



XVI Congres de la Societat Catalano- Balear de
Medicina Interna. Barcelona, 2-3 Juny, 2016

Efectes de la Dieta Mediterrània en la Prevenció de la Malaltia Cardiovascular i el Càncer El Estudi PREDIMED

*Dr. María-Isabel Covas
NUPROAS Handelsbolag (NUPROAS HB)
Cardiovascular Risk and Nutrition Research Group
IMIM – Hospital del Mar Research Institut – Barcelona – Spain
CIBER de Fisiopatología de la Obesidad y Nutrición (CIBEROBN)*



**BEST WEAPONS
AGAINST
CHRONIC DEGENERATIVE
DISEASES:
DIET AND EXERCISE**

Mediterranean Diet Pyramid
A contemporary approach to delicious, healthy eating

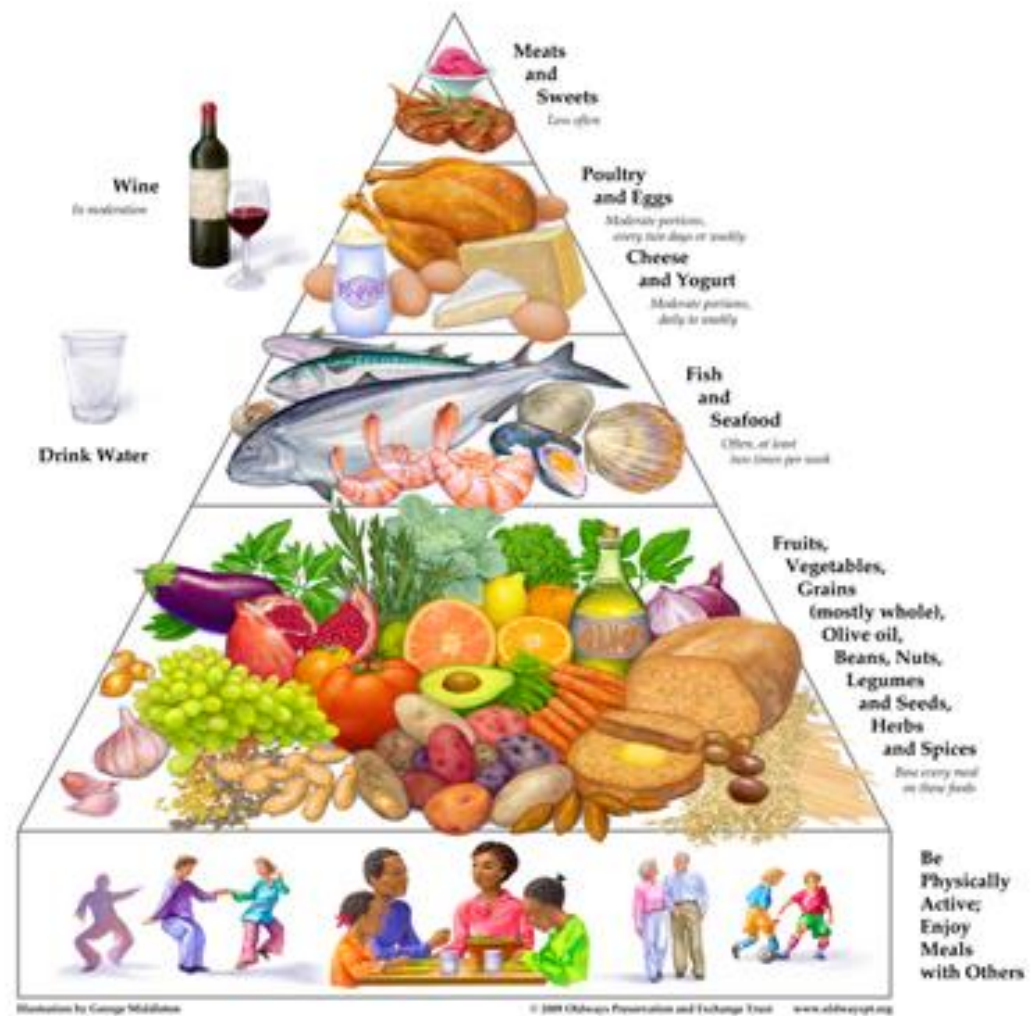
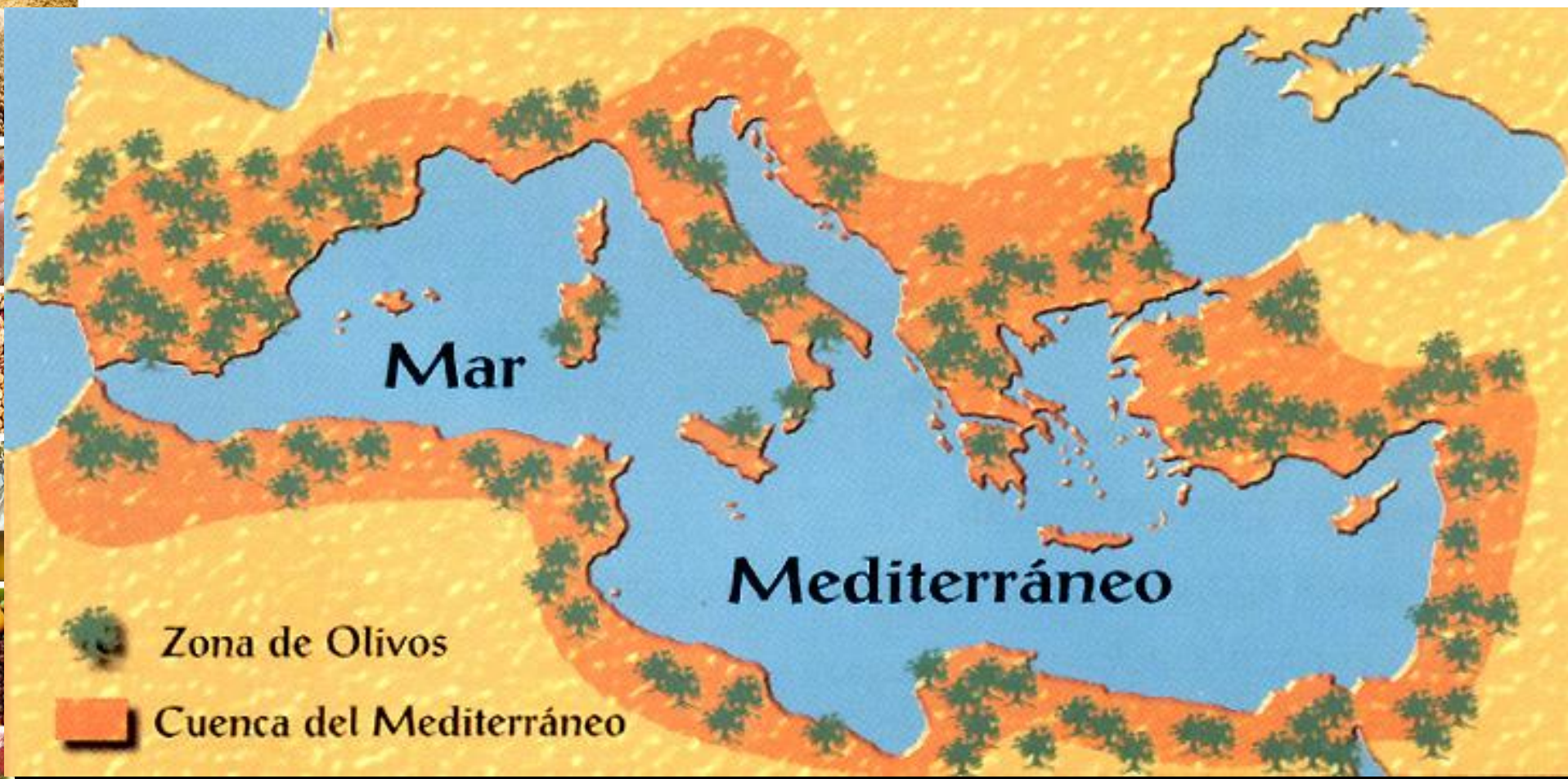


Illustration by George Middleton © 2008 Obispoys Prevention and Exchange Trust www.obisopys.org

Origin of the Mediterranean Diet




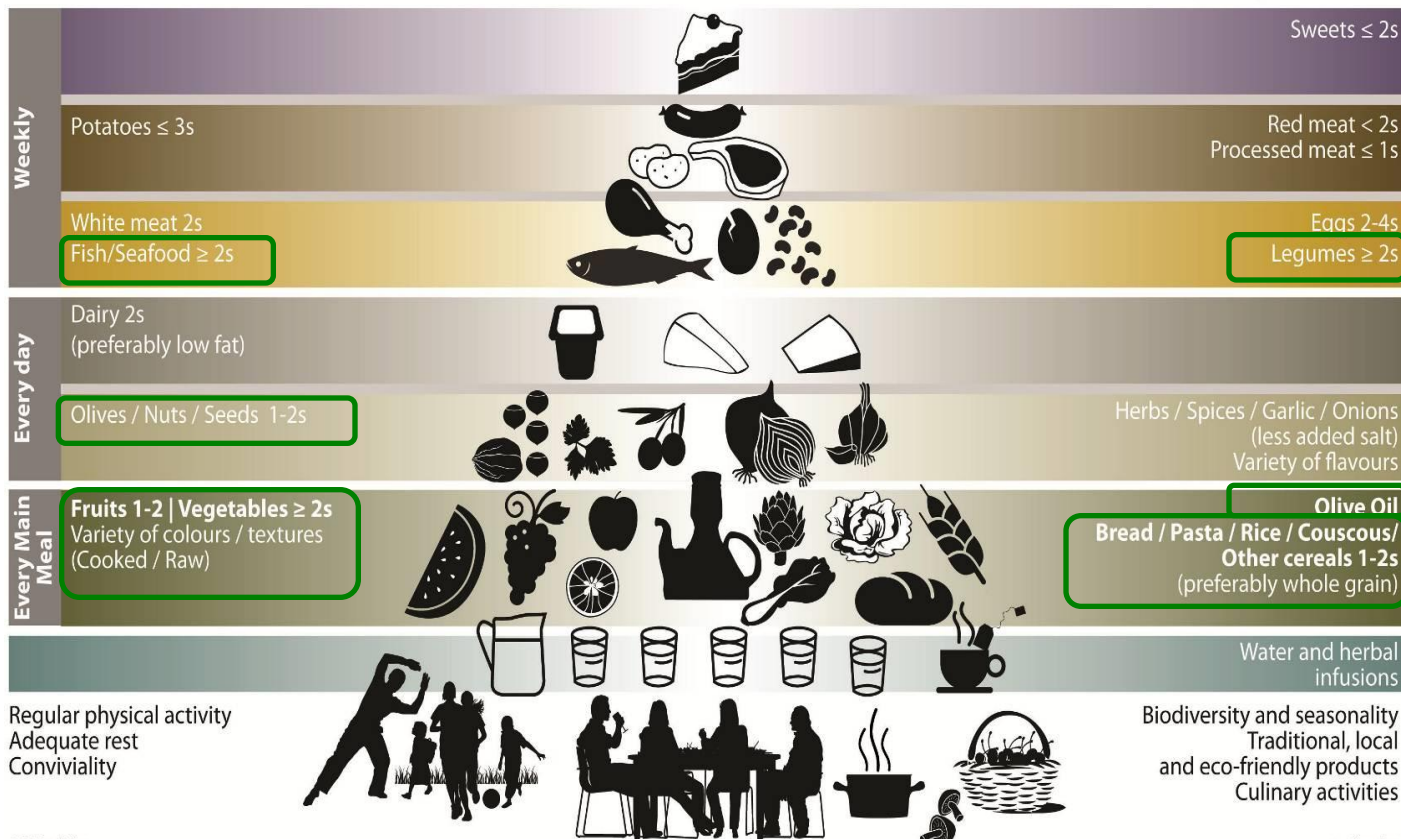
Traditional Mediterranean Diet

HIGH CONSUMPTION

Mediterranean Diet Pyramid: a lifestyle for today
Guidelines for Adult population

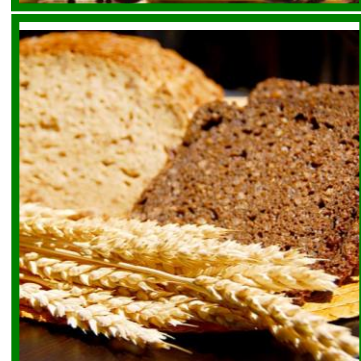
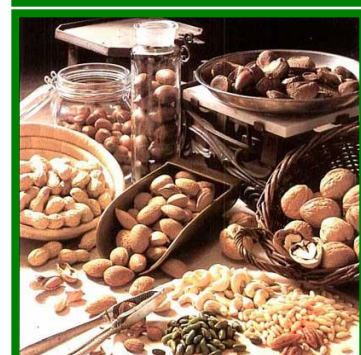
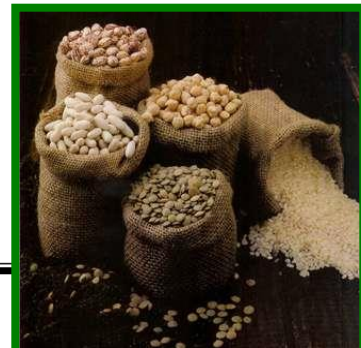
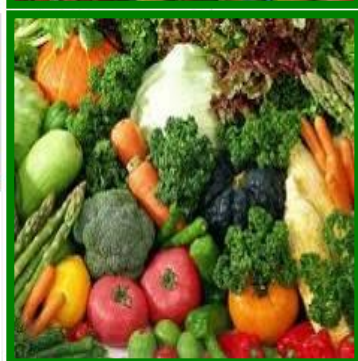
Serving size based on frugality and local habits

 Wine in moderation and respecting social beliefs



Regular physical activity
Adequate rest
Conviviality

Biodiversity and seasonality
Traditional, local and eco-friendly products
Culinary activities



Traditional Mediterranean Diet

MEDIUM/LOW CONSUMPTION

Mediterranean Diet Pyramid: a lifestyle for today
 Guidelines for Adult population

