Cette présentation a été effectuée le 4 décembre 2018 au cours de la journée « La santé cognitive, nouvelle cible de prévention pour la santé publique » dans le cadre des 22es Journées annuelles de santé publique (JASP 2018). L'ensemble des présentations est disponible sur le site Web des JASP à la section Éditions précédentes au : https://www.inspq.qc.ca/jasp.

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

Université de Montréal

EXERCICE, ALIMENTATION ET PRÉVENTION CARDIOVASCULAIRE

MARTIN JUNEAU MD FRCP
INSTITUT DE CARDIOLOGIE DE MONTRÉAL
CENTRE ÉPIC

JASP
4 DÉCEMBBRE 2018

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CONFLITS D'INTÉRÊT

Subventions pour les CLINIQUES de prévention ICM-ÉPIC

BMO :	2 000 000 $ (2007-2017)
Manuvie :	300 000 $ (2008-2013)
Sun Life :	200 000 $ (2007-2009)
Cascades :	250 000 $ (2009-2014)
Banque Scotia:	500 000 $ (2011-2016)
IGA:	270 000 $ (2017-2018)
Saputo:	5 000 000 $ (2016-2021)

Subventions de RECHERCHE

Fondation ÉPIC:150 000 $ /an
Fondation ICM: 100 000 $ /an
Fondation Saputo: 5 000 000$ (2016-2021)

AUCUNE CONFÉRENCE SUR LES MÉDICAMENTS

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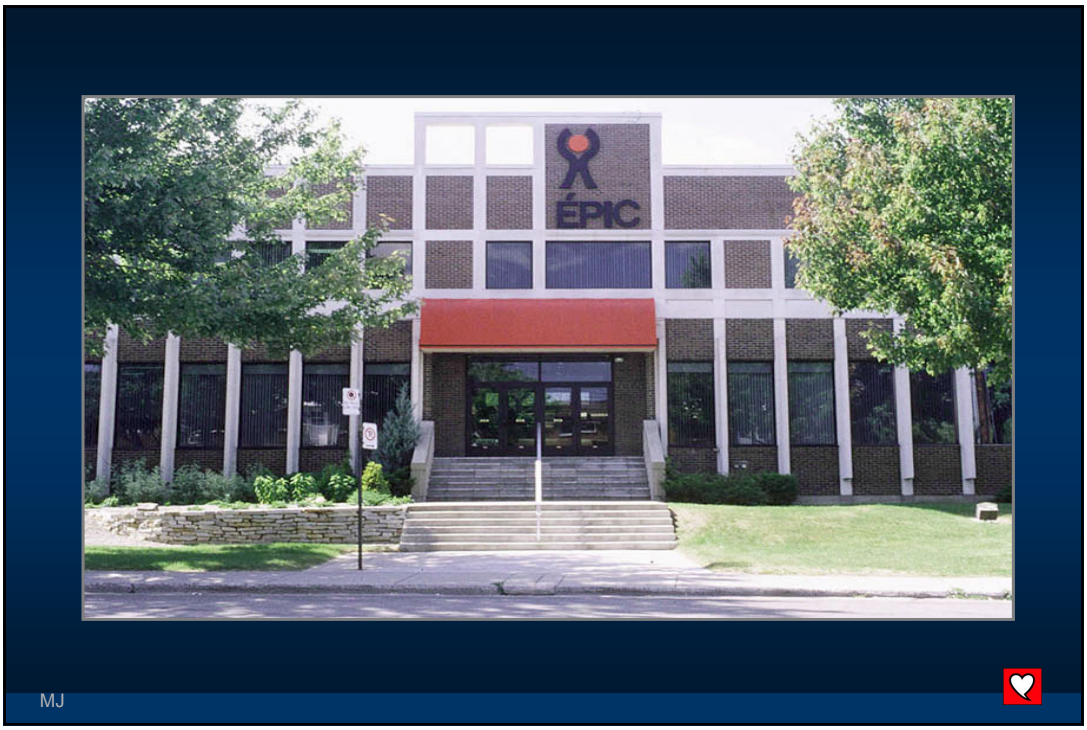
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SPINNING
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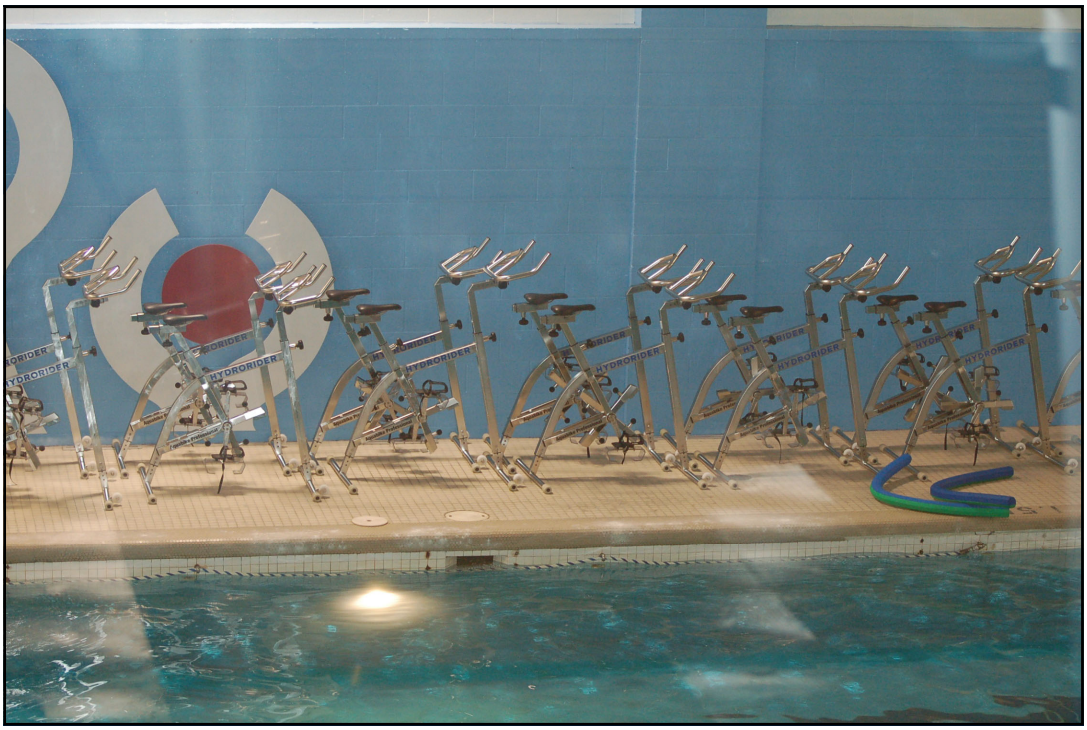
HYDRORIDER


