Healing the Heart with Food and Food Bioactives

Benjamin Brown, ND

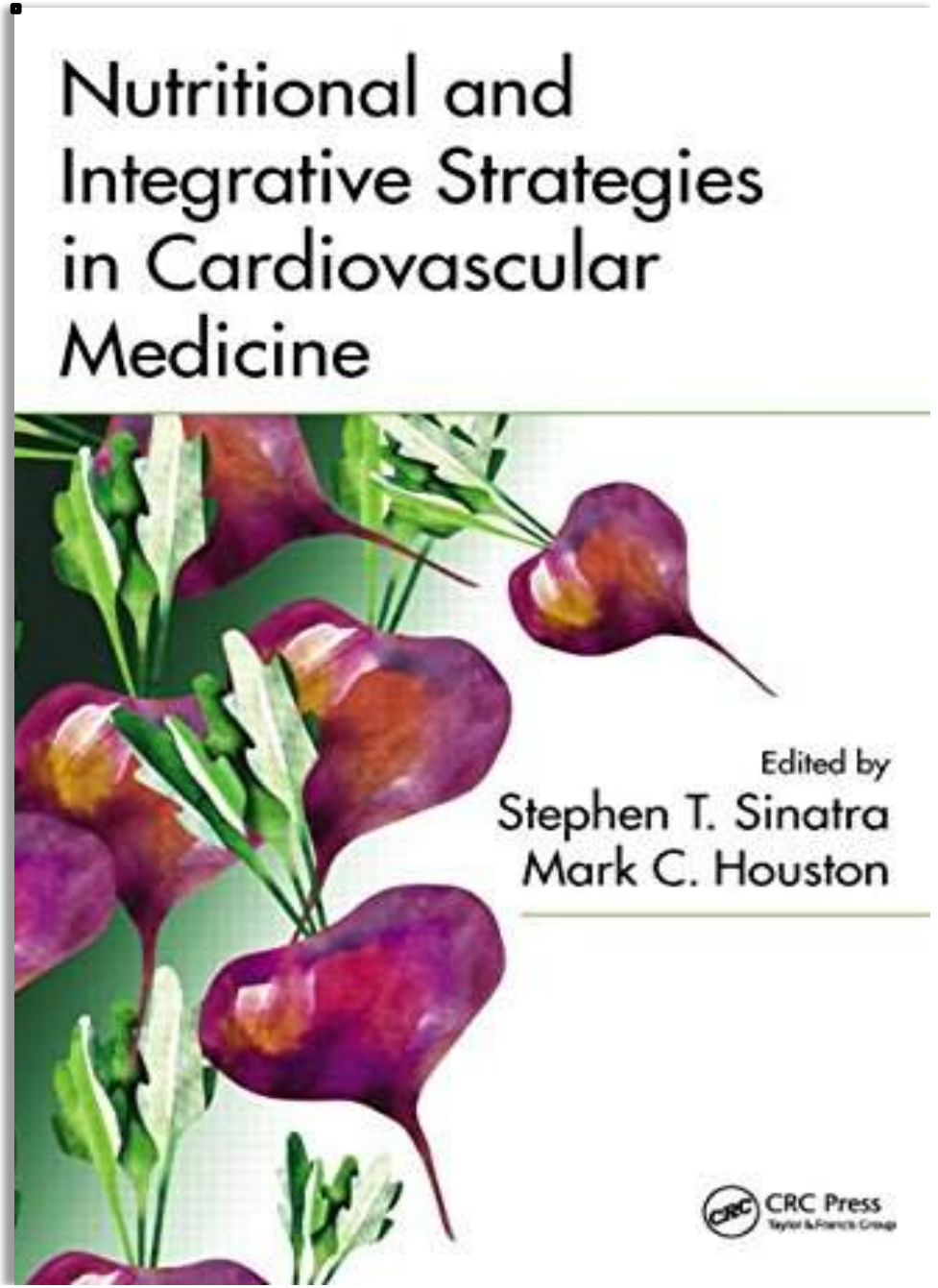
timeforwellness.org

Based on;

Healing the Heart with Whole Foods and Food Bioactives

Deanna Minich and Benjamin Brown

In; Nutritional and Integrative Strategies in Cardiovascular Medicine, 2015 by Stephen T. Sinatra (Editor), Mark C. Houston (Editor). CRC Press; 1st edition (2015)



Nourishment means more than just calories - it's a buffet of what heals, transforms, and connects us to life.

- Deanna Minich, PhD

www.foodandspirit.com

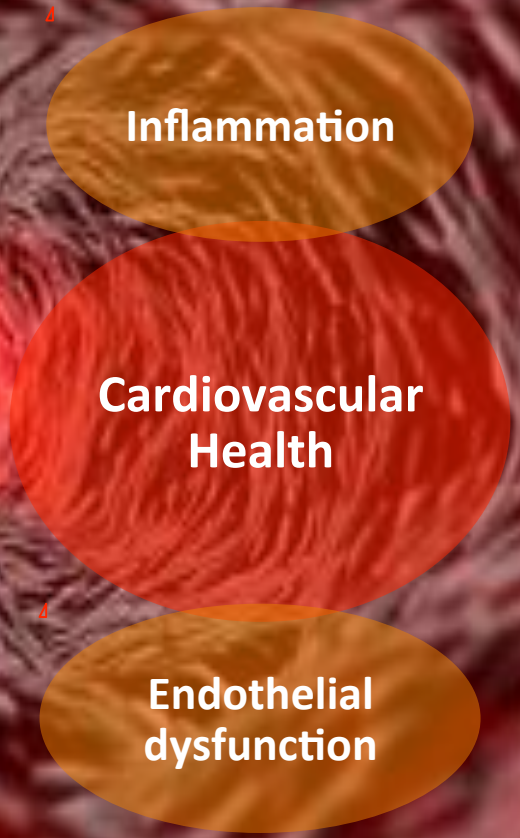
“Cardiovascular diseases (CVDs) are the number 1 cause of death globally: more people die annually from CVDs than from any other cause.”

World Health Organization. Cardiovascular diseases (CVDs).
Fact sheet N°317. Updated January 2015.

Video: atherosclerosis

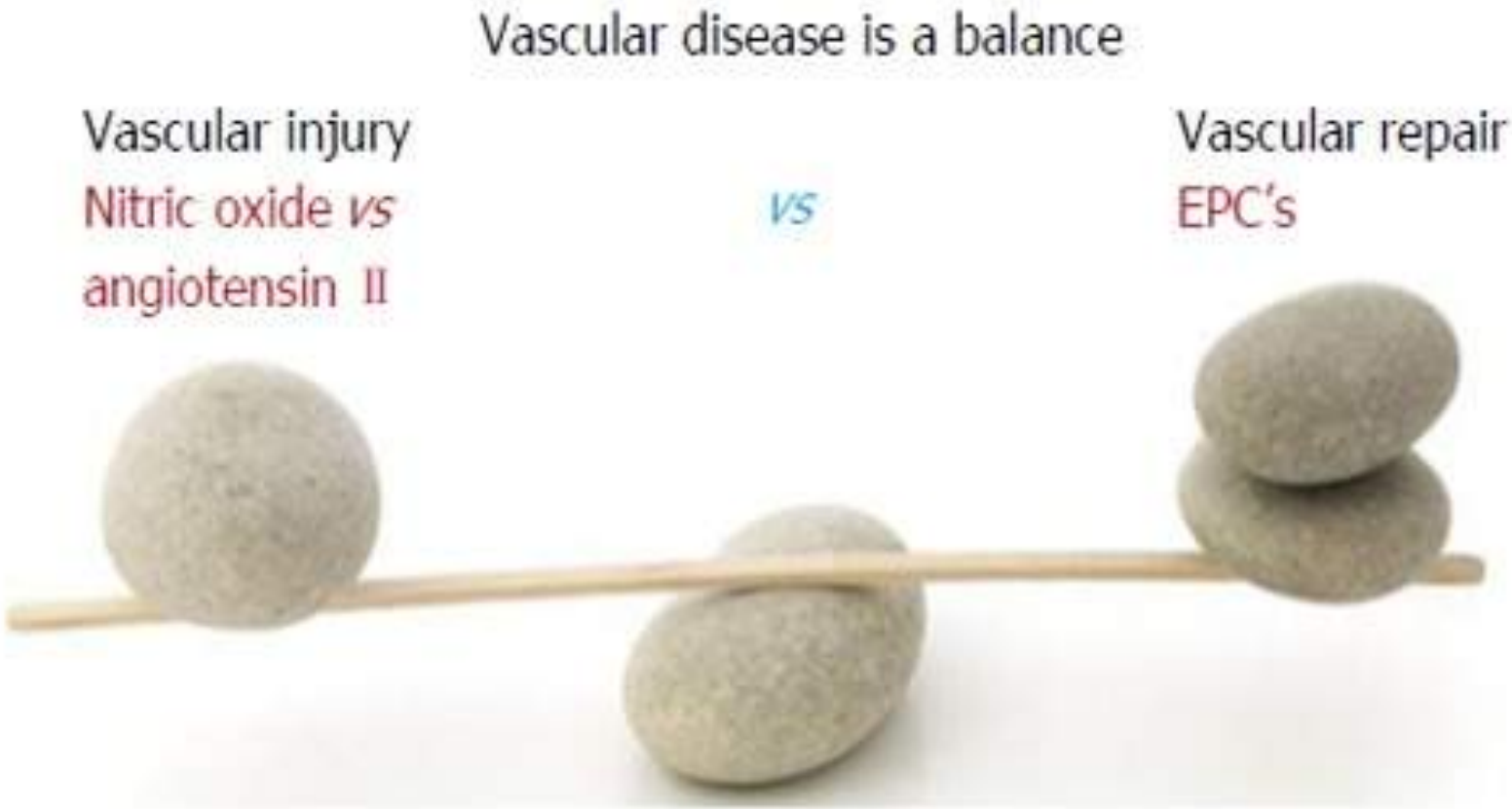
"***Arterial inflammation*** and ***endothelial dysfunction*** play central roles in the pathogenesis of atherosclerosis and adverse cardiovascular events."

"Only about 15% of acute coronary syndromes have a luminal diameter stenosis greater than 70% immediately before the rupture and thrombosis."



Mayo Clin Proc. 2009 Aug;84(8):741-57.

"Various insults that damage the endothelium, lead to endothelial dysfunction (ED) and may induce hypertension and other cardiovascular diseases."



Houston M. The role of nutrition and nutraceutical supplements in the treatment of hypertension. World J Cardiol. 2014 Feb 26;6(2):38-66.

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D.,

The addition of percutaneous coronary intervention to intensive pharmacologic therapy and lifestyle intervention *did not reduce long-term rates of death, nonfatal myocardial infarction,* and hospitalization for acute coronary syndromes.

differences between the PCI group and the medical-therapy group in the composite of death, myocardial infarction, and stroke (20.0% vs. 19.5%; hazard ratio, 1.05; 95% CI, 0.87 to 1.27; P=0.62); hospitalization for acute coronary syndrome (12.4% vs. 11.8%; hazard ratio, 1.07; 95% CI, 0.84 to 1.37; P=0.56); or myocardial infarction (13.2% vs. 12.3%; hazard ratio, 1.13; 95% CI, 0.89 to 1.43; P=0.33).

CONCLUSIONS

As an initial management strategy in patients with stable coronary artery disease, PCI did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when added to optimal medical therapy. (ClinicalTrials.gov number, NCT00007657.)

N Engl J Med. 2007 Apr 12;356(15):1503-16.

"…if you give a statin to a patient [for primary prevention] for about five years we can reduce the chance of a person having a heart attack or a stroke by about one per cent."

James McCormack, Professor of pharmaceutical sciences at the University of British Columbia.

Therapeutics Initiative. Do statins have a role in primary prevention? Therapeutics Letter. Issue 77: Mar - Apr 2010.

"We find that a 150 year old proverb is able to match modern medicine and is likely to have fewer side effects."

BMJ

BMJ 2013;347:f7267 doi: 10.1136/bmj.f7267 (Published 17 December 2013)

RESEARCH

A statin a day keeps the doctor away: comparative proverb assessment modelling study

OPEN ACCESS

Adam D M Briggs *academic clinical fellow*, Anja Mizdrak *researcher*, Peter Scarborough *senior researcher*

Results The estimated annual reduction in deaths from vascular disease of a statin a day, assuming 70% compliance and a reduction in vascular mortality of 12% (95% confidence interval 9% to 16%) per 1.0 mmol/L reduction in low density lipoprotein cholesterol, is 9400 (7000 to 12 500). The equivalent reduction from an apple a day, modelled using the PRIME model (assuming an apple weighs 100 g and that overall calorie consumption remains constant) is 8500 (95% credible interval 6200 to 10 800).

Conclusions Both nutritional and pharmaceutical approaches to the prevention of vascular disease may have the potential to reduce UK mortality significantly. With similar reductions in mortality, a 150 year old health promotion message is able to match modern medicine and is likely to have fewer side effects.

Introduction

"An apple a day keeps the doctor away," a public health message delivered by parents and teachers since the 19th century,[1] is an example of how concise, clear, and accurate Victorian health promotion can truly stand the test of time, whereas other Victorian practices—such as the use of leeches in primary care—have fallen away.

without evidence of significant harm.[4] This has led to calls to use statins for cardiovascular disease prevention at the population level, particularly for people aged 50 years and over.[5]

We set out to test how almost 150 years of Victorian wisdom might compare with the more widespread use of statins in primary prevention. We modelled the effect on vascular mortality of prescribing everybody in the UK over 50 years old either an apple (*Malus domestica*) a day or a statin a day, estimated the number of adverse events, and compared the subsequent drug, or fruit, costs.

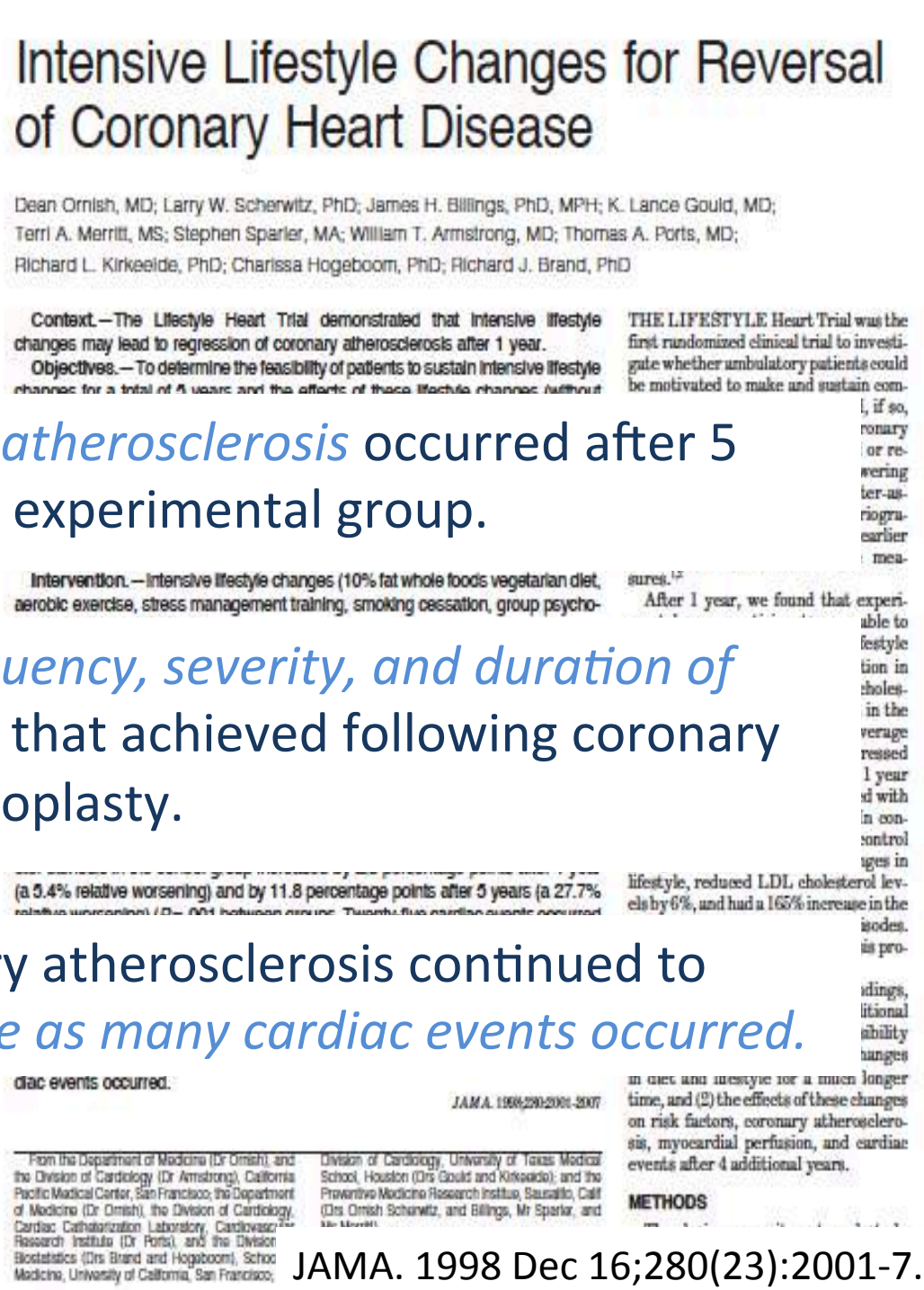
Methods

Data on the effect on vascular mortality (any stroke, cardiac death, or other vascular death) of the UK population of a statin a day came from the Cholesterol Treatment Trialists' meta-analysis, which found that reducing cholesterol with a statin reduces the relative risk of vascular mortality by 12% (95% confidence interval 9% to 16%) per 1.0 mmol/L reduction in low density lipoprotein cholesterol and that on average this is reduced by 1.08 mmol/L over a year of treatment.[6] We applied this annual reduction to age and sex specific vascular mortality

Briggs AD, Mizdrak A, Scarborough P. BMJ 2013; DOI: 10.1136/bmj.f7267.

“I don't understand *why asking people to eat a well-balanced vegetarian diet is considered drastic*, while it is *medically conservative to cut people open* and put them on cholesterol-lowering drugs for the rest of their lives.”

— Dean Ornish, MD



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

Intervention.—Intensive lifestyle changes (10% fat whole foods vegetarian diet, aerobic exercise, stress management training, smoking cessation, group psycho-

(a 5.4% relative worsening) and by 11.8 percentage points after 5 years (a 27.7%

diac 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, Cardiovasc Research Institute (Dr Ports), and the Division Biostatistics (Drs Brand and Hogeboom), Schoo Medicine, University of California, San Francisco; Division of Cardiology, University of Texas Medical School, Houston (Drs Gould and Kirkeeide); and the Preventive Medicine Research Institute, Sausalito, Calif (Drs Ornish Scherwitz, and Billings, Mr Sparler, and

THE LIFESTYLE Heart Trial was the first randomized clinical trial to investigate whether ambulatory patients could be motivated to make and sustain com-

, if so, ronary or re- wering ter-as- riogra- earlier mea-

sures.[12]

After 1 year, we found that experi- able to festyle tion in choles- in the verage ressed 1 year d with n con- ontrol ges in

lifestyle, reduced LDL cholesterol lev- els by 6%, and had a 165% increase in the isodes. is pro-

ddings, litional ability hanges

in diet and lifestyle for a much longer time, and (2) the effects of these changes on risk factors, coronary atherosclero- sis, myocardial perfusion, and cardiac events after 4 additional years.

