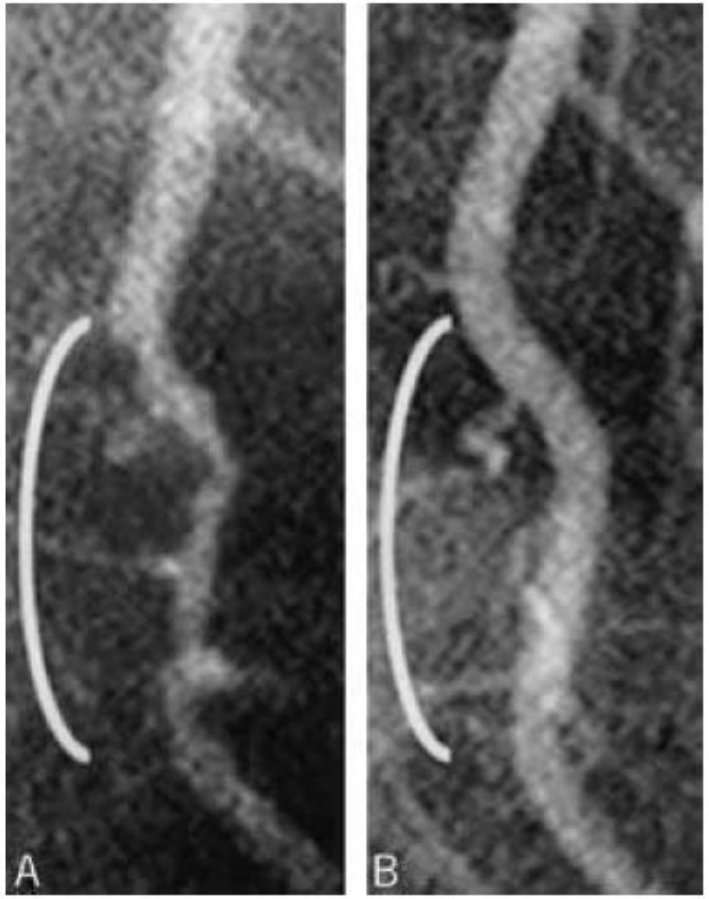
Restoration of myocardial perfusion[2]



Positron emission tomography performed on a patient with coronary artery disease shows an area of myocardium with insufficient blood flow (top). Following only 3 weeks of plant-based nutritional intervention, normal blood flow was restored (bottom).

FIGURE 2

Reversal of coronary artery disease[4]



Coronary angiography reveals a diseased distal left anterior descending artery (A). Following 32 months of a plant-based nutritional intervention without cholesterol-lowering medication, the artery regained its normal configuration (B).

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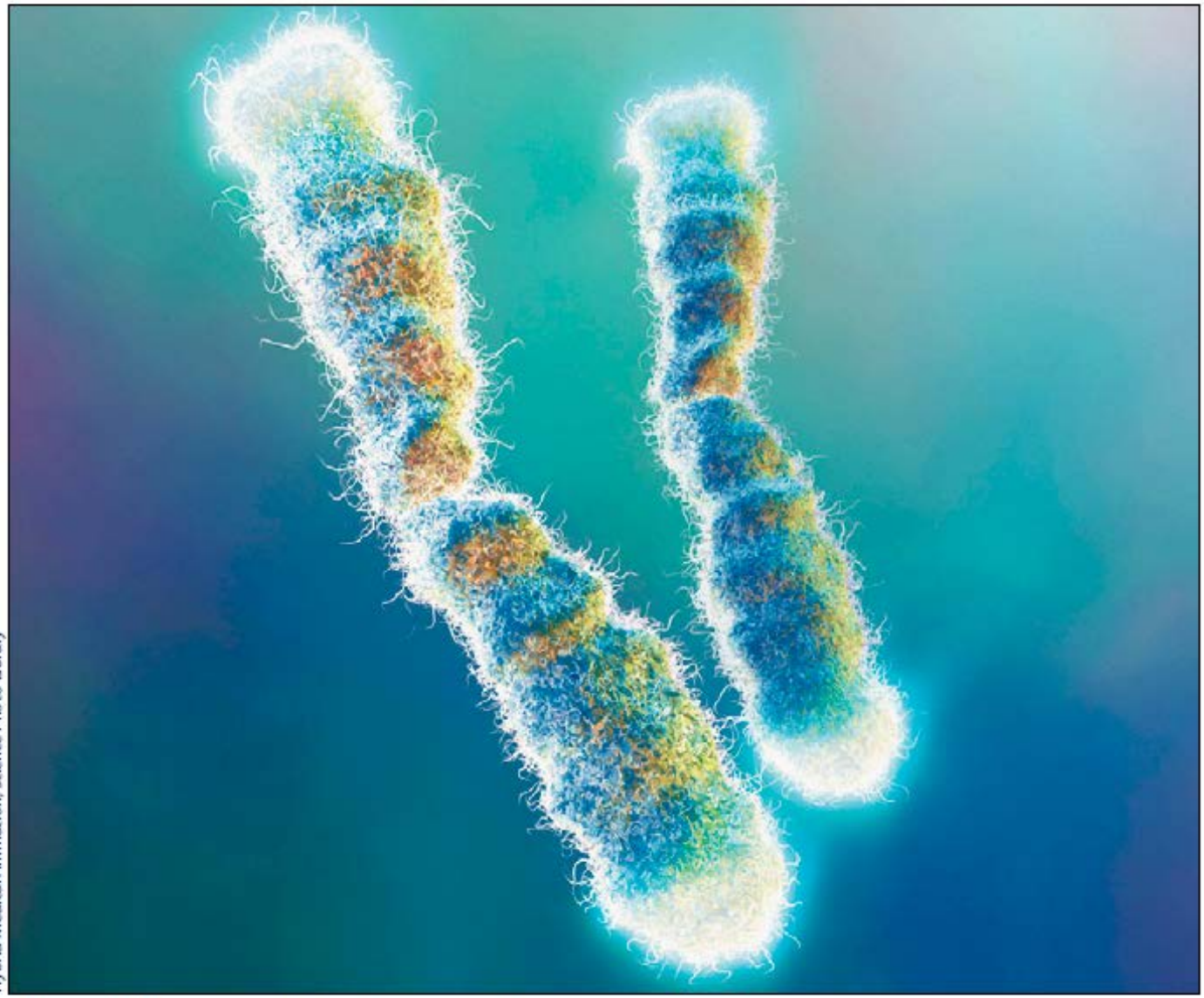