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CANTROL
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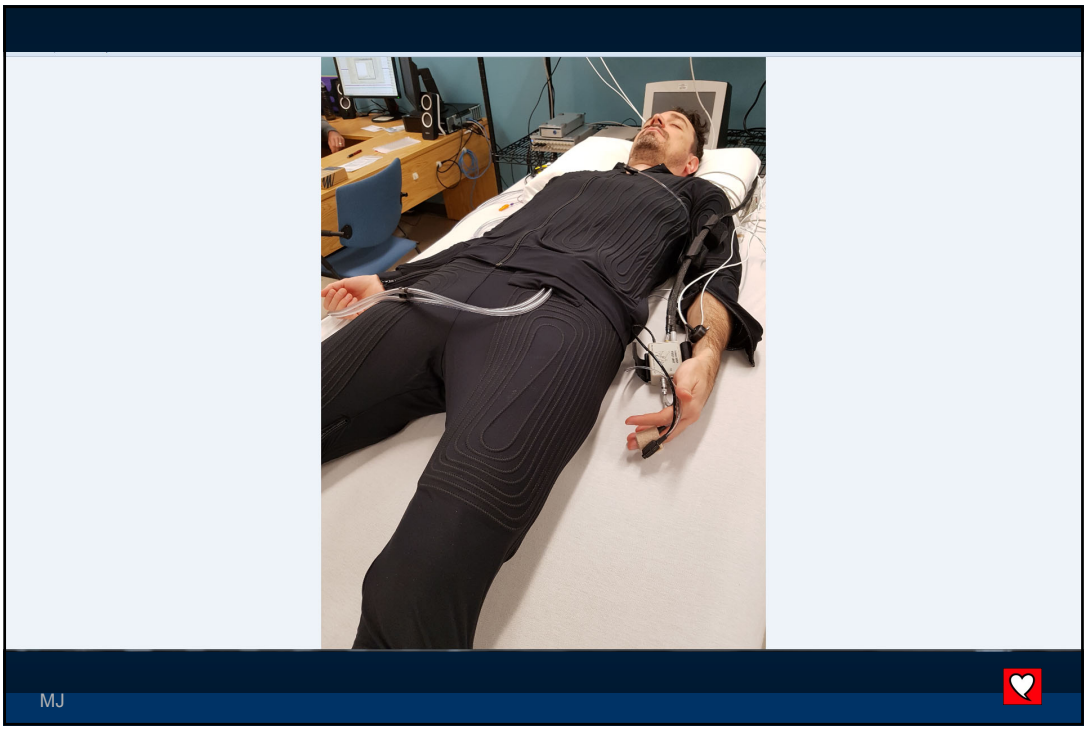
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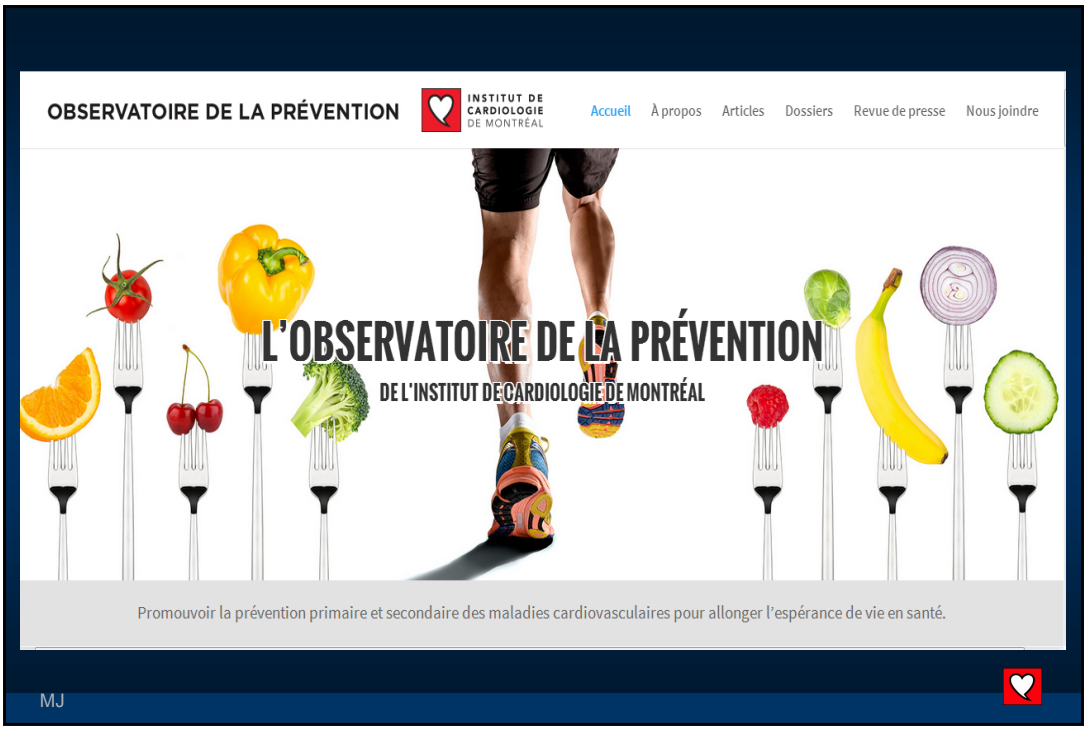
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Promouvoir la prévention primaire et secondaire des maladies cardiovasculaires pour allonger l'espérance de vie en santé.
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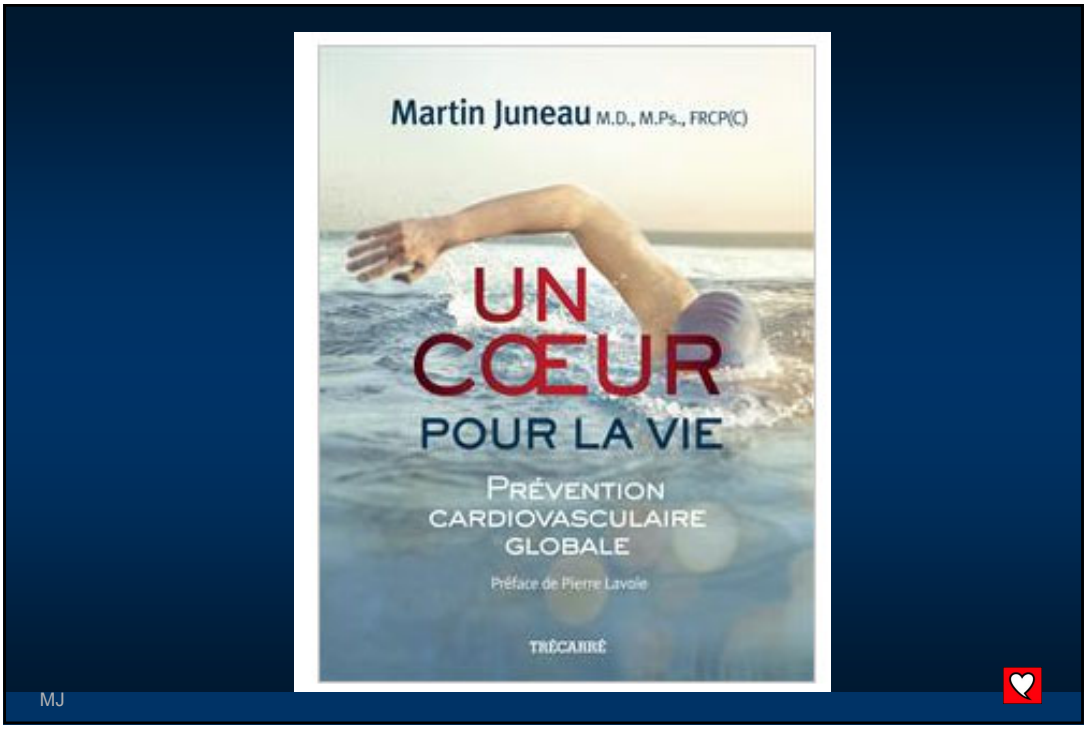
Martin Juneau M.D., M.Ps., FRCP(C)
UN CŒUR POUR LA VIE
PRÉVENTION CARDIOVASCULAIRE GLOBALE
Préface de Pierre Lavoie
TRÉCARRÉ
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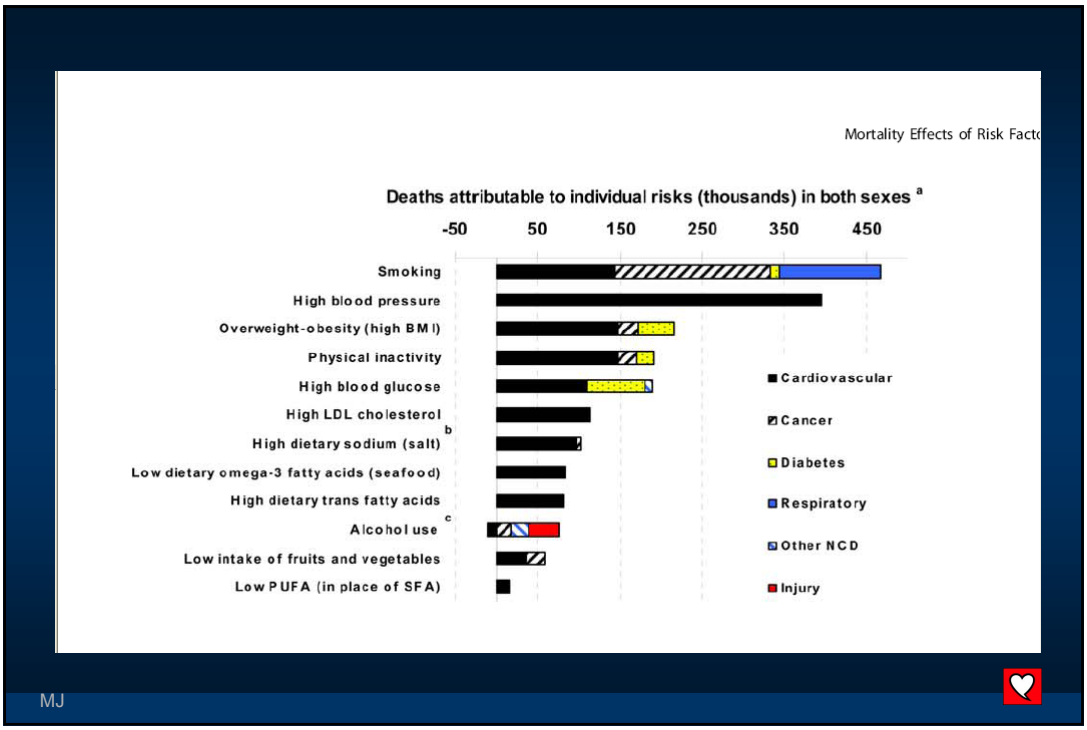
Mortality Effects of Risk Facto
Deaths attributable to individual risks (thousands) in both sexes [a]
-50
50
150
250
350
450
Smoking
High blood pressure
Overweight-obesity (high BMI)
Physical inactivity
High blood glucose
High LDL cholesterol
High dietary sodium (salt) [b]
Low dietary omega-3 fatty acids (seafood)
High dietary trans fatty acids
Alcohol use [c]
Low intake of fruits and vegetables
Low PUFA (in place of SFA)
Cardiovascular
Cancer
Diabetes
Respiratory
Other NCD
Injury
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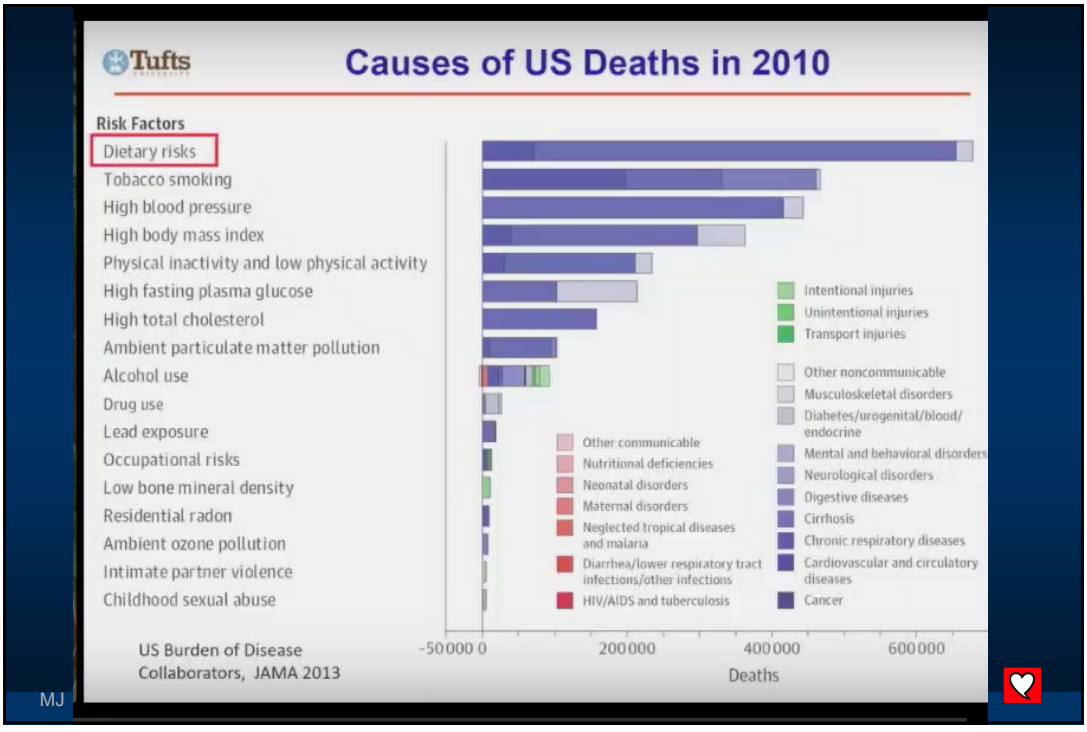
Tufts
Causes of US Deaths in 2010
Risk Factors
Dietary risks
Tobacco smoking
High blood pressure
High body mass index
Physical inactivity and low physical activity
High fasting plasma glucose
High total cholesterol
Ambient particulate matter pollution
Alcohol use
Drug use
Lead exposure
Occupational risks
Low bone mineral density
Residential radon
Ambient ozone pollution
Intimate partner violence
Childhood sexual abuse
Intentional injuries
Unintentional injuries
Transport injuries
Other noncommunicable
Musculoskeletal disorders
Diabetes/urogenital/blood/endocrine
Mental and behavioral disorders
Neurological disorders
Digestive diseases
Cirrhosis
Chronic respiratory diseases
Cardiovascular and circulatory diseases
Cancer
Other communicable
Nutritional deficiencies
Neonatal disorders
Maternal disorders
Neglected tropical diseases and malaria
Diarrhea/lower respiratory tract infections/other infections
HIV/AIDS and tuberculosis
-50000 0
200000
400000
600000
Deaths
US Burden of Disease Collaborators, JAMA 2013
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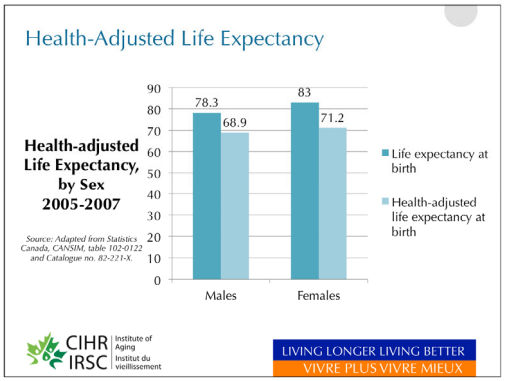
Espérance de vie vs. Espérance de vie en santé



OMS: "Adding health to years"

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

Université de Montréal

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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

Andrew Mente, PhD,*† Salim Yusuf, MBBS, DPhil,*† Shofiqul Islam, MS,* Matthew J. McQueen, MBChB, PhD,*‡ Supachai Tanomsup, MD,§ Churchill L. Onen, MD,‖ Sumathy Rangarajan, MS,* Hertzel C. Gerstein, MD, MS,*† Sonia S. Anand, MD, PhD,*† for the INTERHEART Investigators

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]: 2.46 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

From the *Population Health Research Institute, Hamilton Health Sciences, and the Departments of †Medicine and Clinical Epidemiology and Biostatistics, and ‖Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada; §Division of Cardiology, Ramathibodi Hospital, Bangkok, Thailand; and the ‖Center for Chronic Diseases, Gaborone Private Hospital, Gaborone, Botswana.

This study was supported by the Canadian Institutes of Health Research, the Heart and Stroke Foundation of Ontario, the International Clinical Epidemiology Network, and unrestricted grants from several pharmaceutical companies (with major contributions from AstraZeneca, Novartis, Hoechst Marion Roussel [now Aventis], Knoll Pharmaceuticals [now Abbott], Bristol-Myers Squibb, and Sanofi-Synthélabo), and various national bodies in different countries. Dr. Mente is supported by a Heart and Stroke Foundation of Canada Postdoctoral Research Fellowship. Dr. Yusuf is supported by an endowed chair of the Heart and Stroke Foundation of Ontario and a Senior Scientist Award from the Canadian Institutes of Health Research. Dr. Anand holds the Michael G. DeGroote Heart and Stroke Foundation of Ontario Chair in Population Health Research and the Eli Lilly Canada/May Cohen Chair in Women's Health.

Manuscript received September 28, 2009; revised manuscript received December 14, 2009, accepted December 17, 2009.

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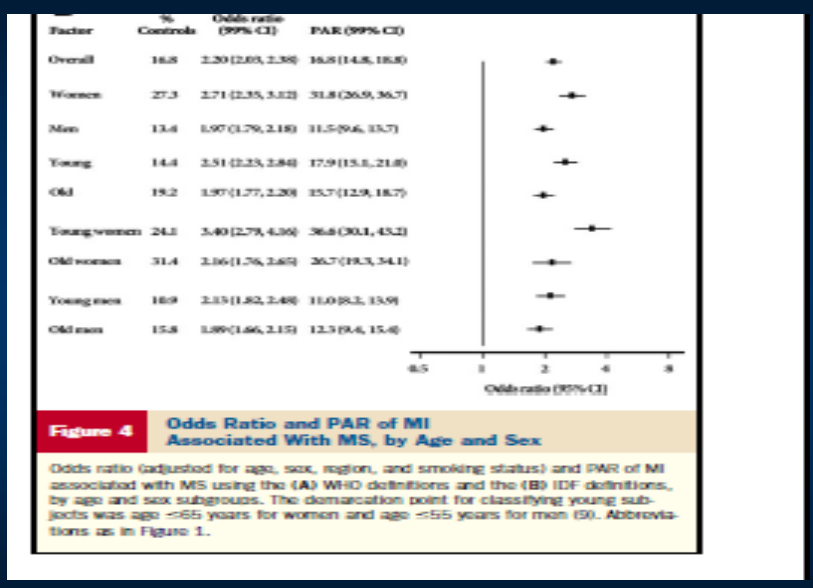

Figure 4 **Odds Ratio and PAR of MI Associated With MS, by Age and Sex**

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 (50). Abbreviations as in Figure 1.

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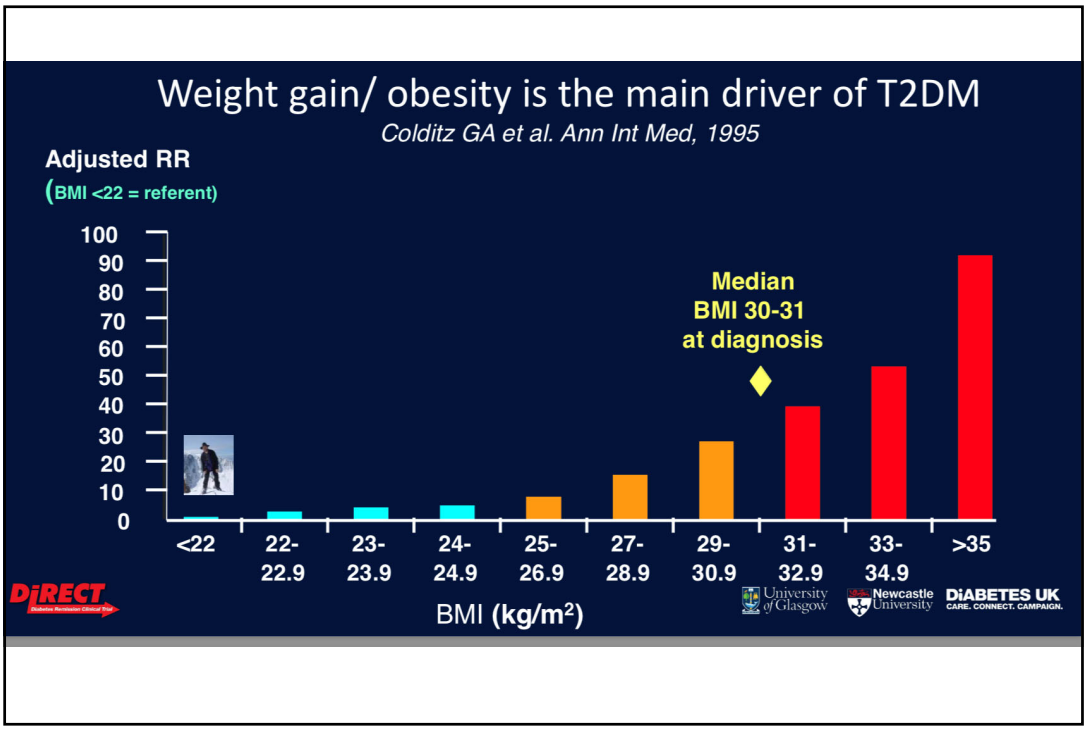
Diabetes: a growing problem in Canada

- Diabetes prevalence in Canada is among the worst of OECD countries (Organisation for Economic Co-operation and Development), according to the International Diabetes Federation.
- In Canada today, one in three people lives with prediabetes or diabetes – 11 million Canadians. Since 2000, the number of Canadians with diabetes has doubled. A 20 year old in Canada now has a 50 per cent chance of developing the disease and this grows to 80 per cent within some Indigenous populations.
- If prevalence grows by 40 per cent in the next decade as projected, the direct costs associated with treating diabetes in Canada will top $39 billion by 2028.