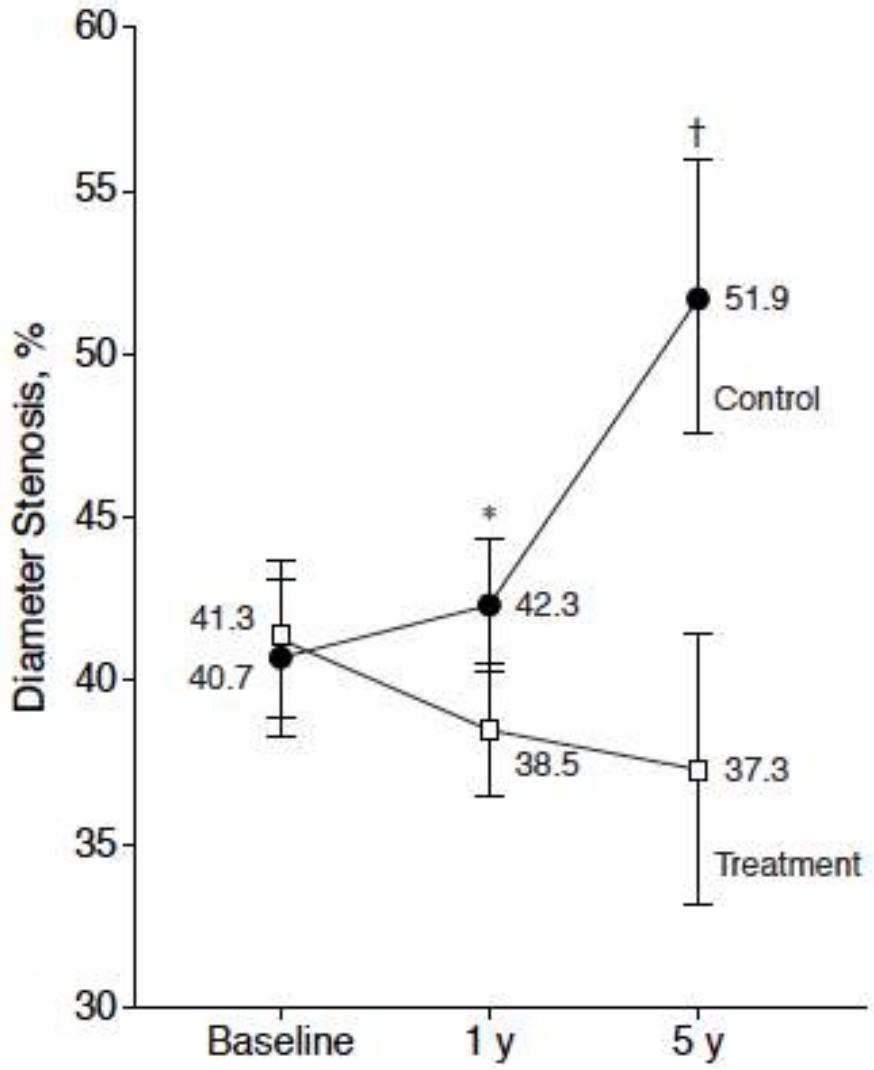
METHODS

- More *regression of coronary atherosclerosis* occurred after 5 years than after 1 year in the experimental group.
- The *marked reduction in frequency, severity, and duration of angina* was comparable with that achieved following coronary artery bypass surgery or angioplasty.
- In the control group, coronary atherosclerosis continued to progress and *more than twice as many cardiac events occurred.*

JAMA. 1998 Dec 16;280(23):2001-7.

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; William T. Armstrong, MD; Thomas A. Ports, MD; boom, PhD; Richard J. Brand, PhD



onstrated that intensive lifestyle therosclerosis after 1 year.
patients to sustain intensive lifestyle of these lifestyle changes (without e.
ucted from 1986 to 1992 using a

e to severe coronary heart disease ge group or to a usual-care control quantitative coronary arteriography. al centers.
0% fat whole foods vegetarian diet, smoking cessation, group psycho-

ntensive lifestyle changes, changes nd cardiac events.
[71%] of 28 patients completed rehensive lifestyle changes for 5 %] of 20 patients completed 5-year e experimental group, the average d 1.75 absolute percentage points by 3.1 absolute percentage points ontrast, the average percent diam- 2.3 percentage points after 1 year ntage points after 5 years (a 27.7% Twenty-five cardiac events occurred in 20 control group patients during the control group, 2.47 [95% con-

y atherosclerosis occurred after 5 up. In contrast, in the control group, and more than twice as many car-

JAMA. 1998;280:2001-2007

on of Cardiology, University of Texas Medical l, Houston (Drs Gould and Kirkeeide); and the ntive Medicine Research Institute, Sausalito, Calif (Drs Ornish Scherwitz, and Billings, Mr Sparler, and

of Medicine (Dr Ornish), the Division of Cardiology, Cardiac Catheterization Laboratory, Cardiovasc Research Institute (Dr Ports), and the Division Biostatistics (Drs Brand and Hogaboom), Schoo Medicine, University of California, San Francisco;

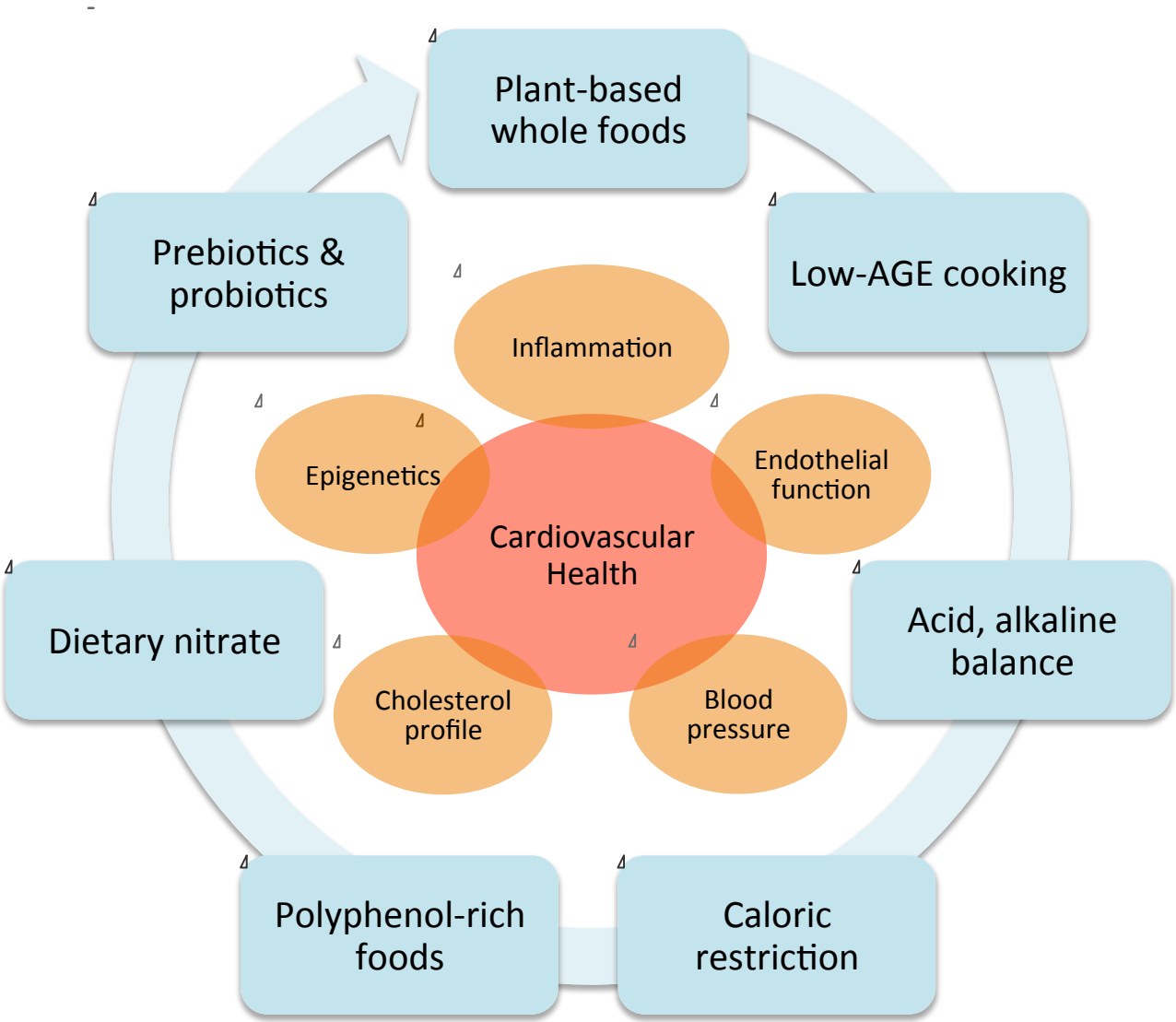
THE LIFESTYLE Heart Trial was the first randomized clinical trial to investigate whether ambulatory patients could be motivated to make and sustain comprehensive lifestyle changes and, if so, whether the progression of coronary atherosclerosis could be stopped or reversed without using lipid-lowering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

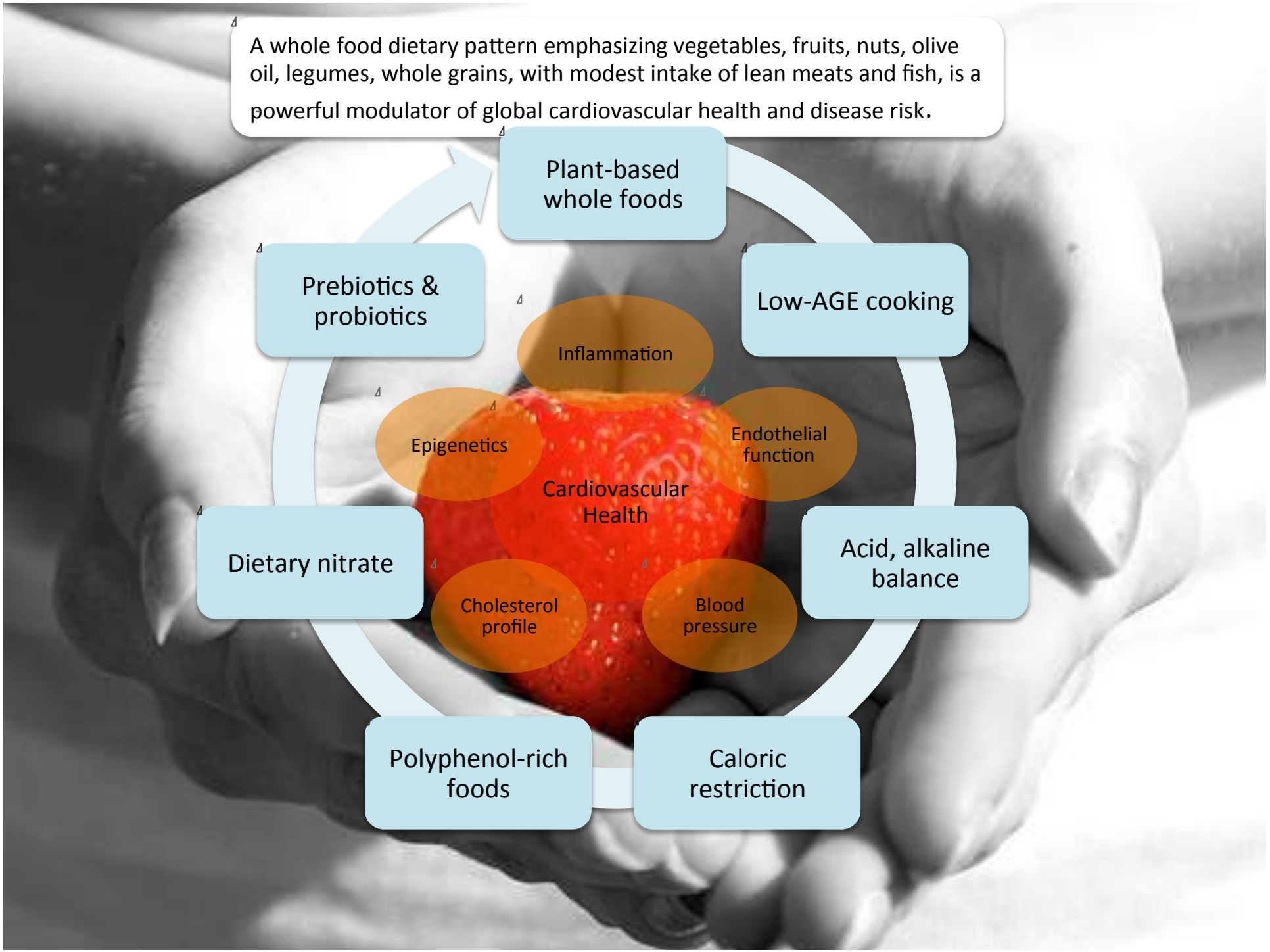
After 1 year, we found that experimental group participants were able to make and maintain intensive lifestyle changes and had a 37.2% reduction in low-density lipoprotein (LDL) cholesterol levels and a 91% reduction in the frequency of anginal episodes.[3] Average percent diameter stenosis regressed 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

JAMA. 1998 Dec 16;280(23):2001-7.


Plant-based whole foods
Low-AGE cooking
Acid, alkaline balance
Caloric restriction
Polyphenol-rich foods
Dietary nitrate
Prebiotics & probiotics
Inflammation
Endothelial function
Blood pressure
Cholesterol profile
Epigenetics
Cardiovascular Health


A whole food dietary pattern emphasizing vegetables, fruits, nuts, olive oil, legumes, whole grains, with modest intake of lean meats and fish, is a powerful modulator of global cardiovascular health and disease risk.
Plant-based whole foods
Low-AGE cooking
Acid, alkaline balance
Caloric restriction
Polyphenol-rich foods
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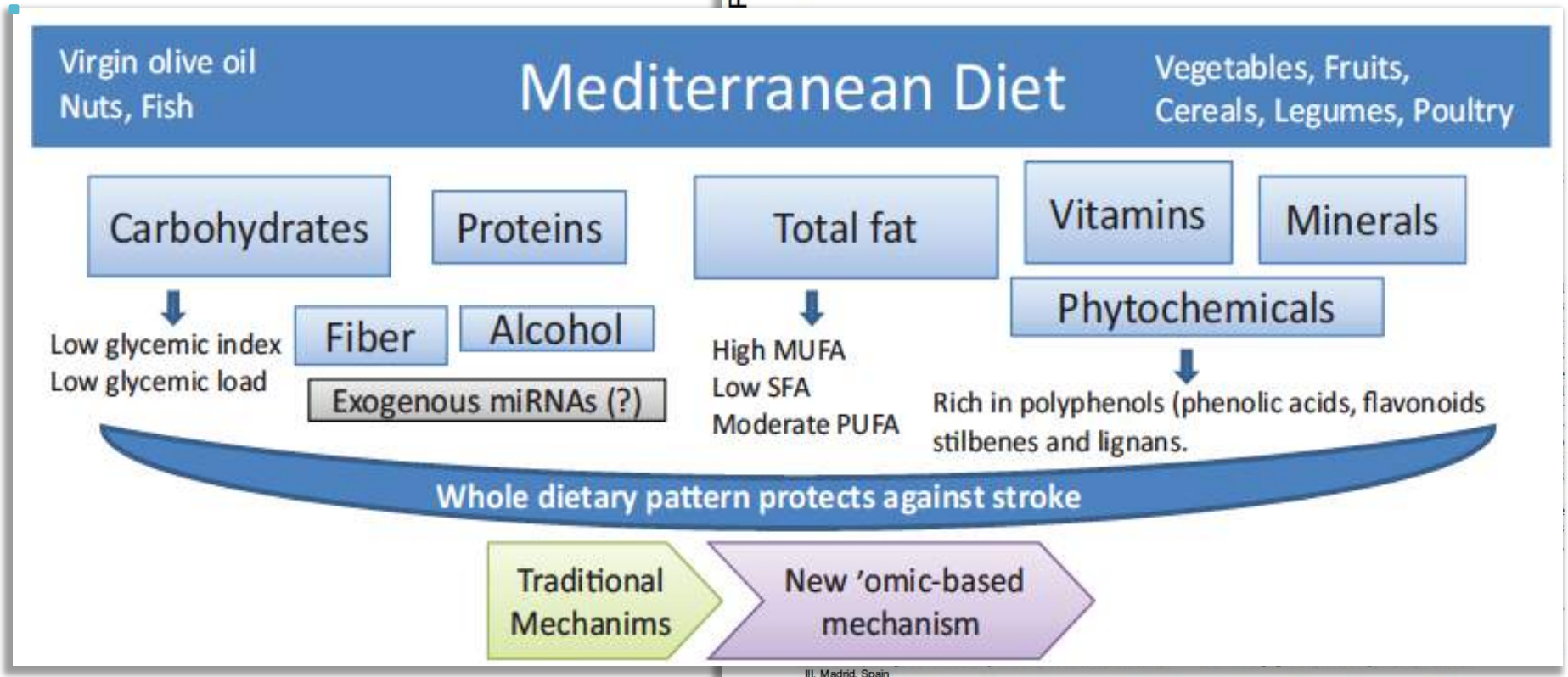
Inflammation
Endothelial function
Blood pressure
Cholesterol profile
Epigenetics
Cardiovascular Health

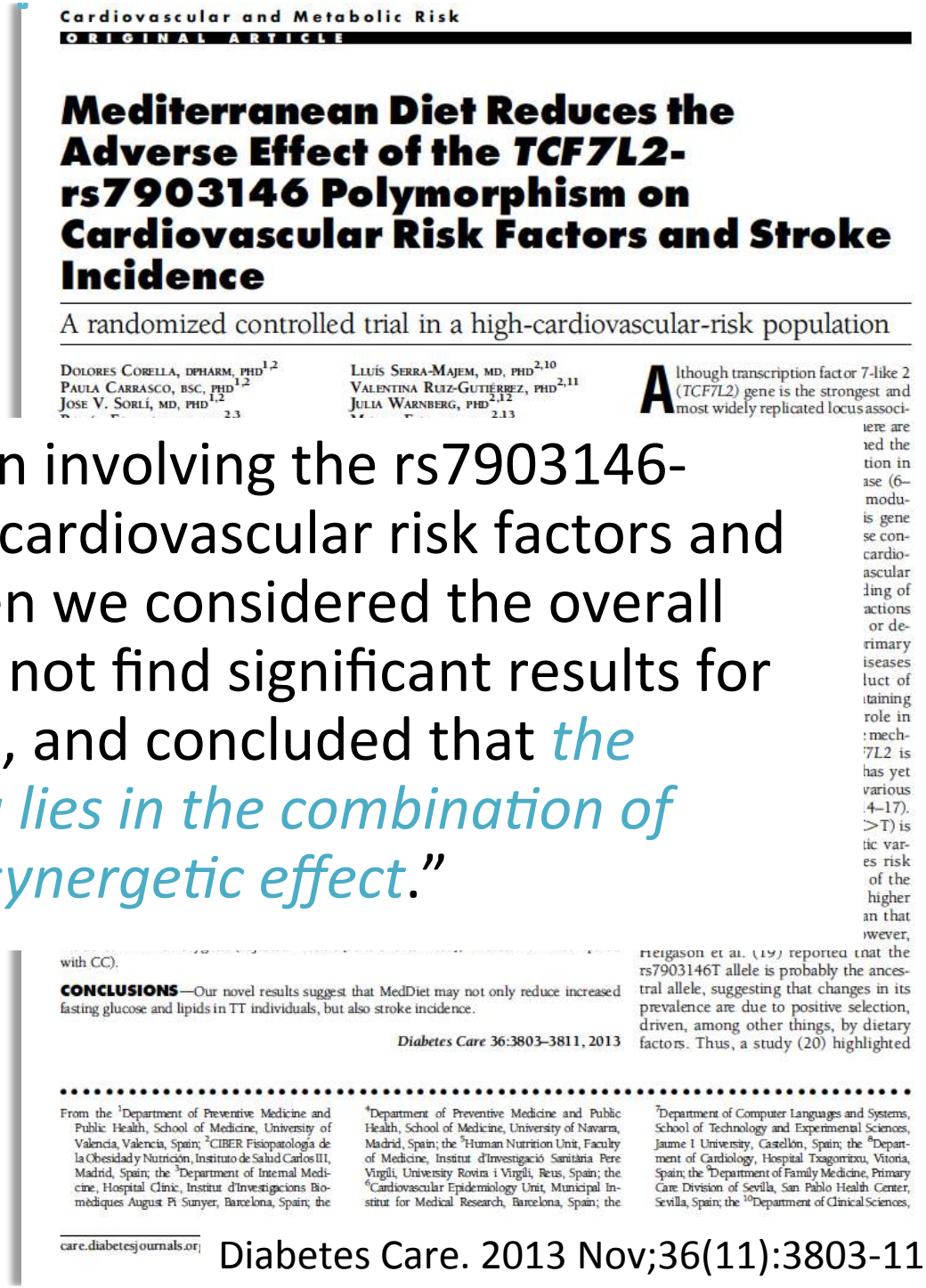
How does the Mediterranean diet promote cardiovascular health? Current progress toward molecular mechanisms



III, Madrid, Spain
[3] Department of Cardiovascular Epidemiology and Population Genetics, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

*Corresponding author:
Dolores Corella
E-mail: dolores.corella@uv.es

Bioessays. 2014 May;36(5):526-37.