Serving size based on frugality and local habits
 Wine in moderation and respecting social beliefs



Regular physical activity
 Adequate rest
 Conviviality

Biodiversity and seasonality
 Traditional, local and eco-friendly products
 Culinary activities





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



Evidence Level

Ia- Meta-analysis

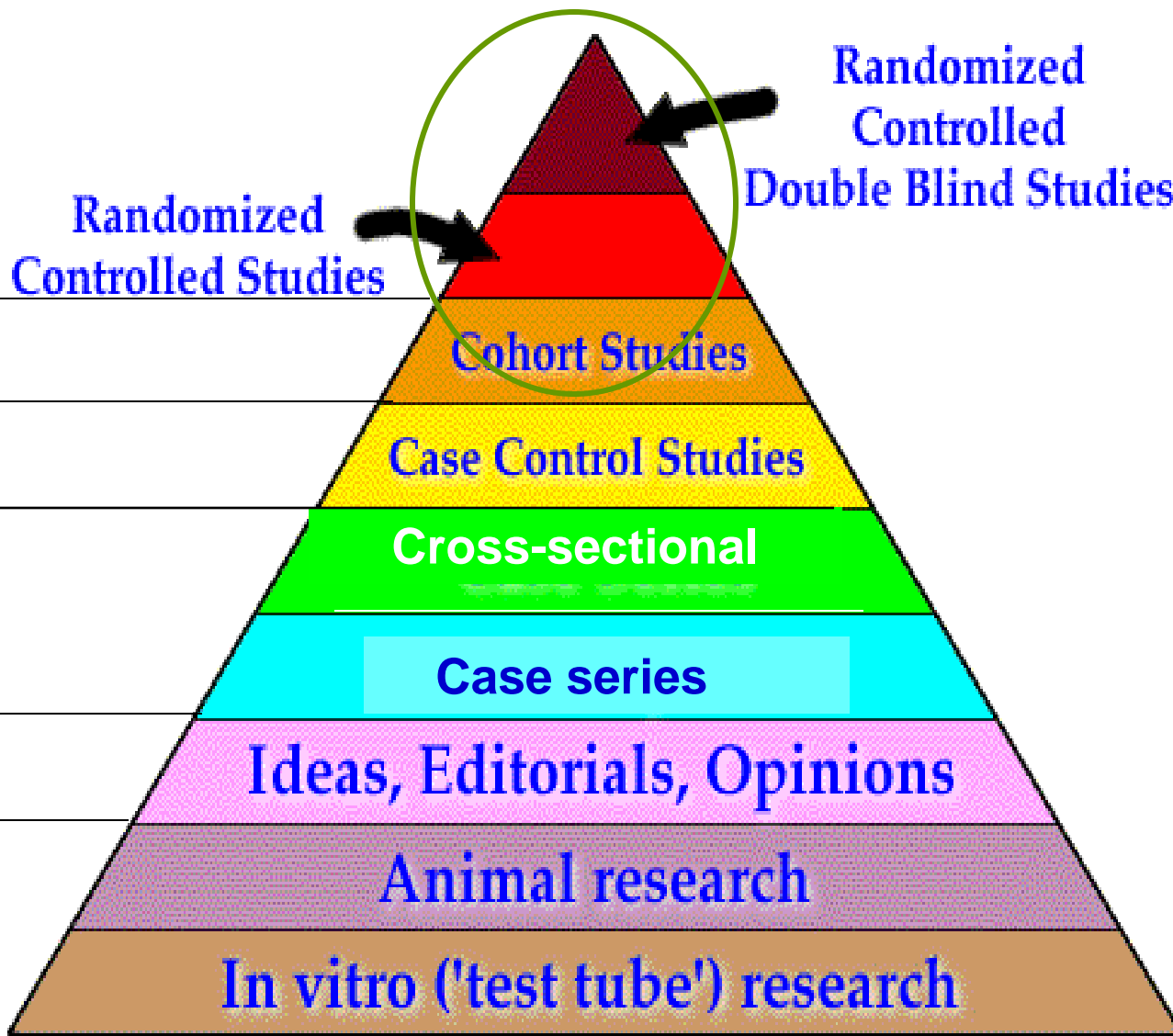
Ib- Individual RCT

IIa,IIb

IIIa, IIIb

IV

V



Canadian Task Force on the Periodic Health Examination. J Clin Epidemiol 1990; 43:891-905; U.S. Preventive Task Force.

Williams and Wilkins 1989; The Swedish Council of Technology Assessment in Health and Care., 1993; Agència d'Avaluació de

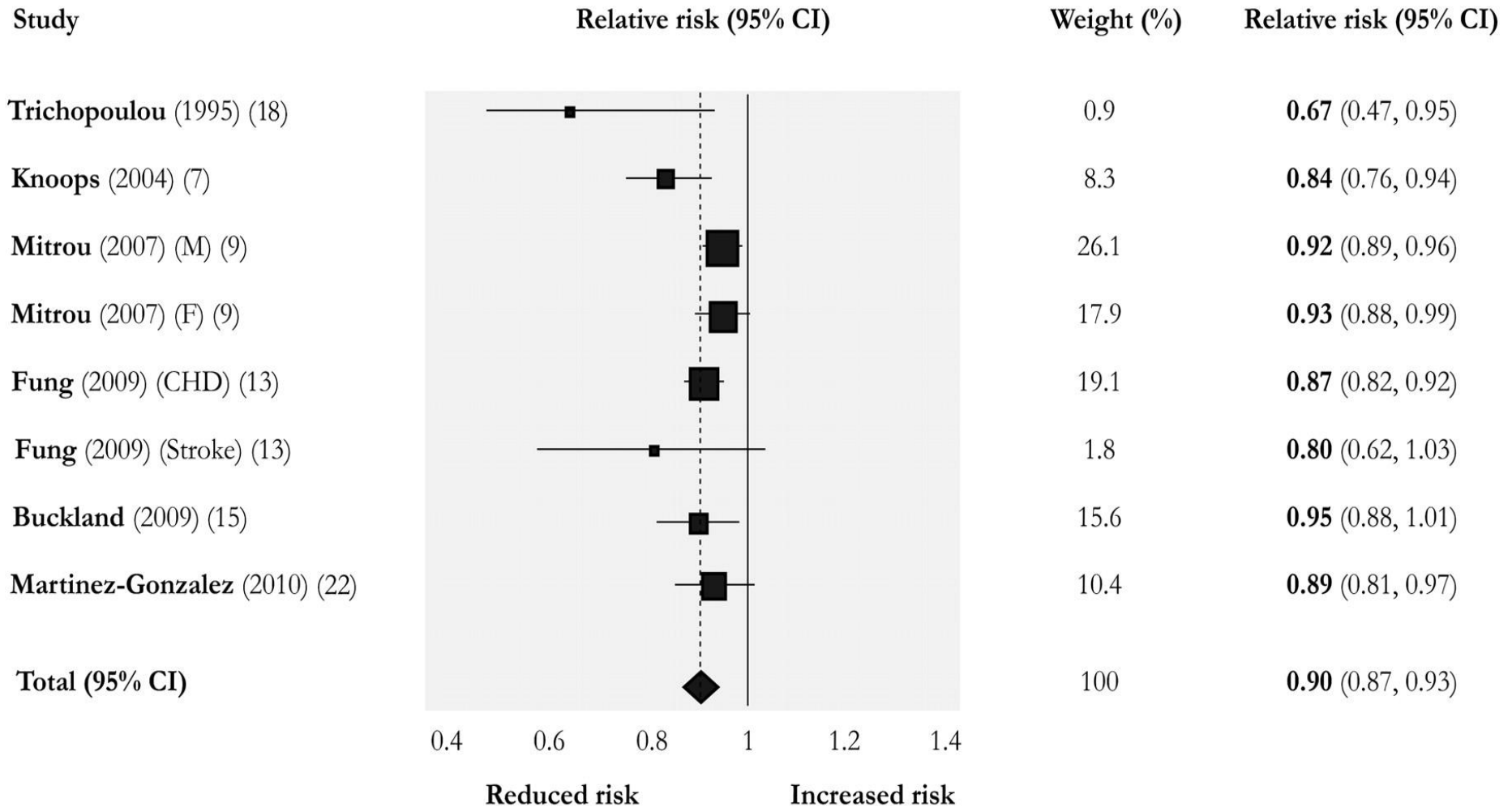
Tecnologia Mèdica de Catalunya. Med Clin (Barc) 1995;105:740-743.

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Mediterranean Diet
and
Cardiovascular Disease



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

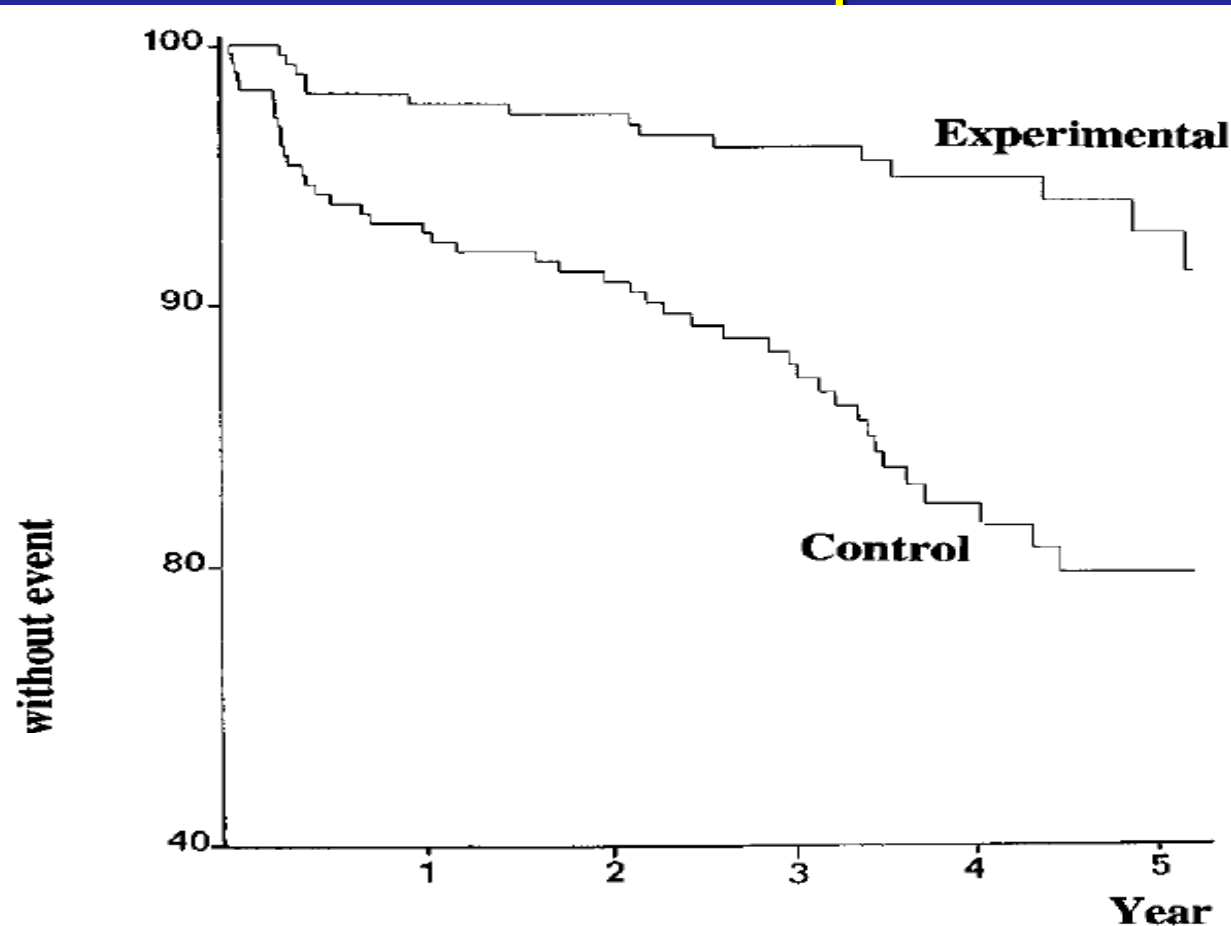
- Randomized
- Mediterranean diet
- when

Intervention

- Mediterranean diet
- enriched

Follow-up

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

OR

NUTS

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

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



**Mediet +
Virgin Olive Oil**



**Mediet +
Nuts**



**Control
Low-fat**

All free of CVD at baseline



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

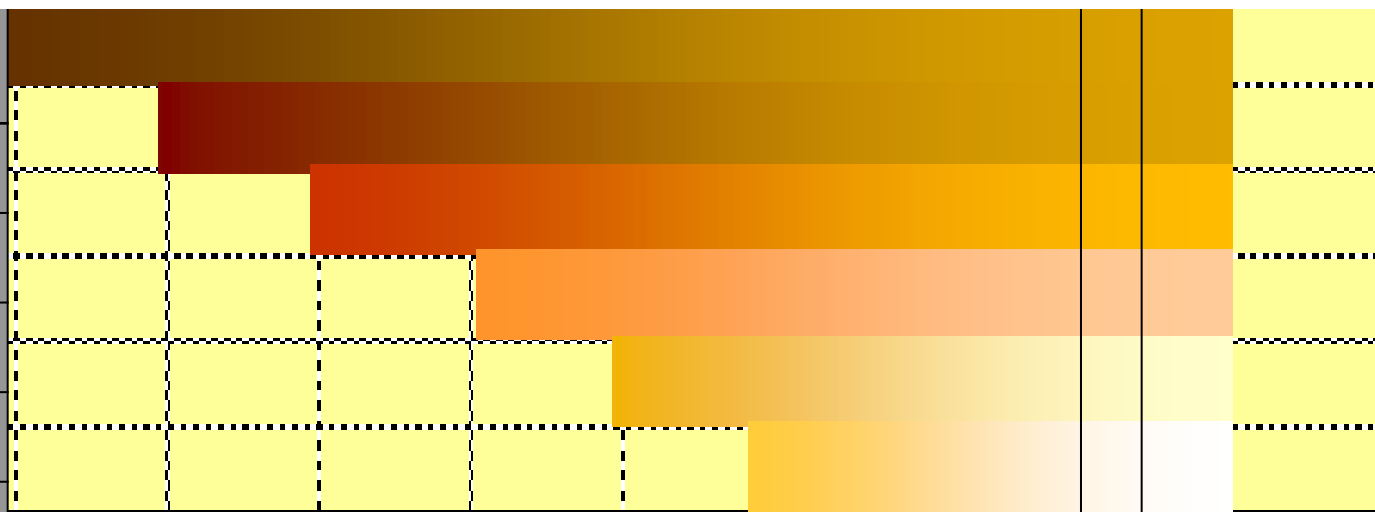
Xavier Pi-Sunyer (chair). *Columbia University, USA*

