

ESTUDIO PREDIMED

**Papel de la Dieta
Mediterránea en la
Diabetes y la
Obesidad
Evidencias
epidemiológicas**



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Origin of the Mediterranean Diet



Seven-country study

1) Prevalence of coronary heart disease:

- United States: 4.6%
- Finland: 3.4%
- Italy: 1.1%
- Greece: 0.5%



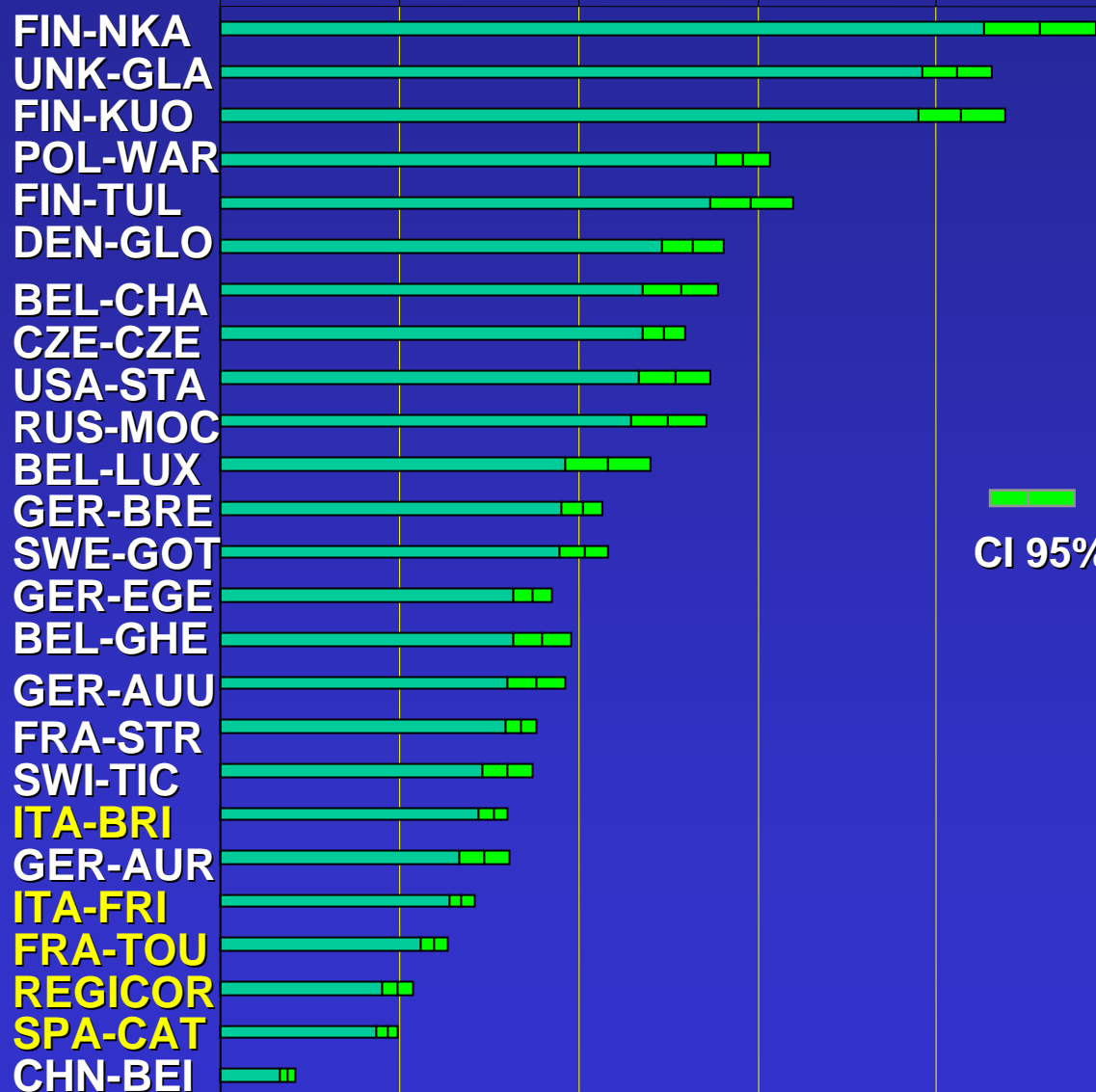
2) 10-year mortality due to coronary heart disease:

- Finland 45.5 / 10,000
- United States 42.4
- Netherlands 31.7
- Italy 20.3
- Greece 6.6

Incidence of AMI/100,000, 35-64 yr: 1985-94

Men

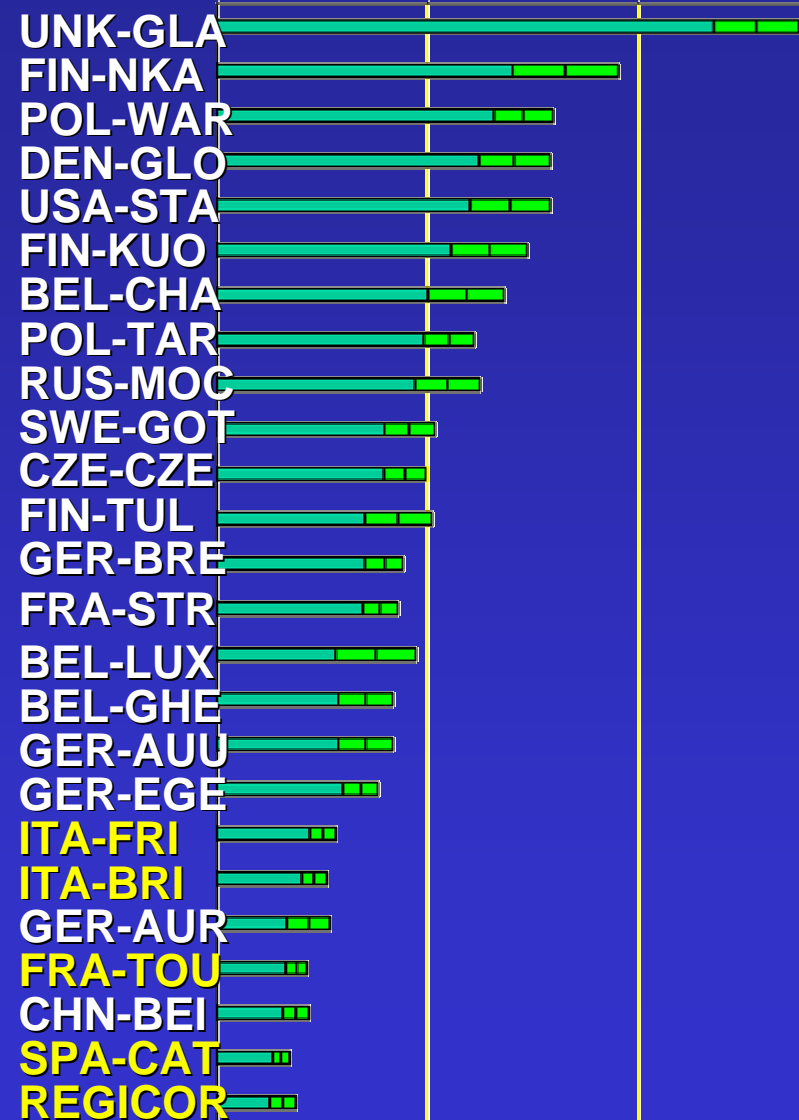
0 200 400 600 800



CI 95%

Women

0 100 200

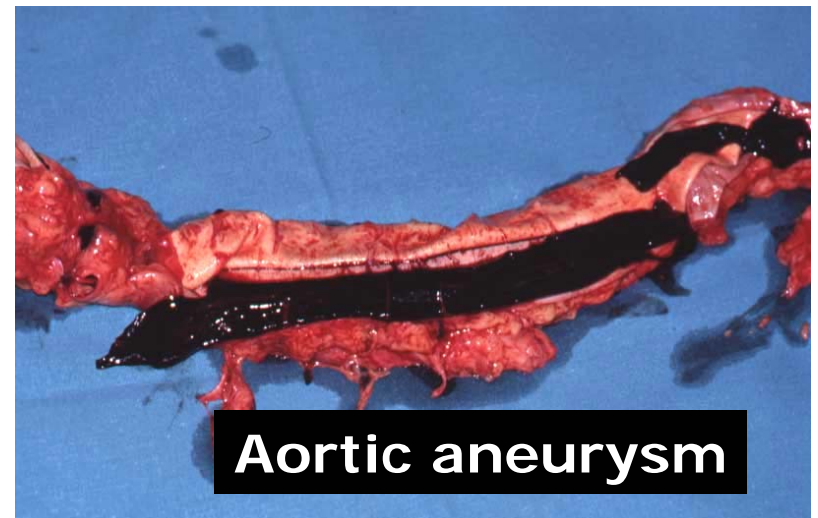
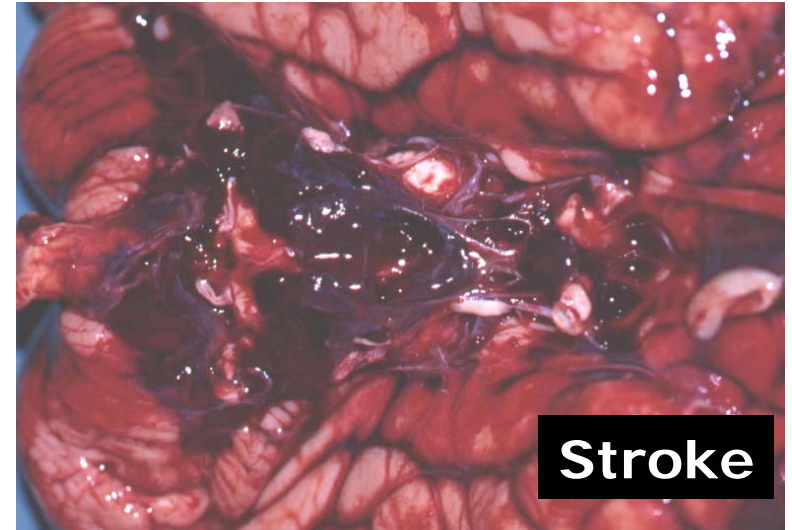
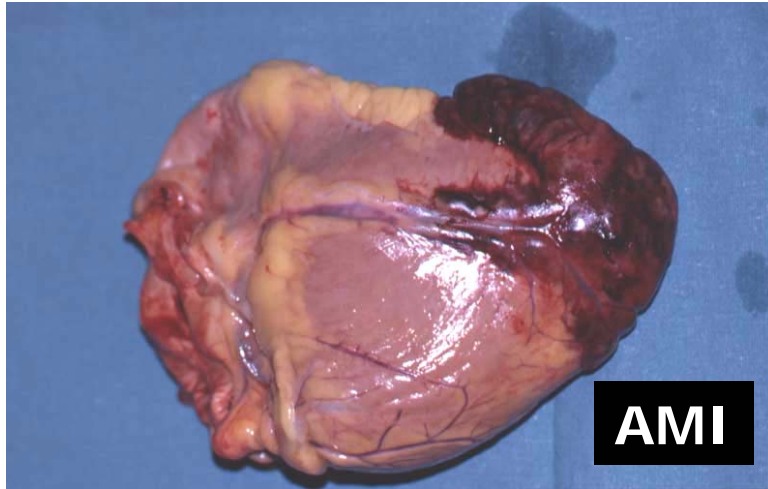


Factors that explain ↓ CV risk in the countries from the South of Europe

- Genetic factors - improbable
- Life habits - probable
 - Mediterranean diet
 - Physical activity

Evidence-based medicine studies are needed

Cardiovascular disease is the main cause of death at the onset of the XXI Century




Risk factors of atherosclerosis

Not modifiable

- Age
- Gender
- Genetics

Modifiable

- Lípids
cLDL, cHDL, TG
- Hypertension
- Diabetes
- Obesity
- Homocystein
- Habits
 - *Smoking*
 - *Atherogenic diets*
 - *High alcohol consumption*
 - *Sedentary*



El tratamiento de los factores de riesgo cardiovascular puede retrasar la progresión de la arteriosclerosis y la aparición de sus principales manifestaciones clínicas: los eventos cardiovasculares

