

THE PREDIMED STUDY

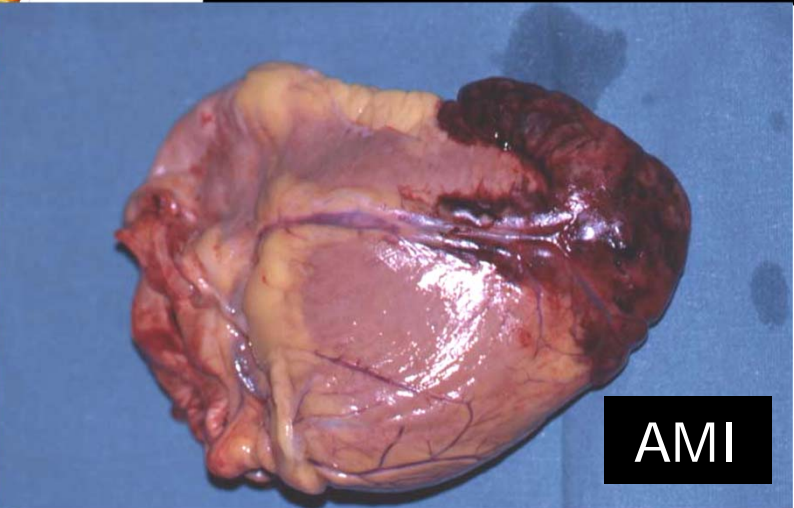
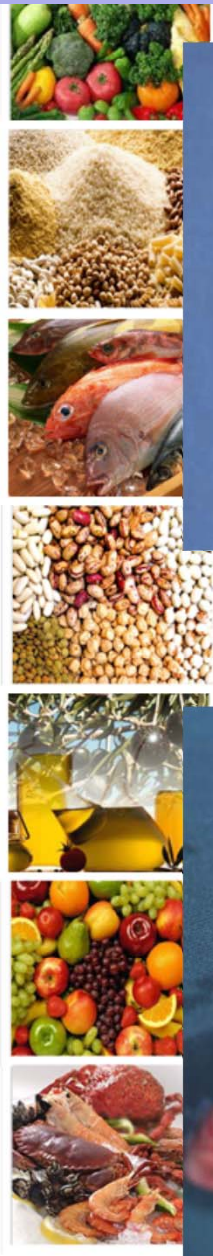
New evidences of the effects of the Mediterranean diet in the prevention of cardiovascular disease



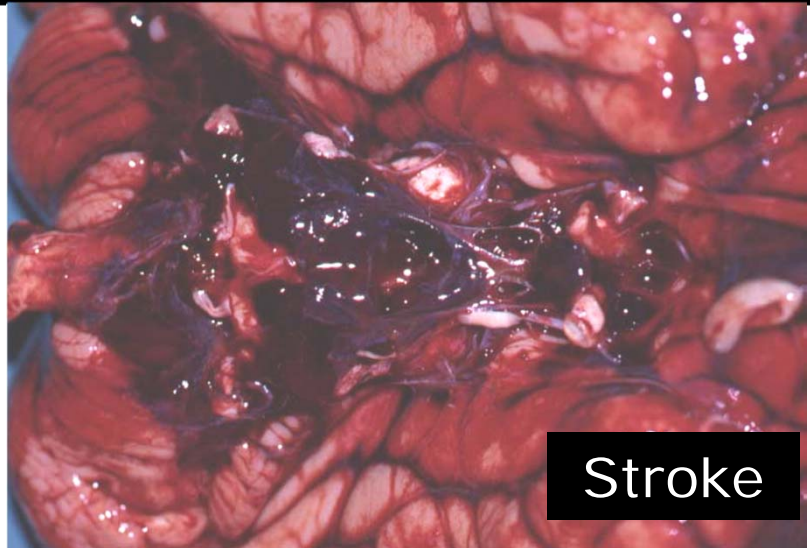
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The REGICOR Study Group*

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CIBER de Fisiopatología de la Obesidad y Nutrición (CIBEROBN)*

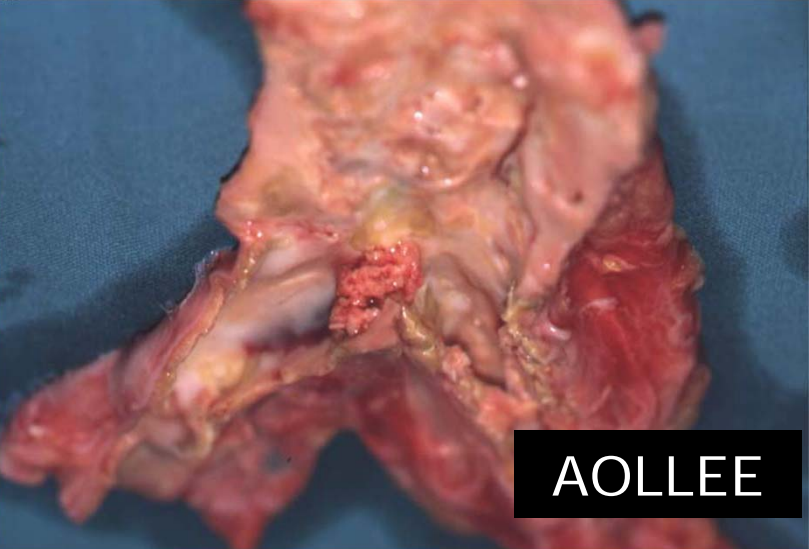
Cardiovascular disease is the main cause of death at the onset of the XXI Century