Source: Diabetes Canada

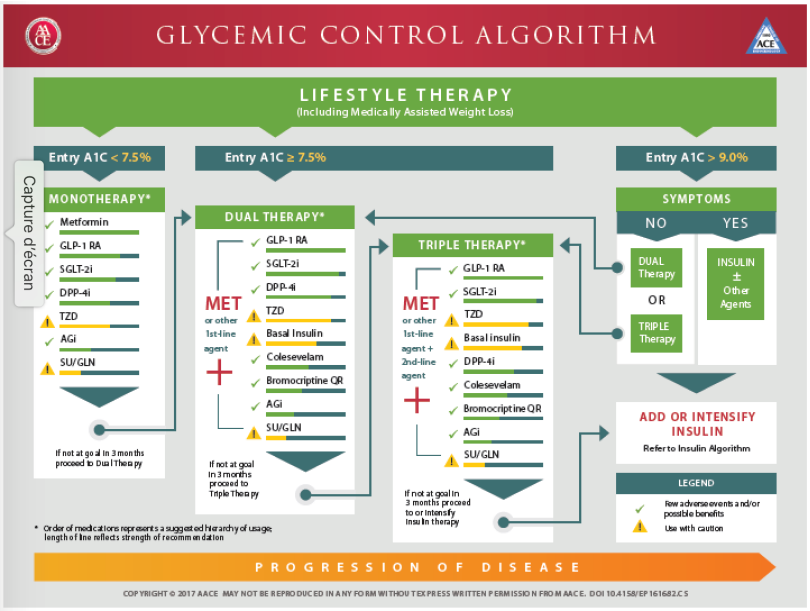


Diabetes is a lifestyle disease

- Type 2 diabetes has long been regarded as inevitably progressive, requiring increasing numbers of oral hypoglycemic agents and eventually insulin.
- This seemingly inexorable deterioration in control has been interpreted to mean that the condition is treatable but not curable.
- But diabetes is first and foremost a lifestyle disease, in most cases caused by excessive fat accumulation.
- Increase in the incidence of obesity is the main driver of the current diabetes epidemics.

Reversal of diabetes

- Since diabetes is caused be excessive fat accumulation of fat in the liver and pancreas, this suggests that normalization of this fat content may reverse the disease.
- The first hint that type 2 diabetes may be a fully reversible syndrome came from bariatric surgery.
- Studies show that blood glucose levels are normalized in obese people with type 2 diabetes undergoing bariatric surgery and 10 years later, almost 90% remained free of diabetes (*Pories WJ et al. Am J Clin Nutr 1992;55(Suppl.):582S–585S*).



N=
123,219

Suivi de
34 ans

Circulation

ORIGINAL RESEARCH ARTICLE

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

Yanping Li, MD, PhD*
An Pan, PhD*
Dong D. Wang, MD, ScD
Xiaoran Liu, PhD
Klodian Dhana, MD, PhD
Oscar H. Franco, MD, PhD
Stephen Kaptoge, PhD
Emanuele Di Angelantonio, MD, PhD
Meir Stampfer, MD, DrPH
Walter C. Willett, MD, DrPH
Frank B. Hu, MD, PhD

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/m², ≥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.

*Drs Li and Pan contributed equally.

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

Sources of Funding, see page XXX

http://circ.ahajournals.org

Circulation 2018;137:00–00. DOI: 10.1161/CIRCULATIONAHA.117.032047 xxx xx, 2018 1

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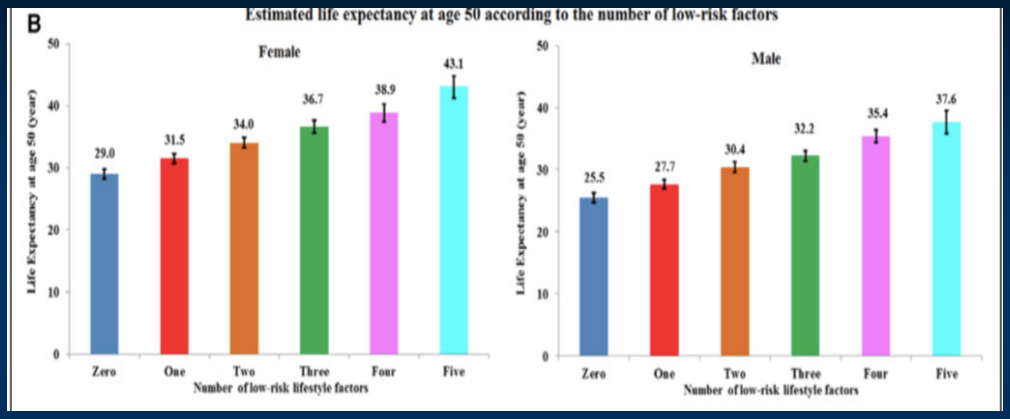

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ORIGINAL INVESTIGATIONS

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

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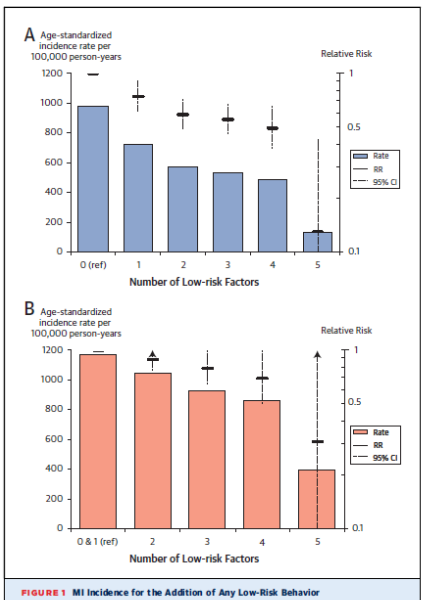

FIGURE 1 MI Incidence for the Addition of Any Low-Risk Behavior

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

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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**[3], **Robert Luben**[3], **Nicholas Day**[3]

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

Funding: EPIC-Norfolk is supported by programme grants from Medical Research Council and Cancer Research United Kingdom with additional support from the Stroke Association, British Heart Foundation, Research into Ageing, and the Academy of Medical Science. The sponsors had no role in the study design, data collection, management, analysis, and interpretation of the data, and preparation, review, or approval of the manuscript.

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

Academic Editor: Alan Lopez, The University of Queensland, Australia

Citation: Khaw KT, Wareham N, Bingham S, Welch A, Luben R, et al. (2008) Combined impact of health behaviours and mortality in men and women: the EPIC-Norfolk Prospective Population study. PLoS Med 5(1): e12. doi:10.1371/journal.pmed.0050012

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Accepted: October 26, 2007
Published: January 8, 2008

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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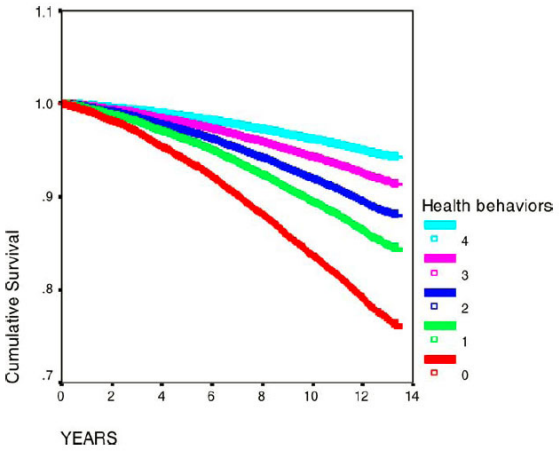

Figure 1. Survival Function According to Number of Health Behaviours in Men and Women Aged 45–79 Years without Known Cardiovascular Disease or Cancer, Adjusted for Age, Sex, Body Mass Index and Social Class, EPIC-Norfolk 1993–2006

doi:10.1371/journal.pmed.0050012.g001

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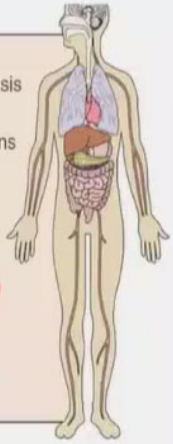
Diet & Health: Modern Science

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

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Articles

Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial

*Peter S Sever, Björn Dahlöf, Neil R Poulter, Hans Wedel, Gareth Beevers, Mark Caulfield, Rory Collins, Sverre E Kjeldsen, Arni Kristinsson, Gordon T McInnes, Jesper Mehlsen, Markku Nieminen, Eoin O'Brien, Jan Östergren, for the ASCOT investigators**

Summary

Background The lowering of cholesterol concentrations in individuals at high risk of cardiovascular disease improves outcome. No study, however, has assessed benefits of cholesterol lowering in the primary prevention of coronary heart disease (CHD) in hypertensive patients who are not conventionally deemed dyslipidaemic.

Methods Of 19 342 hypertensive patients (aged 40–79 years with at least three other cardiovascular risk factors) randomised to one of two antihypertensive regimens in the Anglo-Scandinavian Cardiac Outcomes Trial, 10 305 with non-coronary events (178 *vs* 247, 0·71 [0·59–0·86], p=0·0005) were also significantly lowered. There were 185 deaths in the atorvastatin group and 212 in the placebo group (0·87 [0·71–1·06], p=0·16). Atorvastatin lowered total serum cholesterol by about 1·3 mmol/L compared with placebo at 12 months, and by 1·1 mmol/L after 3 years of follow-up.

Interpretation The reductions in major cardiovascular events with atorvastatin are large, given the short follow-up time. These findings may have implications for future lipid-lowering guidelines.

Lancet 2003; **361:** 1149–58. Published online April 2, 2003

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N=10 305

	Atorvastatin n (%)	Atorvastatin Rate*	Placebo n (%)	Placebo Rate*	Unadjusted hazard ratio (95% CI)	p
Primary endpoint†						
Non-fatal MI‡ plus fatal CHD	100 (1·9)	6·0	154 (3·0)	9·4	0·64 (0·50–0·83)	0·0005
Secondary endpoints†						
Total cardiovascular events and procedures	389 (7·5)	24·1	486 (9·5)	30·6	0·79 (0·69–0·90)	0·0005
Total coronary events	178 (3·4)	10·8	247 (4·8)	15·2	0·71 (0·59–0·86)	0·0005
Non-fatal MI§ plus fatal CHD	86 (1·7)	5·2	137 (2·7)	8·3	0·62 (0·47–0·81)	0·0005
All-cause mortality	185 (3·6)	11·1	212 (4·1)	12·8	0·87 (0·71–1·06)	0·1649
Cardiovascular mortality	74 (1·4)	4·4	82 (1·6)	4·9	0·90 (0·66–1·23)	0·5066
Fatal and non-fatal stroke	89 (1·7)	5·4	121 (2·4)	7·4	0·73 (0·56–0·96)	0·0236
Fatal and non-fatal heart failure	41 (0·8)	2·5	36 (0·7)	2·2	1·13 (0·73–1·78)	0·5794
Tertiary endpoints†						
Silent MI	14 (0·3)	0·8	17 (0·3)	1·0	0·82 (0·40–1·66)	0·5813
Unstable angina	21 (0·4)	1·3	24 (0·5)	1·4	0·87 (0·49–1·57)	0·6447
Chronic stable angina	33 (0·6)	2·0	56 (1·1)	3·4	0·59 (0·38–0·90)	0·0135
Peripheral arterial disease	42 (0·8)	2·5	41 (0·8)	2·5	1·02 (0·66–1·57)	0·9254
Life-threatening arrhythmias	10 (0·2)	0·6	3 (0·1)	0·2	3·31 (0·91–12·01)	0·0540
Development of diabetes mellitus	154 (3·0)	9·4	134 (2·6)	8·2	1·15 (0·91–1·44)	0·2493
Development of renal impairment	31 (0·6)	1·9	24 (0·5)	1·4	1·29 (0·76–2·19)	0·3513

MI=myocardial infarction. *Per 1000 patient-years. †Full definition of endpoints provided in reference 24. ‡Includes silent MI. §Excludes silent MI.

Table 3: **Hazard ratio of atorvastatin treatment on primary, secondary, and tertiary endpoints**

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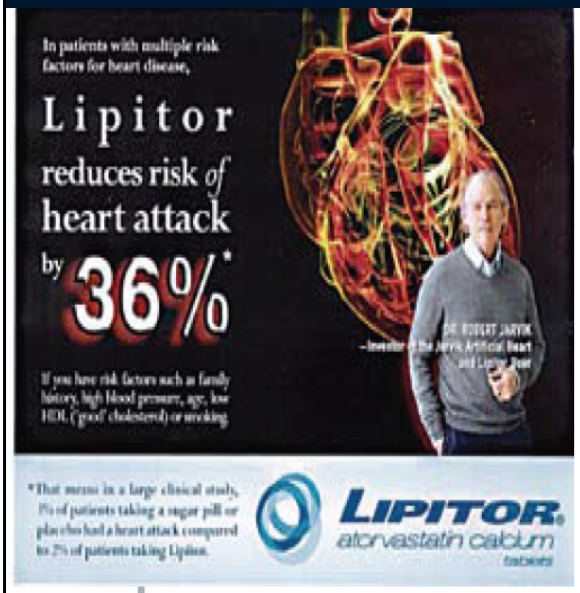

simplement assorti d'un astérisque qui renvoie à quelques lignes composées en petits caractères. Il y est précisé que « lors d'un important essai clinique », 2 % des patients sous Lipitor (1,9 %, en réalité) et 3 % des patients sous placebo ont subi une crise cardiaque. Conclusion : la probabilité *réelle* d'éviter un infarctus est de 1,1 %.