BEST WEAPONS AGAINST CARDIOVASCULAR DISEASE: DIET AND EXERCISE

Mediterranean Diet Pyramid

A contemporary approach to delicious, healthy eating

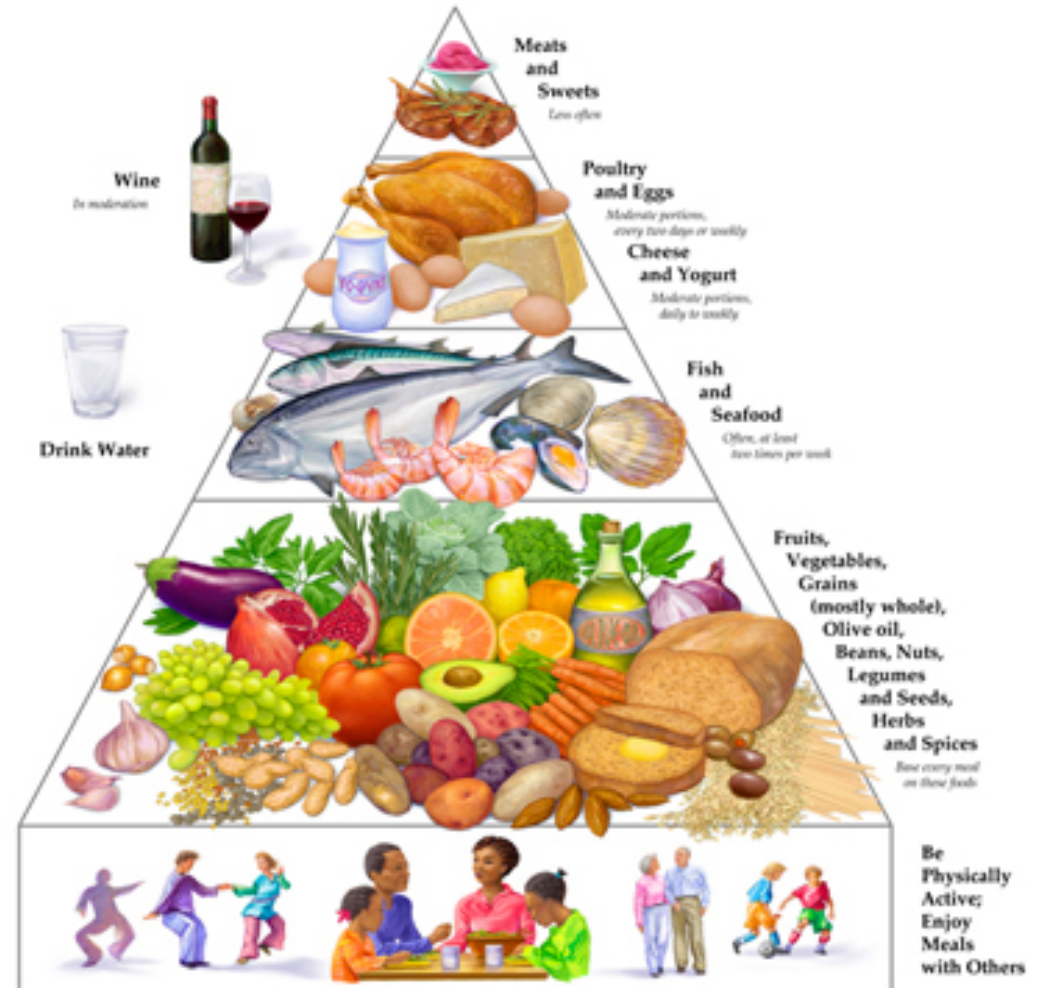


Illustration by George Michalatos

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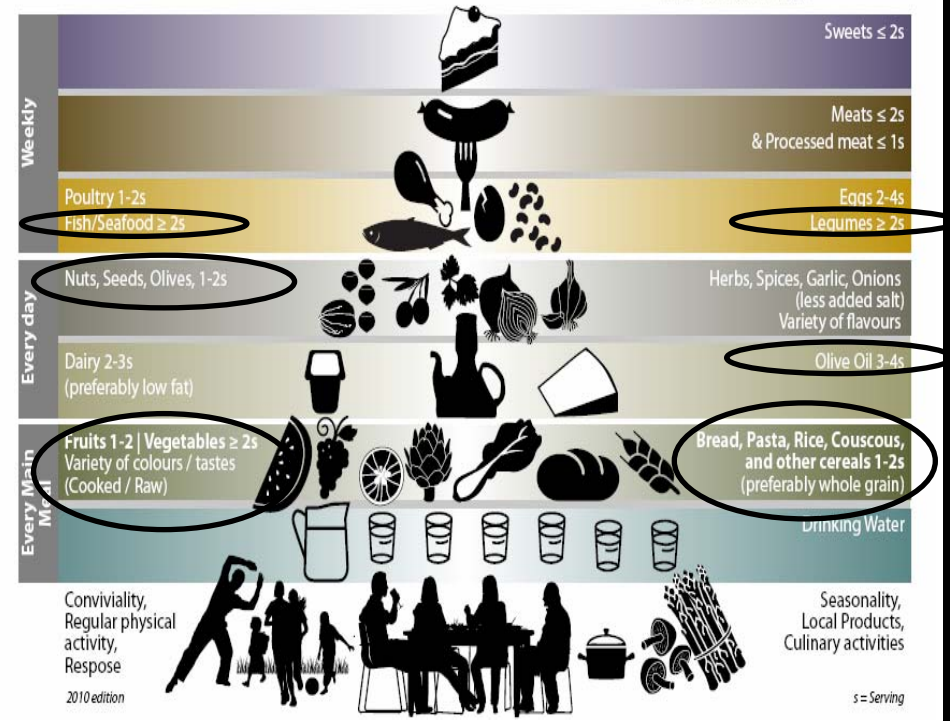
Dieta Mediterránea



Mediterranean Diet Pyramid Today | Adult population

Each country has its own serving size based on frugality

Wine in moderation & respecting religious & social beliefs



high intake

Traditional Mediterranean Diet



Mediterranean Diet Pyramid Today | Adult population

Each country has its own serving size based on frugality

Wine in moderation & respecting religious & social beliefs

Mediterranean Diet Pyramid Today | Adult population

Each country has its own serving size based on frugality

Wine in moderation & respecting religious & social beliefs



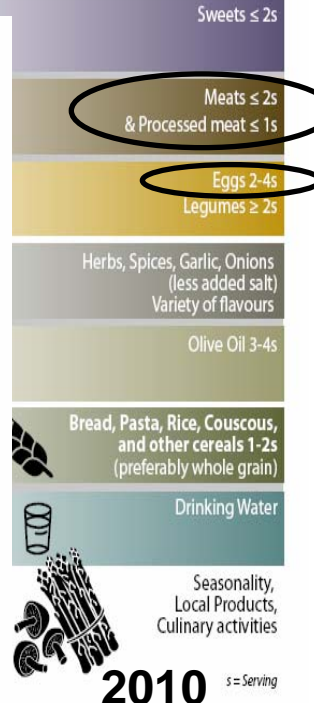
Conviviality, Regular physical activity, Respite