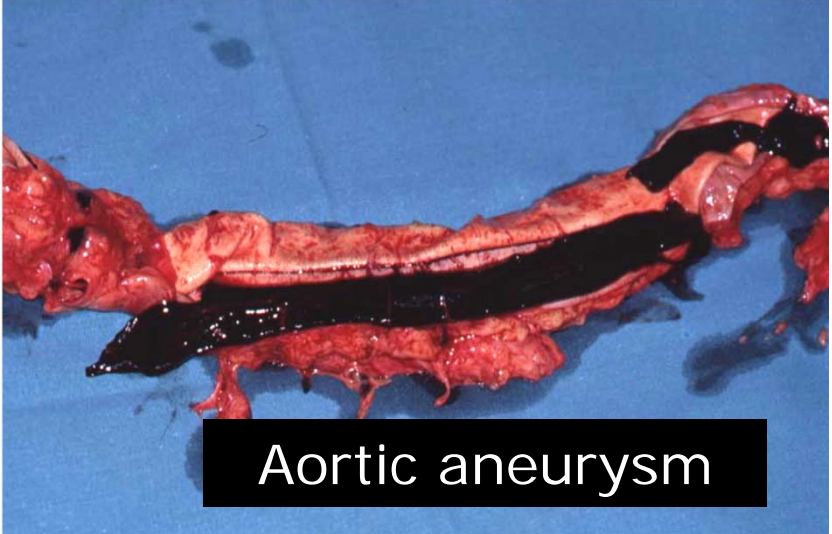
AMI



Stroke



AOLLEE



Aortic aneurysm



**BEST WEAPONS
AGAINST
CARDIOVASCULAR
DISEASE:
DIET AND EXERCISE**

Mediterranean Diet Pyramid
A contemporary approach to delicious, healthy eating

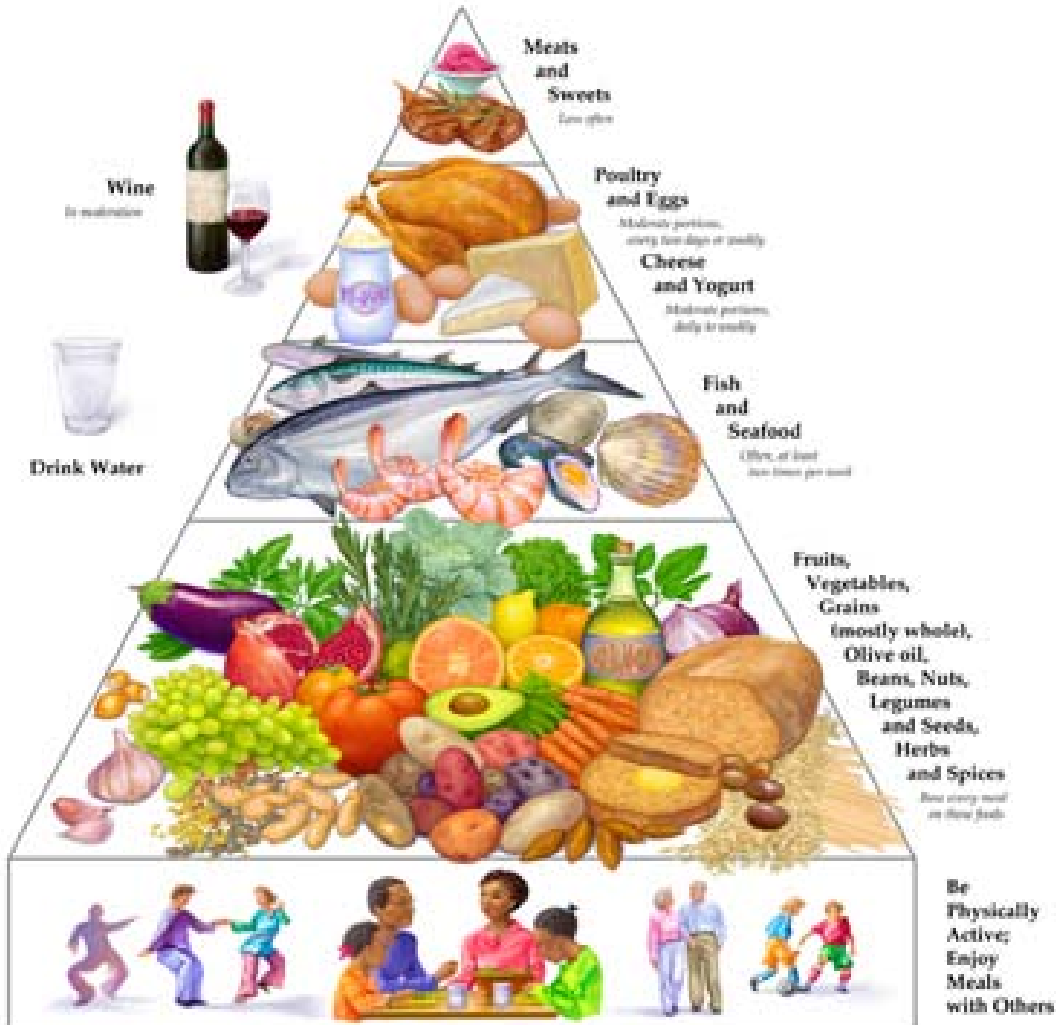


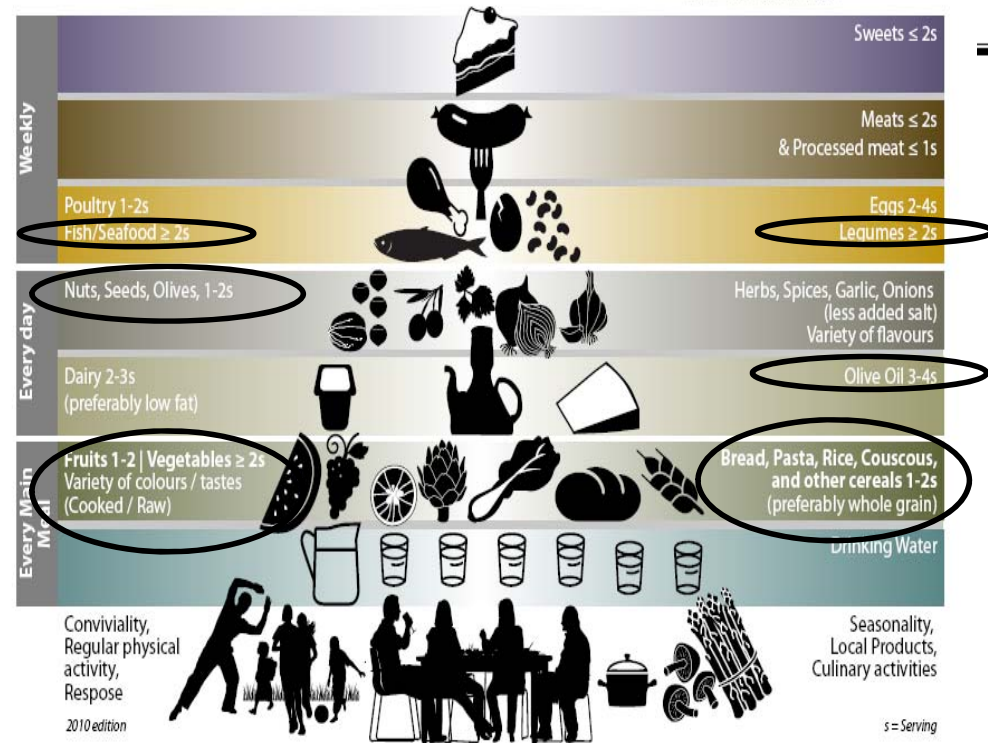
Illustration by George Middlemore © 2009 Oldways Preservation and Exchange Trust www.oldwayspt.org



Mediterranean Diet Pyramid Today | Adult population

Each country has its own serving size based on frugality

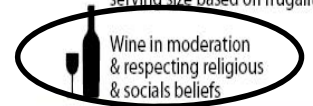
Wine in moderation & respecting religious & social beliefs





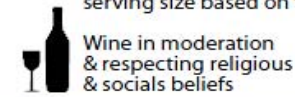
Mediterranean Diet Pyramid Today | Adult population

Each country has its own serving size based on frugality



Mediterranean Diet Pyramid Today | Adult population

Each country has its own serving size based on frugality



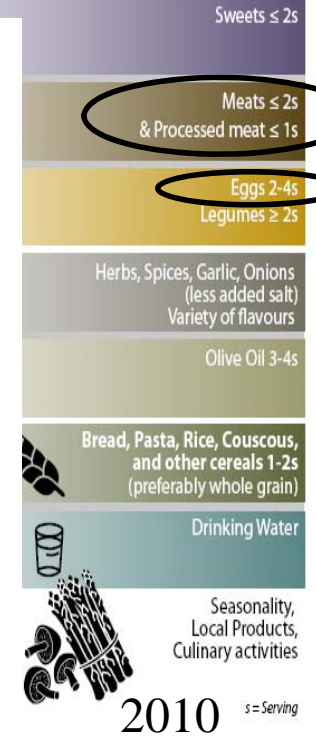
Conviviality,
Regular physical
activity,
Respond