Cardiovascular and Metabolic Risk

ORIGINAL ARTICLE

Mediterranean Diet Reduces the Adverse Effect of the *TCF7L2*-rs7903146 Polymorphism on Cardiovascular Risk Factors and Stroke Incidence

A randomized controlled trial in a high-cardiovascular-risk population

DOLORES CORELLA, DPHARM, PHD[1,2]
PAULA CARRASCO, BSC, PHD[1,2]
JOSE V. SORLÍ, MD, PHD[1,2]
LLUÍS SERRA-MAJEM, MD, PHD[2,10]
VALENTINA RUIZ-GUTIÉRREZ, PHD[2,11]
JULIA WARNBERG, PHD[2,12]

Although transcription factor 7-like 2 (*TCF7L2*) gene is the strongest and most widely replicated locus associ-

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CONCLUSIONS—Our novel results suggest that MedDiet may not only reduce increased fasting glucose and lipids in TT individuals, but also stroke incidence.

Diabetes Care 36:3803–3811, 2013

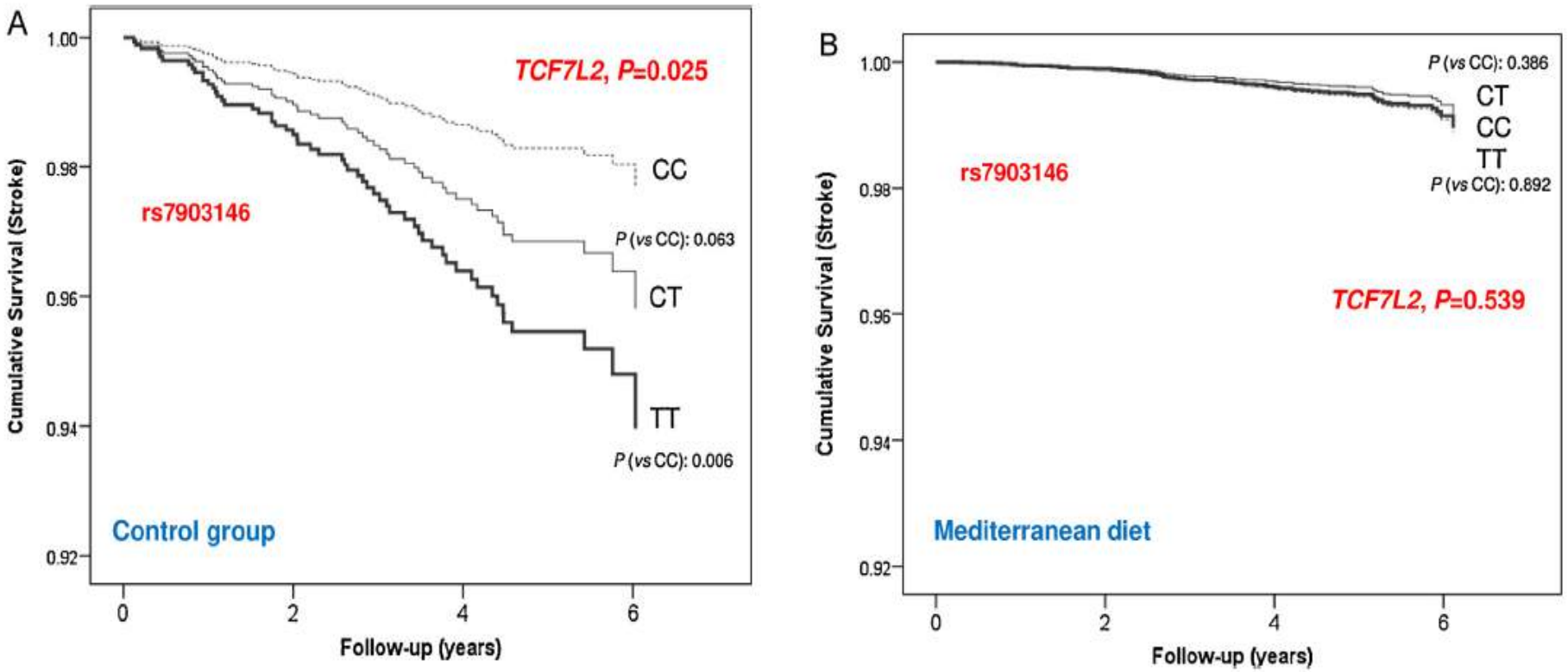
Helgason et al. (19) reported that the rs7903146T allele is probably the ancestral allele, suggesting that changes in its prevalence are due to positive selection, driven, among other things, by dietary factors. Thus, a study (20) highlighted

From the [1]Department of Preventive Medicine and Public Health, School of Medicine, University of Valencia, Valencia, Spain; [2]CIBER Fisiopatología de la Obesidad y Nutrición, Instituto de Salud Carlos III, Madrid, Spain; the [3]Department of Internal Medicine, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi Sunyer, Barcelona, Spain; the [4]Department of Preventive Medicine and Public Health, School of Medicine, University of Navarra, Madrid, Spain; the [5]Human Nutrition Unit, Faculty of Medicine, Institut d'Investigació Sanitària Pere Virgili, University Rovira i Virgili, Reus, Spain; the [6]Cardiovascular Epidemiology Unit, Municipal Institut for Medical Research, Barcelona, Spain; the [7]Department of Computer Languages and Systems, School of Technology and Experimental Sciences, Jaume I University, Castellón, Spain; the [8]Department of Cardiology, Hospital Txagorritxu, Vitoria, Spain; the [9]Department of Family Medicine, Primary Care Division of Sevilla, San Pablo Health Center, Sevilla, Spain; the [10]Department of Clinical Sciences,

"The gene-diet interaction involving the rs7903146-TCF7L2 polymorphism in cardiovascular risk factors and stroke was observed when we considered the overall MedDiet pattern. We did not find significant results for the main individual foods, and concluded that *the importance of our finding lies in the combination of MedDiet components: a synergetic effect*."

Diabetes Care. 2013 Nov;36(11):3803-11

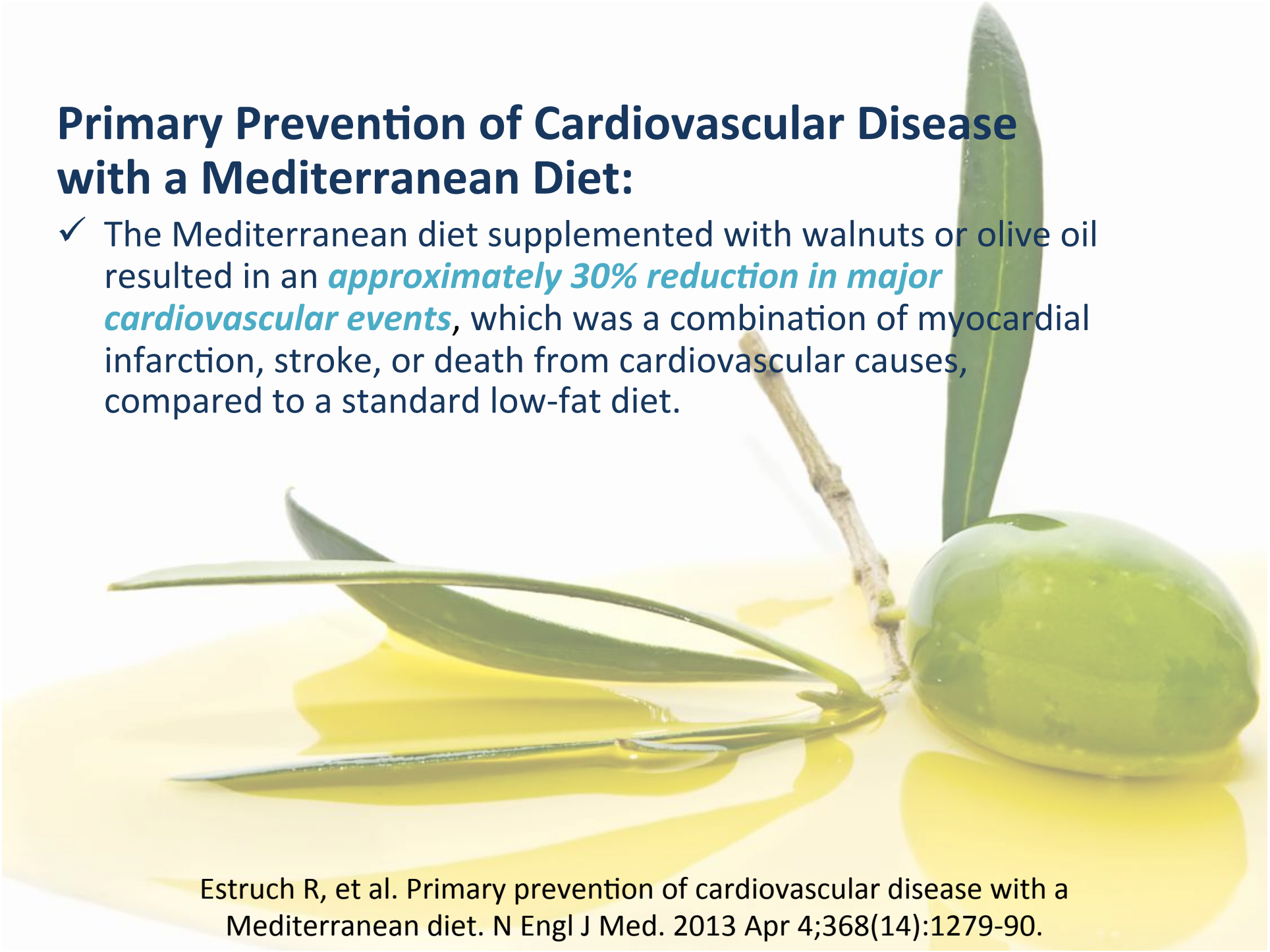
Genetic predisposition quenched by diet



Corella D, et al. Mediterranean diet reduces the adverse effect of the TCF7L2-rs7903146 polymorphism on cardiovascular risk factors and stroke incidence: a randomized controlled trial in a high-cardiovascular-risk population. Diabetes Care. 2013 Nov;36(11):3803-11.

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet:

- ✓ The Mediterranean diet supplemented with walnuts or olive oil resulted in an ***approximately 30% reduction in major cardiovascular events***, which was a combination of myocardial infarction, stroke, or death from cardiovascular causes, compared to a standard low-fat diet.

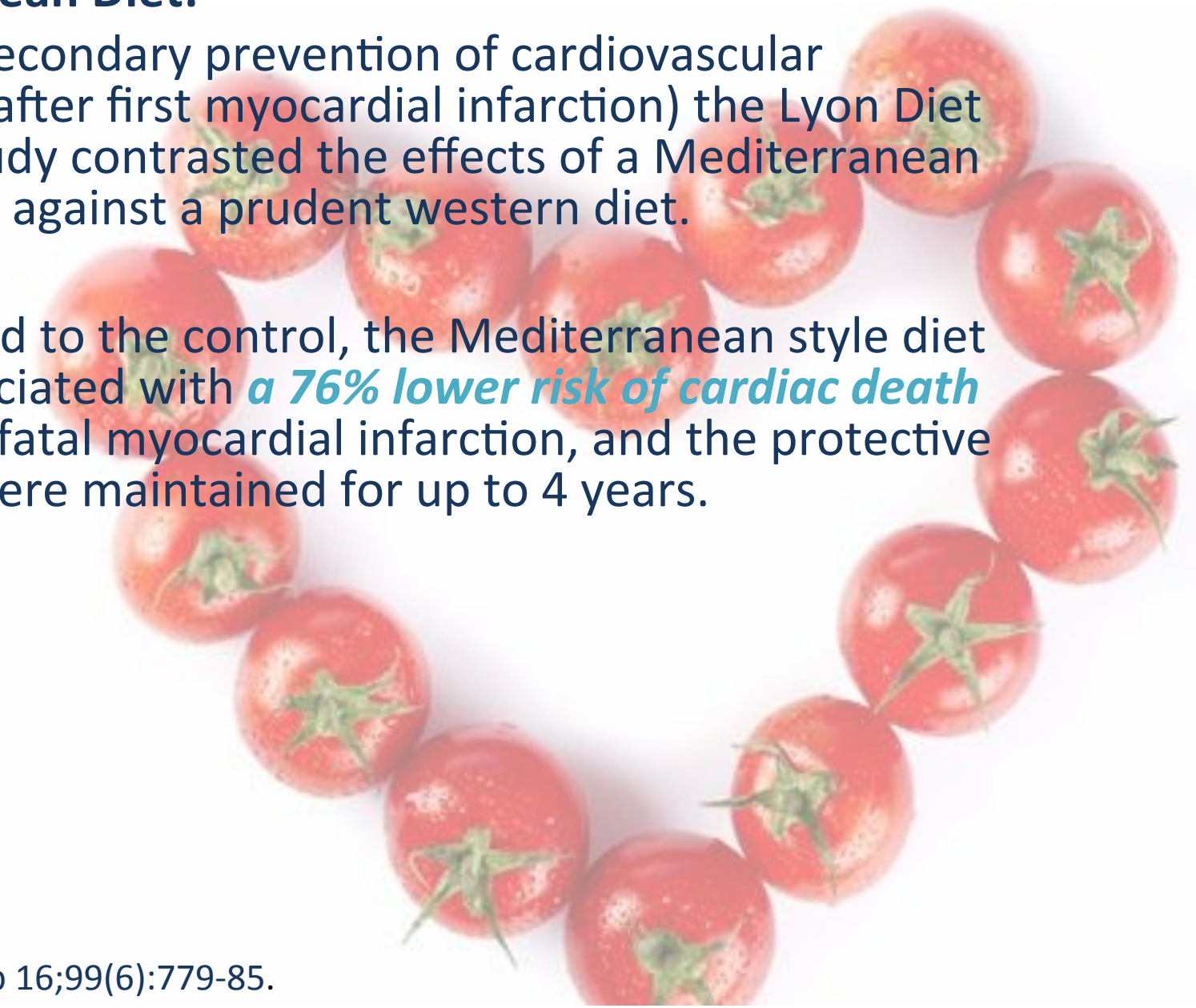


Estruch R, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013 Apr 4;368(14):1279-90.

Secondary Prevention of Cardiovascular Disease with a Mediterranean Diet:

- ✓ For the secondary prevention of cardiovascular disease (after first myocardial infarction) the Lyon Diet Heart Study contrasted the effects of a Mediterranean style diet against a prudent western diet.

- ✓ Compared to the control, the Mediterranean style diet was associated with ***a 76% lower risk of cardiac death*** and non-fatal myocardial infarction, and the protective effects were maintained for up to 4 years.



Circulation. 1999 Feb 16;99(6):779-85.

Clinical Cardiology with a Fork

Prevention of Myocardial Infarction or Cardiac Death

Intervention	Angioplasty/ Stent	Statins	Mediterranean-Style Diet
Primary	N/A	1%	30%
Secondary	No Data	18%	76%

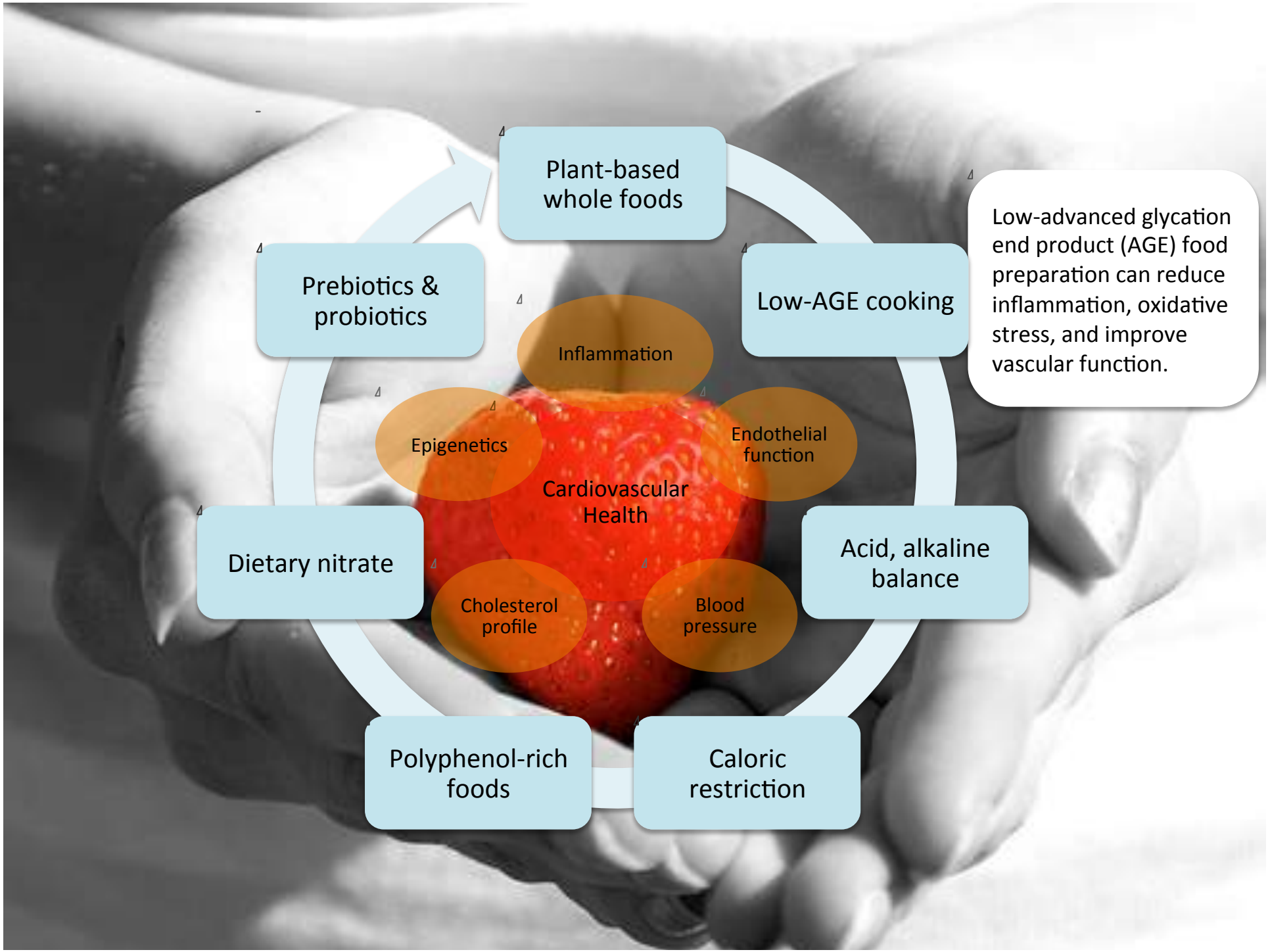
N Engl J Med. 2007 Apr 12;356(15):1503-16

Therapeutics Letter. Issue 77: 2010.