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Telomeres help prevent the loss of genetic information

Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study

Dean Ornish, Jue Lin, June M Chan, Elissa Epel, Colleen Kemp, Gerdi Weidner, Ruth Marlin, Steven J Frenda, Mark Jesus M Magbanua, Jennifer Daubenmier, Ivette Estay, Nancy K Hills, Nita Chainani-Wu, Peter R Carroll, Elizabeth H Blackburn

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Summary

Background Telomere shortness in human beings is a prognostic marker of ageing, disease, and premature morbidity. We previously found an association between 3 months of comprehensive lifestyle changes and increased telomerase activity in human immune-system cells. We followed up participants to investigate long-term effects.

Methods This follow-up study compared ten men and 25 external controls who had biopsy-proven low-risk prostate cancer and had chosen to undergo active surveillance. Eligible participants were enrolled between 2003 and 2007 from previous studies and selected according to the same criteria. Men in the intervention group followed a programme of comprehensive lifestyle changes (diet, activity, stress management, and social support), and the men in the control group underwent active surveillance alone. We took blood samples at 5 years and compared relative telomere length and telomerase enzymatic activity per viable cell with those at baseline, and assessed their relation to the degree of lifestyle changes.

Findings Relative telomere length increased from baseline by a median of 0·06 telomere to single-copy gene ratio (T/S) units (IQR 0·05 to 0·11) in the lifestyle intervention group, but decreased in the control group (−0·03 T/S units