« Un virgule un pour cent divisé par 3 %, ça fait bien 36 %. Mais 36 % de rien, ça reste peu de chose ! La vérité, c'est que vous avez 99 chances sur 100 de ne pas bénéficier du médicament », sou-

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cholesterol Lowering in Intermediate-Risk Persons without Cardiovascular Disease

S. Yusuf, J. Bosch, G. Dagenais, J. Zhu, D. Xavier, L. Liu, P. Pais, P. López-Jaramillo, L.A. Leiter, A. Dans, A. Avezum, L.S. Piegas, A. Parkhomenko, K. Keltai, M. Keltai, K. Sliwa, R.J.G. Peters, C. Held, I. Chazova, K. Yusoff, B.S. Lewis, P. Jansky, K. Khunti, W.D. Toff, C.M. Reid, J. Varigos, G. Sanchez-Vallejo, R. McKelvie, J. Pogue,* H. Jung, P. Gao, R. Diaz, and E. Lonn, for the HOPE-3 Investigators†

ABSTRACT

BACKGROUND

Previous trials have shown that the use of statins to lower cholesterol reduces the risk of cardiovascular events among persons without cardiovascular disease. Those trials have involved persons with elevated lipid levels or inflammatory markers and involved mainly white persons. It is unclear whether the benefits of statins can be extended to an intermediate-risk, ethnically diverse population without cardiovascular disease.

METHODS

In one comparison from a 2-by-2 factorial trial, we randomly assigned 12,705 participants in 21 countries who did not have cardiovascular disease and were at intermediate risk to receive rosuvastatin at a dose of 10 mg per day or placebo. The first coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, and the second coprimary outcome additionally included revascularization, heart failure, and resuscitated cardiac arrest. The median follow-up was 5.6 years.

RESULTS

The overall mean low-density lipoprotein cholesterol level was 26.5% lower in the rosuvastatin group than in the placebo group. The first coprimary outcome occurred in 235 participants (3.7%) in the rosuvastatin group and in 304 participants (4.8%) in the placebo group (hazard ratio, 0.76; 95% confidence interval [CI], 0.64 to 0.91; P=0.002). The results for the second coprimary outcome were consistent with the results for the first (occurring in 277 participants [4.4%] in the rosuvastatin group and in 363 participants [5.7%] in the placebo group; hazard ratio, 0.75; 95% CI, 0.64 to 0.88; P<0.001). The results were also consistent in subgroups defined according to cardiovascular risk at baseline, lipid level, C-reactive protein level, blood pressure, and race or ethnic group. In the rosuvastatin group, there was no excess of diabetes or cancers, but there was an excess of cataract surgery (in 3.8% of the participants, vs. 3.1% in the placebo group; P=0.02) and muscle symptoms (in 5.8% of the participants, vs. 4.7% in the placebo group; P=0.005).

CONCLUSIONS

Treatment with rosuvastatin at a dose of 10 mg per day resulted in a significantly lower risk of cardiovascular events than placebo in an intermediate-risk, ethnically diverse population without cardiovascular disease. (Funded by the Canadian Institutes of Health Research and AstraZeneca; HOPE-3 ClinicalTrials.gov number, NCT00468923.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Yusuf at the Population Health Research Institute, 237 Barton St. E., Hamilton, ON L8L 2X2, Canada, or at yusufs@mcmaster.ca.

*Deceased.

†A complete list of the Heart Outcomes Prevention Evaluation (HOPE)–3 trial investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Table 2. Primary, Secondary, and Other Outcomes.*

Outcome	Rosuvastatin Group (N = 6361)	Placebo Group (N = 6344)	Hazard Ratio (95% CI)	P Value
Coprimary outcomes — no. (%)				
First coprimary outcome	235 (3.7)	304 (4.8)	0.76 (0.64–0.91)	0.002
Second coprimary outcome	277 (4.4)	363 (5.7)	0.75 (0.64–0.88)	<0.001
Secondary outcome — no. (%)	306 (4.8)	393 (6.2)	0.77 (0.66–0.89)	<0.001
Components of the coprimary and secondary outcomes — no. (%)				
Death from cardiovascular causes	154 (2.4)	171 (2.7)	0.89 (0.72–1.11)	
Myocardial infarction	45 (0.7)	69 (1.1)	0.65 (0.44–0.94)	
Stroke	70 (1.1)	99 (1.6)	0.70 (0.52–0.95)	
Resuscitated cardiac arrest	4 (0.1)	4 (0.1)	0.99 (0.25–3.97)	
Revascularization	56 (0.9)	82 (1.3)	0.68 (0.48–0.95)	
Heart failure	21 (0.3)	29 (0.5)	0.72 (0.41–1.26)	
Angina with evidence of ischemia	56 (0.9)	64 (1.0)	0.87 (0.61–1.24)	
Death from any cause — no. (%)	334 (5.3)	357 (5.6)	0.93 (0.80–1.08)	0.32
New-onset diabetes — no. (%)	232 (3.9)	226 (3.8)	1.02 (0.85–1.23)	0.82
Coronary heart disease — no. (%)†	105 (1.7)	140 (2.2)	0.74 (0.58–0.96)	0.02
First and recurrent events of the second coprimary outcome‡				
No. of participants with ≥1 event	277	363		
No. of participants with ≥2 events	68	89		
No. of participants with ≥3 events	6	16		
Total no. of events	353	473	0.75 (0.64–0.89)	0.001
Hospitalizations — no. (%)§				
For cardiovascular causes	281 (4.4)	369 (5.8)	0.75 (0.64–0.88)	<0.001
For noncardiovascular causes	881 (13.9)	879 (13.9)	1.00 (0.91–1.10)	0.99

* The first coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke; the second coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, resuscitated cardiac arrest, heart failure, or revascularization; and the secondary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, resuscitated cardiac arrest, heart failure, revascularization, or angina with evidence of ischemia.
† Coronary heart disease was a post hoc outcome that included fatal or nonfatal myocardial infarction, coronary revascularization, and angina with evidence of ischemia.
‡ The analysis of the recurrent events of the second coprimary outcome was a post hoc analysis that used a proportional-means model. The second coprimary outcome is shown because it comprises all events that were included in the first coprimary outcome as well as resuscitated cardiac arrest, heart failure, and revascularization.
§ Hospitalizations were a prespecified safety outcome.

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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

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

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JAMA Intern Med. 2014;174(7):1038-1045. doi:10.1001/jamainternmed.2014.1927

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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).

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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.

JAMA Intern Med. doi:10.1001/jamainternmed.2014.2266
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Invited Commentary

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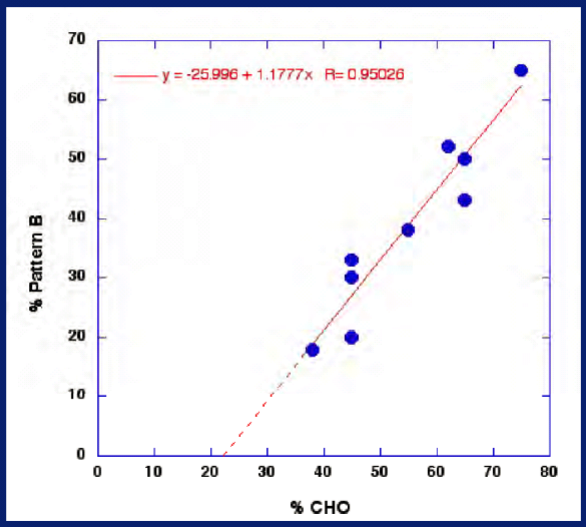
LDL particle size is responsive to dietary CHO



Krauss, J Nutr 131:340S, 2001

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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

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;

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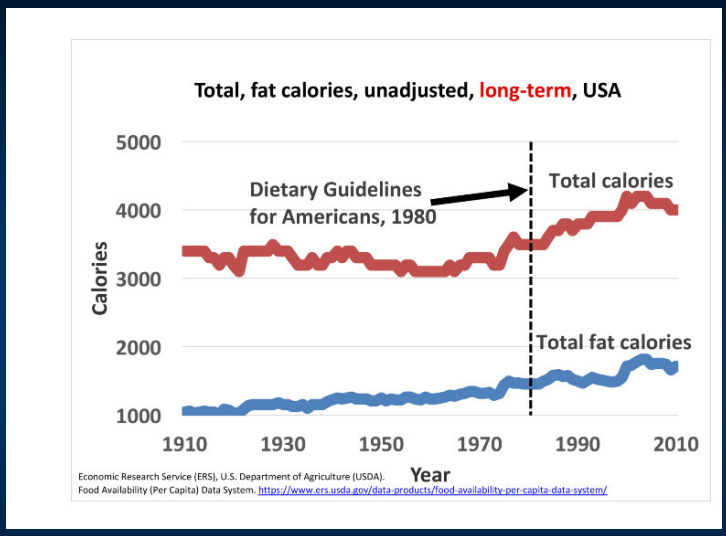
Total, fat calories, unadjusted, long-term, USA
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Economic Research Service (ERS), U.S. Department of Agriculture (USDA).
Food Availability (Per Capita) Data System. https://www.ers.usda.gov/data-products/food-availability-per-capita-data-system/

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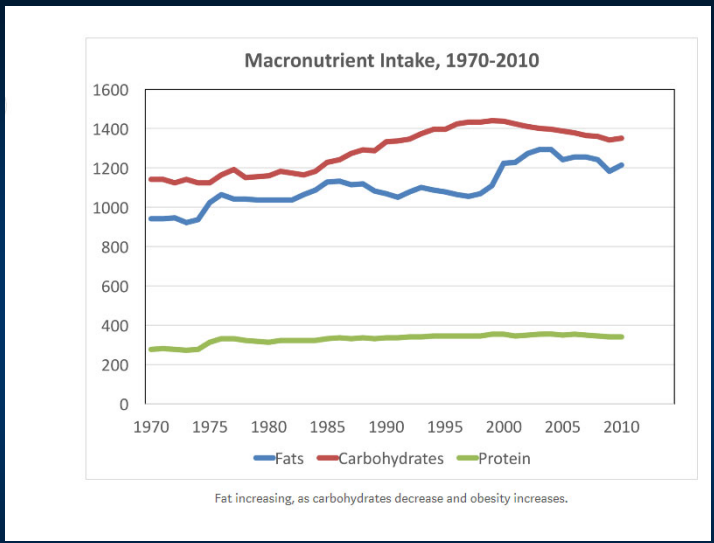
Macronutrient Intake, 1970-2010
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Carbohydrates
Protein
Fat increasing, as carbohydrates decrease and obesity increases.

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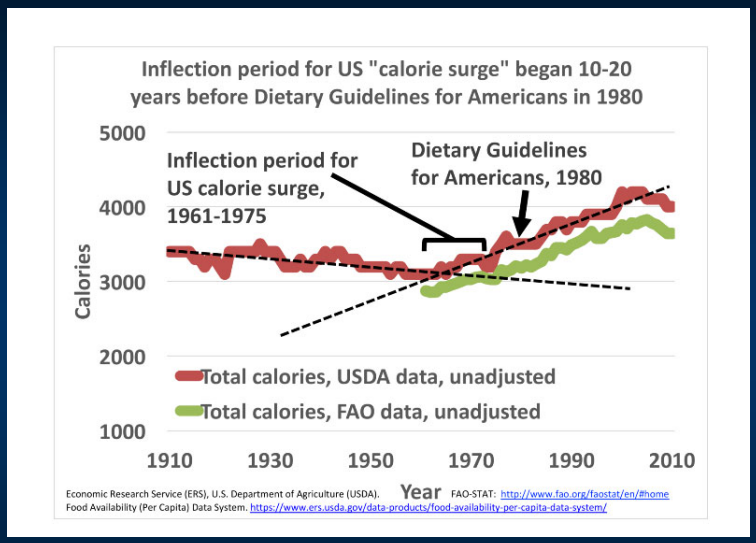

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"There's no question that sedentary lifestyles have caused the obesity crisis to get out of control."

- Indra Nooyi, CEO PepsiCo

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"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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ORIGINAL RESEARCH

American Heart Association | American Stroke Association

Association of Fast-Food and Full-Service Restaurant Densities With Mortality From Cardiovascular Disease and Stroke, and the Prevalence of Diabetes Mellitus

Mohsen Mazidi, PhD; John R. Speakman, DSc

***Background*—**We explored whether higher densities of fast-food restaurants (FFRs) and full-service restaurants are associated with mortality from cardiovascular disease (CVD) and stroke and the prevalence of type 2 diabetes mellitus (T2D) across the mainland United States.

***Methods and Results*—**In this cross-sectional study county-level data for CVD and stroke mortality, and prevalence of T2D, were combined with per capita densities of FFRs and full-service restaurants and analyzed using regression. Mortality and diabetes mellitus prevalence were corrected for poverty, ethnicity, education, physical inactivity, and smoking. After adjustment, FFR density was positively associated with CVD (β=1.104, R^2=2.3%), stroke (β=0.841, R^2=1.4%), and T2D (β=0.578, R^2=0.6%) and full-service restaurant density was positively associated with CVD mortality (β=0.19, R^2=0.1%) and negatively related to T2D prevalence (β=−0.25, R^2=0.3%). In a multiple regression analysis (FFRs and full-service restaurants together in same model), only the densities of FFRs were significant (and positive). If we assume these relationships are causal, an impact analysis suggested that opening 10 new FFRs in a county would lead to 1 extra death from CVD every 42 years and 1 extra death from stroke every 55 years. Repeated nationally across all counties, that would be an extra 748 CVD deaths and 567 stroke deaths (and 390 new cases of T2D) over the next 10 years.