Lancet. 2002;360(9326):7-22.

N Engl J Med 2013; 368:1279-129

Circulation. 1999 Feb 16;99(6):779-85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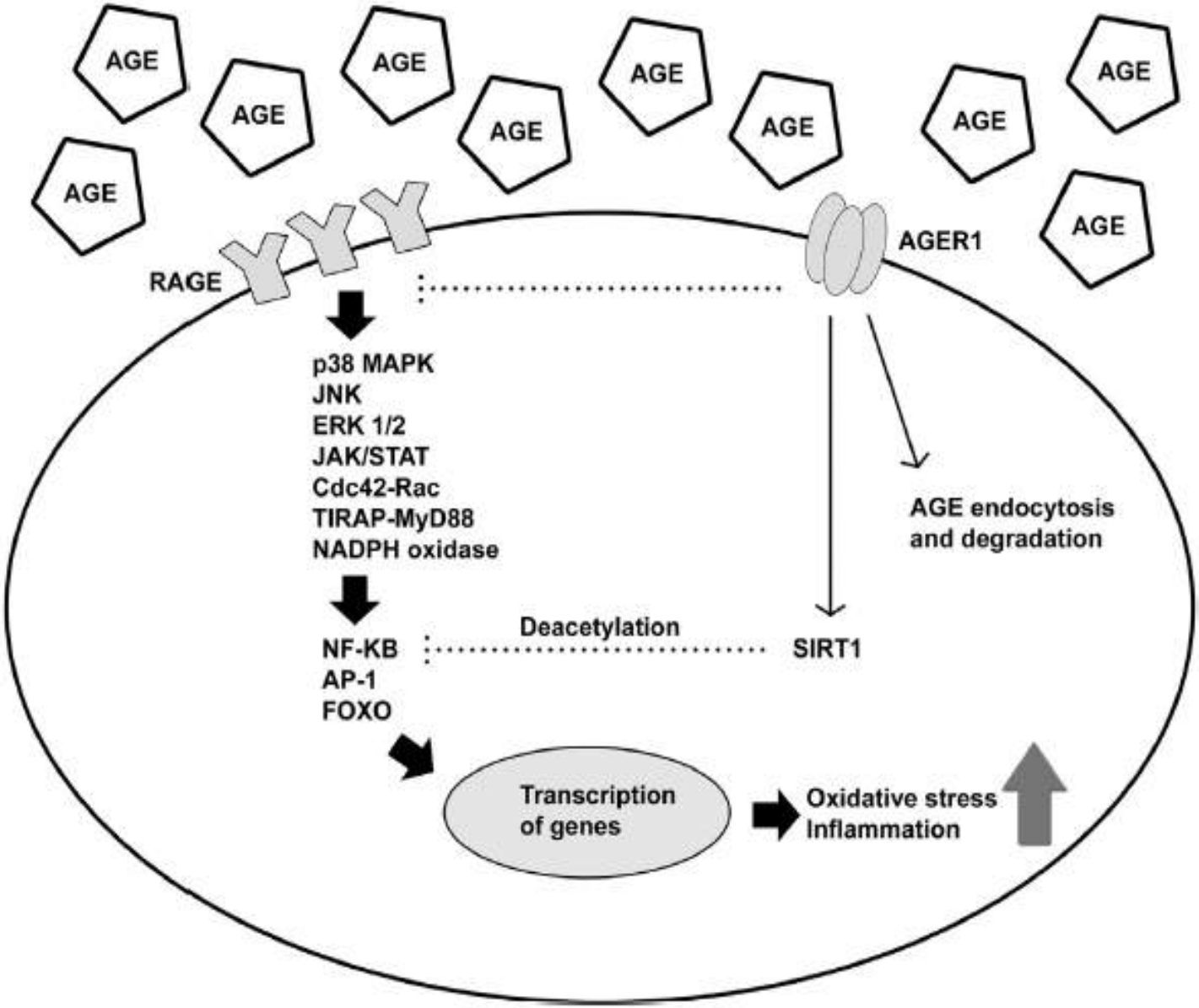
Cholesterol profile
Epigenetics
Cardiovascular Health
Low-advanced glycation end product (AGE) food preparation can reduce inflammation, oxidative stress, and improve vascular function.



Poulsen MW,et al. Advanced glycation endproducts in food and their effects on health. Food Chem Toxicol. 2013 Oct;60:10-37.


Never underestimate the power of a single meal.
- Deanna Minich, PhD

Effects of low- and high-advanced glycation endproduct meals on endothelial function:

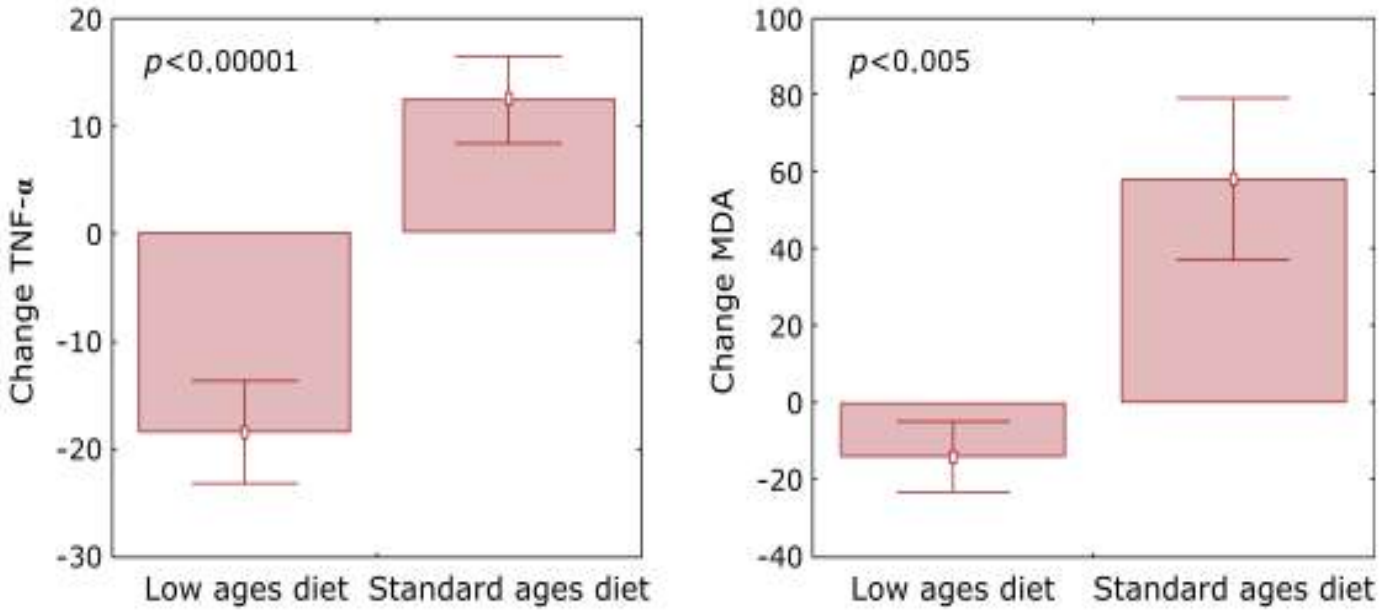
A single “real-life” High-AGE meal induces a *profound impairment of both macro- and microvascular function* (−36.2% and −67.2%, respectively).

These changes are significantly greater than those induced by a meal containing the same ingredients but with a five-fold lower AGE concentration.

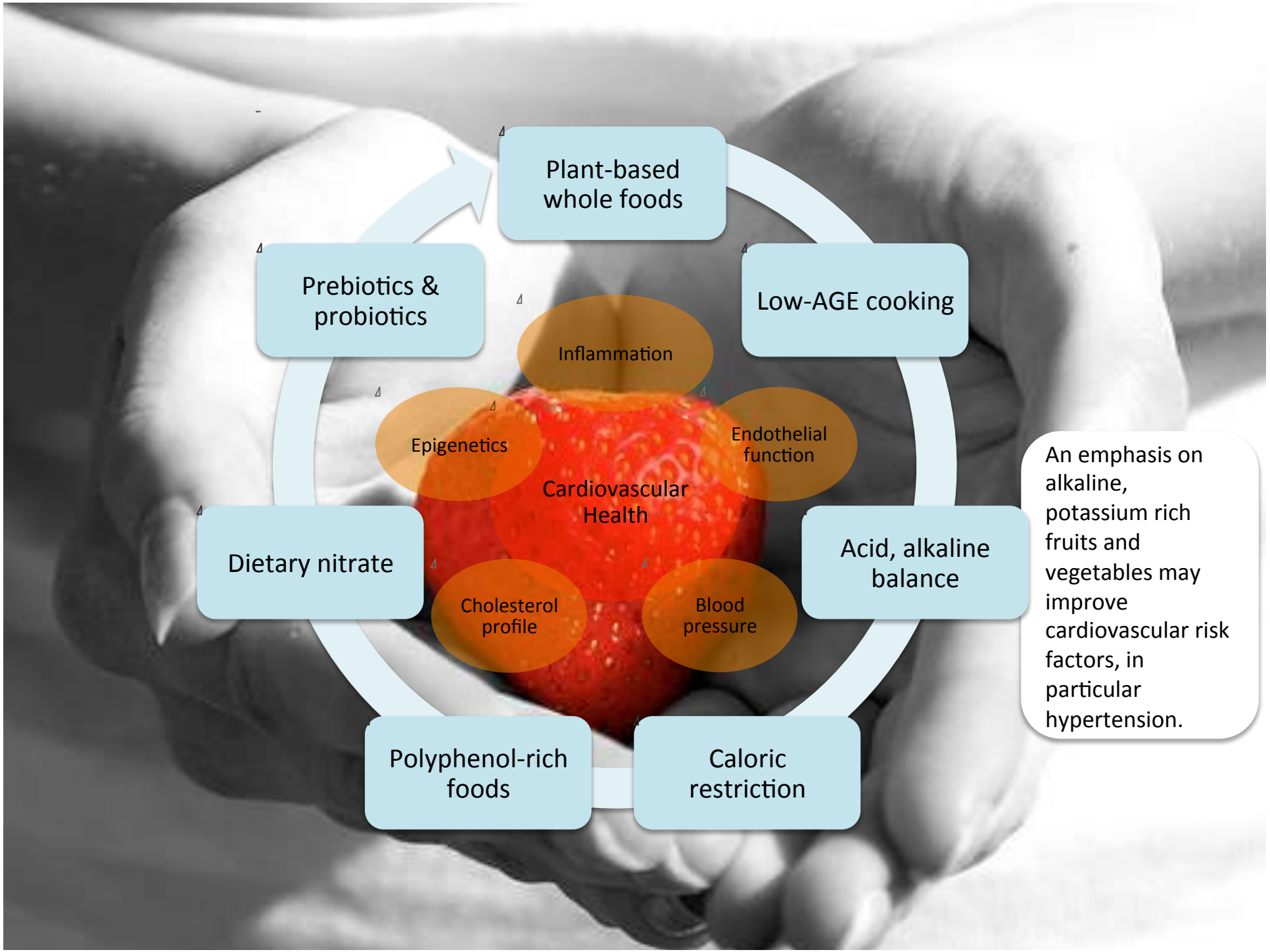
Am J Clin Nutr. 2007 May;85(5):1236-43.

Dietary AGE restriction diminishes inflammation markers and oxidative stress:

A 6-week intervention study with a low AGE diet in diabetic patients demonstrated a *marked reduction in inflammation and oxidative stress* compared to a standard diet.



J Clin Biochem Nutr. 2013 Jan;52(1):22-6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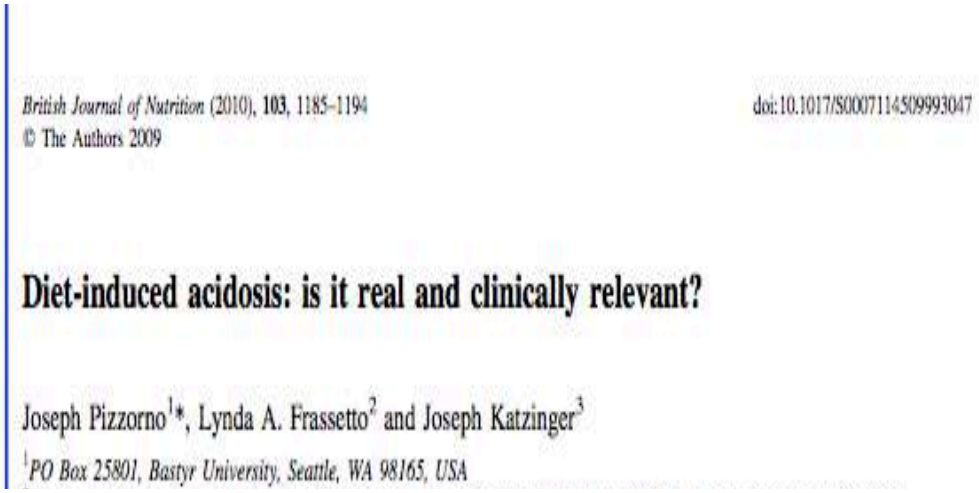
Prebiotics & probiotics
Inflammation
Endothelial function
Blood pressure
Cholesterol profile
Epigenetics
Cardiovascular Health
An emphasis on alkaline, potassium rich fruits and vegetables may improve cardiovascular risk factors, in particular hypertension.



British Journal of Nutrition (2010), 103, 1185–1194
© The Authors 2009

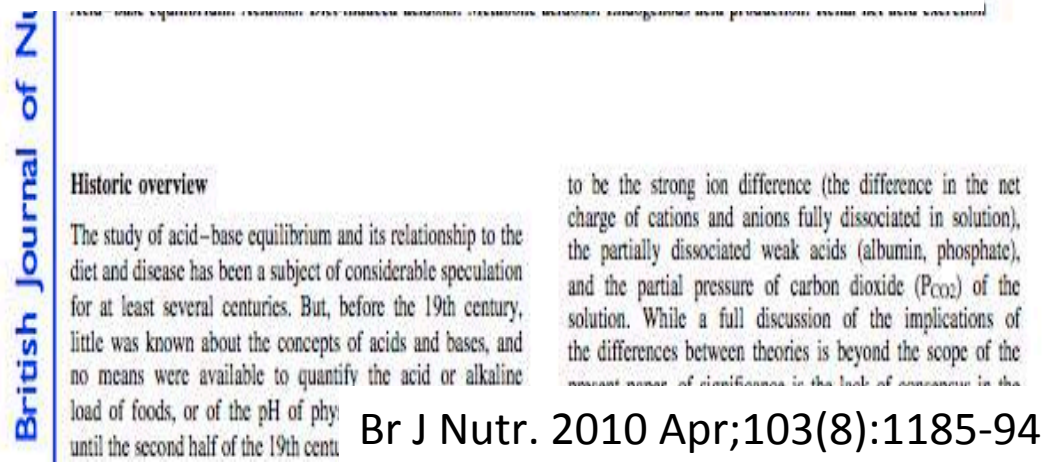
doi:10.1017/S0007114509993047

Diet-induced acidosis: is it real and clinically relevant?

Joseph Pizzorno[1]*, Lynda A. Frassetto[2] and Joseph Katzinger[3]

[1]*PO Box 25801, Bastyr University, Seattle, WA 98165, USA*

"…the available research makes a compelling case that *diet-induced acidosis is a real phenomenon, has significant clinical relevance,* may largely be prevented through dietary changes, *and should be recognized and treated.*"



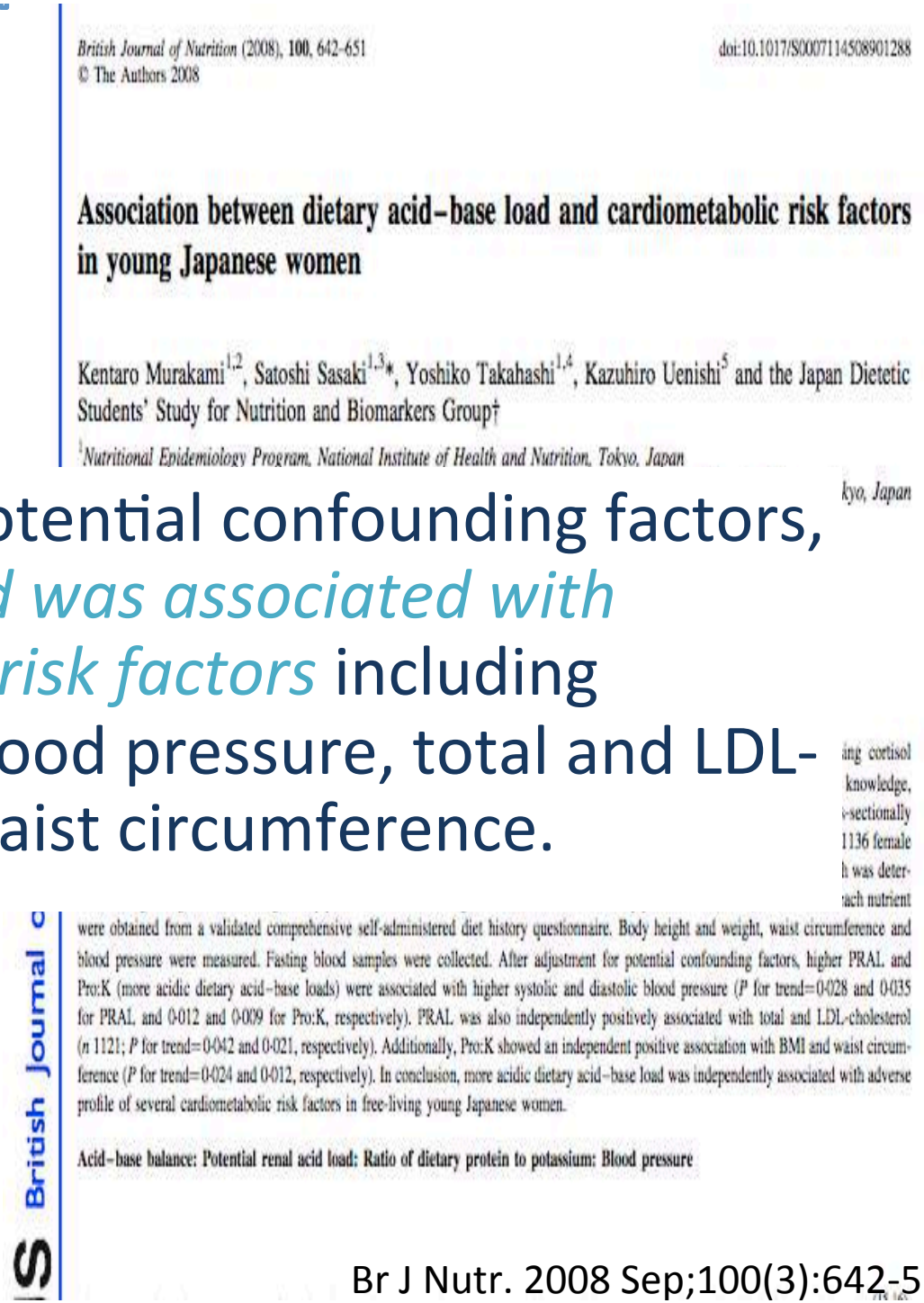
British Journal of Nu

Historic overview

The study of acid–base equilibrium and its relationship to the diet and disease has been a subject of considerable speculation for at least several centuries. But, before the 19th century, little was known about the concepts of acids and bases, and no means were available to quantify the acid or alkaline load of foods, or of the pH of phy until the second half of the 19th centu

to be the strong ion difference (the difference in the net charge of cations and anions fully dissociated in solution), the partially dissociated weak acids (albumin, phosphate), and the partial pressure of carbon dioxide (P_{CO2}) of the solution. While a full discussion of the implications of the differences between theories is beyond the scope of the

Br J Nutr. 2010 Apr;103(8):1185-94.