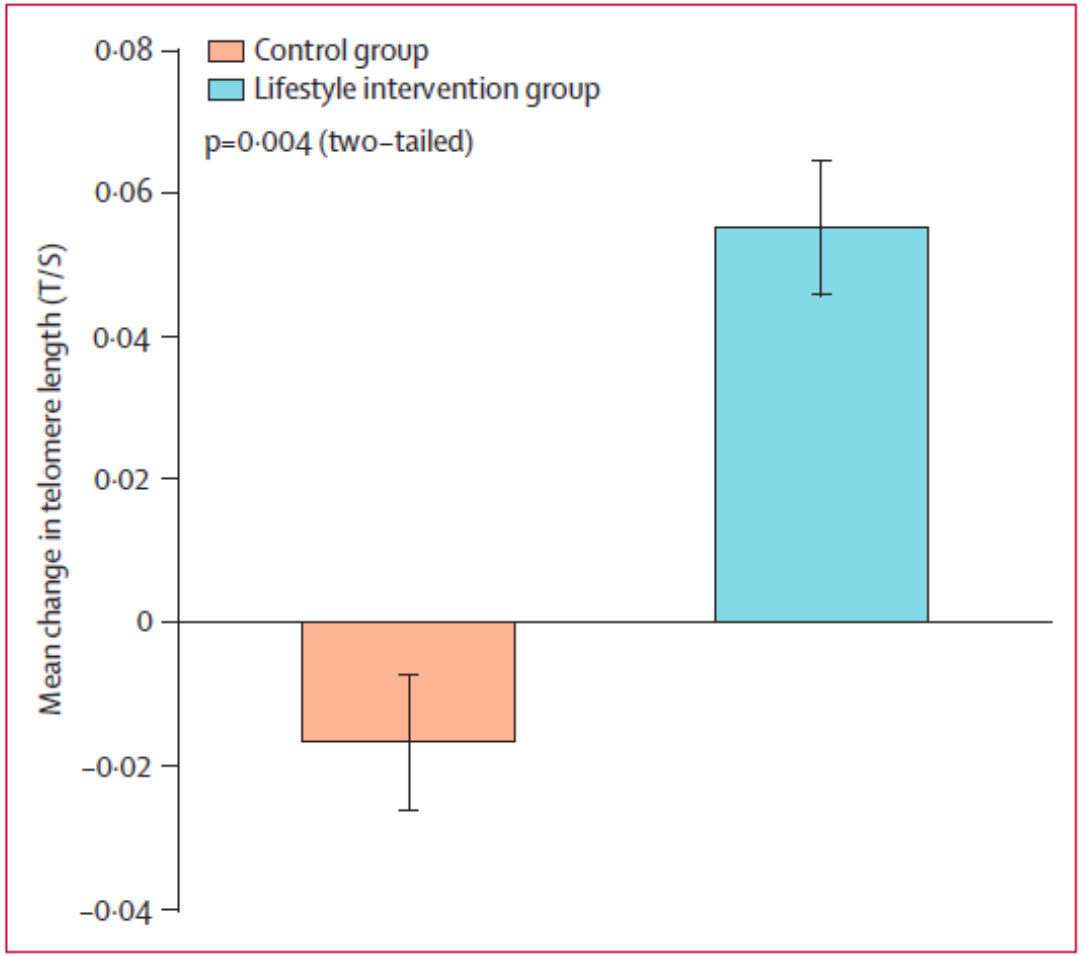

***Figure 1*: Mean change in relative telomere length over 5 years with lifestyle intervention compared with control**

Vertical lines represent 1 SEM. T/S=telomere to single-copy gene ratio units.

ORIGINAL ARTICLE

Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease

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ABSTRACT

BACKGROUND

Both genetic and lifestyle factors contribute to individual-level risk of coronary artery disease. The extent to which increased genetic risk can be offset by a healthy lifestyle is unknown.

METHODS

Using a polygenic score of DNA sequence polymorphisms, we quantified genetic risk for coronary artery disease in three prospective cohorts — 7814 participants in the Atherosclerosis Risk in Communities (ARIC) study, 21,222 in the Women's Genome Health Study (WGHS), and 22,389 in the Malmö Diet and Cancer Study (MDCS) — and in 4260 participants in the cross-sectional BioImage Study for whom genotype and covariate data were available. We also determined adherence to a healthy lifestyle among the participants using a scoring system consisting of four factors: no current smoking, no obesity, regular physical activity, and a healthy diet.

RESULTS

The relative risk of incident coronary events was 91% higher among participants at high genetic risk (top quintile of polygenic scores) than among those at low genetic risk (bottom quintile of polygenic scores) (hazard ratio, 1.91; 95% confidence interval [CI], 1.75 to 2.09). A favorable lifestyle (defined as at least three of the four healthy lifestyle factors) was associated with a substantially lower risk of coronary events than an unfavorable lifestyle (defined as no or only one healthy lifestyle factor), regardless of the genetic risk category. Among participants at high genetic risk, a favorable lifestyle was associated with a 46% lower relative risk of coronary events than an unfavorable lifestyle (hazard ratio, 0.54; 95% CI, 0.47 to 0.63). This finding corresponded to a reduction in the standardized 10-year incidence of coronary events from 10.7% for an unfavorable lifestyle to 5.1% for a favorable lifestyle in ARIC, from 4.6% to 2.0% in WGHS, and from 8.2% to 5.3% in MDCS. In the BioImage Study, a favorable lifestyle was associated with significantly less coronary-artery calcification within each genetic risk category.

CONCLUSIONS

Across four studies involving 55,685 participants, genetic and lifestyle factors were independently associated with susceptibility to coronary artery disease. Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease than was an unfavorable lifestyle. (Funded by the National Institutes of Health and others.)

From the Center for Human Genetic Research and Cardiology Division, Massachusetts General Hospital (A.V.K., P.N., S.K.), and the Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital (N.R.C., D.I.C., P.M.R.), Boston, and the Program in Medical and Population Genetics, Broad Institute, Cambridge (A.V.K., C.A.E., A.G.B., S.K.) — all in Massachusetts; the Department of Clinical Sciences, Lund University, Malmö, Sweden (I.D., O.M., M.O.-M.); the Cardiovascular Institute, Mount Sinai Medical Center, Icahn School of Medicine at Mount Sinai, New York (U.B., R.M., V.F.); Department of Genetics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia (D.J.R.); and the University of Texas Health Science Center School of Public Health, Houston (E.B.). Address reprint requests to Dr. Kathiresan at the Center for Human Genetics Research, Massachusetts General Hospital, 185 Cambridge St., CPZN 5.252, Boston, MA 02114, or at skathiresan1@mgh.harvard.edu.

Drs. Khera and Emdin contributed equally to this article.

