The protective role of Mediterranean diet on cardiovascular disease risk: Environmental Health Perspectives

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Diet & Health: a historical adventure

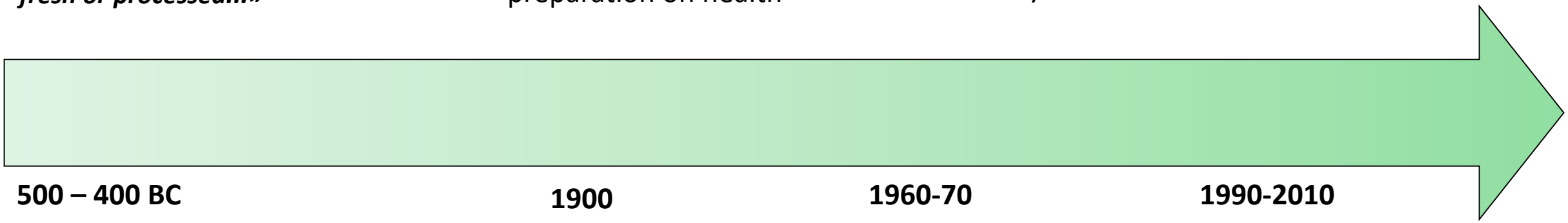
The role of diet on human health was known even from the ancient years, in many populations. Hippocrates said (460 BC) :

«Good health is a matter of the body composition (… genetics?) as well as the foods consumed, both fresh or processed…»

Epidemiologic evidence suggest s the important role of food preservation and preparation on health

First evidence for the role of dietary patterns on CVD risk; the Seven Countries Study

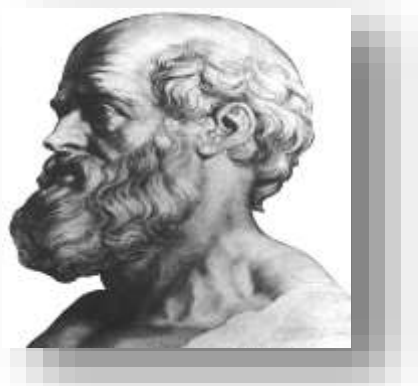
Observational studies and RCTs have established the role of diet on CVD, some types of cancer, and other diseases

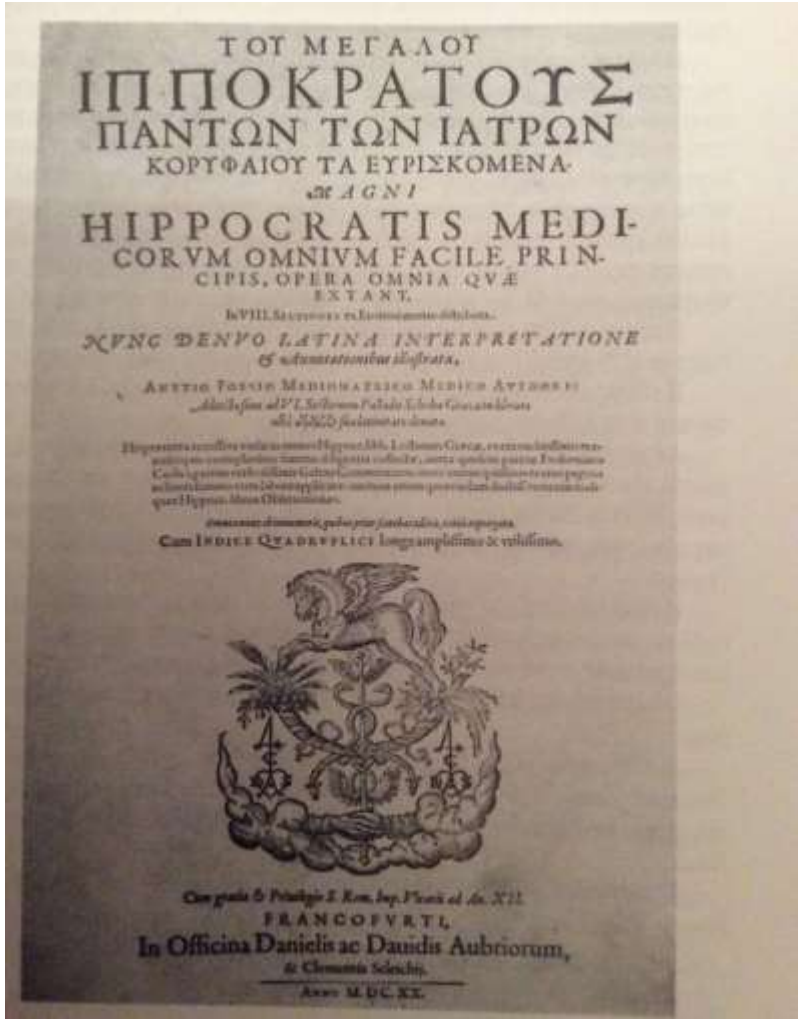


500 – 400 BC **1900** **1960-70** **1990-2010**

Diet and health;

everything should be in moderation and with a variety of choices



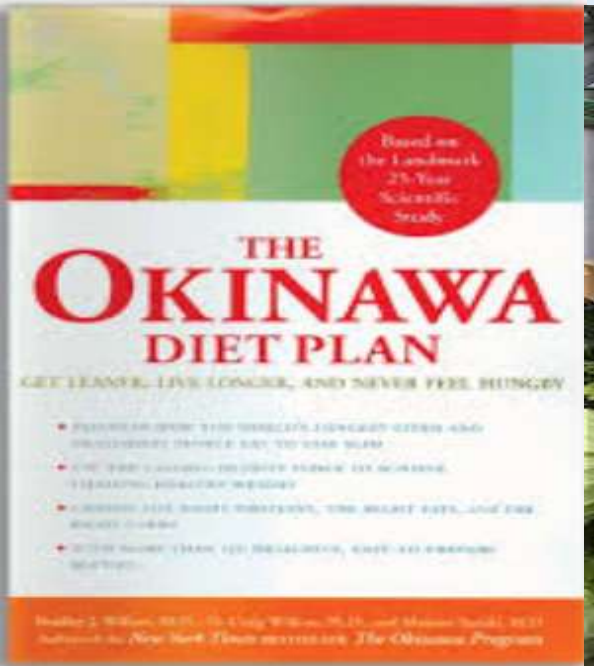


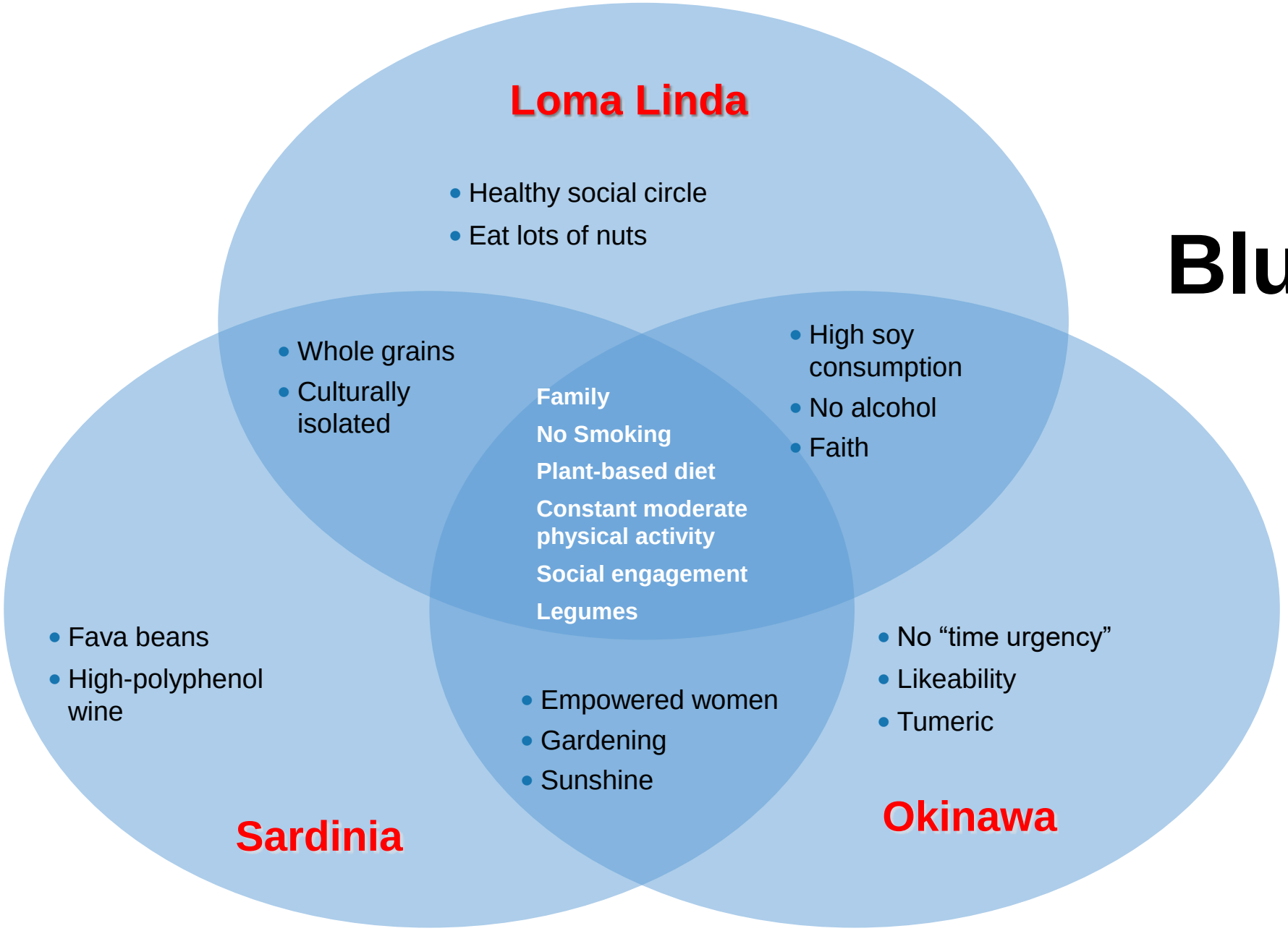
Let food be thy medicine and medicine be thy food.

- *If we could give every individual the **right amount of nourishment and exercise**, not too little and not too much, we would have found the safest way to health …*

***Hippocrates** (460 –370 BC)*

Longevity and Diet.
Myth or pragmatism?





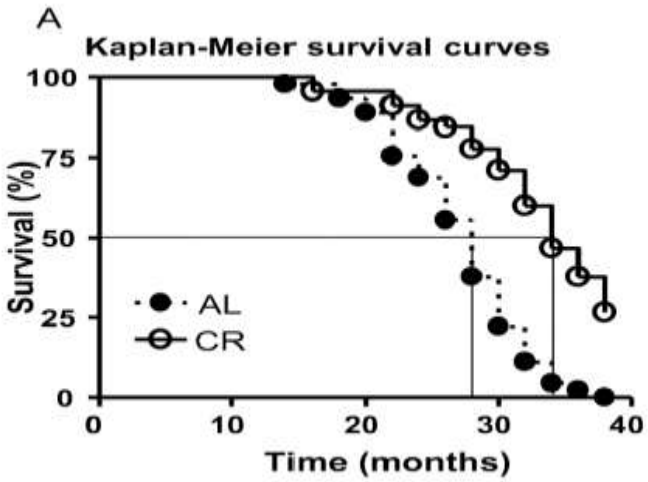
The Blue Zones

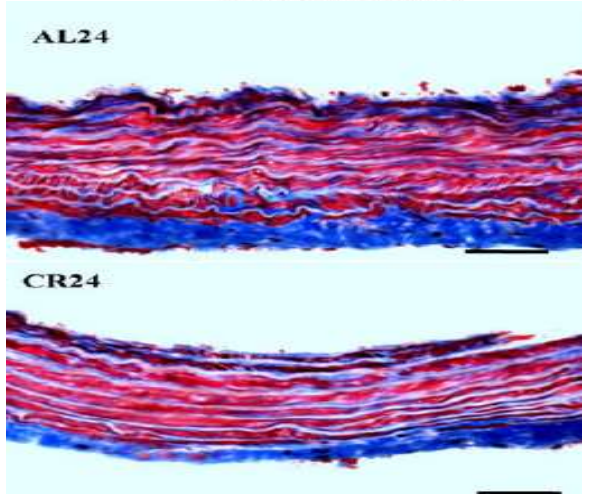
What began as a ***National Geographic*** expedition to find the longest living cultures evolved **into a recipe for living longer …**

Effects of Calorie Restriction on CVD

Caloric Restriction …

• decreases body temperature and oxidative stress
• modulates signaling pathways, including those involving IGF1 insulin, rapamycin target (TOR), DNA methylation, histone acetylation, and genes related to mitochondria metabolism.
• increases adiponectin levels reducing DM and fatty acid accumulation, regulates mitochondrial energy,
• suppresses the formation of inflammatory factors,
• (through reduced glucose intake) also regulates FOXOs which control various cellular functions: apoptosis, cell cycle differentiation, the expression of genes involved in DNA repair and oxidative stress resistance, and the deposition of amyloid in Alzheimer disease





There is no scientific evidence that calorie restriction leads to longevity in human …

J Mol Cell Cardiol. 2011; Aging Cell 2012;11:1110–20.