Carlos A. González. *Institut Catalá 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

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D.,
Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D.,
Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutiérrez, Ph.D., Miquel Fiol, M.D., Ph.D.,
José Lapetra, M.D., Ph.D., Rosa Maria Lamuela-Raventos, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D.,
Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D.,
José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D.,
for the PREDIMED Study Investigators*

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

Mediterranean Diet +

Mediterranean Diet +

n= 2450

n= 2454

n= 2543





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

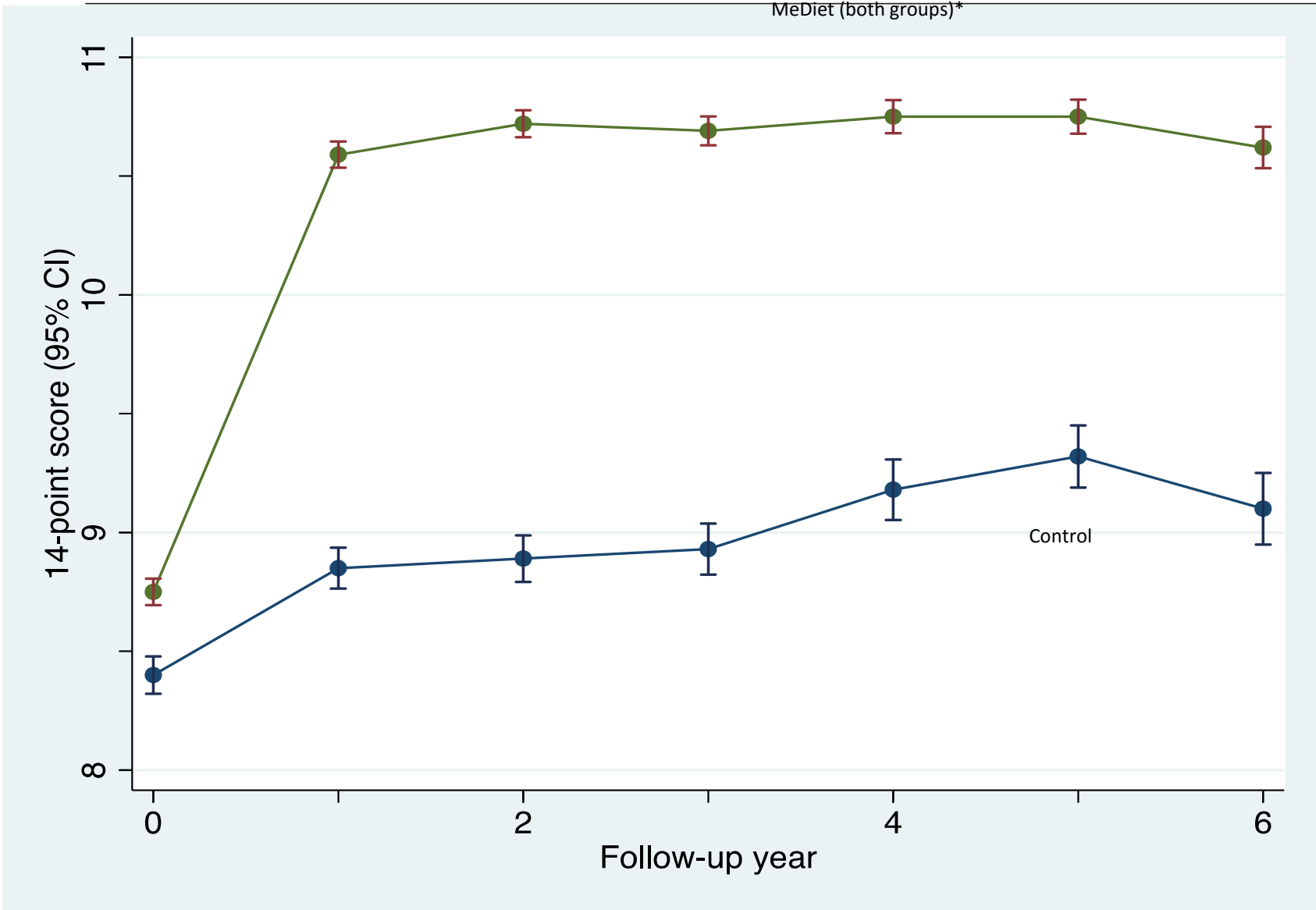


30 g/day

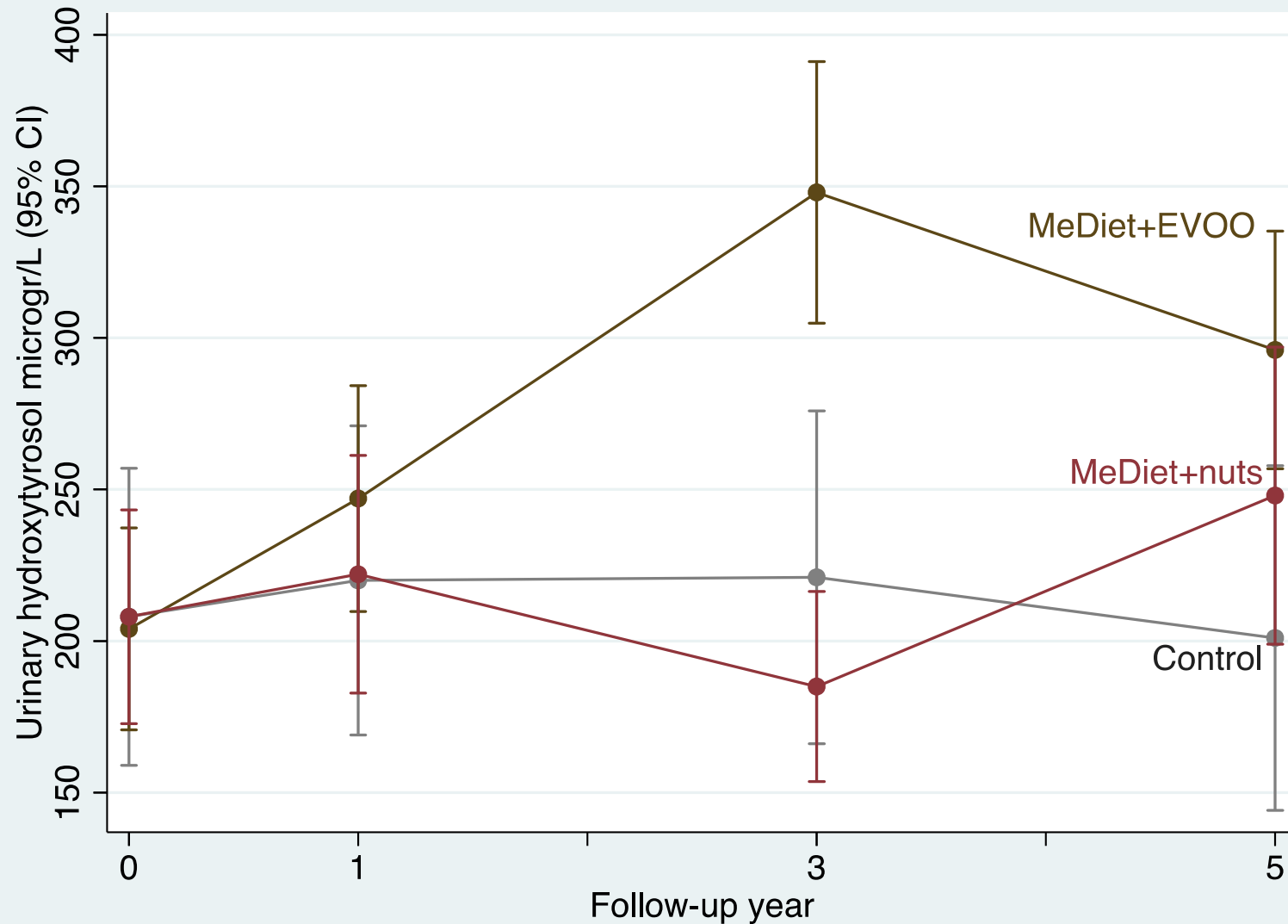


Control Group: Small gifts non-related with food

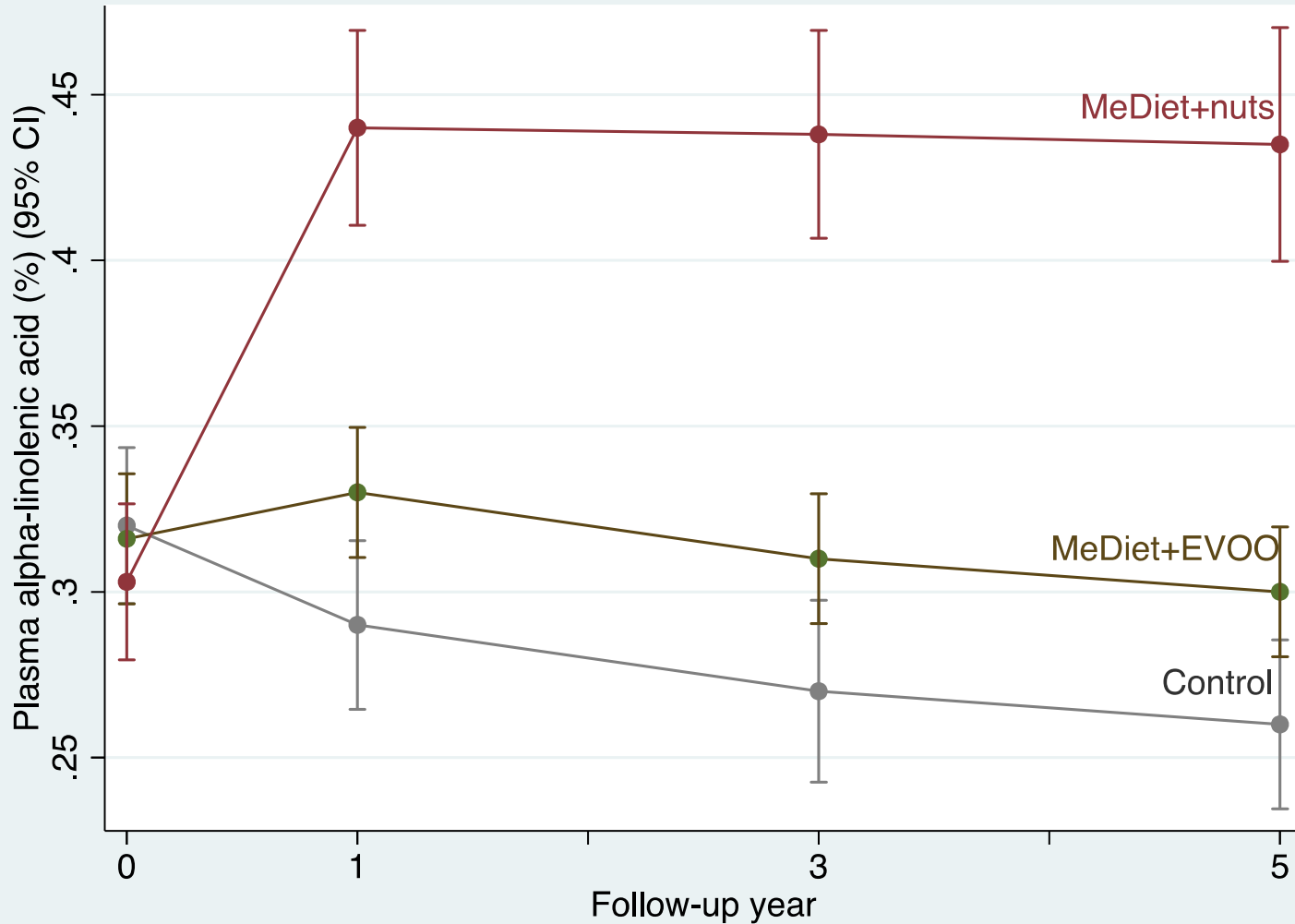
Results-Adherence to Mediterranean Diet (14-points score, Schröder H et al. J Nutr 2011)



