

# Mediterranean Diet: Miracle or Mirage

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# The Mediterranean Diet

## Unique Distinction

- The only major diet whose effectiveness has been demonstrated in controlled trials
- In subjects with a first heart attack, rate of additional cardiac events reduced (secondary prevention of coronary heart disease - CHD)
- In subjects at high risk of CHD (diabetes, smoking, hypertension, elevated LDL-C, decreased HDL-C, obese, family history of premature CHD), rate of CHD events reduced

# The Mediterranean Diet

## Origins

- Ancel Keys observed exceptional longevity and low rate of CHD in southern Italy - 1950s
- Related differing rates of CHD to differences in cholesterol levels
- Further related cholesterol levels to diet, in particular saturated fat content
- Advocated for changes in dietary fat consumption, away from saturated fats (meat & dairy) toward mono- and polyunsaturated fats (vegetable oil, fish, nuts), and limit total to 30% of fuel
- Promoted increased consumption of vegetables, fruits, nuts, legumes, seafood



# Mediterranean Diet

Food	Goal
<b>Mediterranean diet</b>	
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

# Sofrito, Soffritto, Mirepoix

A sauce used as a base in southern Italian cooking

Aromatic ingredients minced and sauteed in oil

- Typically celery, onions, carrots
- Garlic, paprika, peppers, tomatoes common
- Cooked in olive oil or butter

Also found, with variations, in French, Spanish, Portuguese and Latin American cuisine

# Lyon Diet Heart Study: RCT of Mediterranean Diet

## **Mediterranean Diet, Traditional Risk Factors, and the Rate of Cardiovascular Complications After Myocardial Infarction**

### **Final Report of the Lyon Diet Heart Study**

Michel de Lorgeril, MD; Patricia Salen, BSc; Jean-Louis Martin, PhD; Isabelle Monjaud, BSc;  
Jacques Delaye, MD; Nicole Mamelle, PhD

de Lorgeril *Circulation* 1999

# Mediterranean Diet

## Lyon Diet Heart Study

- Patients surviving a first MI, age < 70, clinically stable
- Randomized to two diets
  - Mediterranean diet
  - "Prudent" diet, as advised by personal MD
  - 423 patients accessioned from 1988-92
  - Well-matched on all pertinent risk factors
- Lyon, France

# Lyon Diet Heart Study

## Outcomes Studied

- Composite 1 (CO1): MI or CVD death
- Composite 2 (CO2): MI, CVD death, or major secondary event (e.g., unstable angina)
- Composite 3 (CO3): CO2, or minor secondary event



# Lyon Diet Heart Study

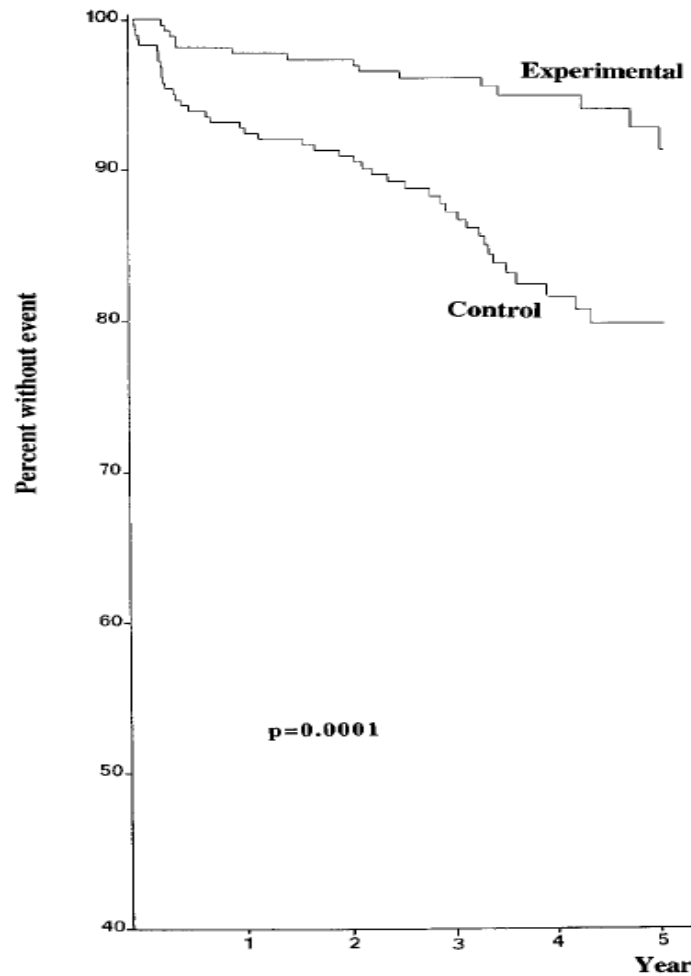
## Intermediate Analysis 1993

- Highly significant difference between groups favoring experimental group
- Scientific Committee of Study decided to terminate the trial