2010 edition

Seasonality,
Local Products,
Culinary activities

2010

s = Serving



moderate and low intake

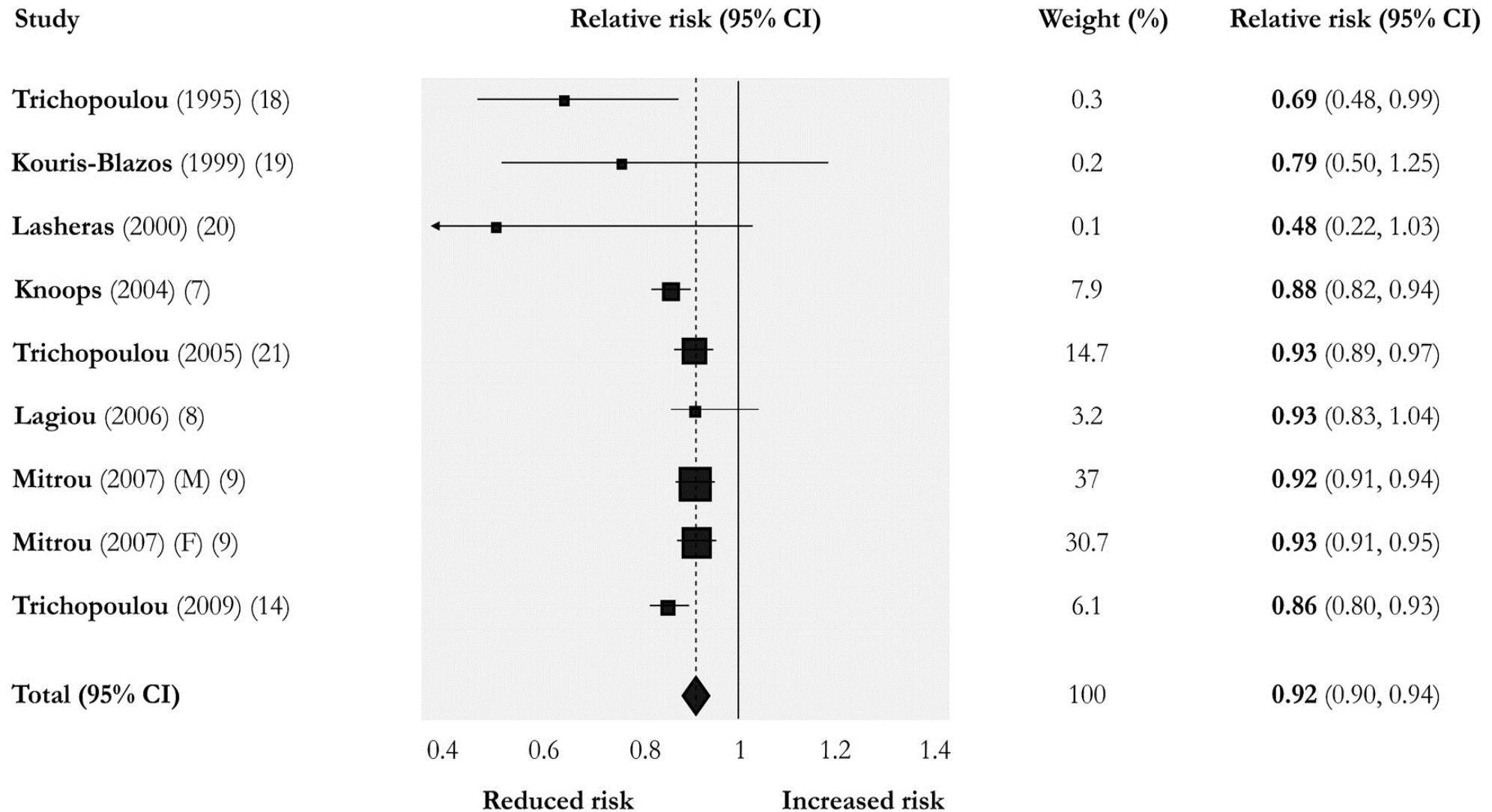
Traditional
Mediterranean Diet



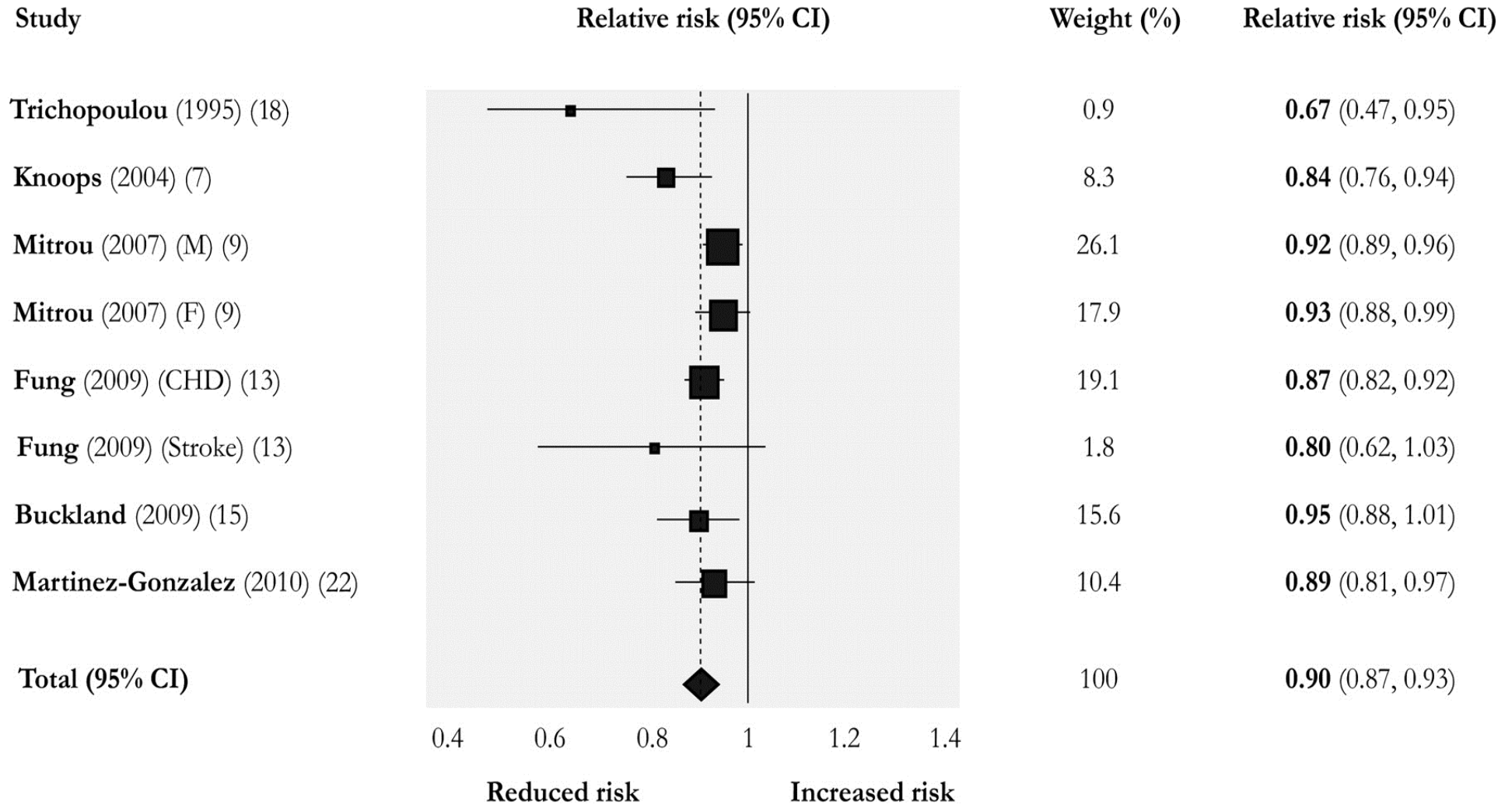
Mediterranean Food Pattern

- Rapidly increasing evidence
 - Increased Longevity
 - Prevention of
 - CV mortality
 - Cancer mortality
 - CVD incidence
 - Metabolic syndrome
 - Diabetes
 - Dementia
 - Depression
- Scarcity of large randomized trials

Forest plot of the association between a 2-point increase of adherence score to the Mediterranean diet and the risk of all-cause mortality.



Forest plot of the association between a 2-point increase of adherence score to the Mediterranean diet and the risk of mortality from or incidence of cardiovascular diseases.



