October 16 - 18
14th EDITION 2015

MY CONFLICT OF INTERESTS ARE

-Small grant by International Nut Council (INC) to my Department for Predimedplus (covers <1% costs)

-Food companies donated the food items given for free to participants in the trials

-They had no role in the the trial's design, data analysis, or the decision to report the results.

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Universidad de Navarra
Facultad de Medicina
Departamento de Medicina Preventiva y Salud Pública

MeDiet

&

Atrial Fibrillation

Miguel A. Martínez-González
University of Navarra, Spain

Circulation 2014;130:18-26

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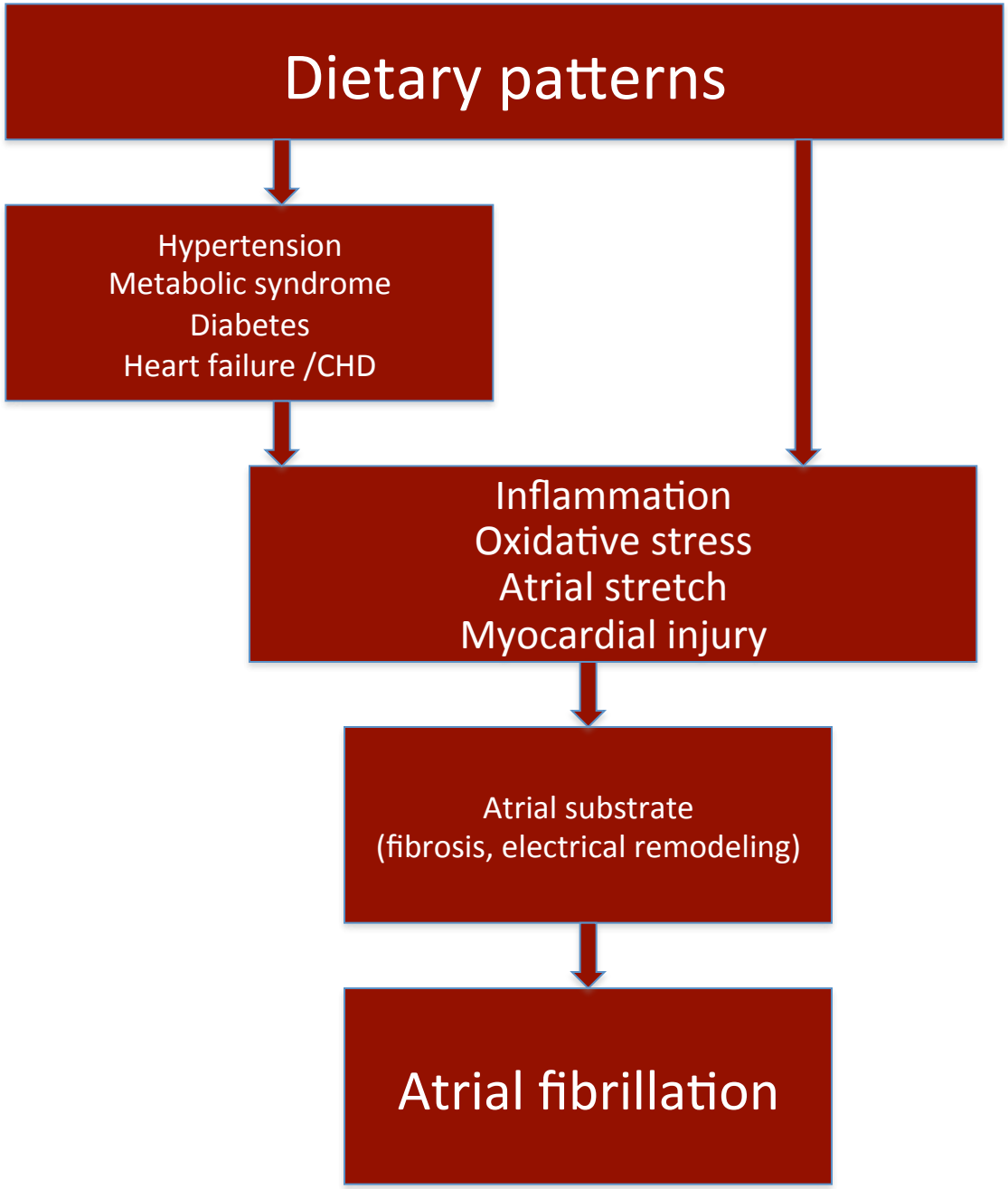
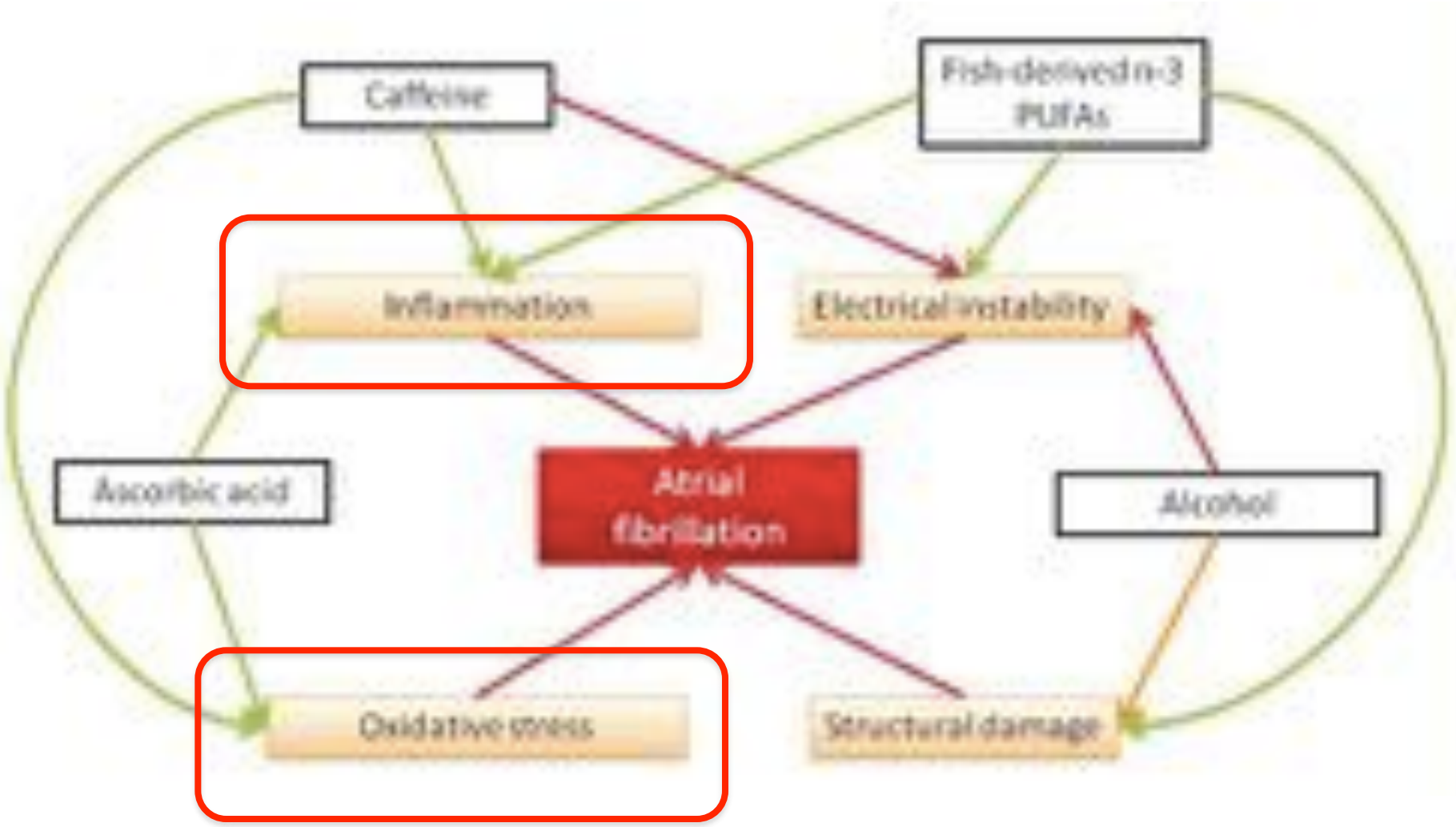

Dietary patterns
Hypertension
Metabolic syndrome
Diabetes
Heart failure /CHD
Inflammation
Oxidative stress
Atrial stretch
Myocardial injury
Atrial substrate
(fibrosis, electrical remodeling)
Atrial fibrillation

Diet & Atrial fibrillation

- Dietary fats have effects on cellular *electrophysiology* and structural *remodeling*, which have been implicated in the development and maintenance of AF (Pharmacol Ther 2013;140:53–80).
- Fat subclasses may influence pathways related to AF *maintenance* rather than initiation (J Nutr 2015;145:2092–101).
- SFAs may promote cardiac structural remodeling through *increased apoptosis in myocytes* (Science 2009;324:343–4) and electrical remodeling through *direct proarrhythmic* effects (Am Heart J 1970;80:671–4).
- Diets high in SFAs may increase *blood pressure*, whereas diets high in MUFAs may reduce blood pressure (JAMA 2005;294:2455–64).
- Fish-derived n-3 PUFAs may prevent AF through several mechanisms: preventing structural heart damage; *inhibiting inflammation*; and inhibiting electrical currents via *myocyte cell membrane stabilization* (*Circ J* 2010;74:2029-38)

Diet & Atrial fibrillation: systematic review
Groonross & Alonso, Circ J 2010



A Randomized Controlled Trial to Prevent Post-Operative Atrial Fibrillation by Antioxidant Reinforcement

J Am Coll Cardiol 2013;62:1457–65

w-3+Vit. C+Vit. E

Ramón Rodrigo, MSc,* Panagiotis Korantzopoulos, MD, PhD,† Mauricio Cereceda, MD,‡ René Asenjo, MD,‡ Jaime Zamorano, MD,‡ Eli Villalabeitia, MD,§ Cristián Baeza, MD,§ Rubén Aguayo, MD,§ Rodrigo Castillo, MD, PhD,‖ Rodrigo Carrasco, MD,* Juan G. Gorman, PhD*

Santiago, Chile; and Ioannina, Greece

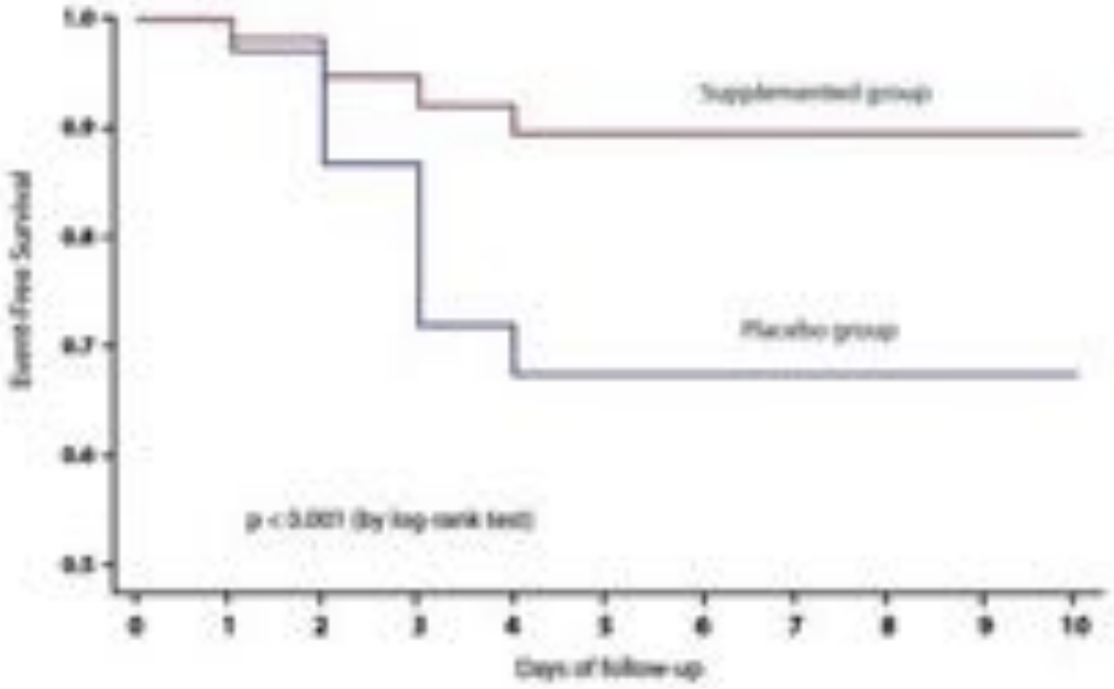
POAF occurred in

- 10 of 103 patients (9.7%) of the supplemented group

versus

- 32 of 100 patients (32.0%) of the placebo group

RR= 0.28 (95% CI: 0.14 to 0.56)
$p < 0.001$



Systematic review, Groonross & Alonso 2010

- Higher **alcohol** intake is consistently related with an increased AF risk
- whereas moderate intake of alcohol and caffeine seem to have **no effect**.
- The association between fish-derived n-3 PUFAs and AF was **inconsistent**, though some evidence exists that these fatty acids might have a protective effect.
- **Further research** to clarify the role of diet in the prevention of AF is warranted