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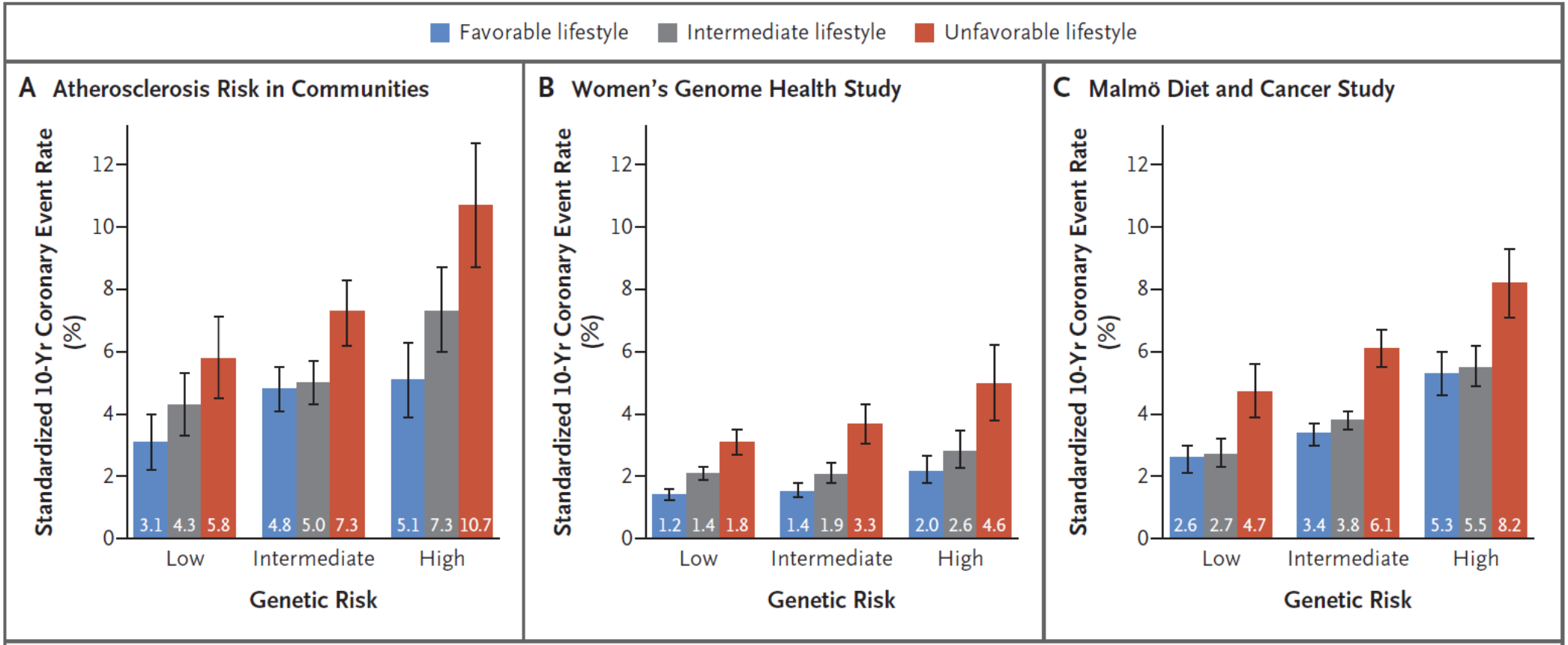

Figure 3. 10-Year Coronary Event Rates, According to Lifestyle and Genetic Risk in the Prospective Cohorts.

Shown are standardized 10-year cumulative incidence rates for coronary events in the three prospective cohorts, according to lifestyle and genetic risk. Standardization was performed to cohort-specific population averages for each covariate. The I bars represent 95% confidence intervals.

Rohrmann et al. BMC Medicine 2013, 11:63
http://www.biomedcentral.com/1741-7015/11/63

Metabolism, diet and disease

BMC Medicine

RESEARCH ARTICLE Open Access

Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition

Sabine Rohrmann[1,2*], Kim Overvad[3], H Bas Bueno-de-Mesquita[4,5], Marianne U Jakobsen[3], Rikke Egeberg[6], Anne Tjønneland[6], Laura Nailler[7,8], Marie-Christine Boutron-Ruault[7,8], Françoise Clavel-Chapelon[7,8], Vittorio Krogh[9], Domenico Palli[10], Salvatore Panico[11], Rosario Tumino[12], Fulvio Ricceri[13], Manuela M Bergmann[14], Heiner Boeing[14], Kuanrong Li[2], Rudolf Kaaks[2], Kay-Tee Khaw[15], Nicholas J Wareham[16], Francesca L Crowe[17], Timothy J Key[17], Androniki Naska[18], Antonia Trichopoulou[18,19], Dimitrios Trichopoulos[19,20,21], Max Leenders[5], Petra HM Peeters[22,23], Dagrun Engeset[24], Christine L Parr[25], Guri Skeie[24], Paula Jakszyn[26], María-José Sánchez[27,28], José M Huerta[27,29], M Luisa Redondo[30], Aurelio Barricarte[28,31], Pilar Amiano[28,32], Isabel Drake[33], Emily Sonestedt[33], Göran Hallmans[34], Ingegerd Johansson[35], Veronika Fedirko[36], Isabelle Romieux[36], Pietro Ferrari[36], Teresa Norat[23], Anne C Vergnaud[23], Elio Riboli[23] and and Jakob Linseisen[2,37]

Abstract

Background: Recently, some US cohorts have shown a moderate association between red and processed meat consumption and mortality supporting the results of previous studies among vegetarians. The aim of this study was to examine the association of red meat, processed meat, and poultry consumption with the risk of early death in the European Prospective Investigation into Cancer and Nutrition (EPIC).