2010 edition

Seasonality, Local Products, Culinary activities

2010

s = Serving

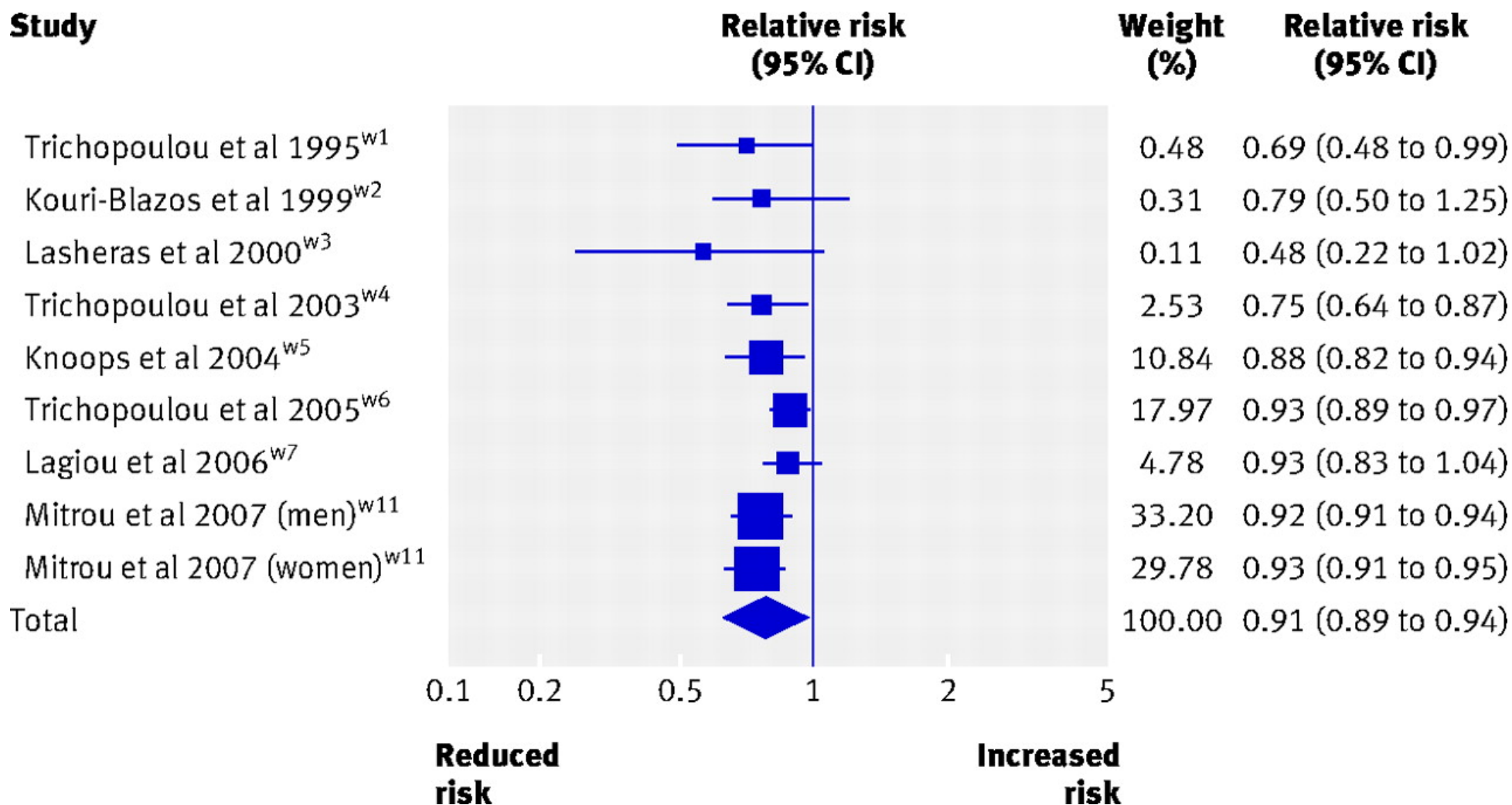


moderate and low intake

Traditional Mediterranean Diet

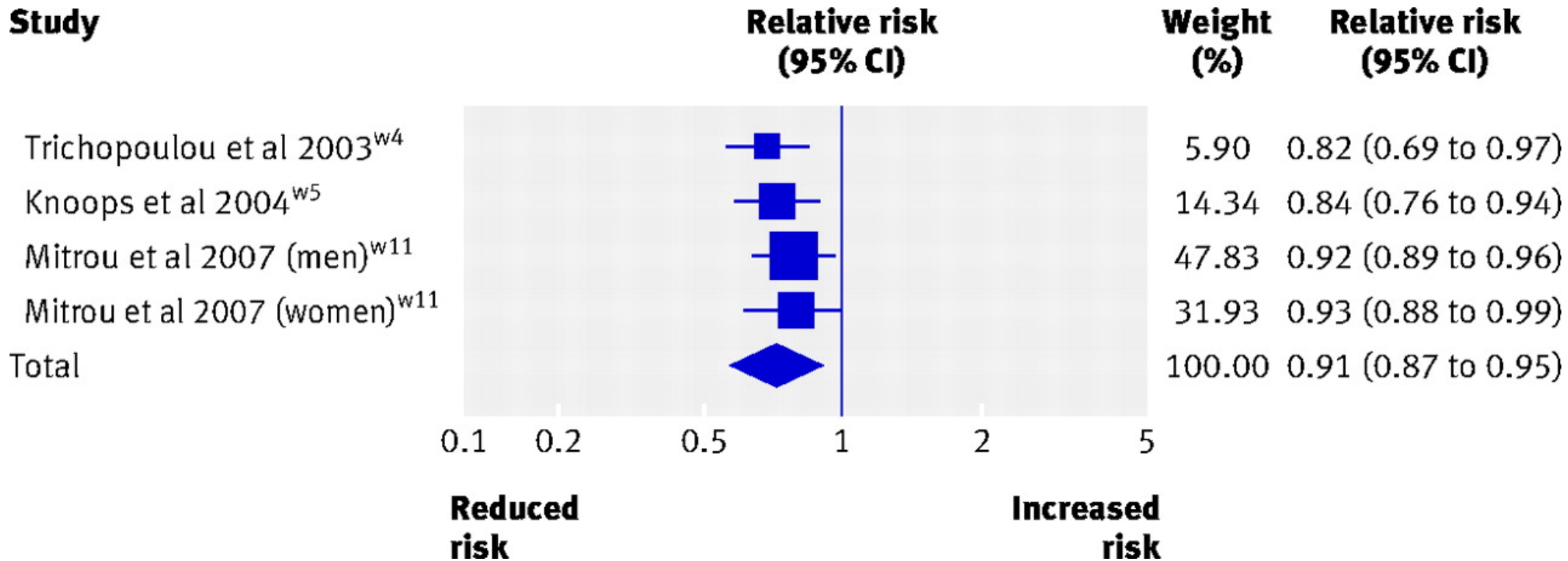


RISK OF ALL CAUSE MORTALITY ASSOCIATED WITH A TWO-POINT INCREASE IN ADHERENCE SCORE FOR THE MEDITERRANEAN DIET



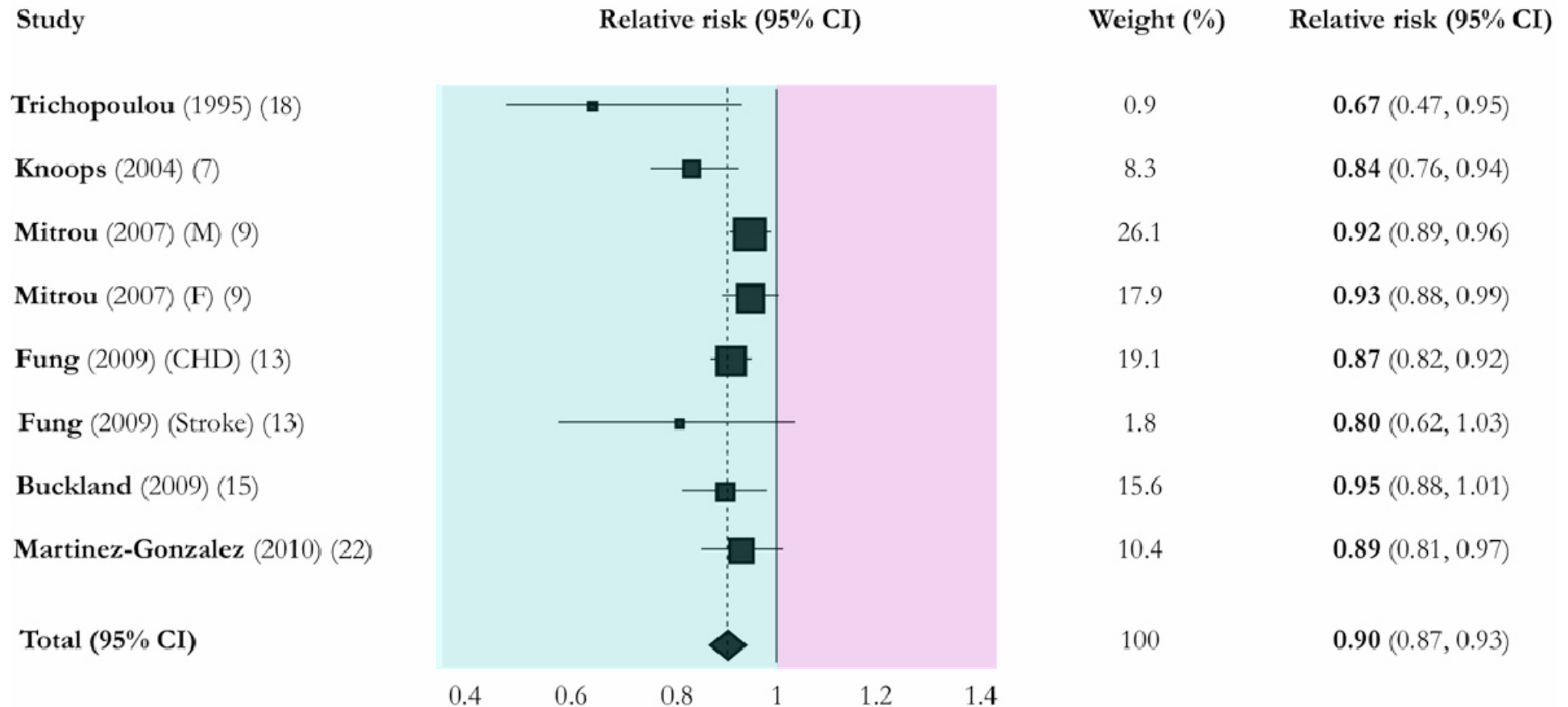
RISK OF MORTALITY BY CARDIOVASCULAR DISEASES ASSOCIATED WITH A TWO-POINT INCREASE IN THE ADHERENCE SCORE FOR THE MEDITERRANEAN DIET

Study



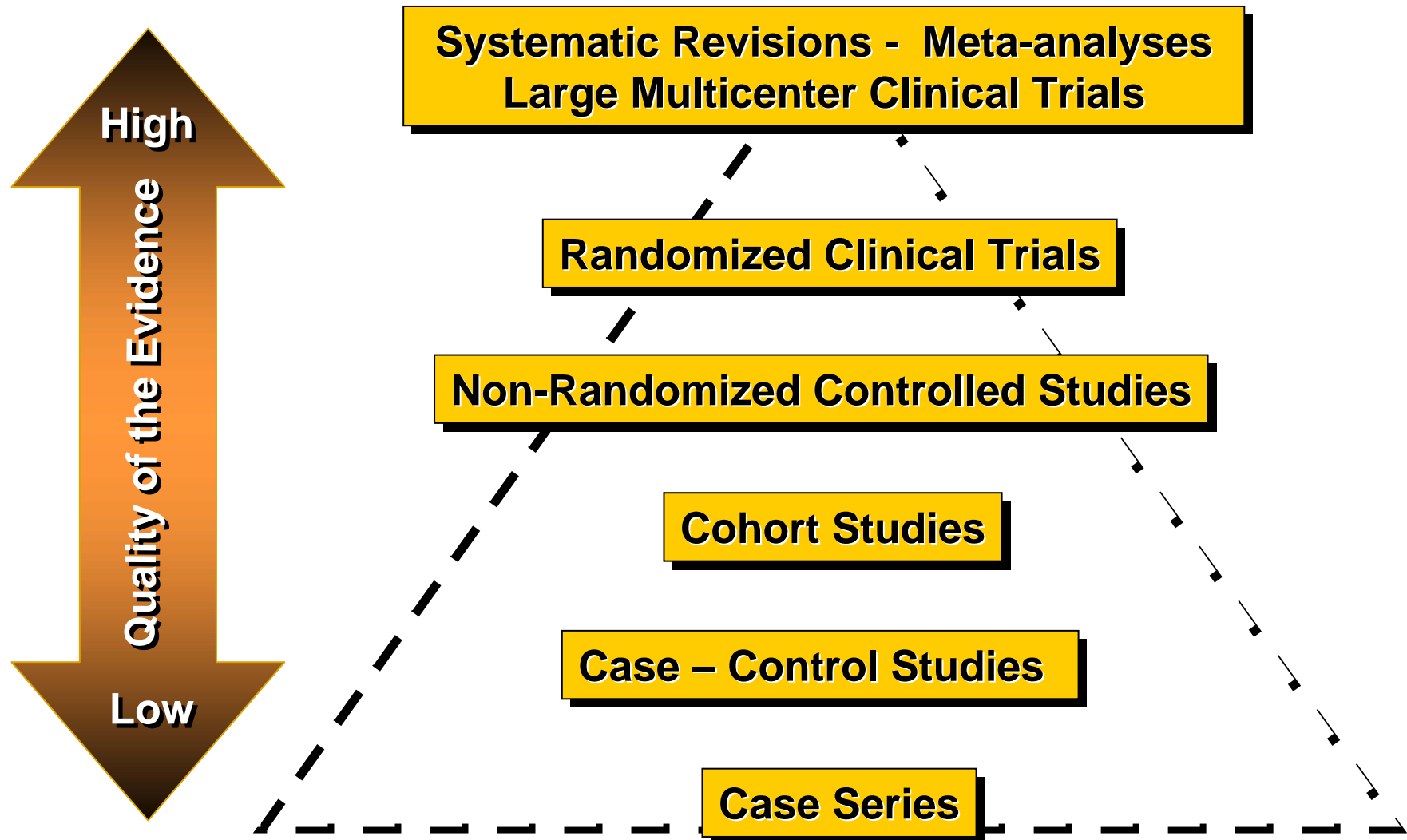
MedDiet & CVD

+2 points (0 to 9)



Accruing evidence about benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis^{1,2} **AJCN 2010**

Hierarchy of Evidence-based Medicine



Mediterranean Diet, Risk Factors and Cardiovascular Events after a Heart Attack: Report of the *Lyon Diet Heart Study*

Design

- Randomized clinical trial on the effects of a Mediterranean-style Diet in a sample of 605 patients who had had a myocardial infarction.

Intervention Groups

- Mediterranean Diet supplemented with margarine enriched with α -linolenic acid (n= 303)
- Step I Diet of the American Association of Cardiology (n= 302)

Follow-up

- 46 months

de Lorgeril M, Salen P, Martin JL, et al. Final Report of the Lyon Diet Heart Study. *Circulation* 1999;99:779-785.

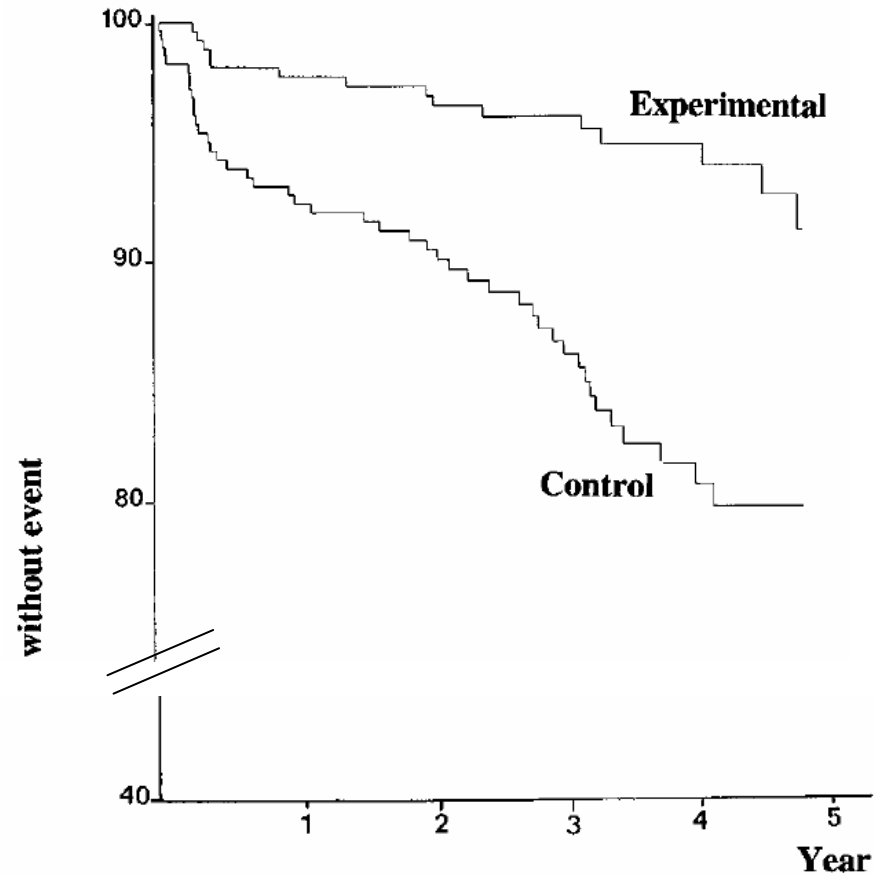


Figure 1. Cumulative survival without nonfatal myocardial infarction (CO 1) among experimental (Mediterranean group) patients and control subjects.



**Effects of the Mediterranean-Style Diet
on the Primary Prevention of
Cardiovascular Disease
*(PREDIMED)***

Primary specific aims

- **To test the effect of a Mediterranean Diet enriched with virgin olive oil on the risk of cardiovascular diseases (a composite endpoint of cardiovascular death, myocardial infarction, and stroke)**
- **To test the effect of a Mediterranean diet enriched with supplementary nuts (walnuts, almonds, and hazelnuts) on the risk of cardiovascular diseases**
- **To test the effect of wine intake on the risk of cardiovascular diseases**

Other specific aims _____

- **To determine the changes in body weight, blood lipids, blood pressure, markers of inflammation and other intermediate markers of cardiovascular risk to better understand how dietary changes are able to modify the risk of clinical events**
- **To identify the subjects with certain phenotypic and genotypic characteristics that benefit more from a Mediterranean diet**

PREDIMED TRIAL: DESIGN

- ❑ Men: 55-80 yr
- ❑ Women: 60-80 yr
- ❑ High CV risk without CVD
type 2 diabetics
3+ risk factors

1. Smoking
2. Hypertension
3. ↑ LDL
4. ↓ HDL
5. Overweight/obese
6. Family history

All free of CVD at baseline

Random



Mediet +
Virgin Olive Oil



Mediet +
Nuts



Control
Low-fat

Sample size and Randomization

7,447 participants



n= 2,482



n= 2,483



n= 2,482



PREDIMED Participants

	Mediet + VOO (n= 2487)	MeDiet + Nuts (n=2396)	Control (n=2349)
Age (SD)	67 (6)	67 (6)	67 (6)
Women (%)	57	54	58
Diabetes (%)	50	47	48
Hypertension (%)	82	82	84
Current smokers (%)	14	15	14
Dyslipidemia (%)	72	73	72
BMI, kg/m ² (SD)	30 (4)	30 (4)	30 (4)
Waist circumf. (SD)	100 (10)	100 (10)	101 (11)
Med Diet 0-14 pts. (SD)	8.7 (2)	8.7 (2)	8.3 (2)

PREDIMED: intervention

Introduce changes in the overall food pattern

- Mediterranean diet: 2 groups
 - Total Fat: *ad libitum*
 - High in
 - MUFA (virgin olive oil)
 - Fish
 - Fruits, vegetables, legumes
 - Low in **meat & dairy products**
 - alcohol permitted: wine
- *Low-fat diet* - Control
 - Reduce every fat
 - Increase CHO
- **No Energy limitation**

tocopherols
polyphenols
flavonoids
phytosterols

PREDIMED INTERVENTION

Strategies for behavior change

- Repeated personal contacts: **every 3-mo.**
- Group sessions: **every 3-mo.**
- Holistic approach
 - Written information
 - Self-monitoring
 - Individualized goal-setting
 - Quick feedback
 - Individual motivational interviews (**every 3-mo.**)
 - adapted to the patient's features
 - clinical condition
 - preferences
 - beliefs
 - expressed in servings/d to improve understanding

PREDIMED INTERVENTION

Strategies for behavior change

- Additional strategies
 - Seasonal buying lists
 - Menus and recipes
- Only in the 2 MeDiet groups
- Provision of key food items for free