Sofi F et al. Am J Clin Nutr 2010;92:1189-1196

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

Design

- Randomized
- Mediterranean diet
- which

Intervention

- Mediterranean diet
- enriched

Follow-up

without event

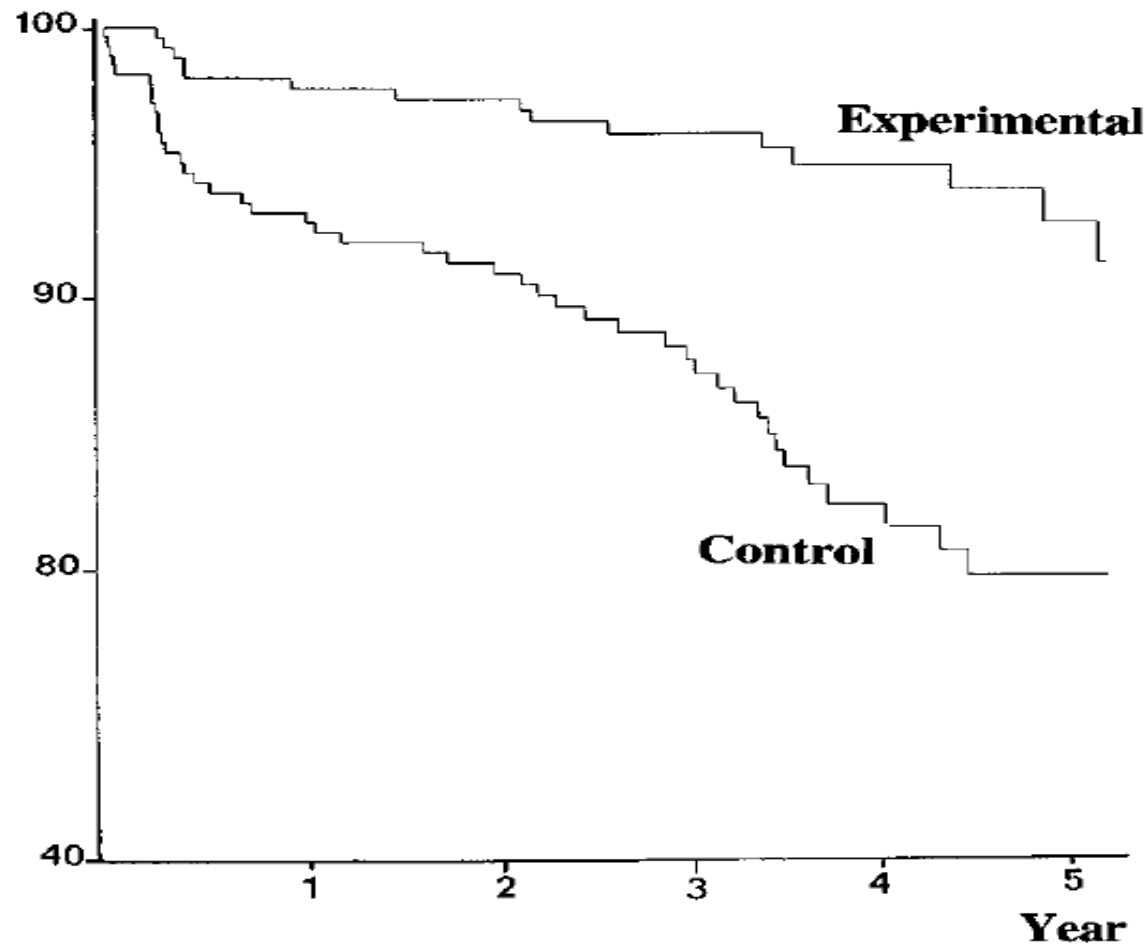


Figure 1. Cumulative survival without nonfatal myocardial infarction (CO 1) among experimental (Mediterranean group) patients and control subjects.

The Effect of the Mediterranean Diet on the Primary Prevention of Cardiovascular Disease. The PREDIMED Study



19 Research Groups of 7 Spanish Regions

10 Recruitment Centers



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 nuts (walnuts, almonds, and hazelnuts) on the risk of cardiovascular diseases (a composite endpoint of cardiovascular death, myocardial infarction, and stroke).
- To test the effect of wine intake on the risk of cardiovascular diseases



Other specific aims

- To determine the changes in blood lipids, blood pressure, markers of oxidation and 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
- To assess the effect of the MedDiet on the nutrigenomic response of atherosclerosis-related genes

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 CHD

Random

All free of CVD at baseline



**Mediet +
Virgin Olive Oil**



**Mediet +
Nuts**



**Control
Low-fat**



PREDIMED Steering Committee

R. Estruch (chair); D. Corella; M.I. Covas; M.A. Martínez-Gonzalez; E. Ros; J. Salas-Salvadó

PREDIMED Independent Data and Safety Monitoring Board

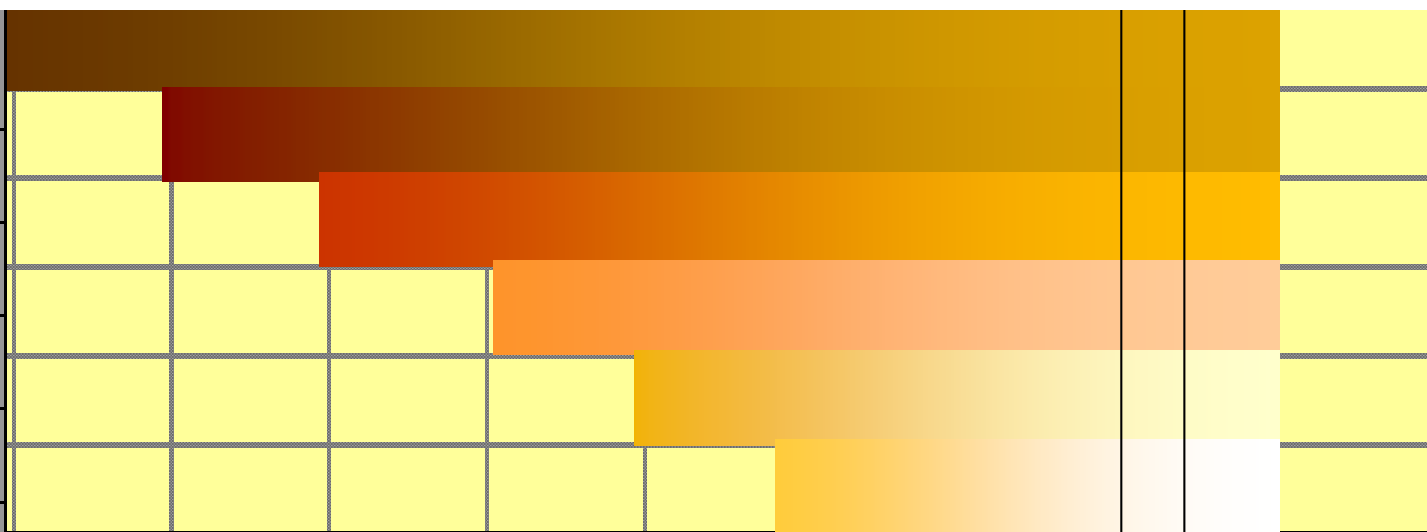
Xavier Pi-Sunyer (chair). *Columbia University, USA*

Carlos A. González. *Institut Català d'Oncologia (ICO), Spain*

Frank B. Hu. *Harvard University, USA*

Joan Sabaté. *Loma Linda University, CA, USA*

Year	% of recruitment	Cum. %
2003	9	9
2004	21	30
2005	28	58
2006	11	69
2007	13	82
2008	17	99
2009	1	100
Total	100	



Interim Analyses with Data until Dec 2010



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Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

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José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D.,
for the PREDIMED Study Investigators*

ABSTRACT

Median Follow-up: 4.8 (2.8 to 5.8)

Participants: 7447

Intention-to-treat-analyses

Sample size and Randomization

7,447 participants

Control Low
Fat Diet

n= 2,543

Mediterranean
Diet
+



n= 2,454

Mediterranean
Diet
+



n= 2,450



PREDIMED Participants

	Mediet + VOO (n= 2543)	MeDiet + Nuts (n=2454)	Control (n=2450)
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)



Table 1. Summary of Dietary Recommendations to Participants in the Mediterranean-Diet Groups and the Control-Diet Group.

Food	Goal
Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day
Tree nuts and peanuts†	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito‡	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<3 servings/wk
Spread fats	<1 serving/day
Red and processed meats	<1 serving/day

Table 1. Summary of Dietary Recommendations to Participants in the Mediterranean-Diet Groups and the Control-Diet Group.

Low-fat diet (control)

Recommended

Low-fat dairy products	≥3 servings/day
Bread, potatoes, pasta, rice	≥3 servings/day
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/wk
Lean fish and seafood	≥3 servings/wk

Discouraged

Vegetable oils (including olive oil)	≤2 tbsp/day
Commercial bakery goods, sweets, and pastries§	≤1 serving/wk
Nuts and fried snacks	≤1 serving /wk
Red and processed fatty meats	≤1 serving/wk
Visible fat in meats and soups¶	Always remove
Fatty fish, seafood canned in oil	≤1 serving/wk
Spread fats	≤1 serving/wk
Sofrito‡	≤2 servings/wk





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



Control Group: Small gifts non-related with food

Measurements

Eligibility questionnaire	X				
General questionnaire	X				
Follow-up questionnaire		X	X	X	X
Food Freq. questionnaire	X	X	X	X	X
14 item score of Med diet	X	X	X	X	X
Physical activity ques.	X	X	X	X	X
EKG, BP, and Anthropometric	X	X	X	X	X
Blood samples *	X	X	X	X	X
Fresh urine sample *	X	X	X	X	X
Toenail sample	X				




* *Specific measurements*
Intervention compliance
assessment

Urinary tyrosol and hydroxytyrosol
 Plasma fatty acid composition (oleic and α -linolenic acids)







PRIMARY END-POINT

Composite of:

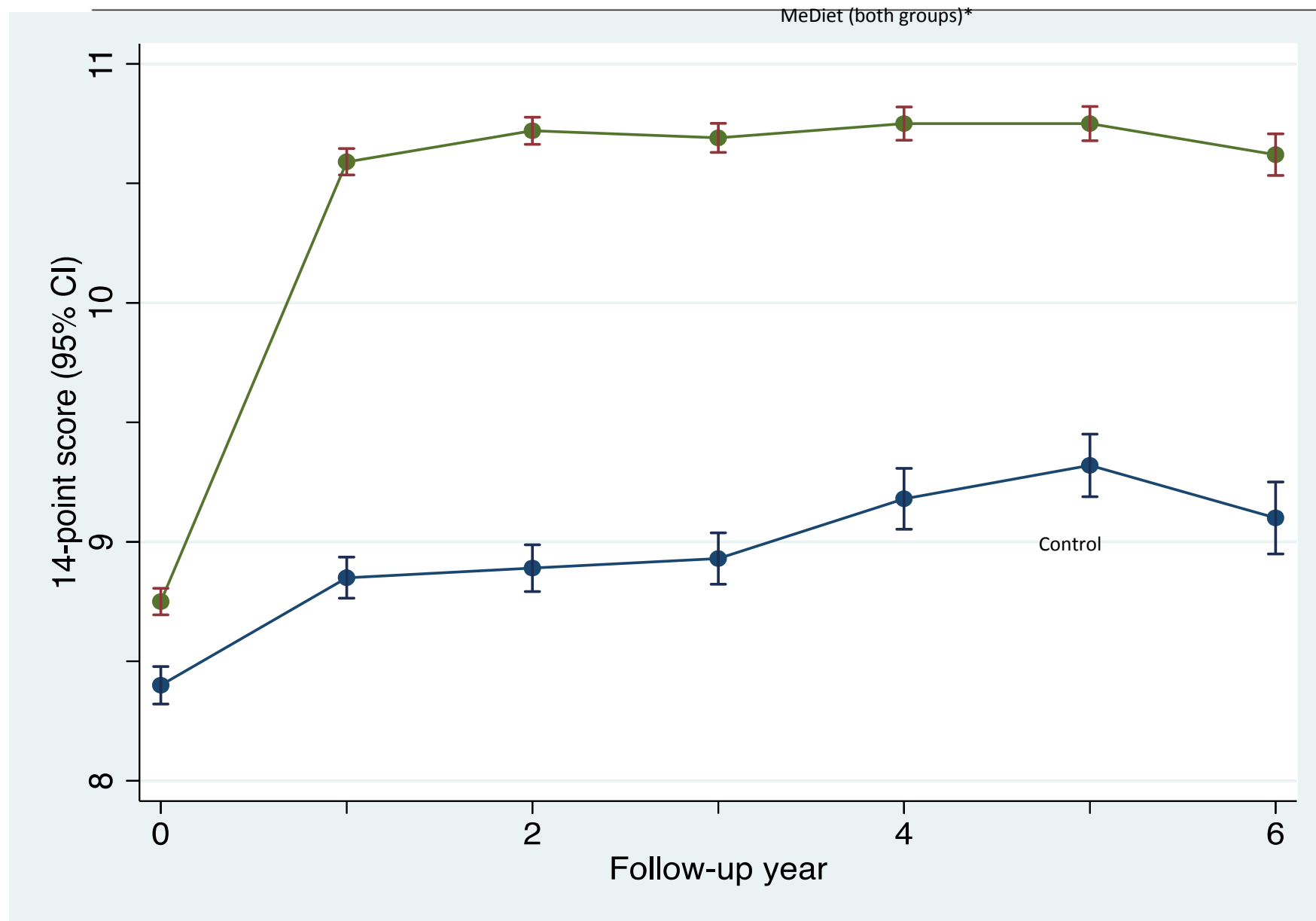
- 
- 
- 
- Cardiovascular death
 - Non-fatal myocardial infarction
 - Non-fatal stroke



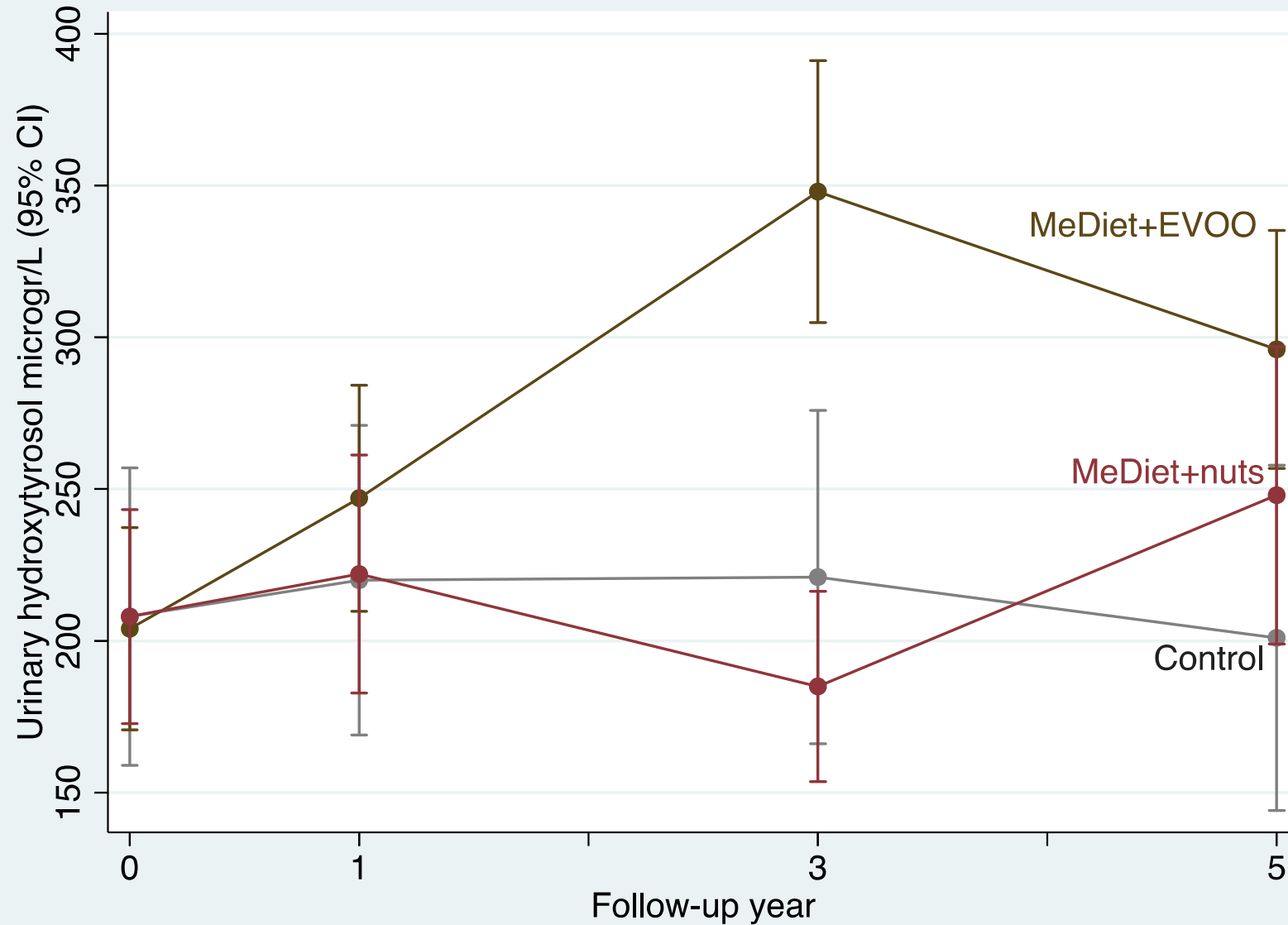
SECONDARY END-POINTS

- 
- 
- 
- 
- Cardiovascular death
 - Non-fatal myocardial infarction
 - Non-fatal stroke
 - Death from any cause
-
- Angina leading to revascularization procedure
 - Heart failure