British Journal of Nutrition (2008), **100**, 642-651
doi:10.1017/S0007114508901288

Association between dietary acid–base load and cardiometabolic risk factors in young Japanese women

Kentaro Murakami[1,2], Satoshi Sasaki[1,3]*, Yoshiko Takahashi[1,4], Kazuhiro Uenishi[5] and the Japan Dietetic Students' Study for Nutrition and Biomarkers Group†

[1]*Nutritional Epidemiology Program, National Institute of Health and Nutrition, Tokyo, Japan*

After adjustment for potential confounding factors, *higher dietary acid load was associated with cardiovascular disease risk factors* including systolic and diastolic blood pressure, total and LDL-cholesterol, BMI and waist circumference.

were obtained from a validated comprehensive self-administered diet history questionnaire. Body height and weight, waist circumference and blood pressure were measured. Fasting blood samples were collected. After adjustment for potential confounding factors, higher PRAL and Pro:K (more acidic dietary acid–base loads) were associated with higher systolic and diastolic blood pressure (*P* for trend=0·028 and 0·035 for PRAL, and 0·012 and 0·009 for Pro:K, respectively). PRAL was also independently positively associated with total and LDL-cholesterol (*n* 1121; *P* for trend=0·042 and 0·021, respectively). Additionally, Pro:K showed an independent positive association with BMI and waist circumference (*P* for trend=0·024 and 0·012, respectively). In conclusion, more acidic dietary acid–base load was independently associated with adverse profile of several cardiometabolic risk factors in free-living young Japanese women.

Acid–base balance: Potential renal acid load: Ratio of dietary protein to potassium: Blood pressure

Br J Nutr. 2008 Sep;100(3):642-51.

European Journal of Clinical Nutrition (2009), 1–9

0954-3007/09 $32.00
www.nature.com/ejcn

ORIGINAL ARTICLE

Metabolic and physiologic improvements from consuming a paleolithic, hunter-gatherer type diet

LA Frassetto, M Schloetter, M Mietus-Synder, RC Morris Jr and A Sebastian

Department of Medicine, University of California San Francisco School of Medicine, San Francisco, CA, USA

A short-term (10-day) intervention with a highly alkaline diet (comprising lean meat, fruits, vegetables and nuts and excluding cereal grains, dairy and legumes) resulted in a marked *increase in potassium intake and improvements in vascular reactivity, blood pressure, glucose tolerance, insulin sensitivity and lipid profiles.*

European Journal of Clinical Nutrition advance online publication, 11 February 2009; doi:10.1038/ejcn.2009.4

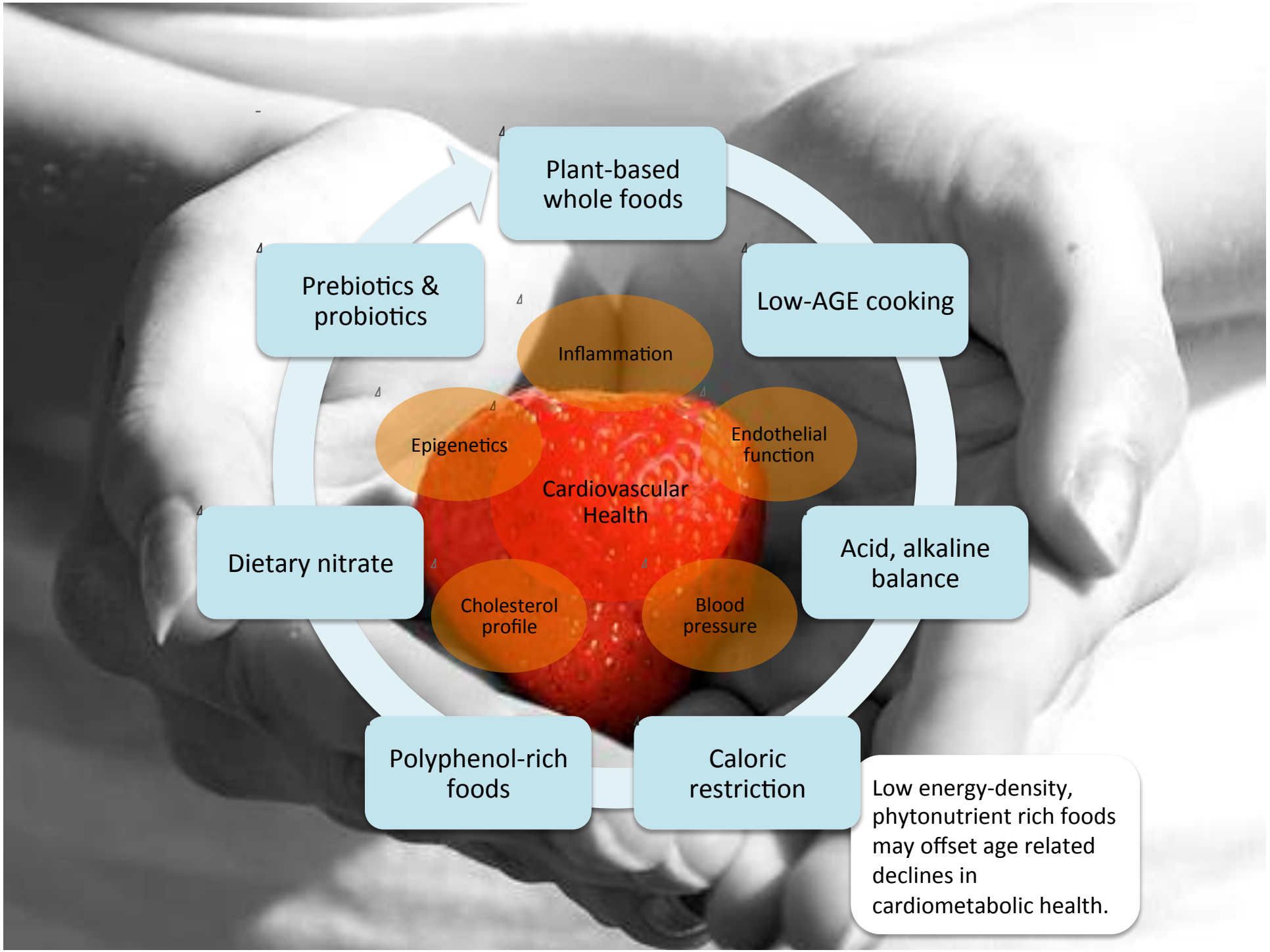
Keywords: paleolithic diet; blood pressure; glucose tolerance; insulin sensitivity; lipids

Introduction

Eur J Clin Nutr. 2009 Aug;63(8):947-55.

Food Group	PRAL (mEq)	
Fruits and fruit juices	-3.1	Alkaline
Vegetables	-2.8	
Red wine	-2.4	
Coffee	-1.4	
Fats and Oils	0	Neutral
Sugar and Honey	0	
Milk	+1	
Bread	+3.5	Acid
Lentils	+3.5	
Flour	+7	
Cheese (low protein)	+8	
Meat and meat products	+9.5	
Cheese (high protein)	+23.6	

Remer T, Manz F. Potential renal acid load of foods and its influence on urine pH. J Am Diet Assoc. 1995 Jul;95(7):791-7.


Plant-based whole foods
Low-AGE cooking
Acid, alkaline balance
Caloric restriction
Polyphenol-rich foods
Dietary nitrate
Prebiotics & probiotics
Inflammation
Endothelial function
Blood pressure
Cholesterol profile
Epigenetics
Cardiovascular Health
Low energy-density, phytonutrient rich foods may offset age related declines in cardiometabolic health.

Okinawa's Ushi Okushima, still gardening at age 109.

Caloric Restriction, the Traditional Okinawan Diet, and Healthy Aging

The Diet of the World's Longest-Lived People and Its Potential Impact on Morbidity and Life Span

BRADLEY J. WILLCOX,[a,b] D. CRAIG WILLCOX,[a,c] HIDEMI TODORIKI,[d] AKIRA FUJIYOSHI,[b] KATSUHIKO YANO,[a] QIMEI HE,[a] J. DAVID CURB,[a,b] AND MAKOTO SUZUKI[e]

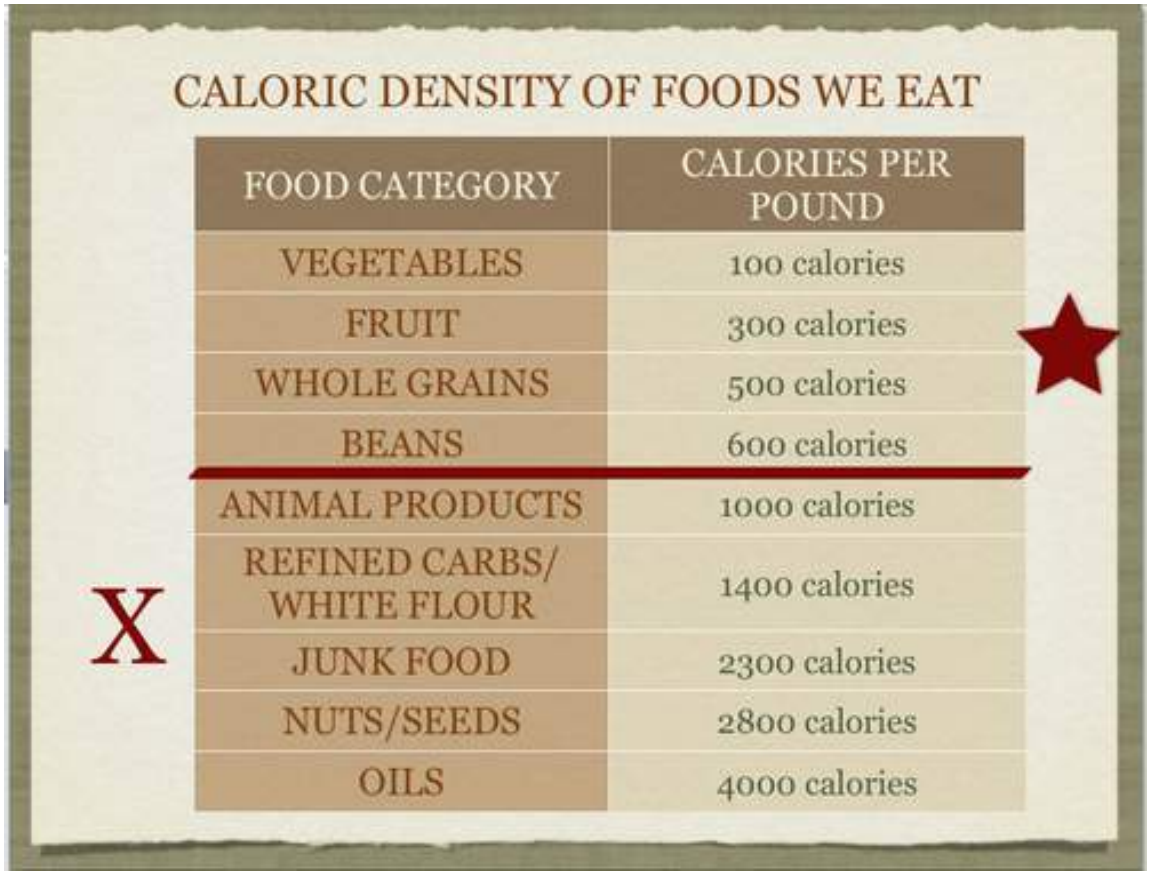
"…we observed *low calorie intake coupled with high physical activity levels that appear to have contributed to a CR phenotype in older Okinawans*. This phenotype includes a life-long low BMI, relatively high plasma levels of DHEA at older ages, reduced mortality from age-associated diseases, and extended average and maximum survival."

been used as an argument to support the CR hypothesis in humans. However, no long-term, epidemiologic analysis has been conducted on traditional dietary patterns, energy balance, and potential CR phenotypes for the specific cohort of Okinawans who are purported to have had a calorically restricted diet. Nor has this cohort's subsequent mortality experience been rigorously studied. Therefore, we investigated six decades of archived population data on the elderly cohort of Okinawans (aged 65-plus) for evidence of CR. Analyses included traditional diet composition, energy intake, energy expenditure, anthropometry, plasma DHEA, mortality from age-related diseases, and current survival patterns. Finding
at younger age

Ann N Y Acad Sci. 2007 Oct;1114:434-55.

What is caloric restriction?

Caloric restriction refers to a state in which energy intake is sufficiently low to achieve or maintain a low-normal body weight status (i.e. body mass index < 21 kg/m^2) without causing malnutrition (i.e. adequate intake of proteins and micronutrients).



Omodei D, Fontana L. Calorie restriction and prevention of age-associated chronic disease. FEBS Lett. 2011 Jun 6;585(11):1537-42.

Am J Physiol Heart Circ Physiol 301: H1205–H1219, 2011.
First published August 12, 2011; doi:10.1152/ajpheart.00685.2011.

Review

Caloric restriction: powerful protection for the aging heart and vasculature

Edward P. Weiss[1,2] and Luigi Fontana[2,3]

[1]*Department of Nutrition and Dietetics, Saint Louis University, Saint Louis, Missouri;* [2]*Division of Geriatrics and Nutritional Sciences, Department of Medicine, Washington University School of Medicine, Saint Louis, Missouri; and* [3]*Division of*

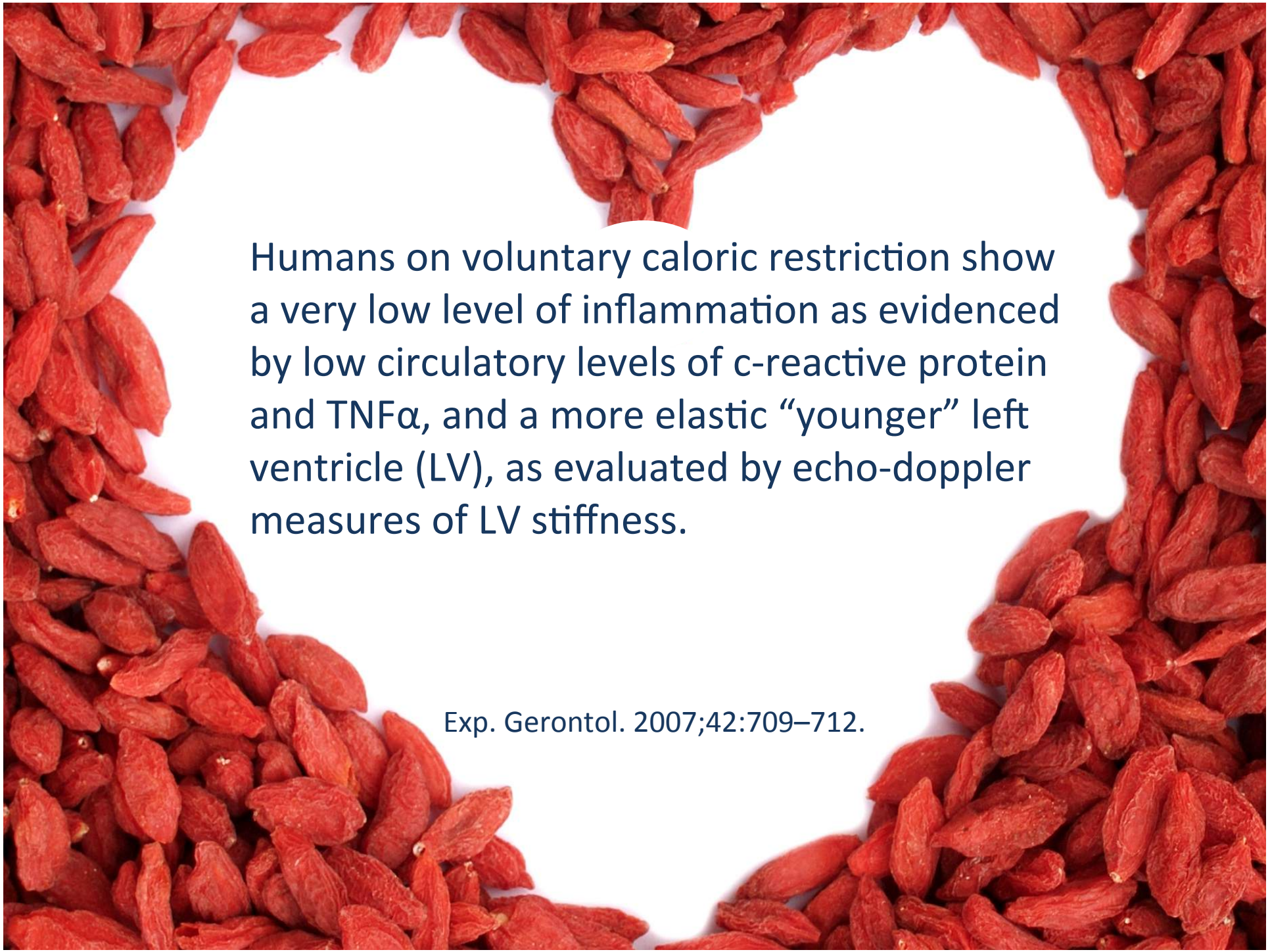
- *In the vasculature*, caloric restriction (CR) appears to protect against endothelial dysfunction and arterial stiffness and attenuates atherogenesis by improving several cardiometabolic risk factors.