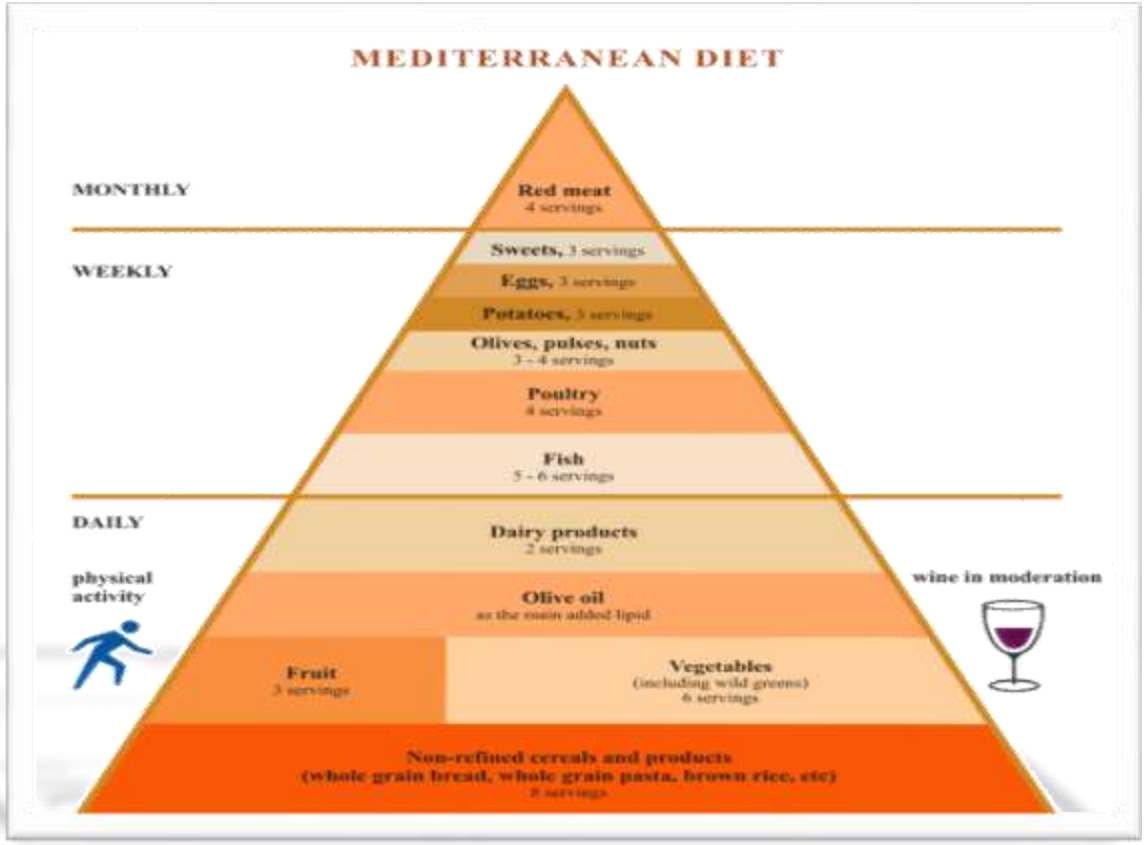
The Mediterranean Diet

- The Mediterranean Diet **is a way of eating**
  - (… and not only)
  - based on the traditional foods and drinks (mainly wine)
    - of the countries surrounding the Mediterranean Sea.
    - It was characterized by a considerable caloric restriction, i.e., 1700 – 1900 Kcal

What is the Mediterranean diet?

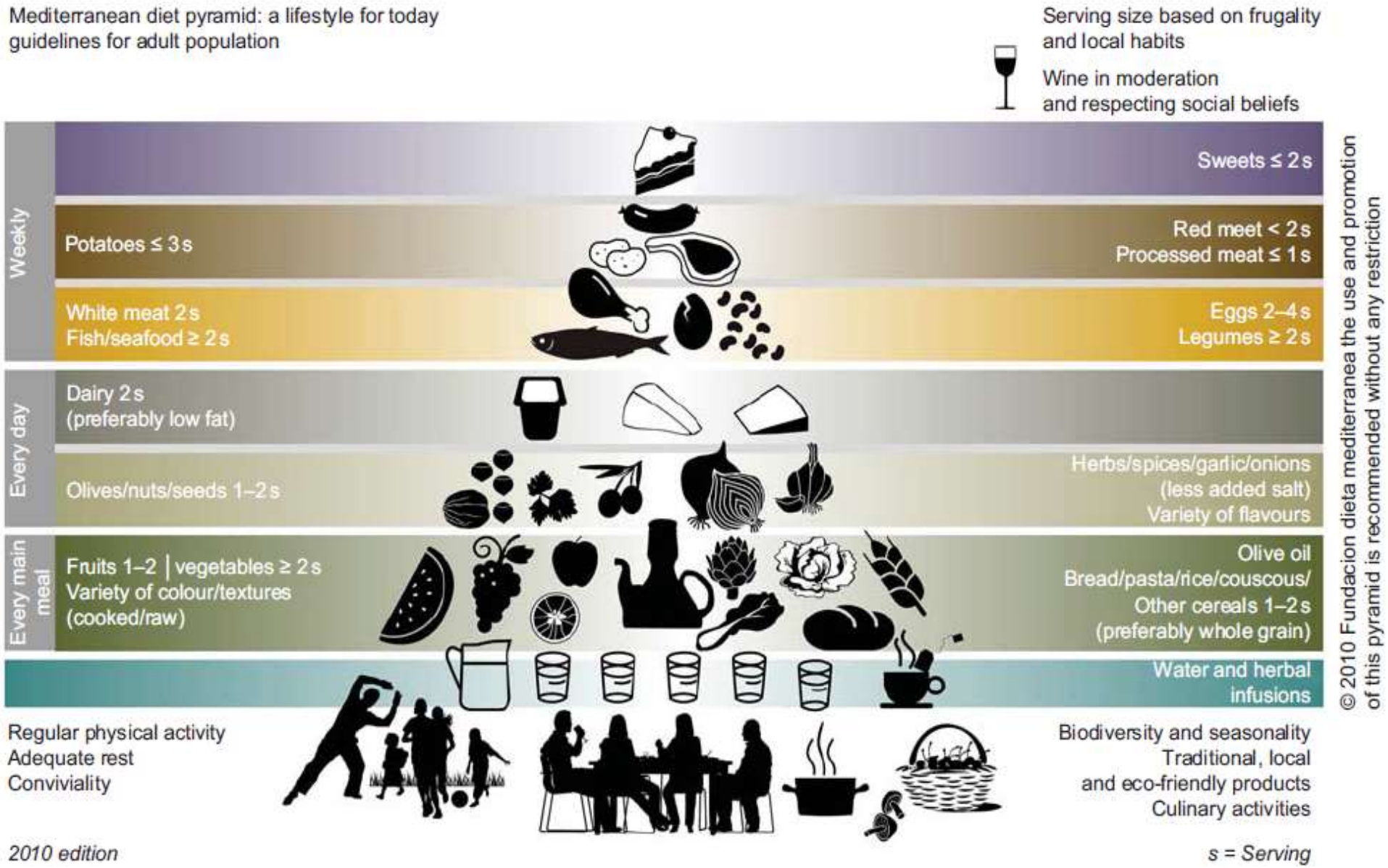
… the "old" definition

- The Mediterranean diet consists of:
  - daily use of olive oil
  - increased consumption of:
    - Fruits
    - Vegetables
    - Whole grain cereals
    - Fish
  - rare consumption
    - Meat & products



The Mediterranean Diet is characterized by a variety of foods consumed…

The …
“modern”
definition



Bach-Faig et al., 2011

The Mediterranean Diet

inscribed in 2013 on the Representative List of the Intangible Cultural Heritage of Humanity

- The Mediterranean diet involves a set of
  - skills, knowledge, rituals, symbols and traditions concerning crops, harvesting, fishing, animal husbandry, conservation, processing, cooking, and particularly the sharing and consumption of food.
  - Eating together is the foundation of the cultural identity and continuity of communities throughout the Mediterranean basin.

United Nations Educational, Scientific and Cultural Organization

Intangible Cultural Heritage

The origins of the Mediterranean Diet

- … *are lost in time* because they sink into the eating habits of the Middle Ages, in which the ancient Roman tradition identified
  - in bread, wine and oil products, sheep cheese, vegetables, little meat and a strong preference for fish and seafood …
    - a symbol of rural culture and agricultural.

The origins of the Mediterranean Diet

- The olive was (… and remains) a main agricultural product of the Mediterranean region,
  - and a cornerstone of the Med Diet.
- Historically,
  - the Romans used the olive tree to reclaim land, and
  - together with the vine and domesticated wheat, the olive supported the development of civilization in areas of the Aegean Sea (Firestone, 2005)

Food has always been an important part of health …

- Evidence of olive cultivation in Greece dates back to 3,500 years ago,
  - and today the Mediterranean basin produces 99% of the world's olive oil of which people of the region consume 87% (Loumou and Giourga, 2003).

Beyond olives & olive oil …

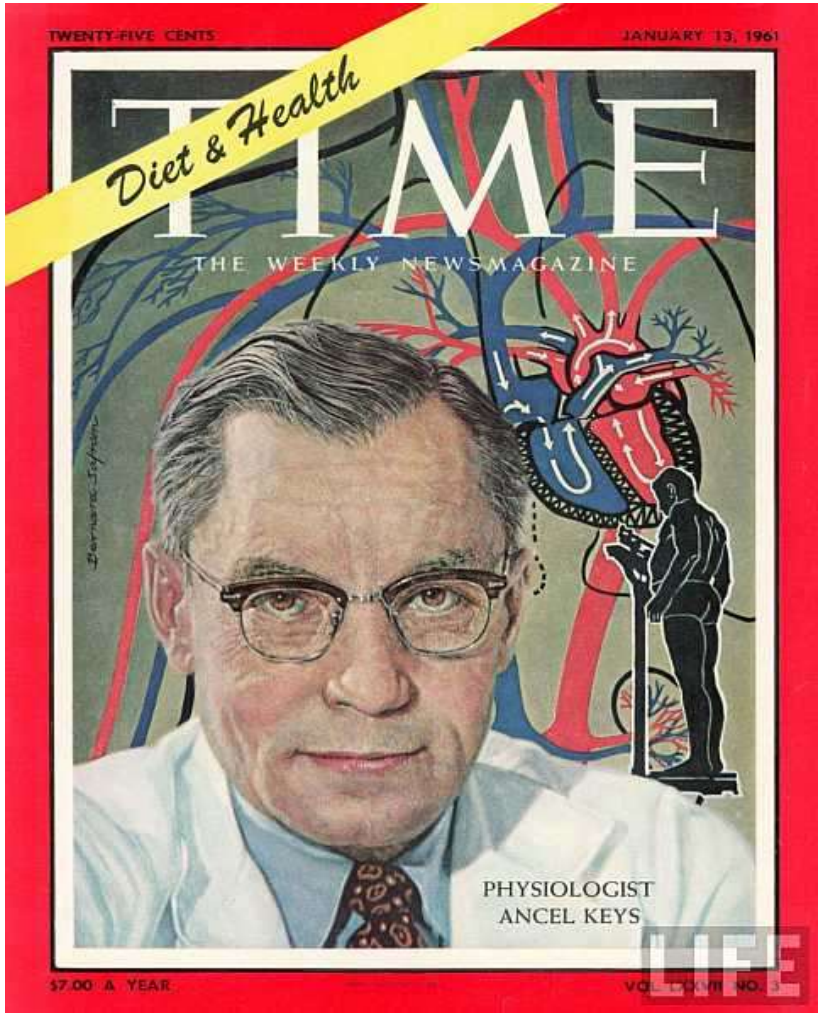
Large quantities of **vegetables** and **fruits** supplement the Mediterranean diet.

Southern Mediterranean cuisines have been known for more than thousands of years for their **distinctive herbs flavors** found in lemon, garlic, tomato and a mixture of herbs including oregano, thyme and basil (Farb and Armelagos, 1980).

The first evidence …

The Seven Countries Study

- The Mediterranean diet was **first "*described*"** in the 1960s by Ancel Keys, as a beneficial dietary pattern that may reduce CVD risk,
  - based on his observations of food habits of some populations in rural Greece…

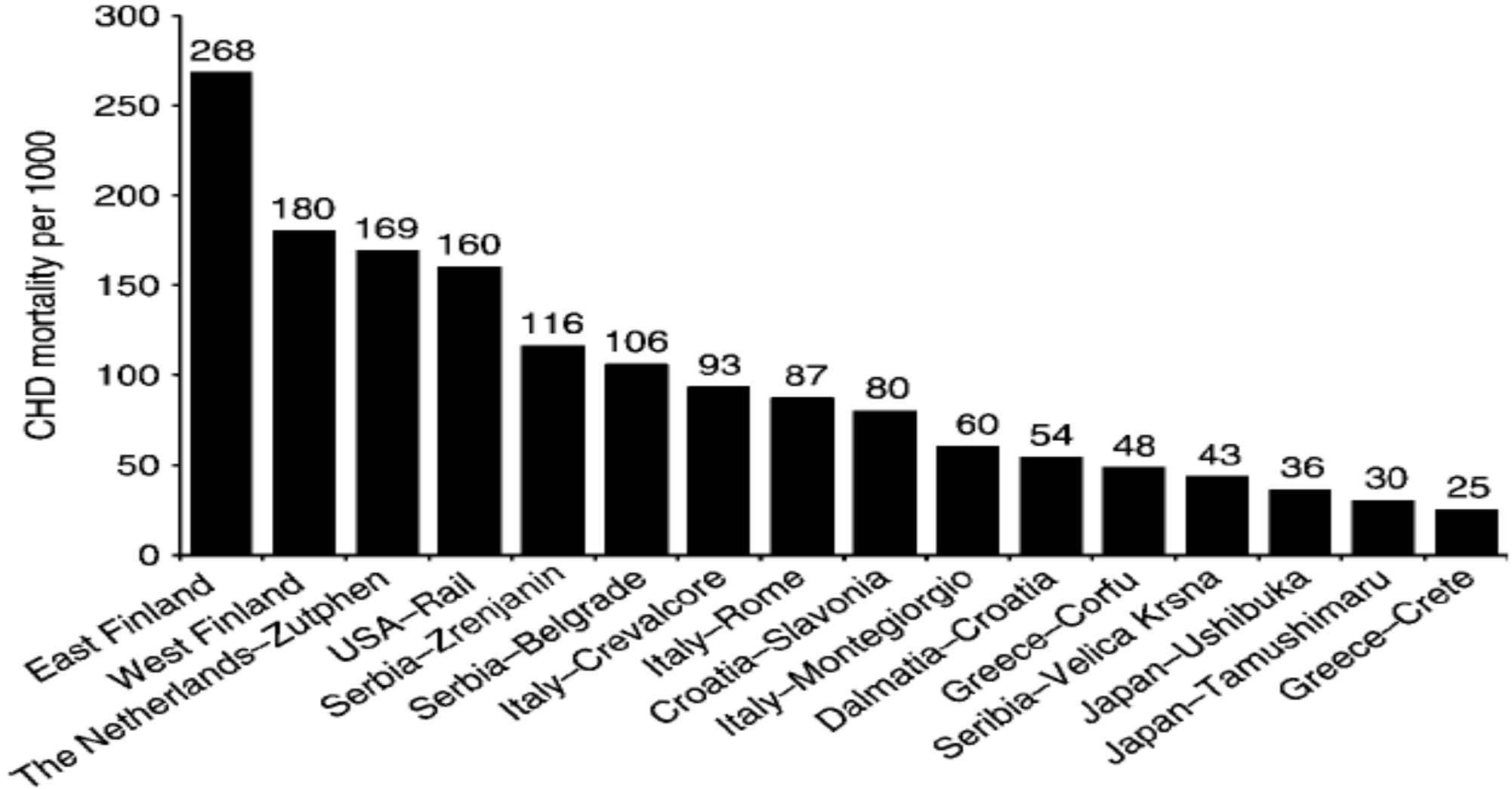


The Seven Countries Study

Area	Year(s) of entry examination	Number of subjects enrolled	Participation rate (%)
U.S. railroad, U.S.A.	1957-1959	2,571	75.0
East Finland, Finland	1959	817	99.3
West Finland, Finland	1959	860	97.0
Zutphen, The Netherlands	1960	878	84.3
Crevalcore , Italy	1960	993	98.5
Montegiorgio, Italy	1960	719	99.0
Rome railroad, Italy	1962	768	80.6
Dalmatia, Croatia, YU	1958	671	98.0
Slavonia, Croatia, YU	1958	696	91.0
Zrenjanin, Serbia, YU	1963	516	98.0
Belgrade, Serbia, YU	1964	538	80.0
Velika Krsna, Serbia, YU	1962	511	96.7
Corfu, Greece	1961	529	95.3
Crete, Greece	1960	686	97.6
Tanushimaru, Japan	1958	508	100.0
Ushibuka, Japan	1960	502	99.6
Total		12,763	90.4