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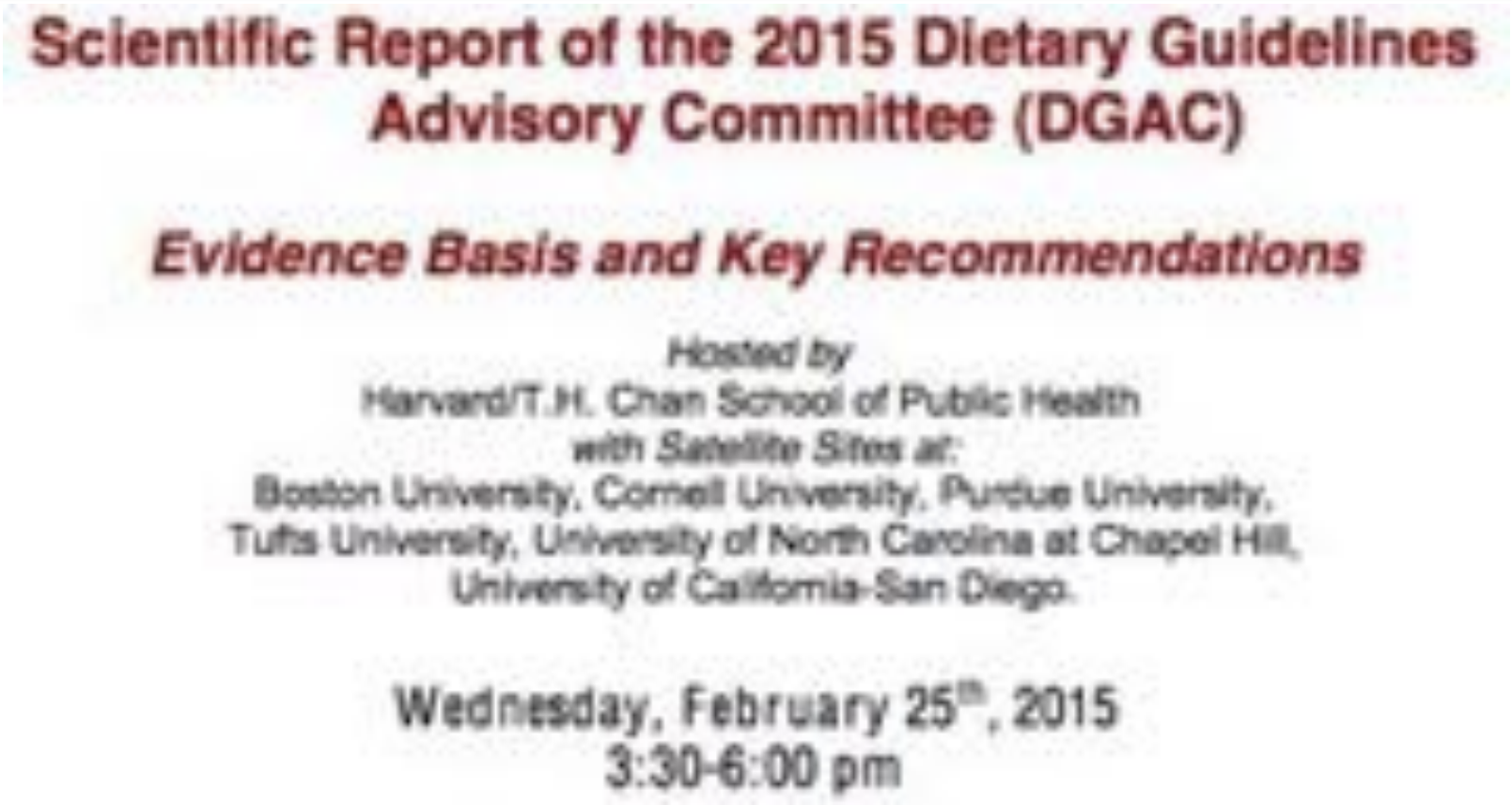
Scientific Report of the 2015 Dietary Guidelines Advisory Committee (DGAC): Evidence Basis and Key Recommendations (Feb 25, 2015)



http://www.health.gov/dietaryguidelines/2015-scientific-report/

Scientific Report of the 2015 Dietary Guidelines Advisory Committee (DGAC): Evidence Basis and Key Recommendations (Feb 25, 2015)

Part D: Science Base

- Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends
- Chapter 2: Dietary Patterns, Foods and Nutrients, and Health Outcomes
- Chapter 3: Individual Diet and Physical Activity Behavior Change
- Chapter 4: Food Environment and Settings
- Chapter 5: Food Sustainability and Safety
- Chapter 6: Cross-Cutting Topics of Public Health Importance
- Chapter 7: Physical Activity

Susan Krebs-Smith

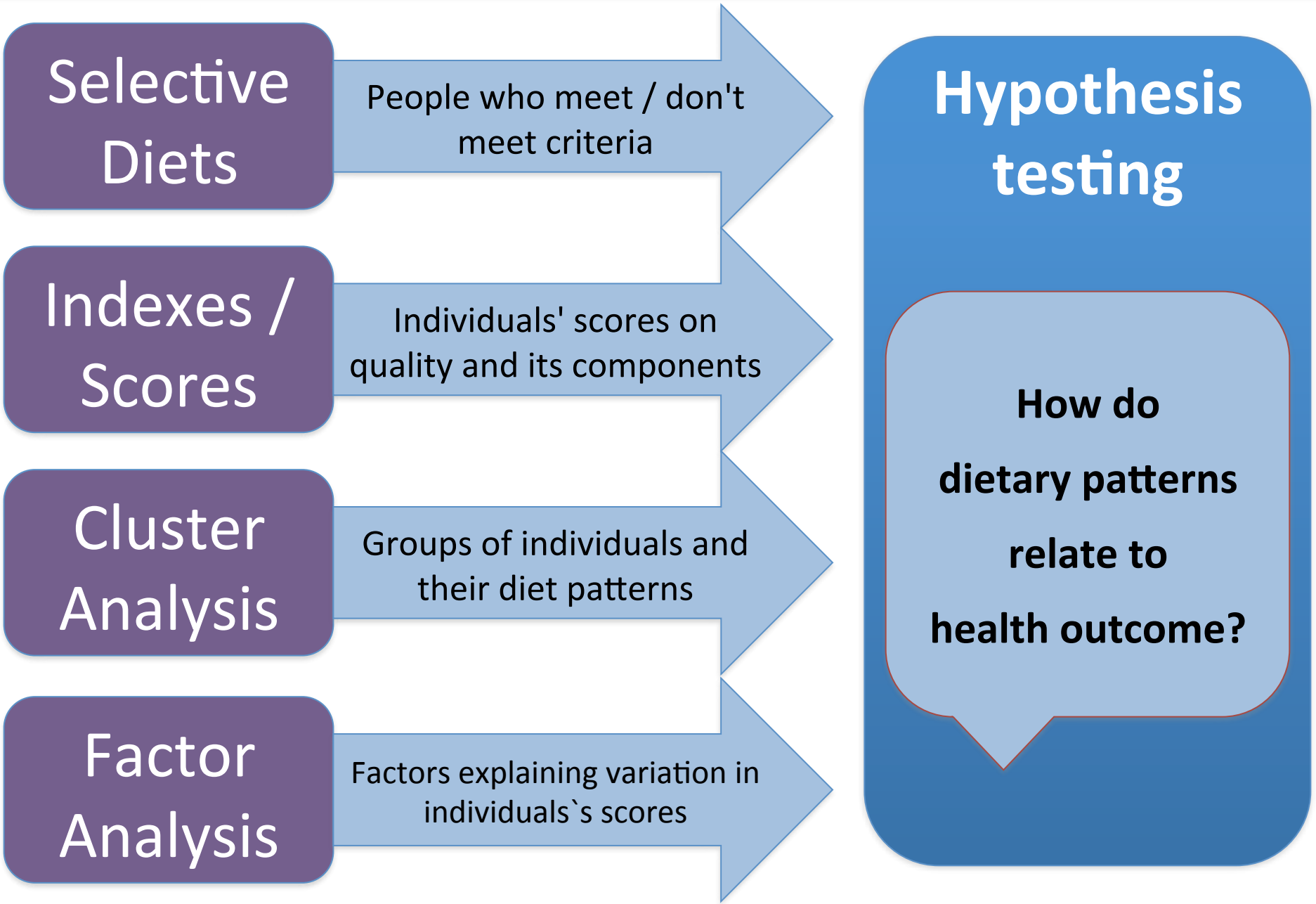
http://www.health.gov/dietaryguidelines/2015-scientific-report/

Scientific Report of the 2015 Dietary Guidelines Advisory Committee (DGAC): Evidence Basis and Key Recommendations (Feb 25, 2015)

Dietary patterns are defined as the

- quantities,
- proportions,
- variety or
- combinations of different foods and beverages in diets,
- and the frequency with which they are habitually consumed.

Dietary patterns methodologies



Dietary patterns: limitations

- **Two general approaches: which is better?**
  - Hypothesis-oriented
  - Data-driven
- **Reproducibility?**
  - Sample-specific medians vs. normative scores
  - Factor or cluster analyses are not reproducible
  - Heterogeneity in dietary assessment tools
- **Confounding?**
  - Lifestyles differ across levels of dietary patterns

Dietary patterns: advantages

- **Interaction**
  - Synergies
  - Antagonisms
- **Confounding**
  - Preempts confounding (other diet. fact.)
- **Statistical power**
  - The isolated effect of a nutrient: too small
  - *Cumulative* exposure = ↑ effect
  - Avoids multicollinearity
  - Avoids issues of multiple comparisons
- **Public health**
  - a sociological reality per se

Scientific Report of the 2015 Dietary Guidelines Advisory Committee (DGAC): Evidence Basis and Key Recommendations (Feb 25, 2015)

http://www.health.gov/dietaryguidelines/2015-scientific-report/

Three beneficial dietary patterns

1. Healthy US-style pattern
2. Healthy Mediterranean-style pattern
3. Healthy Vegetarian pattern

The DGAC had enough descriptive information from existing research and data to model three dietary patterns and to examine their nutritional adequacy. These patterns are the Healthy U.S.-style Pattern, the Healthy Mediterranean-style Pattern, and the Healthy Vegetarian Pattern. These patterns include the components of a dietary pattern associated with health benefits.

The Committee`s examination of the association between dietary patterns and various health outcomes revealed remarkable consistency in the findings

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Perspective

HISTORY OF MEDICINE

Something New under the Sun? The Mediterranean Diet and Cardiovascular Health

Sarah W. Tracy, Ph.D.

N Engl J Med 2013; 368 (17): 1575; April 4, 2013 DOI: 10.1056/NEJMp1302016

www.predimed.es

*Participants: ANCEL KEYS, Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota, U.S.A.; C. ARAVANIS, Evangelismos Hospital Medical Centre, Athens, Greece; the late F. S. P. VAN BUCHEM, Zutphen, The Netherlands; H. BLACKBURN, Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota; R. BUZINA, Institute of Public Health of Croatia, Zagreb, Yugoslavia; B. S. DJORDJEVIĆ, Department of Medicine, University of Belgrade Medical School, Yugoslavia; A. S. DONTAS, Department of Medicine, Accident Hospital, Kifissia (Athens), Greece; F. FIDANZA, Institute of Nutrition and Food Science, University of Perugia, Italy; M. J. KARVONEN, 84060 Pioppi (SA), Italy; N. KIMURA, Kurume University, Japan; A. MENOTTI, Istituto Superiore di Sanità, Rome, Italy; S. NEDELJKOVIĆ, Department of Medicine, University of Belgrade Medical School; V. PUDDU, Clinica Santa Giulia, Rome, Italy; S. PUNSAR, Research Department, Finnish Heart Association, Helsinki, Finland; H. L. TAYLOR, Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota.

TABLE I—TEN YEAR DEATH RATE PER 10 000, STANDARDISED BY SINGLE YEARS OF AGE, OF MEN AGED 40–59 AT ENTRY, AND AVERAGE NUTRIENTS AS % OF CALORIES IN THE DIET

Cohort	No.	Percentage of diet calories from:				Death rate	
		Protein	Fat	Sat FA	Poly	All	CHD
B. Belgrade	538	14	34	12	4	509	288
C. Crevalcore	995	12·8	27	10	3	1261	248
D. Dalmatia	671	14	32	9	2	758	86
E. East Finland	817	12·6	39	22	3	1727	992
G. Corfu	529	11·4	33	7	4	784	144
I. Uzhdsha	502	12	9	5	3	1244	66
K. Crete	686	10·6	40	9	3	543	9
M. Montegiorgio	719	11·2	25	9	3	1080	250
N. Zutphen	878	12·2	40	19	5	1175	420
R. Rome rad	768	13	30	8	3	1027	290
S. Slavonia	696	13·8	33	14	5	1477	214
T. Tanushimaru	508	11	8	3	3	1006	88
U. U.S. rad	2571	14	40	18	5	1088	524
V. Velika Krsna	511	13·5	35	9	3	1078	80
W. West Finland	860	12·2	36	19	3	1118	351
Z. Zvonjanin	534	13·5	37	10	5	1101	152
16 Cohorts	12763	12·6	32·4	11·3	3·8	1071	260

Fat=total fat; Sat FA=saturated fatty acids; Poly=polyunsaturated fatty acids; All=all deaths except from violence; CHD=death from coronary heart disease

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The heart of what we now consider the Mediterranean diet is mainly **vegetarian**:

- **pasta** in many forms,
- **leaves** sprinkled with **olive oil**,
- all kinds of **vegetables** in season,
- and often **cheese**,
- all finished off with **fruit**,
- and frequently washed down with **wine**

Mediterranean diet and public health: personal reflections[1,2]

Ancel Keys

Am J Clin Nutr 1995;61(suppl).1321S

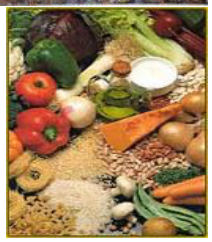
The NEW ENGLAND JOURNAL of MEDICINE

JUNE 26, 2003

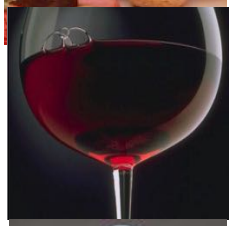
9-item

Adherence to a Mediterranean Diet and Survival in a Greek Population

Antonia Trichopoulou, M.D., Tina Costacou, Ph.D., Christina Bamia, Ph.D., and Dimitrios Trichopoulos, M.D.



- 1 point if >= sex-specific Median
  1. MUFA/SFA ratio
  2. Fruits & nuts
  3. Vegetables
  4. Cereals
  5. Legumes
  6. Fish
- 1 point if <= sex-specific Median
  7. Meat/meat products
  8. Dairy
9. Alcohol: 1 point if
   - Men: between 10-50 g/d
   - Women: between 5-25 g/d



Dietary patterns, Mediterranean diet, and cardiovascular disease

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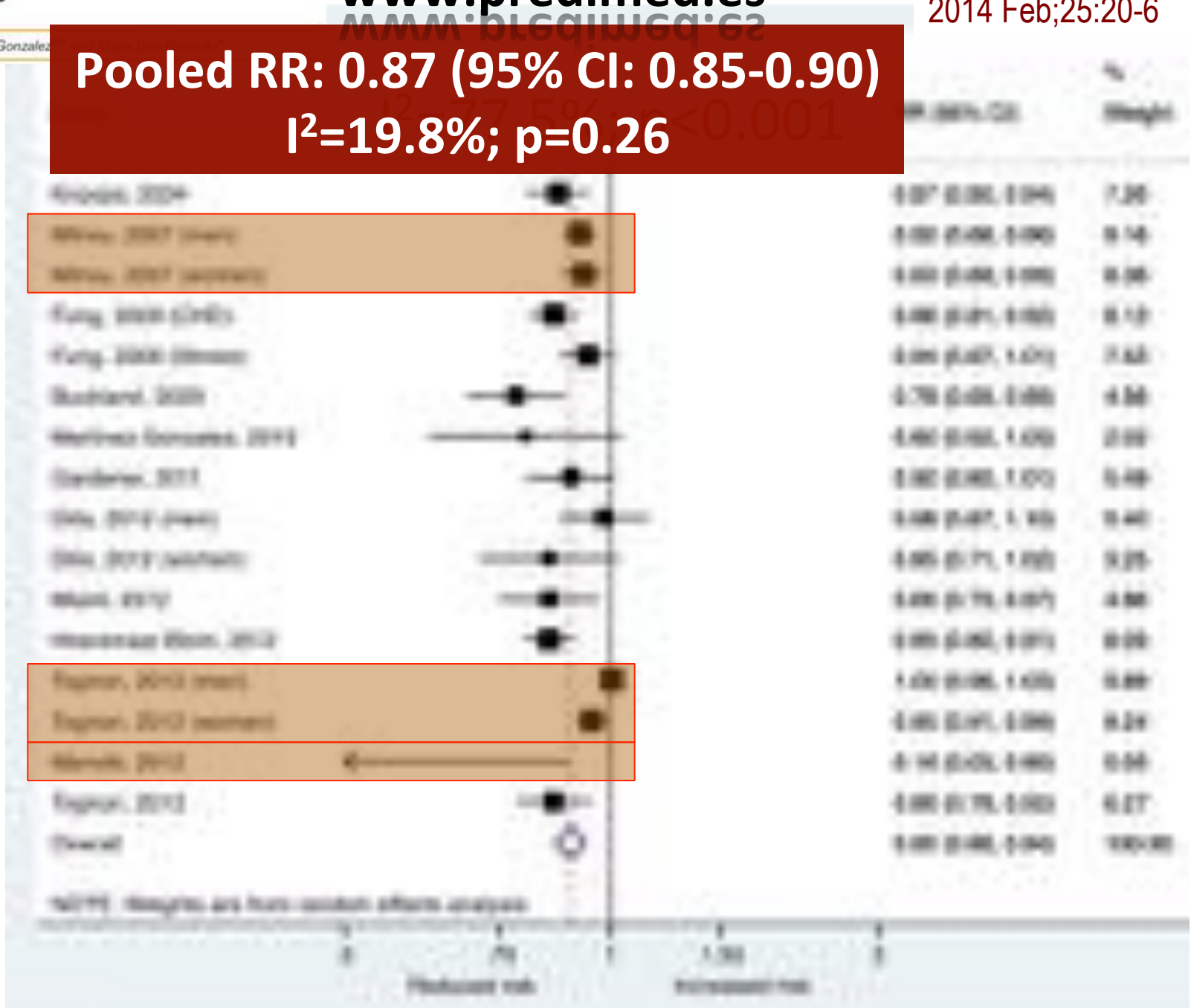
Curr Opin Lipidol
2014 Feb;25:20-6

Miguel Angel Martinez-Gonzalez

Pooled RR: 0.87 (95% CI: 0.85-0.90)
I^2=19.8%; p=0.26



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Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, **crossover trial of the parachute.**

not been subjected to rigorous evaluation by using randomised controlled trials.