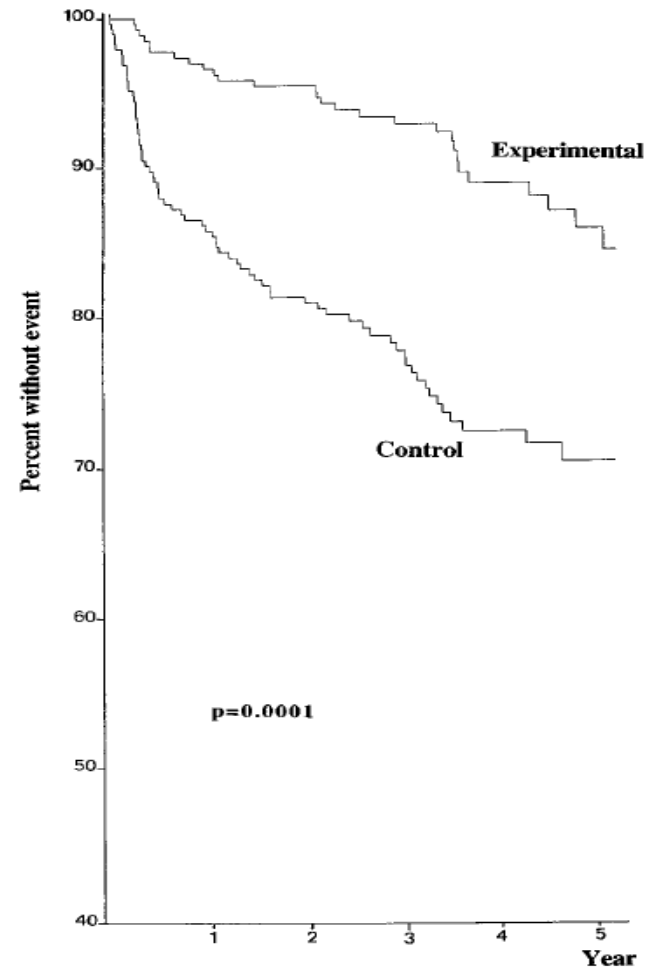
## Final Analysis

- Based on mean follow-up of ~4 years

# Lyon Diet Heart Study



**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).

# Lyon Diet Heart Study

## Results

- Cardiac deaths: 6:19 (MedDiet:Control)
- Non-fatal MI: 8:25 " "
- 72% reduction in CO1
- 67% reduction in CO2
- 47% reduction in CO3
- $P < 0.0002$ , except cardiac death  $p=0.01$

# Lyon Diet Heart Study

## Follow-up on Diet

- Experimental subjects maintained their favorable dietary pattern, even several years after study ended

**TABLE 3. Daily Nutrient Intake Recorded on the Final Visit in 83 Control and 144 Experimental Nonselected Consecutive Patients**

	Control	Experimental	<i>P</i>
Total calories	2088 (490)	1947 (468)	0.033
% calories			
Total lipids	33.6 (7.80)	30.4 (7.00)	0.002
Saturated fats	11.7 (3.90)	8.0 (3.70)	0.0001
Polyunsaturated fats	6.10 (2.90)	4.60 (1.70)	0.0001
18:1( $\omega$ -9) (oleic)	10.8 (4.10)	12.9 (3.20)	0.0001
18:2( $\omega$ -6) (linoleic)	5.30 (2.80)	3.60 (1.20)	0.0001
18:3( $\omega$ -3) (linolenic)	0.29 (0.19)	0.84 (0.46)	0.0001
Alcohol	5.98 (6.90)	5.83 (5.80)	0.80
Proteins, g	16.6 (3.80)	16.2 (3.10)	0.30
Fiber, g	15.5 (6.80)	18.6 (8.10)	0.004
Cholesterol, mg	312 (180)	203 (145)	0.0001

Values are mean (SD).

# Mediterranean Diet - PREDIMED

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

APRIL 4, 2013

VOL. 368 NO. 14

## Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

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for the PREDIMED Study Investigators\*

## Prevención con Dieta Mediterránea - Spain

# PREDIMED

Primary prevention of cardiovascular events in high-risk subjects

- 7557 persons, age 55-80, 57% women, accessioned 2003-09
- No pre-existing CVD
- Type 2 diabetes mellitus or at least three of the following:
  - smoking,
  - hypertension,
  - elevated LDL-C,
  - low HDL-C,
  - overweight or obese,
  - family history of premature CHD.

# PREDIMED

## Intervention

- Two experimental groups, one control group
  - Mediterranean diet supplemented with extra-virgin olive oil (EVOO) 50 g (~4 tbsp)
  - Mediterranean diet supplemented with nut (30 g,  $\frac{1}{2}$  walnuts,  $\frac{1}{4}$  each almonds and hazelnuts)
  - Control group: Low-fat diet, including low-fat dairy, lean fish & seafood, bread, potatoes, pasta, rice, fruits, vegetables, and discouraging vegetable oils, nuts, desserts, red meats, spread fats