1 l/week



30 g/day



Measurements

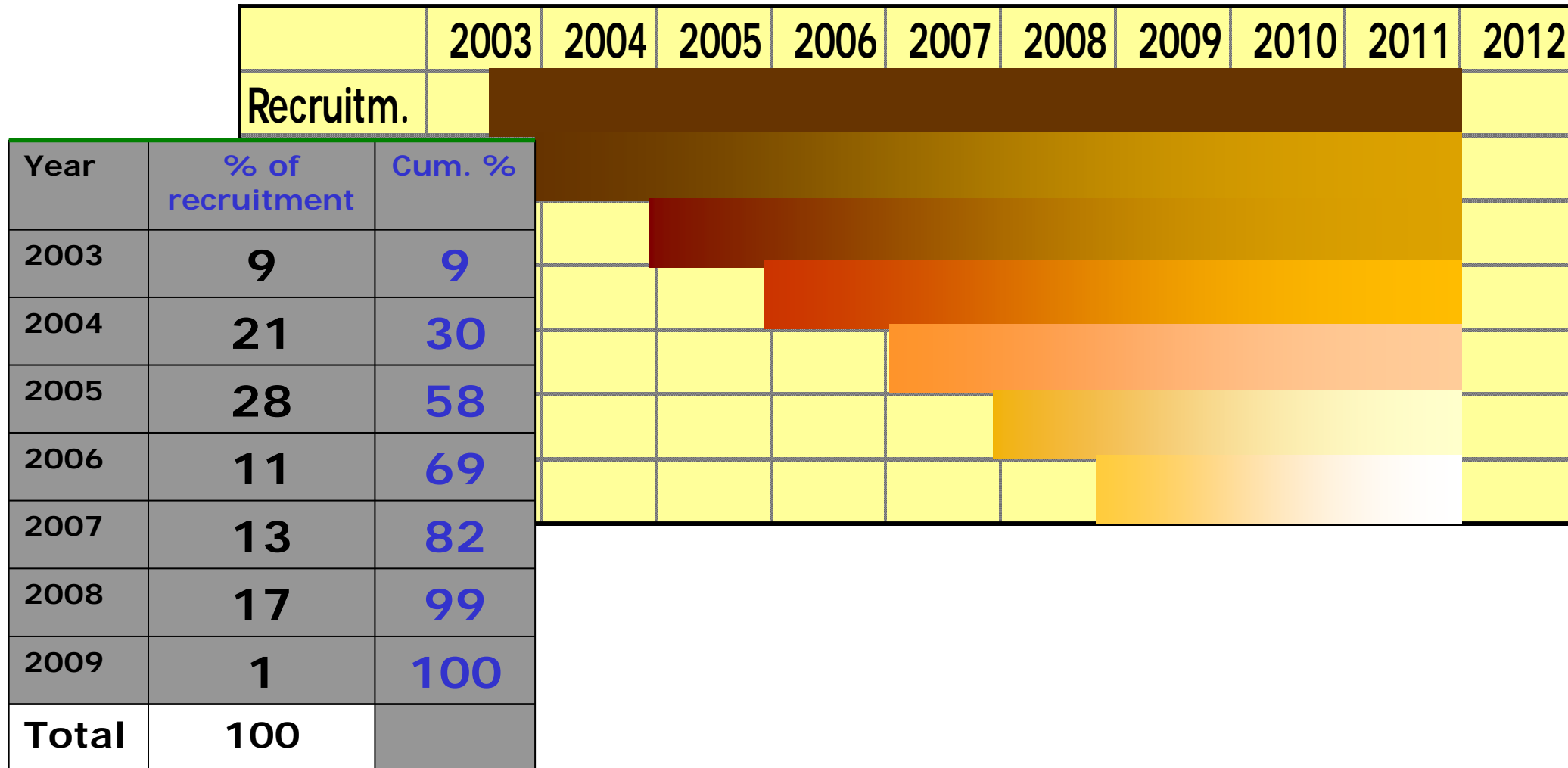
Eligibility questionnaire	X					
General questionnaire	X					
Follow-up questionnaire		X	X	X	X	X
Food Freq. questionnaire	X	X	X	X	X	X
14 item score of Med diet	X	X	X	X	X	X
Physical activity ques.	X	X	X	X	X	X
EKG	X	X	X	X	X	X
Blood samples *	X	X	X	X	X	X
Fresh urine sample *	X	X	X	X	X	X
Toenail sample	X					
	0	1	2	3	4	Years

** Specific measurements
Intervention compliance
assessment*

Compliance assessment (random sample of 750 subjects)

- **Urinary tyrosol and hydroxytyrosol**
- **Plasma fatty acid composition (oleic and α -linolenic acids)**
- **Total urine polyphenol content**
- **Resveratrol in urine**
- **Alcohol in urine**

Projected follow-up = 6 years (median)



PRIMARY END-POINTS

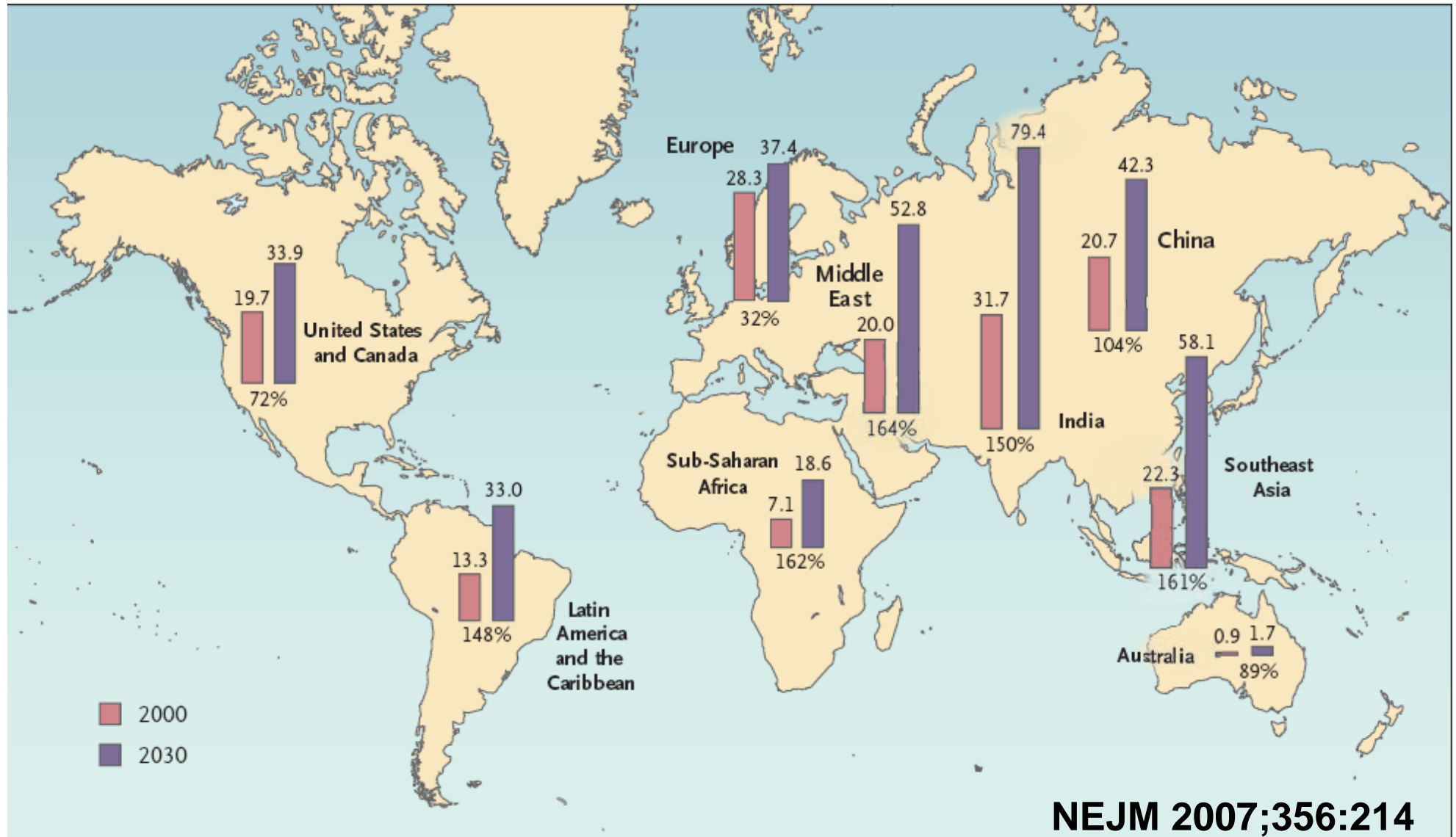
- **Cardiovascular death**
- **Non-fatal myocardial infarction**
- **Non-fatal stroke**

SECONDARY END-POINTS

- **Death from any cause**
- **Angina leading to revascularization procedure**
- **Heart failure**
- **Diabetes**
- **Cancer**

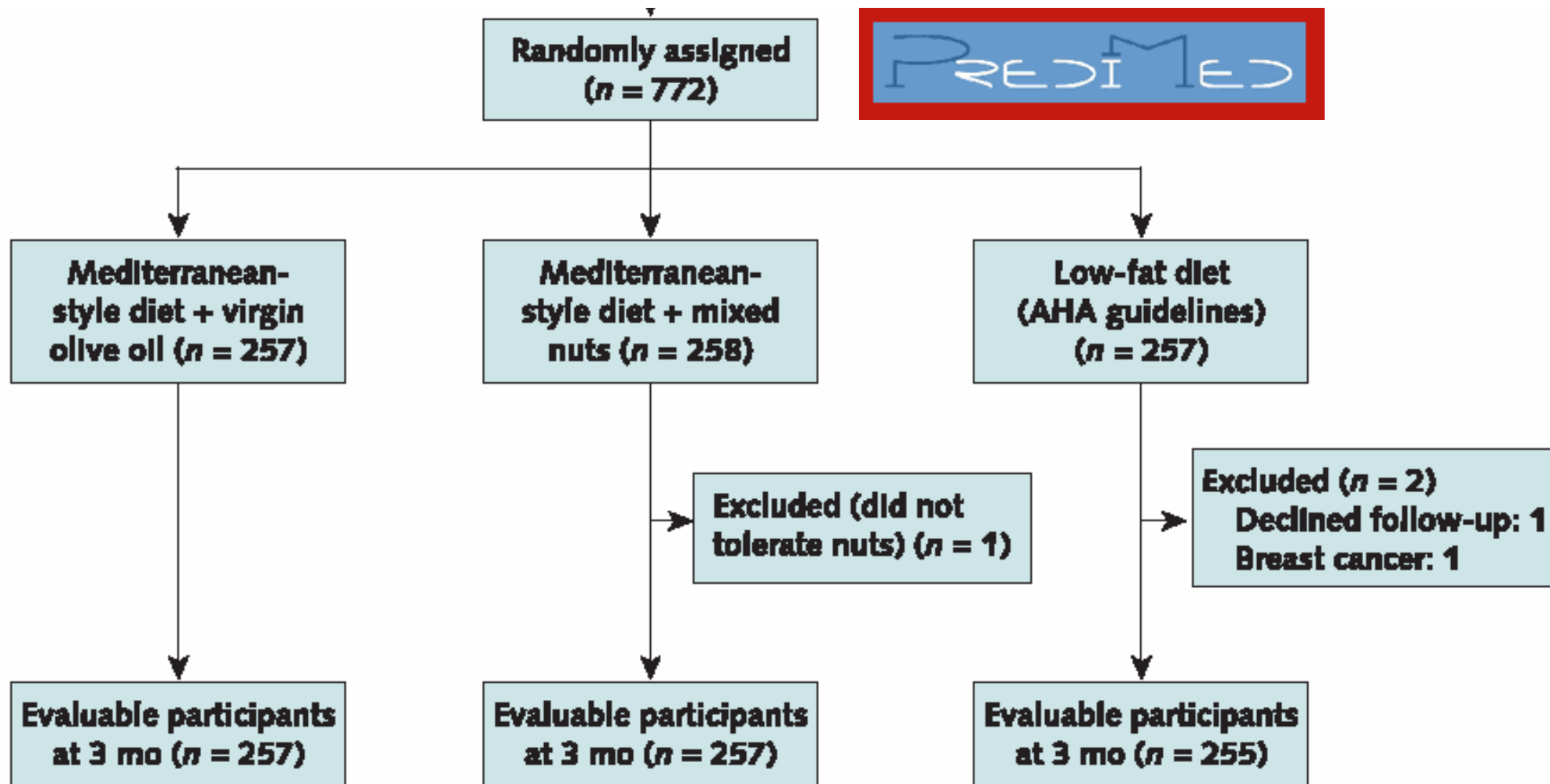
Efectos de la Dieta Mediterránea sobre la Diabetes y la Obesidad

