



# WINE, MEDITERRANEAN DIET AND NEURODEGENERATIVE DISORDERS

**Ramon Estruch**  
**Dept. Internal Medicine – Hospital Clinic**  
**University of Barcelona, Spain**

# Global health status in 2020

....3 out of 5 persons will die from chronic diseases

- 50 million with Alzheimer's Disease, numbers predicted to double every 20 years
- 7% of the world population will have diabetes

➤ It is critical to emphasize prevention!



# Lifestyle & Cognitive Function

## Persuasive evidence in humans

Association of improved cognition with:

- Educational level
- Professional achievement
- Intensity of social interactions
- Physical activity
- **Improved nutrition**





# Diet & Cognitive Function

## Persuasive evidence from animal experiments

Protection against deterioration of brain function and improvement in motor and cognitive tasks with extracts of:

- *Ginkgo biloba*
- curcumin (curry)
- apples
- berries
- grape juice
- walnuts
- cocoa
- spinach

# Diet & Cognitive Function: Weak evidence from epi studies/RCTs in humans

Association  $\pm$  of better cognitive function or reduced risk of dementia with diets rich in:

- fruits and vegetables
- seeds (whole grains, nuts, legumes, coffee)
- vitamins C, E &  $\beta$ -carotene
- folate & vitamin B<sub>12</sub>
- flavonoids
- olive oil
- fish (n-3 fatty acids)
- alcoholic beverages (red wine)
- tea





# Diet & Cognitive Function

Where the “single nutrient” approach has failed, perhaps the “whole diet” might help.

The current paradigm in nutritional epidemiology is to analyze dietary patterns instead of isolated foods or nutrients because they can capture the cumulative effects of the overall diet and the synergistic interaction of its food and nutrient components.

Mediterranean diet: paradigm of a healthy diet

# Mediterranean Diet

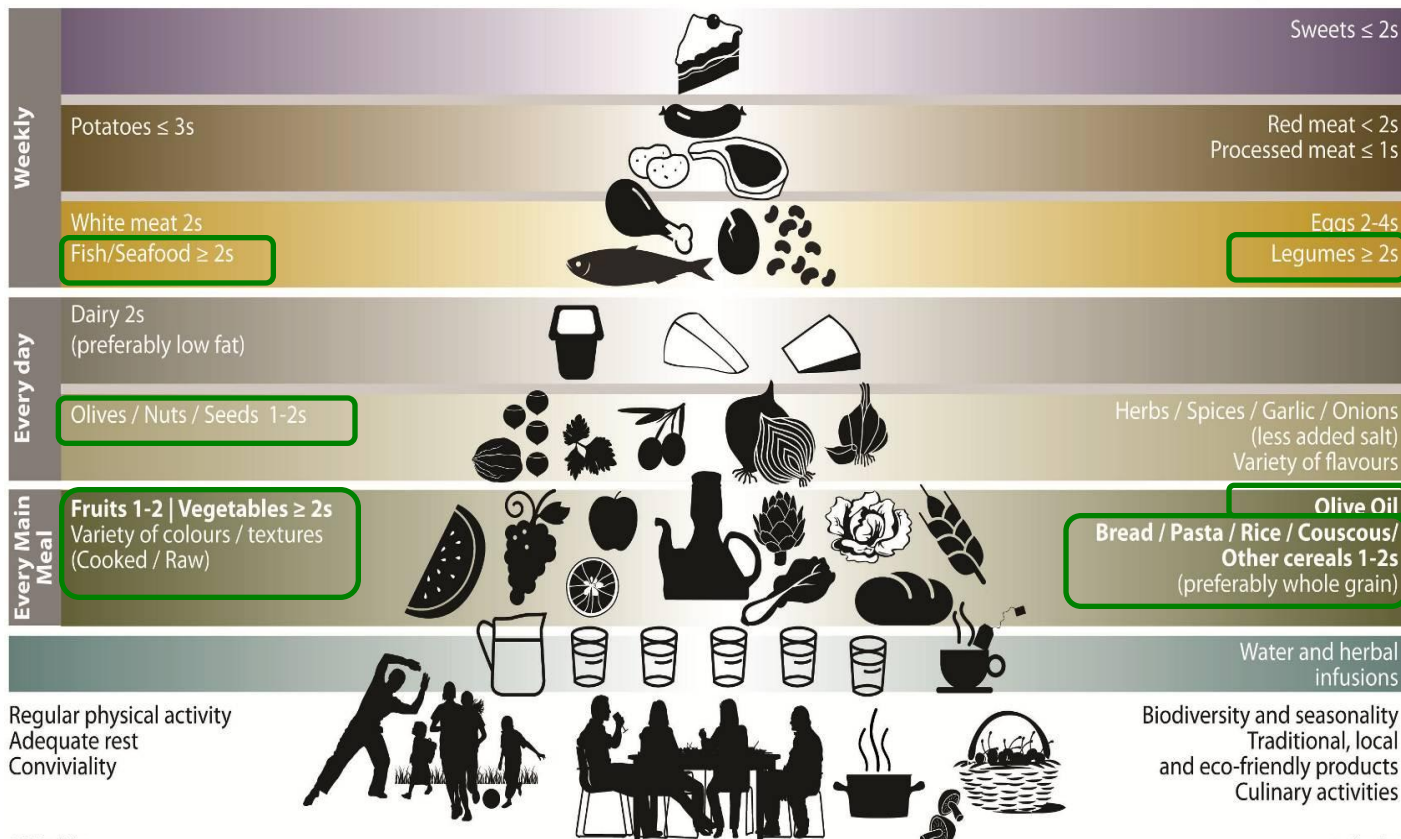
## HIGH INTAKE

### 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



2010 edition

# Mediterranean Diet

## MODERATE TO LOW INTAKE

### 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



# Recent reviews/meta-analyses on MeDiet & cognition/AD

*Proceedings of the Nutrition Society* (2013), **72**, 140–152  
© The Authors 2012

doi:10.1017/S0029665112002959

## Potential benefits of adherence to the Mediterranean diet on cognitive health

Catherine Féart\*, Cecilia Samieri, Benjamin Allès and Pascale Barberger-Gateau  
*INSERM; University of Bordeaux, ISPED, Centre INSERM U897-Epidemiologie-Biostatistique, F-33000  
Bordeaux, France*