Men, aged 40 – 59 yrs

Age-standardised 25-year mortality per 1000 from coronary heart disease (CHD) in 16 cohorts of the Seven Countries Study



The Seven Countries Study

Insights from the Seven Countries Study

Table 1 Average amount of vegetable and animal foods consumed per person in g per day in 1960: selected cohorts of the Seven Countries Study

Cohort	Bread	Cereals	Potatoes	Legumes	Vegetables	Fruit
U. S. railroad	97	26	124	1	171	233
Zutphen	252	17	252	2	227	82
Crete	380	30	190	30	191	464

Cohort	Meat	Fish	Eggs	Cheese	Milk
U. S. railroad	273	3	40	18	231
Zutphen	138	12	27	31	447
Crete	35	18	25	13	235

Table 2 Average amount of visible fats and other foods consumed per person in g per day in 1960: selected cohorts of the Seven Countries Study

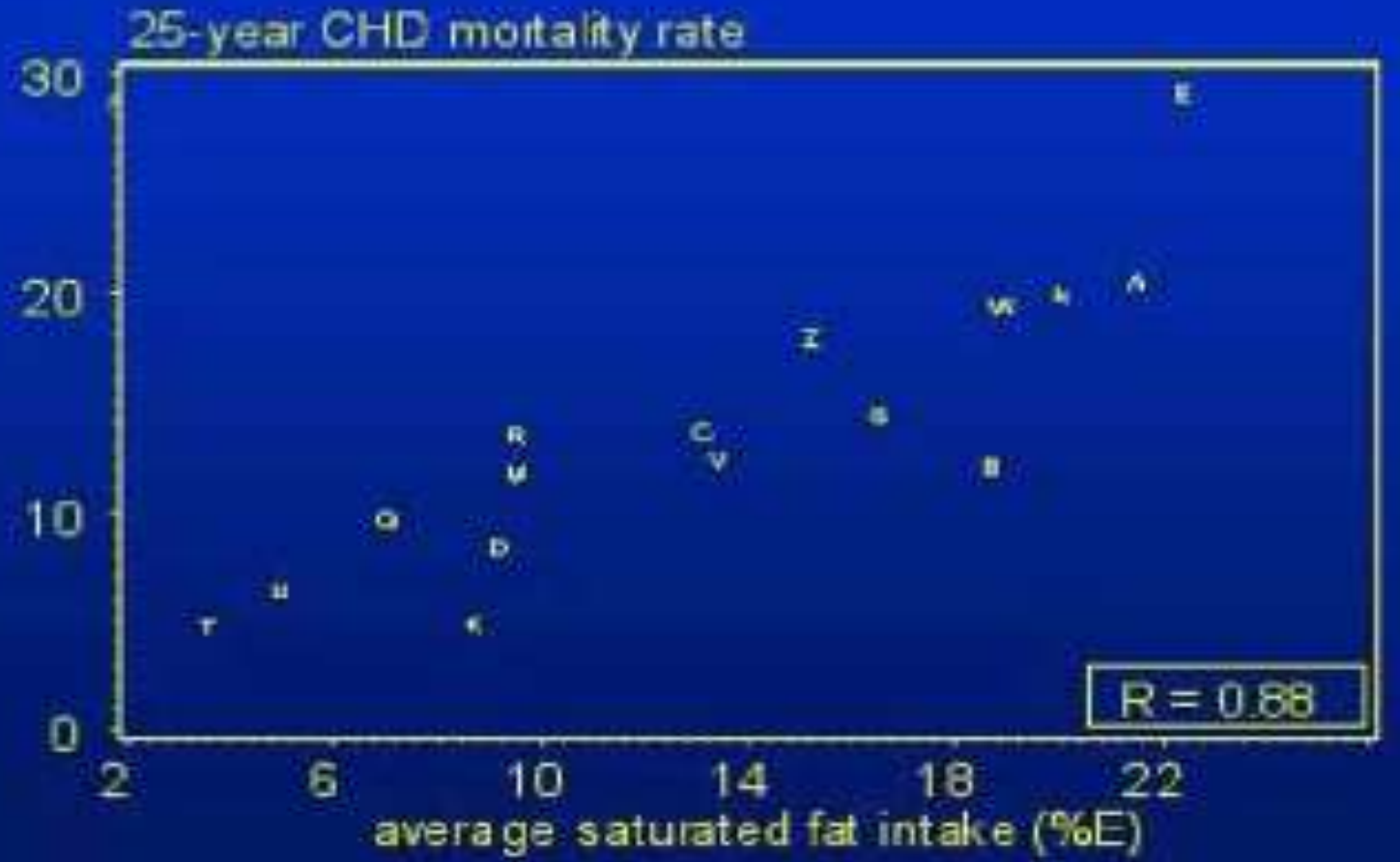
Cohort	Butter	Margarine	Lard	Olive oil	Other
U. S. railroad	26	4			3[a]
Zutphen	21	56	2		
Crete				95	

Cohort	Edible fats	Sugar products	Pastries	Alcohol 100%	Rest
U. S. railroad	33	24	95	6	91
Zutphen	79	72	29	3	29
Crete	95	20	0	15	107

[a] soy bean oil

Kok et al., Eur J Nutr 2004

Average intake of saturated fatty acids (%E) in 1960 and 25-year age-adjusted mortality rates from CHD



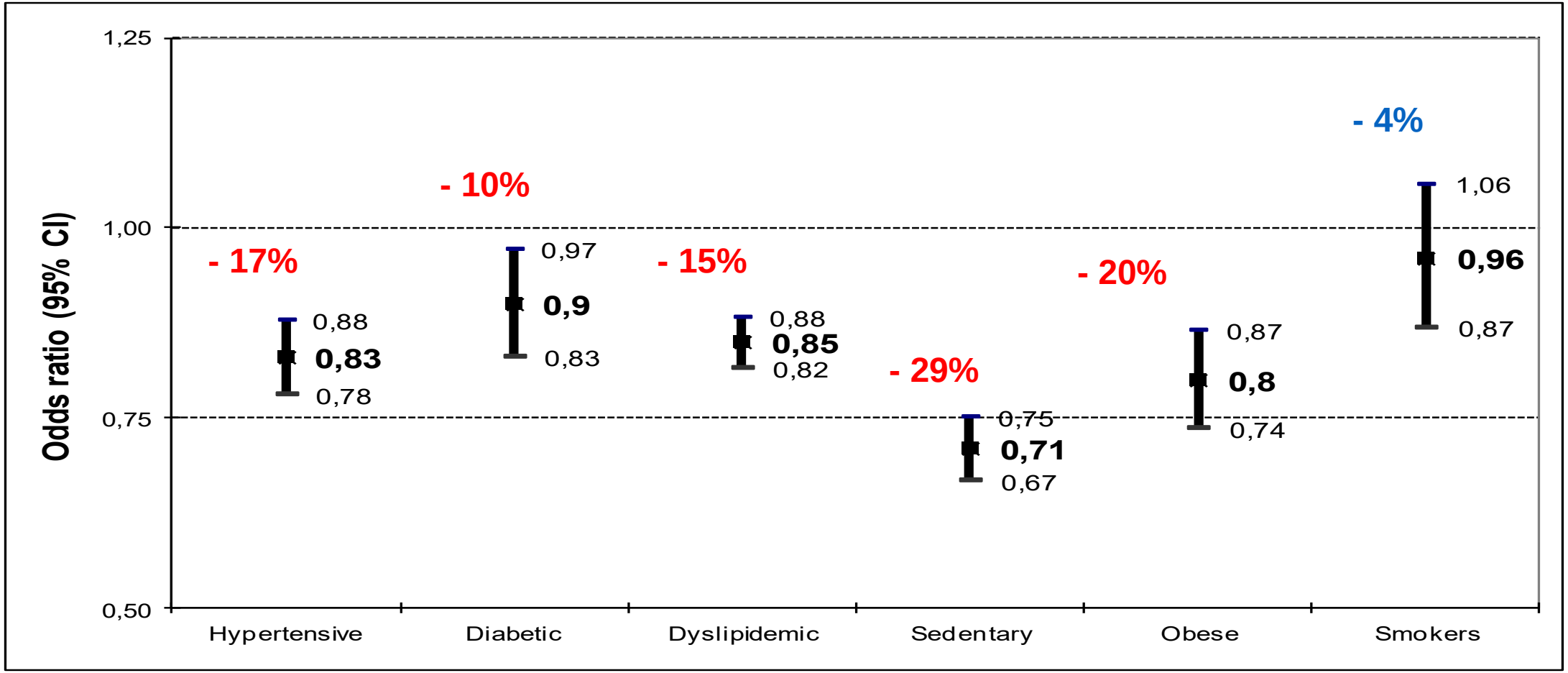
Kromhout et al Prev Med 1995,24:308-15.

Mediterranean diet and CVD

- The traditional Mediterranean diet has long been associated with low risk of CVD, ın
  - observational studies and RCT.

The CARDIO2000 case-control study:

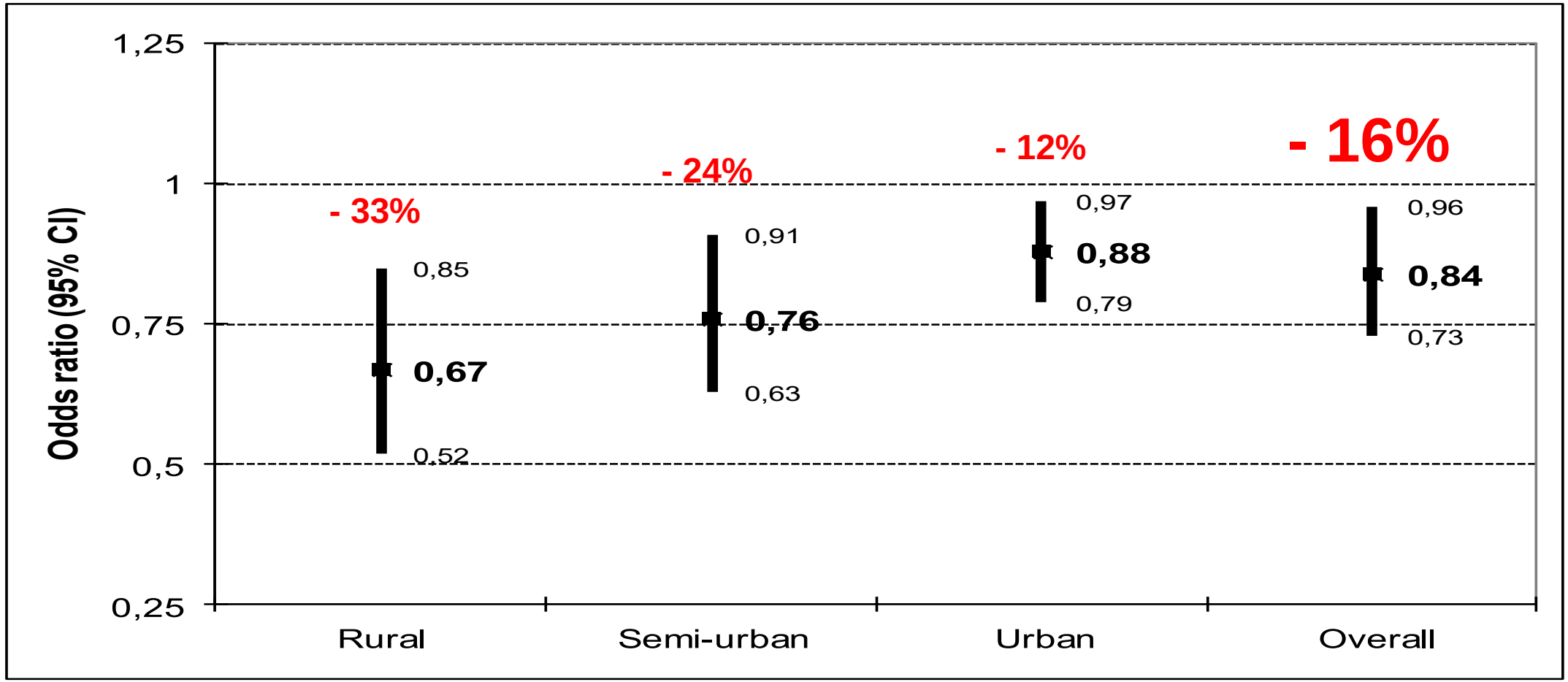
848 ACS pts – 1078 healthy controls



Panagiotakos DB, et al. E Med J PH 2002

The CARDIO2000 case-control study:

848 ACS pts – 1078 healthy controls



Panagiotakos DB, et al. Int J Cardiol 2005

The EPIC study

- The Greek EPIC-Study is one of the first studies that systematically evaluated the effect of Mediterranean diet on health and has reported that …
  - 2/9 increase in the Med diet adherence score was associated with
    - 25% reduction in all-cause mortality
    - 33% reduction in CVD mortality.

Trichopoulou A, et al. NEJM 2003

The HALE study

Healthy Ageing: Longitudinal study in Europe

- A multi-disciplinary approach to healthy ageing and its determinants in **11 European countries**
  - 5th Framework programme EU
    - Quality of Life and Management of Living Resources
    - Key action “The ageing population and their disabilities”
      - Grant no.: QRLT-2000-00211

Knoops KT, de Groot LC, Kromhout D, et al. JAMA 2004

Diet, lifestyle and 10-year mortality in *n*=2339 elderly men and women free from chronic diseases in the HALE project

Table 2. Cox Proportional Hazard Ratios for Dietary Pattern and 3 Lifestyle Factors for 10-Year All-Cause and Cause-Specific Mortality in Elderly Europeans

Variables	Causes of Death, Hazard Ratio (95% Confidence Interval)*				
	All Causes	Coronary Heart Disease	Cardiovascular Disease	Cancer	Other Causes
No. at risk	2339	2152	2152	2152	2145
No. of events	935	122	371	233	145
Protective factors†					
Mediterranean diet	0.77 (0.68-0.88)	0.61 (0.43-0.88)	0.71 (0.58-0.88)	0.90 (0.70-1.17)	0.61 (0.44-0.85)
Moderate alcohol consumption	0.78 (0.67-0.91)	0.60 (0.40-0.88)	0.74 (0.59-0.93)	0.73 (0.54-0.98)	0.63 (0.44-0.90)
Physical activity	0.63 (0.55-0.72)	0.72 (0.48-1.07)	0.65 (0.52-0.81)	0.64 (0.48-0.84)	0.52 (0.37-0.74)
Nonsmoking	0.65 (0.57-0.75)	0.80 (0.54-1.17)	0.68 (0.54-0.85)	0.47 (0.36-0.62)	0.92 (0.59-1.24)

*Model adjusted for the other dietary and lifestyle factors, age, sex, number of years of education, body mass index, and study.
†To achieve protective factors in each category, participants must have scored at least 4 points for the Mediterranean diet score, consumed more than 0 g of alcohol a day, scored in the intermediate or highest tertile for either the Voorrips or Morris questionnaires, and were nonsmokers or had quit smoking for at least 15 years.

