



# “Más vale prevenir que curar: la evidencia de la Prevención cardiovascular”

*Miguel A. Martínez-González*  
*Universidad de Navarra*  
Palma, 12 Diciembre, 2016



**Epidemiol. descriptiva**

**Factores de riesgo**

**Vida simple'7**

**Patrones: MedDiet**

**PREDIMED-PLUS**



# Epidemiol. descriptiva

Factores de riesgo

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Población  
Nacim./año  
Muertes/año

Causas de Muerte

Cáncer  
VIH/sida  
A. Tráfico  
Diabetes  
ECV  
Cirrosis  
Paludismo  
Tuberculosis  
EPOC  
Alzheimer/demencias  
Suicidio



**Población 7.500 M**

**Nacim./año 135 M**

**Muertes/año 57 M**

## Causas de Muerte

**ECV 17,5 M**

**Cáncer 8,2 M**

**EPOC 3,1 M**

**Diabetes 1,5 M**

**Cirrosis 1,0 M**

**Alzh./dem. 0,7 M**

**VIH/sida 1,5 M**

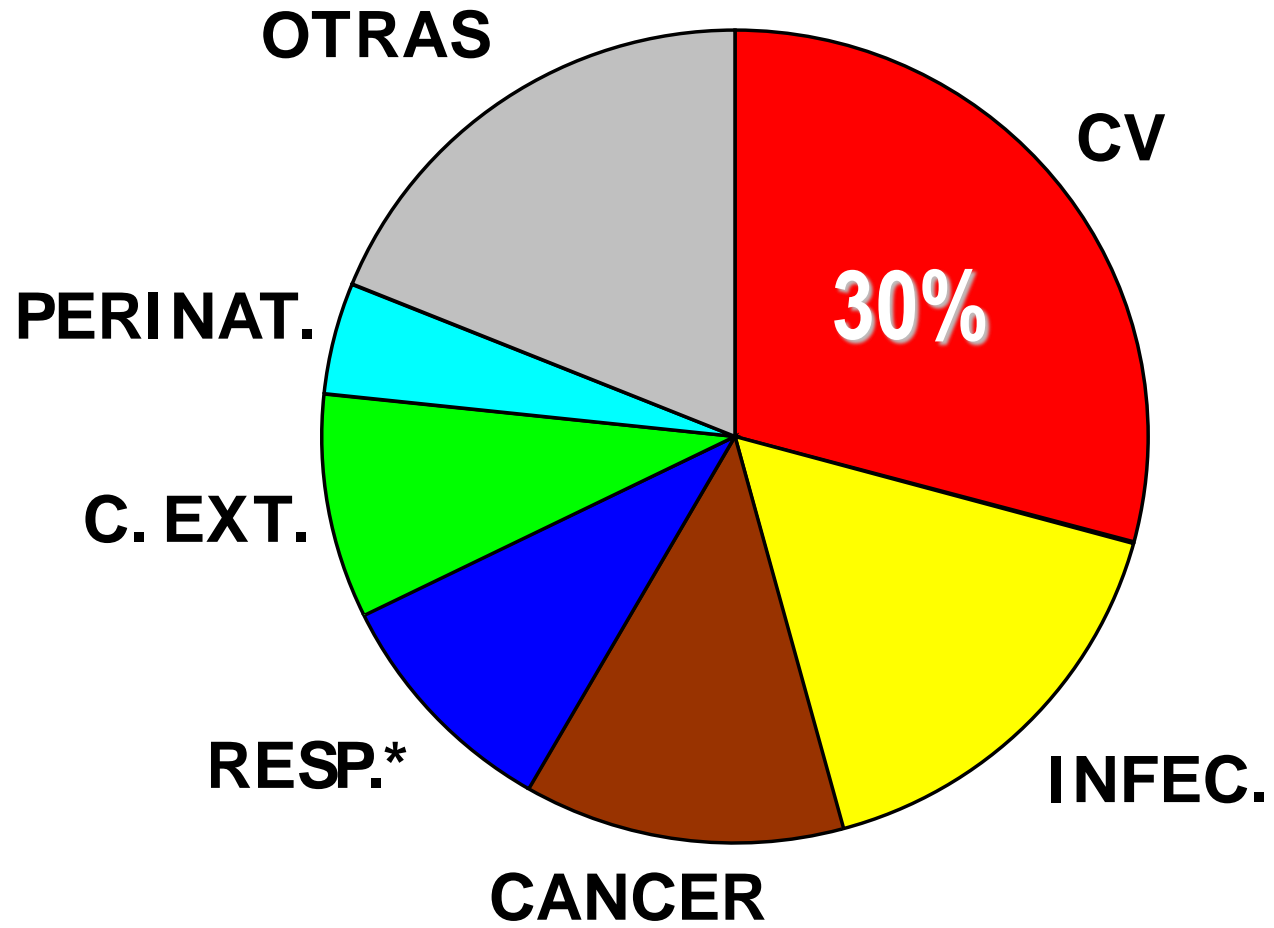