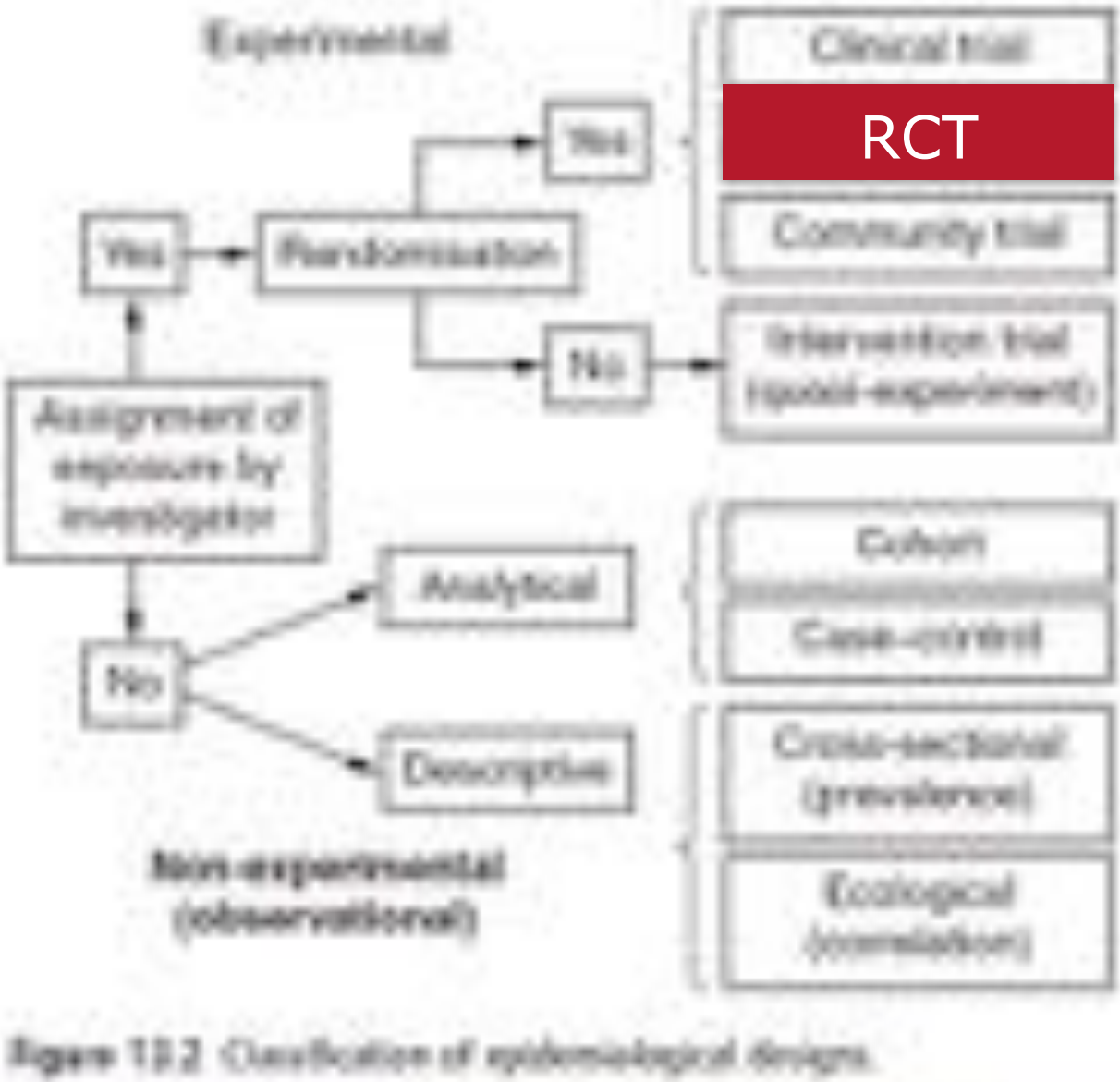
BMJ 2003;327:1459-61

Research designs

Source: Martinez JA & Martinez-Gonzalez MA.

Nutrition Research Methodology: the scientific method and nutritional research.

In: Gibney MJ, et al. *Introduction to Human Nutrition. The Nutrition Society Textbook series*. London: Blackwell Science, 2009.



- Strength of association
- Temporal sequence
- Graduality

- Consistency
- Coherence
- Biological plausibility
- Specificity
- Analogy
- Experimental evidence

Long-term fish consumption is associated with protection against arrhythmia in healthy persons in a Mediterranean region—the ATTICA study[1–3]

Am J Clin Nutr 2007; 85:1385–91.

Christina Chrysohoou, Demosthenes B Panagiotakos, Christos Pitsavos, John Skoumas, Xenofon Krinos, Yannis Chloptsios, Vassilios Nikolaou, and Christodoulos Stefanadis

compared with fish nonconsumers, those who consumed >300 g fish/wk had a 29.2% lower likelihood of having QTc intervals >0.45 s (*P* =0.03)

Associations of Plasma Phospholipid and Dietary Alpha Linolenic Acid With Incident Atrial Fibrillation in Older Adults: The Cardiovascular Health Study

Amanda M. Fretts, PhD, MPH; Dariush Mozaffarian, MD, DrPH; David S. Siscovick, MD, MPH; Susan R. Heckbert, MD, PhD; Barbara McKnight, PhD; Irena B. King, PhD; Eric B. Rimm, ScD; Bruce M. Psaty, MD, PhD; Frank M. Sacks, MD; Xiaoling Song, PhD; Donna Spiegelman, ScD; Rozenn N. Lemaitre, PhD, MPH

J Am Heart Assoc. 2013;2:e003814

no association of plasma phospholipid ALA and incident AF

Postoperative atrial fibrillation and total dietary antioxidant capacity in patients undergoing cardiac surgery: The Polyphemus Observational Study

J Thorac Cardiovasc Surg 2015;149:1175-82

Simona Costanzo, MSc, PhD,[a] Amalia De Curtis, BSc,[a] Veronica di Niro, BN,[b] Marco Olivieri, IT,[c] Mariarosaria Morena, BN,[d] Carlo Maria De Filippo, MD,[d] Eugenio Caradonna, MD,[d] Vittorio Krogh, MD,[e] Mauro Serafini, MSc,[f] Nicoletta Pellegrini, MSc, PhD,[g] Maria Benedetta Donati, MD, PhD,[a] Giovanni de Gaetano, MD, PhD,[a] and Licia Iacoviello, MD, PhD,[a] on behalf of the Polyphemus Observational Study Investigators

patients in the highest tertile of **dietary total antioxidant capacity** had a lower risk of postoperative atrial fibrillation than patients in the 2 lowest tertiles
OR = 0.46 (95% CI: 0.22-0.95)

Dietary factors and incident atrial fibrillation: the Framingham Heart Study[1–3]

Am J Clin Nutr 2011;93:261–6.

Jian Shen, Victor M Johnson, Lisa M Sullivan, Paul F Jacques, Jared W Magnani, Steven A Lubitz, Shivda Pande Daniel Levy, Ramachandran S Vasan, Paula A Quatromoni, Mireia Junyent, Jose M Ordovas, and Emelia J Benja

alcohol, caffeine, fiber, and fish-derived PUFAs no significantly associated with AF risk.
adverse association of **dark fish** and AF merits further investigation.

Adherence to Mediterranean diet and intake of antioxidants influence spontaneous conversion of atrial fibrillation☆

Nutrition, Metabolism & Cardiovascular Diseases 2013;23:115-21

A.V. Mattioli [a,*], C. Miloro [b], S. Pennella [c], P. Pedrazzi [b], A. Farinetti [d]

MeDiet **Olive oil**

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G 03/140: 2003-2005 (Clinic)
RD 06/0045: 2006-2013 (UNAV)
CIBERobn: 2013–

Instituto de Salud Carlos III

1. Clinic (Barcelona)- Ramón Estruch
2. URV (Reus)- Jordi Salas
3. IMIM (Barcelona)- Montse Fitó
4. U. Valencia- Dolores Corella
5. Hosp. Univ. Álava (Vitoria)- Fernando Arós
6. U. Málaga- Enrique Gómez-Gracia
7. CS S. Pablo (Sevilla)- José Lapetra
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9. U. Las Palmas- Lluis Serra-Majem
10. H. Bellvitge (Barcelona)- Xavier Pintó
11. U. Navarra / Osasunbidea – Miguel A. Martínez-González

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COHORT PROFILE

Cohort Profile: Design and methods of the PREDIMED study

Miguel Ángel Martínez-González,[1,7] Dolores Corella,[2,3] Jordi Salas-Salvadó,[3,4] Emilio Ros,[3,5] María Isabel Covas,[3,6] Miquel Fiol,[3,7] Julia Wärnberg,[3,8] Fernando Arós,[9] Valentina Ruiz-Gutiérrez,[10] Rosa María Lamuela-Raventós,[11] Jose Lapetra,[3,12] Miguel Ángel Muñoz,[13] José Alfredo Martínez,[3,14] Guillermo Sáez,[15] Lluís Serra-Majem,[16] Xavier Pintó,[17] María Teresa Mitjavila,[18] Josep Antoni Tur,[19] María del Puy Portillo[20] and Ramón Estruch[3,21], for the PREDIMED Study Investigators

Int J Epidemiol. 2012;41:377-85.
Epub 2010 Dec 20

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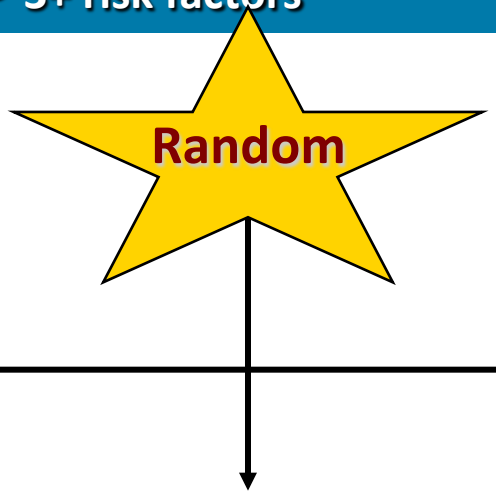
DESIGN OF THE PREDIMED TRIAL

www.predimed.es
n = 7447

- 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

WITHOUT CVD at baseline



American Heart Association®

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GOBIERNO DE ESPAÑA MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

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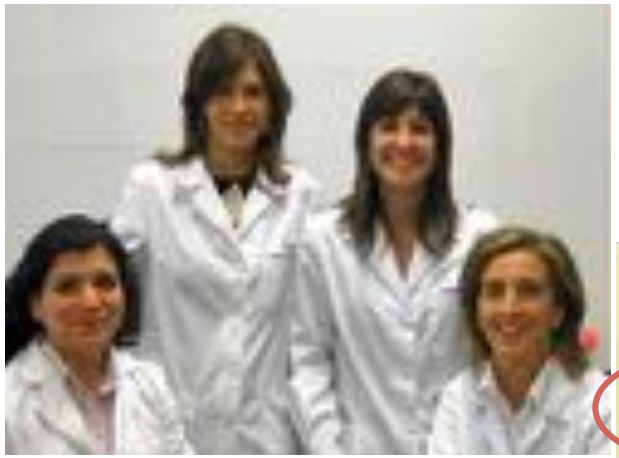
14-point score

1. Olive oil main culinary fat
2. Olive oil >=4 tablespoons/d
3. Vegs>=2 serv./d
4. Fruits>=3 serv./d
5. Red meats<1/d
6. Butter, marg, cream<1/d
7. Soda drinks<1/d
8. Wine >=7 glasses/wk
9. Legumes >=3/wk
10. Fish & seafood >=3/wk
11. Cakes, sweets <3/wk
12. Nuts >=3/wk
13. Poultry > red meats
14. Sofrito



J Nutr 2011;141:1140

A Short Screener Is Valid for Assessing Mediterranean Diet Adherence among Older Spanish Men and Women [1–3]

Helmut Schröder, [4,5]* Montserrat Fitó, [4,5] Ramón Estruch, [3,6] Miguel A. Martínez-González, [8]

Eur J Clin Nutr 2004;58:1550

Development of a short dietary intake questionnaire for the quantitative estimation of adherence to a cardioprotective Mediterranean diet

MA Martínez-González[1]*, E Fernández-Jarne[1], M Serrano-Martínez[1], M Wright[1] and E Gomez-Gracia[2]

Zazpe et al for the PREDIMED group, J Am Diet Assoc 2008;108:1134-44

N Engl J Med 2013

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

Low-fat diet (control)	
Recommended	
Low-fat dairy products	≥3 servings/day
Bread, potatoes, pasta, rice	≥2 servings/day
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
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

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Prevención con Dieta Mediterránea

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 meats & dairy**
  - **alcohol permitted: wine**
- ***Low-fat diet* - Control**
  - **Reduce every fat**
  - **Increase CHO**
- **No Energy limitation**
- **No Physical activity**
- **No goals for weight loss**

tocopherols
polyphenols
flavonoids
phytosterols

Nutrition Reviews 2013;71:511–27

The purpose of the present literature review was to investigate and summarize the current evidence on associations between dietary patterns and biomarkers of inflammation, as derived from epidemiological studies. A systematic literature search was conducted using PubMed, Web of Science, and EMBASE, and a total of 46 studies were included in the review. These studies predominantly applied principal component analysis, factor analysis, reduced rank regression analysis, the Healthy Eating Index, or the Mediterranean Diet Score. No prospective observational study was found. Patterns identified by reduced rank regression as being statistically significantly associated with biomarkers of inflammation were almost all meat-based or "Western" patterns. Studies using principal component analysis or a priori-defined diet scores found that meat-based or "Western-like" patterns tended to be positively associated with biomarkers of inflammation, predominantly C-reactive protein, while vegetable- and fruit-based or "healthy" patterns tended to be inversely associated. While results of the studies were inconsistent, interventions with presumed healthy diets resulted in reductions of almost all investigated inflammatory biomarkers. In conclusion, prospective studies are warranted to confirm the reported findings and further analyze associations, particularly by investigating dietary patterns as risk factors for changes in inflammatory markers over time.