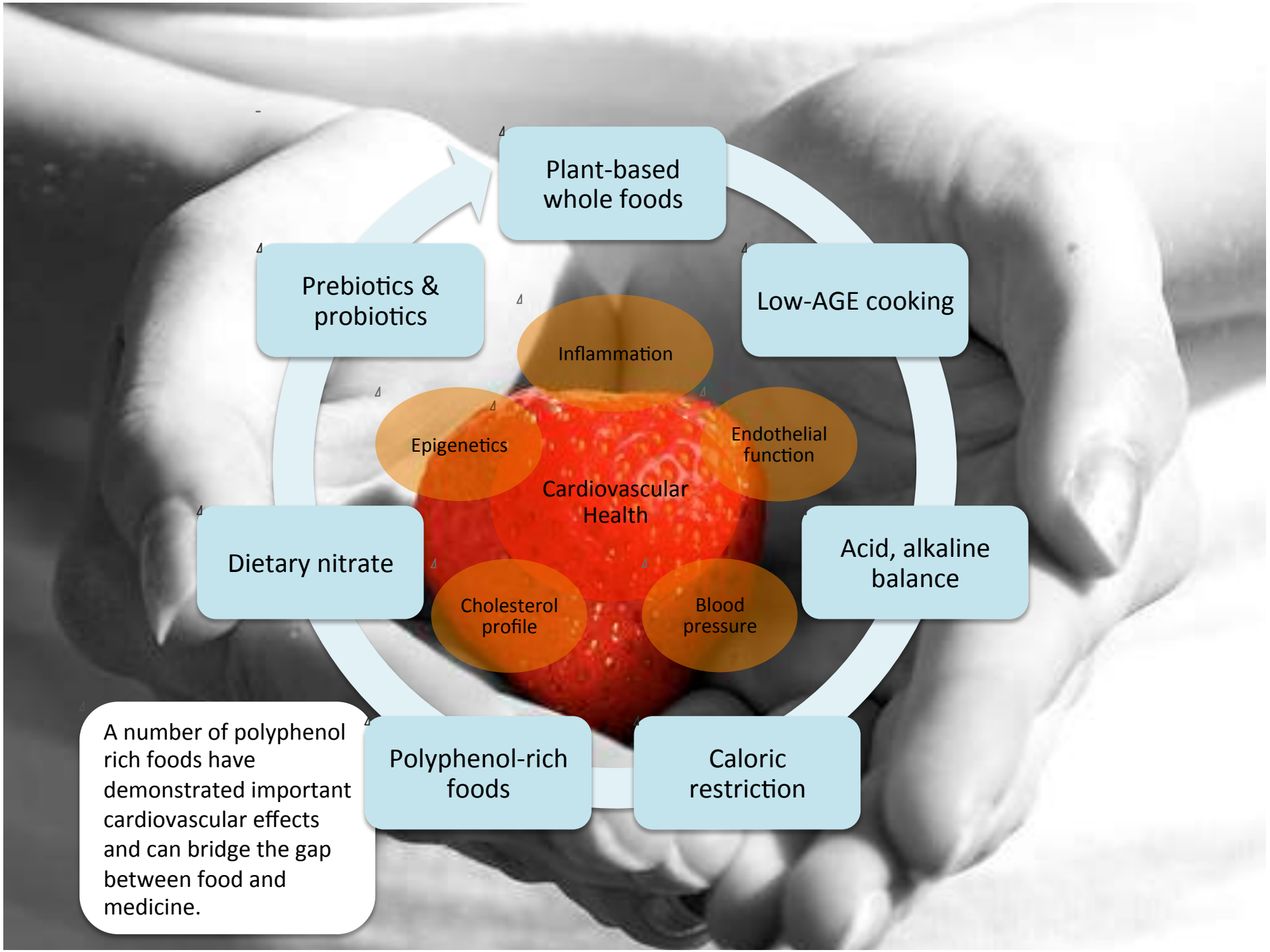
States. Research has shown that the majority of the cardiometabolic alterations

- *In the heart,* CR attenuates age-related changes in the myocardium (i.e., CR protects against fibrosis, reduces cardiomyocyte apoptosis, prevents myosin isoform shifts, etc.) and preserves or improves left ventricular diastolic function.

related to reductions in inflammation and oxidative stress. In the vasculature, CR appears to protect against endothelial dysfunction and arterial stiffness and attenuates atherogenesis by improving several cardiometabolic risk factors. In the heart, CR attenuates age-related changes in the myocardium (i.e., CR protects against fibrosis, reduces cardiomyocyte apoptosis, prevents myosin isoform shifts, etc.) and preserves or improves left ventricular diastolic function. These effects, in combi-

Am J Physiol Heart Circ Physiol. 2011 Oct; 301(4):H1205-19.


Humans on voluntary caloric restriction show a very low level of inflammation as evidenced by low circulatory levels of c-reactive protein and TNFα, and a more elastic “younger” left ventricle (LV), as evaluated by echo-doppler measures of LV stiffness.
Exp. Gerontol. 2007;42:709–712.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Dietary nitrate
Prebiotics & probiotics
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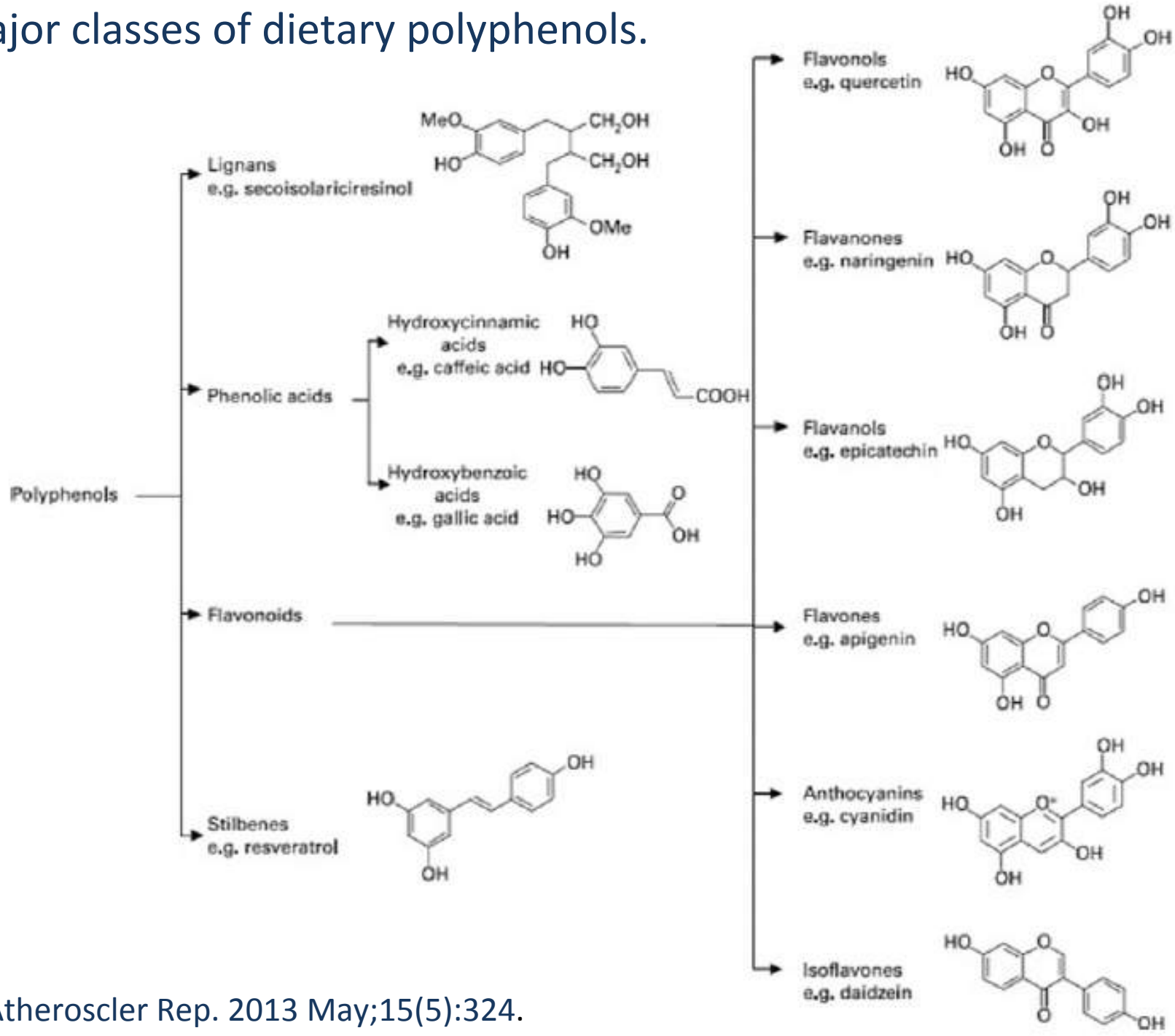
Endothelial function
Blood pressure
Cholesterol profile
Epigenetics
Cardiovascular Health
A number of polyphenol rich foods have demonstrated important cardiovascular effects and can bridge the gap between food and medicine.

Major classes of dietary polyphenols.



Curr Atheroscler Rep. 2013 May;15(5):324.

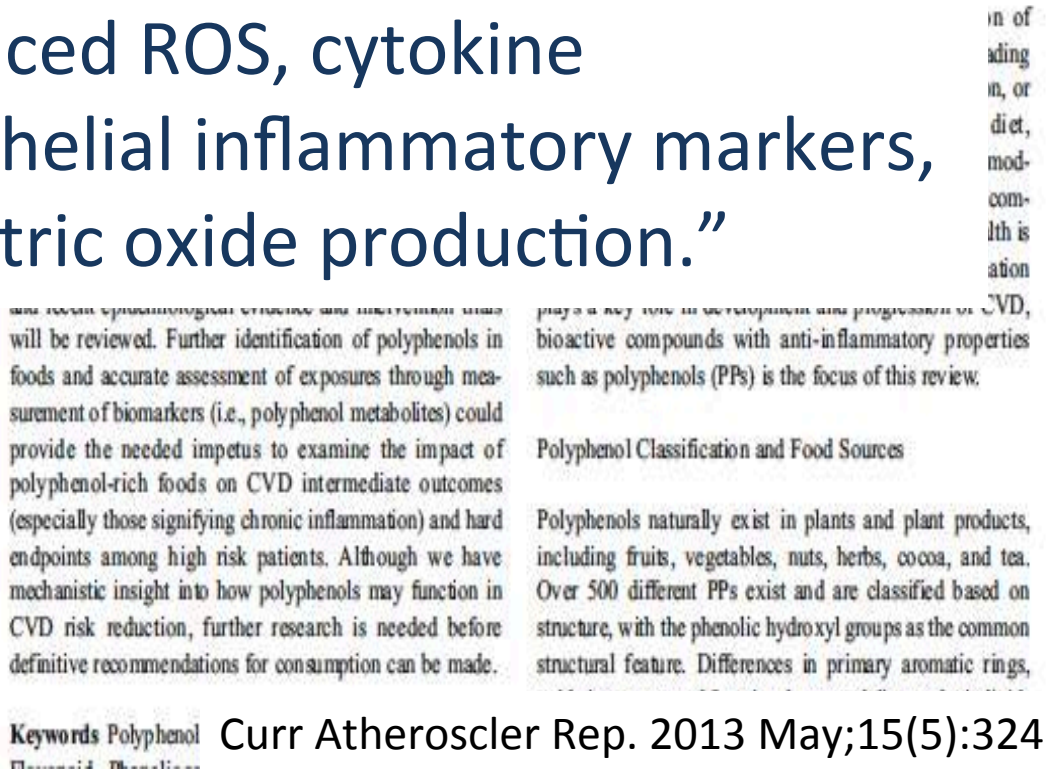
Curr Atheroscler Rep (2013) 15:324
DOI 10.1007/s11883-013-0324-x

VASCULAR BIOLOGY (RS ROSENSON, SECTION EDITOR)

Polyphenols, Inflammation, and Cardiovascular Disease

Christy C. Tangney · Heather E. Rasmussen

"*Recent mechanistic insights provide support for the potential role of polyphenols in the inflammatory process* including reduced ROS, cytokine expression, and endothelial inflammatory markers, as well as increased nitric oxide production."



will be reviewed. Further identification of polyphenols in foods and accurate assessment of exposures through measurement of biomarkers (i.e., polyphenol metabolites) could provide the needed impetus to examine the impact of polyphenol-rich foods on CVD intermediate outcomes (especially those signifying chronic inflammation) and hard endpoints among high risk patients. Although we have mechanistic insight into how polyphenols may function in CVD risk reduction, further research is needed before definitive recommendations for consumption can be made.

bioactive compounds with anti-inflammatory properties such as polyphenols (PPs) is the focus of this review.

Polyphenol Classification and Food Sources

Polyphenols naturally exist in plants and plant products, including fruits, vegetables, nuts, herbs, cocoa, and tea. Over 500 different PPs exist and are classified based on structure, with the phenolic hydroxyl groups as the common structural feature. Differences in primary aromatic rings,

Keywords Polyphenol

Curr Atheroscler Rep. 2013 May;15(5):324.

See corresponding editorial on page 271.

Flavonoid intake and cardiovascular disease mortality in a prospective cohort of US adults[1–4]

Marjorie L McCullough, Julia J Peterson, Roshni Patel, Paul F Jacques, Roma Shah, and Johanna T Dwyer

ABSTRACT

Background: Flavonoids are plant-based phytochemicals with cardiovascular protective properties. Few studies have comprehensively examined flavonoid classes in relation to cardiovascular

nuts, cocoa, and beverages such as tea and wine, are bioactive polyphenolic, noncaloric, nonnutrient secondary metabolites in plants that cannot be synthesized by humans. Many have potent

a lower risk of fatal CVD (RR: 0.82; 95% CI: 0.73, 0.92; *P*-trend = 0.01). Five flavonoid classes—anthocyanidins, flavan-3-ols, flavones, flavonols, and proanthocyanidins—were individually associated with lower risk of fatal CVD (all *P*-trend < 0.05). In men, total flavonoid intakes were more strongly associated with stroke mortality (RR: 0.63; 95% CI: 0.44, 0.89; *P*-trend = 0.04) than with ischemic heart disease (RR: 0.90; 95% CI: 0.72, 1.13). Many associations appeared to be nonlinear, with lower risk at intakes above the referent category.

Conclusions: Flavonoid consumption was associated with lower risk of death from CVD. Most inverse associations appeared with intermediate intakes, suggesting that

of flavonoid-rich foods may be b

2012;95:454–64.

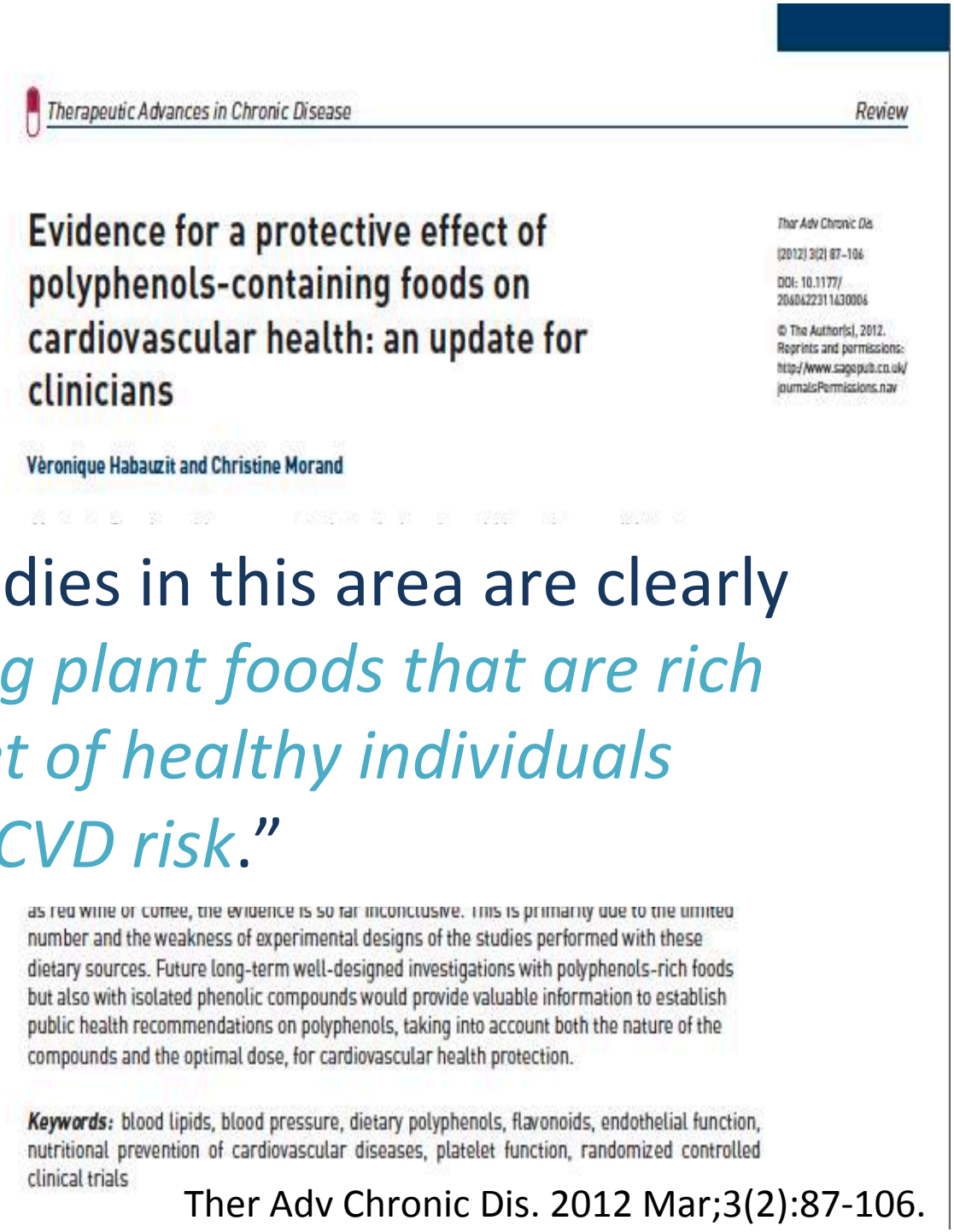
investigation of other classes of flavonoids, including anthocyanidins, flavanones, isoflavones, and proanthocyanidins, in relation to CVD risk in Western populations has been limited (13–15). In the past decade, new flavonoid composition databases (16–18) have enabled more in-depth evaluation of the role of these dietary constituents in chronic disease prevention.

Given the limited evidence relating flavonoid intake to CVD risk in Western populations, we examined the relation between

[1] From the Epidemiology Research Program, American Cancer Society,

"In this large prospective cohort of US men and women, a *greater intake of total flavonoids, and of most flavonoid classes, was associated with a lower risk of fatal CVD* in men and women after several important CVD risk factors were controlled for."

Am J Clin Nutr. 2012 Feb;95(2):454-64.



Therapeutic Advances in Chronic Disease Review

Evidence for a protective effect of polyphenols-containing foods on cardiovascular health: an update for clinicians

Ther Adv Chronic Dis
(2012) 3(2) 87–106
DOI: 10.1177/2040622311430006

Véronique Habauzit and Christine Morand

"While additional studies in this area are clearly needed, *incorporating plant foods that are rich in flavanols in the diet of healthy individuals could help to reduce CVD risk*."