**Tubercul. 0,9 M**

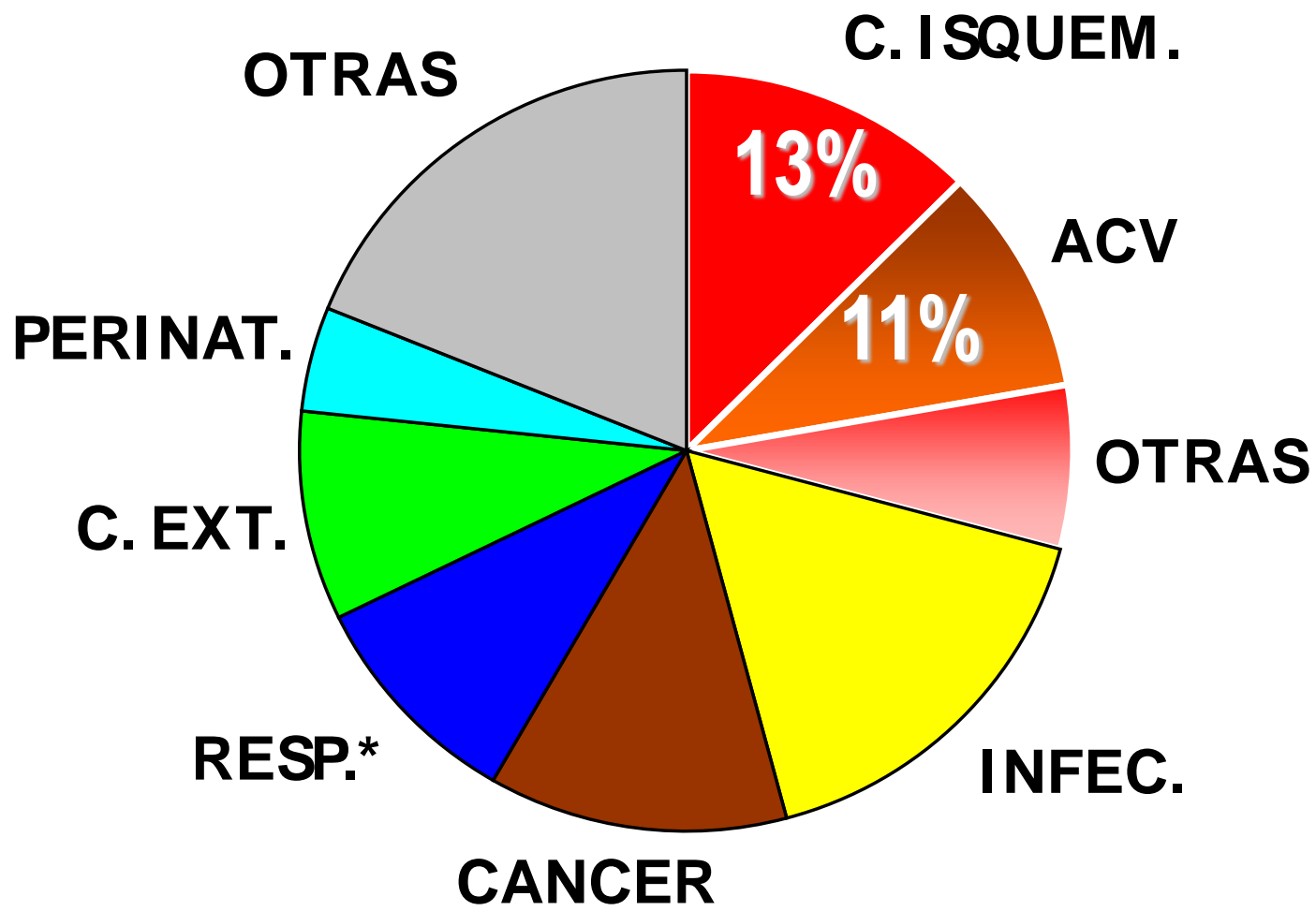
**Paludismo 0,8 M**

**A. tráfico 1,3 M**

**Suicidio 1,0 M**









# Non Communicable Diseases (NCDs)



**2011 UN High-level meeting on NCDs**  
General Assembly • United Nations • New York  
19–20 September 2011

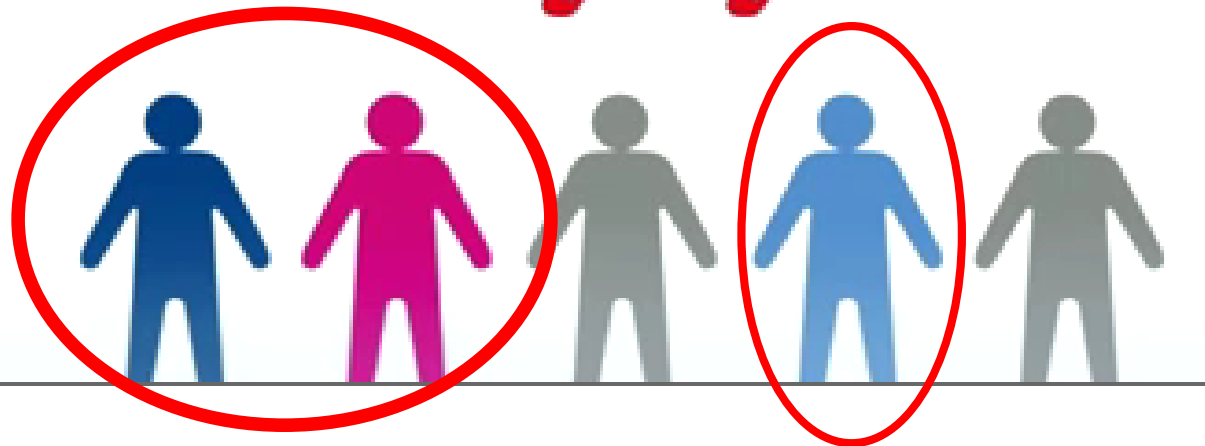
**UNITE IN THE FIGHT AGAINST NCDs**



**World Health  
Organization**

**UN High-level Meeting on NCDs**  
*(New York, 19-20 September 2011)*