### REVIEW ARTICLE

## Mediterranean Diet, Cognitive Function, and Dementia *A Systematic Review*

Ilianna Lourida,<sup>a</sup> Maya Soni,<sup>b</sup> Joanna Thompson-Coon,<sup>a</sup> Nitin Purandare,<sup>a†</sup> Iain A. Lang,<sup>a,c</sup>  
Obioha C. Ukoumunne,<sup>a</sup> and David J. Llewellyn<sup>b</sup>

(*Epidemiology* 2013;24: 479–489)

## Mediterranean Diet, Stroke, Cognitive Impairment, and Depression: A Meta-Analysis

Theodora Psaltopoulou, PhD,<sup>1</sup> Theodoros N. Sergentanis, MD,<sup>1</sup>  
Demosthenes B. Panagiotakos, PhD,<sup>2</sup> Ioannis N. Sergentanis, MD,<sup>1,3</sup>  
Rena Kosti, PhD,<sup>1</sup> and Nikolaos Scarmeas, MD, MSc, PhD<sup>4,5</sup>

*ANN NEUROL* 2013;74:580–591

*Journal of Alzheimer's Disease* 22 (2010) 715–740  
DOI 10.3233/JAD-2010-100942  
IOS Press

715

### Review

## Nutraceutical Properties of Mediterranean Diet and Cognitive Decline: Possible Underlying Mechanisms

Vincenza Frisardi<sup>a,\*</sup>, Francesco Panza<sup>b,\*</sup>, Davide Seripa<sup>b</sup>, Bruno P. Imbimbo<sup>c</sup>, Gianluigi Vendemiale<sup>d</sup>,  
Alberto Pilotto<sup>b</sup> and Vincenzo Solfrizzi<sup>a</sup>

*Journal of Alzheimer's Disease* 39 (2014) 271–282  
DOI 10.3233/JAD-130830  
IOS Press

271

## Association of Mediterranean Diet with Mild Cognitive Impairment and Alzheimer's Disease: A Systematic Review and Meta-Analysis

Balwinder Singh<sup>a,d</sup>, Ajay K. Parsaik<sup>a</sup>, Michelle M. Mielke<sup>b</sup>, Patricia J. Erwin<sup>c</sup>, David S. Knopman<sup>a</sup>,  
Ronald C. Petersen<sup>a,b</sup> and Rosebud O. Roberts<sup>a,b,\*</sup>

# Adherence to MeDiet & risk for cognitive impairment/AD

## 4.3 Highest vs Lowest MeDi tertile

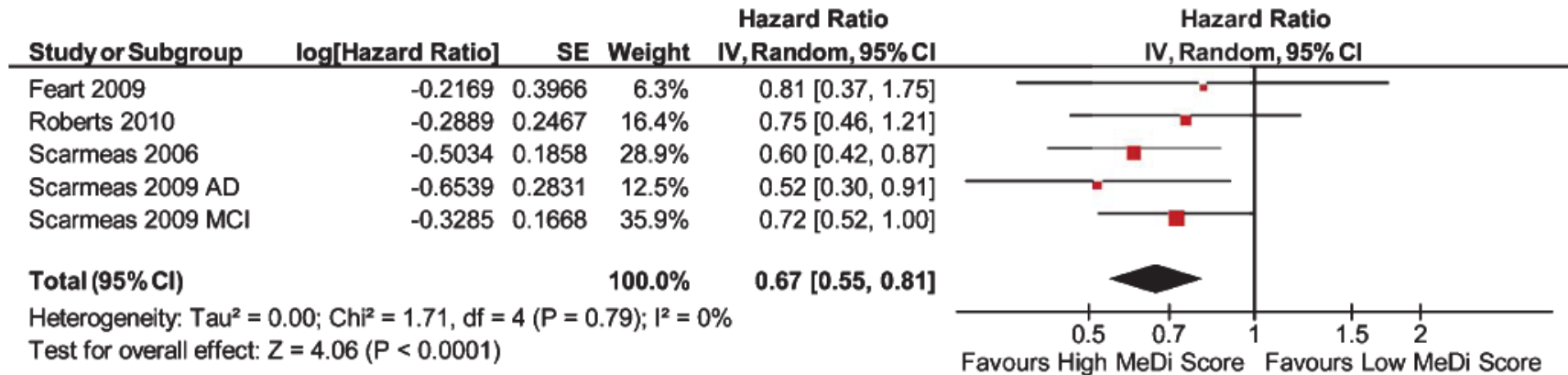


Fig. 4. Summary adherence to the Mediterranean diet and risk of cognitive impairment.

## 3.3 Highest vs Lowest MeDi tertile

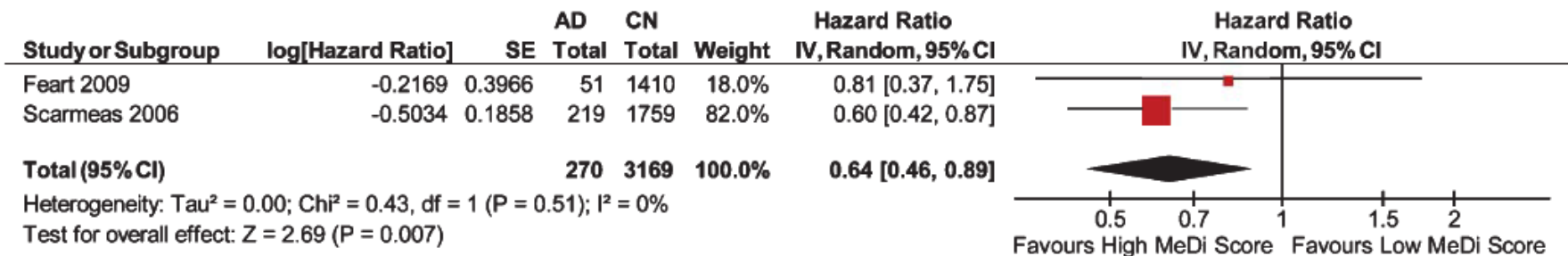


Fig. 3. Summary of adherence to the Mediterranean diet and risk of Alzheimer's disease among cognitively normal individuals at baseline.