***Conclusions*—**These results suggest that an increased density of FFRs is associated with increased risk of death from CVD and stroke and increased T2D prevalence, but the maximal impact (assuming the correlations reflect causality) of each individual FFR is small.

***Clinical Trial Registration*—**URL: http://www.clinicaltrials.gov. Unique identifier: NCT03243253. (*J Am Heart Assoc.* 2018;7: e007651. DOI: 10.1161/JAHA.117.007651.)

Key Words: cardiology • epidemiology • statistical analysis • stroke

Cardiovascular diseases (CVDs) are the main global cause of death, currently accounting for >17.3 million deaths annually, a figure that is predicted to increase to >23.6 million by 2030.[1] Likewise, CVDs were the leading cause of death in the United States in 2015, accounting for 864 000 deaths.[2] There is little controversy over the benefit to cardiovascular health of eating a well-balanced diet and keeping active, as demonstrated in several large cohort studies.[1,3–5] These health behaviors also play an important role in other noncommunicable diseases, such as type 2 diabetes mellitus (T2D).[6,7]

Money spent on food away from home and energy consumed away from home have increased steadily in the United States over the past 50 years, paralleled by an increase in the availability and consumption of both fast foods and foods consumed at full-service establishments.[8–11] Fast foods are quickly served, convenient, relatively inexpensive, and liked by people of most age groups.[12] However, fast foods have high calorie densities; high contents of fat, sugar, and salt; large portion sizes; and high palatability.[13] It has been suggested that consuming fast food leads to weight and adiposity increases, which are a major risk factor for CVDs, noncommunicable diseases, and metabolic abnormalities, such as insulin resistance.[9–13] However, the evidence linking

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Received September 18, 2017; accepted April 11, 2018.

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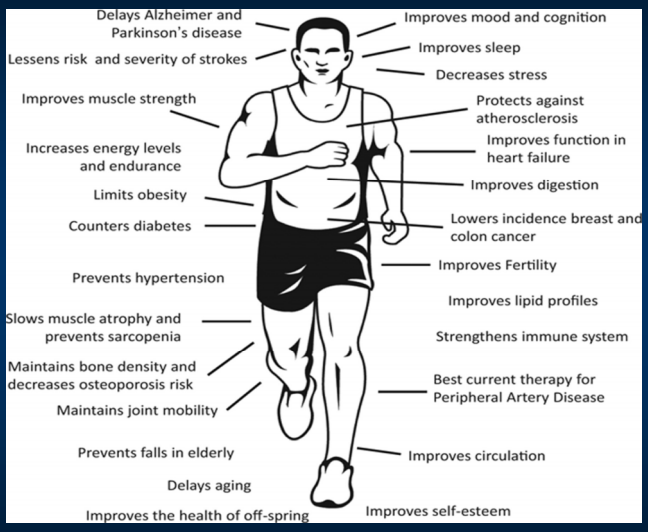
The many long-term benefits of regular endurance exercise.



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

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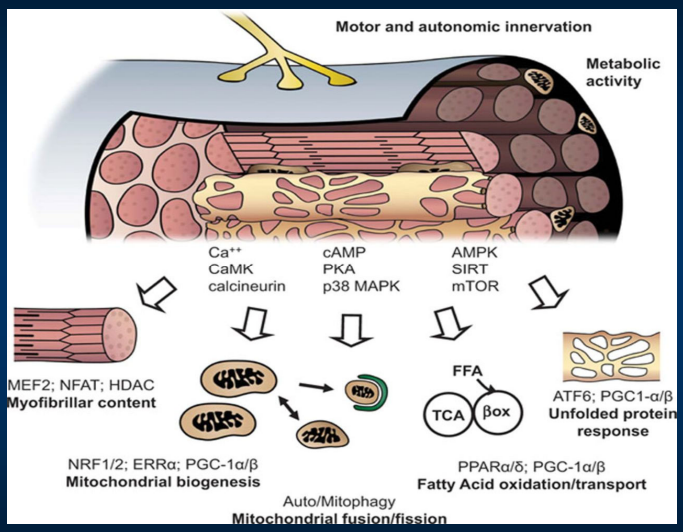
Modular signaling pathways that underpin muscular adaptations to endurance exercise.



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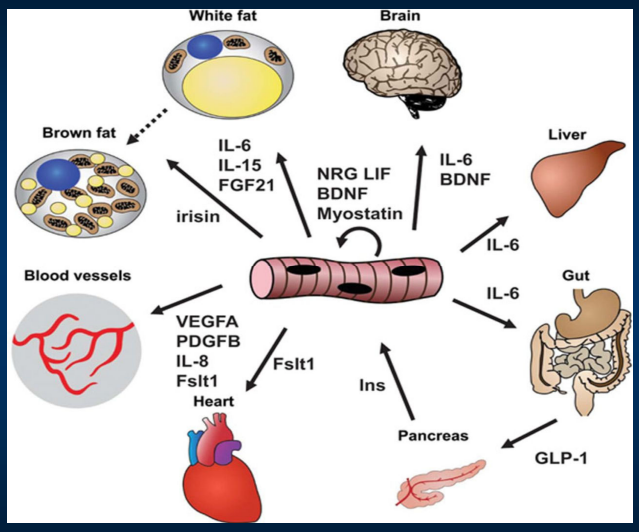
Muscle as an endocrine organ.



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

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Articles

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

Published Online August 16, 2011 DOI:10.1016/S0140-6736(11)60749-6

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

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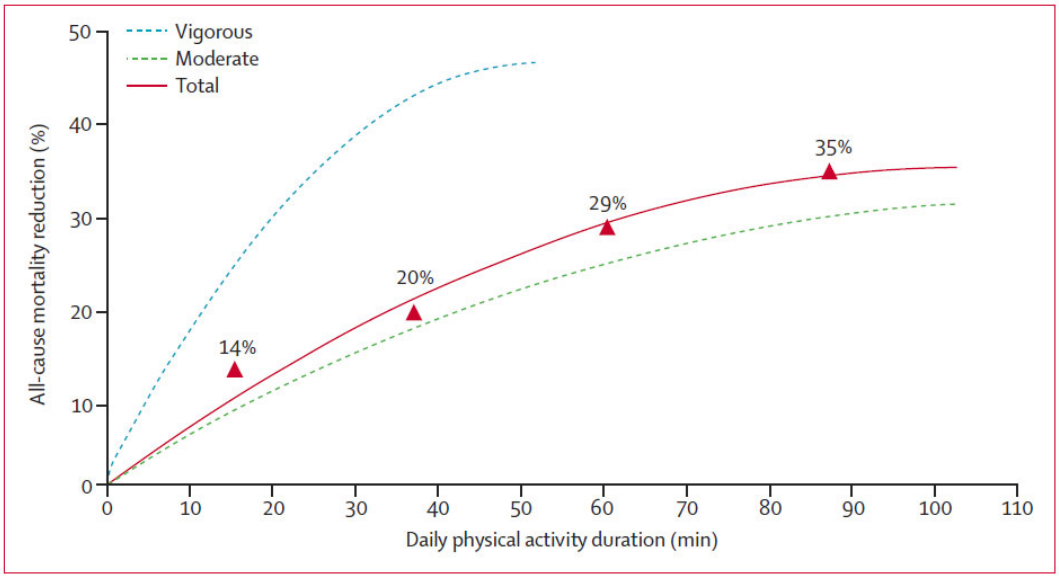

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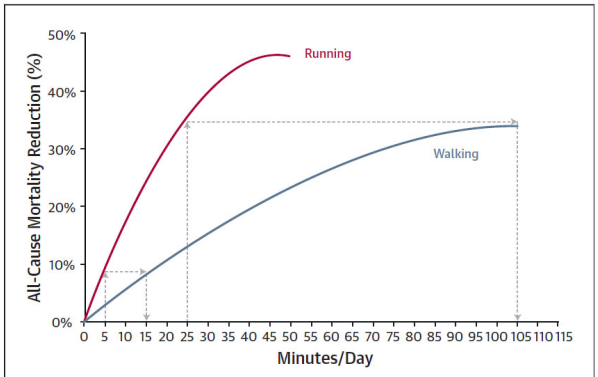

FIGURE 1 Comparison of Benefits Between Walking and Running

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.

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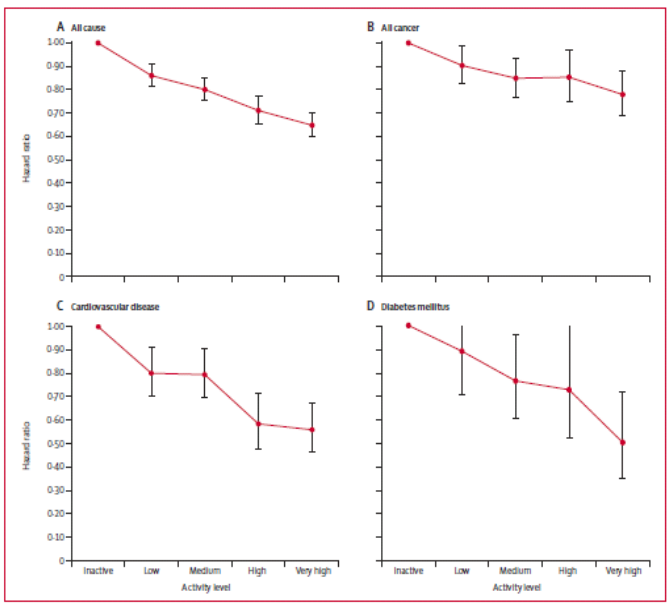

Figure 1: Relation between physical activity volume and mortality reduction compared with individuals in the inactive group
Bars show 95% CIs.

MJ

Articles

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, Dorisjela 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, Harry Swaton, 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 4·4% 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] 23% of the world's population is estimated to be insufficiently active[5] and WHO has recommended a decrease in insufficient physical activity of 10% (of the aforementioned 23%) by 2020.[5]

Many studies from high-income countries have reported significant inverse associations of physical activity with mortality and CVD morbidity,[6] but such data from low-

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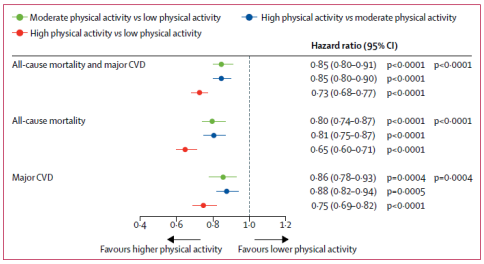

Figure 1: **Hazard ratios and 95% CI for all-cause mortality and major CVD, all-cause mortality, or major CVD by level of physical activity**

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.

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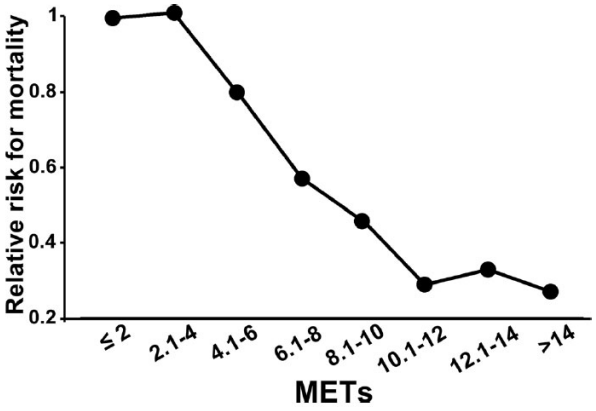

Figure 7 Mortality risk at different exercise capacities. Significant reductions in mortality do not occur less than 4 metabolic equivalents of resting metabolism (METs), become less at approximately 4 to 6 METs and an asymptote occurring at approximately 10 METs in 15,000 US veterans of wars. [Reproduced,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

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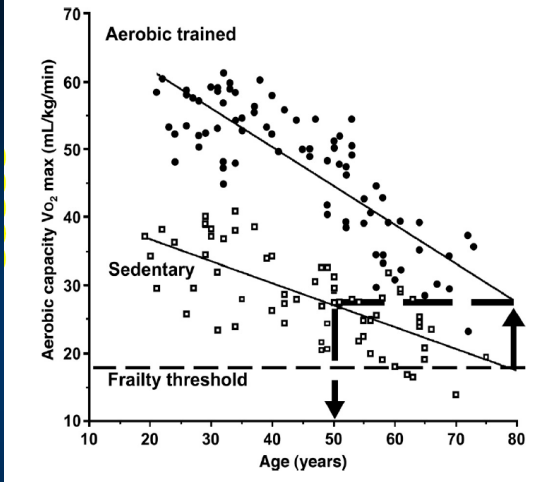

Figure 4 Best-fit linear lines are shown for aerobic capacities of two cross-sectional groups (aerobic trained and sedentary) as a function of their increasing chronological age. At the chronological age of 80 years, a horizontal line is extended from the endurance-trained line to the left where it intersects 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

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Cardiovascular Risk

Relationship of Sedentary Behavior and Physical Activity to Incident Cardiovascular Disease

Results From the Women's Health Initiative

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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).