3 out of 5  
people who die  
every year



# **NCDs**

Every year NCDs kill

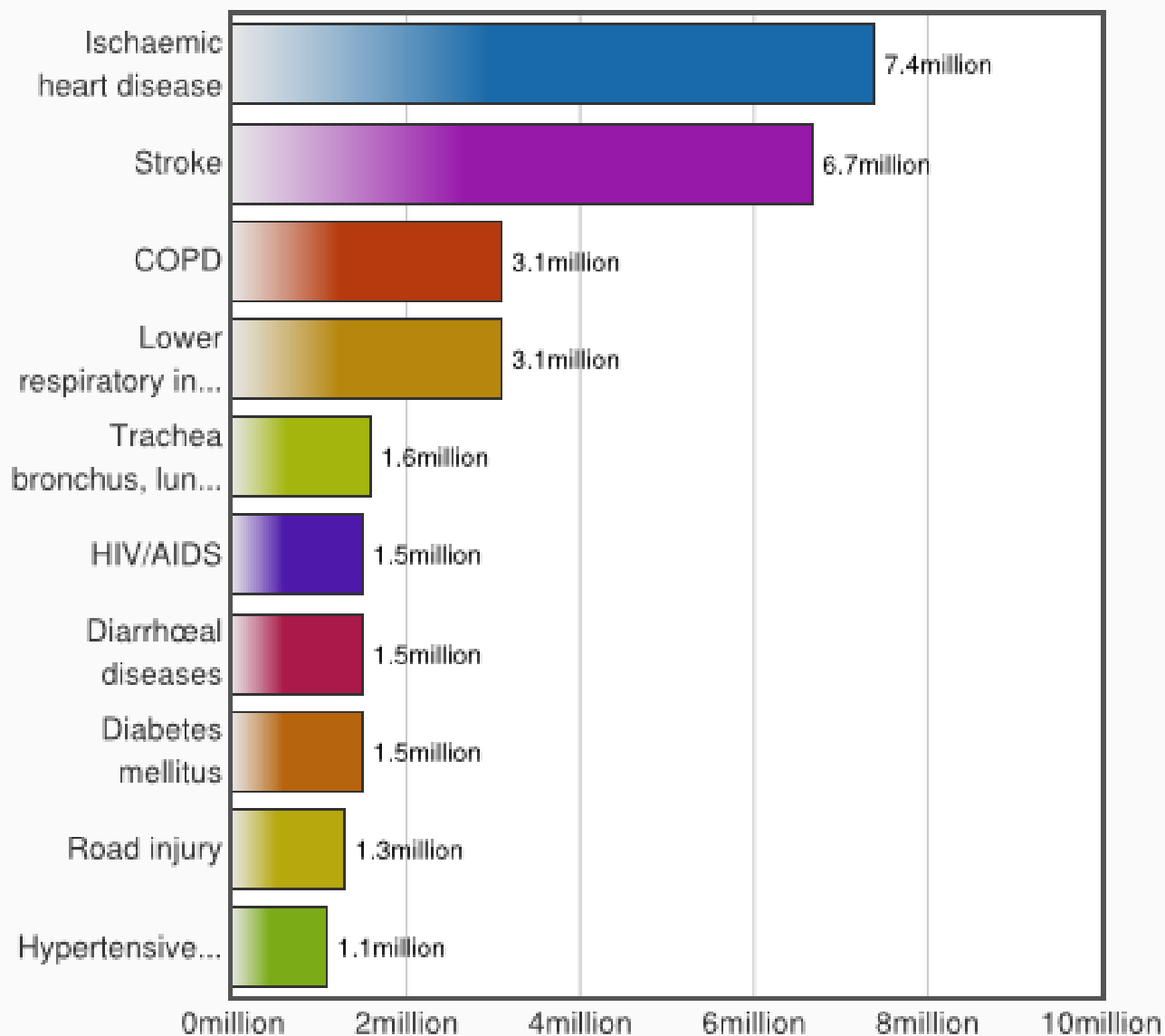
**36 million people**

# NCDs, like

- heart disease and stroke
- diabetes
- cancer
- chronic lung disease



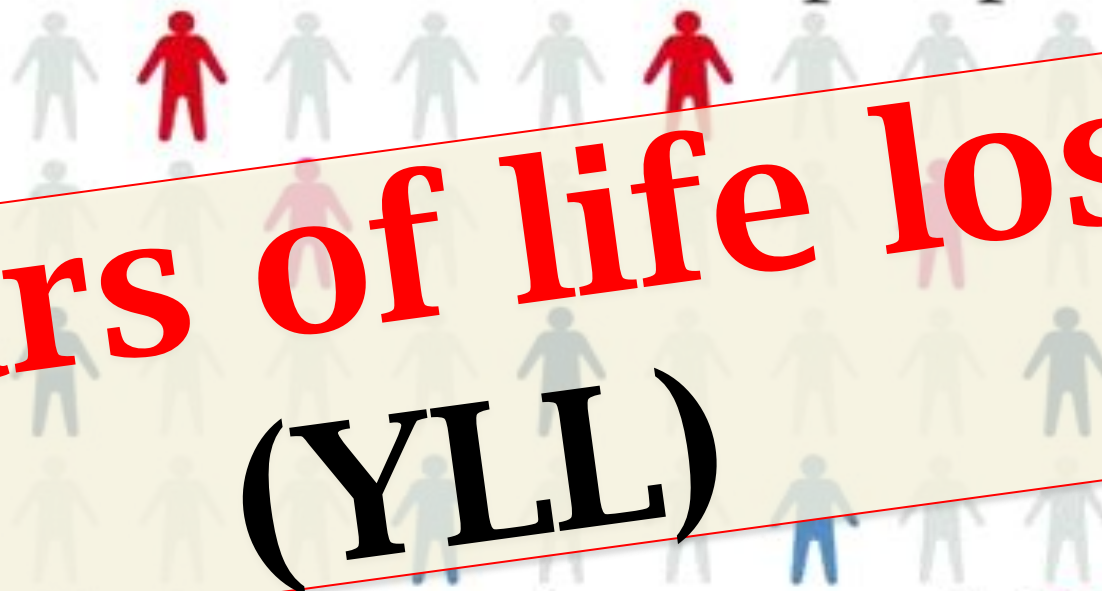
## The 10 leading causes of death in the world 2012





# NCDs

9 million of these people



years of life lost  
(YLL)