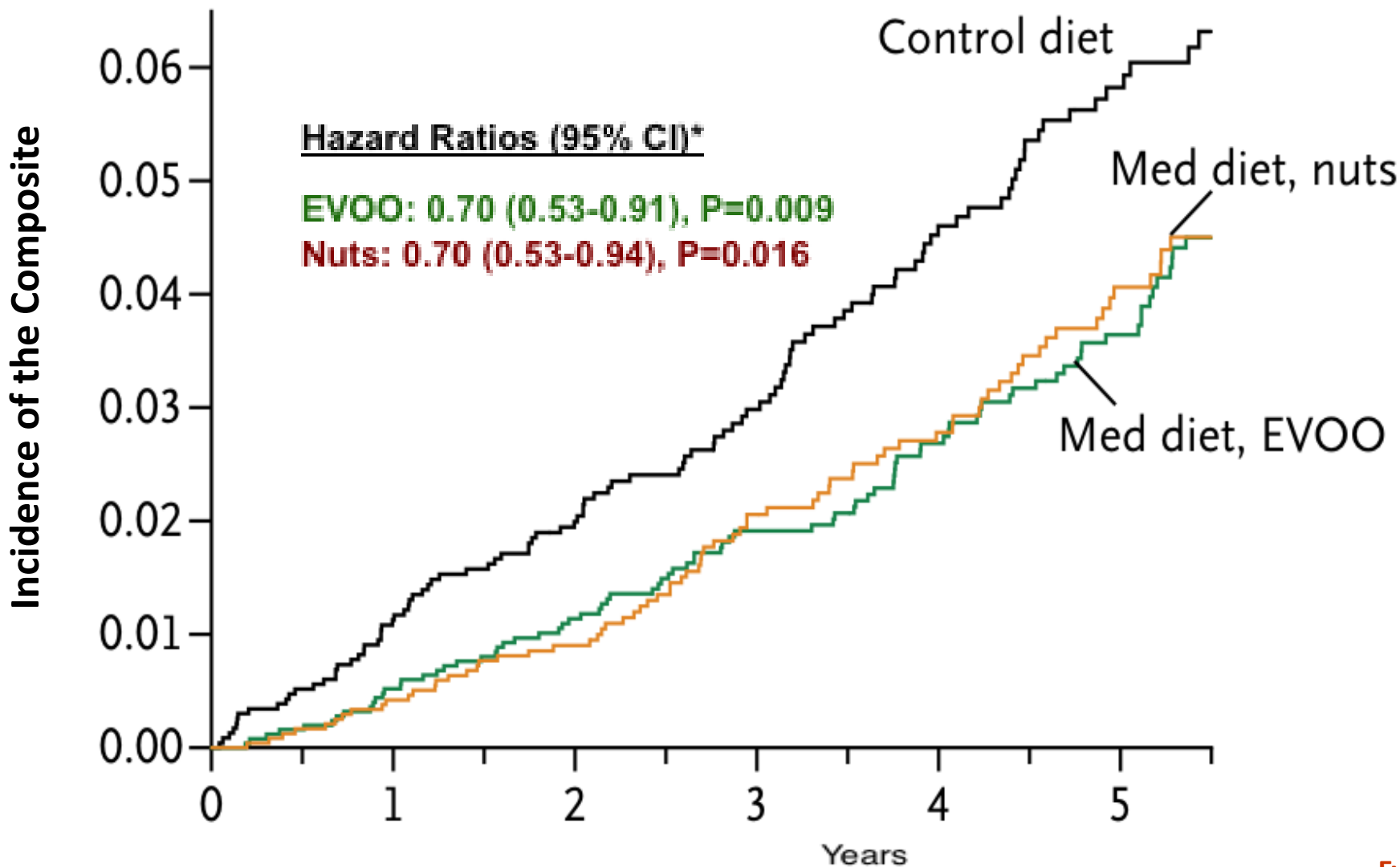
Adherence to MedDiet plus Virgin Olive Oil intervention



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	Events
Control group	2450	2268	2020	1583	1268	946	109
MeDiet+EVOO	2543	2486	2320	1987	1687	1310	96
MeDiet+Nuts	2454	2343	2093	1657	1389	1031	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

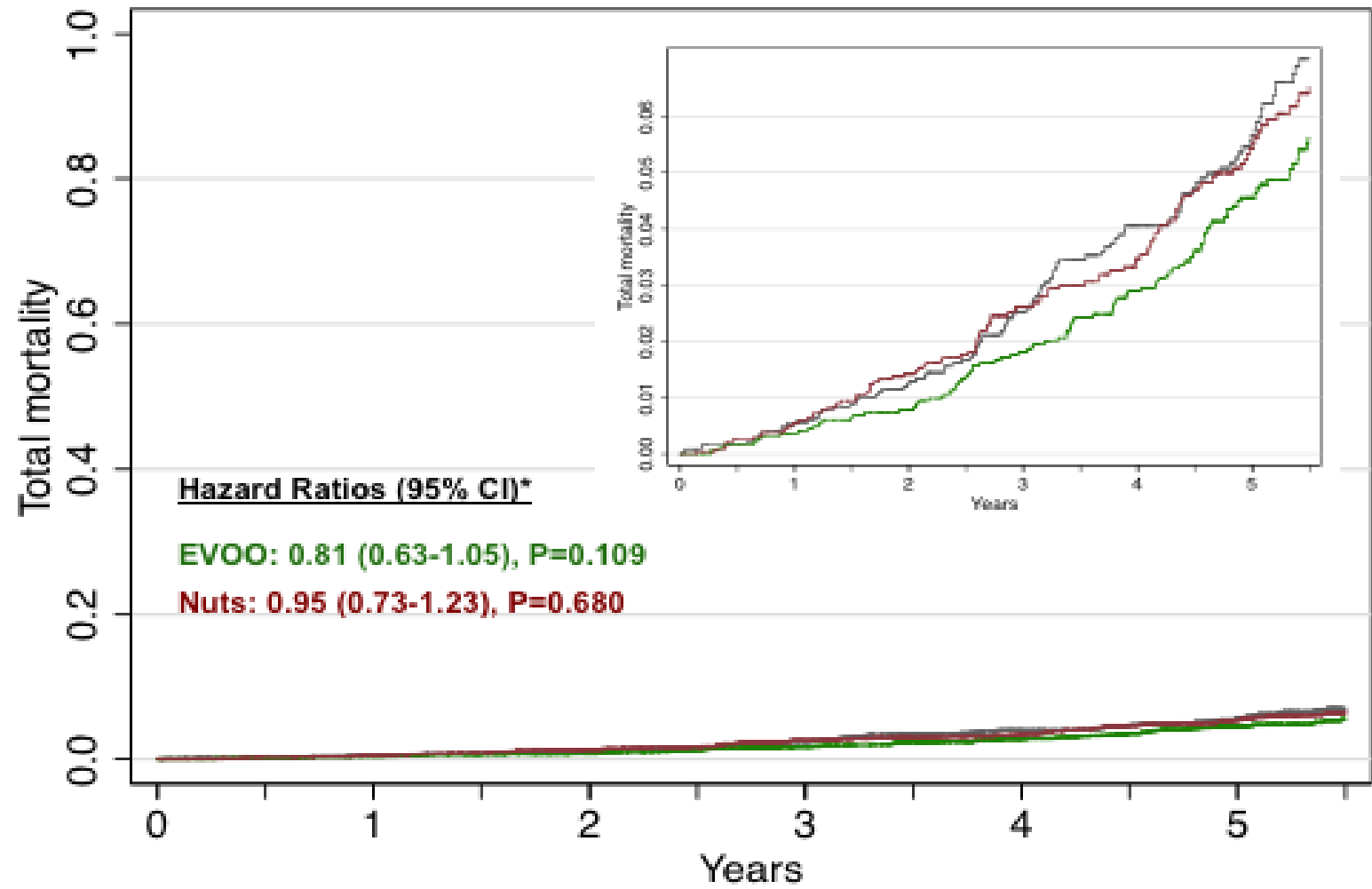
∫ Stratified by recruiting Center and adjusted by age, sex, family history of CHD, and smoking

¶ 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)



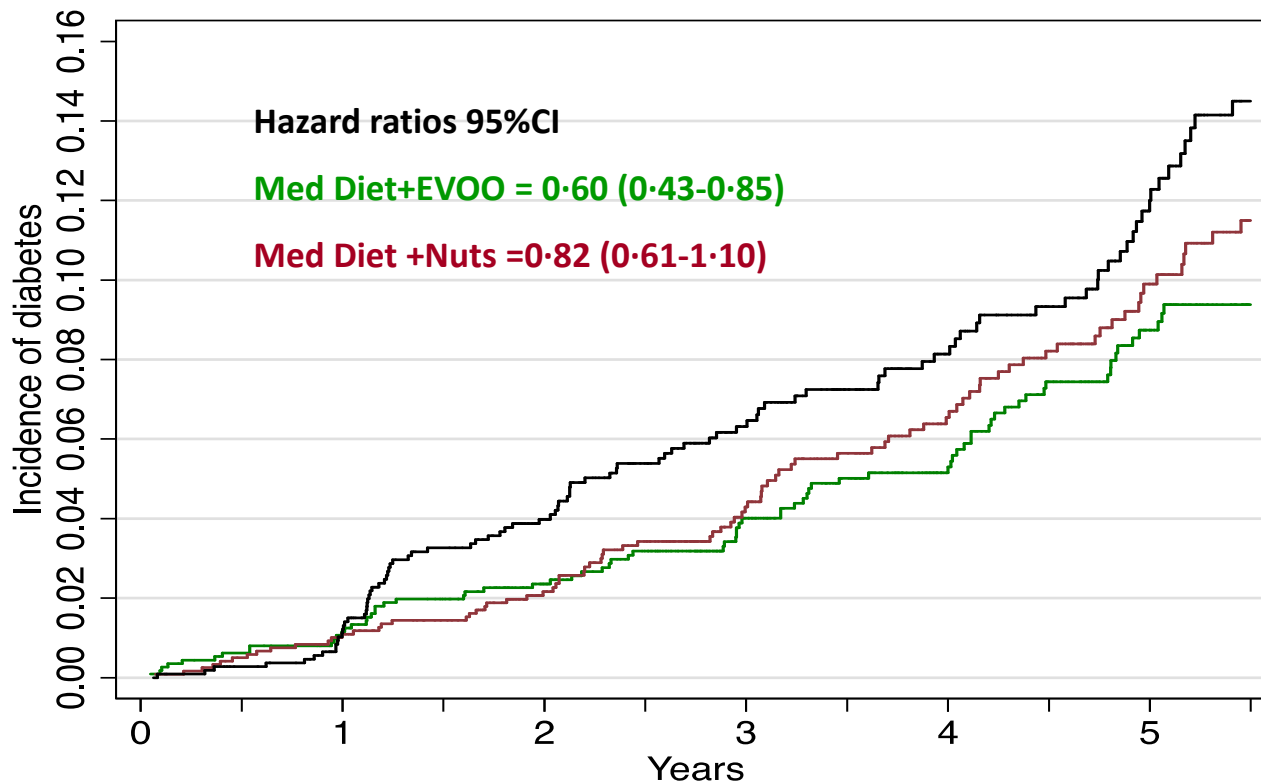
Number at risk	0	1	2	3	4	5
Control group	2450	2268	2026	1585	1272	948
MeDiet+EVOO	2543	2485	2322	1988	1690	1308
MeDiet+Nuts	2454	2345	2097	1662	1395	1037

The PREDIMED Study-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.**



The PREDIMED Study (n= 3541 non-diabetes at baseline). Cumulative diabetes incidence by group of intervention. Aalen-Nelson curves with outcome of diabetes onset and exposure to MedDiet intervention group vs. control



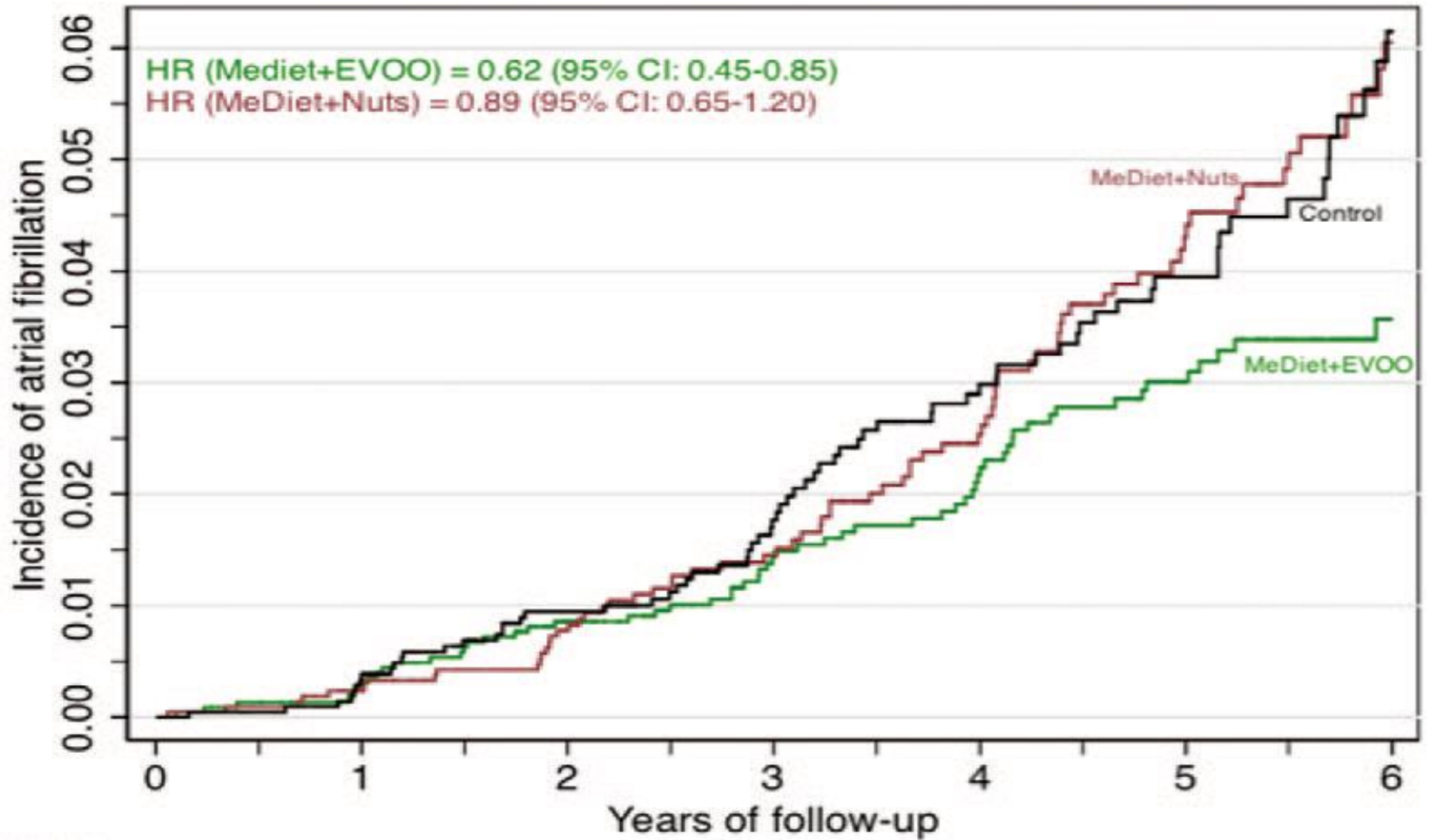
Number at risk

Group = MeDiet+EVOO	1135	1109	996	830	681	488
Group = MeDiet+nuts	1201	1172	1000	774	629	427
Group = Control	1092	1052	901	678	522	367

Extra-Virgin Olive Oil Consumption Reduces Risk of Atrial Fibrillation

The PREDIMED (Prevención con Dieta Mediterránea) Trial.