Knoops KT, de Groot LC, Kromhout D, et al. JAMA 2004

The ATTICA Study

3000+ healthy volunteers; 10 yr Follow up

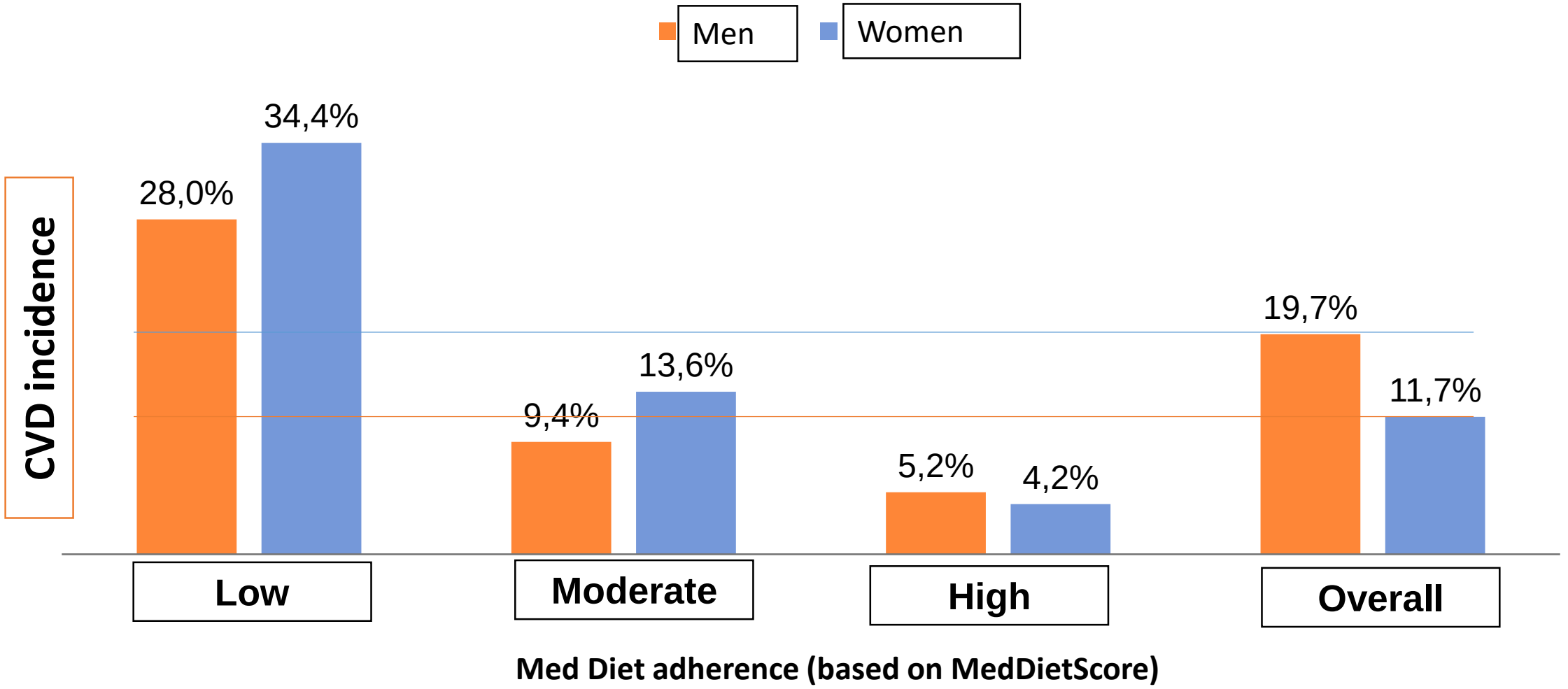
According to the ATTICA Study, participants who where in the **highest tertile** of the MedDietScore had on average

- 20% lower C-reactive protein levels
- 17% lower interleukin-6 levels
- 15% lower homocysteine levels
- 14% lower white blood cell counts
- 6% lower fibrinogen levels (all p-values<0.05)

as compared to those who were in the **lowest tertile**.

Chrysohoou C, Panagiotakos D, Pitsavos C et al. J Am Coll Cardiol 2004

10-year (2002-2012) incidence of CVD and adherence to the Mediterranean Diet (the ATTICA Study)



Panagiotakos D, et al. Nutr Metab CVD 2014

Exploring the path of the Med Diet

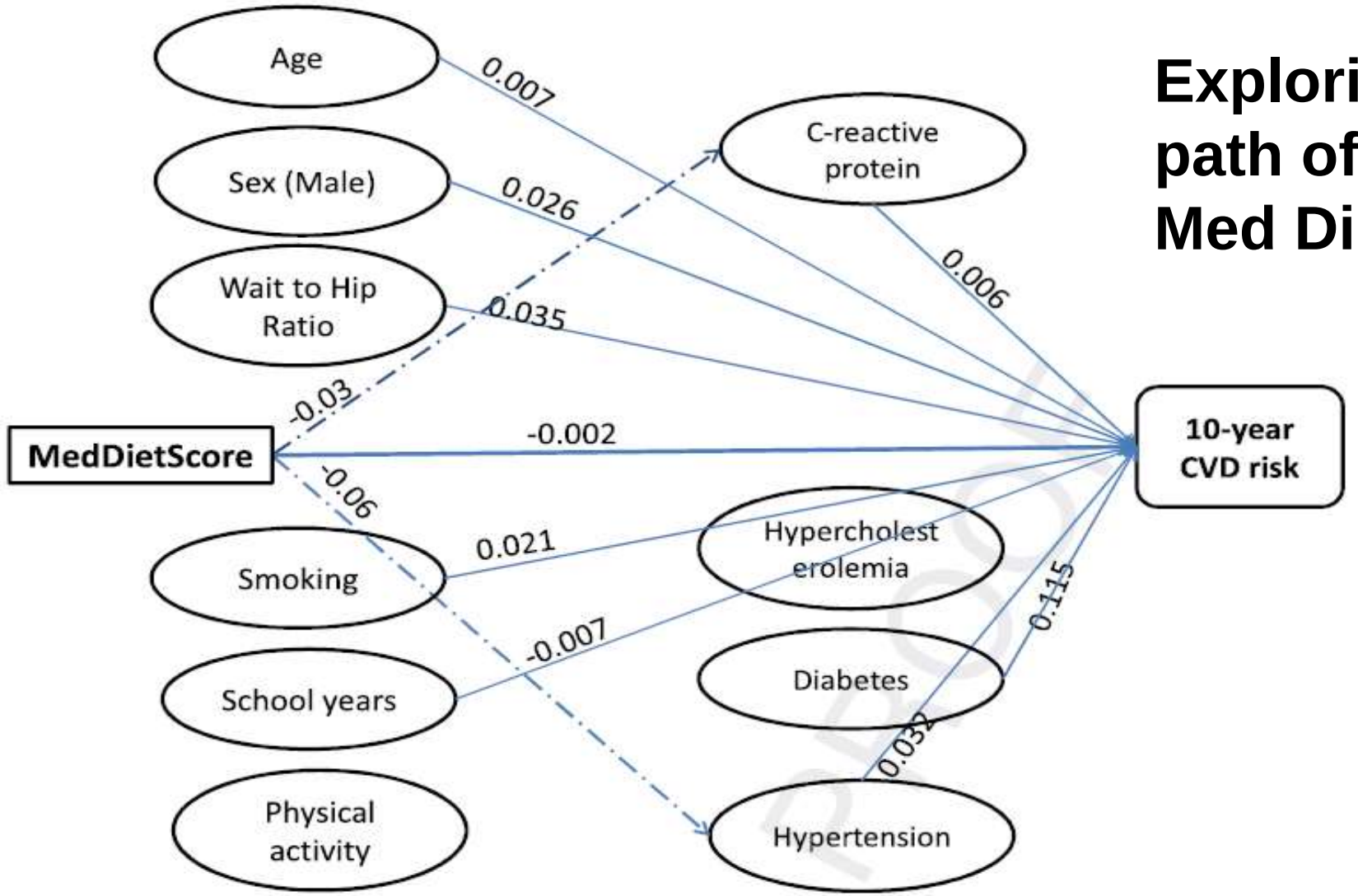


Figure 2 Path analysis for direct (compact lines) and indirect (dotted lines) effects of MedDietScore through age, sex, waist-to-hip ratio, smoking habits, school years, and physical activity status, as well as history of diabetes, hypercholesterolemia, hypertension, and C-reactive protein levels, on CVD risk. Values represent regression coefficients derived from SEM analysis (negative values suggest an inverse relationship with CVD risk).

Panagiotakos D, et al. Nutr Metab CVD 2014

Mediterranean Dietary Pattern and Prediction of All-Cause Mortality in a US Population

Results From the NIH-AARP Diet and Health Study

Panagiota N. Mitrou, PhD; Victor Kipnis, PhD; Anne C. M. Thiébaut, PhD; Jill Reedy, PhD; Amy F. Subar, PhD; Elisabet Wirfält, PhD; Andrew Flood, PhD; Traci Mouw, MPH; Albert R. Hollenbeck, PhD; Michael F. Leitzmann, MD, DrPH; Arthur Schatzkin, MD, DrPH

Table 3. Results of Statistical Analysis for the Mediterranean Dietary Pattern (aMED) and All-Cause Mortality[a]

Characteristic	aMED Score 0-3	aMED Score 4-5	aMED Score 6-9	*P* Value for Trend	aMED Score 0-3	aMED Score 4-5	aMED Score 6-9	*P* Value for Trend
	All Subjects							
	Men (n=214 284)				Women (n=166 012)			
Cases, No.	7616	6903	3607		4073	3891	1709	
Age-adjusted rates[b]	1167.6	870.5	658.5		782.1	583.2	462.1	
Age-adjusted HR	1 [Reference]	0.74 (0.72-0.77)	0.56 (0.54-0.59)	<.001	1 [Reference]	0.75 (0.71-0.78)	0.59 (0.56-0.63)	<.001
Multivariate HR[c]	1 [Reference]	0.89 (0.87-0.93)	0.77 (0.74-0.80)	<.001	1 [Reference]	0.88 (0.84-0.92)	0.78 (0.74-0.83)	<.001
Multivariate HR[d]	1 [Reference]	0.91 (0.88-0.94)	0.79 (0.76-0.83)	<.001	1 [Reference]	0.89 (0.85-0.93)	0.80 (0.75-0.85)	<.001
	Never Smokers							
	Men (n=68 971)				Women (n=75 740)			
Cases, No.	1236	1578	996		1106	1269	608	
Age-adjusted rates[b]	692.6	611.7	502.6		466.8	395.1	340.8	
Age-adjusted HR	1 [Reference]	0.88 (0.82-0.95)	0.72 (0.67-0.79)	<.001	1 [Reference]	0.85 (0.78-0.92)	0.73 (0.66-0.81)	<.001
Multivariate HR[e]	1 [Reference]	0.95 (0.88-1.02)	0.83 (0.76-0.90)	<.001	1 [Reference]	0.89 (0.82-0.97)	0.80 (0.73-0.89)	<.001

Can a Mediterranean diet moderate the development and clinical progression of coronary heart disease? A systematic review

Demosthenes B. Panagiotakos[1], Christos Pitsavos[2], Evangelos Polychronopoulos[1], Christine Chrysohoou[2], Antonis Zampelas[1], Antonia Trichopoulou[3]

[1] Department of Dietetics and Nutrition, Harokopio University, Athens, Greece
[2] First Cardiology Clinic, School of Medicine, University of Athens, Athens, Greece
[3] Department of Hygiene and Epidemiology, School of Medicine, University of Athens, Athens, Greece

Review Article

Med Sci Monit, 2004; 10(8): RA193-198

Table 1. A summary of studies that assessed the effect of Mediterranean diet on coronary heart disease.

Study	Population	Type of study	Outcome	Odds ratio or relative risk
Panagiotakos et al. [12]	661 with ACS and 661 controls	Case - control	First event of ACS	0.84; 0.73–0.96
Pitsavos et al. [13]	534 with ACS and 399 controls with hypercholesterolemia	Case - control	First event of ACS	0.88; 0.82–0.94
Pitsavos et al. [14]	418 with ACS and 303 controls with hypertension	Case - control	First event of ACS	0.92; 0.85–0.98
Pitsavos et al. [15]	307 with ACS and 198 controls with metabolic syndrome	Case - control	First event of ACS	0.64; 0.44–0.95
Trichopoulou et al. [16]	22034 men and women adults	Population based prospective	Fatal CHD	0.67; 0.47–0.94
Martinez-Gonzalez MA et al. [17]	171 with AMI and 171 controls	Case-control	First event of AMI	0.55; 0.42–0.73

BMJ

Adherence to Mediterranean diet and health status: meta-analysis

Francesco Sofi, Francesca Cesari, Rosanna Abbate, Gian Franco Gensini and Alessandro Casini

BMJ 2008;337:a1344
doi:10.1136/bmj.a1344

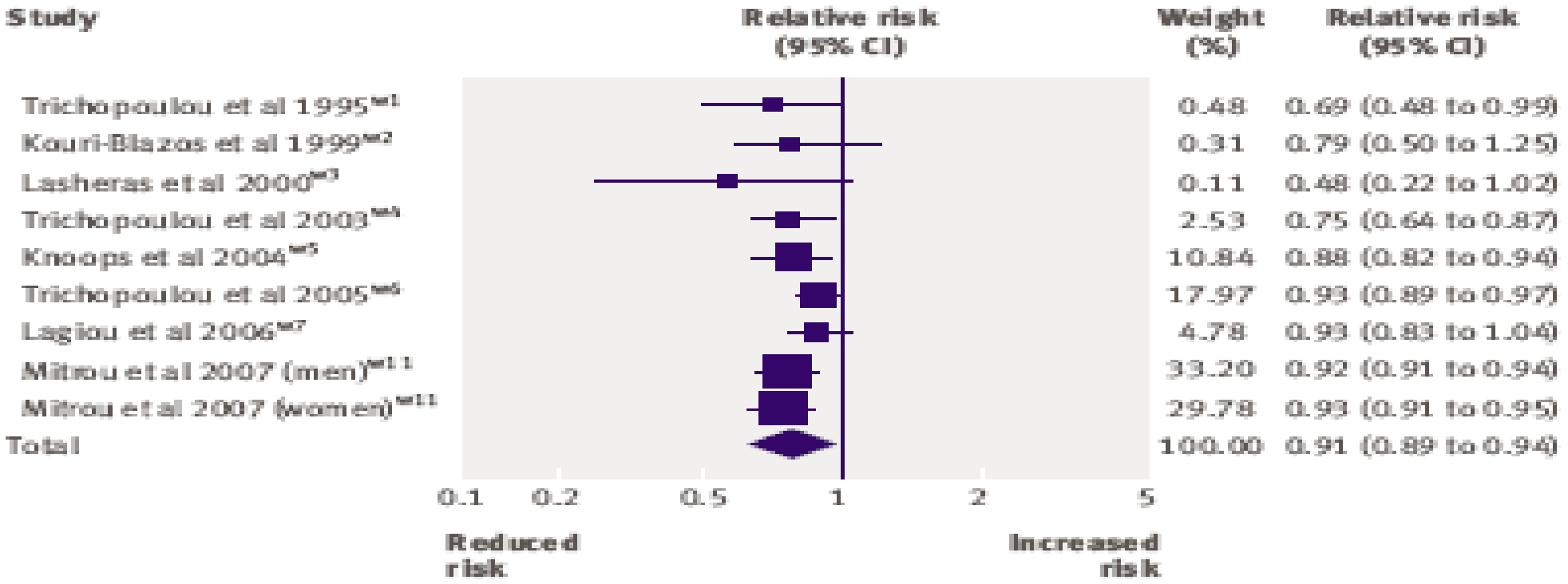


Fig 2| Risk of all cause mortality associated with two point increase in adherence score for Mediterranean diet. Squares represent effect size; extended lines show 95% confidence intervals; diamond represents total effect size

Mediterranean Diet and secondary prevention of CVD

The Lyon Heart Study (RCT) ; 605 AMI pts

Lyon Heart Study (RCT)

- Random allocation to
  - Med Diet
  - Step I AHA diet
- Early stopped
  - 27 mo after start intervention because of a incredible reduction in **70% of recurrent events in Med Diet Group**
- … the attributable risk was **244%**!