Methods: Included in the analysis were 448,568 men and women without prevalent cancer, stroke, or myocardial infarction, and with complete information on diet, smoking, physical activity and body mass index, who were between 35 and 69 years old at baseline. Cox proportional hazards regression was used to examine the association of meat consumption with all-cause and cause-specific mortality.

Results: As of June 2009, 26,344 deaths were observed. After multivariate adjustment, a high consumption of red meat was related to higher all-cause mortality (hazard ratio (HR) = 1.14, 95% confidence interval (CI) 1.01 to 1.28, 160+ versus 10 to 19.9 g/day), and the association was stronger for processed meat (HR = 1.44, 95% CI 1.24 to 1.66, 160+ versus 10 to 19.9 g/day). After correction for measurement error, higher all-cause mortality remained significant only for processed meat (HR = 1.18, 95% CI 1.11 to 1.25, per 50 g/d). We estimated that 3.3% (95% CI 1.5% to 5.0%) of deaths could be prevented if all participants had a processed meat consumption of less than

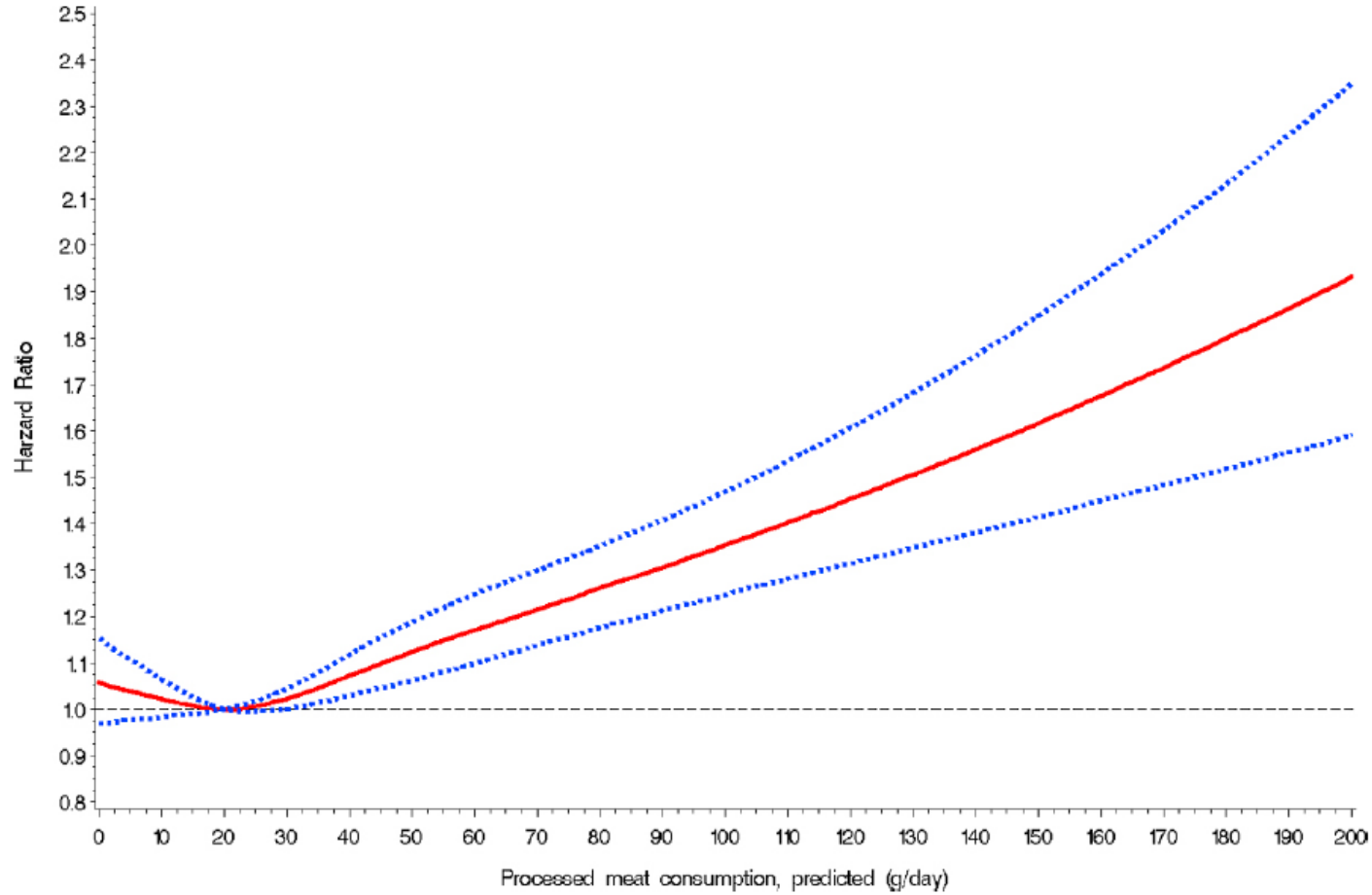

Figure 1 Nonparametric regression curve for the relation of processed meat intake at recruitment with all-cause mortality, European Prospective Investigation into Cancer and Nutrition (EPIC), 1992-2009. Solid line, effect estimate; dotted lines, 95 percent confidence interval.