# **MeDiet & cognitive impairment/AD.**

## **Epidemiology**

Recent epidemiological studies provide suggestive evidence that higher adherence to a Mediterranean-type diet could be associated with:

- Slower cognitive decline
- Reduced risk of progression from MCI to AD
- Reduced risk of AD
- Decreased mortality in AD patients
- Decreased risk of depression and stroke

# Hierarchy of Evidence-based Medicine



**Systematic Revisions - Meta-analyses**  
**Large Multicenter Clinical Trials**

**Randomized Clinical Trials**

**Non-Randomized Controlled Studies**

**Cohort Studies**

**Case – Control Studies**

**Case Series**

# Effects of Mediterranean Diet on Primary Prevention of Cardiovascular Disease (PREDIMED Study)





# Primary Aims

---

- To test the effect of a **Mediterranean Diet** enriched with **extra 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 moderate **wine** and **beer** intake on the risk of cardiovascular diseases

# PREDIMED TRIAL: DESIGN

All free of CVD at baseline

- ☐ 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

Random



Mediet +  
Virgin Olive Oil

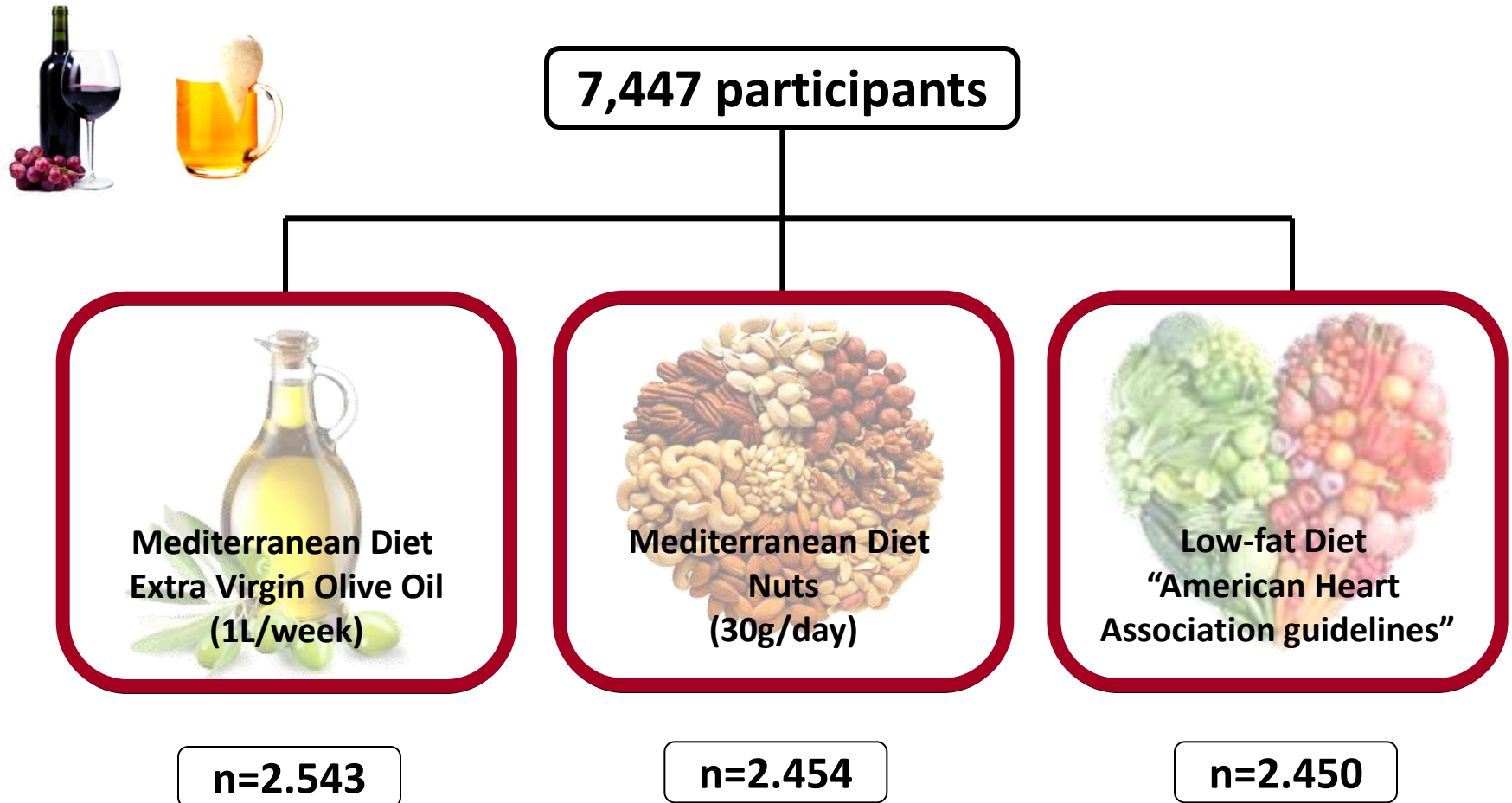


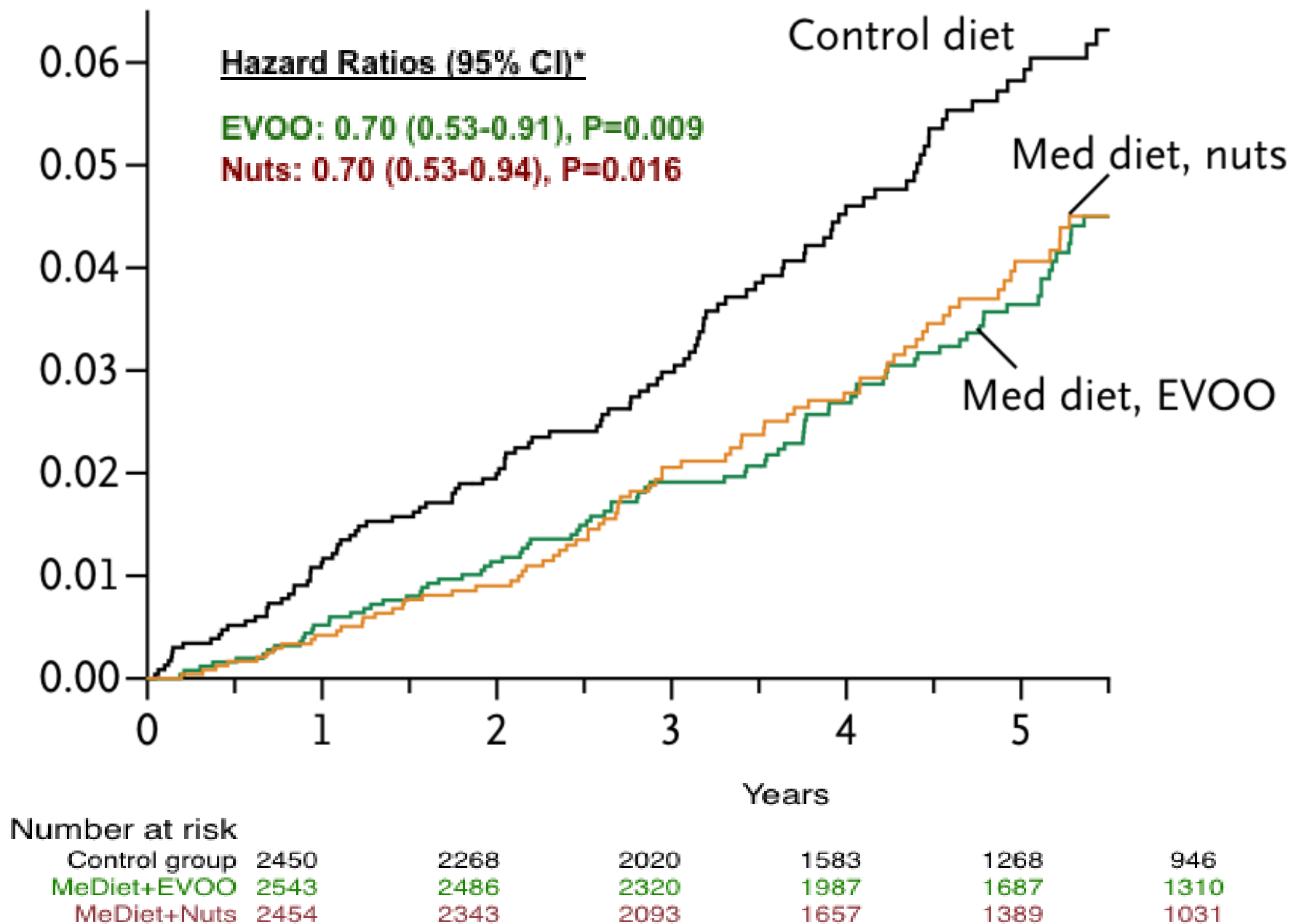
Mediet +  
Nuts



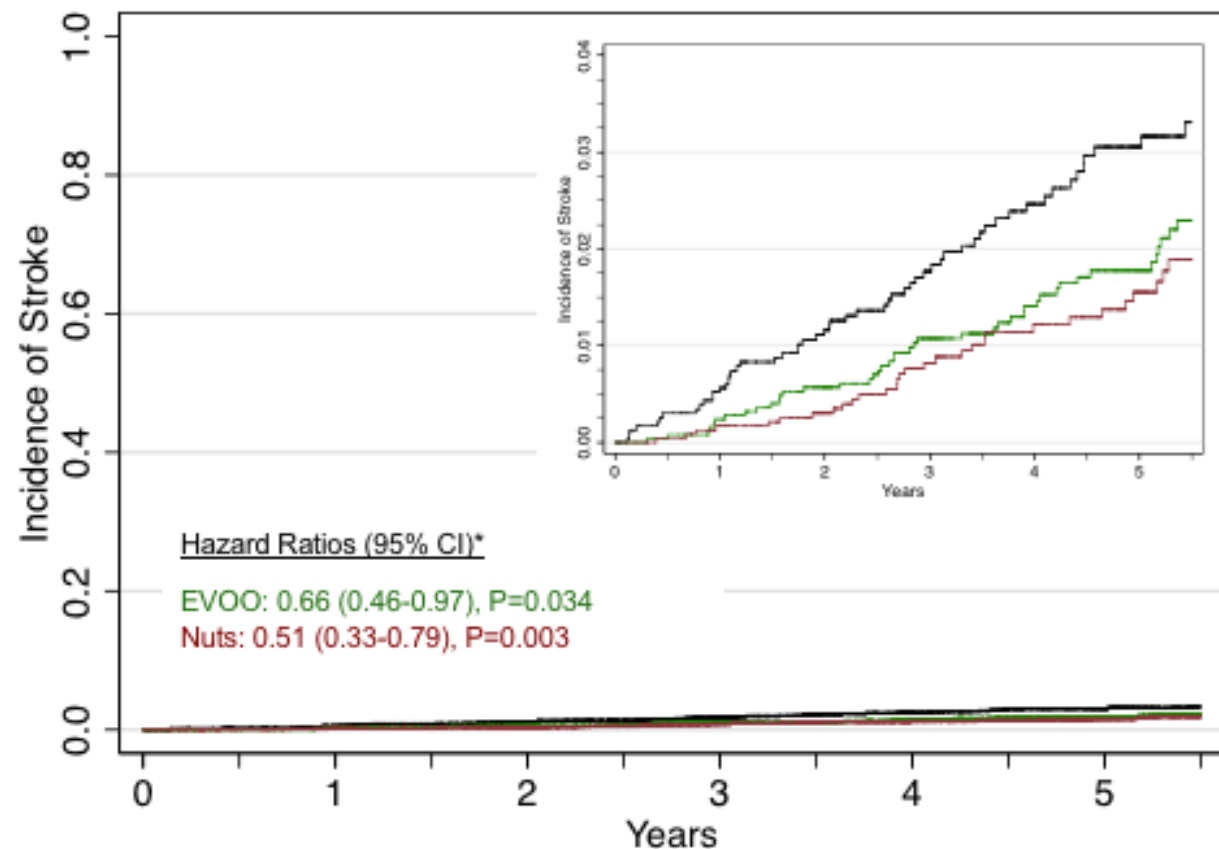
Control  
Low-fat

# Sample Size and Randomization





# Results: Stroke



Number at risk

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



# **PREDIMED sub study. Association of dietary habits with cognitive performance**

## **Aim**

**To assess whether consumption of key foods of the Mediterranean diet is associated with cognitive performance in older persons at high cardiovascular risk.**