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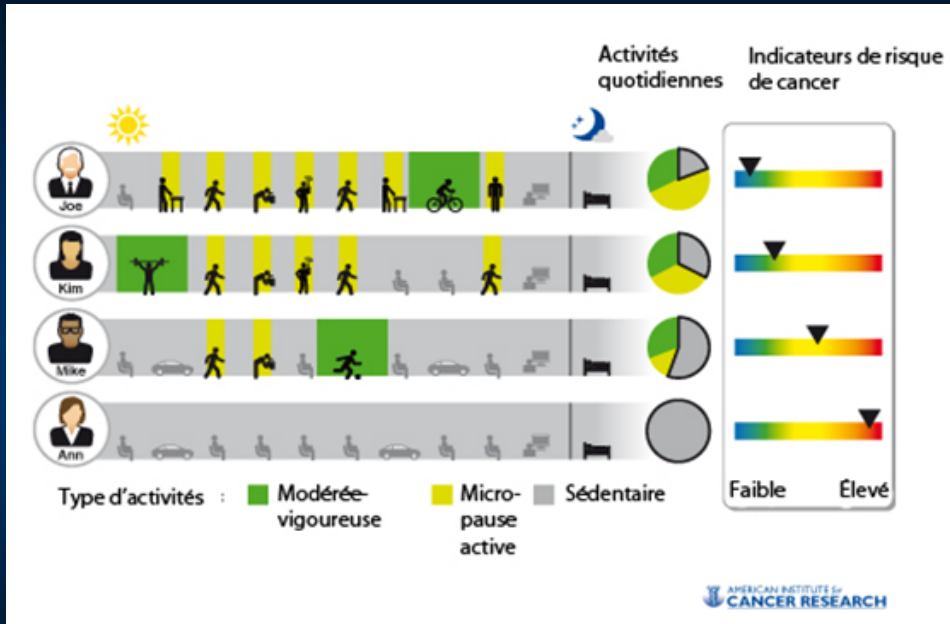

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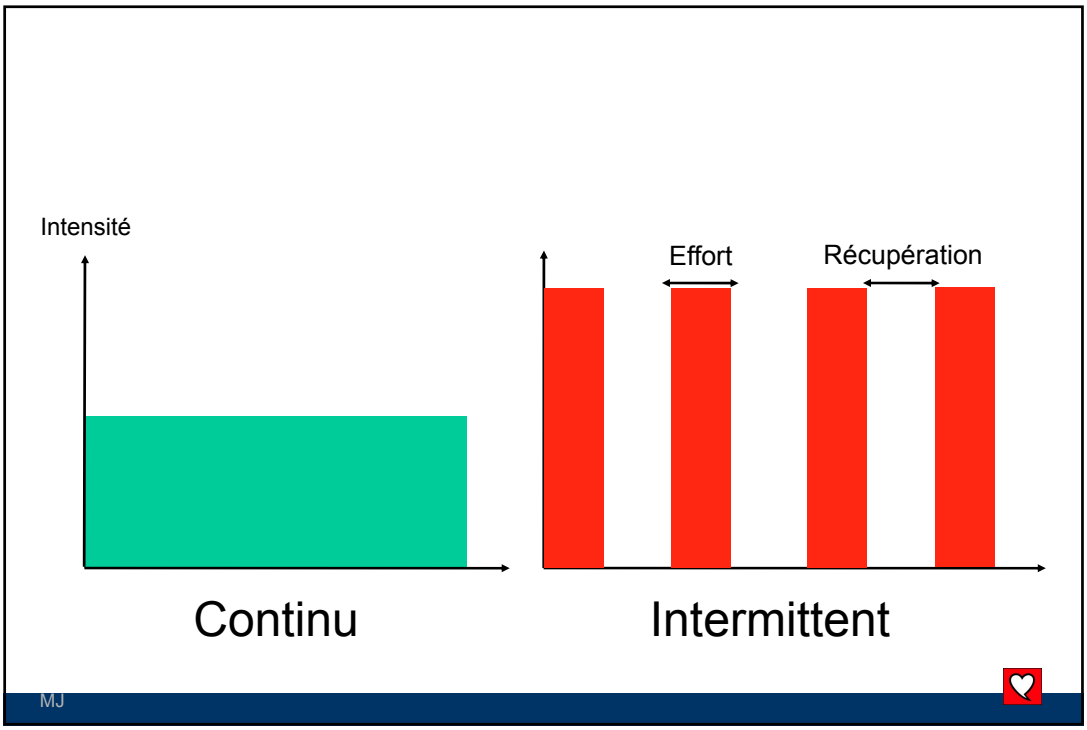
Intensité
Effort
Récupération
Continu
Intermittent
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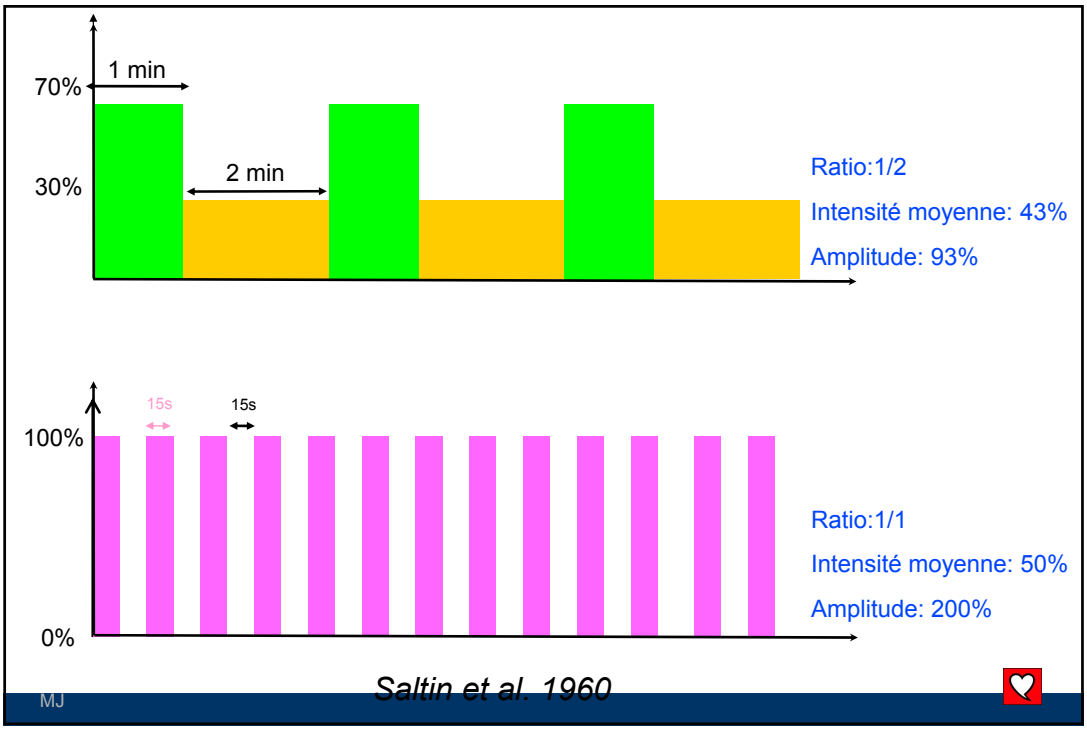
1 min
70%
2 min
30%
Ratio:1/2
Intensité moyenne: 43%
Amplitude: 93%
15s
15s
100%
0%
Ratio:1/1
Intensité moyenne: 50%
Amplitude: 200%
Saltin et al. 1960
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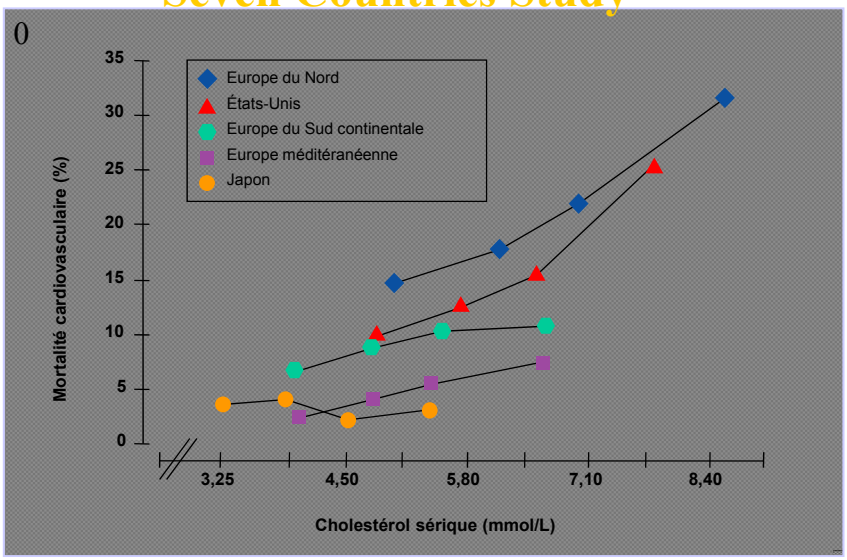
Mortalité cardiovasculaire sur 25 ans

Seven Countries Study



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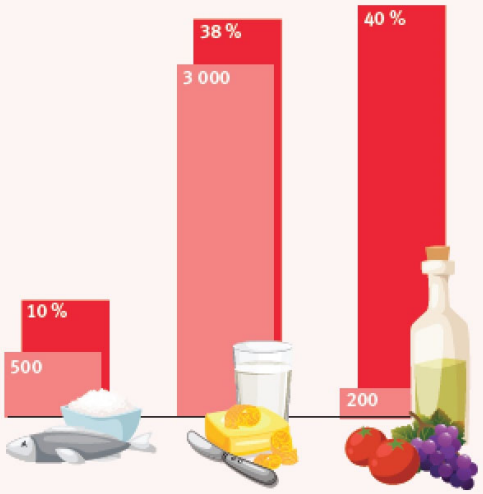
BIEN CHOISIR SES GRAS
POUR PRÉVENIR LES MALADIES CARDIOVASCULAIRES



Même si [illegible]% 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 Stampler et Willett (2006)

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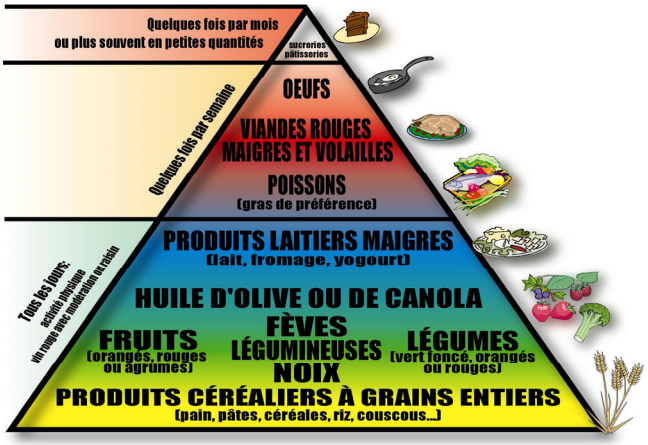
Alimentation Méditerranéenne Modifiée

ÉPIC



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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*

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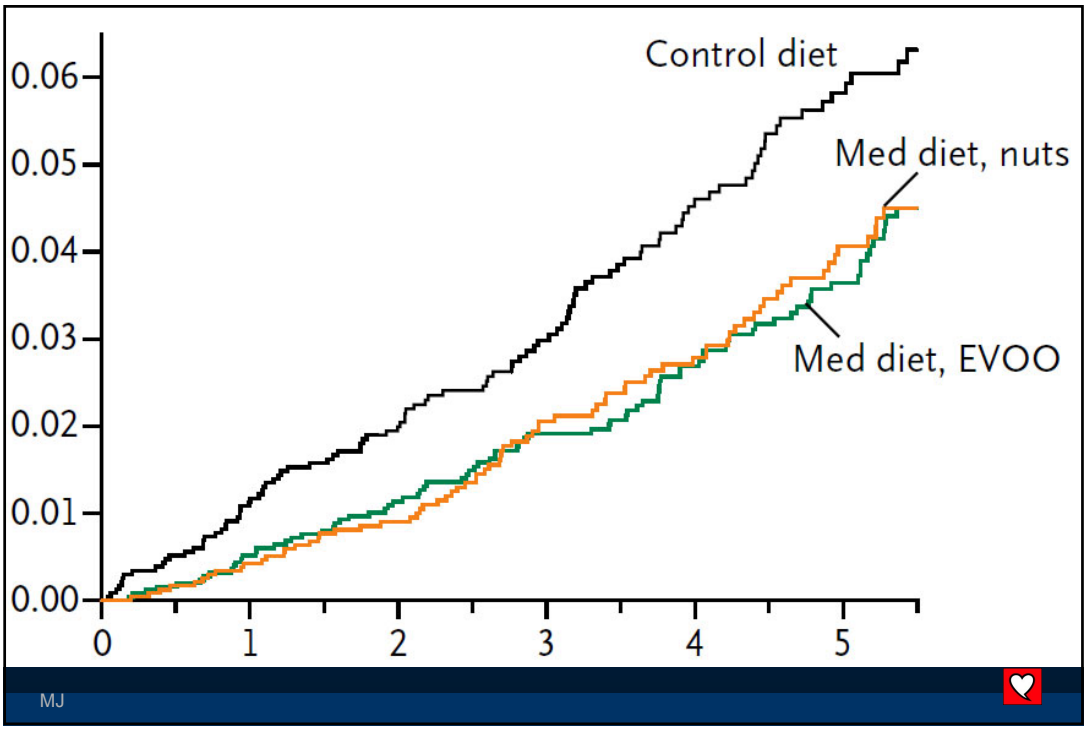

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Research

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)

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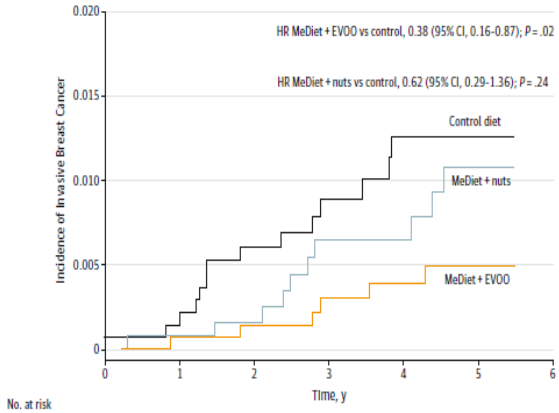
Figure 1. Incidence of Invasive Breast Cancer, According to the Intervention Group



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.