3-mo changes
n= 772

Annals of Internal Medicine | ARTICLE

Effects of a Mediterranean-Style Diet on Cardiovascular Risk Factors

A Randomized Trial

Ann Intern Med 2006;145:1-11

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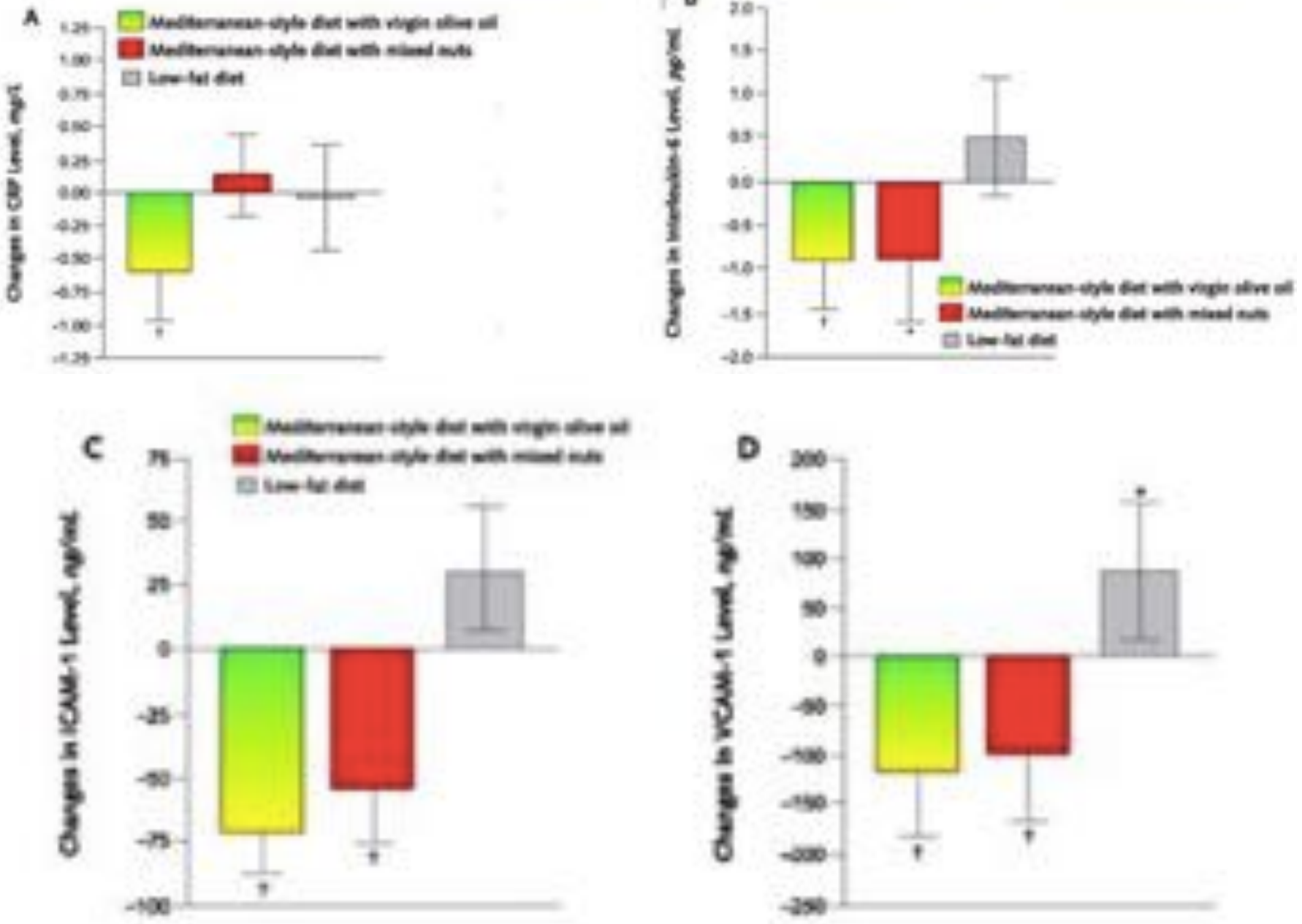
3-mo changes in Risk Factors

Ann Intern Med 2006;145:1-11



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Primary end-point: either

- myocardial infarction
- stroke
- cardiovascular death

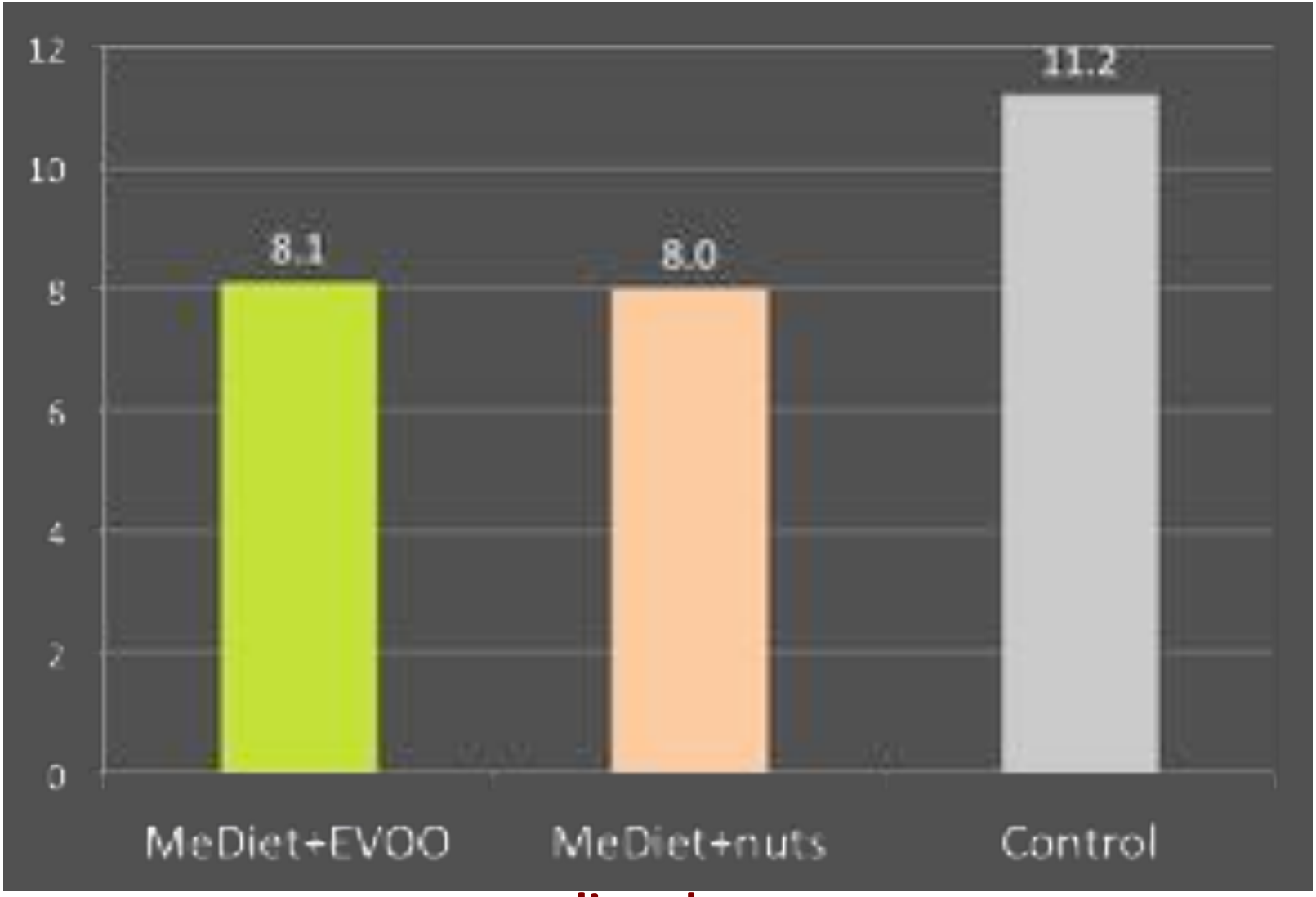
Figure 1: The authors: double blinded versus single blinded

Blinding in randomised trials: hiding who got what

Lancet 2002

Kenneth F Schulz, David A Grimes

Primary end-point (MI, stroke or death from CV causes)
Crude rates / 1000 person-years



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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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., María 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 María Lamuela-Raventós, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D., Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Ángel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D., José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Ángel Martínez-González, M.D., Ph.D., for the PREDIMED Study Investigators*

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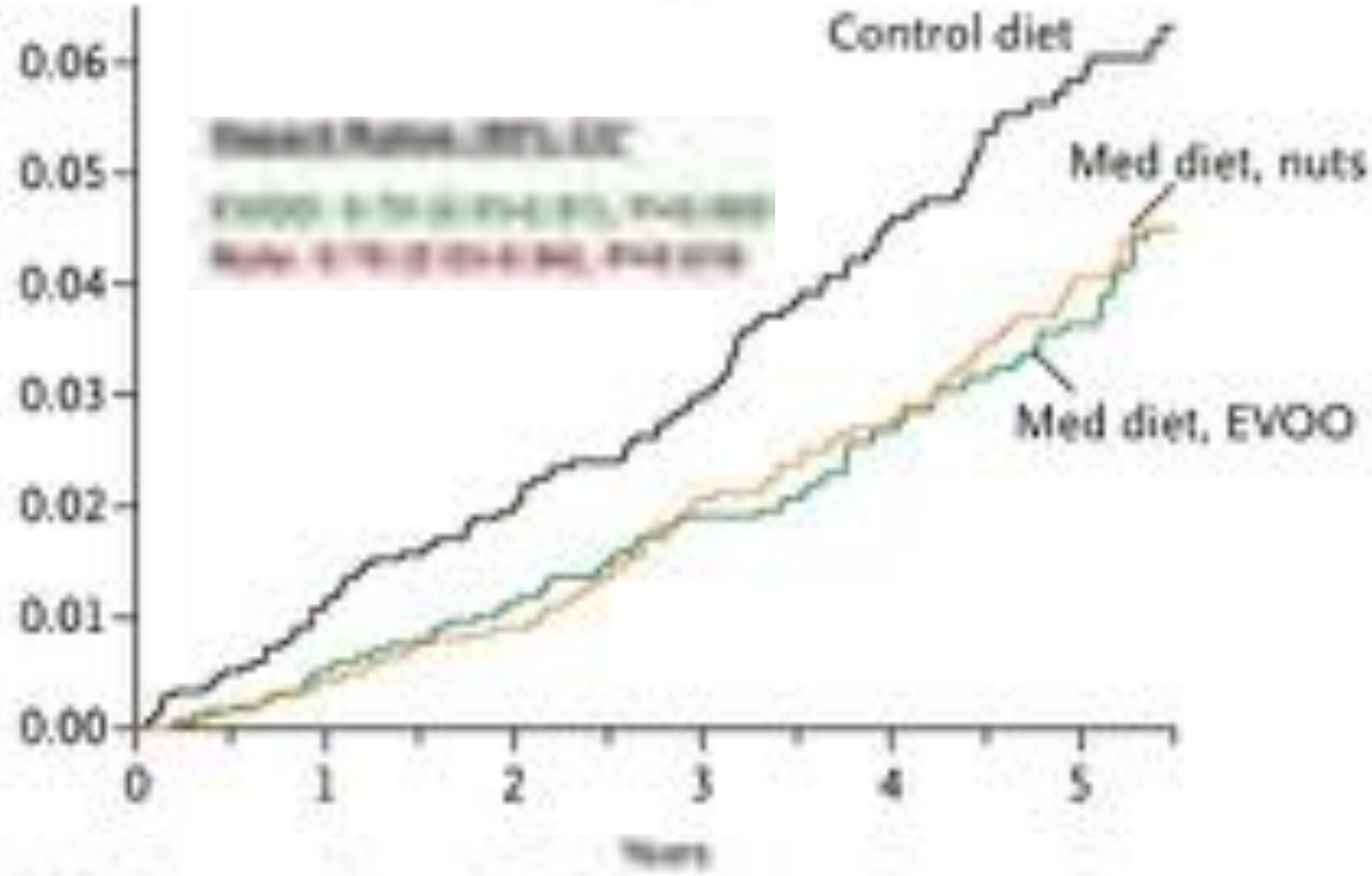
4/4/13

Primary end-point (MI, stroke or death from CV causes)



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Benefits of the Mediterranean Diet: Insights From the PREDIMED Study

Miguel A. Martínez-González[a,b,c,*], Jordi Salas-Salvadó[b,c,d], Ramón Estruch[b,c,e], Dolores Corella[c,f], Montse Fitó[c,g], Emilio Ros[c,e], for the PREDIMED INVESTIGATORS[2]

Mediterranean Diet and Cardiovascular Health: Teachings of the PREDIMED Study[1–3]

Adv Nutr 2014;5:330S-6S.