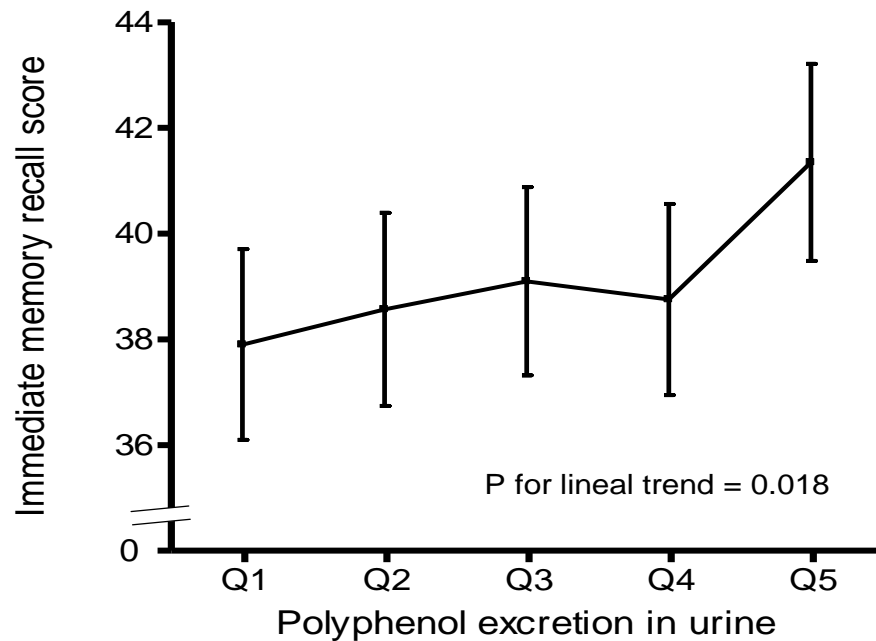
# PREDIMED – Diet & Cognition

NEUROPSYCHOLOGICAL TESTS	INDEPENDENT VARIABLES	B COEFFICIENT	BETA	P
MMSE (Overall cognitive function)	<b>Wine, per 200 ml/d</b>	<b>0.252</b>	<b>0.096</b>	<b>0.044</b>
	Age, per 10 y	-0.405	-0.170	<0.001
	Education level, per 5 y	0.529	0.238	<0.001
	Diabetes	-0.289	-0.104	0.032
	Hypertension	-0.419	-0.132	0.006
RAVLT (Immediate recall)	<b>Total olive oil, per 10 g/d</b>	<b>0.755</b>	<b>0.109</b>	<b>0.014</b>
	<b>Cereal intake, per 40 g/d</b>	<b>-0.431</b>	<b>-0.098</b>	<b>0.032</b>
	Age, per 10 y	-5.079	-0.329	<0.001
	Sex (female)	2.549	0.142	0.002
	Education level, per 5 y	3.304	0.231	<0.001
RAVLT (Delayed recall)	<b>Virgin olive oil, per 10 g/d</b>	<b>0.163</b>	<b>0.094</b>	<b>0.037</b>
	<b>Coffee, per 50 ml/d</b>	<b>0.294</b>	<b>0.106</b>	<b>0.016</b>
	<b>Cereal intake, per 40 g/d</b>	<b>-0.235</b>	<b>-0.149</b>	<b>0.001</b>
	<b>Meat &amp; meat products, per 100 g/d</b>	<b>-0.845</b>	<b>-0.109</b>	<b>0.020</b>
	Age, per 10 y	-1.606	-0.288	<0.001
	Sex (female)	1.443	0.223	<0.001
	Education level, per 5 y	0.838	0.162	<0.001
	Hypertension	-0.735	0.098	0.003
Reverse digits (Working memory)	<b>Walnut intake, per 30 g/d</b>	<b>1.191</b>	<b>0.149</b>	<b>0.039</b>
	Education level, per 5 y	0.365	0.220	0.003

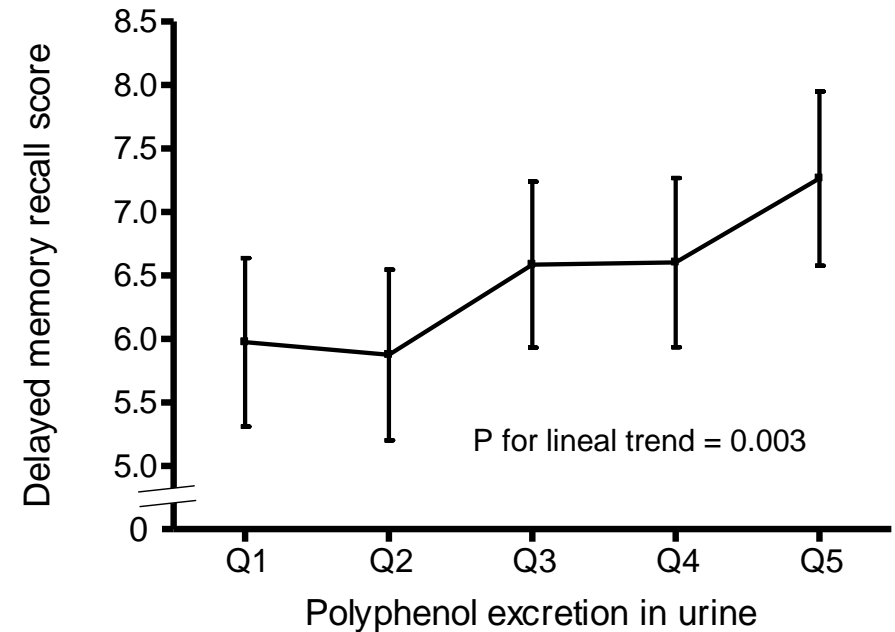
# PREDIMED – Diet & Cognition (I). Results (II)