Martínez-González et al. Circulation 2014



Number at risk		0	1	2	3	4	5	6
MeDiet+EVOO	2292	2234	2097	1798	1511	1144	496	
MeDiet+Nuts	2210	2113	1899	1499	1244	903	387	
Control	2203	2044	1837	1438	1152	851	358	

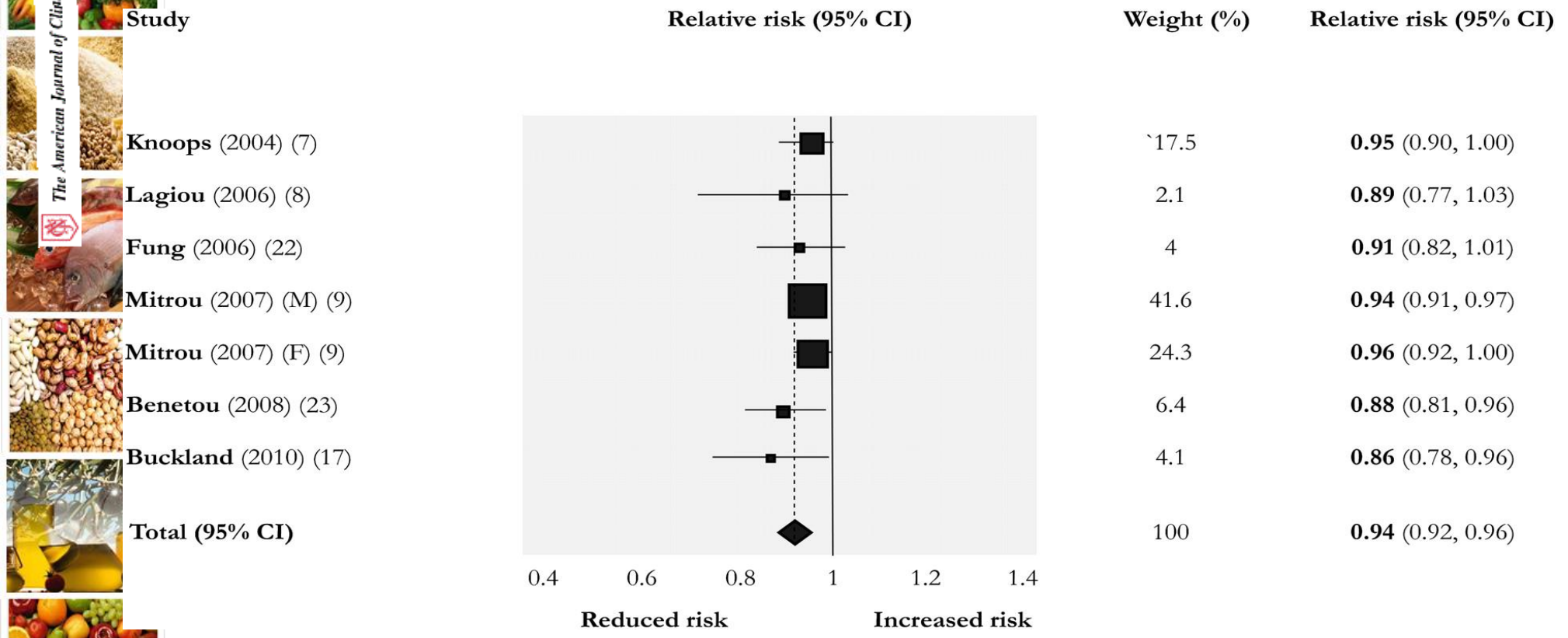
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Mediterranean Diet and Cancer



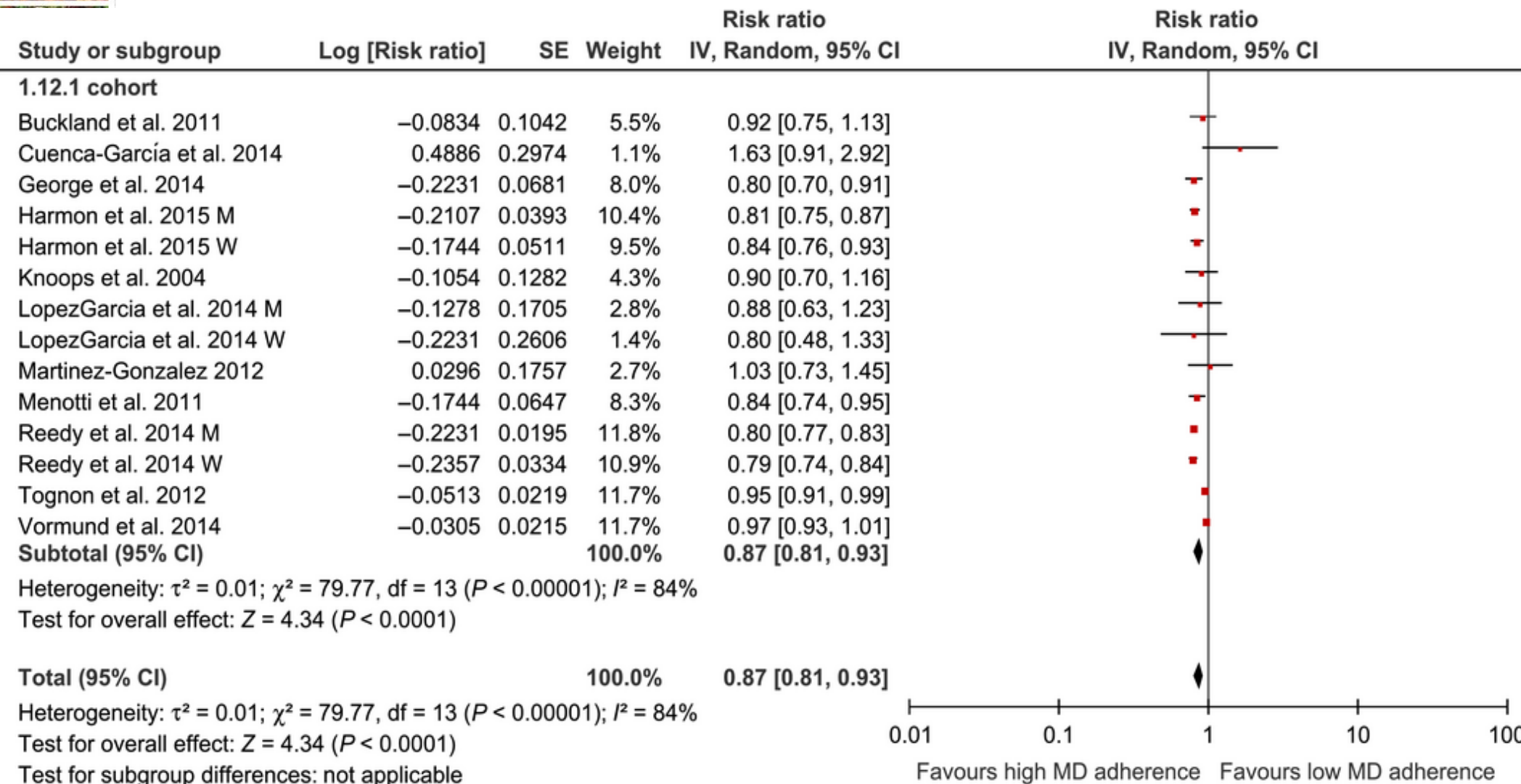
Forest plot of the association between a 2-point increase of adherence score to the Mediterranean diet and the risk of mortality from or incidence of neoplastic diseases

The American Journal of Clinical Nutrition



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

Adherence to Mediterranean diet and risk of cancer: an updated systematic review and meta-analysis of observational studies. Overall cancer mortality





RISK RATIO/ODDS RATIO OF CANCER TYPE INCIDENCE ASSOCIATED WITH THE HIGHEST ADHERENCE TO MEDITERRANEAN DIETARY PATTERN.

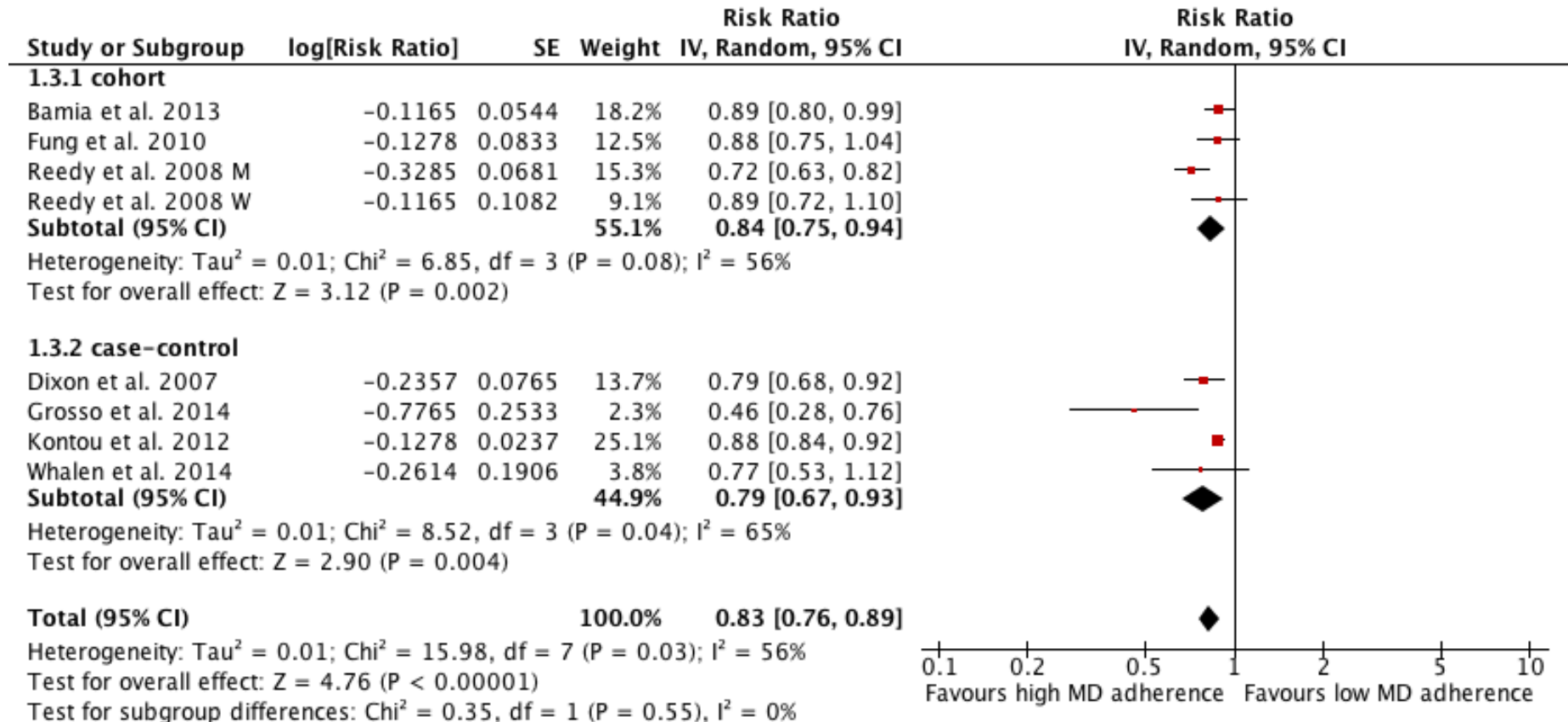
Outcome	No of studies	Study type	Risk ratio/odds ratio 95% CI
Colorectal	7	Combined	0.83
	3	Cohort	0.84
	4	Case-control	0.79
Breast	12	Combined	0.93
	4	Cohort	0.99

No significant association was observed between adherence to a Mediterranean Diet and risk of mortality among cancer survivors or cancer recurrence.