# PREDIMED - Control diet

## Low-fat diet (control)

### Recommended

Low-fat dairy products  $\geq 3$  servings/day

Bread, potatoes, pasta, rice  $\geq 3$  servings/day

Fresh fruits  $\geq 3$  servings/day

Vegetables  $\geq 2$  servings/wk

Lean fish and seafood  $\geq 3$  servings/wk

### Discouraged

Vegetable oils (including olive oil)  $\leq 2$  tbsp/day

Commercial bakery goods, sweets, and pastries§  $\leq 1$  serving/wk

Nuts and fried snacks  $\leq 1$  serving /wk

Red and processed fatty meats  $\leq 1$  serving/wk

Visible fat in meats and soups¶ Always remove

Fatty fish, seafood canned in oil  $\leq 1$  serving/wk

Spread fats  $\leq 1$  serving/wk

Sofrito‡  $\leq 2$  servings/wk



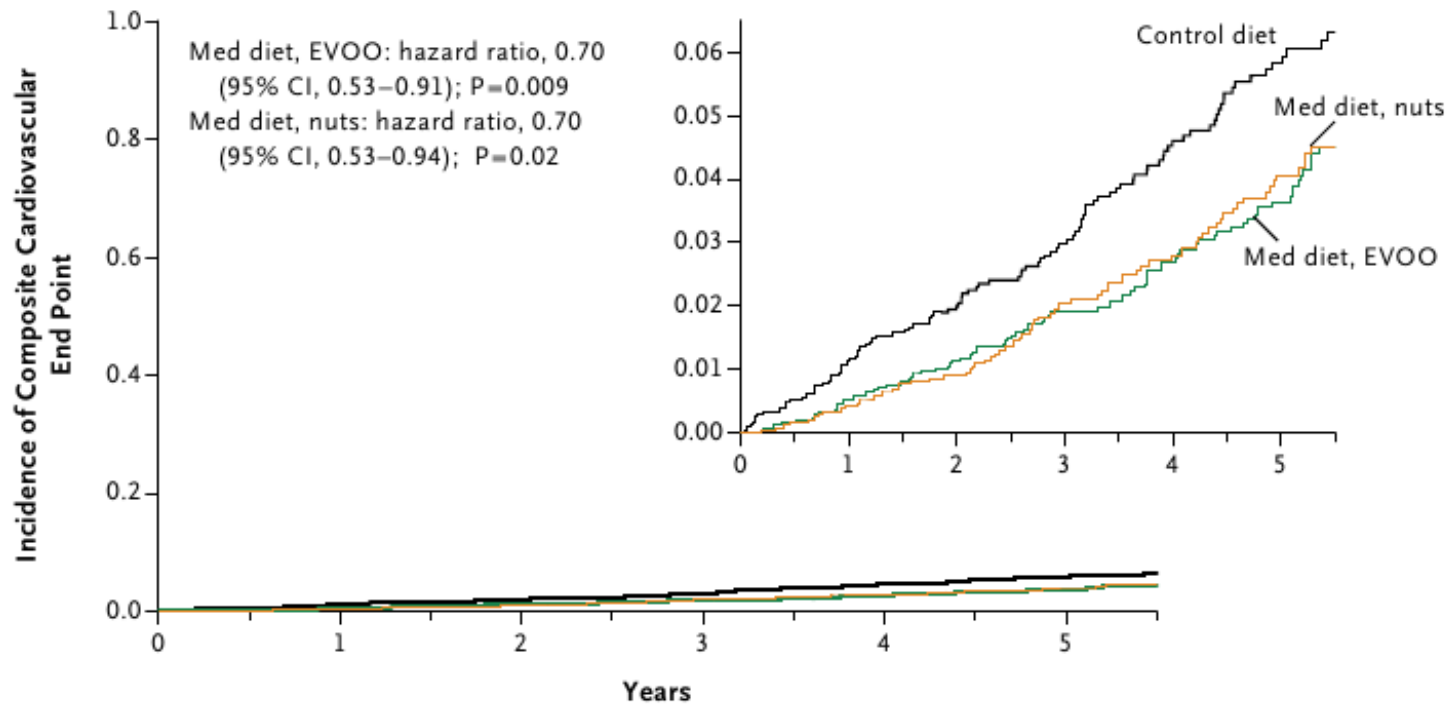
# PREDIMED

## Results

- Interim analyses after 2 years of follow-up
  - Stopping boundary reached 2011
- Median follow-up: 4.8 years
- Good adherence to diet: score 8.7/14
- Primary end point (MI or CVA or CVD death)
  - 8.1% : 8.0% : 11.2% (MedEVOO:MedNuts:Control)
  - RR 0.70 for both Med groups vs. Control ( $p < 0.01$ )

# PREDIMED

**A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)**



**No. at Risk**

Control diet	2450	2268	2020	1583	1268	946
Med diet, EVOO	2543	2486	2320	1987	1687	1310
Med diet, nuts	2454	2343	2093	1657	1389	1031

# Mediterranean Diet - Conclusions

People who have had their first MI, or who have not had CVD but have strong risk factors, may reduce their risk of having an MI or death from CHD by following a Mediterranean diet by comparison to following a low-fat diet

These conclusions were demonstrated in RCT; therefore, one may draw valid conclusions about causality

However, follow-ups are short in both Lyon Diet Heart Study and PREDIMED study; stay tuned to this channel for future developments