## RAVLT memory test scores by quintiles of urinary polyphenol excretion

### Immediate recall



### Delayed recall



# Polyphenol-Rich Foods in the Mediterranean Diet are Associated with Better Cognitive Function in Elderly Subjects at High Cardiovascular Risk

Cinta Valls-Pedret<sup>a,b</sup>, Rosa Maria Lamuela-Raventós<sup>b,c,d</sup>, Alexander Medina-Remón<sup>b,c,d</sup>,  
Melibea Quintana<sup>a</sup>, Dolores Corella<sup>b,e</sup>, Xavier Pintó<sup>d,f</sup>, Miguel Ángel Martínez-González<sup>d,g</sup>,  
Ramon Estruch<sup>b,h</sup> and Emilio Ros<sup>a,b,\*</sup>

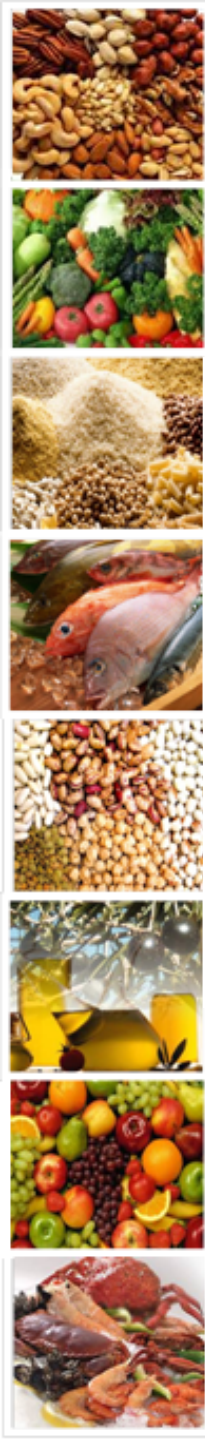
- **Better neuropsychological test scores with increased consumption:**
  - **Wine**
  - **Total and virgin olive oil**
  - **Coffee**
  - **Walnuts**
  