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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

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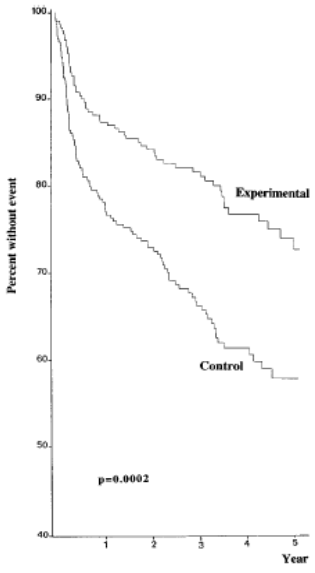

Figure 3. Cumulative survival without nonfatal infarction, without major secondary end points, and without minor secondary end points (CO 3).

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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%

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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).

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Research

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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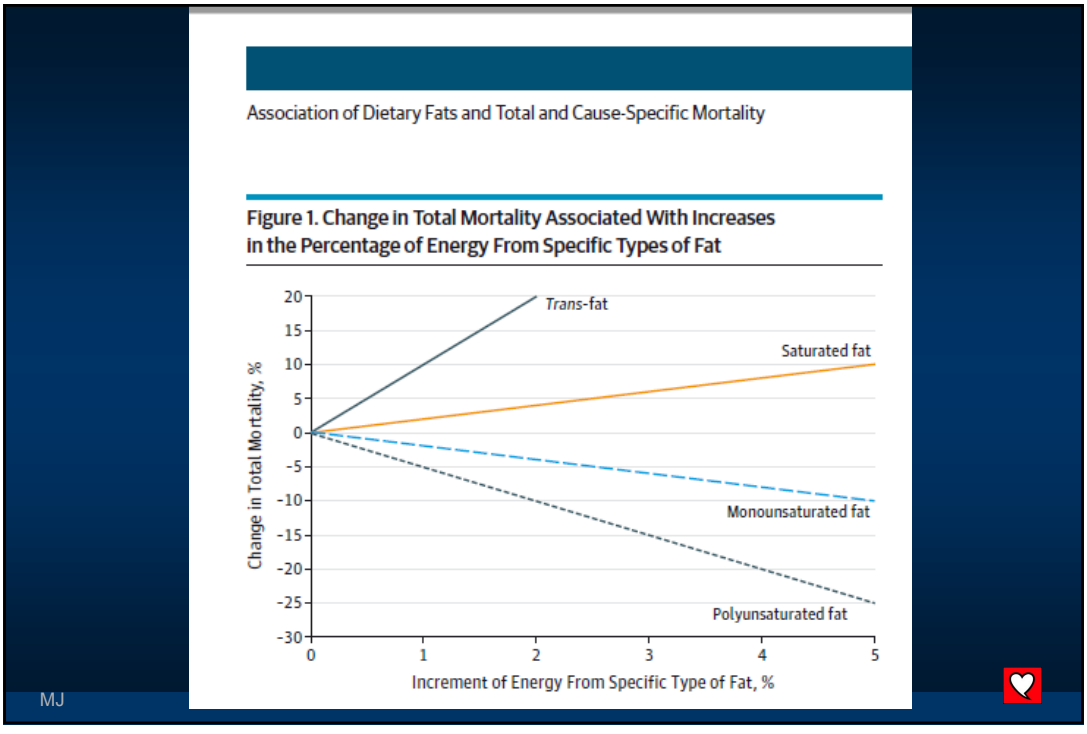

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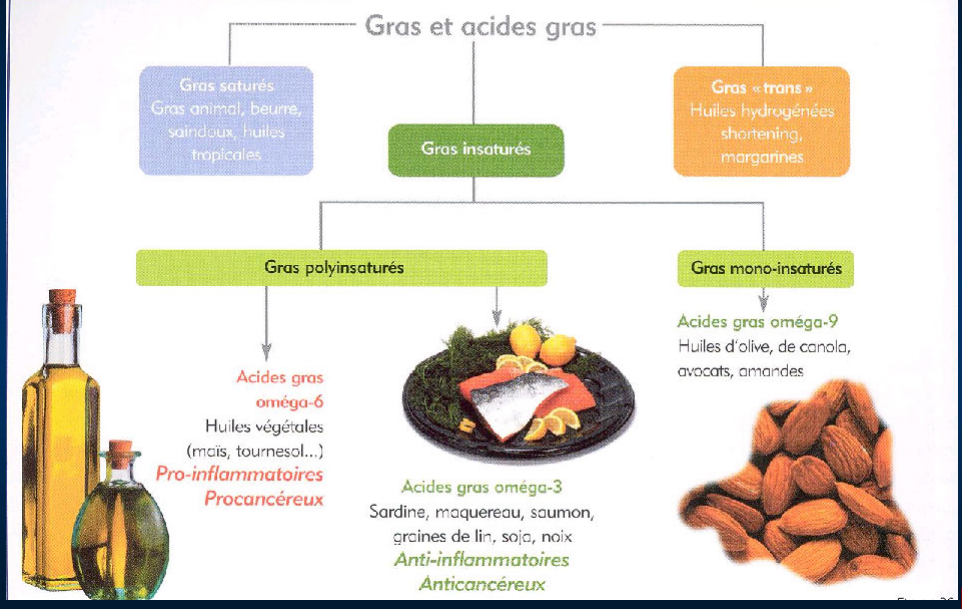
LES MATIÈRES GRASSES DE L'ALIMENTATION



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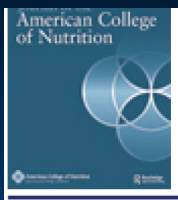

Journal of the American College of Nutrition

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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

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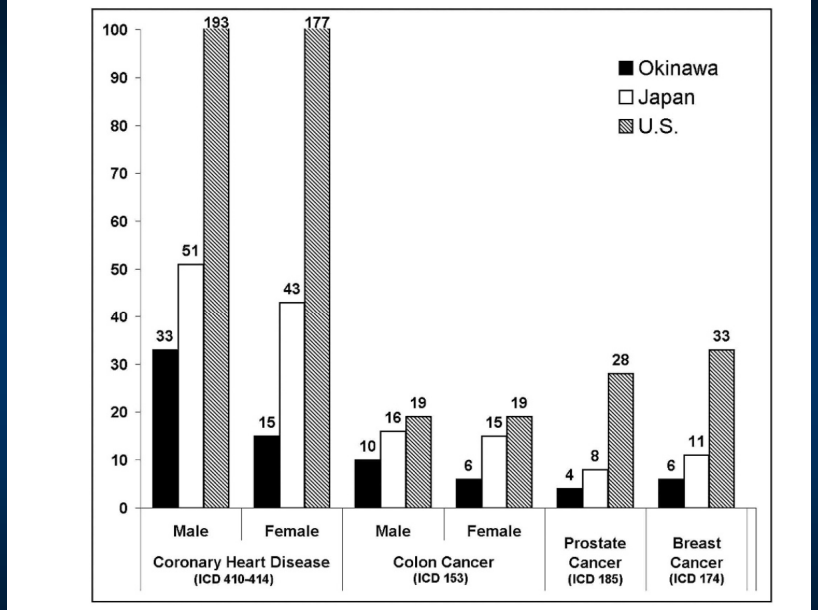

. Mortality rates from coronary heart disease and cancers in Okinawans, Japanese, and Americans [1].

MJ

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."

MJ

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 (Dr Gould and Kirkeeide); and the Preventive Medicine Research Institute, Sausalito, Calif (Drs Ornish Scherwitz, and Billings, Mr Sparler, and Ms Merritt).

Reprints: Dean Ornish, MD, Preventive Medicine Research Institute, 900 Bridgeway, Suite 1, Sausalito, CA 94965 (e-mail: DeanOrnish@aol.com).

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.[3,4] In brief, we recruited men and women

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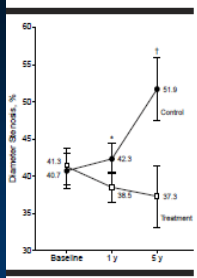

Figure 1.—Mean percentage diameter stenosis in treatment and control groups at baseline, 1 year, and 5 years. Error bars represent SEM; asterisk, $P = .02$ by between-group 2-tailed test; dagger, $P = .001$ by between-group 2-tailed test.

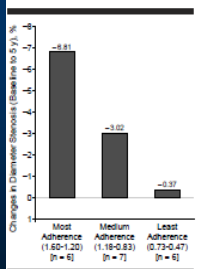

Figure 2.—Changes in percentage diameter stenosis by 5-year adherence tertiles for the experimental group.

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Caldwell B. Esselstyn Jr, MD; Gina Gendy, MD; Jonathan Doyle, MCS; Mladen Golubic, MD, PhD; Michael F. Roizen, MD
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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.

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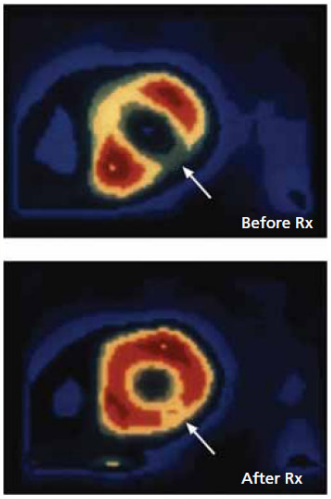
FIGURE 1

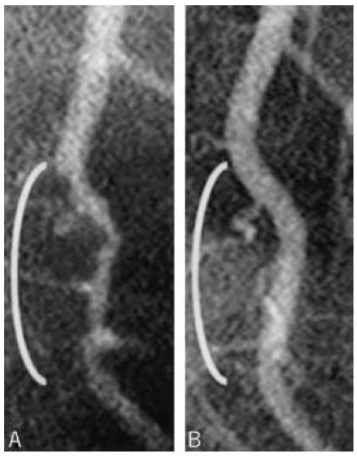
Restoration of myocardial perfusion[2]



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).

MJ

Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial

Michael EJ Lean, Wilma S Leslie, Alison C Barnes, Naomi Brosnahan, George Thom, Louise McCombie, Carl Peters, Sviatlana Zhyzhneuskaya, Ahmad Al-Mrabeh, Kieren G Hollingsworth, Angela M Rodrigues, Lucia Rehackova, Ashley J Adamson, Falko F Sniehotta, John C Mathers, Hazel M Ross, Yvonne McIlvenna, Renae Stefanetti, Michael Trenell, Paul Welsh, Sharon Kean, Ian Ford, Alex McConnachie, Naveed Sattar, Roy Taylor**

- 306 individuals aged 20–65 years (BMI of 27–45 kg/m^2) who had been diagnosed with type 2 diabetes within the past 6 years, and were not receiving insulin.
- The intervention group comprised withdrawal of antidiabetic and antihypertensive drugs, total diet replacement (825–853 kcal/day formula diet for 3–5 months), stepped food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance. Control group was assigned to a best-practice care by guidelines.
- Co-primary outcomes were weight loss of 15 kg or more, and remission of diabetes, defined as glycated haemoglobin (HbA_{1c}) of less than 6·5% (< 48 mmol/mol) after at least 2 months off all antidiabetic medications, from baseline to 12 months.

Volume 391, Issue 10120, 10–16 February 2018, Pages 541-551

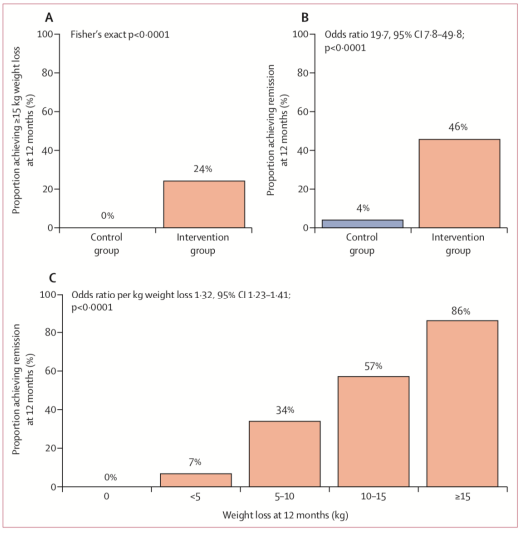


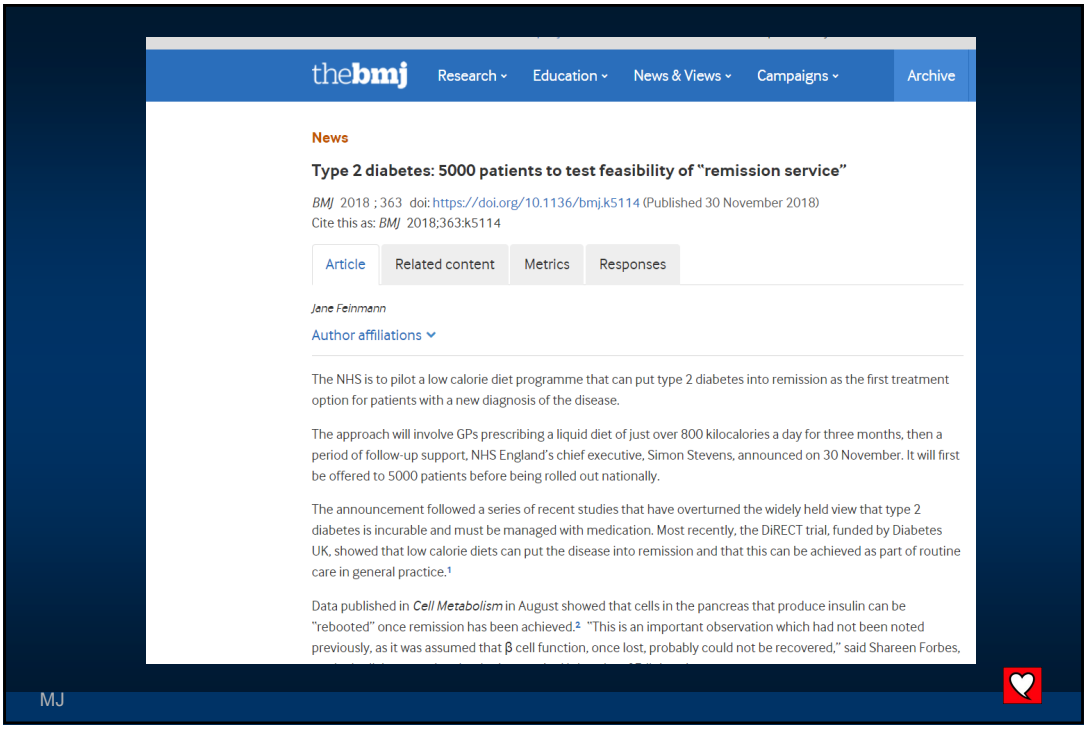
Figure 2: **Primary outcomes and remission of diabetes in relation to weight loss at 12 months**
(A) First co-primary outcome: achievement of at least 15 kg weight loss at 12 months. (B) Second co-primary outcome: remission of diabetes (glycated haemoglobin <6·5% [48mmol/mol], off antidiabetic medication for 2 months). (C) Remission of diabetes, in relation to weight loss achieved at 12 months (both groups combined).