Emilio Ros,[4,5]* Miguel A. Martínez-González,[6,7] Ramon Estruch,[1,6] Jordi Salas-Salvadó,[6,9] Montserrat Fitó,[6,10] José A. Martínez,[6,8] and Dolores Corella[6,11]

[4]Lipid Clinic, Endocrinology and Nutrition Service and [1]Department of Internal Medicine, Institut d'Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Hospital Clinic, University of Barcelona, Barcelona, Spain; [5]CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III, Spanish Government, Spain; Departments of [7]Preventive Medicine and Public Health and [8]Nutrition and Food Sciences, Physiology, and Toxicology, University of Navarra, Pamplona, Spain; [9]Human Nutrition Department, Sant Joan University Hospital, Pere Virgili Health Research Institute, Rovira i Virgili University, Reus, Spain; [10]Cardiovascular and Nutrition Research Group and Regicor Study Group, Hospital del Mar Research Institute, Barcelona, Spain; and [11]Department of Preventive Medicine, University of Valencia, Valencia, Spain

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Extravirgin Olive Oil Consumption Reduces Risk of Atrial Fibrillation

The PREDIMED (Prevención con Dieta Mediterránea) Trial

Miguel Á. Martínez-González, MD, PhD; Estefanía Toledo, MD, PhD; Fernando Arós, MD, PhD; Miquel Fiol, MD, PhD; Dolores Corella, DPharm, PhD; Jordi Salas-Salvadó, MD, PhD; Emilio Ros, MD, PhD; María I. Covas, DPharm, PhD; Joaquín Fernández-Crehuet, MD, PhD; José Lapetra, MD, PhD; Miguel A. Muñoz, MD, PhD; Monserrat Fitó, MD, PhD; Luis Serra-Majem, MD, PhD; Xavier Pintó, MD, PhD; Rosa M. Lamuela-Raventós, DPharm, PhD; Jose V. Sorlí, MD, PhD; Nancy Babio, BSc, PhD; Pilar Buil-Cosiales, MD, PhD; Valentina Ruiz-Gutierrez, PhD; Ramón Estruch, MD, PhD; Alvaro Alonso, MD, PhD; for the PREDIMED Investigators*

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

2014;130:18-26

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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

2014;130:18-26

	MeDiet+EVOO	MeDiet+nuts	Control
n	**2292**	**2210**	**2203**
Women (%)	58.6	54.3	60.1
Age	66.9	66.6	67.4
Smokers (%)	13.9	14.3	13.4
BMI	30.0	29.8	30.3
Height	160	160	159
Hypertension (%)	82.8	83.2	84.2
Type 2 diabetes (%)	50.2	46.2	48.6
History arrhythmia* (%)	6.7	7.4	7.4

*It does not include AF

Extravirgin Olive Oil Consumption Reduces Risk of Atrial Fibrillation

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Miguel Á. Martínez-González, MD, PhD; Estefanía Toledo, MD, PhD; Fernando Arós, MD, PhD; Miquel Fiol, MD, PhD; Dolores Corella, DPharm, PhD;

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
2014;130:18-26

annual review of all outpatient and inpatient medical records of each participant and from yearly ECGs performed during follow-up examinations in the healthcare centers. If AF was mentioned anywhere in the medical record or AF was present in the ECG, all relevant documentation was submitted to the Adjudication Committee. Even though AF was not a primary end point in the trial, the Adjudication Committee reviewed the medical charts and ECGs from potential AF cases and made a final decision about the presence or absence of AF. For the purposes of the PREDIMED trial and the present analysis, a diagnosis of AF was made only if both AF was present in an ECG tracing and an explicit medical diagnosis of AF was made by a physician. AF events associated with myocardial infarction or cardiac surgery were not included.

253 cases

Extravirgin Olive Oil Consumption Reduces Risk of Atrial Fibrillation
The PREDIMED (Prevención con Dieta Mediterránea) Trial

Miguel Á. Martínez-González, MD, PhD; Estefanía Toledo, MD, PhD; Fernando Arós, MD, PhD; Miquel Fiol, MD, PhD; Dolores Corella, DPharm, PhD;

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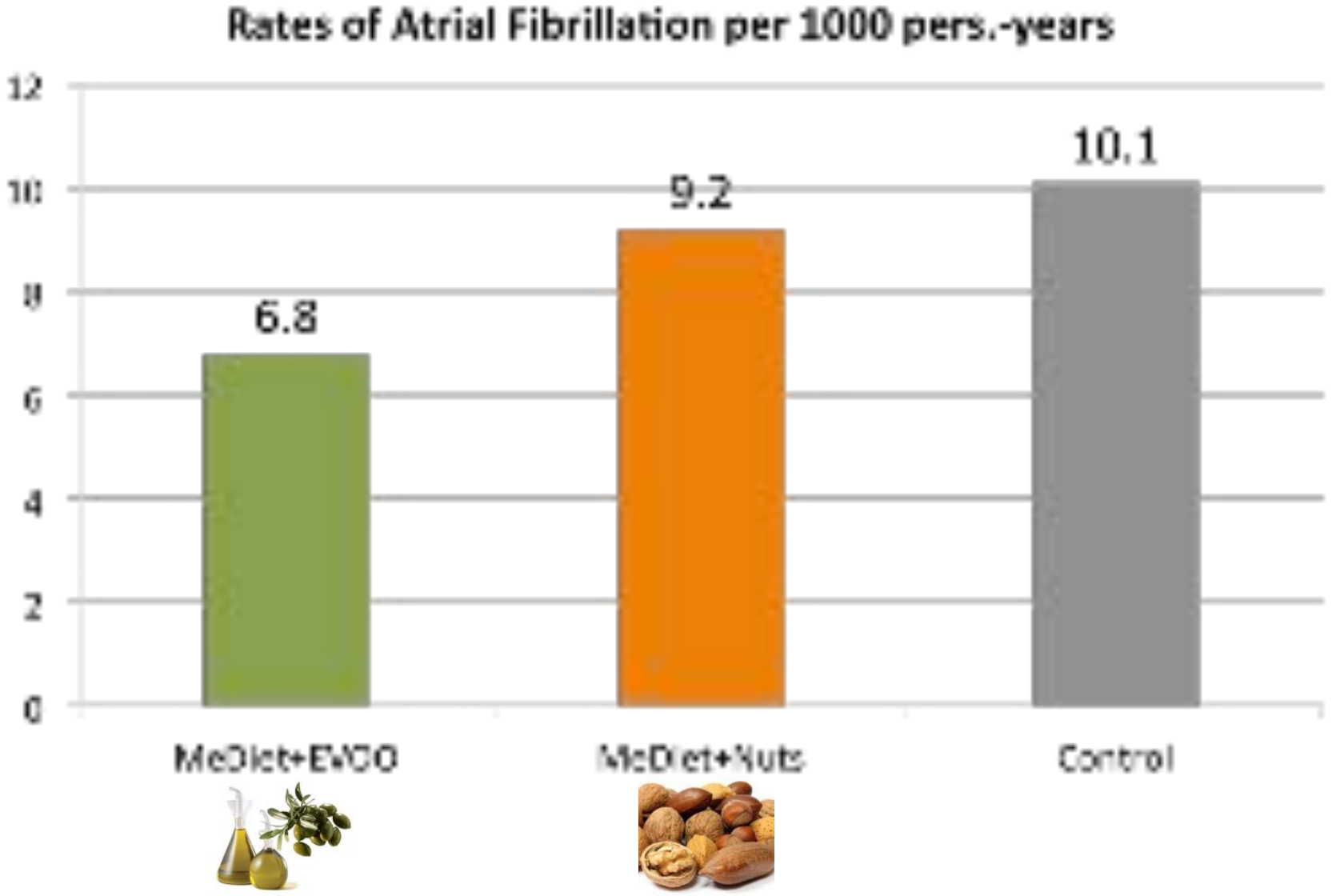

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Extravirgin Olive Oil Consumption Reduces Risk of Atrial Fibrillation

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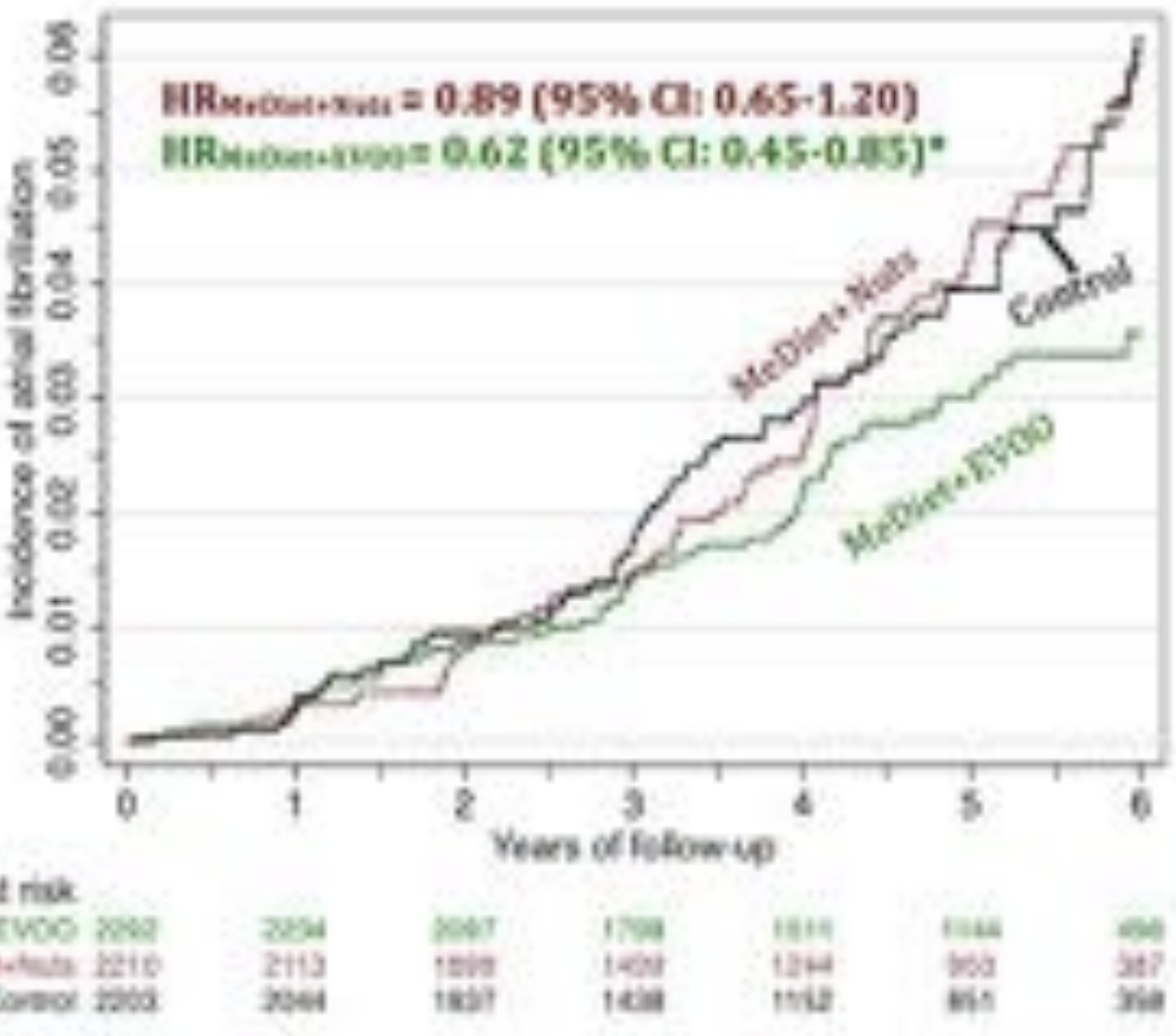

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Hazard Ratios (HR) of Atrial Fibrillation (95% CI) in multivariable-adjusted Cox models

	MeDiet+EVOO	MeDiet+nuts	Control
Cases	72	92	89
Persons-years	10,634	9,333	8,851
HR (1)	*0.64 (0.46-0.88)*	0.90 (0.66-1.22)	1 (ref.)
HR (2)	*0.62 (0.44-0.85)*	0.86 (0.63-1.17)	1 (ref.)
HR (3)	*0.62 (0.44-0.86)*	0.87 (0.64-1.18)	1 (ref.)
HR (4)	*0.62 (0.45-0.88)*	0.90 (0.66-1.23)	1 (ref.)

HR (1) adjusted for age & sex

HR (2) Additionally adjusted for smoking, educational level, baseline height, body mass index, waist to height ratio, diabetes, hypertension, LDL, HDL, BP, antihypertensive treatment, statin use, baseline adherence to the MeDiet, and preexisting arrhythmias (other than AF).

HR (3) additionally adjusted for the nonfatal component of the primary end point (myocardial infarction, stroke) of the PREDIMED trial as a time-dependent covariate.

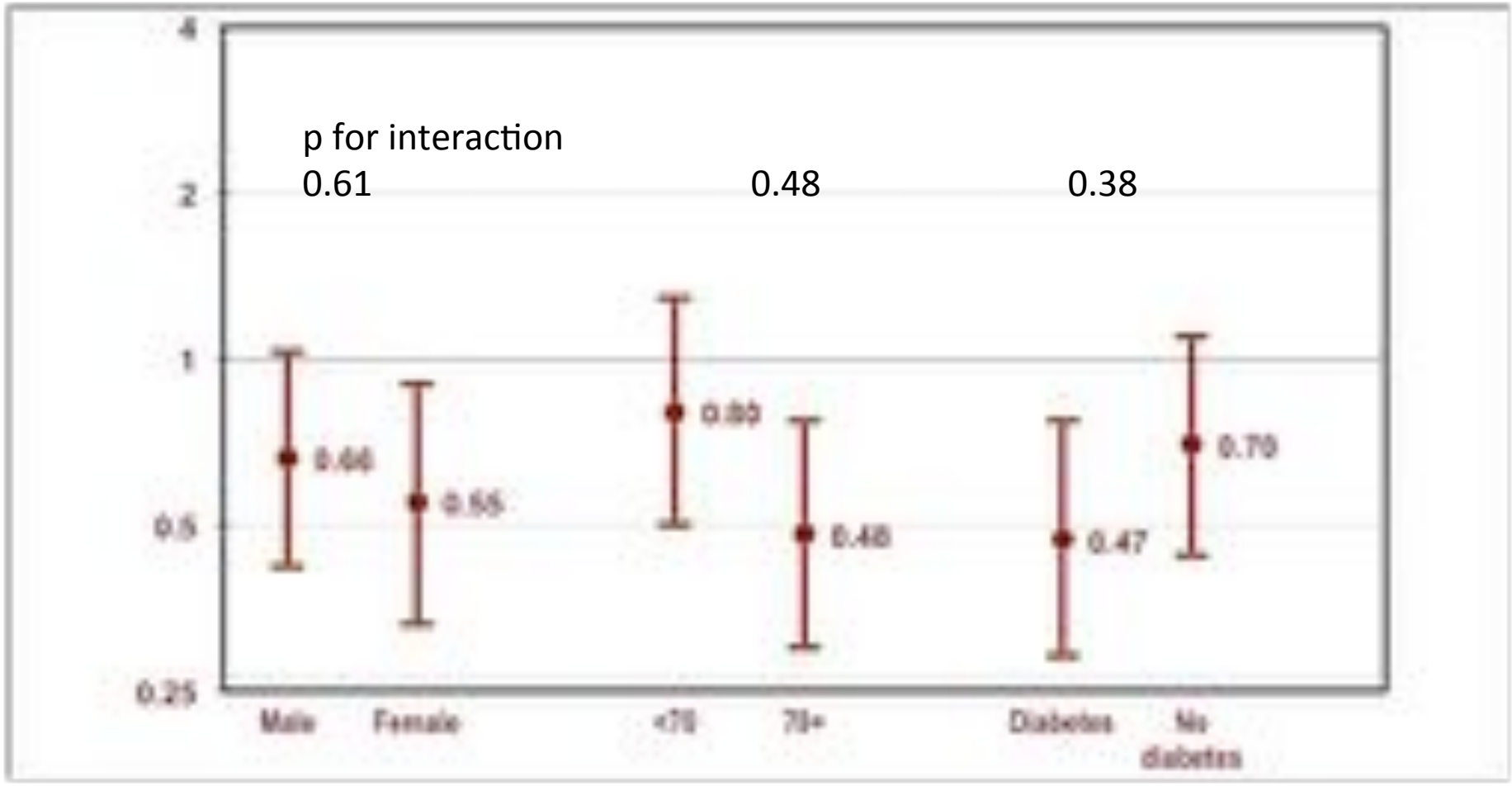
HR (4) Additionally censoring participants at the time of nonfatal primary end points (AMI, stroke).

Hazard Ratios (HR) of Atrial Fibrillation (95% CI) or mayor CVD (primary end-point)

	MeDiet+EVOO	MeDiet+nuts	Control
Crude model	0.67 (0.54-0.84)	0.83 (0.67-1.03)	1 (ref.)
Adjusted*	0.71 (0.57-0.88)	0.85 (0.68-1.05)	1 (ref.)