ARTICLES

nature medicine

Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis

Robert A Koeth[1,2], Zeneng Wang[1,2], Bruce S Levison[1,2], Jennifer A Buffa[1,2], Elin Org[3], Brendan T Sheehy[1], Earl B Britt[1,2], Xiaoming Fu[1,2], Yuping Wu[4], Lin Li[1,2], Jonathan D Smith[1,2,5], Joseph A DiDonato[1,2], Jun Chen[6], Hongzhe Li[6], Gary D Wu[7], James D Lewis[6,8], Manya Warrier[9], J Mark Brown[9], Ronald M Krauss[10], W H Wilson Tang[1,2,5], Frederic D Bushman[5], Aldons J Lusis[3] & Stanley L Hazen[1,2,5]

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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.

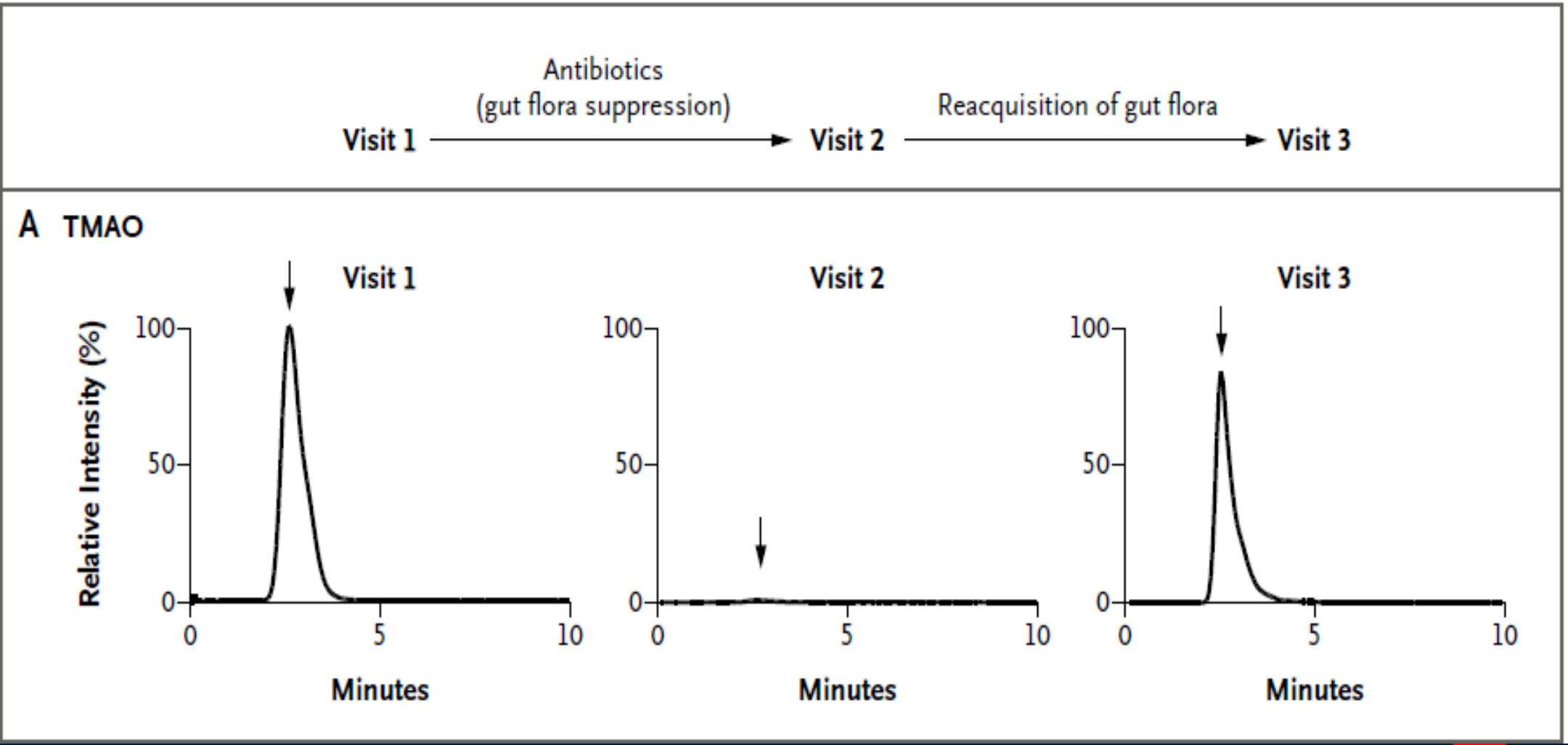

Antibiotics
(gut flora suppression)
Visit 1
Visit 2
Reacquisition of gut flora
Visit 3
A TMAO
Visit 1
Visit 2
Visit 3
Relative Intensity (%)
100
50
0
0
5
10
Minutes