CASES OF **DIABETES** IN 2000 AND FORECASTS FOR 2030

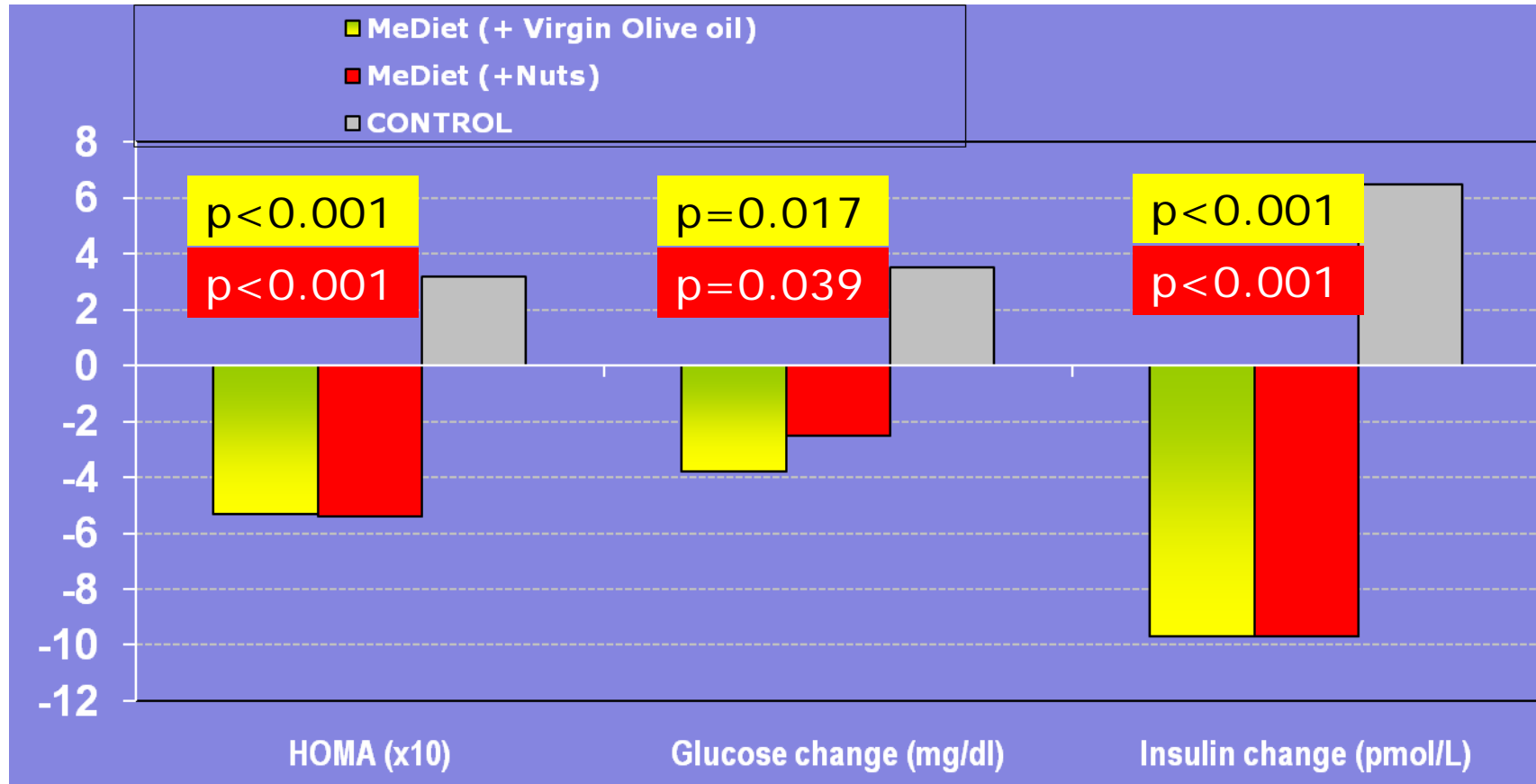


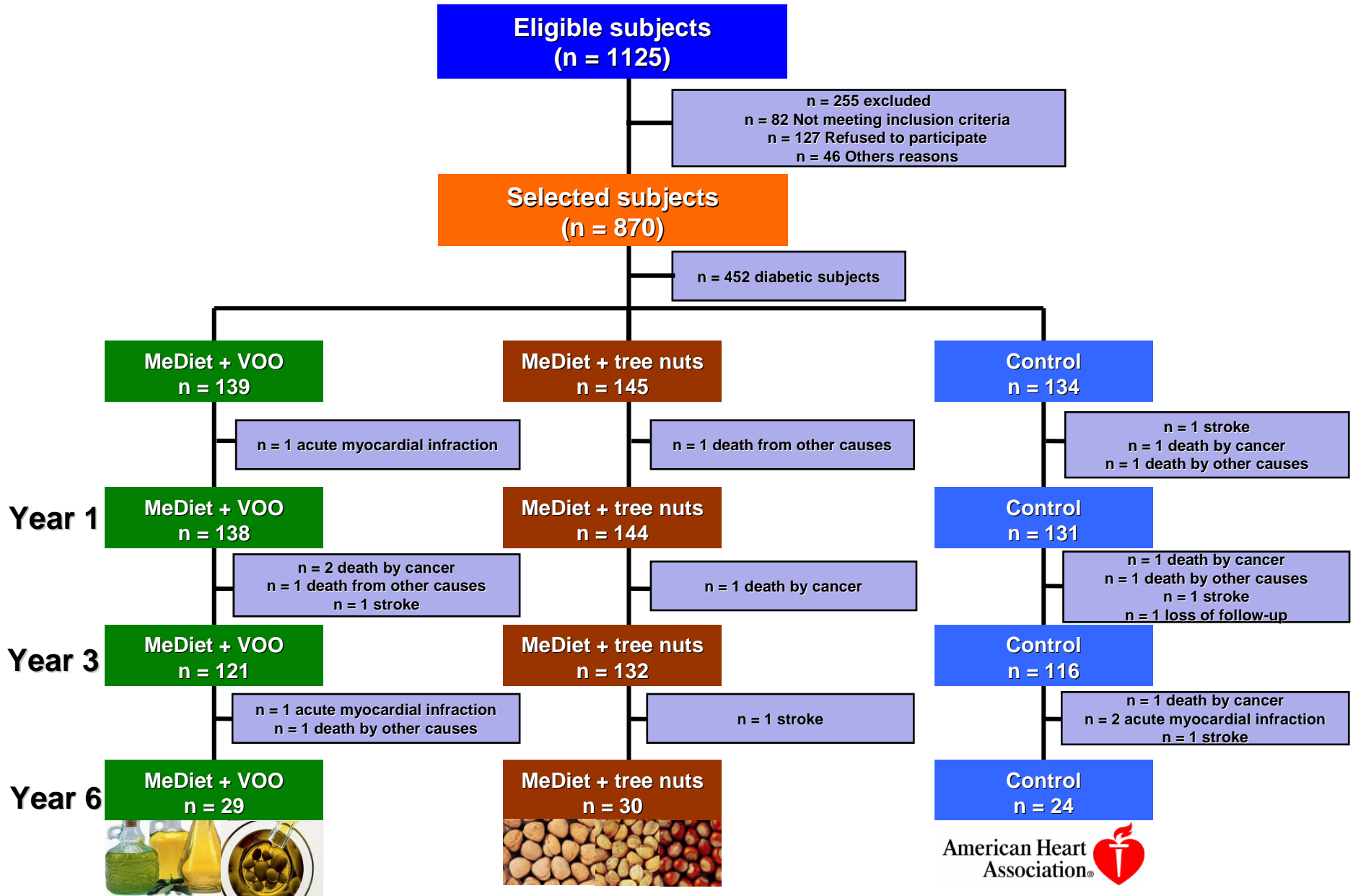
PREDIMED STUDY

3-mo. changes in risk factors



PREDIMED TRIAL: 3-mo. changes





BASELINE CHARACTERISTICS OF PARTICIPANTS

	MedDiet + VOO	MedDiet + tree nuts	Control group
n	139	145	134
Male	55 (40)	68 (47)	51 (38)
Age - yr	67.4 (6.1)	66.6 (5.8)	67.8 (6.1)
Body mass index - kg/m ²	29.7 (3.3)	29.6 (3.1)	30.0 (3.3)
Fasting plasma glucose-mmol/l	5.5 (0.8)	5.5 (0.9)	5.5 (0.9)
HOMA index	1.41 (0.87)	1.34 (0.87)	1.60 (1.17)
Physical activity Kcal/day	400 (283)	427 (306)	373 (238)
Current smokers -no. (%)	15 (11)	21 (15)	20 (15)

Median (SD)

GOALS ATTAINED ACCORDING TO INTERVENTION GROUP

	MedDiet + VOO	MedDiet + tree nuts	Control group	P-value †
% weight loss \geq 5%	10.6	9.8	12.8	0.72
Physical activity: % highest baseline tertile	43.9	42.1	32.8	0.148
% 14-point score of MedDiet \geq 10	61.2	68.3	23.9‡	<0.001
% MUFA:SFA Ratio \geq 2	84.9	83.4	65.7‡	<0.001
% Olive oil \geq 20 g/1000 Kcal/d	86.3	65.5	59.7‡	<0.001
% Dietary fiber intake \geq 14 g/1000 Kcal/d	10.8	13.1	11.9	0.83

Abbreviations: MedDiet, Mediterranean diet; VOO, virgin olive oil; MUFA, monounsaturated fatty acids; SFA, saturated fatty acids
 † P values for differences among the three diet groups were calculated by the chi-square test.
 ‡ The value for the low-fat diet group is significantly different from the value for the two Mediterranean-diet groups (P<0.05).

CUMULATIVE INCIDENCE OF DIABETES ACCORDING TO INTERVENTION GROUP

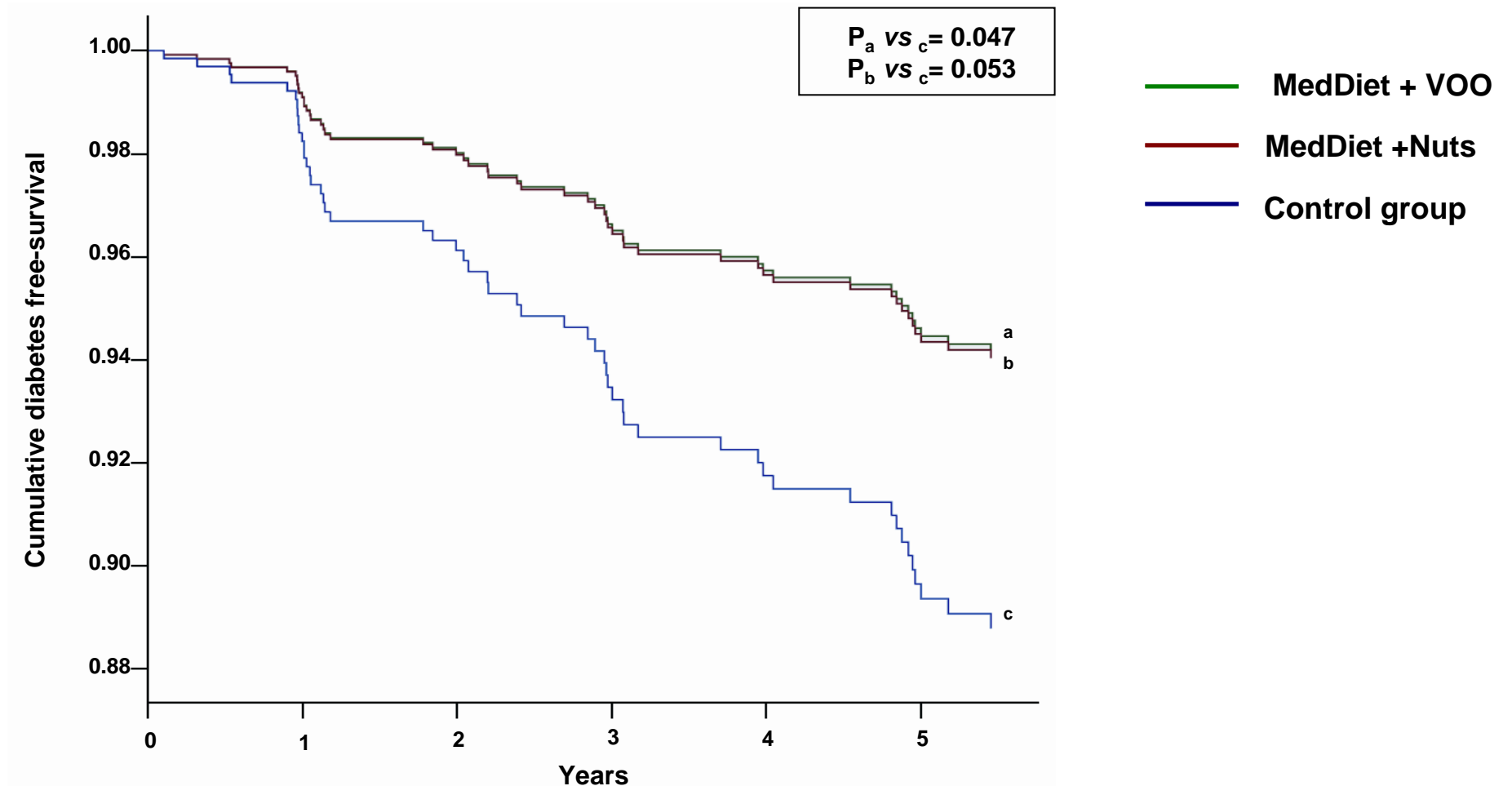
	MedDiet with VOO group (n=139)	MedDiet with nuts group (n=145)	Control diet group (n=134)
Person-years, No.	570	598	515
New cases of diabetes, No.	14	16	24
Rate per 1000 person-years	24.6 (13.5 to 40.8)	26.8 (15.3 to 43.0)	46.6 (30.1 to 68.5)
Cumulative incidence (95% CI)	10.1 (5.1 to 15.1)	11.0 (5.9 to 16.1)	17.9 (11.4 to 24.4)

HAZARD RATIOS (95% CONFIDENCE INTERVALS) OF DIABETES ACCORDING TO THE INTERVENTION GROUP

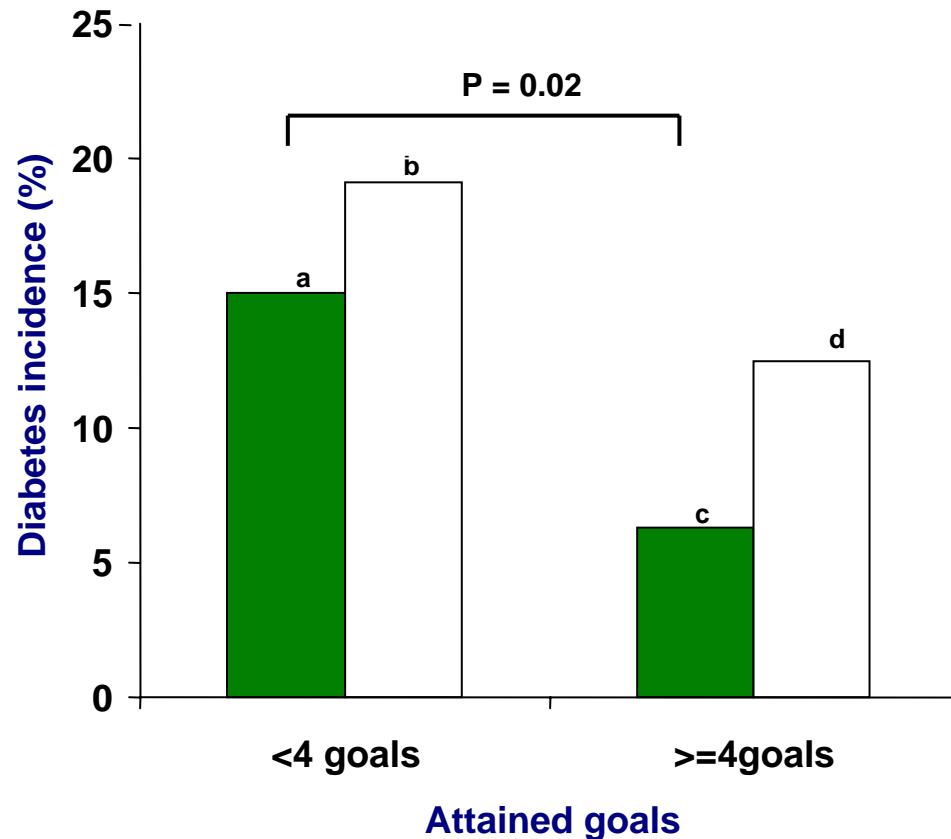
	MedDiet + VOO vs. control	MedDiet + Tree nuts vs. control	2 MedDiet groups vs. control group
Crude	0.53 (0.27-1.90)	0.58 (0.31-1.10)	0.55 (0.32-0.95)
Age- and sex-adjusted	0.52 (0.27-1.00)	0.55 (0.29-1.00)	0.53 (0.31-0.92)
Multivariate adjusted ^a	0.49 (0.25-0.97)	0.48 (0.24-0.96)	0.48 (0.27-0.86)