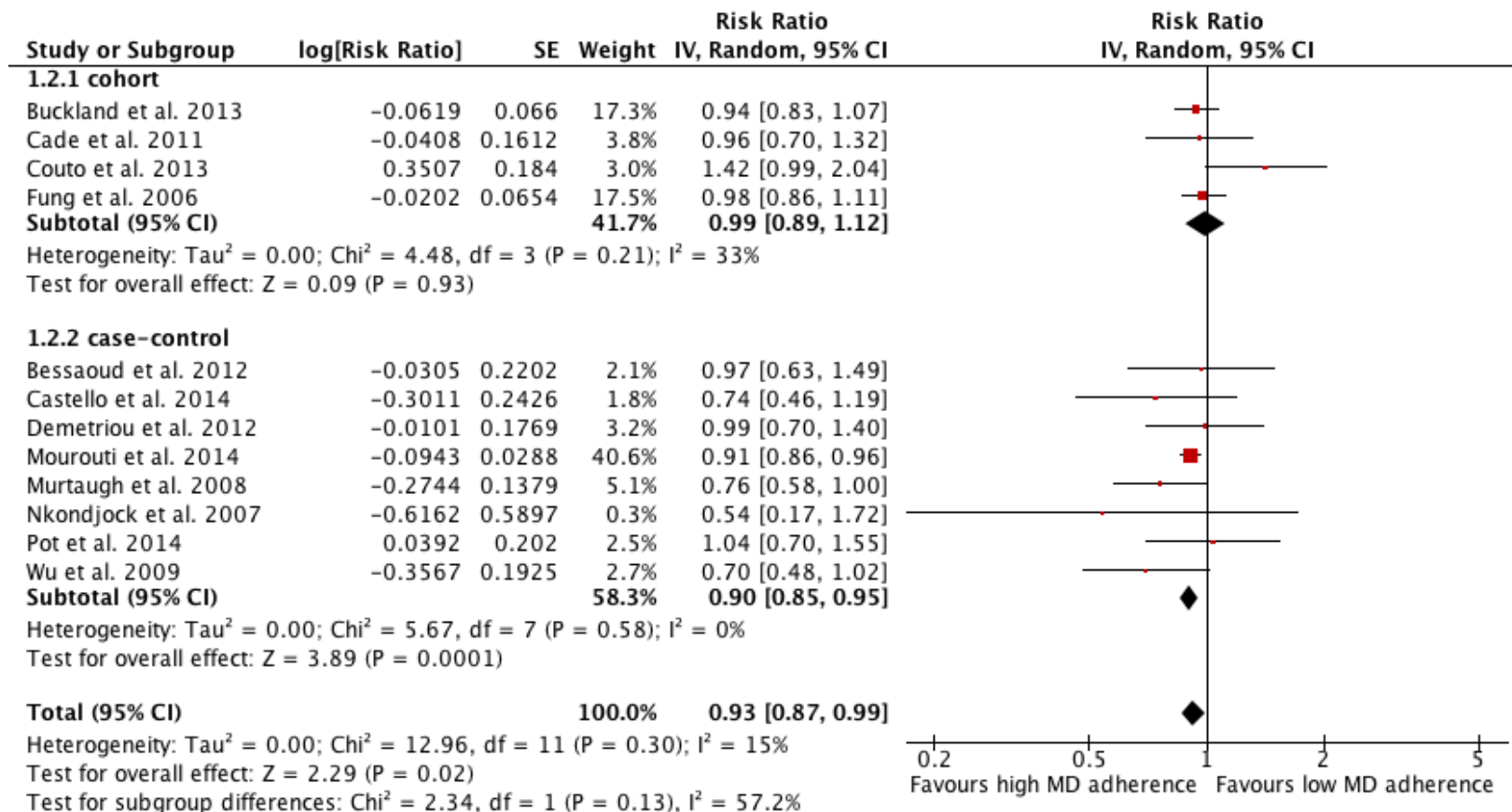
- **Prostate**
- **Gastric cancer**
- **Liver cancer**
- **Esophageal**
- **Head and neck**
- **Endometrial**
- **Respiratory**
- **Bladder**
- **Pancreatic**

	1	Cohort	0.51	0.55-1.14
	3	Case-control	0.32	0.19-0.55
	3	Combined	0.72	0.40-1.31
	1	Cohort	0.98	0.82-1.17
	2	Case-control	0.61	0.29-1.29
	1	Cohort	0.10	0.10-0.70
	1	Cohort	0.84	0.69-1.02
	1	Case-control	0.48	0.35-0.66

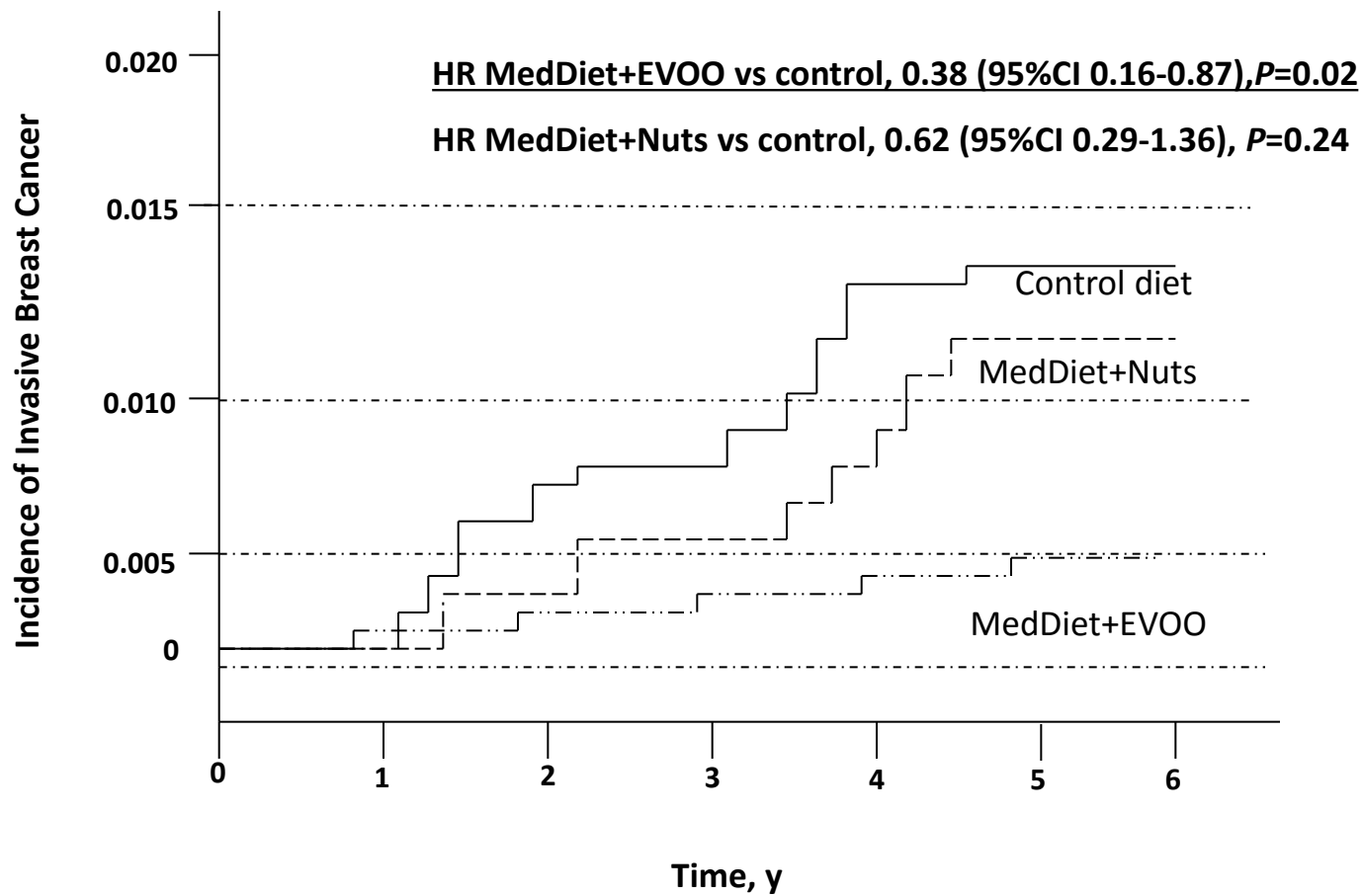
Forest plot showing pooled risk ratio (RRs) with 95% CI for risk of colorectal cancer for 3 cohort studies, and 4 case-control studies.



Forest plot showing pooled risk ratio (RRs) with 95% CI for risk of breast cancer for 4 cohort studies and 8 case-control studies.



The PREDIMED Study. Incidence of Invasive Breast Cancer According to Intervention Group





Conclusions

Adherence to a Mediterranean Diet is associated with lower risk of overall incidence and cancer mortality

Current data points out to an inverse association between the adherence to the Mediterranean Diet and colorectal, breast, and prostate cancers.

More data are needed to define an inverse association between the adherence to the Mediterranean Diet and gastric, liver, and respiratory cancers.



Mediterranean Diet, Cardiovascular Disease and Cancer

Evidence on the benefits of the
Mediterranean Diet on Secondary End
Points (Mechanisms)

Oxidation and Inflammation

The PREDIMED Study. Adjusted 1year Changes in Heart Failure Biomarkers. (n= 930). Mean (95%CI).



TMD + VOO TMD + Nuts Low-fat diet

P<0.05

P=0.004

P=0.038



NT-ProBNP ***-28 (-74 to -18)*** ***- 42 (-84 to -0.4)*** ***43 (-0.4 to 86)***

OxLDL ***-10 (-14 to -6)*** ***-6 (-10 to - 1.7)*** ***-1.5 (-5 to 1.5)***

Lp(a) ***0.7 (-2 to 3)*** ***2 (-0.2 to 5)*** ***5 (2 to 8)***

Adjusted by sex, age, centre, and physical activity. Adjusted by LDL/HDL cholesterol ratio for lipid variables

The PREDIMED Study. MedDiet improves systemic oxidative damage in female with Metabolic Syndrome (n= 110). Mean \pm SD

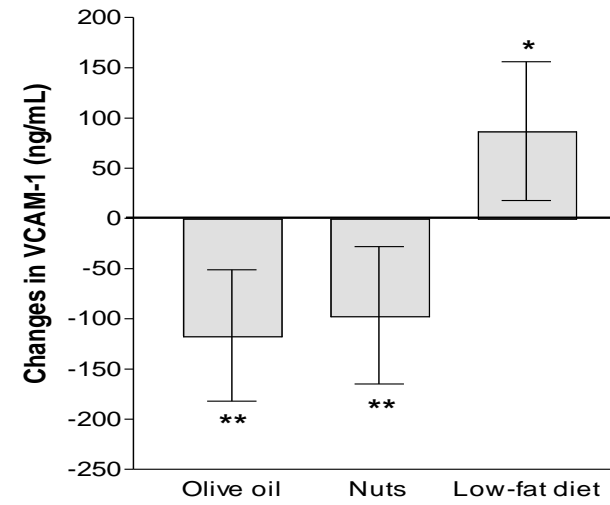
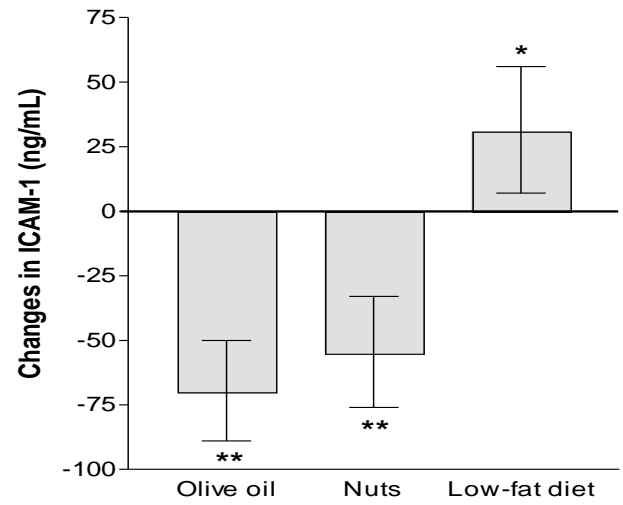
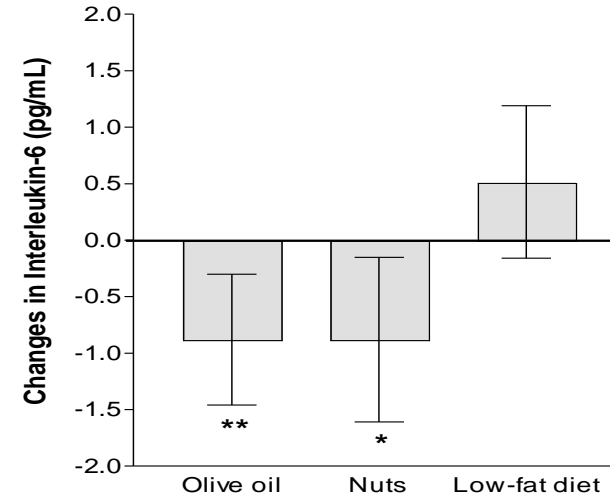
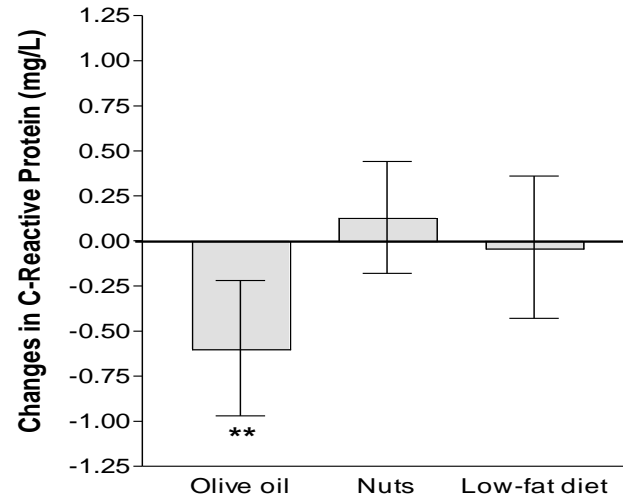
	MedDiet + VOO	MedDiet + Nuts	Low-fat diet
 8-oxo-dGuo	-9.8 (0.58)*	- 11.0 (0.60)*	-1.3 (0.58)*
 F2-isoprostanes	-13.7 (1.94)*	-14.8 (1.81)*	-9.3 (1.73)*

P < 0.001

Adjusted by baseline and prevalence of the blood pressure MetS component

** P < 0.001 vs its baseline*

Changes from baseline in plasma inflammatory biomarkers. The PREDIMED Study (n = 772)




Estruch et al. Ann Int Med, 2006. Olive oil and Nuts, traditional Mediterranean diet enriched with virgin olive oil or nuts, respectively



Metanalysis of randomized controlled trials assessing the effects of an MedDiet on outcomes of endothelial function and inflammation.