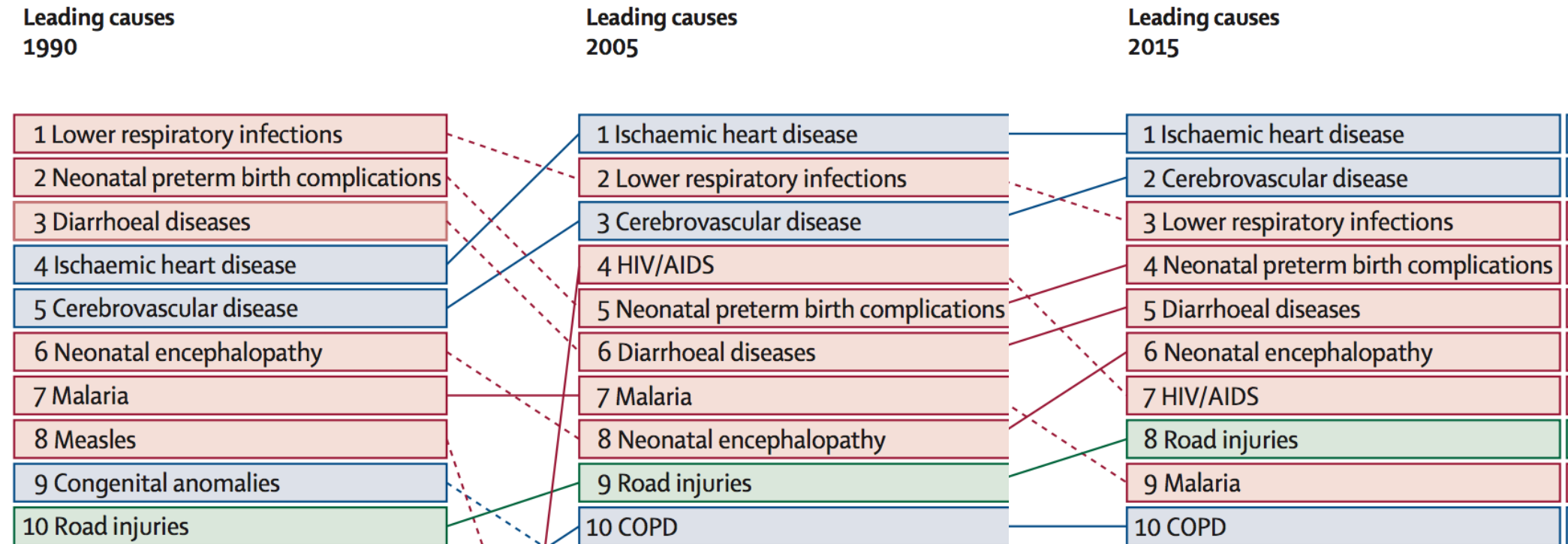
die before the age of 60

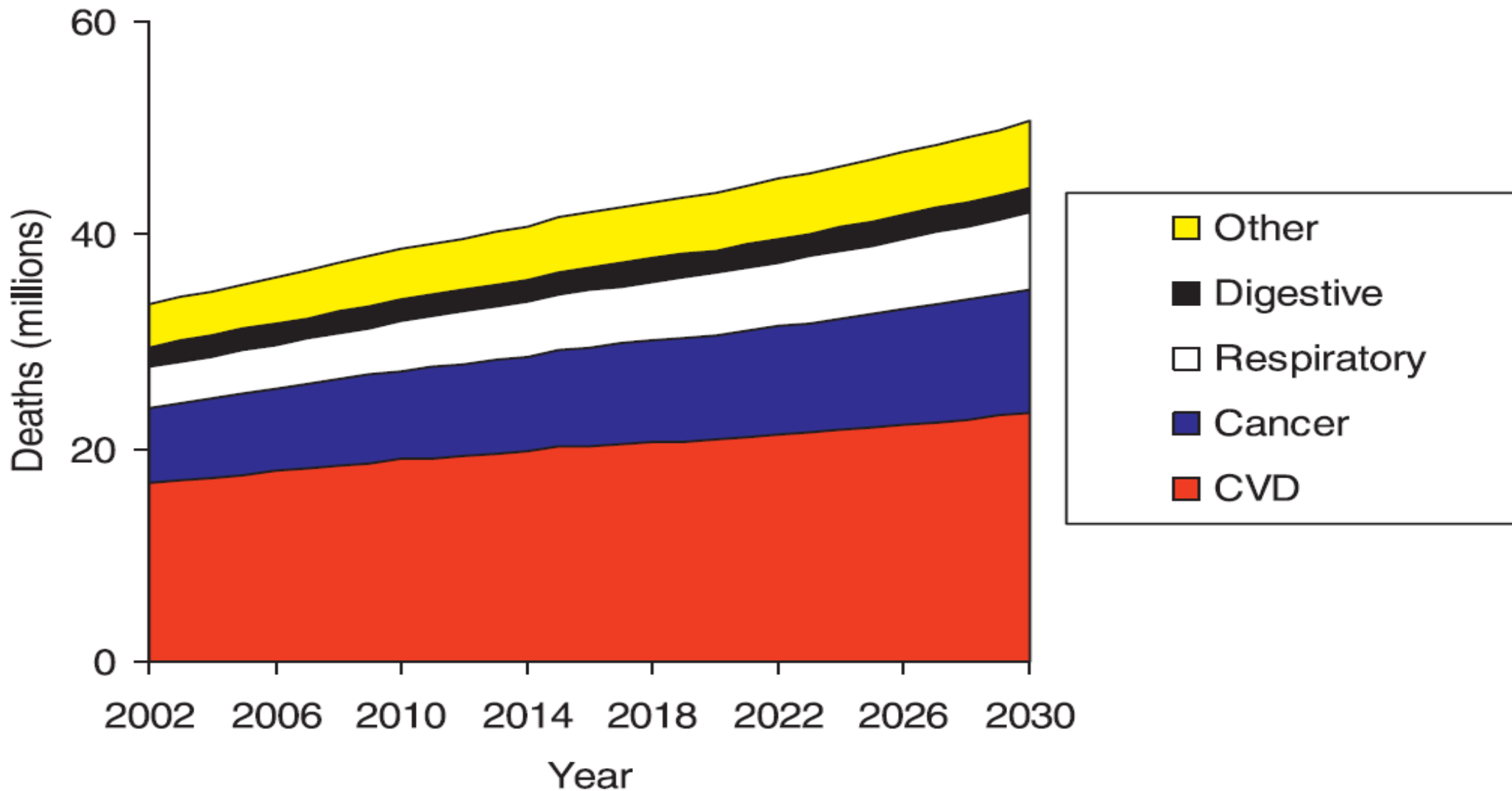
# Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015