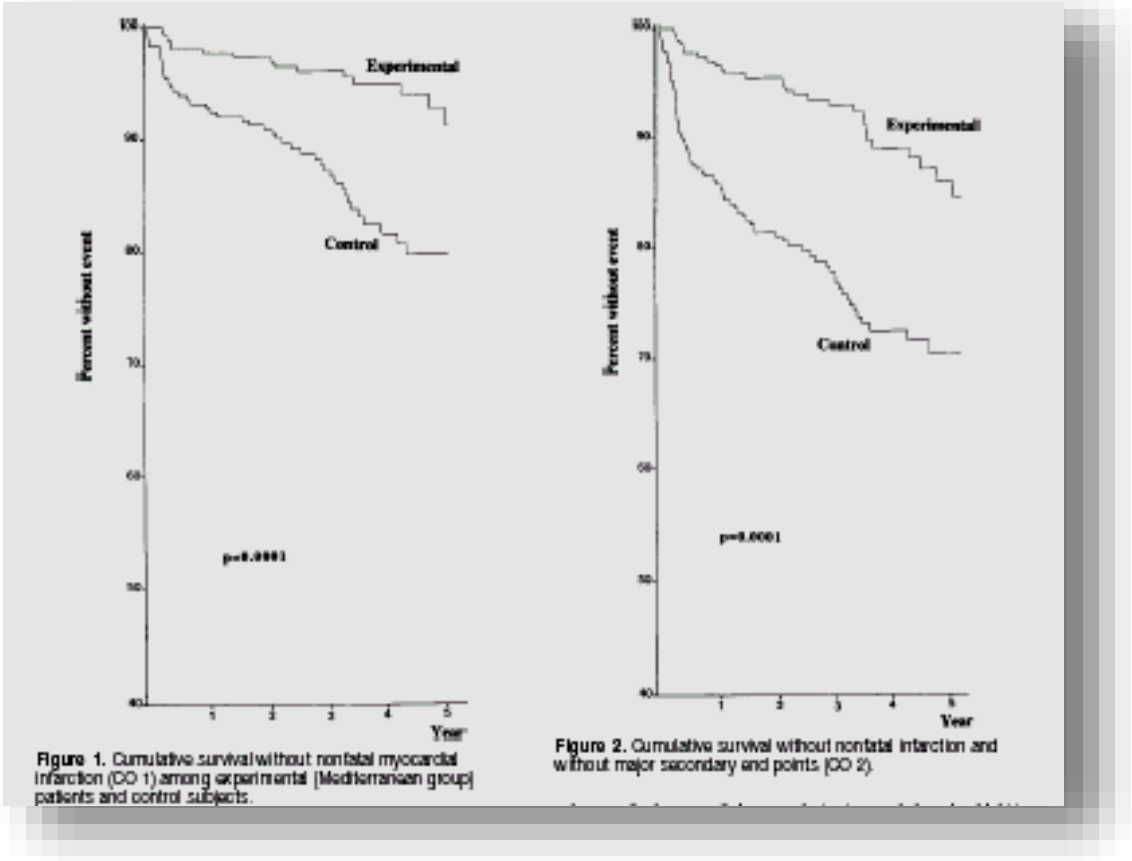


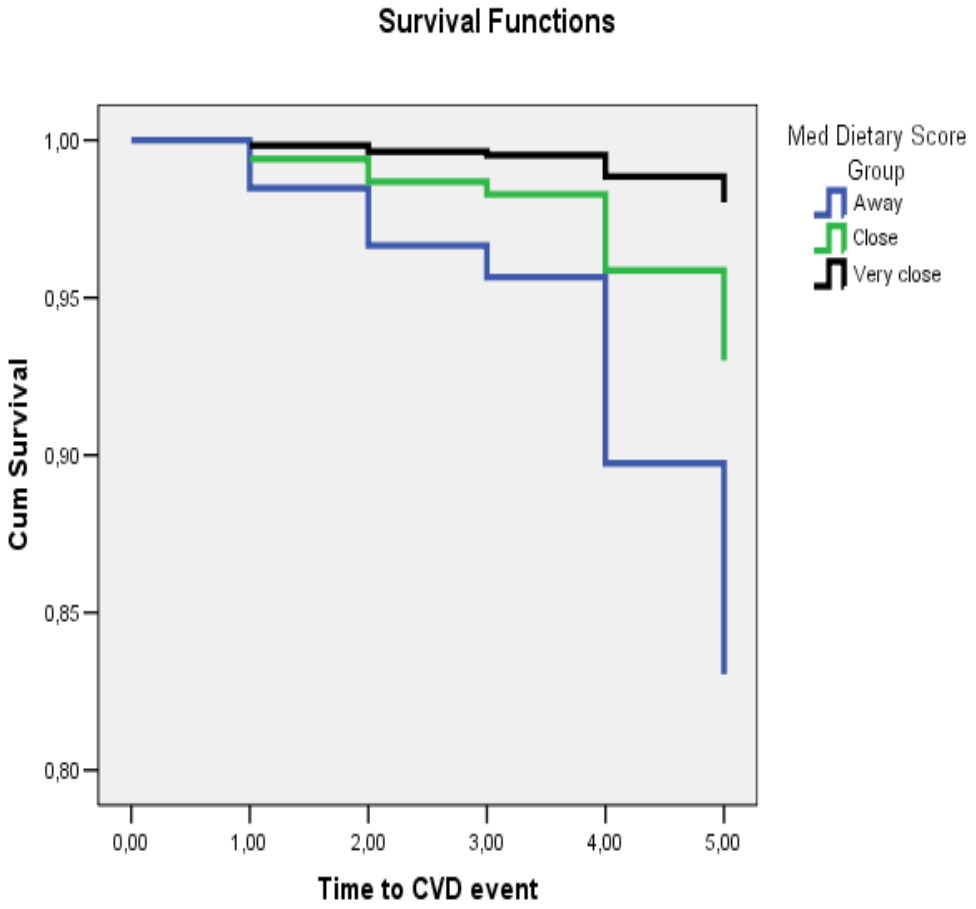
Figure 1. Cumulative survival without nonfatal myocardial infarction (CO 1) among experimental [Mediterranean group] patients and control subjects.

Figure 2. Cumulative survival without nonfatal infarction and without major secondary end points (CO 2).

De Lorgeril M et al. Circulation 1999

Mediterranean Diet and Secondary prevention of CVD

The GREECS Study; 2172 ACS pts, 10-yr Follow up



Our findings suggest that greater adherence to the Mediterranean diet results in a less severe ACS, in terms of cardiac troponin I, CK, and CK-MB levels, making it more probable for the patient to experience UA than MI as a first ACS. Furthermore, we observed that clinical status at presentation or at discharge was highly associated with inhospital mortality and 30-d event rates. The status of the patients mainly explained the observed inverse association of adherence to the Mediterranean diet with an adverse event during hospitalization or 30 d after.

Panagiotakos DB, Pitsavos C, et al., Nutr 2006

Mediterranean Diet & CVD

Potential mechanisms

- Pleiotropic effects :
  - Antioxidant
  - Anti-inflammatory
  - Low glycaemic index
  - Reduced insulin resistance
  - …

… the obesity hypothesis!

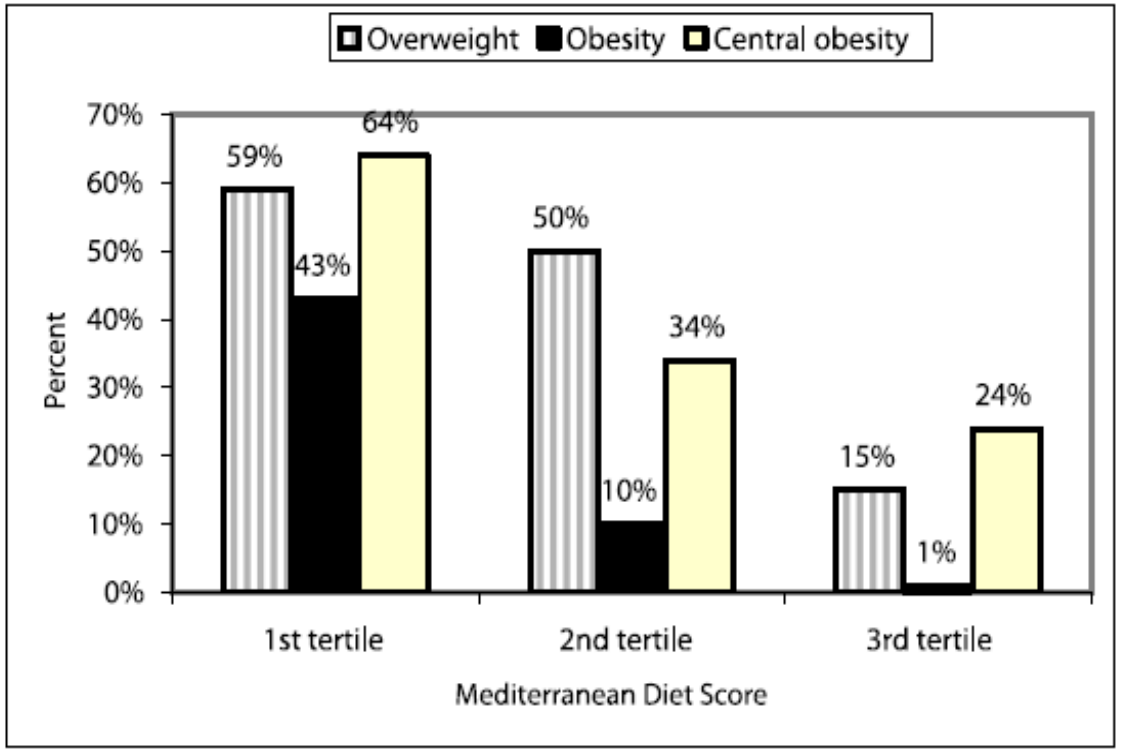


Fig. 2. Prevalences of overweight (striped bars), obesity (black bars), and central obesity (white bars) by tertile of the Mediterranean diet score.

ELSEVIER

Nutrition 22 (2006) xxx–xxx

NUTRITION

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Applied nutritional investigation

Association between the prevalence of obesity and adherence to the Mediterranean diet: the ATTICA study

Demosthenes B. Panagiotakos, Ph.D.[a,*], Christina Chrysohoou, M.D., Ph.D.[b], Christos Pitsavos, M.D., Ph.D.[b], and Christodoulos Stefanadis, M.D., Ph.D.[b]

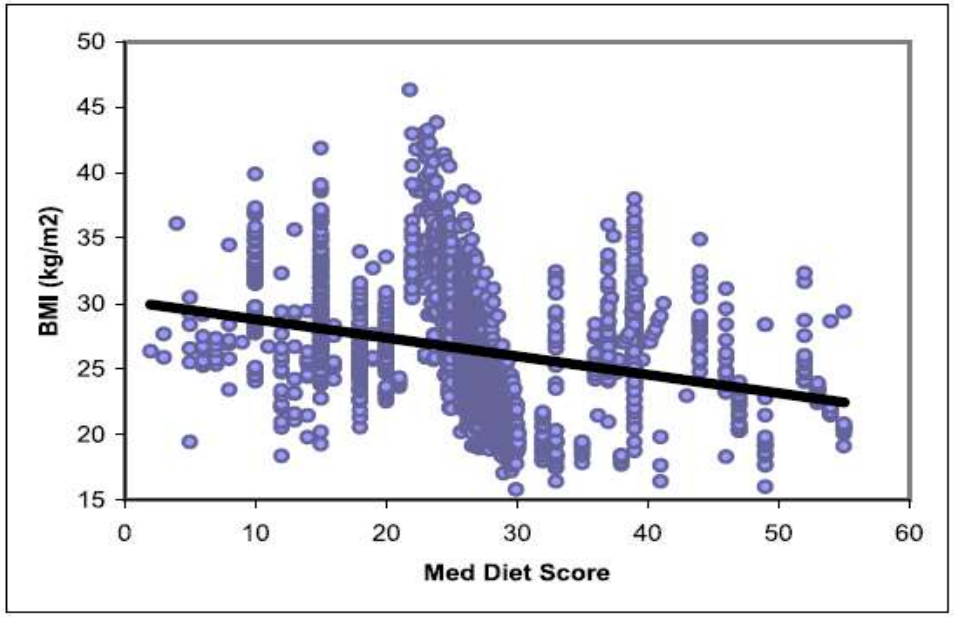

Fig. 1. BMI and Mediterranean diet score. BMI, body mass index; Med, Mediterranean.