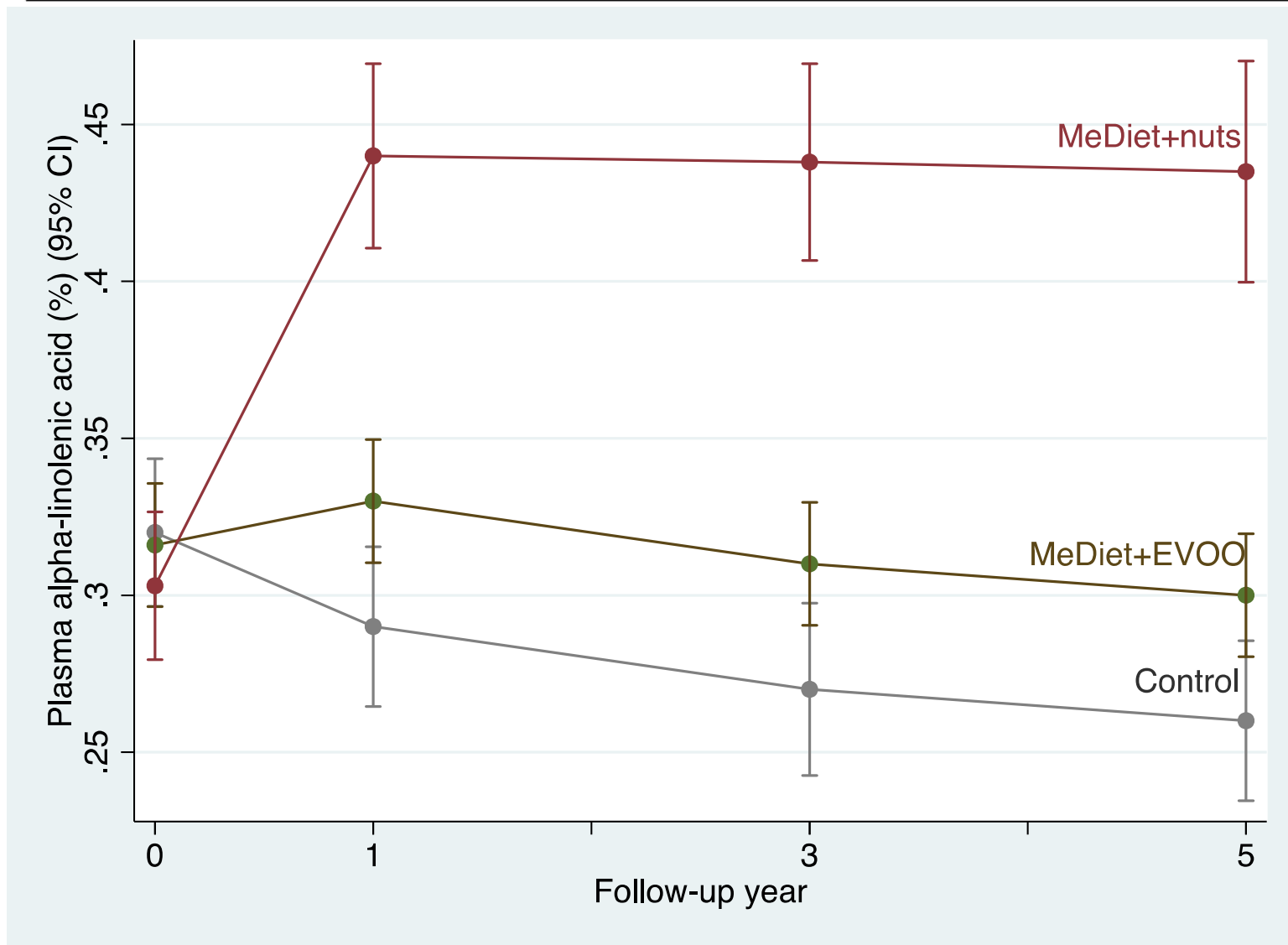
Results-Adherence to Mediterranean Diet



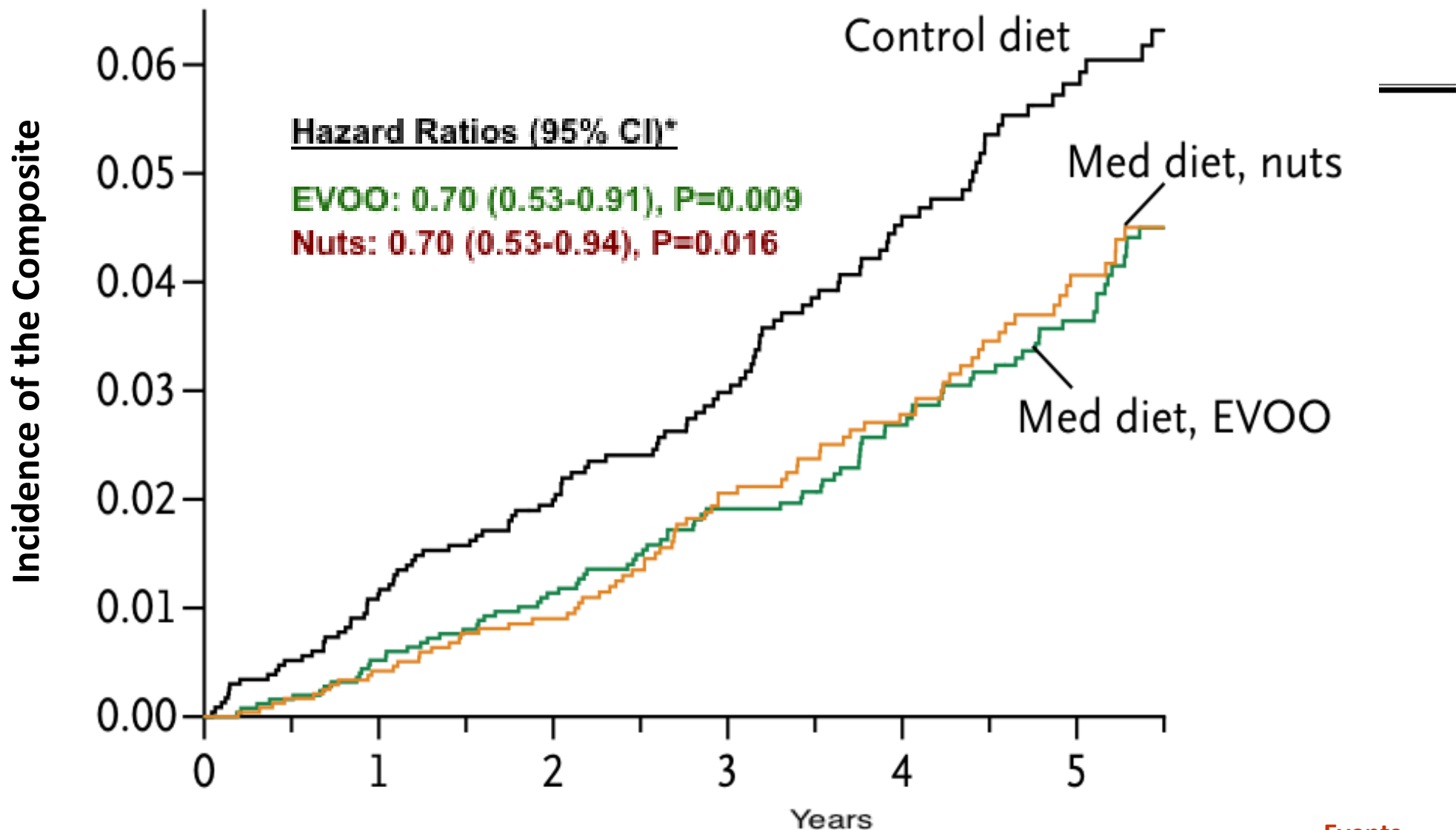
Adherence to MedDiet plus Virgin Olive Oil intervention



Adherence to the MedDiet plus nuts Intervention



Kaplan-Meier Estimates of the Incidence of the Primary End-point



Number at risk

	0	1	2	3	4	5
Control group	2450	2268	2020	1583	1268	946
MeDiet+EVOO	2543	2486	2320	1987	1687	1310
MeDiet+Nuts	2454	2343	2093	1657	1389	1031

Events

Control group	109
MeDiet+EVOO	96
MeDiet+Nuts	83



Table 3. Outcomes According to Study Group.*

End Point	Mediterranean Diet with EVOO (N=2543)	Mediterranean Diet with Nuts (N=2454)	Control Diet (N=2450)	P Value†
				Mediterranean Diet with EVOO vs. Control Diet Mediterranean Diet with Nuts vs. Control Diet

┆ Stratified by recruiting Center and adjusted by age, sex, family history of CHD, smoking, BMI, Waist-to height, and hypertension, dyslipidemia and diabetes at baseline