17 trials (N= 2300) MetDiet adherence resulted in a decrease [WMD, 95% CI] of :

- 1) **hs CRP** [-0.98 mg/l, -1.48 to -0.49, $p < 0.0001$]
- 2) **Interleukin-6** [-0.42 pg/ml, -0.73 to -0.11, $p = 0.008$]
- 3) **ICAM-1** [-23.73 ng/ml, -41.24 to -6.22 $p = 0.008$]



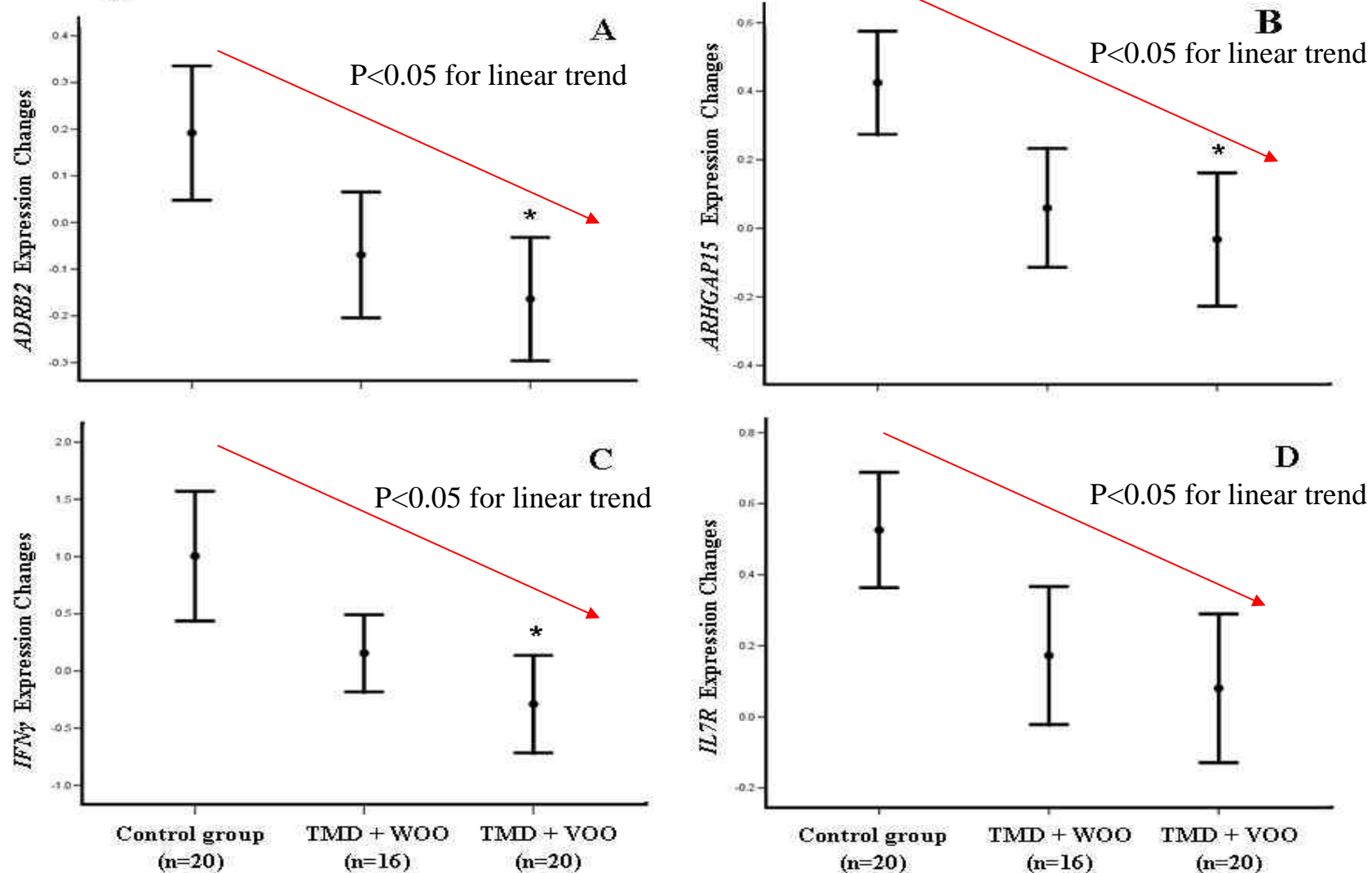
Molecular mechanisms by which the Mediterranean Diet can exert benefits for health

Nutrigenomics

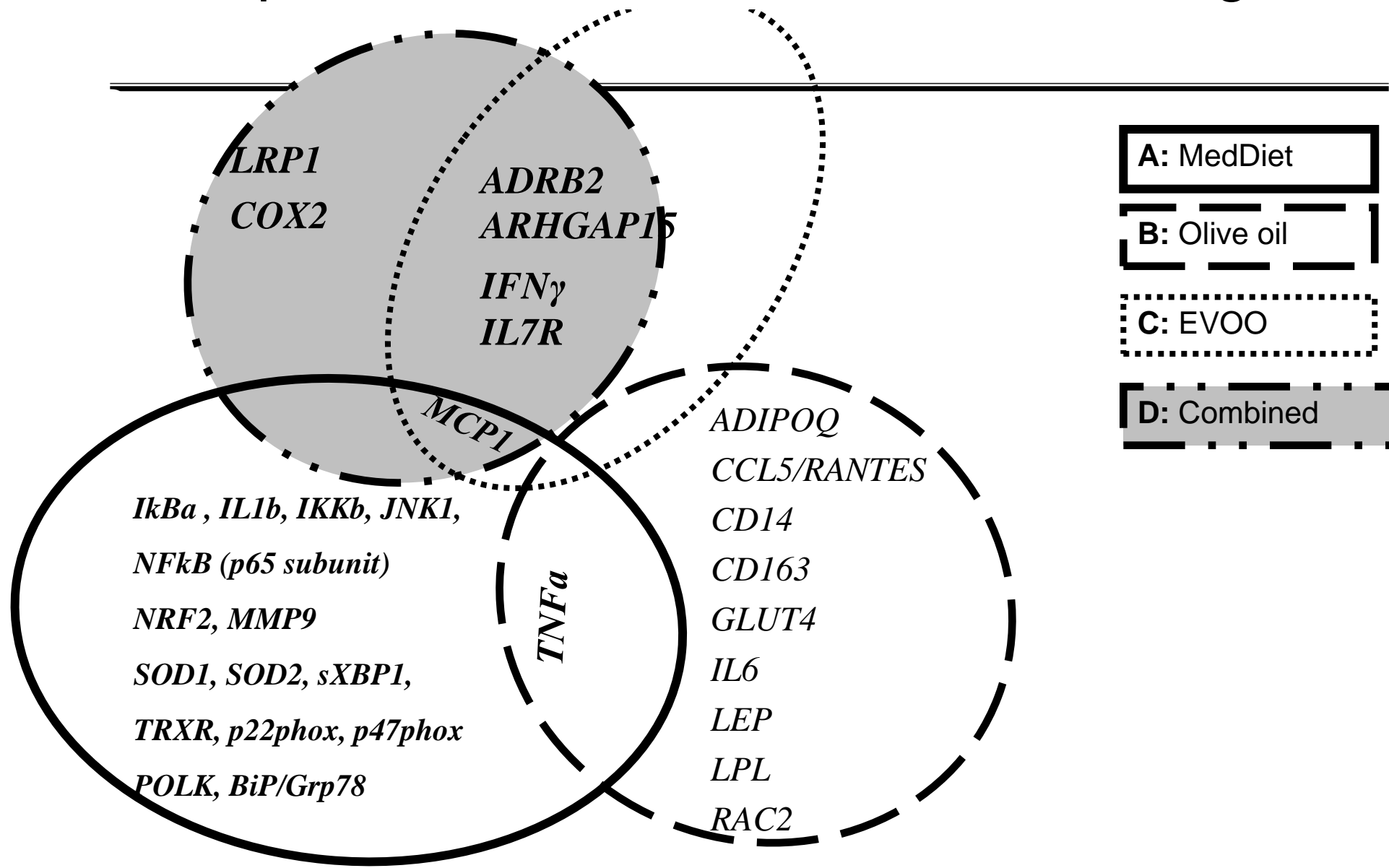
Mediterranean diet modulate the expression of
atherosclerosis-related genes toward a
protective mode

Changes in inflammatory genes after 3-month consumption of Habitual diet (Control) and Mediterranean diet with washed virgin olive oil (TMD+WOO) or virgin olive oil (PC=366 mg/kg) (TMD+VOO) (n =90, healthy volunteers)

Figure 3.

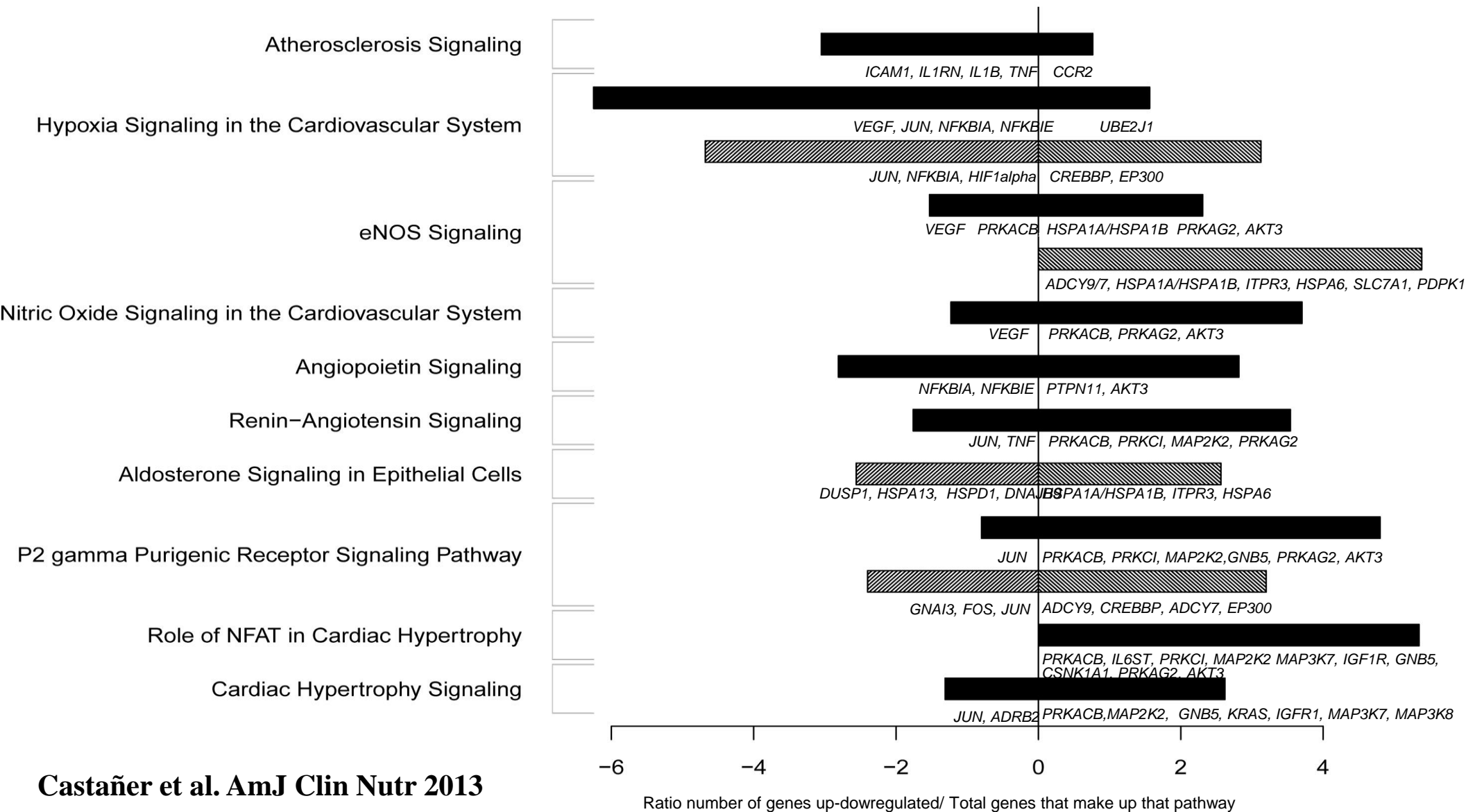


Decreased expression of atherosclerosis-related genes



The PREDIMED Study. PREDIGENE substudy (n=30, Microarray)

- TMD+VOO
- ▨ TMD+NUTS
- LFD-CONTROL





Conclusions

The Mediterranean Diet is an useful tool for protecting against cardiovascular disease and cancer

This protection involves a reduction of the lipid and DNA oxidative damage and of the chronic and acute inflammation

Molecular mechanisms involved *in vivo* in humans

A nutrigenomic effect regulating the expression of atherosclerosis-related genes toward a protective mode

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.