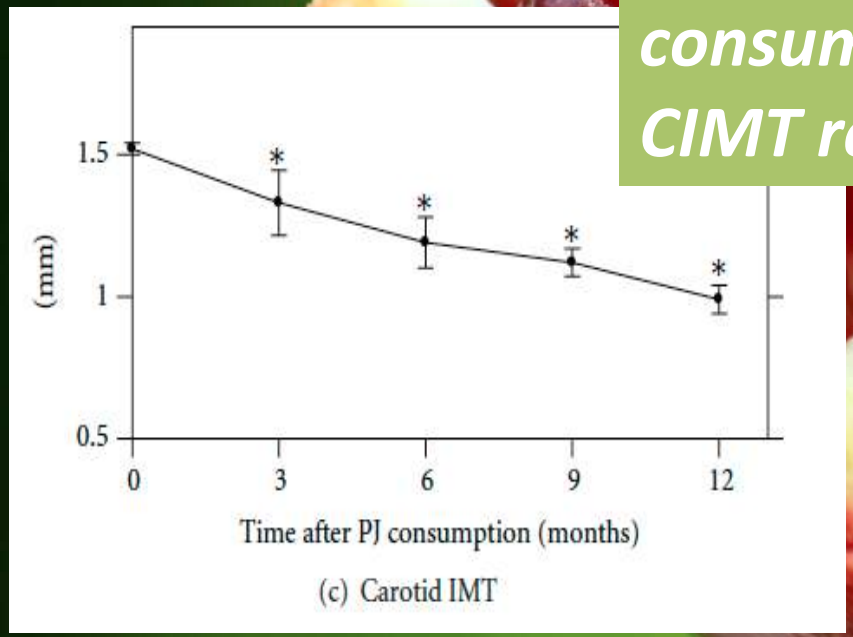
as red wine or coffee, the evidence is so far inconclusive. This is primarily due to the limited number and the weakness of experimental designs of the studies performed with these dietary sources. Future long-term well-designed investigations with polyphenols-rich foods but also with isolated phenolic compounds would provide valuable information to establish public health recommendations on polyphenols, taking into account both the nature of the compounds and the optimal dose, for cardiovascular health protection.

Keywords: blood lipids, blood pressure, dietary polyphenols, flavonoids, endothelial function, nutritional prevention of cardiovascular diseases, platelet function, randomized controlled clinical trials

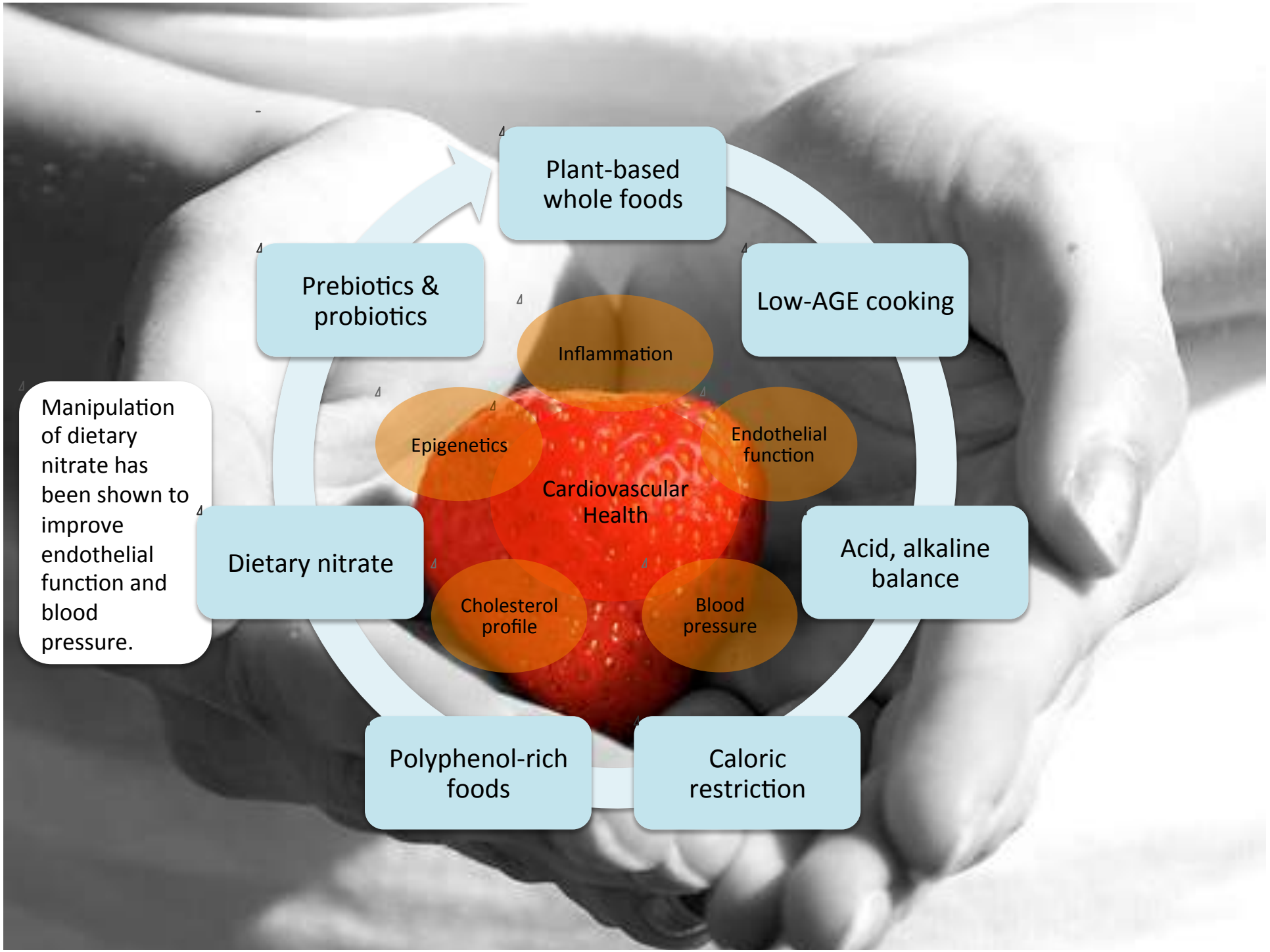
Ther Adv Chronic Dis. 2012 Mar;3(2):87-106.

People with carotid artery stenosis (CAS) drank 240 mL/day of pomegranate juice (PJ) over a year.

While in the control group (no PJ) carotid intima-media thickness (CIMT) increased by 10% after 1 year, ***PJ consumption resulted in a significant CIMT reduction, by up to 35%.***



Evid Based Complement Alternat Med. 2012;2012:382763.


Plant-based whole foods
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Dietary nitrate
Prebiotics & probiotics
Inflammation
Endothelial function
Epigenetics
Cardiovascular Health
Cholesterol profile
Blood pressure
Manipulation of dietary nitrate has been shown to improve endothelial function and blood pressure.

NUTRITION REVIEWS 70 YEARS 1942-2012

Emerging Science

Inorganic nitrate: a major player in the cardiovascular health benefits of vegetables?

Ajay Machha and Alan N Schechter

Epidemiological evidence suggests a higher consumption of vegetables confers a protective effect against the risk of cardiovascular disease. Impaired bioavailability

"…it appears that inorganic nitrate may play a major role in the cardiovascular health benefits of vegetables, presumably through enhancing nitric oxide (NO) bioavailability in the vasculature."

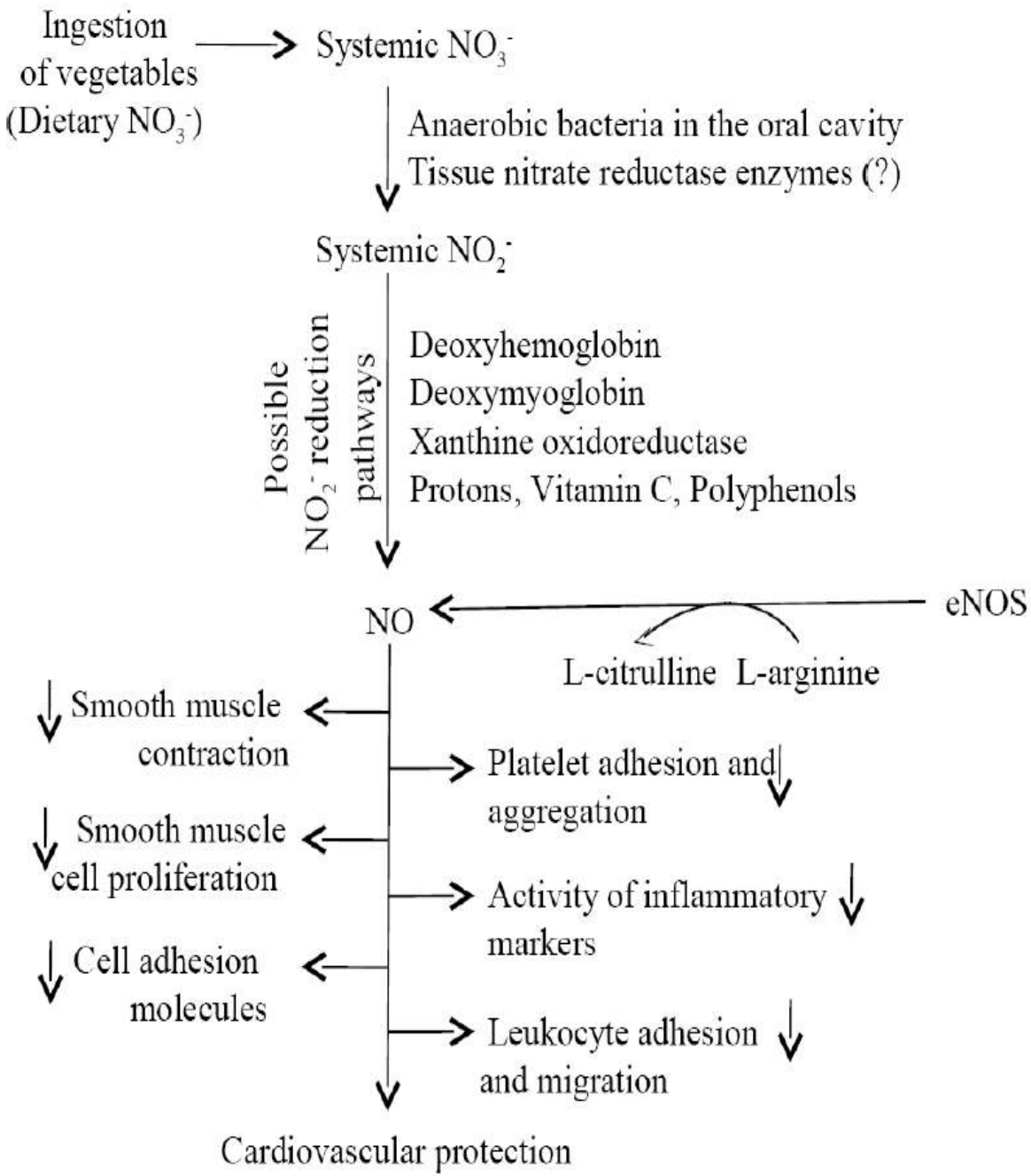
nitrite remains less clear and must be studied in prospective controlled studies. This brief review discusses the potential role of inorganic dietary nitrate in the cardiovascular health benefits of vegetables.

INTRODUCTION

Epidemiological evidence suggests that increased consumption of vegetables reduces the risk of cardiovascular disease, which is the leading cause of mortality in the Western world.[1-5] Although this benefit was traditionally postulated to be linked to the antioxidant factors in vegetables, studies over the past two decades many nonantioxidant factors as likely can

clinical studies show that dietary nitrate supplementation at doses commonly found in vegetable-rich diets exerts beneficial effects on the cardiovascular system.[10-16] These beneficial effects of nitrate are largely thought to be mediated by the reduction of nitrate to nitric oxide (NO) in the body, since NO is a critical regulator of vascular homeostasis.[10-16] Current data suggest that nitrate under-

Nutr Rev. 2012 Jun;70(6):367-72.



Nutr Rev. 2012 Jun;70(6):367-72.

Dietary nitrate in Japanese traditional foods lowers diastolic blood pressure in healthy volunteers:

- ✓ A randomized, cross-over trial examining the effect of a 10-day period of Japanese traditional diet (JTD) on blood pressure in 25 healthy volunteers.

- ✓ Plasma and salivary levels of ***nitrate and nitrite were higher*** at the end of the JTD period.

- ✓ ***Diastolic BP decreased*** on average 4.5 mm Hg during JTD compared to the control diet (P = 0.0066) while systolic BP was not affected.

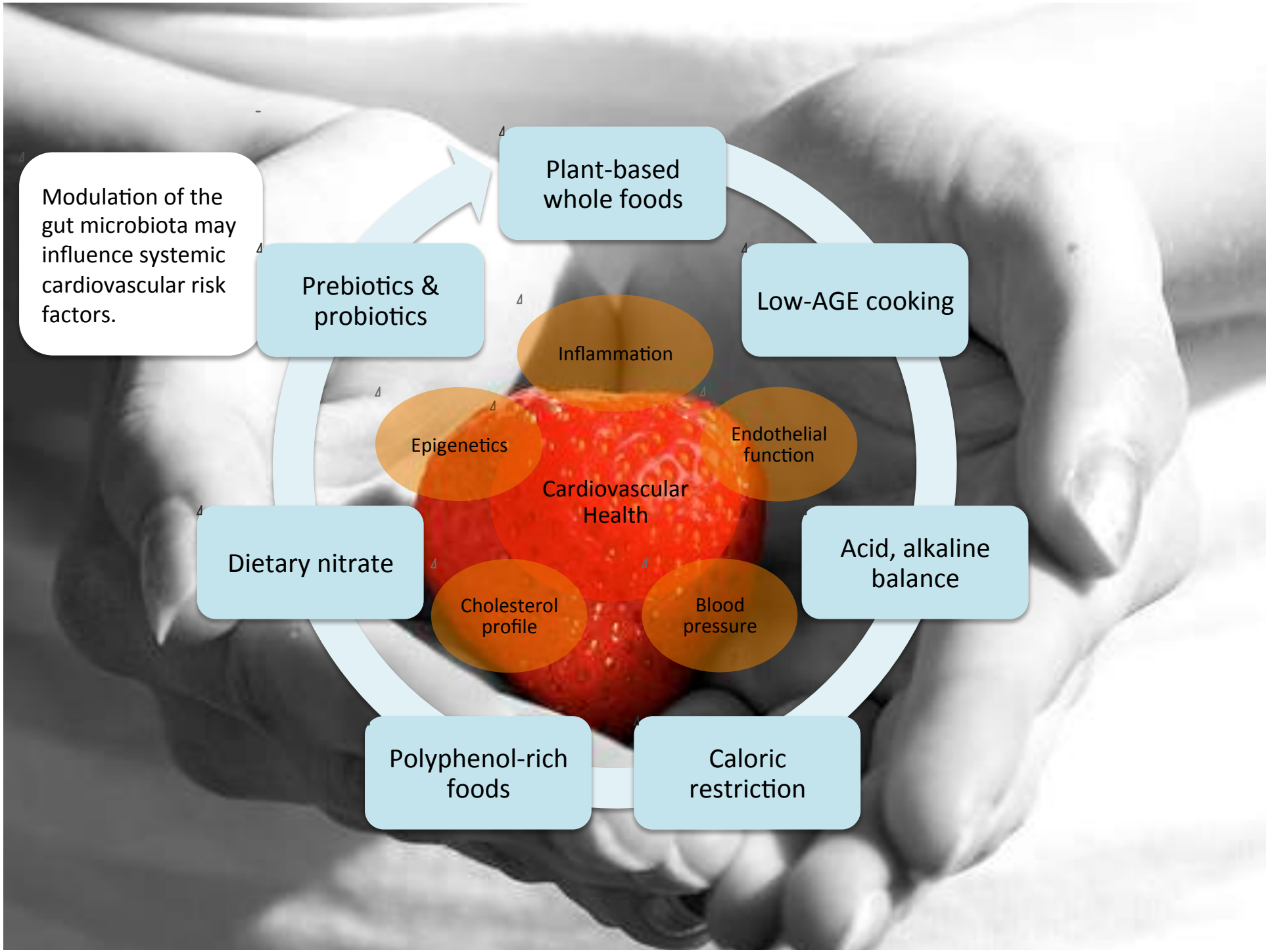
Nitric Oxide. 2010 Feb 15;22(2):136-40.

Beeting Heart Disease:

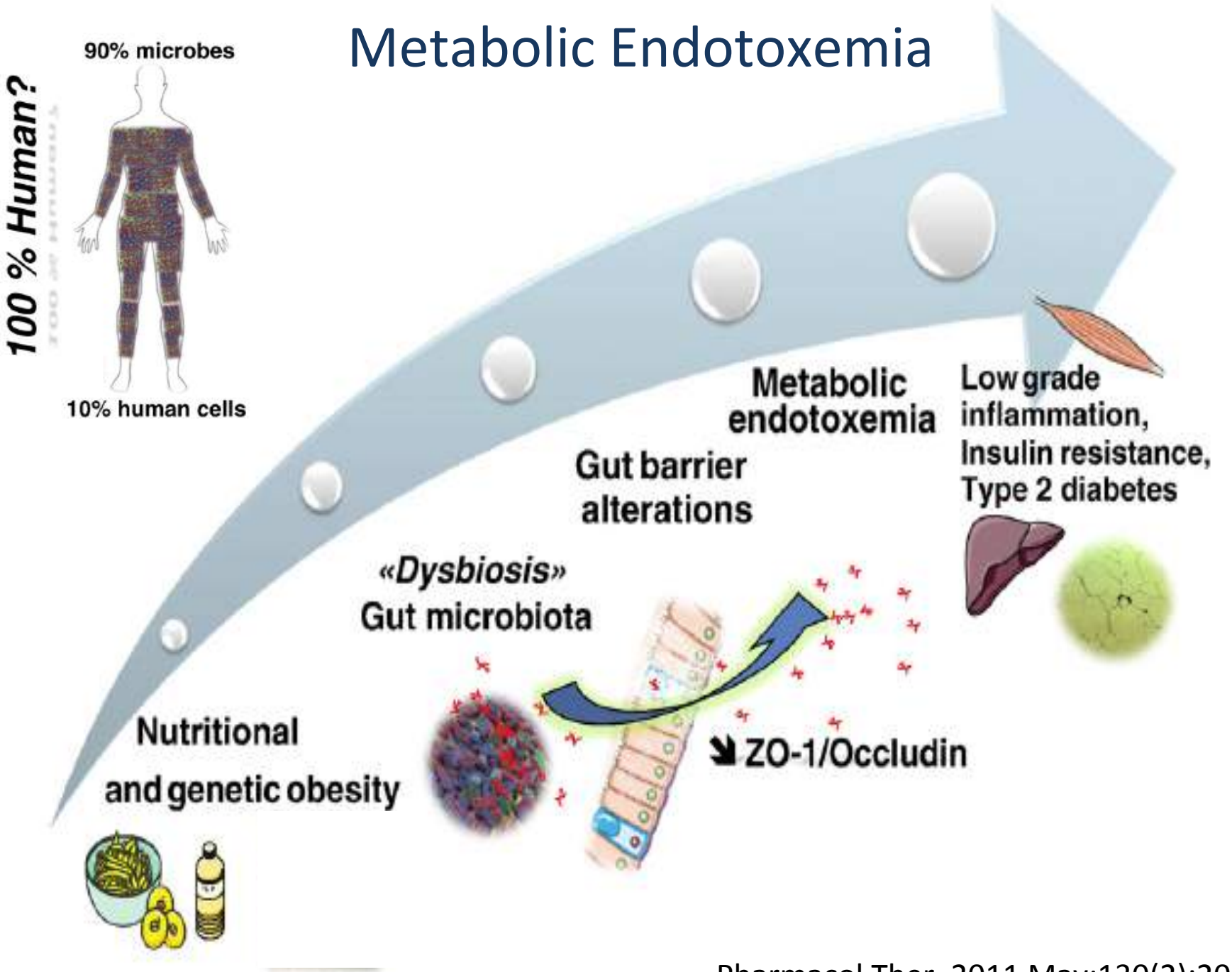
Hypertensive patients were randomized to receive either dietary nitrate (250mL daily, as beetroot juice) or a placebo (nitrate-free beet juice) for 4-weeks.