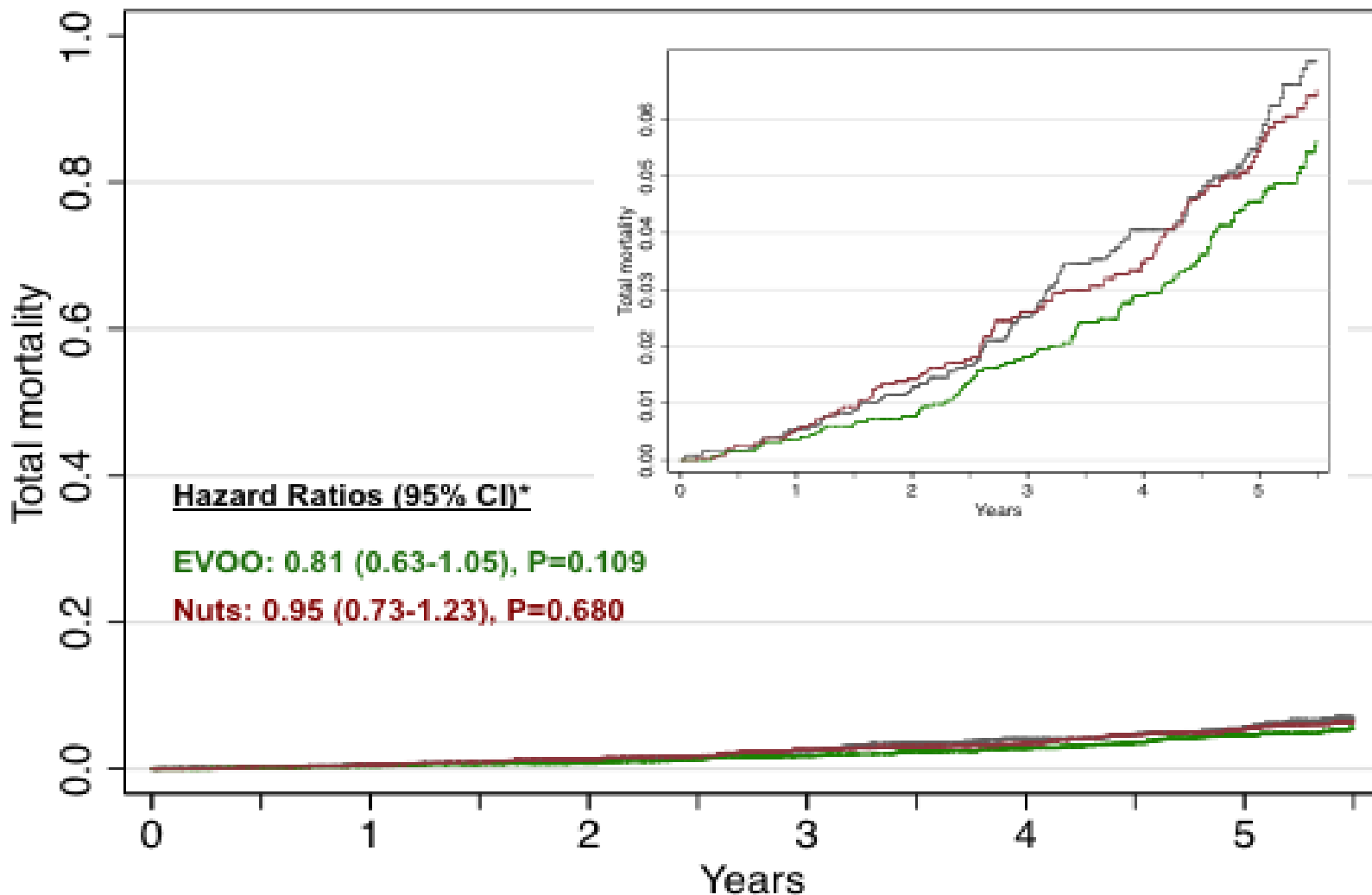
┆ Stratified by recruiting Center and adjusted by age, sex, family history of CHD, and smoking

¶ Additionally adjusted by BMI, Waist-to height, and hypertension, dyslipidemia and diabetes at baseline



Kaplan-Meier Estimates of the Incidence of Total Mortality

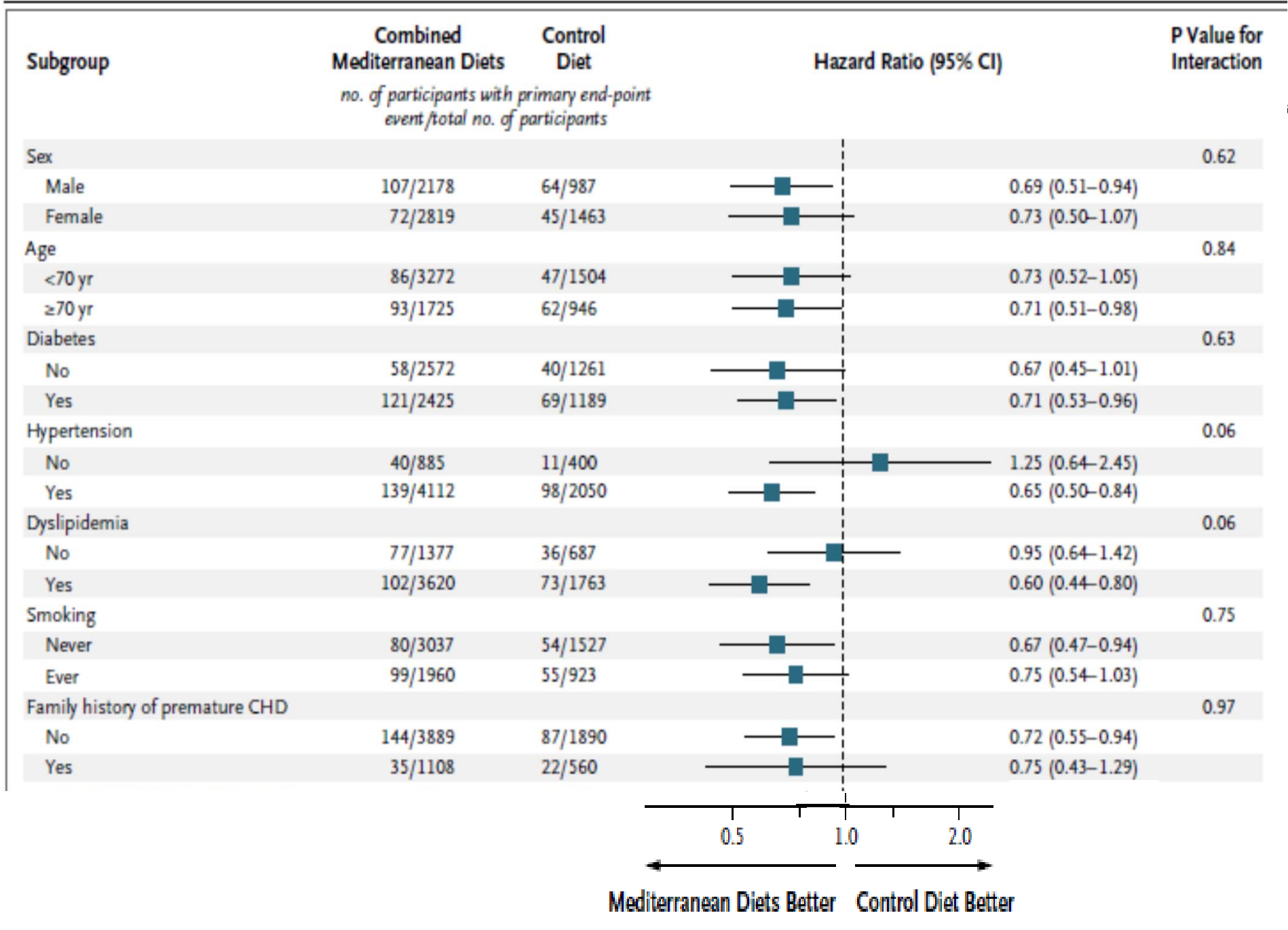
	MeDiet+EVOO	MedDiet+Nuts	Low-Fat
No. of events:	118	116	114
Crude rate/1000 person-yr (95% CI):	10.0 (8.2–11.9)	11.2 (9.3–13.4)	11.7 (9.6–14.0)