- **Improved memory function with increased polyphenol intake**

# **PREDIMED – Diet & Cognition Conclusion**

---

**Polyphenol-rich foods in the  
Mediterranean diet might  
counteract age-related cognitive  
decline.**





# PREDIMED – Neurodegenerative Disorders

Research

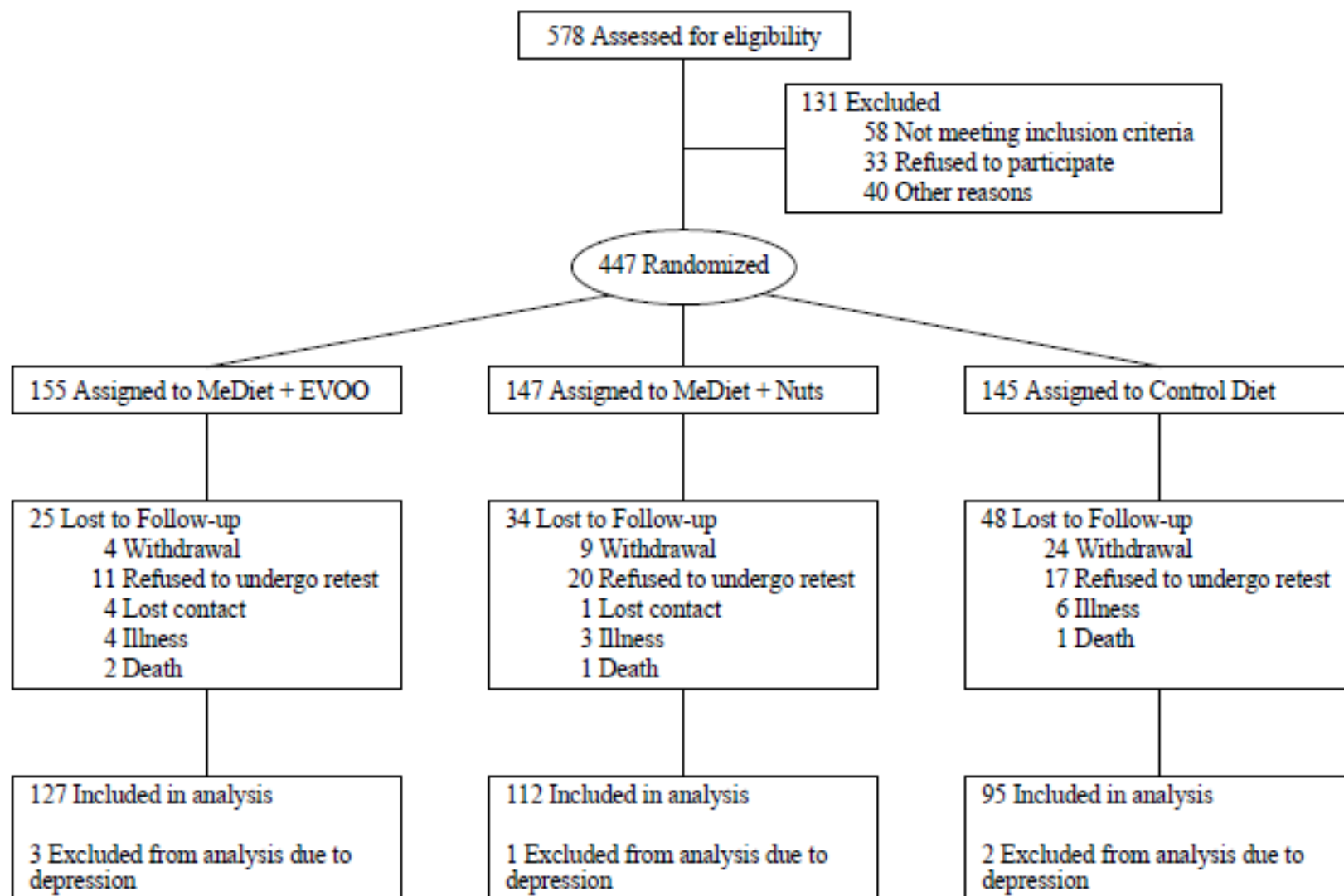
Original Investigation

## Mediterranean Diet and Age-Related Cognitive Decline A Randomized Clinical Trial

Cinta Valls-Pedret, MSc; Aleix Sala-Vila, DPharm, PhD; Mercè Serra-Mir, RD; Dolores Corella, DPharm, PhD; Rafael de la Torre, DPharm, PhD; Miguel Ángel Martínez-González, MD, PhD; Elena H. Martínez-Lapiscina, MD, PhD; Montserrat Fitó, MD, PhD; Ana Pérez-Heras, RD; Jordi Salas-Salvadó, MD, PhD; Ramon Estruch, MD, PhD; Emilio Ros, MD, PhD

**JAMA Intern Med. 2015;175(7):1094-1103.**

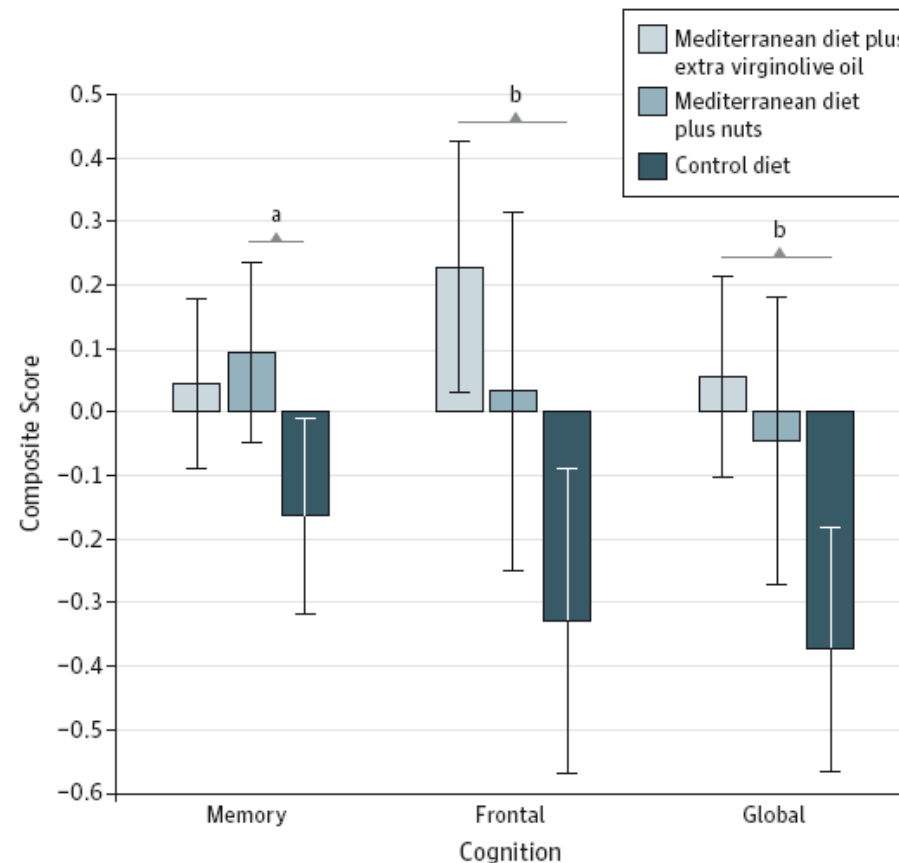
# PREDIMED sub study: Diet & Cognition



# PREDIMED sub study: Diet & Cognition

## Longitudinal evaluation of 447 participants

Changes of mean z scores (final minus baseline)



# **PREDIMED sub study: Diet & Cognition**

---

**Mediterranean diet  
supplemented with (polyphenol-  
rich) extra-virgin olive oil slow  
down age-related cognitive  
decline.**





# **Other brain health-related outcomes from the PREDIMED trial**

**MeDiet intervention in the whole cohort and:**

- Reduction of incident stroke
- Decreased rates of depression
- Prevention of diabetes

**MeDiet intervention in sub-cohorts and:**

- Regression of carotid atherosclerosis
- Higher plasma BDNF concentrations



# **WHAT WAS ALREADY KNOWN ON THIS TOPIC**

---

**Several prospective cohort studies  
have indicated that  
conformity to the traditional  
Mediterranean diet is associated with  
longevity**

**No study has investigated the relative  
importance of individual components  
of the Mediterranean diet score  
in the generation of this association**



# Anatomy of health effects of Mediterranean diet: Greek EPIC prospective cohort study.

---

**Objective:** To investigate the relative importance of individual components of the Med diet in generating the inverse association of increased adherence to this diet and overall mortality.

**Design:** Prospective cohort study.

**Setting:** Greek segment of the EPIC

**Participants:** 23 349 men and women, not previously diagnosed with cancer, coronary heart disease or diabetes mellitus

**Follow-up:** 8.5 years

**Main outcome measure:** All cause mortality.



# Anatomy of health effects of Mediterranean diet: Greek EPIC prospective cohort study.

---

- Follow-up of 8.5 years
- 652 deaths from any cause had occurred among 12,694 participants with Mediterranean diet scores 0-4 (poor adherence)
- 423 among 10,655 participants with scores of 5 or more (good adherence).
- Controlling for potential confounders, higher adherence to a Mediterranean diet was associated with a statistically significant reduction in total mortality (adjusted mortality ratio, per two unit increase in score, 0.864; 95% confidence interval 0.802 to 0.932).