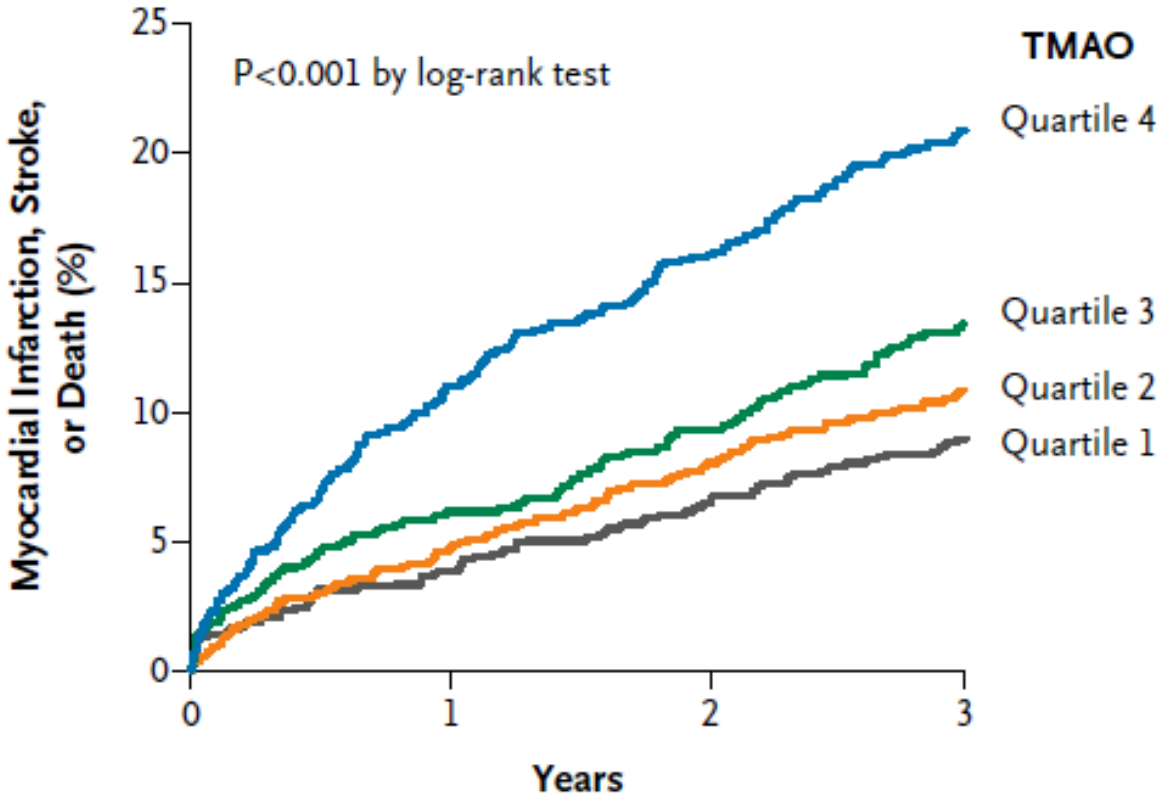
Table 2. Risk of a Major Adverse Cardiovascular Event at 3 Years, According to Quartile of TMAO Level.*

Risk of Event	TMAO Level					
	Quartile 1	Quartile 2		Quartile 3		Quartile 4	
	reference	hazard ratio (95% CI)	P value	hazard ratio (95% CI)	P value	hazard ratio (95% CI)	P value
Unadjusted hazard ratio	1.00	1.24 (0.93–1.66)	0.15	1.53 (1.16–2.02)	0.003	2.54 (1.96–3.28)	<0.001
Adjusted hazard ratio							
Model 1†	1.00	1.14 (0.86–1.53)	0.37	1.29 (0.98–1.71)	0.07	1.88 (1.44–2.44)	<0.001
Model 2‡	1.00	1.08 (0.79–1.48)	0.61	1.15 (0.85–1.56)	0.36	1.49 (1.10–2.03)	0.01
Model 3§	1.00	1.06 (0.77–1.45)	0.72	1.11 (0.82–1.51)	0.50	1.43 (1.05–1.94)	0.02

* A major adverse cardiovascular event was defined as death, myocardial infarction, or stroke. The quartiles of TMAO levels are as follows: quartile 1, less than 2.43 μM; quartile 2 2.43 to 3.66 μM; quartile 3, 3.67 to 6.18 μM; and quartile 4, more than 6.18 μM. Hazard ratios and P values are for the comparison with quartile 1.

† In model 1, hazard ratios were adjusted for traditional risk factors (age, sex, smoking status, systolic blood pressure, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, and status with respect to diabetes mellitus), plus log-transformed high-sensitivity C-reactive protein level.