^a Adjusted for sex, age, baseline energy intake, BMI, waist circumference, physical activity (tertiles), smoking, fasting glucose Mediterranean diet score, lipid lowering drugs and weight changes during the study

CUMULATIVE INCIDENCE OF DIABETES IN THE CONTROL GROUP AND THE INTERVENTION GROUPS DURING 5.5 YEARS



INCIDENCE OF DIABETES IN THE TWO MED DIET GROUPS POOLED AND THE CONTROL DIET GROUP BY ATTAINMENT OF INTERVENTION GOALS



■ Both MedDiet groups
□ Control group

Dietary MUFA:SFA ratio ≥ 2

Olive oil ≥ 20 g/1000 kcal/d

Nut consumption ≥ 10 g/1000 kcal/d

Dietary fiber intake ≥ 14 g/1000 kcal/d

14-point MedDiet SCORE ≥ 10

Weight loss $\geq 5\%$ of initial body weight

Highest physical activity tertile (>395 kcal/d)

CONCLUSIONES

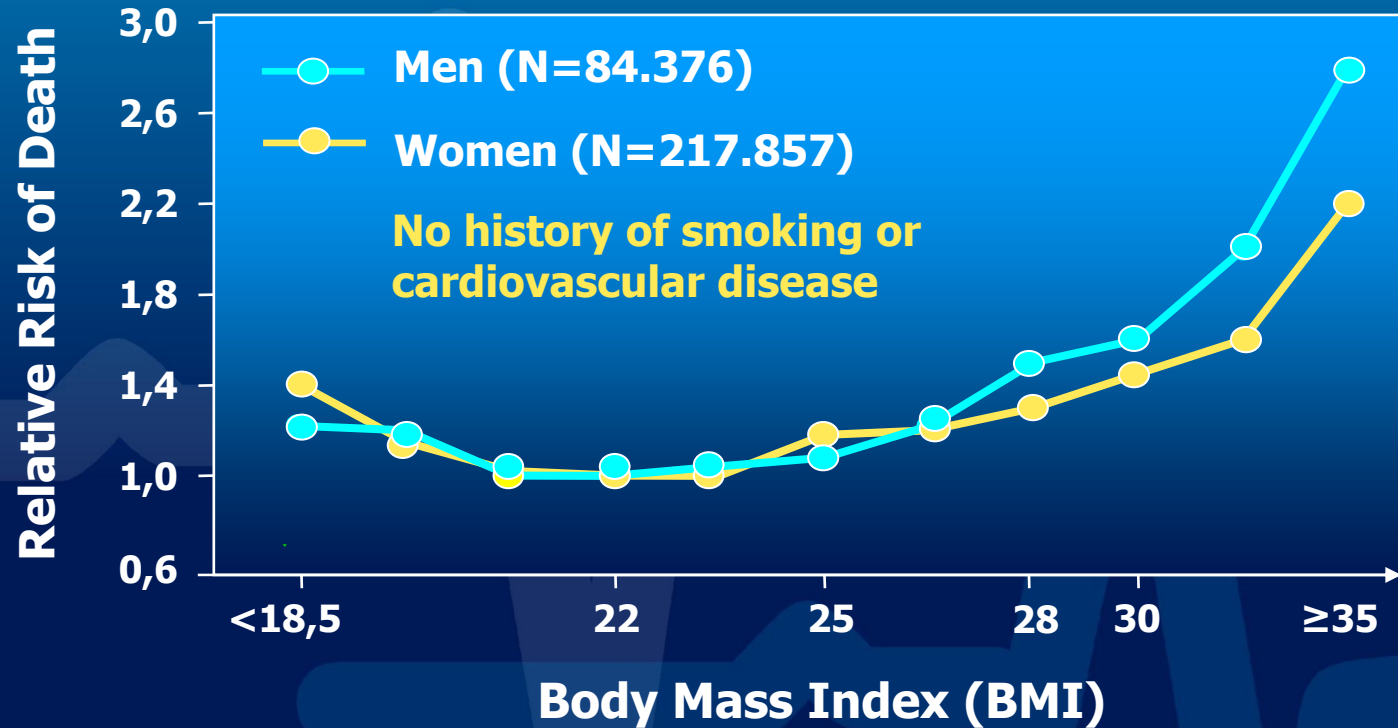
Los resultados de este sub-estudio del PREDIMED indican que una Dieta Mediterránea *ad libitum* y alta en grasa no saturada y antioxidantes es una herramienta útil en la prevención de la diabetes.

No obstante, es preciso realizar más estudios para dilucidar los mecanismos de reducción del riesgo de diabetes, independientes de una pérdida de peso.

THE XXI CENTURY EPIDEMIA : OBESITY

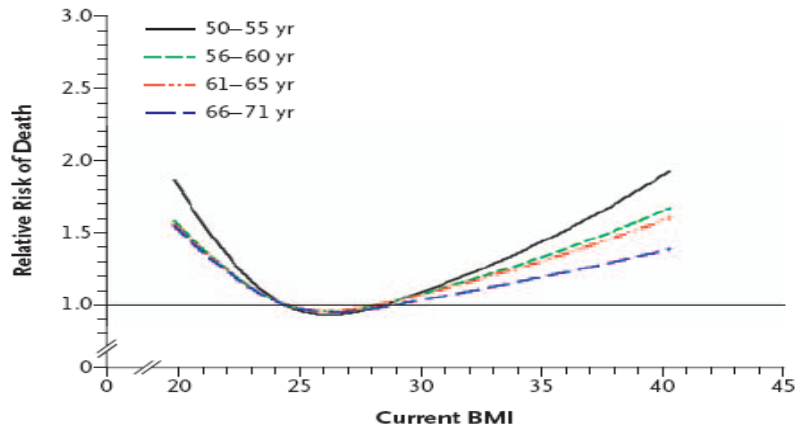


Obesity increases the risk of cardiovascular disease

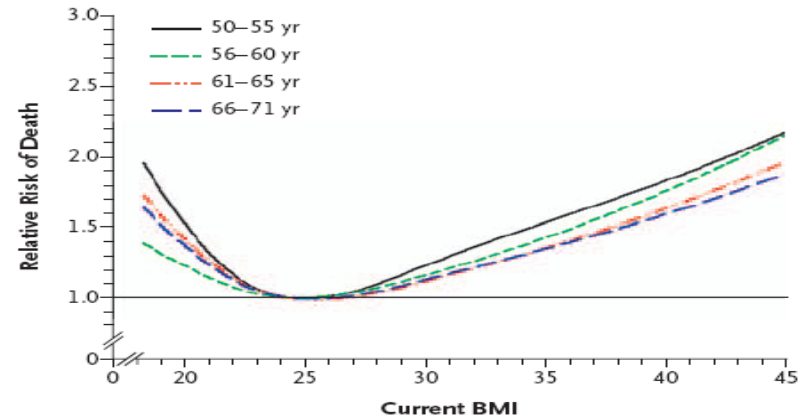


Overweight increases the risk of cardiovascular disease

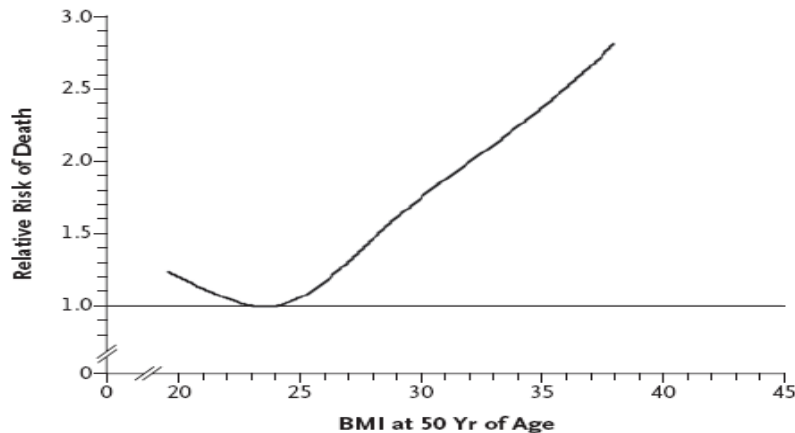
B Men According to Age (N=313,047; 42,173 deaths)



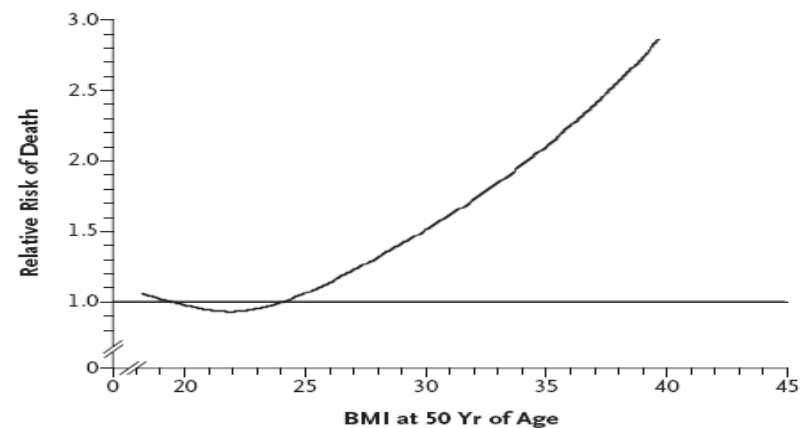
B All Women According to Age (N=214,218; 19,144 deaths)



D Men Who Had Never Smoked (N=54,925; 4079 deaths)



D Women Who Had Never Smoked (N=56,156; 2867 deaths)



Characteristics of the Participants

n = 3,089

	OLIVE OIL (n = 1049)	NUTS (n = 1028)	LOW-FAT (n = 1012)
Age, mean (SD)	67.0 ± 6.1	66.8 ± 5.9	67.3 ± 6.3
Gender, N (%) Male	441 (42)	473 (46)	415 (41)
Family history, N (%)	220 (21)	206 (20)	202 (20)
Smoking, N (%)	147 (14)	144 (14)	142 (14)
Diabetes Mellitus, N (%)	514 (49)	483 (47)	486 (48)
Hypertension, N (%)	850 (81)	822 (80)	840 (83)
Dyslipidemia, N (%)	724 (69)	720 (70)	698 (69)
BMI, mean (SD), kg/m²	30.1 ± 3.7	29.7 ± 3.7	30.2 ± 4.1
Overweight/Obesity, N (%)	976 (93)	936 (91)	931 (92)

1 vs. 2-year assessment

BODY WEIGHT

	Baseline Mean (SD)	1-year Mean (SD)	2-year Mean (DE)	P
1. Low Fat Diet	76.1 ± 12.0	76.0 ± 12.3	76.0 ± 12.4	
2. MedDiet + Olive Oil	76.5 ± 11.8	75.6 ± 11.8	75.5 ± 12.0	< 0.001 vs. 1 & 3
3. MedDiet + Nuts	76.1 ± 12.0	76.0 ± 12.0	76.0 ± 11.8	

Repeated measures analysis of variance:

P time < 0.001

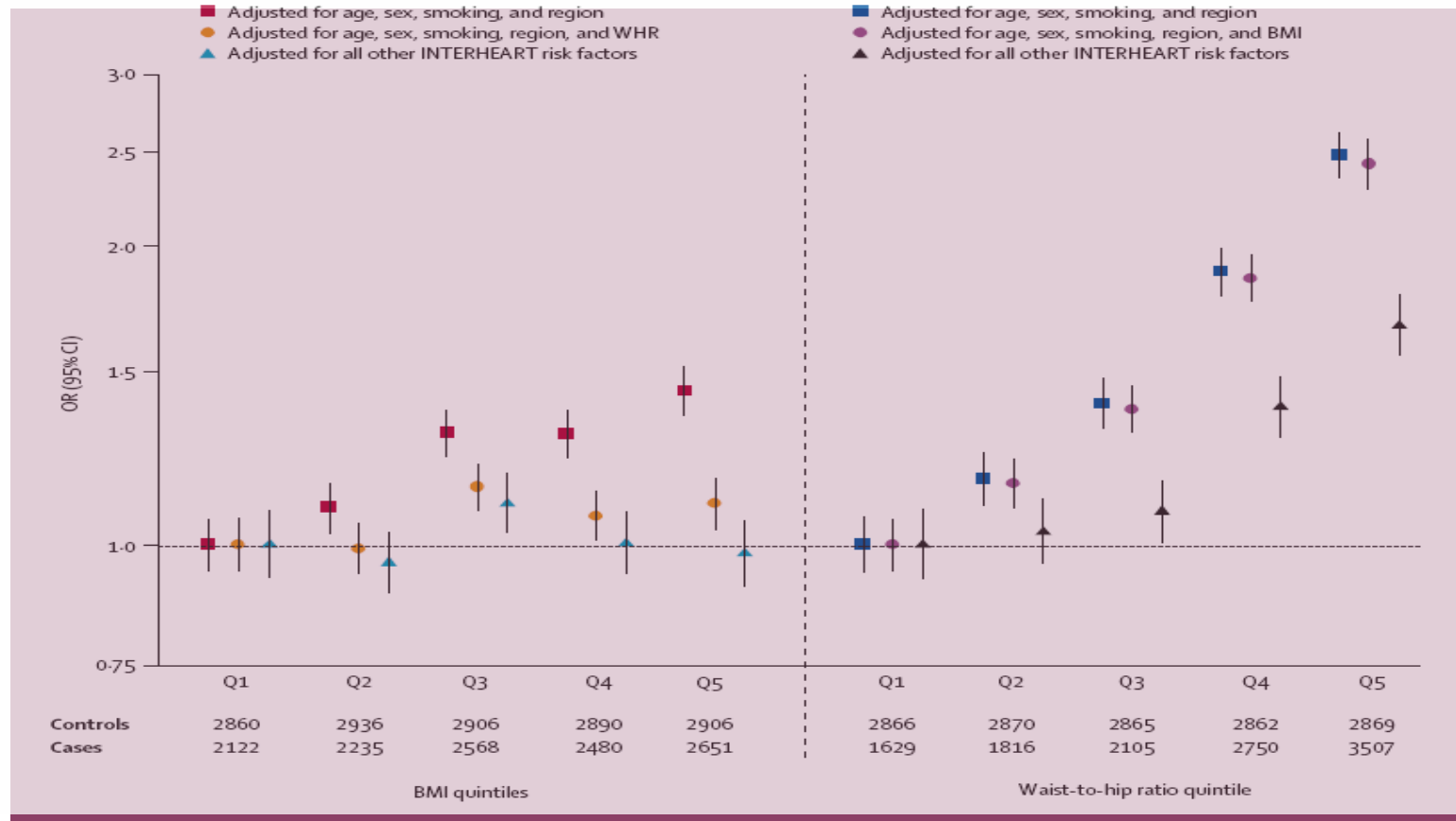
P group = 0.389

P interaction < 0.001

Abdominal fat and myocardial infarction

INTERHEART Study

Importance of the central distribution of fat



1 vs. 2-year assessment

WAIST PERIMETER

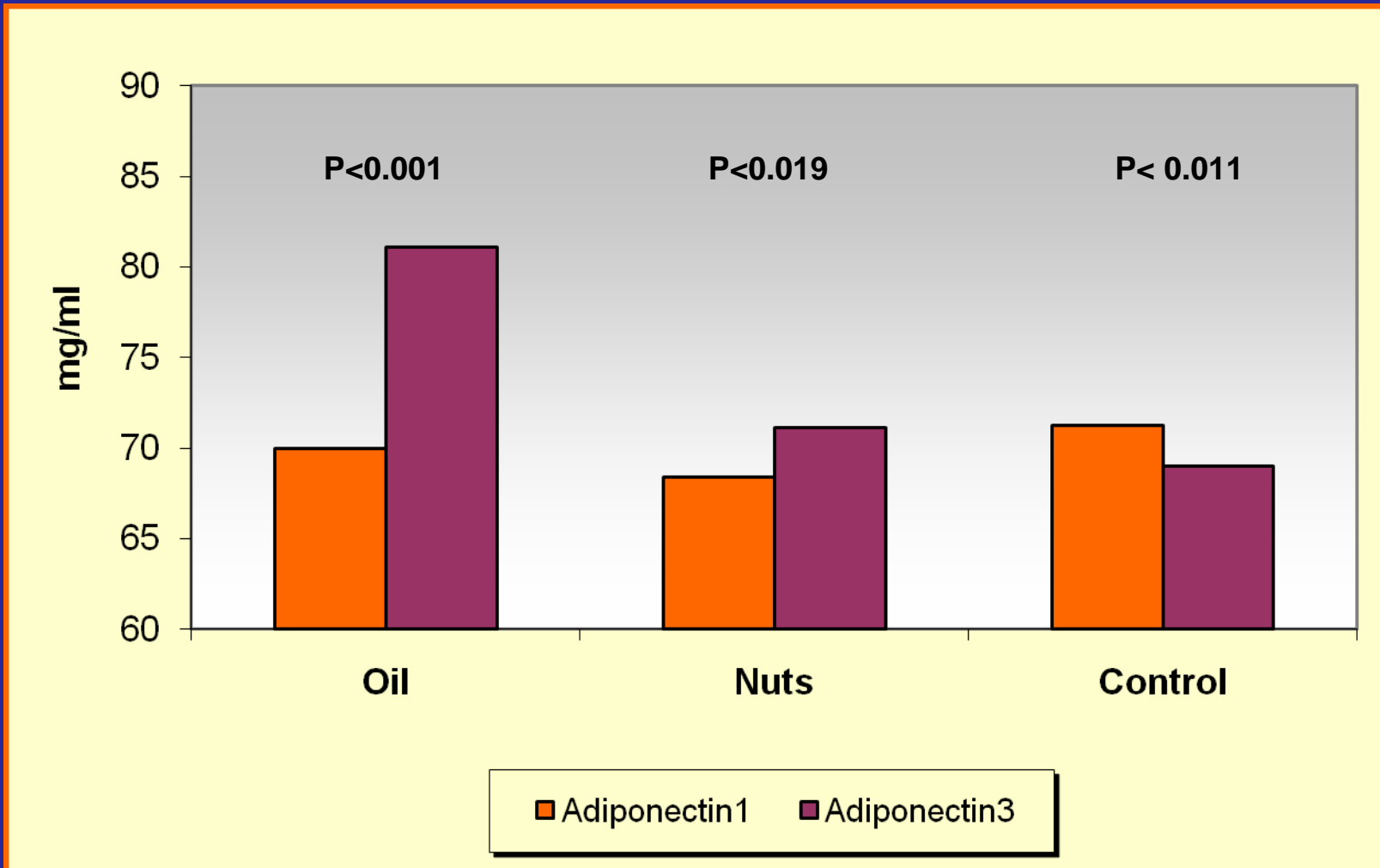
	Baseline Mean (SD)	1 -year Mean (SD)	2-year Mean (SD)	p*
1. Low Fat Diet	99.8 ± 10.5	99.8 ± 10.3	99.9 ± 10.8	
2. MedDiet + Olive Oil	99.8 ± 9.9	98.7 ± 9.8	98.7 ± 10.3	0.001 vs. 1 & 3
3. MedDiet + Nuts	99.6 ± 10.2	99.3 ± 10.3	99.4 ± 10.8	