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Nutrition, Metabolism & Cardiovascular Diseases

ELSEVIER

EVIEW

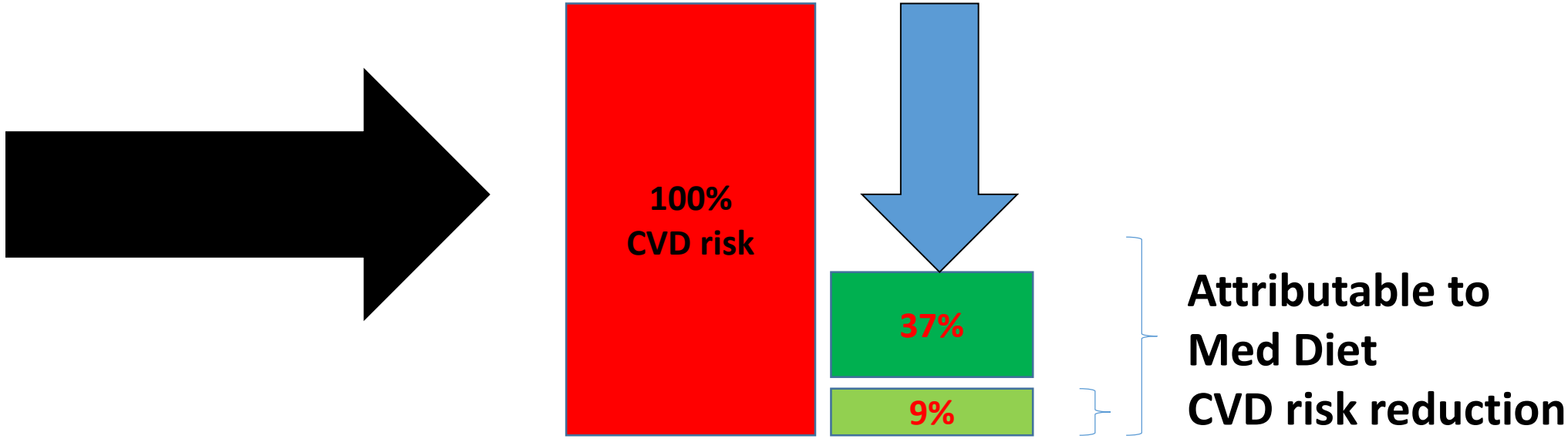
Mediterranean diet and coronary heart disease: s obesity a link? — A systematic review

.M. Kastorini [a,b], H.J. Milionis [b], J.A. Goudevenos [b], D.B. Panagiotakos [a,*]

dietary pattern is a pattern well-known its beneficial effects on human health and cardiovascular health, in particular. The Mediterranean diet protects against the development of coronary heart disease risk factors, diabetes, hyperlipidemia, hypertension, oxidative stress and inflammation [7,9—12,69—71]. Although not all studies show a protective effect of the Mediterranean diet on body weight and obesity, the evidence suggests a possible beneficial role of this dietary pattern. Thus adherence to the Mediterranean dietary pattern may have a protective role against obesity, positively influencing other CVD risk factors through the reduction of body weight, exerting an even more beneficial role. Finally, the Mediterranean diet is a pattern that the majority of people can follow in the long term; therefore, its adoption for preventing or delaying coronary heart disease is of considerable importance.

Conclusion

The studies that have included dietary assessment to a CVD risk model reported a considerable increase in model's accuracy. Moreover, the vast majority of the discussed studies reported an independent effect of dietary patterns on CVD risk, with the attributable to unhealthy dietary patterns risk ranging from 9% to 37%. All these emerge the need for further studies that will evaluate the role of dietary assessment on the accuracy of CVD risk prediction. Innovative methodology on diet measurement approach (i.e., latent class analysis, which uses maximum likelihood for estimating the membership probability in each class) could provide more accurate information regarding dietary habits (Linda, 2010).



Georgousopoulou et al., Int J Food Sci Nutr 2014

Mediterranean Diet

www.healthandlovepage.com

illustrates

is

conferred

the food pyramid

a sustainable diet

Intangible Cultural Heritage

ensuring

awarded by

UNESCO

leads to

fair and affordable prices

healthy citizens

eco-friendly practices

sensitivity to biodiversity and ecosystems

cultural maintenance

enhance

represent

protect

strengthens

the economy

a healthy society

the environment

culture

form

is divided into

high consumption

moderate consumption

low to moderate consumption

low consumption

of

of

of

of

contribute to

provide

contribute to

contribute to

contribute to

contribute to

antioxidants and vitamins

essential for

good health

11% of GHG

11% of GHG

18% of GHG

10% of GHG

30% of GHG

by reducing

lead to

several diseases

such as

colon cancer

heart disease

MedDietScore has been incorporated into CVD risk charts

Table 3
Predicting 10-year CHD risk (%) in men and women from the ATTICA study (2001–02, in Athens metropolitan area), by group of the Mediterranean Diet Score

Age	Mediterranean diet score									
	0–5	6–10	11–15	16–20	21–25	26–30	31–35	36–40	41–45	>45
Men										
<30	4%	3%	3%	3%	3%	3%	2%	2%	1%	0%
30–35	5%	5%	4%	4%	4%	3%	3%	3%	2%	1%
36–40	6%	5%	5%	5%	5%	5%	4%	3%	3%	2%
41–50	7%	7%	6%	6%	6%	5%	5%	4%	4%	3%
51–55	8%	8%	7%	7%	7%	6%	6%	5%	5%	4%
56–60	10%	9%	8%	7%	7%	7%	7%	6%	6%	5%
61–65	12%	12%	9%	9%	8%	7%	7%	6%	6%	6%
66–70	14%	14%	11%	10%	9%	9%	9%	8%	7%	7%
71–75	17%	16%	12%	11%	11%	10%	9%	9%	8%	8%
>75	19%	16%	14%	13%	12%	11%	11%	10%	9%	9%
Women										
<30	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%
30–35	1%	1%	1%	1%	1%	1%	0%	0%	0%	0%
36–40	2%	2%	1%	1%	1%	1%	1%	1%	1%	1%
41–50	3%	3%	2%	2%	2%	2%	2%	1%	1%	1%
51–55	4%	4%	3%	3%	3%	3%	2%	2%	2%	2%
56–60	5%	5%	4%	4%	3%	3%	3%	2%	2%	2%
61–65	6%	6%	5%	5%	4%	4%	4%	4%	3%	2%
66–70	7%	7%	6%	6%	5%	5%	5%	5%	4%	3%
71–75	8%	8%	7%	7%	7%	6%	6%	6%	5%	4%
>75	9%	8%	7%	7%	7%	6%	6%	6%	5%	4%

The probabilities were estimated using the Framingham equations that incorporated age, blood cholesterol, HDL cholesterol, blood pressure, cigarette smoking and diabetes mellitus, and classified by the dietary score categories. The 10-year risk estimates (%) are presented smoothed, using linear interpolation of the logit of the Framingham probabilities, and rounded.

Panagiotakos DB, et al., Prev Med 2007

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Metabolic Syndrome

The Effect of Mediterranean Diet on Metabolic Syndrome and its Components

A Meta-Analysis of 50 Studies and 534,906 Individuals

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Katherine Esposito, MD, PhD,‡ Dario Giugliano, MD, PhD,‡ John A. Goudevenos, MD, PhD,†
Demosthenes B. Panagiotakos, PhD*

The results of the present meta-analysis suggest that adherence to the Mediterranean dietary pattern was associated with lower MS prevalence and progression. Moreover, greater adherence to this traditional dietary pattern was associated with favorable effects on the MS components. These results are of considerable public health importance, because this dietary pattern can be easily adopted by all population groups and various cultures (65) and cost-effectively serve for the primary and secondary prevention of the MS and its individual components.

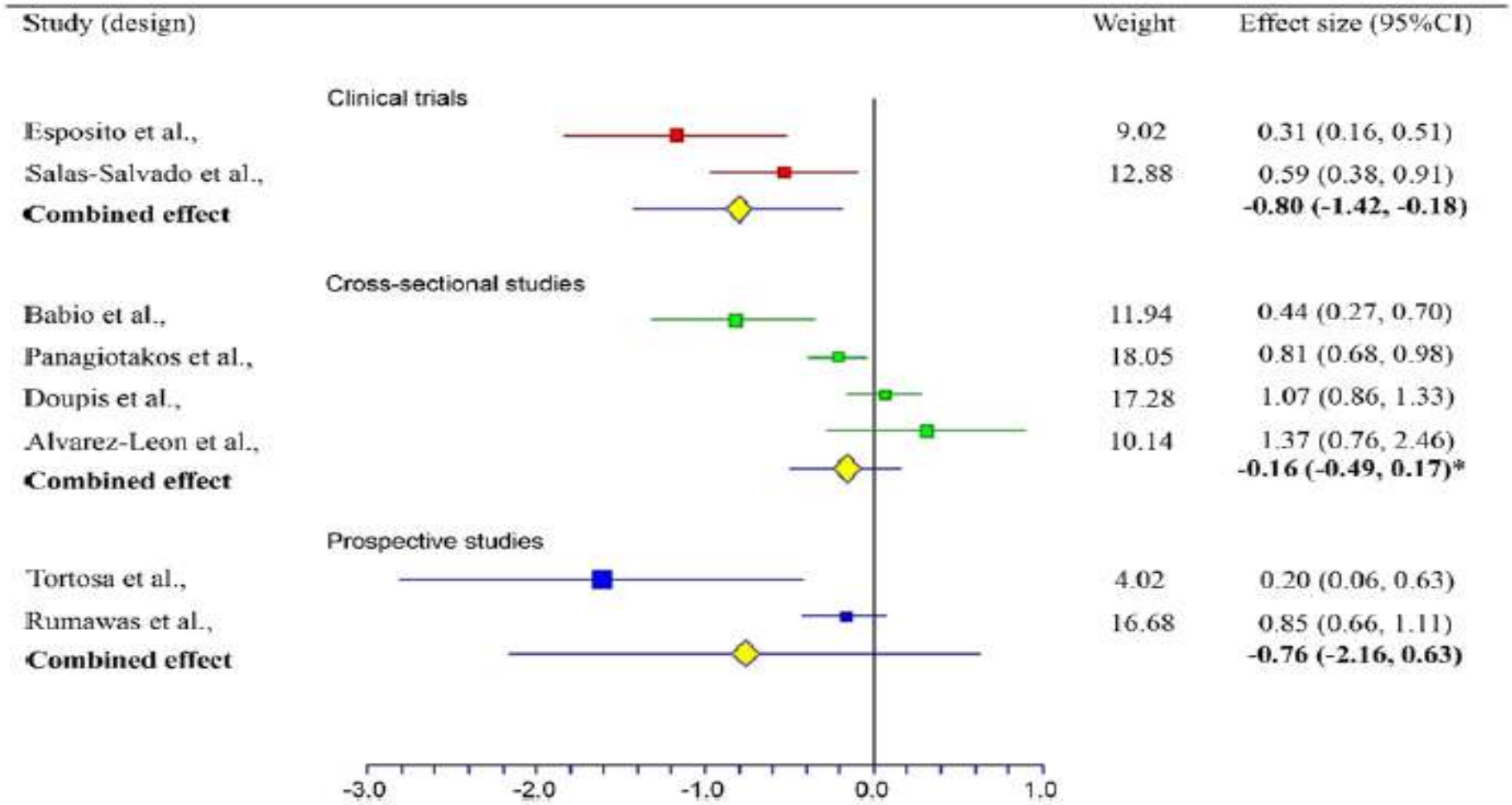


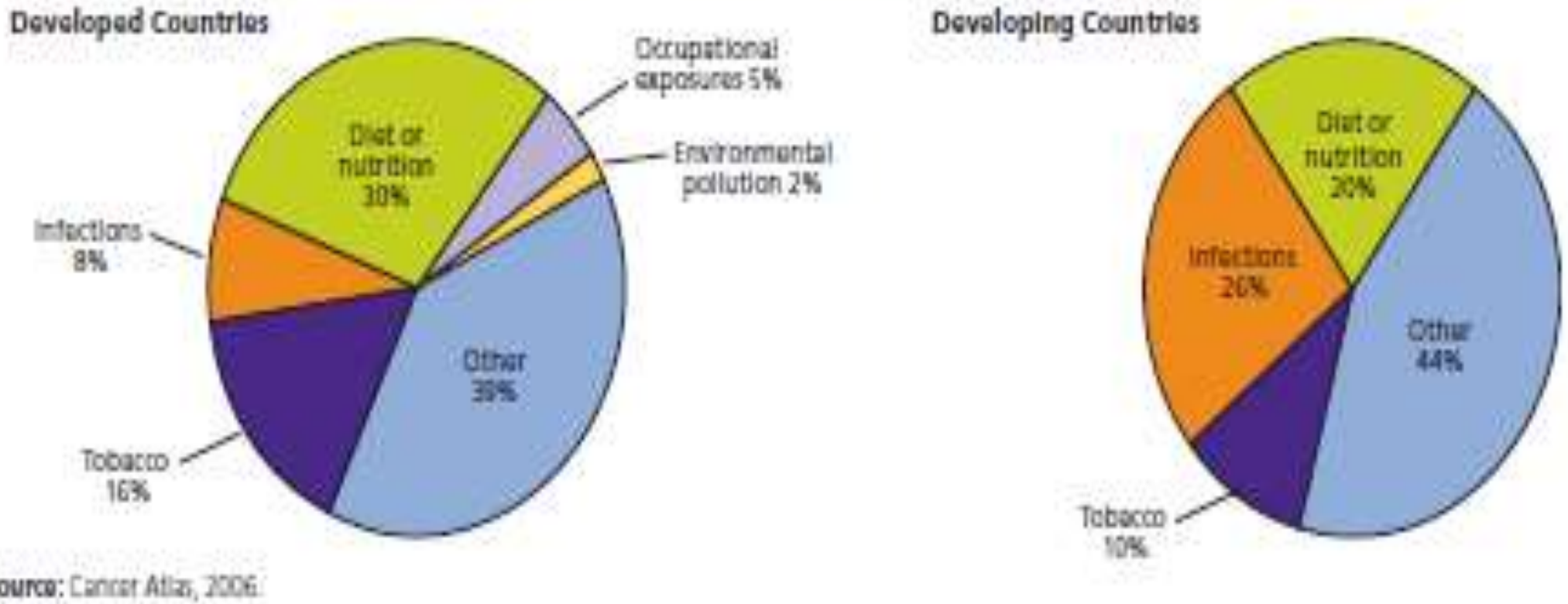
Figure 2 **Mediterranean Diet and Metabolic Syndrome**

Forest plot of studies that evaluated the effect of Mediterranean diet on the presence of the metabolic syndrome (**squares** and **diamonds** represent effect size; **extended lines** show 95% confidence intervals [CIs]). Adherence to the Mediterranean diet was associated with a protective effect in 2 of 2 clinical trials, 2 of 4 cross-sectional studies, and 1 of 2 prospective studies, as compared with lower compliance with this pattern or with a control diet. The combined effect of both clinical trials and prospective studies was highly protective (log-hazard ratio: −0.69, 95% CI: −1.24 to −1.16). *Log(odds ratio) or log(relative risk).

Cancer and Diet

- In 2012 about **14.1 million new cases of cancer occurred globally** (not including skin cancer other than melanoma).
  - Caused about 8.2 million deaths (14.6% of all human deaths).
    - … common types of cancer in males are lung cancer, prostate cancer, colorectal cancer, and stomach cancer, and
    - in females, the most common types are breast cancer, colorectal cancer, lung cancer, and cervical cancer.