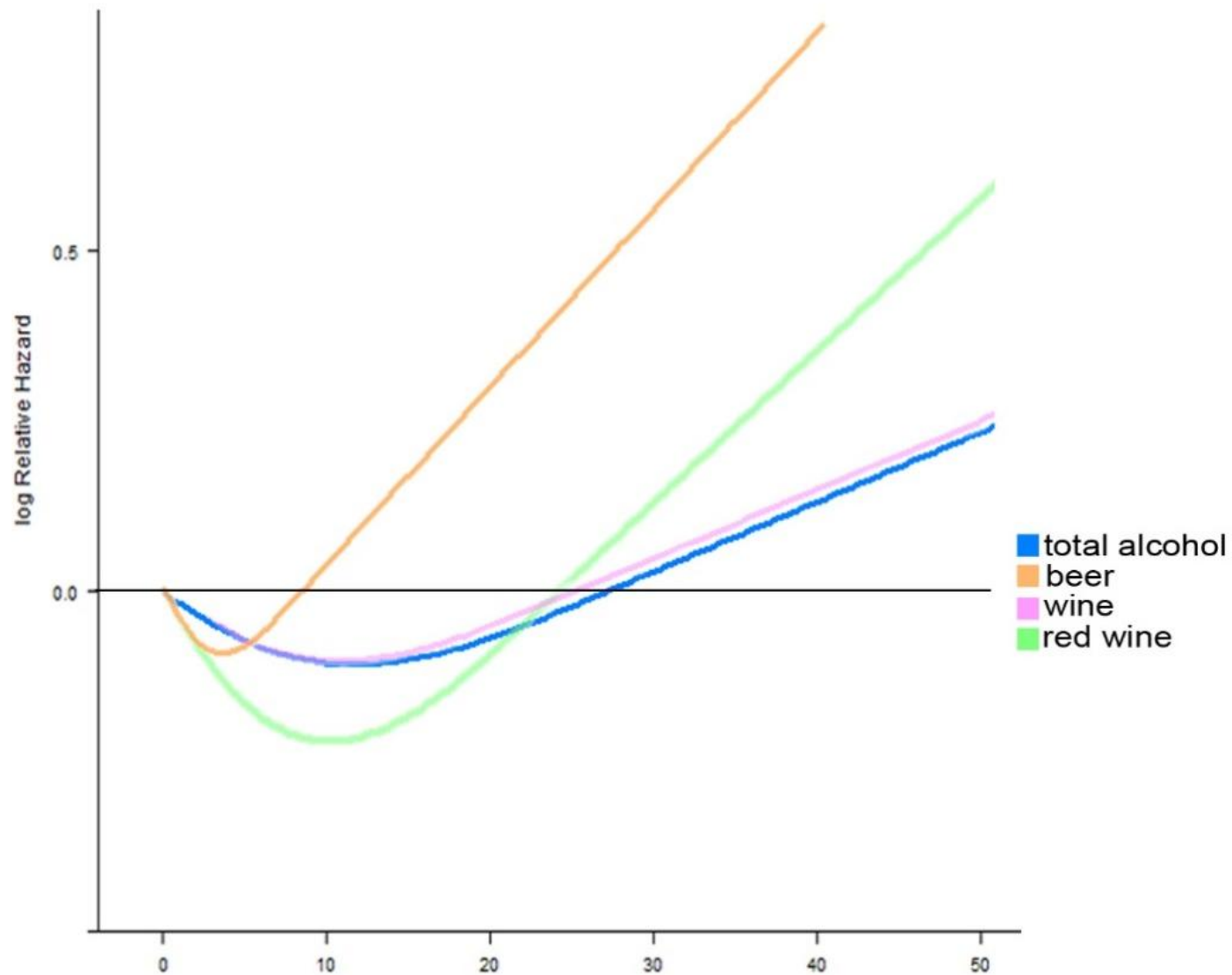
# Anatomy of health effects of Mediterranean diet: Greek EPIC prospective cohort study.

---

The contributions of the individual components of the Med diet to this association were :

- 23.5% moderate ethanol consumption,
- 16.6% low consumption of meat and meat products
- 16.2% high vegetable consumption
- 11.2% high nut consumption,
- 10.6% high monounsaturated to saturated lipid ratio
- 9.7% high legume consumption

The contributions of high cereal consumption and low dairy consumption and fish intake were minimal.



**Relative hazard of cardiovascular events according to the accumulative consumption of alcohol (g/day) – PREDIMED TRIAL**

# Wine consumption and CVD

## Adjusted Relative Hazard (95% CI) of tertile 3 of wine consumption compared to tertile 1

Wine (all) 0.65 (0.47 – 0.89)

Old wine 0.64 (0.43 – 0.94)

Young wine 0.53 (0.47 – 0.86)

White wine 0.97 (0.65 – 1.46)

Work in progress

# Conclusions

1. Among persons at high cardiovascular risk, a Mediterranean Diet supplemented with extra-virgin olive oil or nuts reduce the incidence of major cardiovascular events (cardiovascular death, acute myocardial infarction and stroke) by 30%, compared to a control low-fat diet.
2. The results of this study support the benefits of the Mediterranean diet for the primary prevention of cardiovascular disease with the highest level of scientific evidence.



## Conclusions - II

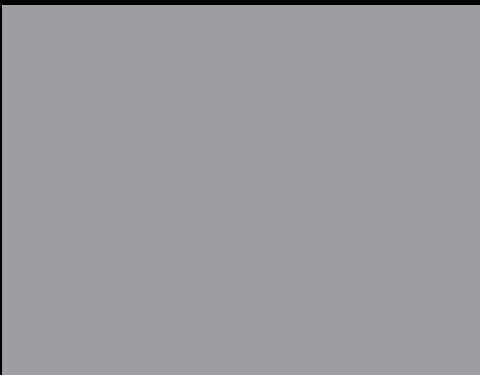
3. Moderate wine consumption protects (by itself) against the appearance of cardiovascular events (stroke) and cognitive-aging decline in subjects at high cardiovascular risk
4. A Mediterranean diet enhanced with high-fat, high-unsaturated fat foods (EVOO and nuts):
  - a) Does not lead to weight gain and may even help lose weight and reduce waist circumference.
  - b) May help reduce diabetes risk.
  - c) Is associated with lower blood pressure by ambulatory monitoring (an objective marker)





Email: [restruch@clinic.ub.es](mailto:restruch@clinic.ub.es)

Twitter: @restruch\_MD



Thank you for your attention