Repeated measures analysis of variance: *P time* = 0.010

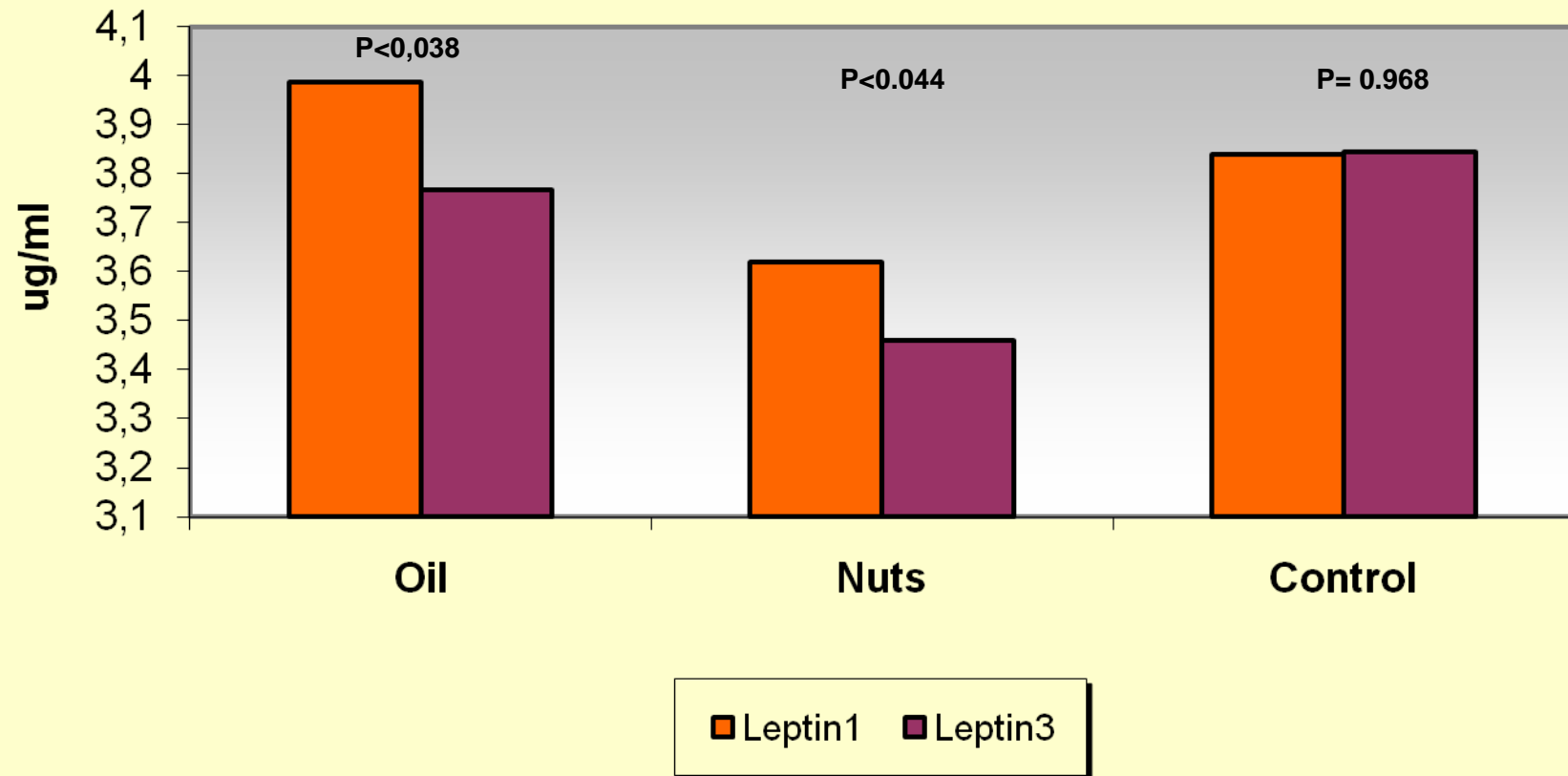
P group = 0.069

P interaction < 0.001

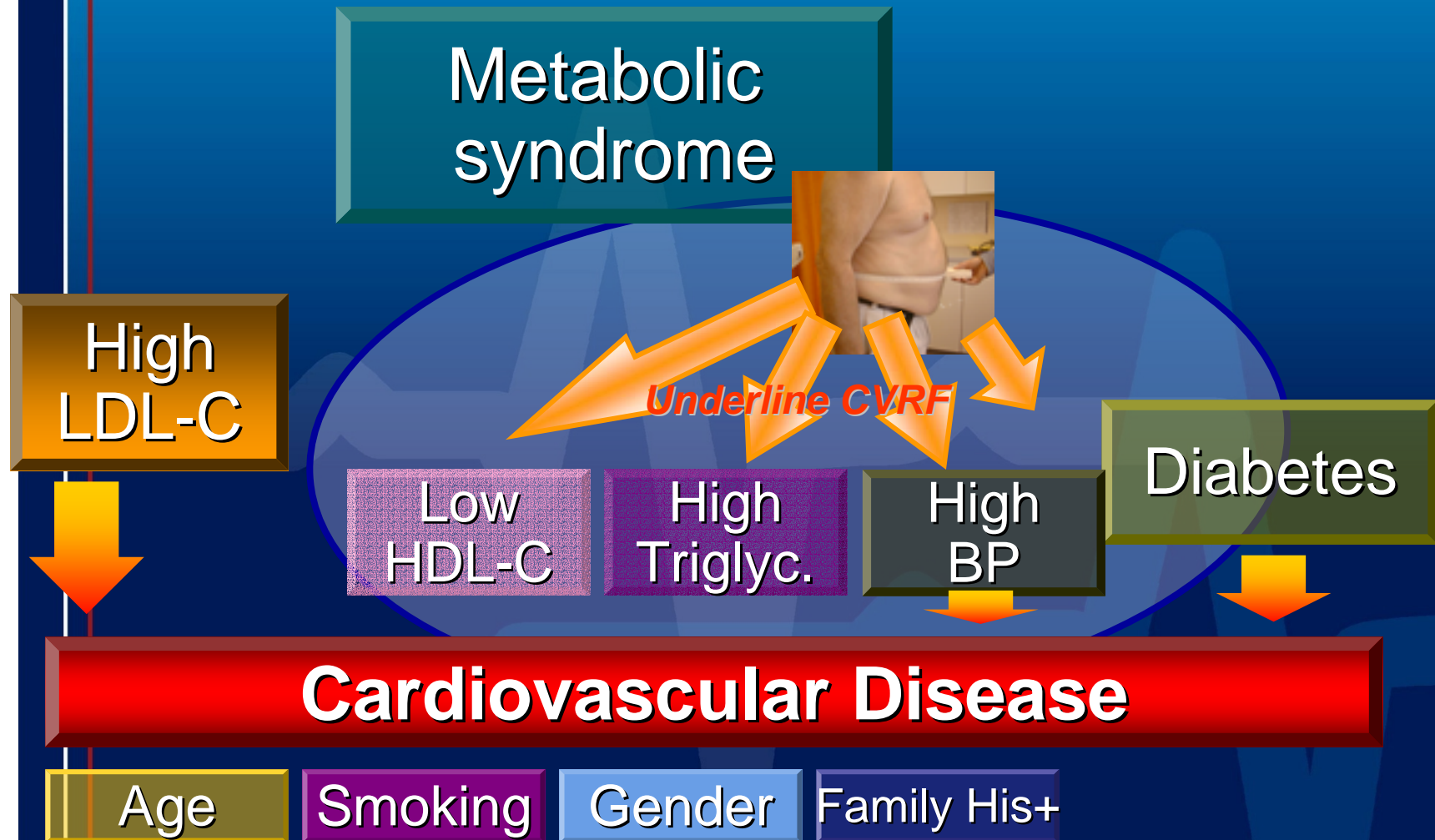
CHANGES IN SERUM ADIPONECTIN



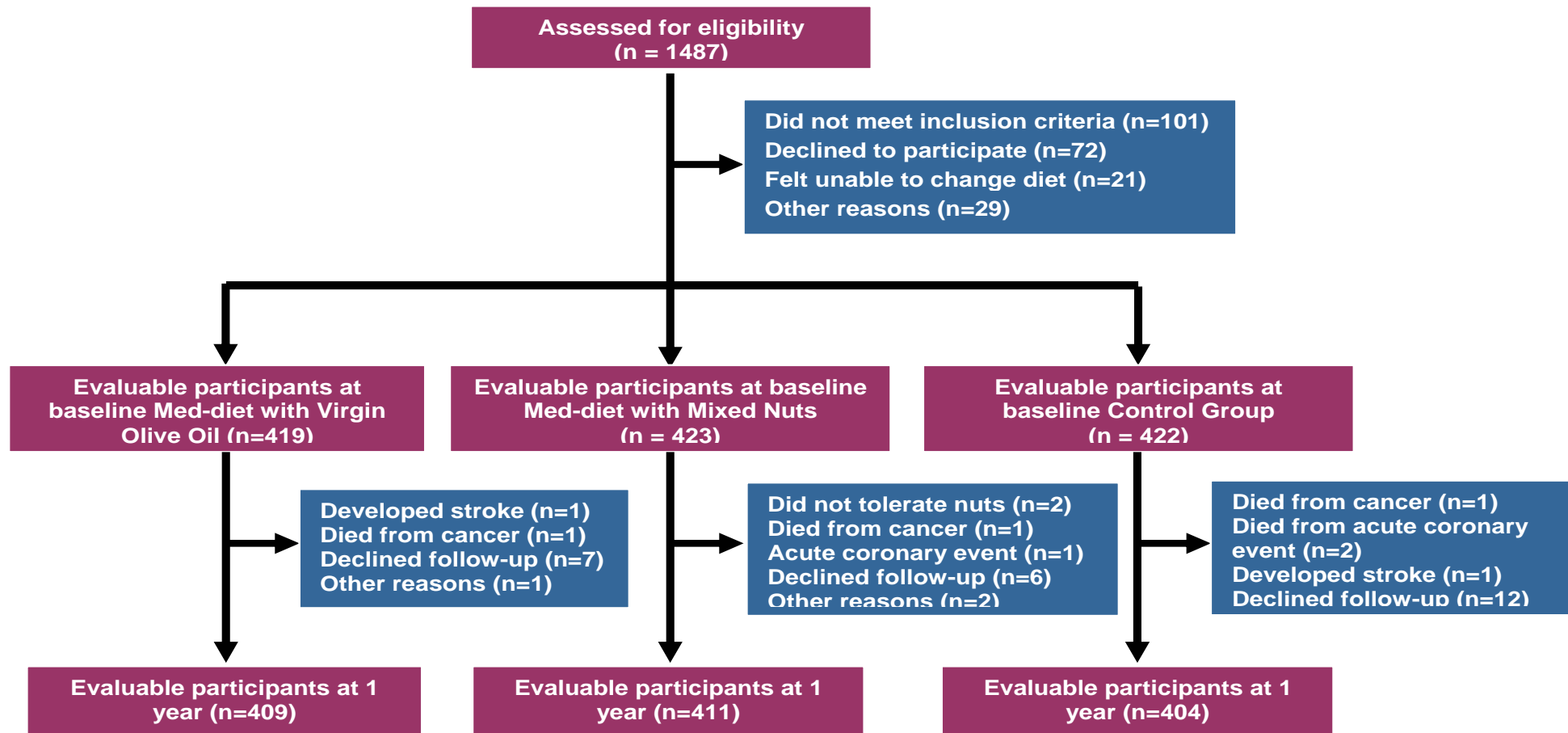
CHANGES IN SERUM LEPTIN LEVELS



Overweight and cardiovascular disease



PREDIMED STUDY FLOW CHART



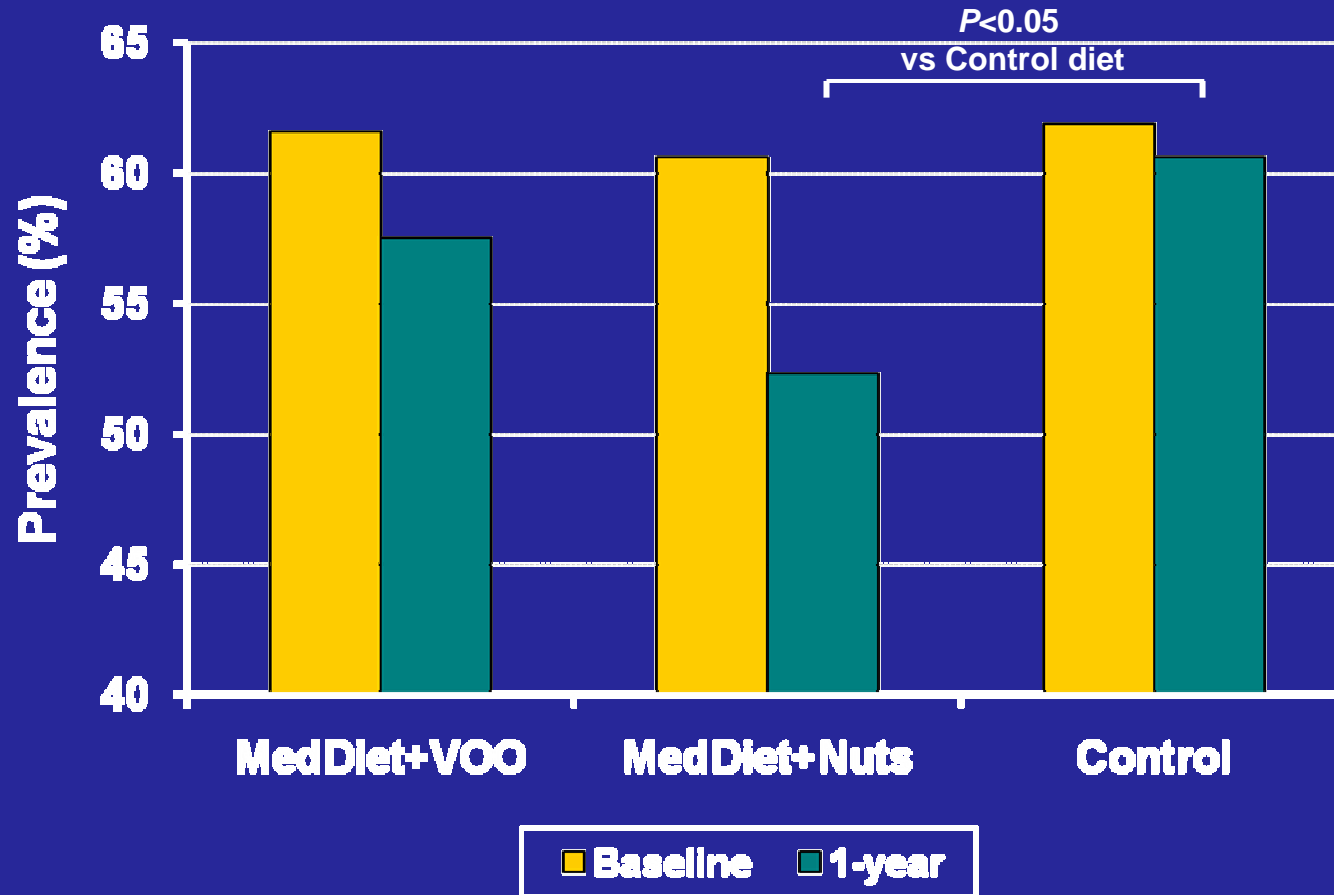
METABOLIC SYNDROME STATUS AND ITS COMPONENTS AT BASELINE

	MedDiet+VOO (n=409)	MedDiet+Nuts (n=411)	Control Diet (n=404)	<i>P</i>
Metabolic syndrome	61.6 (252)	60.6 (249)	61.9 (250)	0.92
Waist circumference	65.3 (267)	64.5 (265)	69.8 (282)	0.22
Low level of HDL cholesterol	26.4 (108)	21.2 (87)	24.0 (97)	0.12
High triglyceride levels	29.8 (122)	29.0 (119)	31.4 (127)	0.74
High fasting serum glucose	67.5 (276)	66.7 (274)	66.6 (269)	0.96
High blood pressure	97.1 (397)	95.1 (391)	95.0 (384)	0.27

Percentage (number)

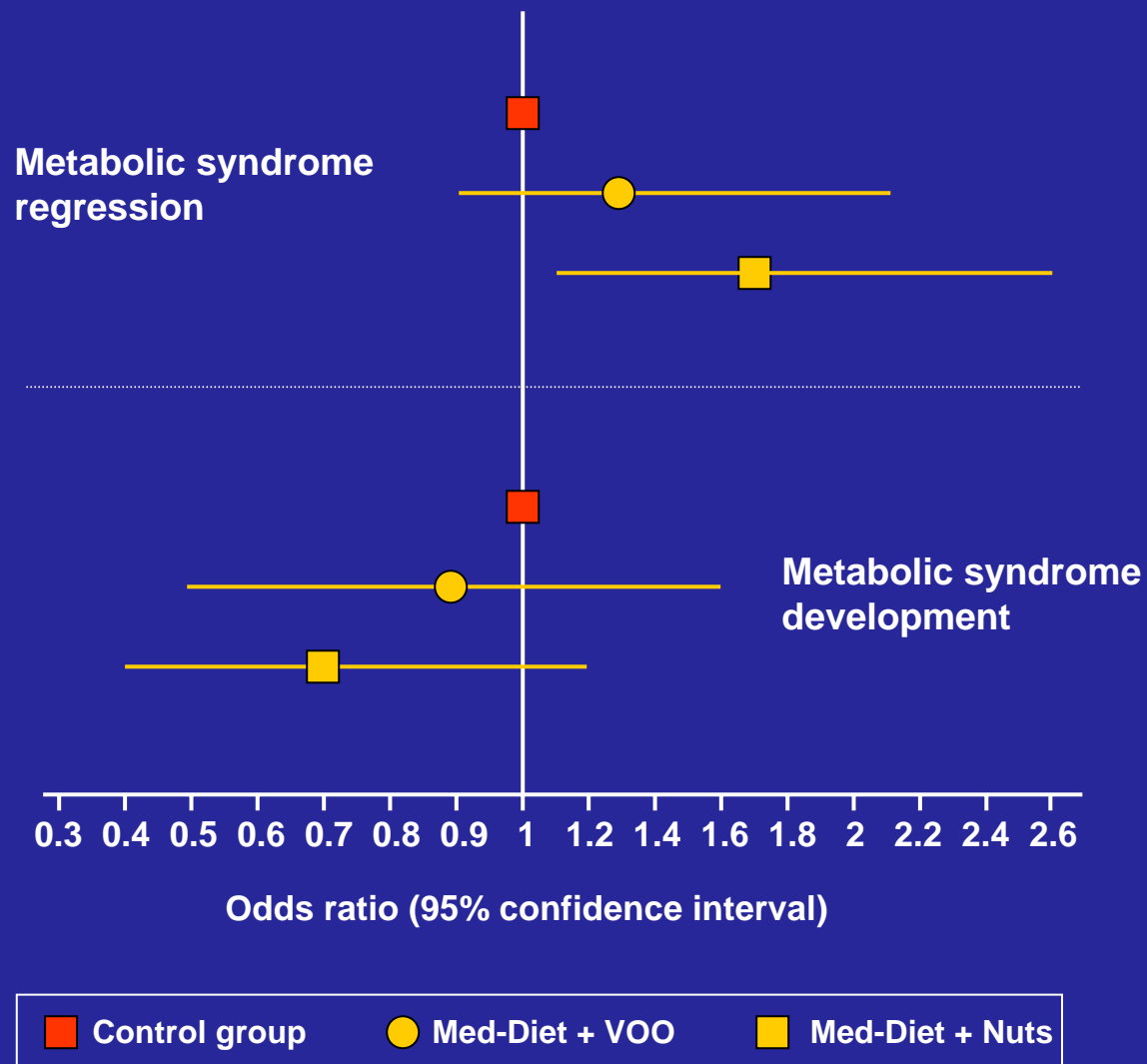
P value for comparisons across groups with Pearson's chi-square test for categorical variables or one-way ANOVA for numerical variables.

BASELINE AND 1-YEAR PREVALENCE OF METABOLIC SYNDROME BY DIET ASSIGNMENT



MedDiet, Mediterranean diet; VOO, virgin olive oil.

ODDS RATIOS AND 95% CONFIDENCE INTERVALS OF 1-YEAR RESOLUTION (TOP) AND INCIDENCE (BOTTOM) OF THE METS IN THE 2 MED-DIET GROUPS IN COMPARISON WITH THE CONTROL DIET



The logistic regression model was adjusted for sex, age, and weight changes.

CONCLUSIONES

- 1. Nunca es tarde para cambiar los hábitos dietéticos con una mejoría significativa de los marcadores “subrogados” de riesgo vascular.**
- 2. Una Dieta Mediterránea, alta en alimentos ricos en grasa insaturada (aceite de oliva y frutos secos):**
 - a) Reduce el riesgo de diabetes.**
 - b) Se acompaña de pérdida de peso y disminución de la circunferencia de la cintura.**
 - c) Se asocia a una menor prevalencia de síndrome metabólico.**

GRACIAS