Lancet 2016; 388:  
1459–544

GBD 2015 Mortality and Causes of Death Collaborators\*

## Leading causes of global YLLs for both sexes combined for 1990, 2005, and 2015





OPEN ACCESS Freely available online

PLoS MEDICINE

## Projections of Global Mortality and Burden of Disease from 2002 to 2030

Colin D. Mathers\*, Dejan Loncar

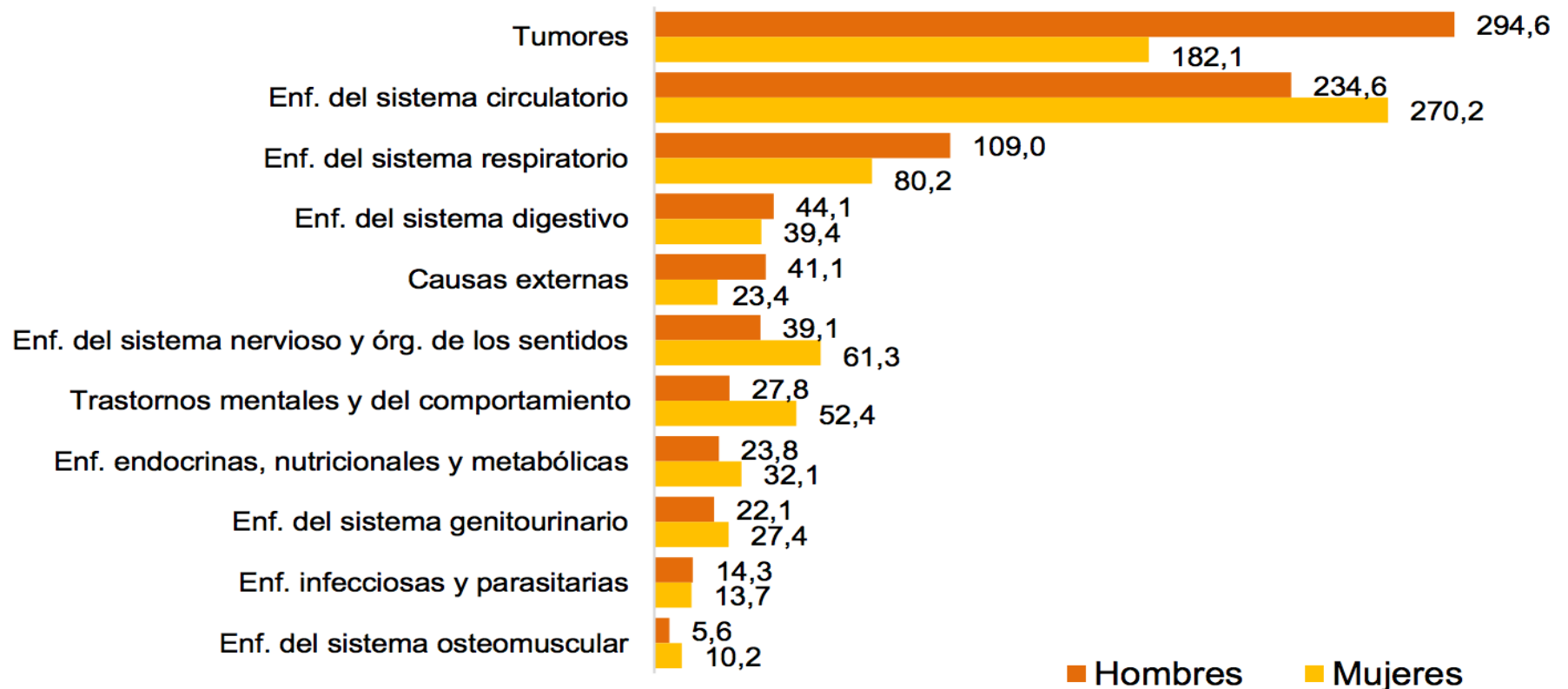
Evidence and Information for Policy Cluster, World Health Organization, Geneva, Switzerland

PLoS Med. 2006 Nov;3(11):e442.





## Tasas brutas de mortalidad por 100.000 habitantes según causa de muerte (capítulos CIE-10) y sexo. Año 2014



# Número de defunciones según las causas de muerte más frecuentes (\*)

Año 2014

	Total	Hombres	Mujeres
<b>Total enfermedades</b>	395.830	201.571	194.259
Enfermedades isquémicas del corazón	32.564	19.101	13.463
Enfermedades cerebrovasculares	27.579	11.573	16.006
Cáncer de bronquios y pulmón	21.251	17.194	4.057
Demencia	17.883	5.838	12.045
Insuficiencia cardiaca	17.095	6.214	10.881
Enf. crónicas de las vías respiratorias inferiores (ECVRI)	15.546	11.434	4.112
Enfermedad de Alzheimer	14.022	4.099	9.923
Cáncer de colon	11.797	6.964	4.833
Enfermedad hipertensiva	11.573	3.699	7.874
Diabetes mellitus	9.625	4.100	5.525
Neumonía	8.445	4.357	4.088
Insuficiencia renal	6.395	2.975	3.420
Cáncer de mama	6.325	94	6.231
Cáncer de páncreas	6.287	3.199	3.088
Cáncer de próstata	5.863	5.863	-