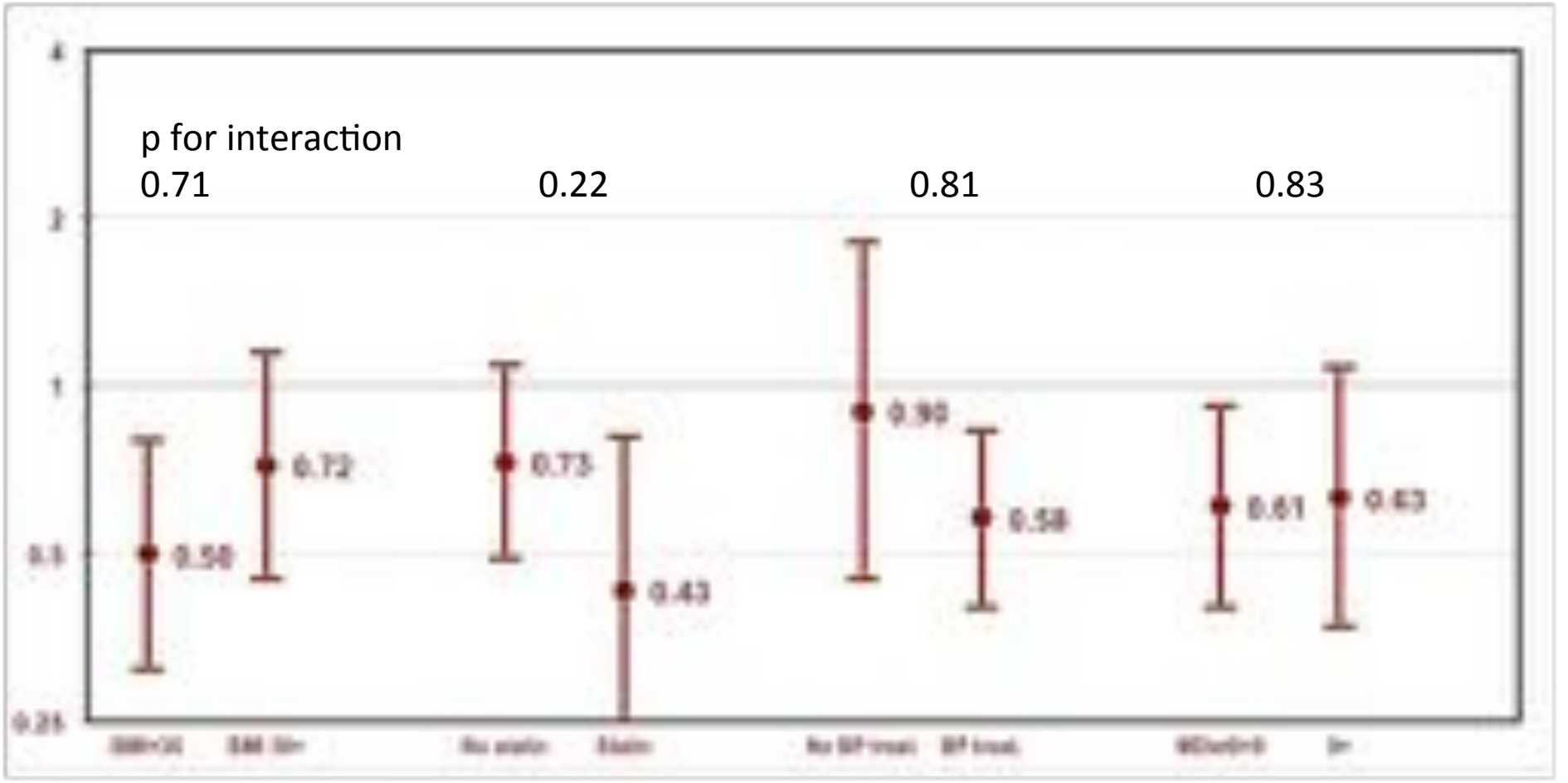
*** Age, sex, smoking, educational level, baseline height, body mass index, waist to height ratio, diabetes, hypertension, LDL, HDL, BP, antihypertensive treatment, statin use, baseline adherence to the MeDiet, and preexisting arrhythmias (other than AF).**

Hazard Ratios (HR) of Atrial Fibrillation (95% CI) in MeDiet+EVOO vs. control within subgroups



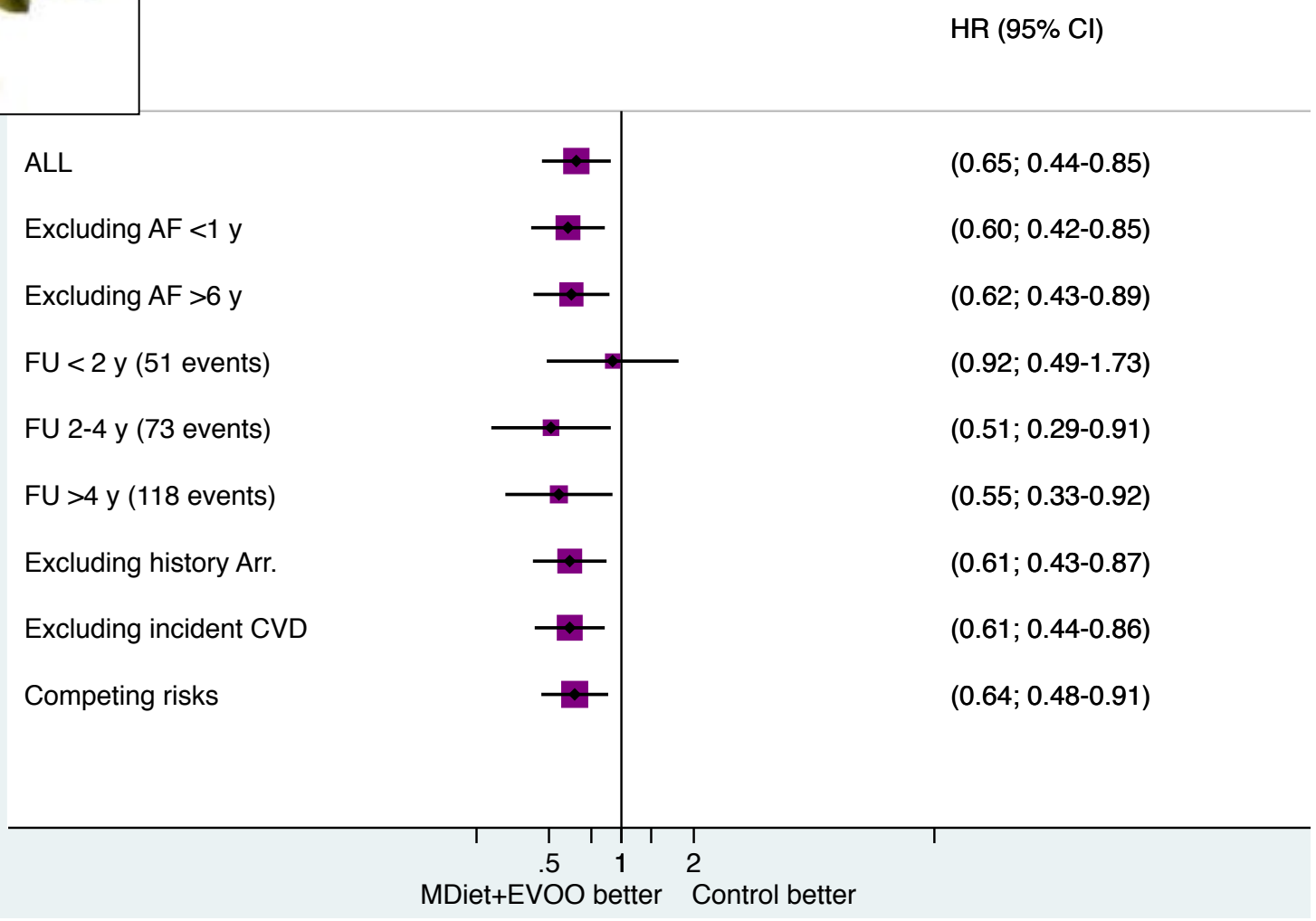
*** Aadjusted for age, sex, smoking, educational level, baseline height, body mass index, waist to height ratio, diabetes, hypertension, LDL, HDL, BP, antihypertensive treatment, statin use, baseline adherence to the MeDiet, and preexisting arrhythmias (other than AF).**

Hazard Ratios (HR) of Atrial Fibrillation (95% CI) in MeDiet+EVOO vs. control within subgroups



*** Adjusted for age, sex, smoking, educational level, baseline height, body mass index, waist to height ratio, diabetes, hypertension, LDL, HDL, BP, antihypertensive treatment, statin use, baseline adherence to the MeDiet, and preexisting arrhythmias (other than AF).**

Sensitivity analyses



*** Adjusted for age, sex, smoking, educational level, baseline height, body mass index, waist to height ratio, diabetes, hypertension, LDL, HDL, BP, antihypertensive treatment, statin use, baseline adherence to the MeDiet, and preexisting arrhythmias (other than AF).**

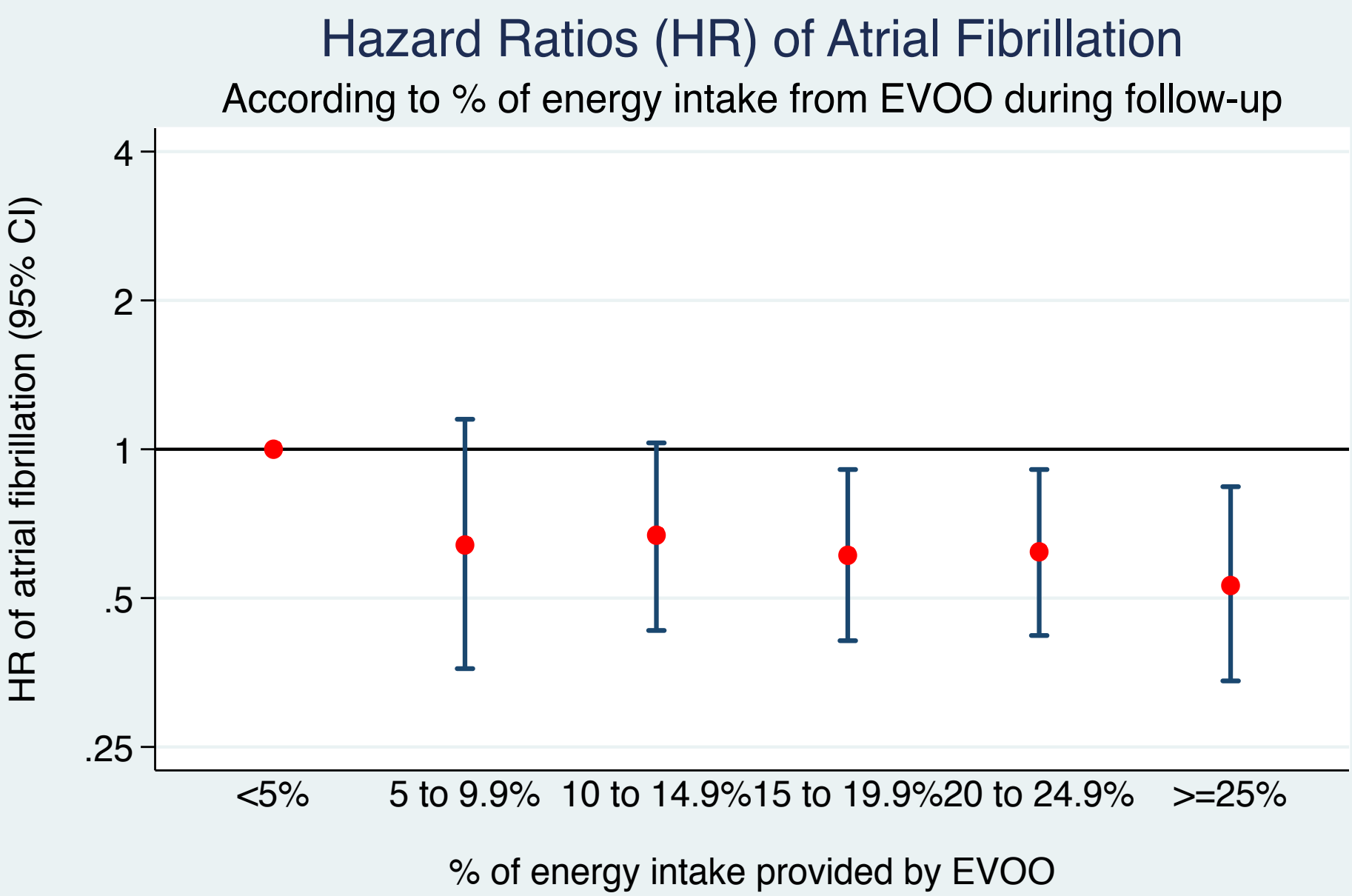
Supplemental Table 1. Association of selected baseline characteristics with the incidence of AF. Hazard Ratios (HR) and 95% confidence intervals (CI). The PREDIMED trial, 2003-2010.

	HR (95% CI)	P-value
Male sex	1.01 (0.68, 1.51)	0.95
Age, 5 years increment	1.29 (1.16, 1.44)	<0.001
Smoking		
Never smoker	1 (ref)	
Former smoker	1.17 (0.83, 1.65)	0.38
Current smoker	1.27 (0.83, 1.94)	0.27
Height, 10 cm increment	1.29 (1.01, 1.64)	0.04
Weight, 11 kg increment	1.37 (1.11, 1.68)	0.004
Diabetes	0.96 (0.73, 1.27)	0.77
Hypertension	1.20 (0.85, 1.69)	0.84
Systolic blood pressure,		
10 mmHg increment	1.08 (0.97, 1.21)	0.22
Diastolic blood pressure,		
10 mmHg increment	0.84 (0.73, 0.97)	0.007
BP lowering medication	1.70 (1.18, 2.44)	0.005
Use of statins	0.84 (0.63, 1.11)	0.22

Cox proportional hazards model adjusting for all covariates in the table plus assigned treatment, education, LDL-c, and PREDs, stratified by center and using robust variance estimations.

Supplemental Table 3. Incidence of AF according to attained consumption of extra virgin olive oil during the follow up period. Per protocol analysis. The PREDIMED trial 2003-2013.