‡ In model 2, hazard ratios were adjusted for all factors in model 1, plus myeloperoxidase level, log-transformed estimated glomerular filtration rate, total white-cell count, body-mass index, and status with respect to receipt of certain medications



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.

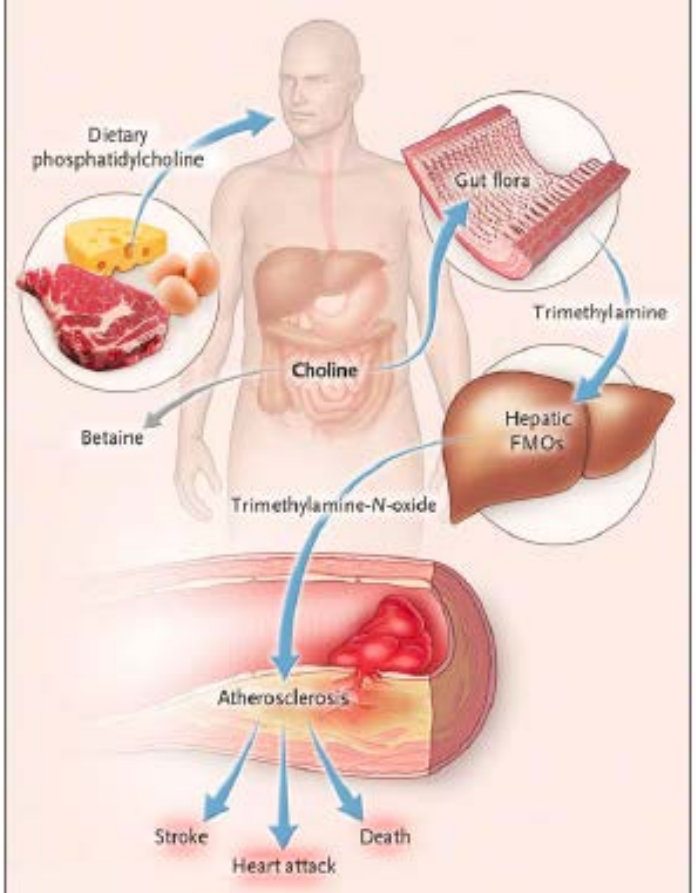


Figure 3. Pathways Linking Dietary Phosphatidylcholine, Intestinal Microbiota, and Incident Adverse Cardiovascular Events.

Ingested phosphatidylcholine (lecithin), the major dietary source of total choline, is acted on by intestinal lipases to form a variety of metabolic products, including the choline-containing nutrients glycerophosphocholine, phosphocholine, and choline. Choline-containing nutrients that reach the cecum and large bowel may serve as fuel for intestinal microbiota (gut flora), producing trimethylamine (TMA). TMA is rapidly further oxidized to trimethylamine-*N*-oxide (TMAO) by hepatic flavin-containing monooxygenases (FMOs). TMAO enhances the accumulation of cholesterol in macrophages, the accumulation of foam cells in artery walls, and atherosclerosis,[7] all factors that are associated with an increased risk of heart attack, stroke, and death. Choline can also be oxidized to betaine in both the liver and kidneys.[20] Dietary betaine can serve as a substrate for bacteria to form TMA[21] and presumably TMAO.

EUROPEAN SOCIETY OF CARDIOLOGY®

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REVIEW

Nutrition in cardiovascular disease

The gut microbiome as novel cardio-metabolic target: the time has come!

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Energy and Health 5

Food, livestock production, energy, climate change, and health

Anthony J McMichael, John W Powles, Colin D Butler, Ricardo Uauy

Food provides energy and nutrients, but its acquisition requires energy expenditure. In post-hunter-gatherer societies, extra-somatic energy has greatly expanded and intensified the catching, gathering, and production of food. Modern relations between energy, food, and health are very complex, raising serious, high-level policy challenges. Together with persistent widespread under-nutrition, over-nutrition (and sedentarism) is causing obesity and associated serious health consequences. Worldwide, agricultural activity, especially livestock production, accounts for about a fifth of total greenhouse-gas emissions, thus contributing to climate change and its adverse health consequences, including the threat to food yields in many regions. Particular policy attention should be paid to the health risks posed by the rapid worldwide growth in meat consumption, both by exacerbating climate change and by directly contributing to certain diseases. To prevent increased greenhouse-gas emissions from this production sector, both the average worldwide consumption level of animal products and the intensity of emissions from livestock production must be reduced. An international contraction and convergence strategy offers a feasible route to such a goal. The current global average meat consumption is 100 g per person per day, with about a ten-fold variation between high-consuming and low-consuming populations. 90 g per day is proposed as a working global target, shared more evenly, with not more than 50 g per day coming from red meat from ruminants (ie, cattle, sheep, goats, and other digastric grazers).

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This is the fifth in a **Series** of six papers about energy and health

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L'ombre portée
de l'élevage
impacts environnementaux et
options pour leur atténuation
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