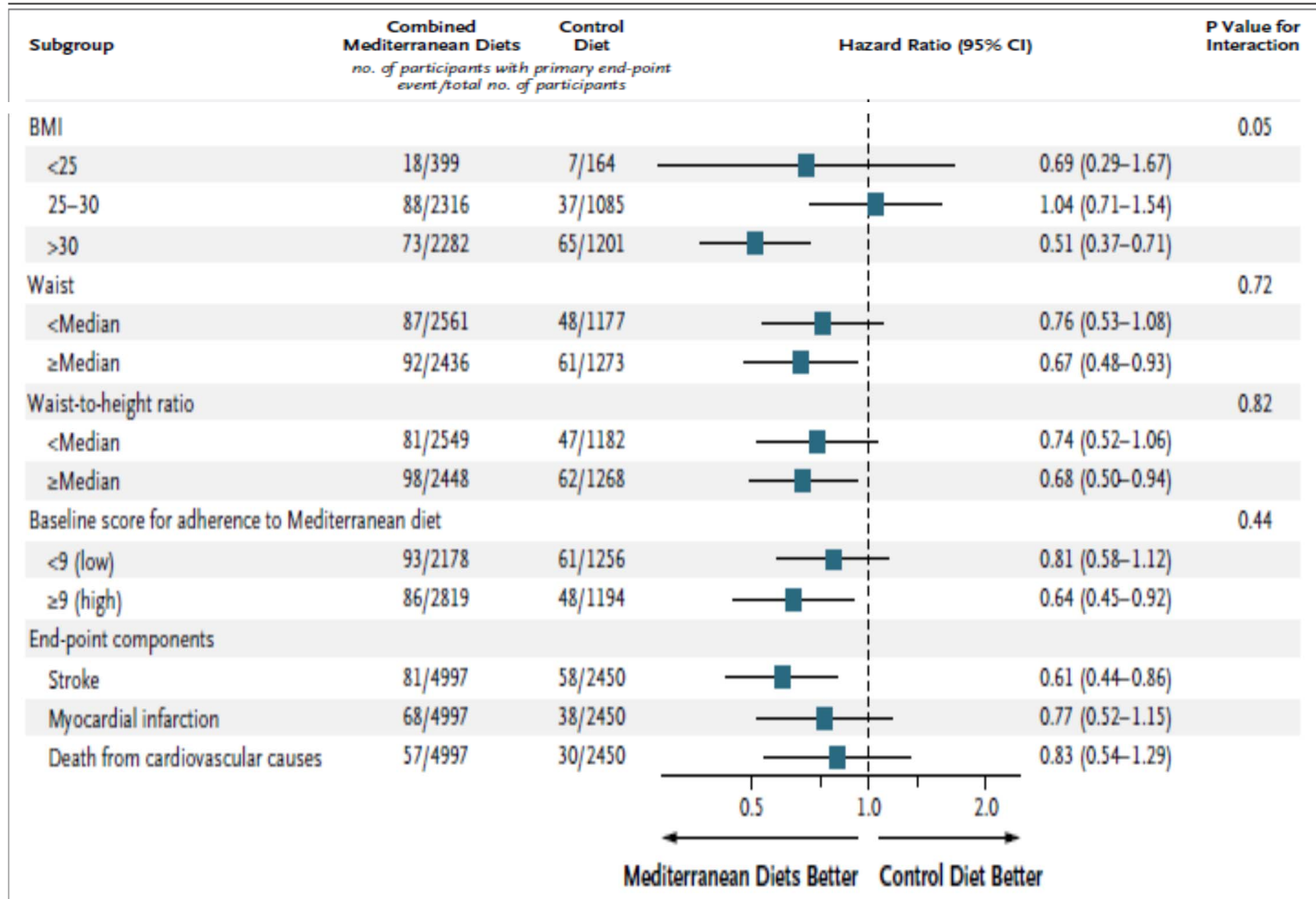
Number at risk

	0	1	2	3	4	5
Control group	2450	2268	2026	1585	1272	948
MeDiet+EVOO	2543	2485	2322	1988	1690	1308
MeDiet+Nuts	2454	2345	2097	1662	1395	1037

The PREDIMED Study. Subgroup analyses



The PREDIMED Study. Subgroup analyses





Limitations

The protocol for the control group was changed halfway through the trial (October 2006). A lower intensity of dietary intervention for the control group during the first few years might have caused a bias toward a benefit in the Mediet groups, since the participants in these groups received a more intensive intervention during that time.

However, we found no significant interaction between the period of trial enrollment (before vs. after the protocol change) and the benefit in the Mediet groups.

Limitations

The generalizability of our findings is limited because all the study participants lived in a Mediterranean country and were at high cardiovascular risk.

Whether the results can be generalized to persons at lower risk or to other settings requires further research.



Conclusions

- 1. Among individuals at cardiovascular risk, a traditional Mediterranean diet supplemented with Extra Virgin Olive Oil or with Nuts promoted a 30% reduction in the incidence of major cardiovascular events.**
- 2. Results of the PREDIMED Study provide first level evidence on the benefits of the traditional Mediterranean diet on the primary prevention of cardiovascular disease.**



Primary Prevention by the Mediterranean Diet

The PREDIMED Study



We thank the participants in the trial for their enthusiastic and sustained collaboration and Joan Vila from Institut Municipal d'Investigació Mèdica, Barcelona, for expert assessment in the statistical analyses.



ACKNOWLEDGEMENTS

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Centro de Investigación Biomédica En Red
Fisiopatología de la Obesidad y Nutrición

Centro de Investigaciones Biomédicas en Red
Physiopathology of Obesity and Nutrition.
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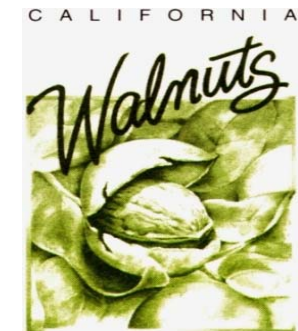


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www.gencat.cat



LA MORELLA NUTS



THANK YOU FOR YOUR ATTENTION

Encuesta de 14 puntos

1. ¿Usa usted el aceite de oliva como principal grasa para cocinar?

Sí = 1 punto

2. ¿Cuanto aceite de oliva consume en total al día (incluyendo el usado para freír, comidas fuera de casa, ensaladas, etc.)?

4 o más cucharadas = 1 punto

3. ¿Cuántas raciones de verdura u hortalizas consume al día?

(las guarniciones o acompañamientos = 1/2 ración) 1 ración = 200g.

2 o más (al menos una de ellas en ensalada o crudas) = 1 punto

4. ¿Cuántas piezas de fruta (incluyendo zumo natural) consume al día?

3 o más al día = 1 punto

5. ¿Cuántas raciones de carnes rojas, hamburguesas, salchichas o embutidos consume al día? (ración: 100 - 150 g)

menos de 1 al día = 1 punto

6. ¿Cuántas raciones de mantequilla, margarina o nata consume al día?

(porción individual: 12 g)


menos de 1 al día = 1 punto

7. ¿Cuántas bebidas carbonatadas y/o azucaradas (refrescos, colas, tónicas, bitter) consume al día?

menos de 1 al día = 1 punto



Encuesta de 14 puntos



8. ¿Bebe usted vino? ¿Cuánto consume a la semana?

7 o más vasos a la semana = 1 punto

9. ¿Cuántas raciones de legumbres consume a la semana?

(1 plato o ración de 150 g)

3 o más a la semana = 1 punto

10. ¿Cuántas raciones de pescado-mariscos consume a la semana?

(1 plato pieza o ración: 100 - 150 de pescado o 4-5 piezas o 200 g de marisco)

3 o más a la semana = 1 punto

11. ¿Cuántas veces consume repostería comercial (no casera) como galletas, flanes, dulce o pasteles a la semana?

menos de 2 a la semana = 1 punto

12. ¿Cuántas veces consume frutos secos a la semana? (ración 30 g)

3 o más a la semana = 1 punto

13. ¿Consume usted preferentemente carne de pollo, pavo o conejo en vez de ternera, cerdo, hamburguesas o salchichas? (carne de pollo: 1 pieza o ración de 100 - 150 g)

Sí = 1 punto

14. ¿Cuántas veces a la semana consume los vegetales cocinados, la pasta, arroz u otros platos aderezados con salsa de tomate, ajo, cebolla o puerro elaborada a fuego lento con aceite de oliva (sofrito)?

2 o más a la semana = 1 punto



8. ¿Bebe usted vino? ¿Cuánto consume a la semana?

7 o más vasos a la semana = 1 punto

9. ¿Cuántas raciones de legumbres consume a la semana?

(1 plato o ración de 150 g)

3 o más a la semana = 1 punto

10. ¿Cuántas raciones de pescado-mariscos consume a la semana?

(1 plato pieza o ración: 100 - 150 de pescado o 4-5 piezas o 200 g de marisco)

3 o más a la semana = 1 punto

11. ¿Cuántas veces consume repostería comercial (no casera) como galletas, flanes, dulce o pasteles a la semana?

menos de 2 a la semana = 1 punto

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2 o más a la semana = 1 punto