	Attained consumption of energy-adjusted EVOO (++ 3 upper quintiles)	
	No	Yes
Cases	109	144
Person-years of follow up	7 016	21 805
Crude rate/1000 person-years (95% CI)	15.5 (12.8-18.7)	6.6 (5.6-7.8)
Hazard ratios of AF (95% CI) entire sample		
Crude model*	1 (ref.)	0.34 (0.26-0.45)
Age- and sex-adjusted model*	1 (ref.)	0.36 (0.27-0.47)
Multivariate adjusted model* (a)	1 (ref.)	0.35 (0.27-0.47)
Additionally adjusted for both intervention groups (a)	1 (ref.)	0.36 (0.28-0.50)
Hazard ratios of AF (95% CI) in each arm		
Within the Mediterranean-EVOO* (a)	1 (ref.)	0.31 (0.20-0.51)
Within the Mediterranean* (a)	1 (ref.)	0.41 (0.31-0.60)
Within the Control group* (a)	1 (ref.)	0.39 (0.24-0.64)
p for interaction (2 df)		0.66
p for interaction (1 df)		0.33


Hazard Ratios (HR) of Atrial Fibrillation
According to % of energy intake from EVOO during follow-up
HR of atrial fibrillation (95% CI)
4
2
1
.5
.25
<5%
5 to 9.9%
10 to 14.9%
15 to 19.9%
20 to 24.9%
>=25%
% of energy intake provided by EVOO

Dietary Fat Intake Is Differentially Associated with Risk of Paroxysmal Compared with Sustained Atrial Fibrillation in Women[1–3]

Stephanie E Chiuve,[4,5,7]* Roopinder K Sandhu,[5,8] M Vinayaga Moorthy,[5] Robert J Glynn,[5] and Christine M Albert[4,5,6]

J Nutr 2015;145:2092–101

Women's Health Study

- 33,665 women <45 y without CVD and AF at baseline in 1993.
- 1441 cases of incident AF (929 paroxysmal and 467 persistent/chronic)

Only observed associations **for persistent/chronic AF**, but not for paroxysmal AF

- RR for a 5% increment of energy from **SFAs**: **1.47 (95% CI: 1.04, 2.09)**
- RR for a 5% increment for **MUFAs** was **0.67 (95% CI: 0.46, 0.98)** for persistent/chronic
- No association with the American-adopted version of MeDiet

"Adherence to the Mediterranean diet in US populations such as the WHS

often **does not reflect the traditional Mediterranean diet** in other parts of the world

or the dietary pattern tested in the PREDIMED trial"

J Nutr 2015;145:2092–101

VENICE 2015
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Venice, Italy. October 16-18 2015

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1. Diet & AF
2. Dietary patterns & MeDiet
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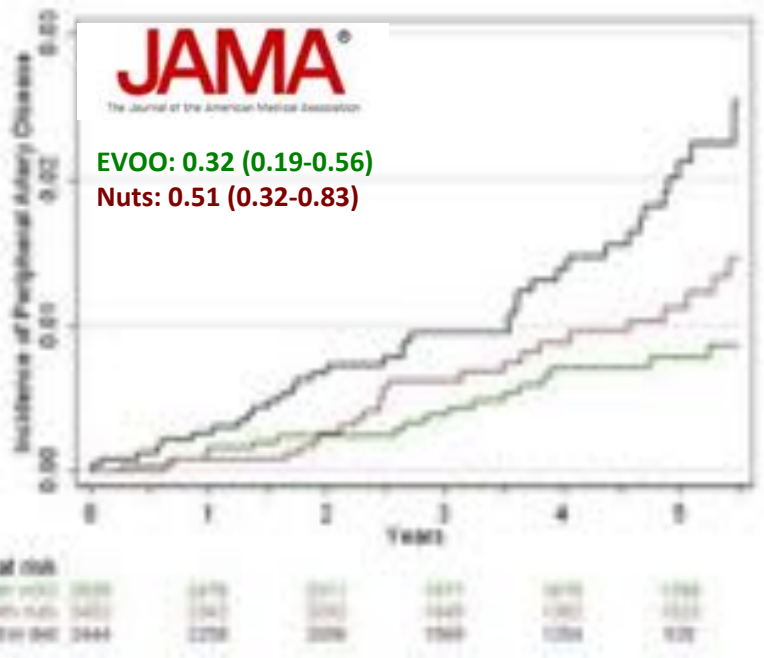
CVD

EVOO: 0.70 (0.53-0.91)
Nuts: 0.70 (0.53-0.94)

PAD



EVOO: 0.32 (0.19-0.56)
Nuts: 0.51 (0.32-0.83)

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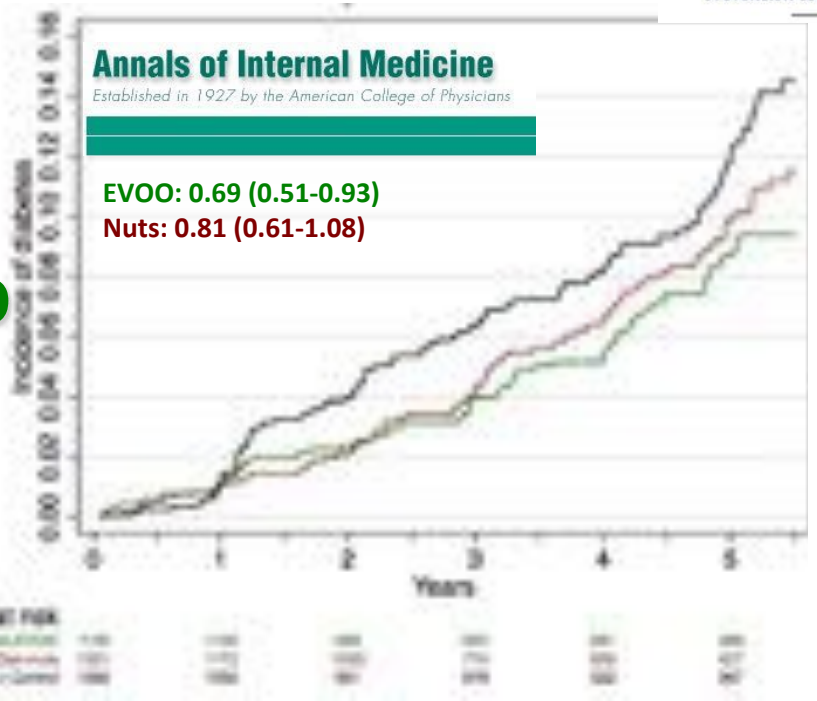
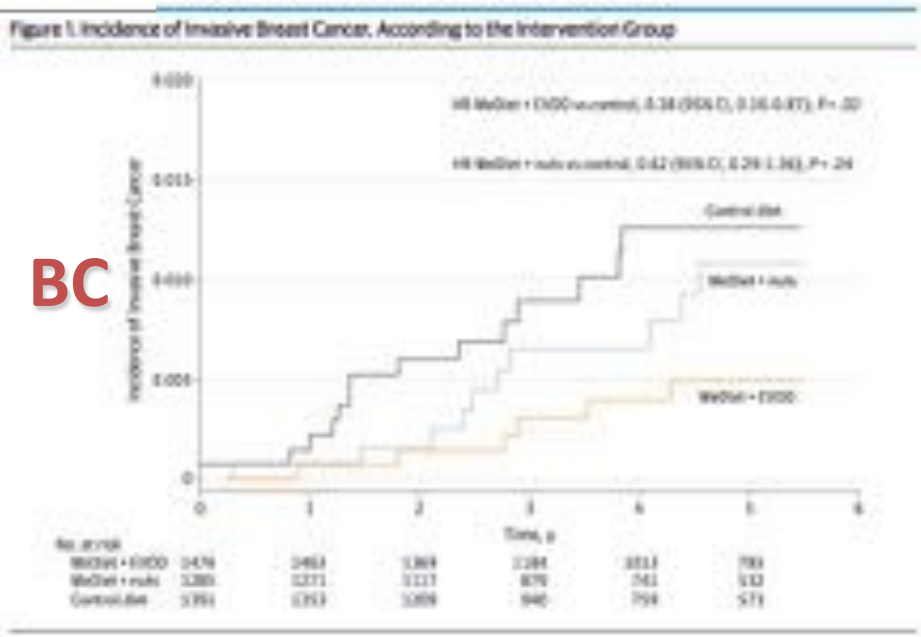
Prevención con Dieta Mediterránea

T2D



EVOO: 0.69 (0.51-0.93)
Nuts: 0.81 (0.61-1.08)

BC



Eur J Nutr
DOI 10.1007/s00394-014-0828-3

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ORIGINAL CONTRIBUTION

Nutritional adequacy according to carbohydrates and fat quality

Ana Sánchez-Taínta · Itziar Zazpe · Maira Bes-Rastrollo · Jordi Salas-Salvadó · Mónica Bullo · José Vicente Sorlí · Dolores Corella · Mª Isabel Covas · Fernando Arós · Mario Gutiérrez-Bedmar · Miquel Fiol · F. García de la Corte · Lluis Serra-Majem · Xavier Pinto · Helmut Schröder · Emilio Ros · M. Carmen López-Sabater · Ramón Estruch · Miguel Angel Martínez-González · For the PREDIMED study investigators

www.predimed.es

Received: 26 May 2014 / Accepted: 23 December 2014
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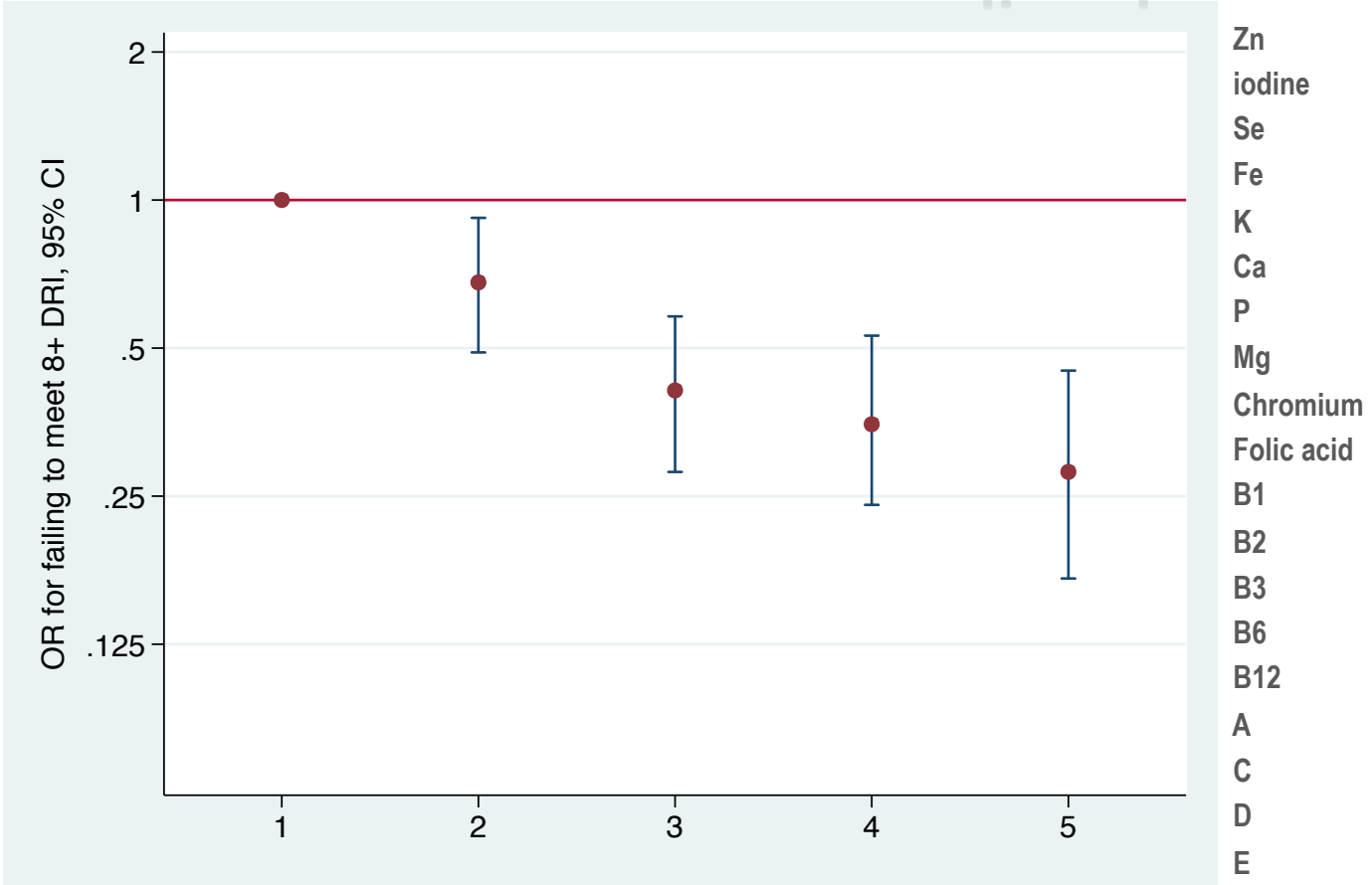
MeDiet:
a high-quality diet



Quintiles of adherence to the Mediterranean diet (PREDIMED 14-item score)

The **Mediterranean diet** has passed the tests of

- long-term sustainability,
- effectiveness and
- nutritional quality.

A low-calorie Mediterranean diet might be the most sensible approach for **weight loss** and prevention of **cardiovascular** disease in patients with diabetes.

[redacted]

CORRESPONDENCE

Intensive Lifestyle Intervention in Type 2 Diabetes

N Engl J Med 2013; 369:2356-2359 | December 12, 2013 | DOI: 10.1056/NEJMc1312802

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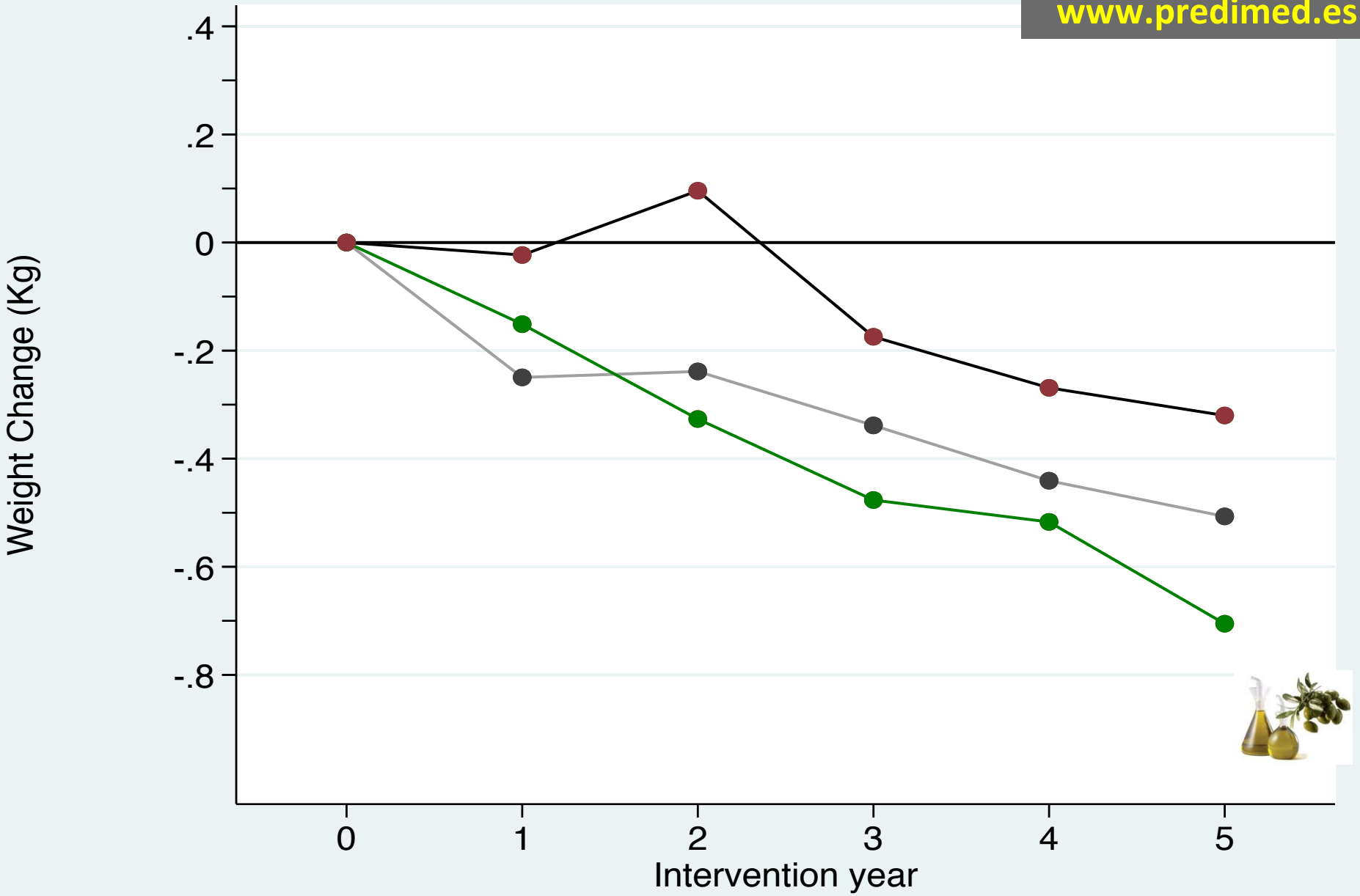

www.predimed.es

PLos One 2012;7: e43134

OPEN ACCESS Freely available online

PLOS ONE

A 14-Item Mediterranean Diet Assessment Tool and Obesity Indexes among High-Risk Subjects: The PREDIMED Trial