Figure 2. Proportion of Cancer Causes by Major Risk Factors and Level of Economic Development



Source: Cancer Atlas, 2006

AACR American Association for Cancer Research
Cancer Research

Landmarks in the History of Cancer Epidemiology: 1900–Present

U.S. Surgeon General reports smoking causes cancer and bronchitis. (9)
1972

Diethylstilbestrol (DES) associated with vaginal adenocarcinoma in daughters of DES-treated women. (35)
1970s

Epidemiological and experimental evidence shows cigarette and tobacco constituents responsible for lung cancer. (6,8)
1950

U.S. Surgeon General: first report on smoking and health. (9)
1964

Cytologic Pap test for cervical cancer, the first early-detection method. (72)
1943

Link between asbestos exposure and lung cancer. (17)
1955

Tobacco smoking may be linked to lung cancer. (5)
1912

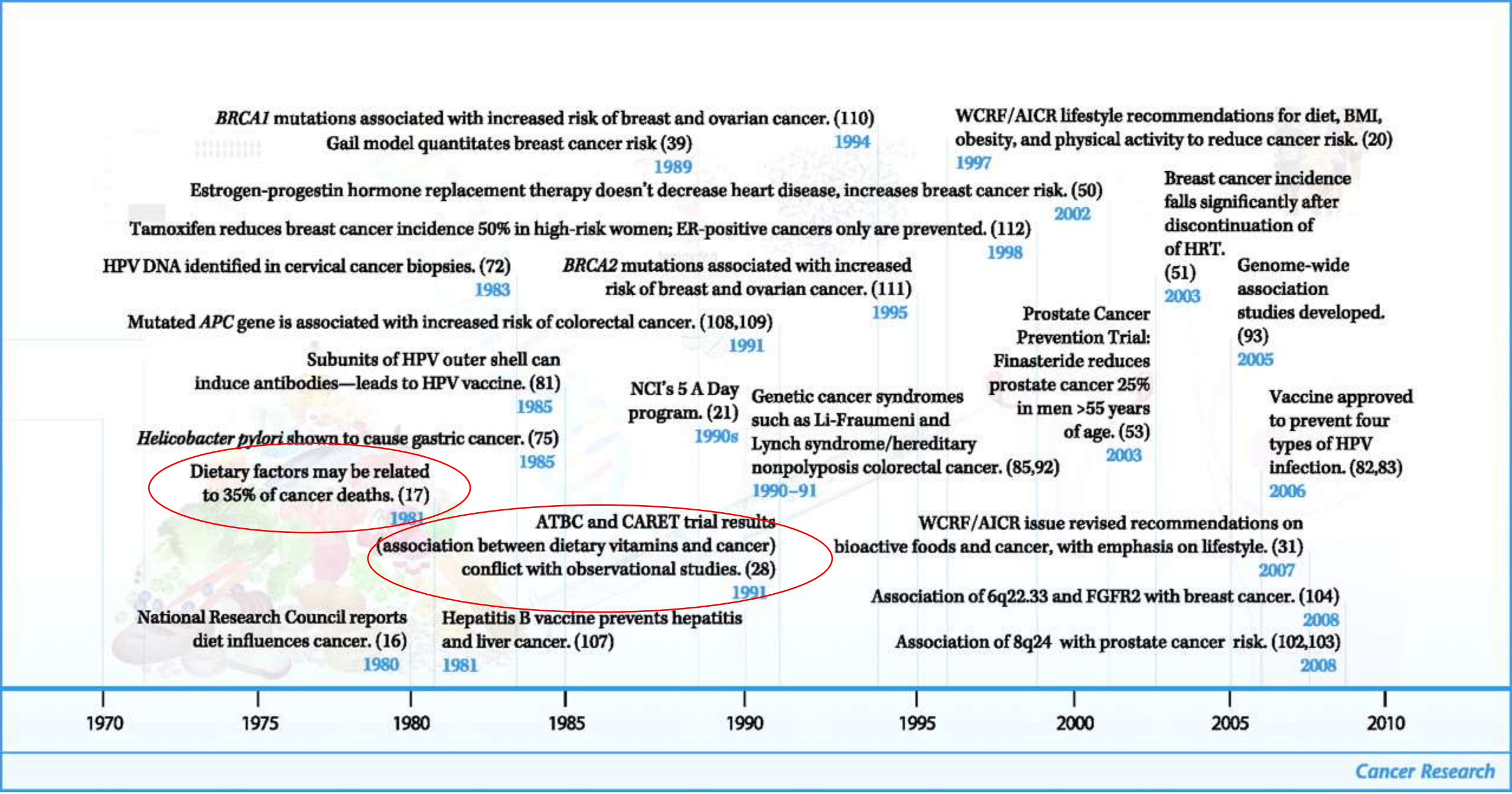
Congress establishes the National Cancer Institute (NCI).
1937

Warning labels on cigarettes in the U.S. (9)
1965

1900 1905 1910 1915 1920 1925 1930 1935 1940 1945 1950 1955 1960 1965

AACR Centennial Series

Peter Greenwald, and Barbara K. Dunn Cancer Res 2009



Peter Greenwald, and Barbara K. Dunn Cancer Res 2009

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REVIEW

The Mediterranean Diet in Cancer Prevention: A Review

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E ROLE OF MEDITERRANEAN DIET ON CANCER RISK

			Participants (n)	*Age range (y)*	*Main findings*
cohort and cancer of oral cavity and pharynx; Bosetti *et al.*,[28] Franceschi *et al.*[29]	Italy	1992–1997	598 cases, 1491 controls	22–77 (oral cavity cancer) 32–76 (pharynx cancer) 20–78 (controls)	MD was inversely associated with cancer of oral cavity and pharynx.
Italian cohort and risk of squamous cell esophageal cancer; Bosetti *et al.*[28,30]	Italy	1992–1997	304 cases, 743 controls	39–77 (cases) 36–77 (controls)	MD was inversely associated with esophageal cancer.
Italian cohort and laryngeal cancer risk; Bosetti *et al.*[28,31]	Italy	1992–2000	527 cases, 1297 controls	30–79 (cases) 31–79 (controls)	MD was inversely associated with laryngeal cancer.
French Canadian families; Nkondjock and Ghadirian[44]	Canada	1995	280 (89 cases, 48 controls–A, 46 controls–B)	42–68 (cases) 39–63 (controls–A) 39–71 (controls–B)	MD did not have any association with *BRCA*-associated breast cancer risk.
Los Angeles County study; Wu *et al.*[45]	U.S.	1995–2001	1248 cases, 1148 controls	25–74	MD was inversely associated with breast cancer risk.
The San Francisco Bay Area; Dalvi *et al.*[43]	U.S.	1996–1999	500 cases, 470 controls	35–79	MD was not associated with endometrial cancer risk.
Four-Corners Breast Cancer study; Murtaugh *et al.*[46]	U.S.	1999–2004	Hispanic (757 cases, 867 controls) Non-Hispanic (1524 cases, 1598 controls)	25–79	MD (and native Mexican) pattern was associated with lower risk for breast cancer.

Mediterranean diet and risk of cancer

Based on … 21 cohort studies including **1,368,736** subjects and 12 case–control studies with **62,725** subjects, that were meta-analysed …

The highest adherence to MD category resulted in a significantly risk reduction for

- **overall cancer** mortality/incidence
  - (cohort; RR: 0.90, 95% CI 0.86–0.95, $p < 0.0001$; $I^2 = 55\%$),
  - **colorectal**
    - (cohort/case–control; RR: 0.86, 95% CI 0.80–0.93, $p < 0.0001$; $I^2 = 62\%$],
  - **prostate**
    - (cohort/case–control; RR: 0.96, 95% CI 0.92–0.99, $p = 0.03$; $I^2 = 0\%$)
  - and **aerodigestive** cancer
    - (cohort/case–control; RR: 0.44, 95% CI 0.26–0.77,$p = 0.003$; $I^2 = 83\%$).

Non-significant changes could be observed for

- breast cancer, gastric cancer and pancreatic cancer.

Schwingshackl L, Hoffmann G. IJC 2014

Conclusions

- Epidemiological evidence suggest that
  - Mediterranean diet protects against the development of CVD,
    - as well as diabetes and hypertension,
  - not only because of its beneficial role regarding CVD risk factors, but also due to a possible effect on body weight and obesity.
  - The level of evidence as regards cancer prevention are still sparse and conflicting … (*but promising*!).

Two questions should be answered …

- Is the Mediterranean diet an **integral entity**, or
  - the **sum of identifiable components** that can and should be **separately considered** in the development of guidelines?

- Is the Mediterranean diet or its major components **transferable to other populations living far from the Mediterranean area**?

What do we eat now?

Table 3 Comparison of the Mediterranean adequacy index (MAI computed) between countries in the study in the periods 1961–1963 and 1998–2000

			95% CI			
		Mean ± SD	Lower bound	Upper bound	*F*	*P*
MAI 61–63	Mediterranean Europe	3.39 ± 1.12	2.35	4.42		
	Eastern Europe	2.67 ± 1.45	0.87	4.47		
	Northern Europe	0.78 ± 0.18	0.63	0.93	14.27	0.0002
MAI 98–00	Mediterranean Europe	1.48 ± 0.39	1.12	1.84		
	Eastern Europe	1.36 ± 0.52	0.72	2.00		
	Northern Europe	0.86 ± 0.14	0.74	0.98	6.53	0.0079

SD – standard deviation; CI – confidence interval.

Balanza et al., Pub Health Nutr 2007

What do we eat now?

Table 1 Total energy availability and percentage of energy availability from fat, protein, carbohydrate and alcohol per capita per day in the periods 1961–1963 and 1998–2000 in the three European regions

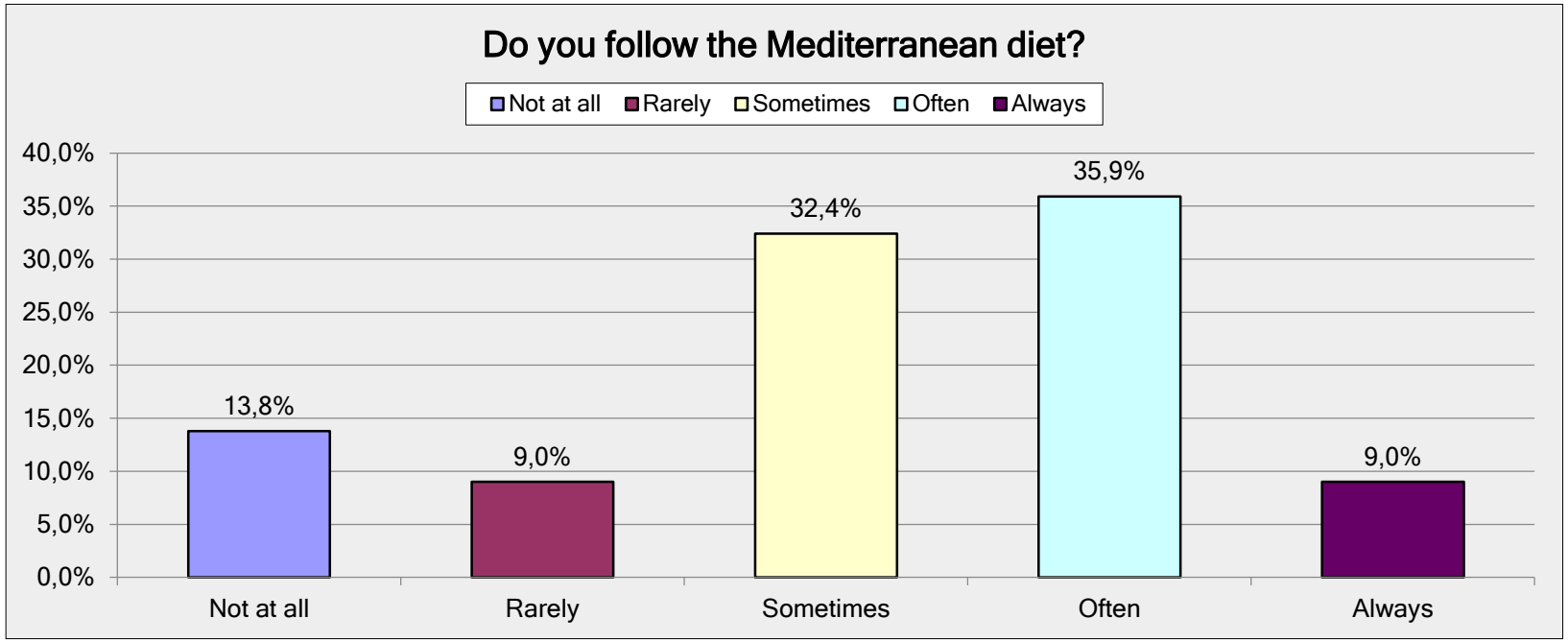
	Mediterranean		Northern Europe		Eastern Europe	
	1961–1963	1998–2000	1961–1963	1998–2000	1961–1963	1998–2000
Total energy (kJ)	12 343 ± 1046	14 819 ± 753	12 765 ± 794	14 070 ± 439	13 292 ± 786	13 602 ± 828‡
Total fats (%)	26.4 ± 3.1	39.1 ± 2.8	36.9 ± 1.5*	38.3 ± 1.2	23.8 ± 3.8§	29.9 ± 3.7*,§
Vegetable	12.9 ± 3.7	18.8 ± 4.1	10.4 ± 2.4	16.3 ± 2.1	6.9 ± 2.3‡	12.2 ± 1.8‡
Animal	13.5 ± 6.1	20.3 ± 4.9	26.5 ± 3.0*	22.0 ± 1.3	17.0 ± 5.3‖	17.7 ± 3.1
Total protein (%)	11.9 ± 0.7	12.9 ± 0.3	11.3 ± 0.4	11.7 ± 0.6†	11.6 ± 0.4	11.8 ± 0.6‡
Vegetable	6.8 ± 0.9	5.1 ± 0.6	4.7 ± 0.2*	4.8 ± 0.3	7.2 ± 1.1§	6.0 ± 0.9‖
Animal	5.1 ± 1.4	7.7 ± 0.8	6.6 ± 0.4	6.9 ± 0.6	4.4 ± 0.9‖	5.8 ± 0.5†
Carbohydrates (%)	54.5 ± 5.3	43.3 ± 3.4	46.9 ± 1.5†	43.5 ± 1.6	61.2 ± 4.1§	53.4 ± 4.3*,§
Total ethanol (%)	7.2 ± 2.1	4.8 ± 1.0	4.9 ± 1.2	6.5 ± 1.3	3.4 ± 1.2†	5.0 ± 1.4
Wine	5.8 ± 1.6	2.6 ± 0.6	0.4 ± 0.3*	1.0 ± 0.3*	0.8 ± 0.8*	0.7 ± 0.6*

Mean ± standard deviation. Comparisons among groups were performed by univariant analysis of variance with *post hoc* analysis (Bonferroni test). Data were weighted by the average number of inhabitants in each geographical area over the period of time.
Comparisons versus Mediterranean Europe in the same period of time: *$P < 0.001$; †$P < 0.01$; ‡$P < 0.05$.
Comparisons between Northern and Eastern Europe in the same period of time: §$P < 0.001$; ‖$P < 0.05$.