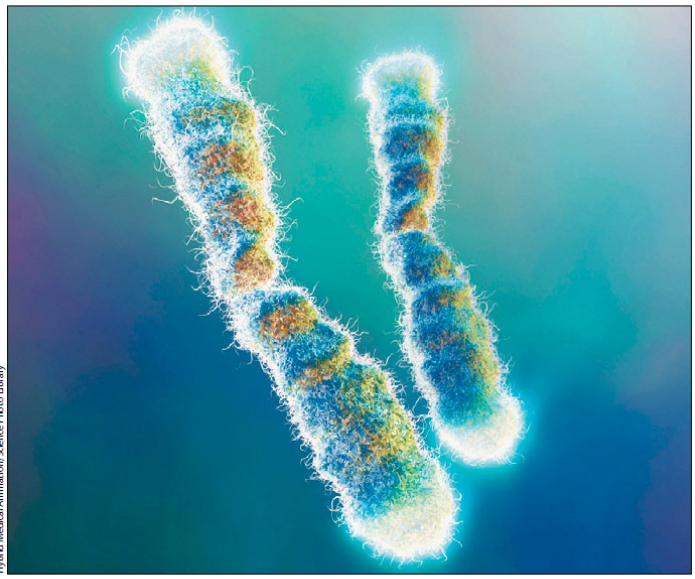
Criteria for diabetes remission

McCombie et coll. BMJ 2017; 358: j4030

Table 1| **Published and proposed criteria for diabetes in remission**

	Criteria for remission	Confirmation
ADA Consensus Group[8]	**Partial remission (no longer having diabetes):** Both HbA_{1c} < 6.5% (<48 mmol/mol) and fasting blood glucose 5.6-6.9 mmol/L without antidiabetes drugs (time not specified)	Maintained for 1 year
	Complete remission (no longer having prediabetes): Both HbA_{1c} < 6% (<42 mmol/mol) and fasting blood glucose <5.6 mmol/L without antidiabetes drugs (time not specified)	Maintained for 1 year
Buchwald et al[9] (systematic review after bariatric surgery)	HbA_{1c} < 6% (42 mmol/mol) or fasting blood glucose<5.6 mmol/L without antidiabetic drugs (time not specified)	None
Authors' proposal for coding in routine practice	Previous diagnosis of type 2 diabetes by WHO criteria. HbA_{1c} <6.5% (<48 mmol/mol) or fasting blood glucose<7 mmol/L and 2 hour glucose<11 mmol/L after at least 2 months without antidiabetes medication	Two non-diabetic test results, at least 2 months apart then reviewed annually





Telomeres help prevent the loss of genetic information

MJ

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

Lancet Oncol 2013; 14: 1112–20

Published Online September 17, 2013 http://dx.doi.org/10.1016/S1470-2045(13)70366-8

Department of Medicine (Prof D Ornish MD, J Daubenmier PhD), Department of Biochemistry and Biophysics (J Lin PhD, Prof E H Blackburn PhD), Department of Psychiatry (E Epel PhD), Department of Orofacial Sciences (N Chainani-Wu DMD), Department of Urology, Helen

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;

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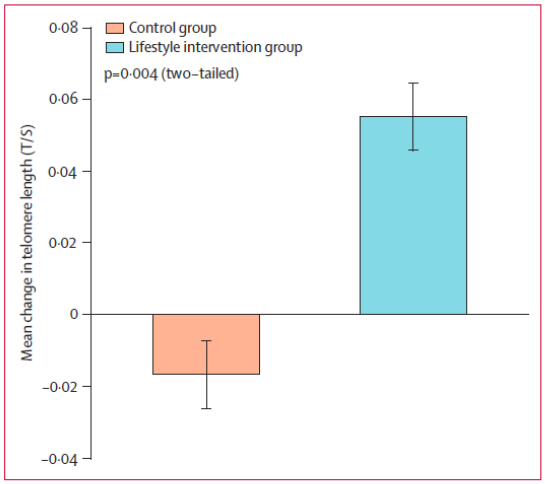

***Figure 1*: Mean change in relative telomere length over 5 years with lifestyle intervention compared with control**
Vertical lines represent 1 SEM. T/S=telomere to single-copy gene ratio units.

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

BMC Medicine

Metabolism, diet and disease

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], Dimitirios 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

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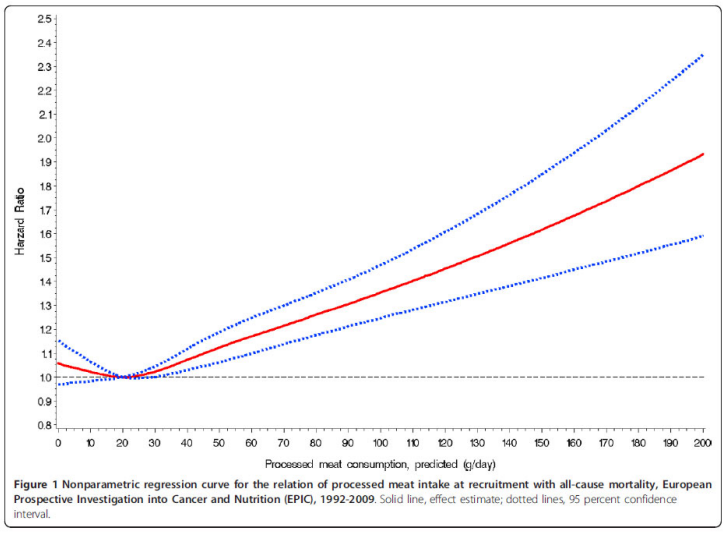

Figure 1 Nonparametric regression curve for the relation of processed meat intake at recruitment with all-cause mortality, European Prospective Investigation into Cancer and Nutrition (EPIC), 1992-2009. Solid line, effect estimate; dotted lines, 95 percent confidence interval.

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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]

MJ

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 25, 2013 VOL. 368 NO. 17

Intestinal Microbial Metabolism of Phosphatidylcholine and Cardiovascular Risk

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

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The NEW ENGLAND JOURNAL of MEDICINE

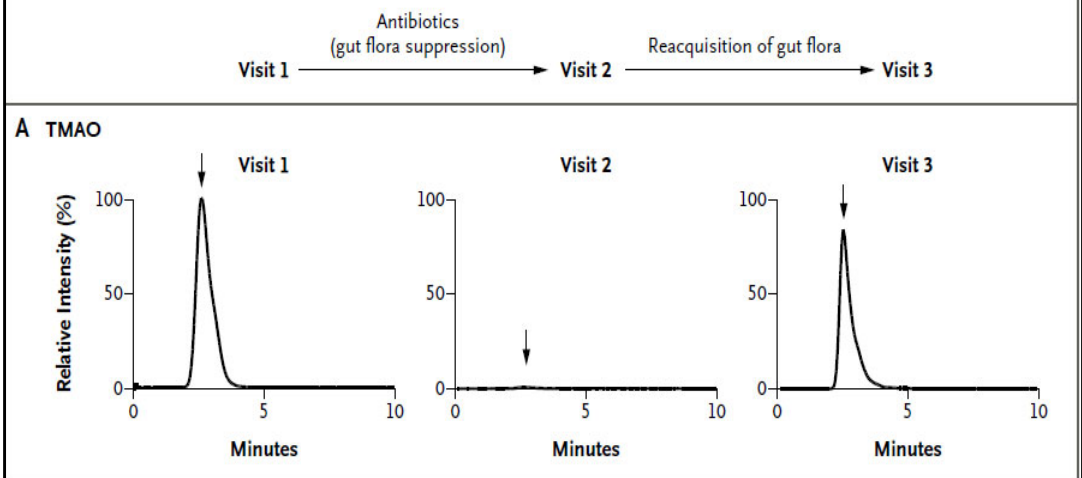

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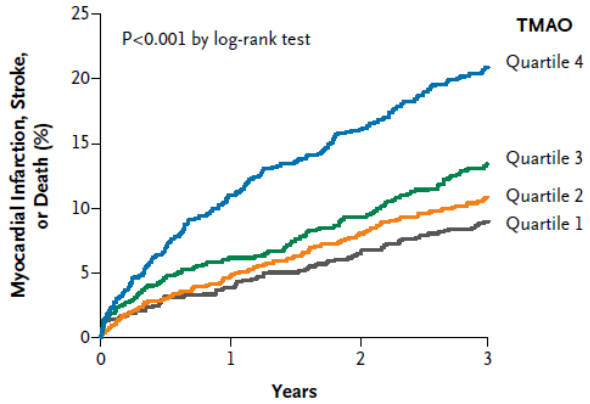
Table 2. Risk of a Major Adverse Cardiovascular Event at 3 Years, According to Quartile of TMAO Level.*

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.

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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).

Lancet 2007; 370: 1253–63

Published Online September 13, 2007 DOI:10.1016/S0140-6736(07)61256-2

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

National Centre for Epidemiology and Population Health, The Australian National University, Canberra, Australia (Prof A J McMichael PhD, C D Butler PhD); **Institute of Public Health, Cambridge University, Cambridge, UK** (J W Powles PhD); **Nutrition and Public Health Interventions Research Unit, London School of Hygiene and Tropical**

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We need to talk about meat

Humans and the livestock they consume is a tale that impacts lives in a deep and meaningful sense. Human history is interwoven with production of meat for consumption, and its availability and nutritional value as a source of protein has played a major part in diet as far back as we can imagine, shaping regional identities and global movements. The emotionally charged debate over the ethical suitability of meat consumption may never reach a conclusion, but it is only comparatively recently that the climate impact of livestock rearing, and the nutritional and health issues caused by meat have become a pressing concern.

Achieving a healthy diet from a sustainable source is a struggle new enough to countries with an abundance of food that it has proven difficult to enact meaningful change. Government efforts to curb consumption and thus curb weight gain in high-income countries are yet to display a meaningful effect, and most of these efforts are focused on sugar or fat. Similarly, the global ecological sustainability of farming habits has not been a major topic of conversation until the last few decades. It's only now that we're beginning to have a conversation about the role of meat in both of these debates, and the evidence suggests a reckoning with our habits is long overdue.

Meat production doesn't just affect the ecosystem by production of gases, and studies now question the system of production's direct effect on global freshwater use, change in land use, and ocean acidification. A recent paper in *Science* claims that even the lowest-impact meat causes "much more" environmental impact than the least sustainable forms of plant and vegetable production. Population pressures, with global population predicted to increase by a third between 2010 and 2050, will push us past these breaking points.

Another important addition to the conversation around meat is the *PLoS One* paper discussing health-related taxes for red meat. The paper offers up some compelling claims as justification, including the suggestion that the health-related costs directly attributable to the consumption of red and processed meat will be US$285 billion in 2020, or 0·3% of worldwide gross GDP. 4·4% of all deaths worldwide would be caused by red or processed meat. Of course, this causal mathematical model should be taken with a pinch of salt, but it does follow on from the 2015 WHO classification of some meats as proven carcinogens, based on the International Agency For Research On Cancer assessment of a "strong" link between red meat and the mechanistic evidence for carcinogenicity.

The question of what can be done is more challenging than the question of what should be done. Countries, and their citizens, should look to limit their consumption of intensively farmed meats, both for health and environmental reasons. The issue of how this change comes about is part of a wider conversation that we all need to start having about meat. Will a simple tax on red and processed meat change habits to the extent required? A simple measure enacted alone runs the risk of unfairly targeting those whose budgets only stretched to the cheaper processed meats. Stating that those who can suddenly not afford meat should just switch to a vegetarian diet anyway is not a balanced addition to the debate over meat's role in society. However, targeted taxation has shown positive results in areas of strong health concern such as tobacco, although these successes are similarly accompanied by discussions of the regressive nature of such a tax.

The likelihood is that action will need to take a wider systems approach, with a very public conversation about meat informing a host of measures from deciding the appropriate application of government farming subsidies and finding a way to ameliorate the true costs to humans and the planet of certain processing methods, all the way through to slowly changing consumer habits over time, possibly through use of targeted taxation but certainly through an engaging, balanced conversation. No one system fits every country. Meat might be common to almost every society but its role in each is different and deeply culturally engrained.

So what is a healthy amount of red or processed meat? It's looking increasingly like the answer, for both the planet and the individual, is very little. Saying this is one thing. Getting the world to a place where we have the ability to balance the desire to eat whatever we want with our need to preserve the ecosystem we rely on to sustain ourselves is quite another. The conversation has to start soon. ■ *The Lancet*

For more on the **effect of the food system on freshwater use** see *Nature* 2018; 562: 519–25.
For more on the **lowest-impact meat's environmental impact** see *Science* 2018; 360: 987–92.
For more on **meat taxation** see *PLoS One*; published online Nov 6, 2018. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0206139
For more on **carcinogenicity of consumption of red and processed meat** see *News Lancet Oncol* 2015; 16: 1599–600
For more on the **effects of tobacco taxation and pricing on smoking behaviour in high risk populations** see *Int J Environ Res Public Health* 2011; 8: 4118–39

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