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ciberobn

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Physiopathology of Obesity and Nutrition.
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Ministry of Science and Innovation

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RETICS RD06/0045/0003

Programa INGENIO CONSOLIDER 2010, FUN-C-
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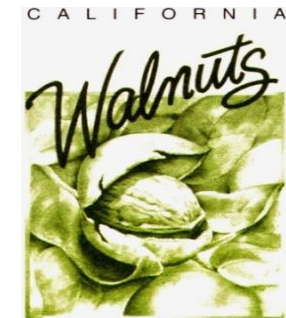


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LA MORELLA NUTS



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GRACIES PER LA VOSTRA ATENCIÓ

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

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



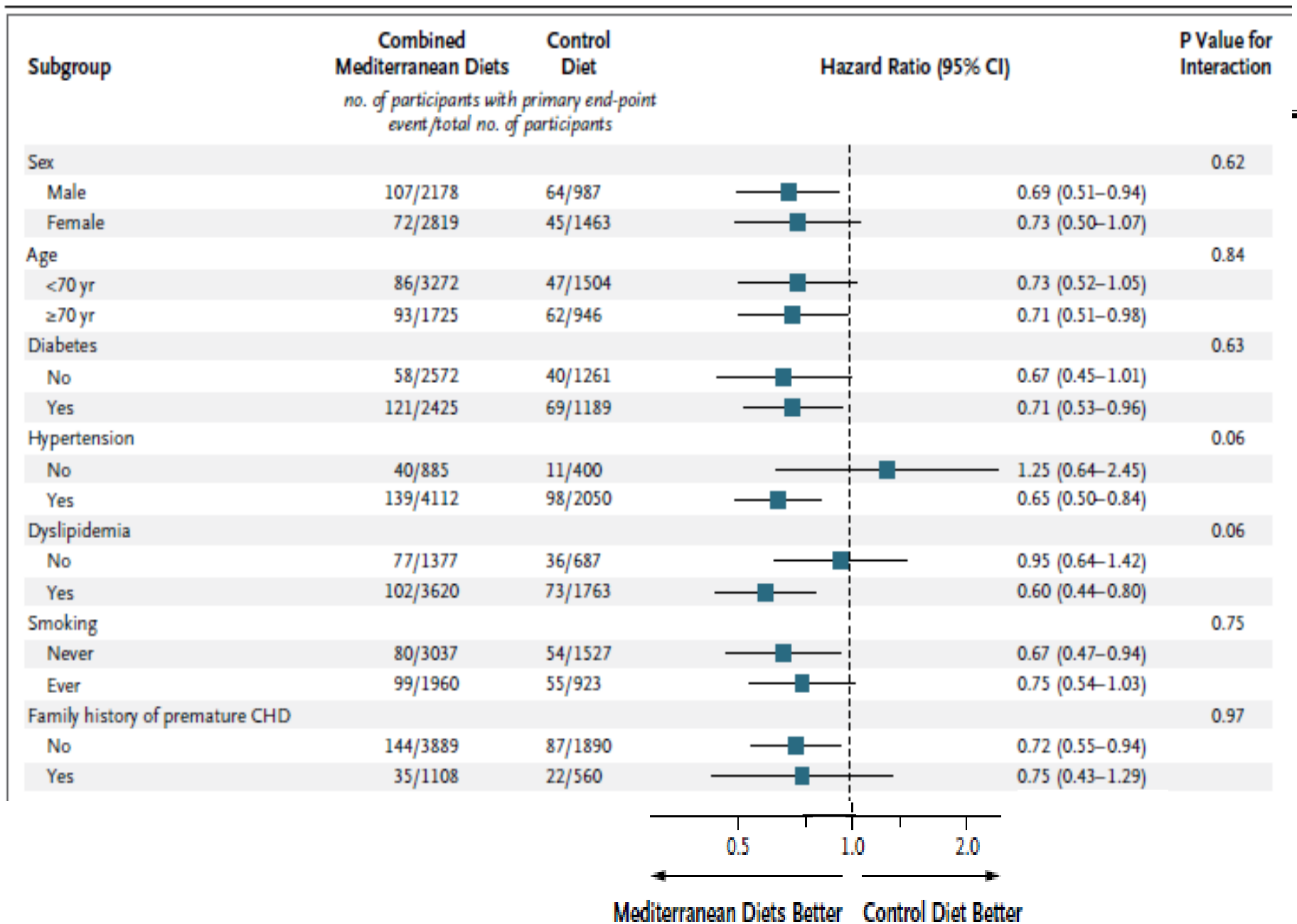
Measurements

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				

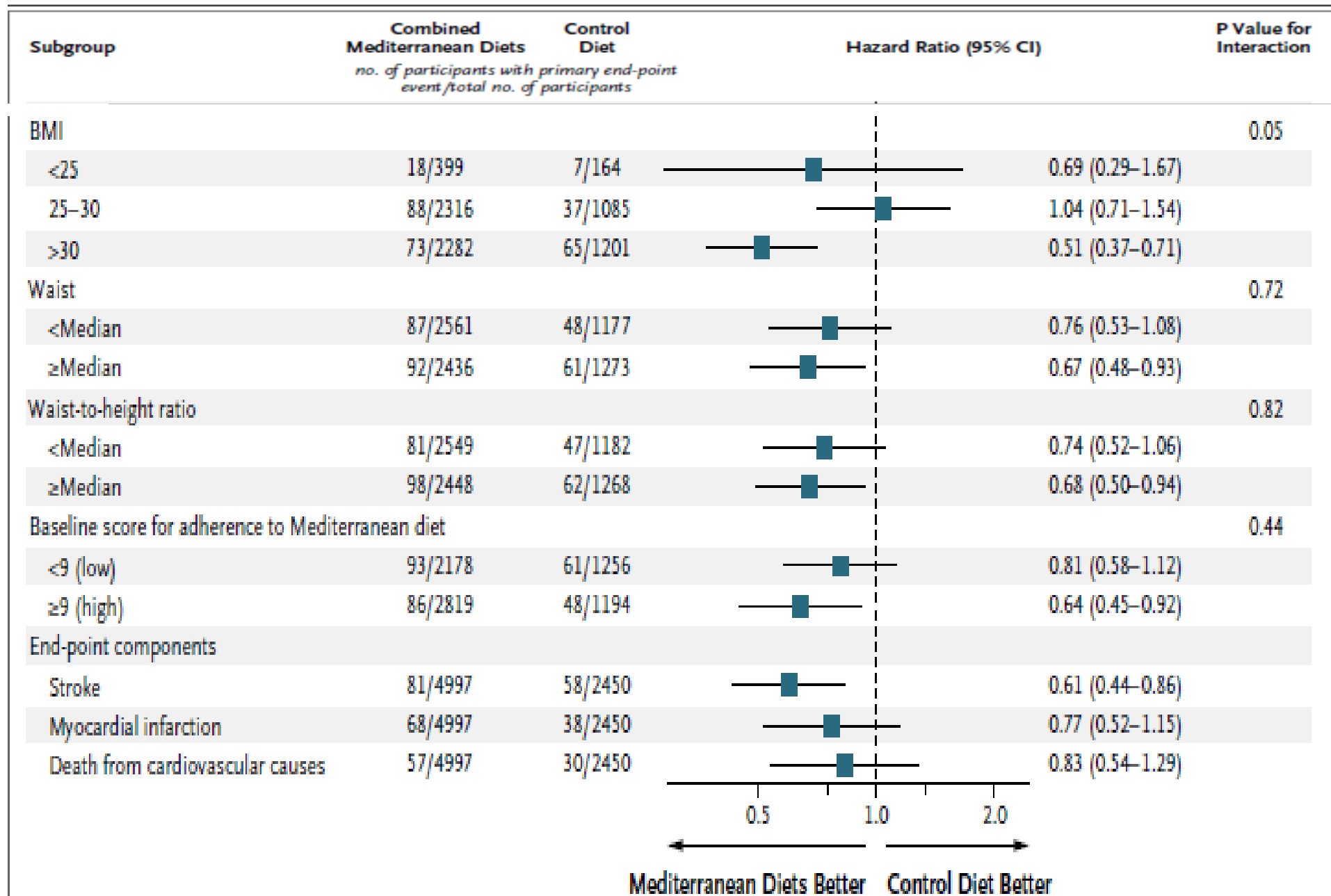
* *Specific measurements*
Intervention compliance
assessment

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

The PREDIMED Study. Subgroup analyses



The PREDIMED Study. Subgroup analyses





2. RISK RATIO/ODDS RATIO ASSOCIATED WITH THE HIGHEST ADHERENCE TO MEDITERRANEAN DIETARY PATTERN.

Outcome	No of studies	Study type	Risk ratio/odds ratio	95% CI	I ² (%)
Colorectal cancer	7	Combined	0.83	0.76–0.89	56
	3	Cohort	0.84	0.75–0.94	56
	4	Case-control	0.79	0.67–0.93	65
Breast cancer	12	Combined	0.93	0.87–0.99	15
	4	Cohort	0.99	0.89–1.12	33
	8	Case-control	0.90	0.85–0.95	0
Prostate cancer	4	Combined	0.96	0.92–1.00	0
	3	Cohort	0.96	0.92–1.00	0
	1	Case-control	1.03	0.81–1.31	n.a
Gastric cancer	3	Combined	0.73	0.55–0.97	66
	2	Cohort	0.82	0.61–1.10	49
	1	Case-control	0.57	0.45–0.72	n.a
Liver cancer	2	Combined	0.58	0.46–0.73	
	1	Cohort	0.62	0.47–0.82	n.a
	1	Case-control	0.51	0.34–0.77	n.a
Esophageal cancer	2	Combined	0.49	0.22–1.09	83
	1	Cohort	0.68	0.34–1.36	n.a
	1	Case-control	0.26	0.13–0.52	n.a
Head and neck cancer	4	Combined	0.40	0.24–0.66	90
	1	Cohort	0.61	0.33–1.14	n.a
	3	Case-control	0.32	0.19–0.55	83
Endometrial cancer	3	Combined	0.72	0.40–1.31	94
	1	Cohort	0.98	0.82–1.17	n.a
	2	Case-control	0.61	0.29–1.29	89
Respiratory cancer	1	Cohort	0.10	0.10–0.70	n.a
Bladder cancer	1	Cohort	0.84	0.69–1.02	n.a
Pancreatic cancer	1	Case-control	0.48	0.35–0.66	n.a

. With respect to types of cancer, the positive effects of an MD on colorectal carcinoma demonstrated in the first analysis could be confirmed by the inclusion of new studies. Additional evidence could be found with respect to distinct types of cancer such as liver cancer, or head and neck cancer, which were either not depicted in the original analysis due to lack of corresponding studies or had to be rearranged to fit into the adapted classification of cancer types used for the update. Furthermore, an inverse association could be observed for breast cancer and gastric cancer risk (taking into account the exclusion of Tognon et al., who reported only on cancer-specific mortality cases). Some data must be interpreted with caution, since the number of observations dealing with these types of cancer are still low (e.g., liver cancer). Likewise, the effects of an MD on breast cancer will remain a matter of debate. The inverse association of an MD dietary pattern after pooling only case-control studies was present in the original analysis and is now further substantiated by three additional studies. However, pooling cohort studies (which are characterized by a higher level of evidence) did not confirm these results (there are no additional cohorts in this update). For future studies, it might be interesting to differentiate between post and premenopausal breast cancer or even to classify breast cancer according to receptor type.

. However, we could not find a significant correlation between adherence to an MD and risk of cancer mortality and cancer recurrence.



The PREDIMED Study-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.



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

The PREDIMED Study-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.








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



Evidence pro the Mediterranean type Diet . Clinical Trials. Secondary End Points

Effect of a Mediterranean-Style Diet, on Endothelial Dysfunction, Vascular Inflammation in the metabolic Syndrome.

Esposito K , Marfella R, Ciotola M, et al. JAMA 2004;292:1440-1446



180 Italians with Metabolic Syndrome. 2 years-Intervention study.

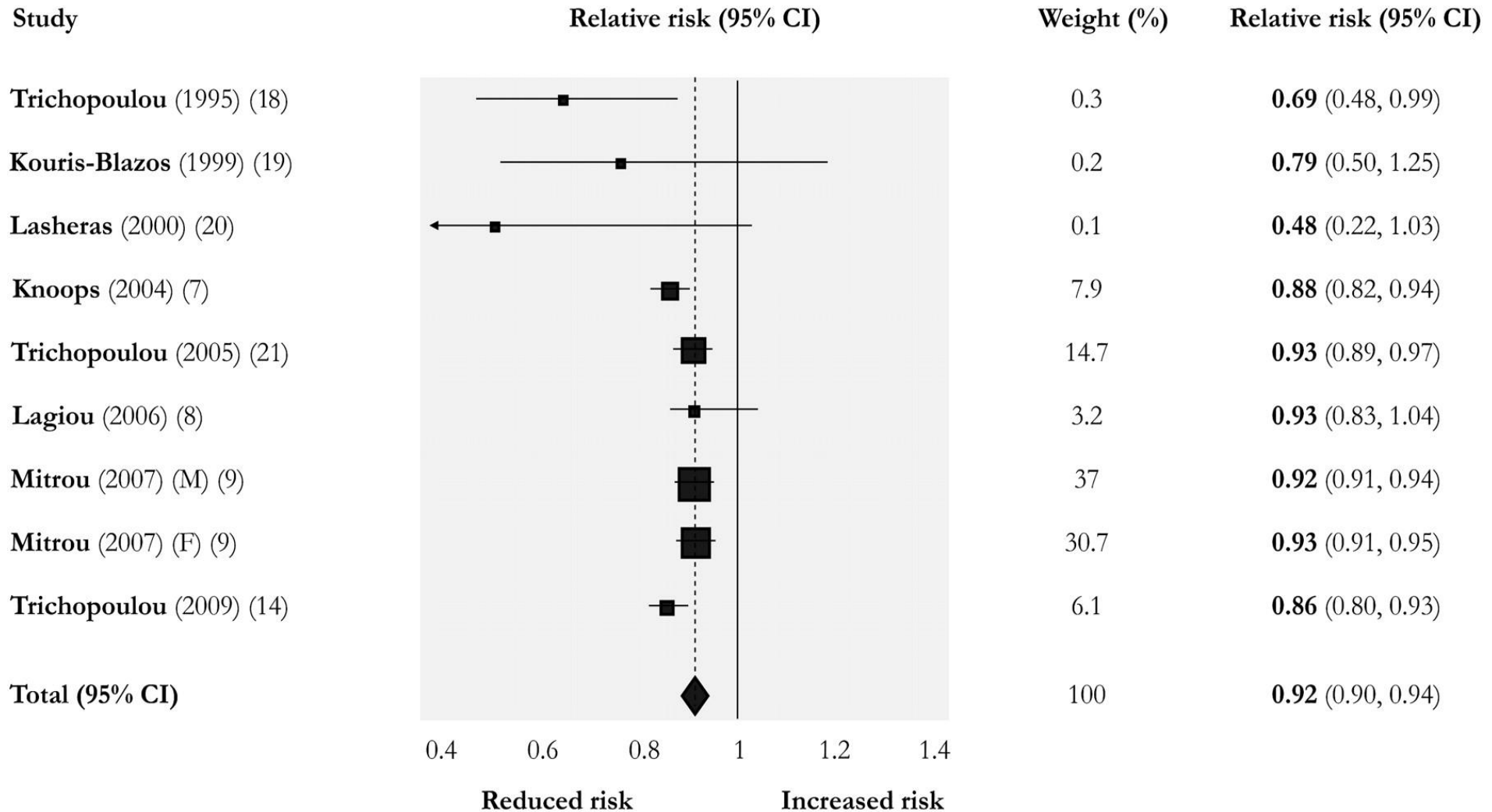
Significative reductions in :

- hs-CRP , Interleukines ,
- BMI,
- Glucose. Insulin, HOMA
- SBP and DBP
- Total cholesterol and triglycerides

Increase in HDL cholesterol



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



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/m² (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)