Balanza et al., Pub Health Nutr 2007

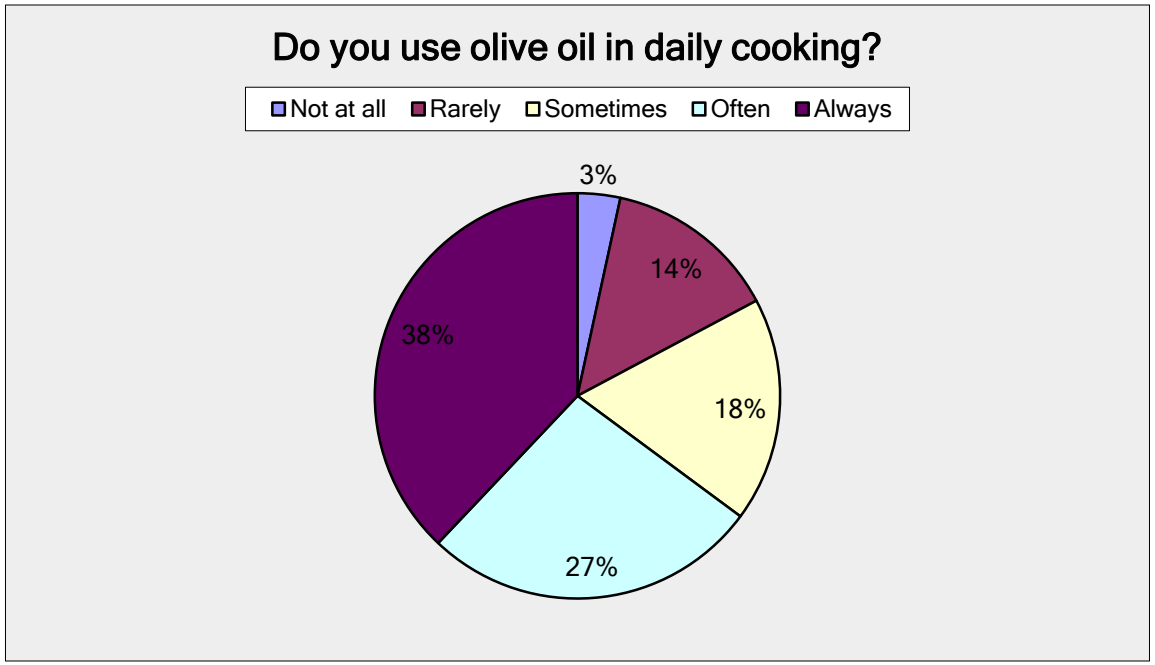
What do we eat … in this room!

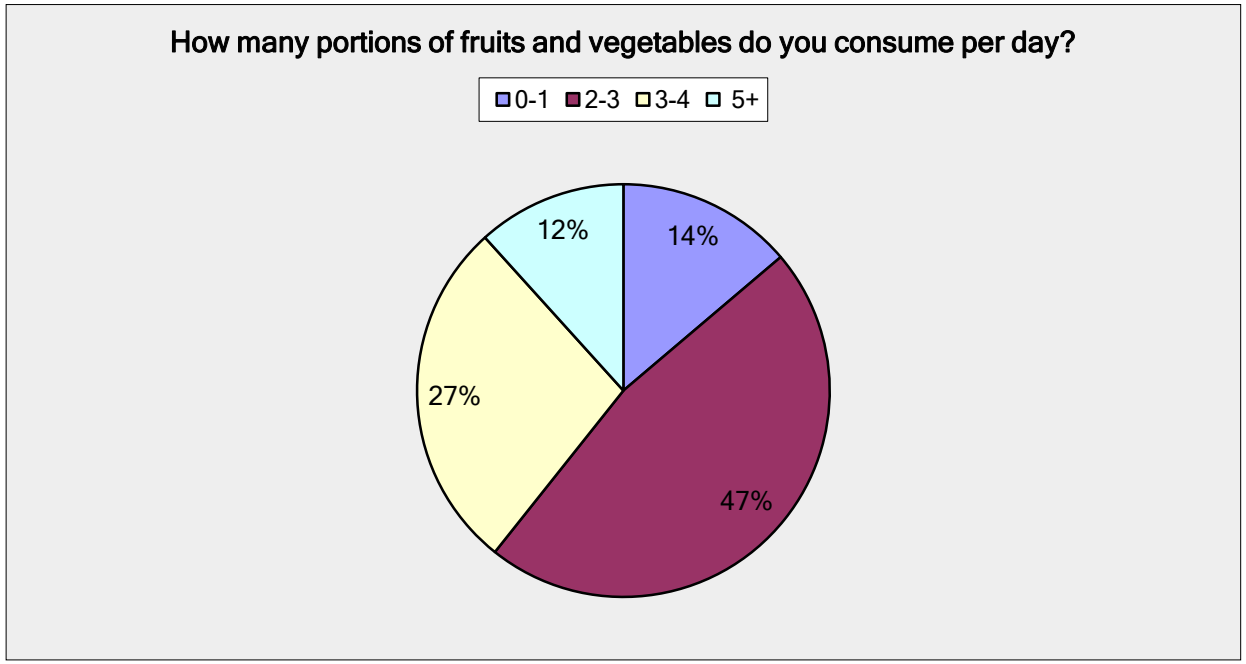
- An electronic survey was conducted to IFCC Conference participants between February 27th and March 7th.
  - 145 individuals (50±14 years, 65 females), from various places around the world, responded to the 8-item questionnaire.

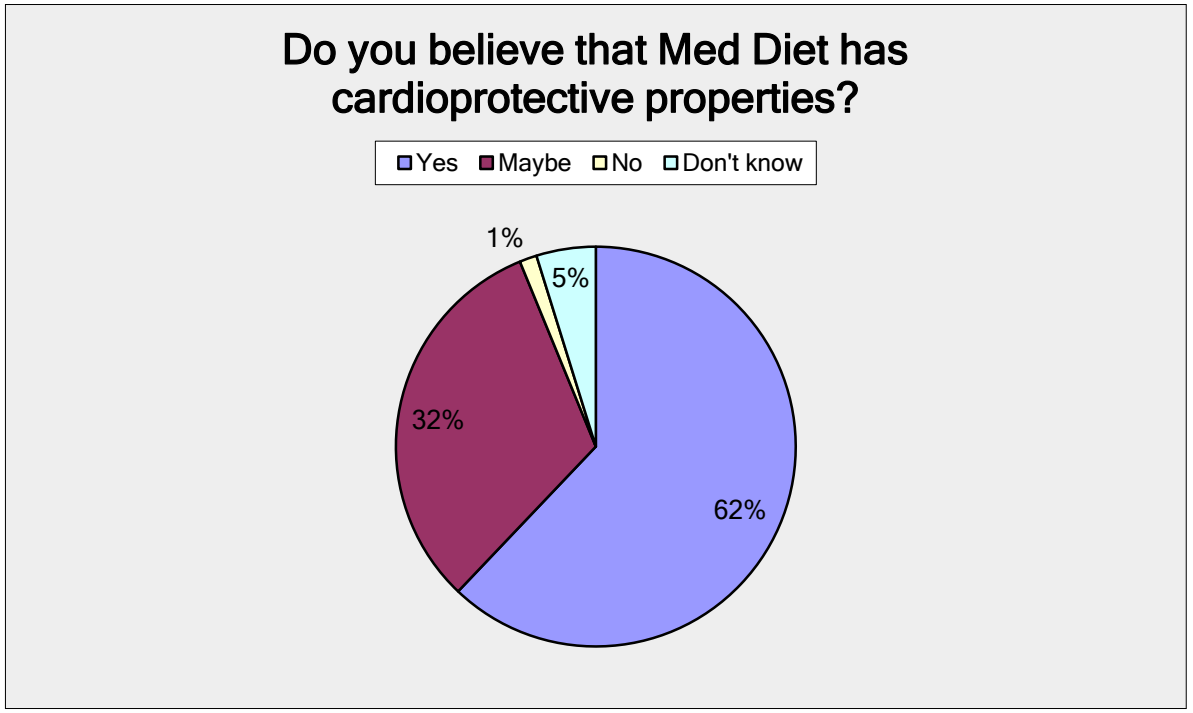


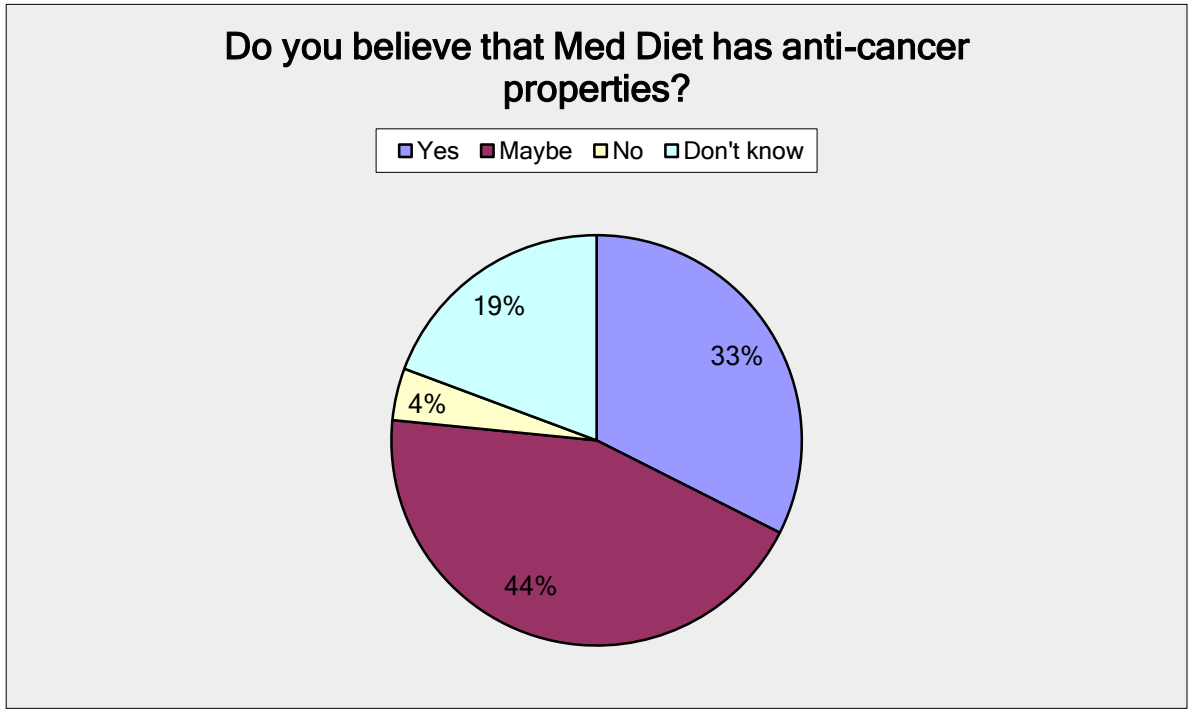
Women: 54% vs. **Men**: 47%

Med Region: 56% vs.
no-Med region: 44%



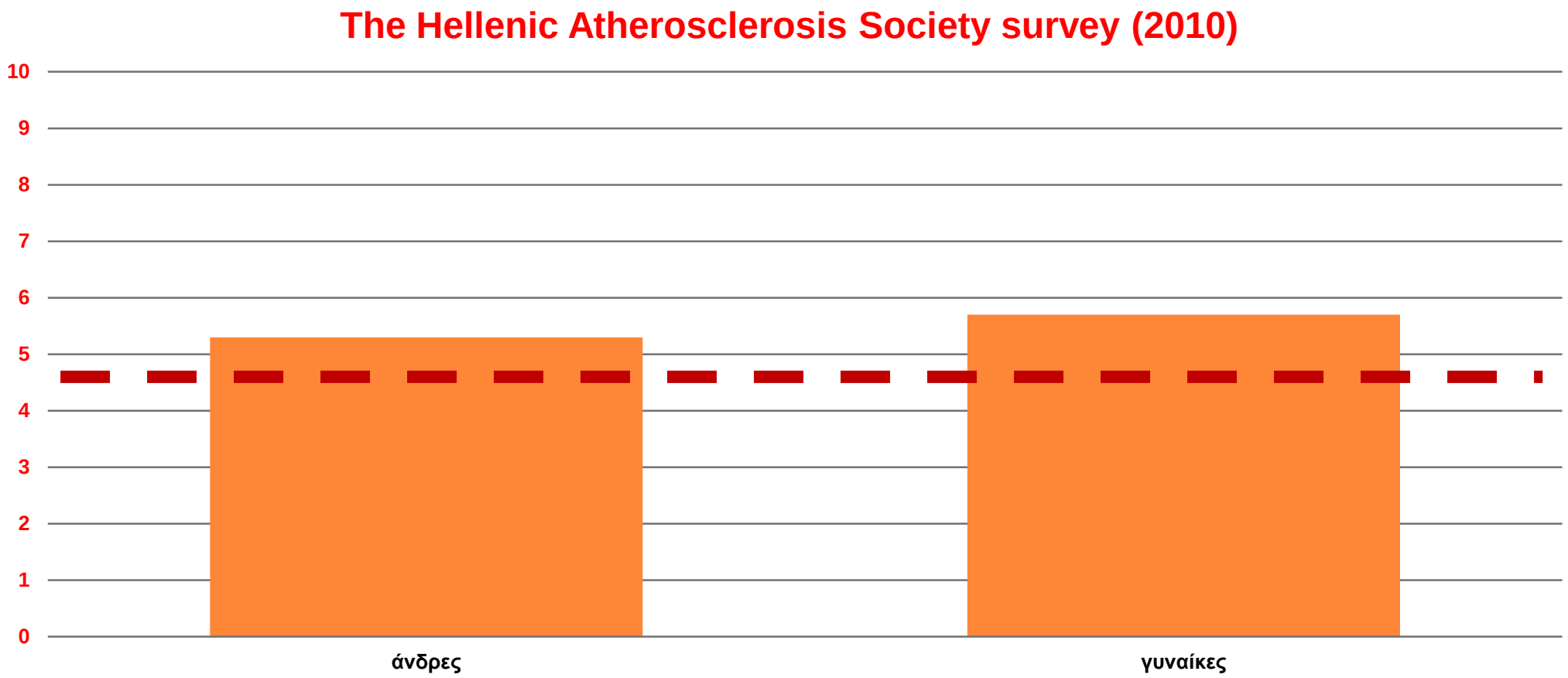






The responses of the participants are in line with the current scientific evidence as regards the cardioprotective effects of Med diet on heart disease and cardiometabolic disorders.
However, they seem more optimistic as regards the anticancer properties.

A test of basic knowledge as regards nutrition facts, among 10.000 Greek adults



Nutrition Education from early stages of life …

Efforts from…

Evidence exists to remind us that the lifestyle habits of our ancestors are a suitable (non pharmaceutical) means for the benefit of our health and quality of life!

THANK YOU!