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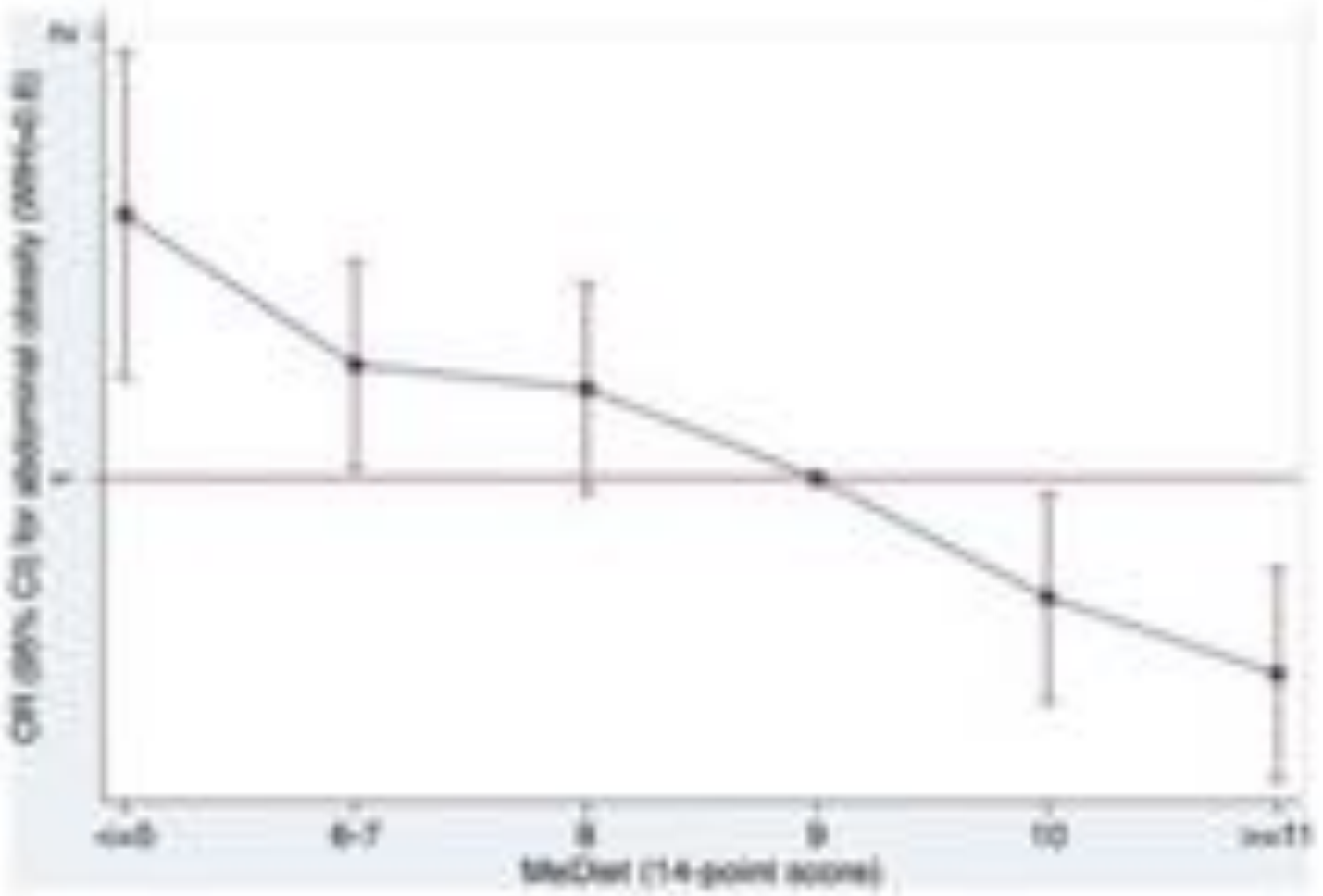

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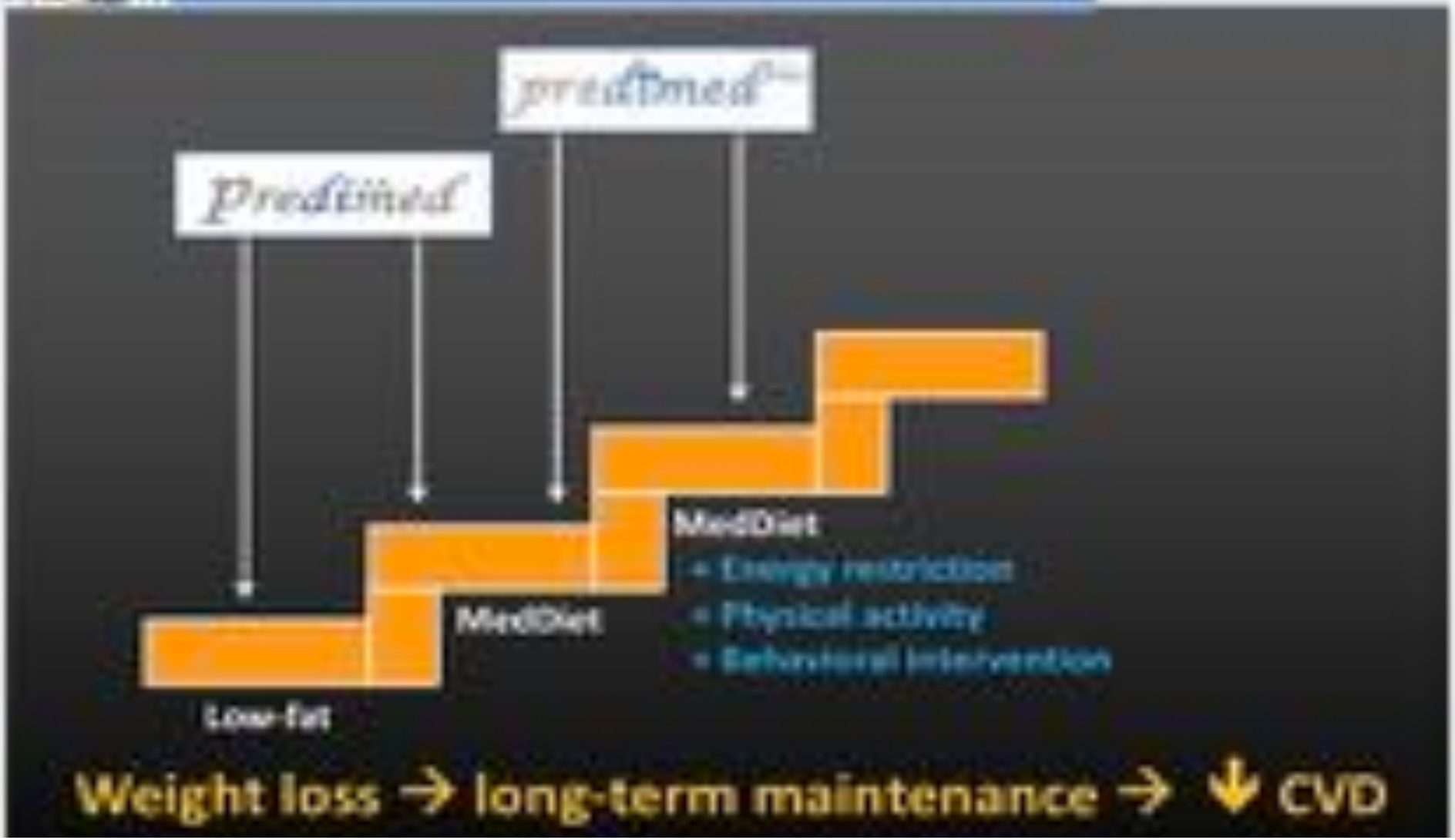
PREDIMED-PLUS DESIGN



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DESIGN AND METHODS OF THE PREDIMED PLUS TRIAL

predimed plus

n = 6000

Eligible participants

Random

n = 3000

n = 3000

Intensive weight-loss lifestyle intervention

Usual care (MedDiet)

Energy-restricted Mediterranean diet
+
Physical activity
+
Behavioral intervention

Data Safety and Monitoring Board

preadmed

Chairman:

Prof. Meir Stampfer (Harvard School of Public Health)

Members:

Prof. Joan Sabaté (Loma Linda University)

Dr. Anne Astrup (Copenhagen University)

Prof. Francisco Fernández-Avilés (Universidad Complutense of Madrid)

Honorary member:

Prof. Xavier Pi-Sunyer (Columbia University)

To ensure the smooth running of the trial and the safety of participants

Up to Sept 20, 2015

predimed

n=2274

NODO	n	%
10-Navarra (Preventiva)	358	34,86
07 - Reus	230	10,11
06 - IMIM	227	9,98
12-Valencia	196	8,62
03-Navarra (Nutrición)	163	7,08
04-Baleares (S. Espases)	157	6,9
13-Las Palmas	134	5,89
05-Clínic (M. Interna)	121	5,32
11-Vitoria	114	5,01
01-Málaga (Preventiva)	112	4,93
15-Córdoba	96	4,13
18-Malaga Endocr.	70	3,08
14-Bellvitge	60	2,64
02-Sevilla	56	2,46
08 - Granada	53	2,33
20- Clínic (Endocrino)	50	2,2
19-Baleares (Fisiol.)	36	1,58
21 - Alicante	35	1,54
09-F. Jiménez Díaz	23	1,01
16-IMDEA	8	0,35
17-Clínico Madrid	5	0,22

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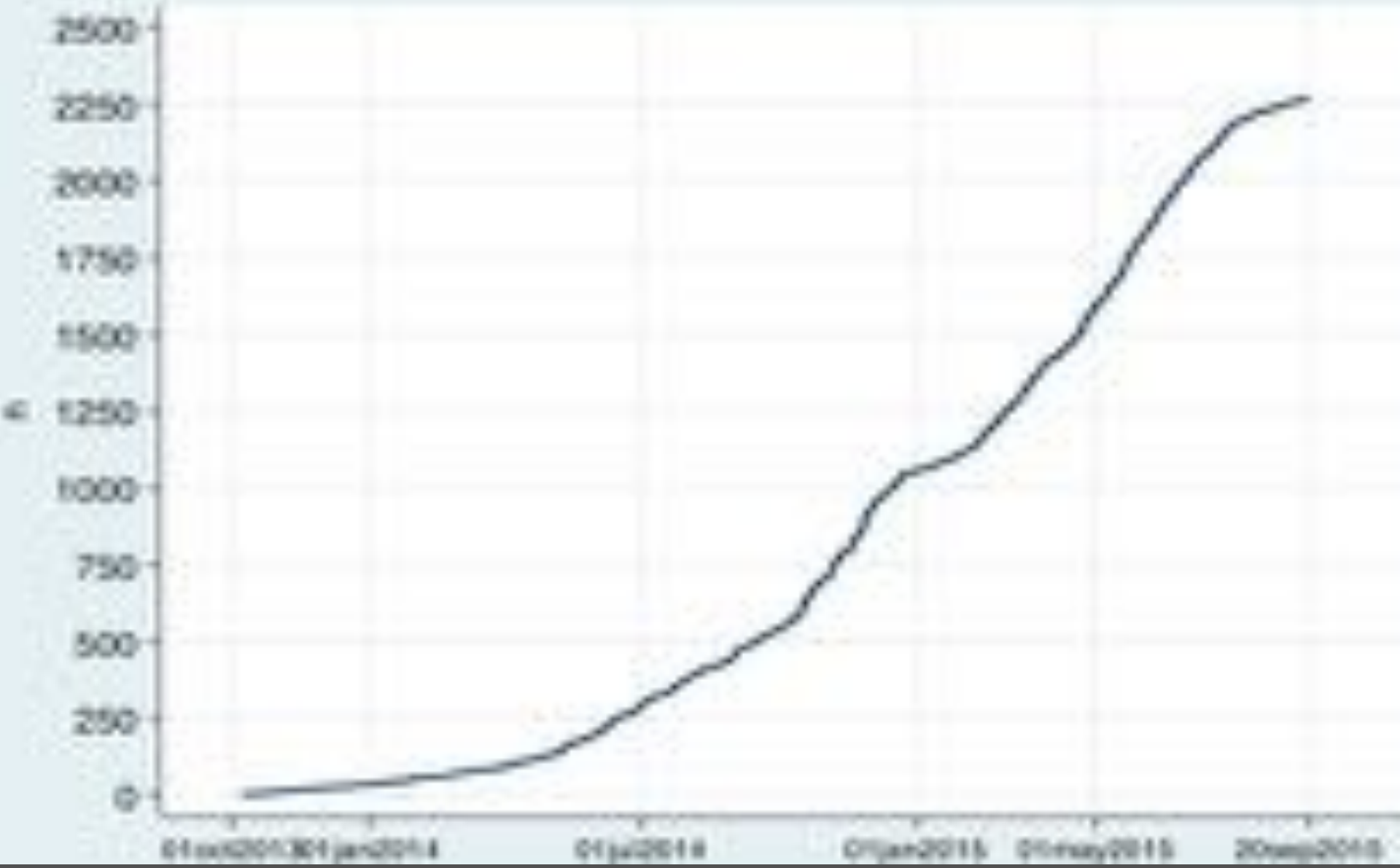

VENICE 2015 ARRHYTHMIAS
Venice, Italy. October 16-18 2015

Predimed
Prevención con Dieta Mediterránea

Universidad de Navarra
Facultad de Medicina
Departamento de Medicina Preventiva y Salud Pública

MeDiet & **Atrial Fibrillation**

Thank you!

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www.predimed.es