Home blood pressure was reduced by 8.1mmHg. Endothelial function improved by ~20% and arterial stiffness was reduced, with no change after placebo.

Hypertension. 2015 Feb;65(2):320-7.


Modulation of the gut microbiota may influence systemic cardiovascular risk factors.
Plant-based whole foods
Low-AGE cooking
Acid, alkaline balance
Caloric restriction
Polyphenol-rich foods
Dietary nitrate
Prebiotics & probiotics
Inflammation
Endothelial function
Blood pressure
Cholesterol profile
Epigenetics
Cardiovascular Health

Metabolic Endotoxemia



Pharmacol Ther. 2011 May;130(2):202-12.

ELSEVIER

Atherosclerosis 203 (2009) 494–502

ATHEROSCLEROSIS

www.elsevier.com/locate/atherosclerosis

Ethnic and sex differences in circulating endotoxin levels: A novel marker of atherosclerotic and cardiovascular risk in a British multi-ethnic population

Michelle A. Miller[a,*], Philip G. McTernan[a], Alison L. Harte[a], Nancy F. da Silva[a], Pasquale Strazzullo[b], K. George M.M. Alberti[c],

- Endotoxin levels were positively associated with waist, waist-hip ratio, total cholesterol, serum triglycerides and serum insulin levels and negatively associated with serum HDL-cholesterol.
- A graded increase in endotoxin levels from black Africans to whites to South Asians, which is consistent with the ethnic difference in CHD risk.

Abstract

Background: Circulating endotoxin levels are associated with atherosclerosis. Moreover, ethnic differences in pro-inflammatory markers may

high-
sians
Heart

[95%
toxin

levels were positively associated with waist, waist-hip ratio, total cholesterol, serum triglycerides and serum insulin levels and negatively associated with serum HDL-cholesterol. Serum hs-CRP and plasma sCD14 varied by ethnic group ($p<0.001$) but was not associated with endotoxin.

Conclusions: This study is the first to indicate a graded increase in endotoxin levels from black Africans to whites to South Asians, which is consistent with the ethnic difference in CHD risk. Whilst these findings support the concept that the innate immune system (IIS) may contribute significantly to the metabolic component underlying the development of CVD and CHD risk, further studies are required to see whether endotoxin levels are causally related to the development of CHD.

Keywords: Ethnicity; Ather

Atherosclerosis. 2009 Apr;203(2):494-502.

The unhealthy meal increased plasma enotoxin concentration and oxidative and inflammatory stress.

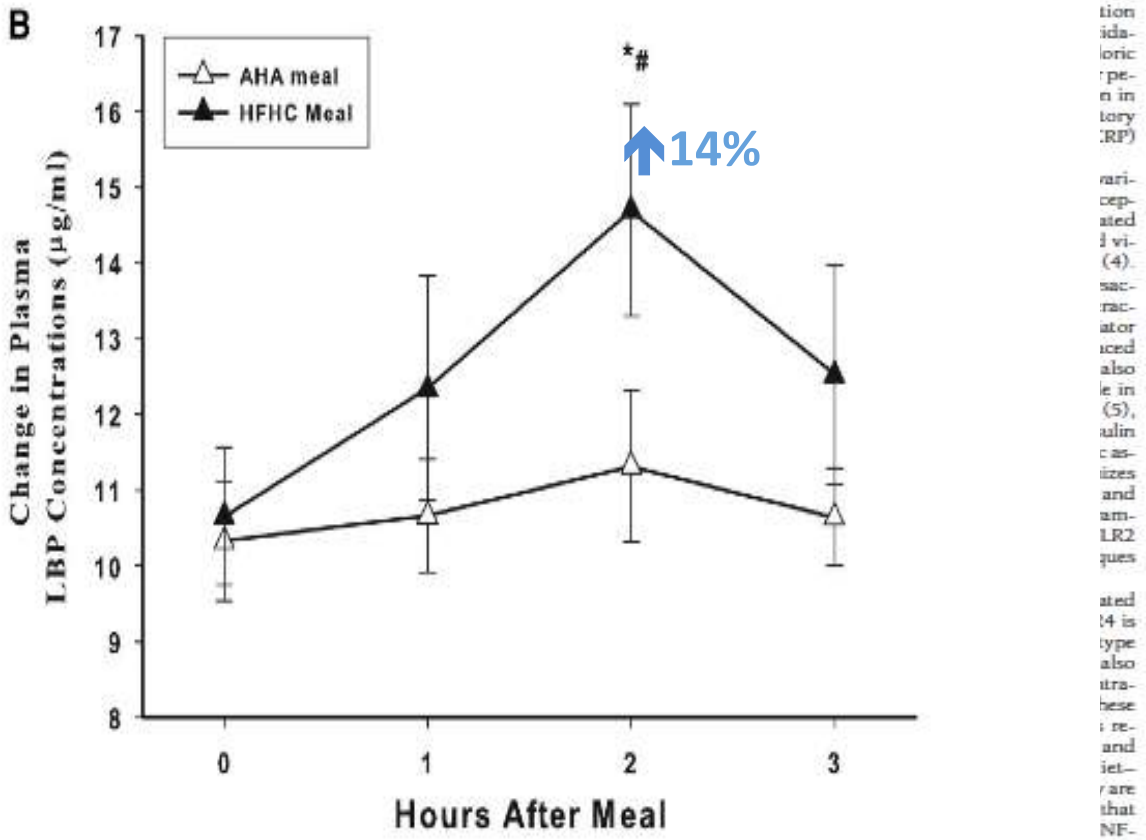
These increases were totally absent after the meal rich in fiber and fruit.

Pathophysiology/Complications
ORIGINAL ARTICLES

Increase in Plasma Endotoxin Concentrations and the Expression of Toll-Like Receptors and Suppressor of Cytokine Signaling-3 in Mononuclear Cells After a High-Fat, High-Carbohydrate Meal

Implications for insulin resistance

HUSAM GHANIM, PHD[1]
SANAA ABUAYSHEH, BS[1]
AJAY CHAUDHURI, MD[2]
JOSE MANUEL FERNANDEZ-REAL, MD[1]



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caloric restriction (2) and weight loss in human obesity over a period of 4 weeks

kB–mediated inflammation and the development of insulin resistance (6). We have recently shown that a low-dose in-

Diabetes Care. 2009 Dec;32(12):2281-7.

The Western-style diet induced a *71% increase* in plasma levels of endotoxin activity (endotoxemia).

A prudent-style diet *reduced levels by 31%*.

GASTROENTEROLOGY 2012;142:1100–1101

BRIEF REPORTS

A High-Fat Diet Is Associated With Endotoxemia That Originates From the Gut

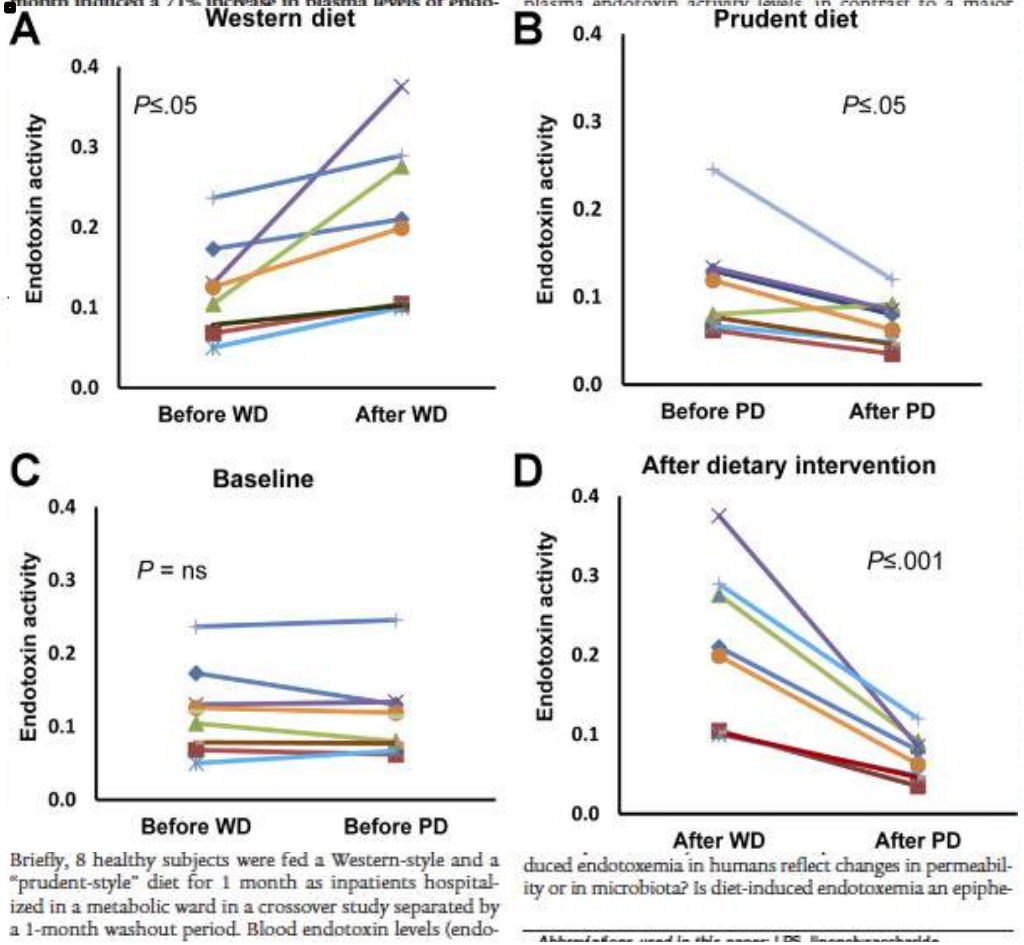
SWAROOP PENDYALA, JEANNE M. WALKER, and PETER R. HOLT

Laboratory of Biochemical Genetics and Metabolism, The Rockefeller University, New York, New York

Endotoxemia, characterized by an excess of circulating bacterial wall lipopolysaccharide, is associated with systemic inflammation and the metabolic syndrome. Placing 8 healthy subjects on a Western-style diet for 1 month induced a 71% increase in plasma levels of endo-

tration for this purpose. Serum cytokines were determined before and after each dietary study period.

Our study shows that 4 weeks of feeding a Western-style diet induced highly significant increases (by 71%) in plasma endotoxin activity levels, in contrast to a major



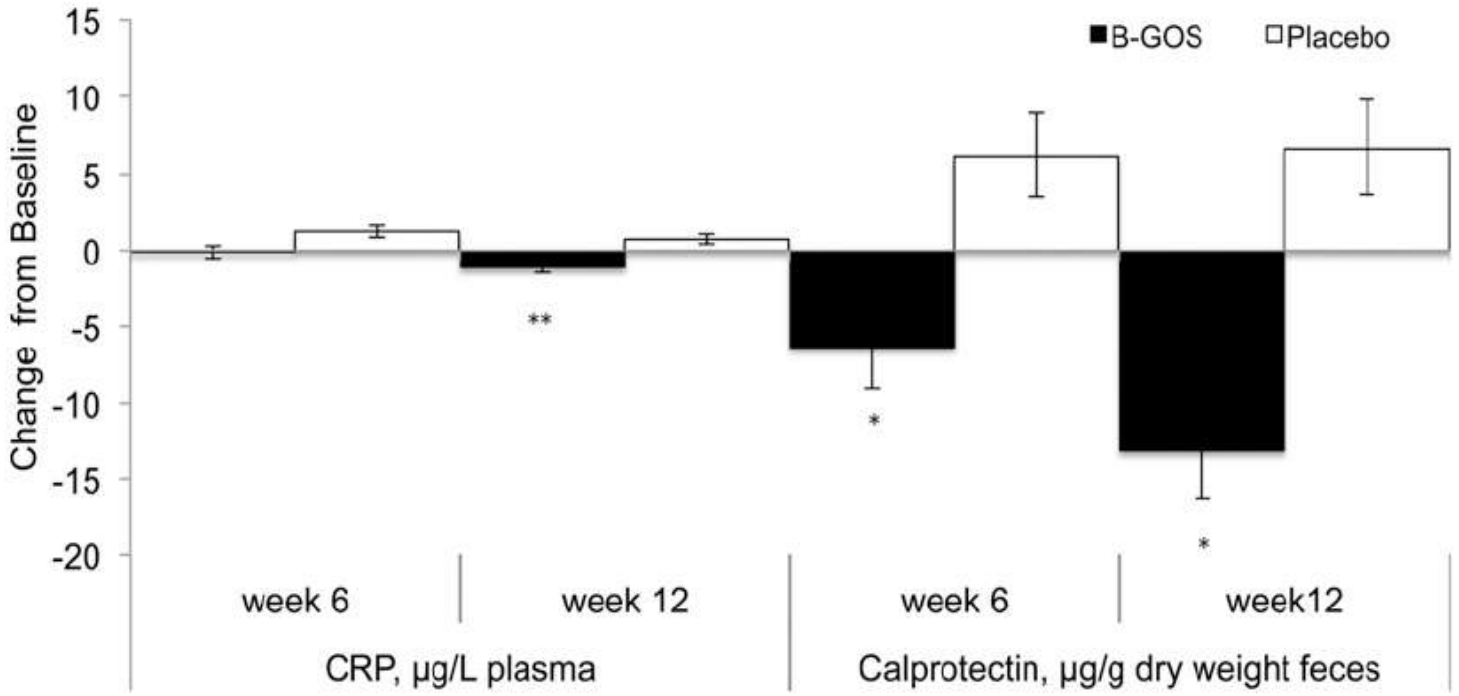
Briefly, 8 healthy subjects were fed a Western-style and a "prudent-style" diet for 1 month as inpatients hospitalized in a metabolic ward in a crossover study separated by a 1-month washout period. Blood endotoxin levels (endo-

duced endotoxemia in humans reflect changes in permeability or in microbiota? Is diet-induced endotoxemia an epiphe-

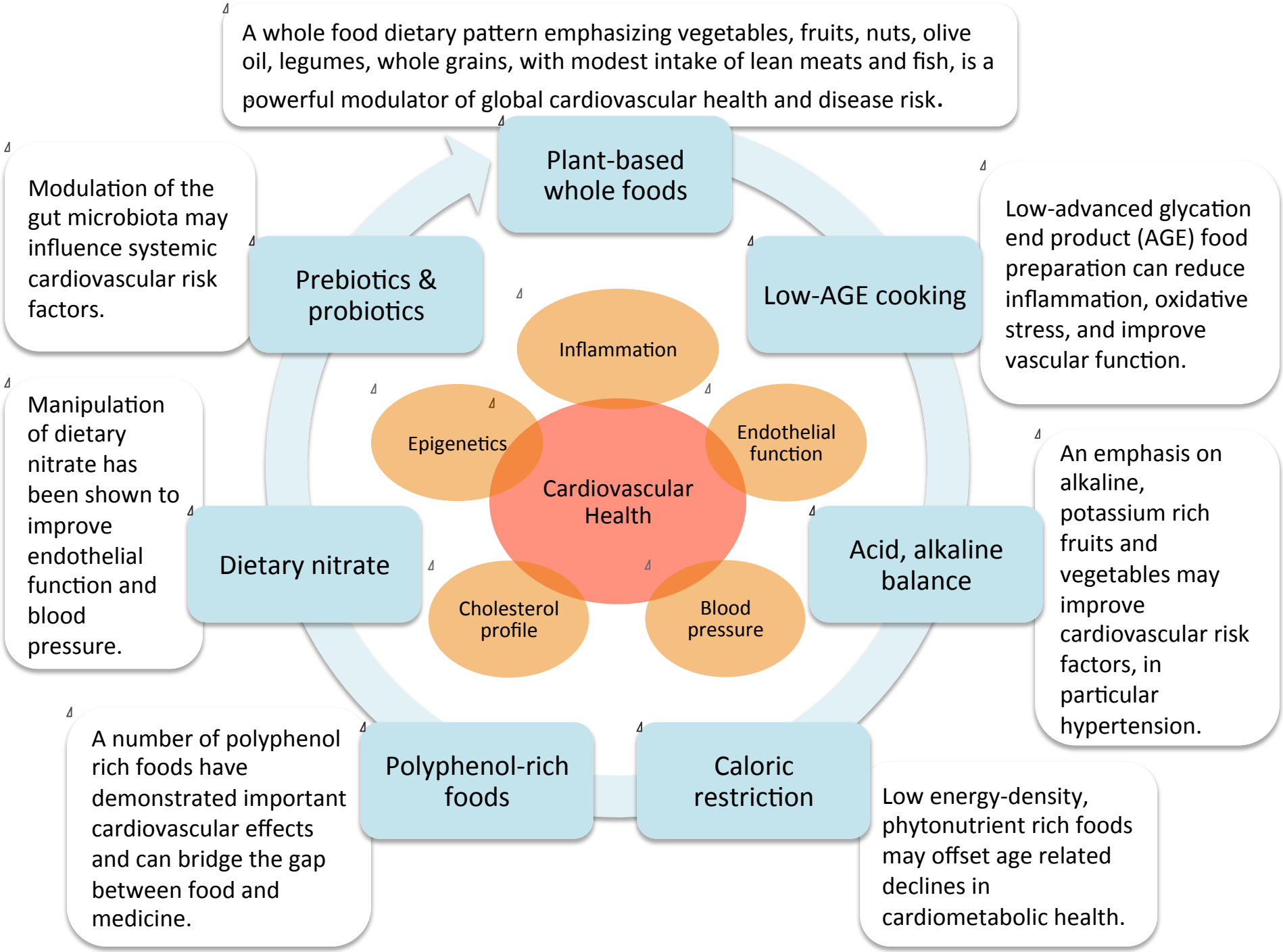
Gastroenterology. 2012 May;142(5):1100-1101.e2.

Galactooligosaccharides reduce markers of metabolic syndrome and modulates the fecal microbiota:

A galactooligosaccharide mixture *increased the number of fecal bifidobacteria* at the expense of less desirable groups of bacteria. Increases in fecal secretory IgA and *decreases in fecal calprotectin, plasma C-reactive protein, insulin, total cholesterol (TC), TG, and the TC:HDL cholesterol* ratio were also observed.



J Nutr. 2013 Mar;143(3):324-31.


A whole food dietary pattern emphasizing vegetables, fruits, nuts, olive oil, legumes, whole grains, with modest intake of lean meats and fish, is a powerful modulator of global cardiovascular health and disease risk.
Plant-based whole foods
Low-advanced glycation end product (AGE) food preparation can reduce inflammation, oxidative stress, and improve vascular function.
Low-AGE cooking
An emphasis on alkaline, potassium rich fruits and vegetables may improve cardiovascular risk factors, in particular hypertension.
Acid, alkaline balance
Low energy-density, phytonutrient rich foods may offset age related declines in cardiometabolic health.
Caloric restriction
A number of polyphenol rich foods have demonstrated important cardiovascular effects and can bridge the gap between food and medicine.
Polyphenol-rich foods
Manipulation of dietary nitrate has been shown to improve endothelial function and blood pressure.
Dietary nitrate
Modulation of the gut microbiota may influence systemic cardiovascular risk factors.
Prebiotics & probiotics
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