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**PREDIMED-PLUS**



# Epidemiol. descriptiva

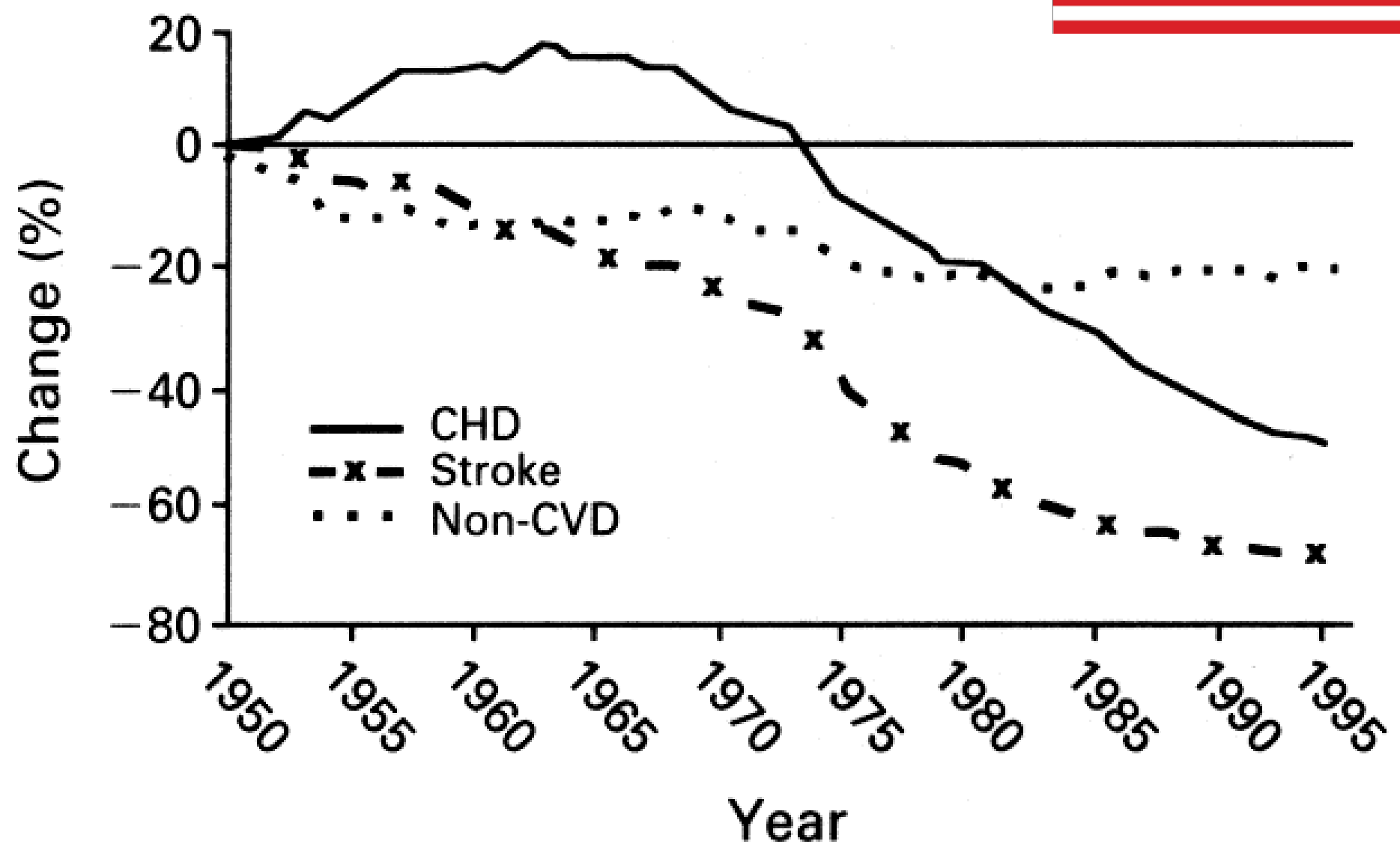
## Factores de riesgo

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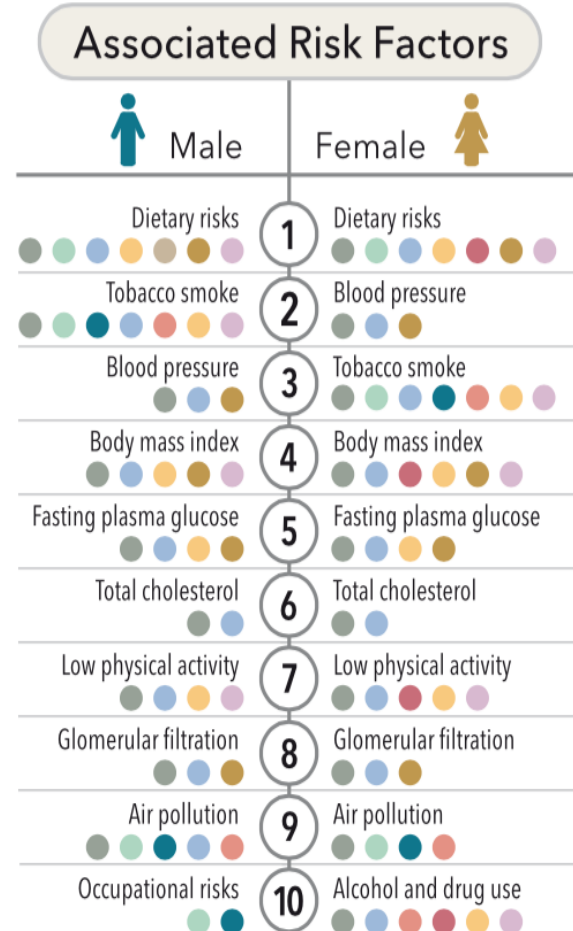
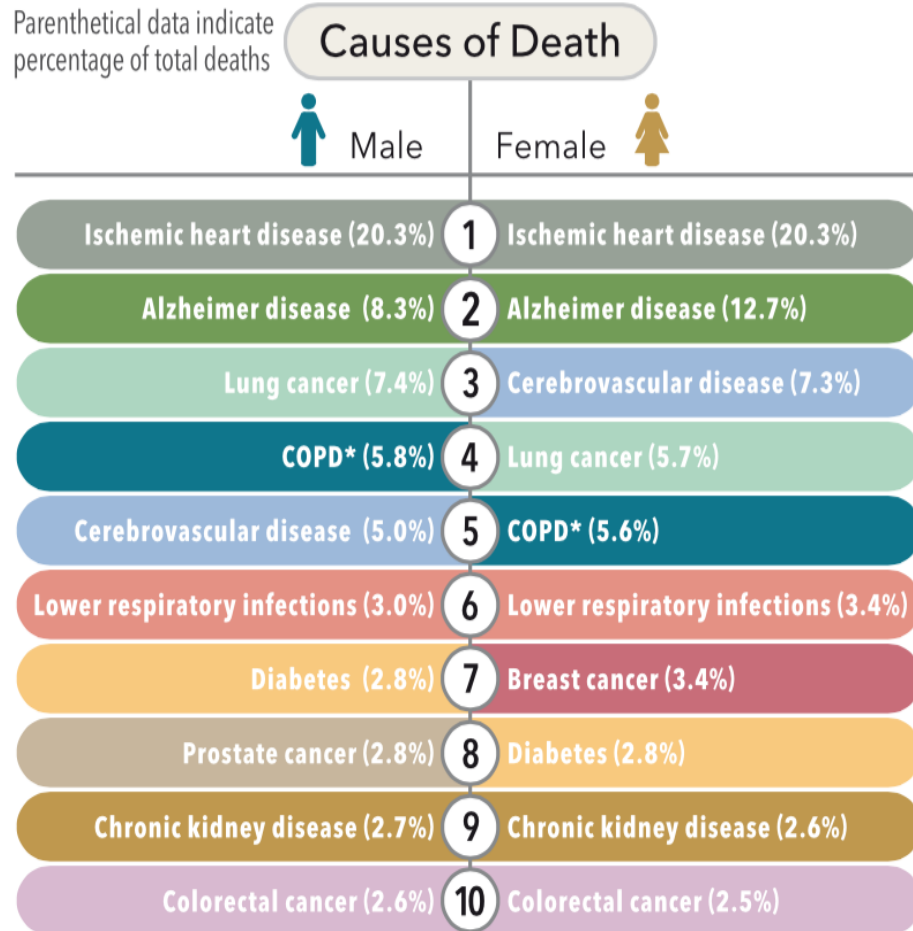
PREDIMED-PLUS





### Top 10 Causes of Death and Associated Risk Factors in the United States, All Ages, 2013

Parentetical data indicate percentage of total deaths



\*Chronic obstructive pulmonary disease

**Authors:** Laurie Marczak, PhD; Kevin O'Rourke, MFA; Dawn Shepard, BA, for the Institute for Health Metrics and Evaluation.

**Sources:** 1. GBD 2013 Mortality and Causes of Death Collaborators. *Lancet*. 2015;385(9963):117-171.  
 2. GBD 2013 Risk Factors Collaborators. *Lancet*. 2015;386(10010):2287-2323.  
 Please cite as *JAMA*. 2016;315(3):241.  
 10.1001/jama.2015.17599



IHME



The JAMA Network

dad  
rra

**McKinlay J.** A case for refocussing **upstream**: the political economy of illness.  
En: Proceedings of American Heart Association Conference.  
Washington: junio de 1974.





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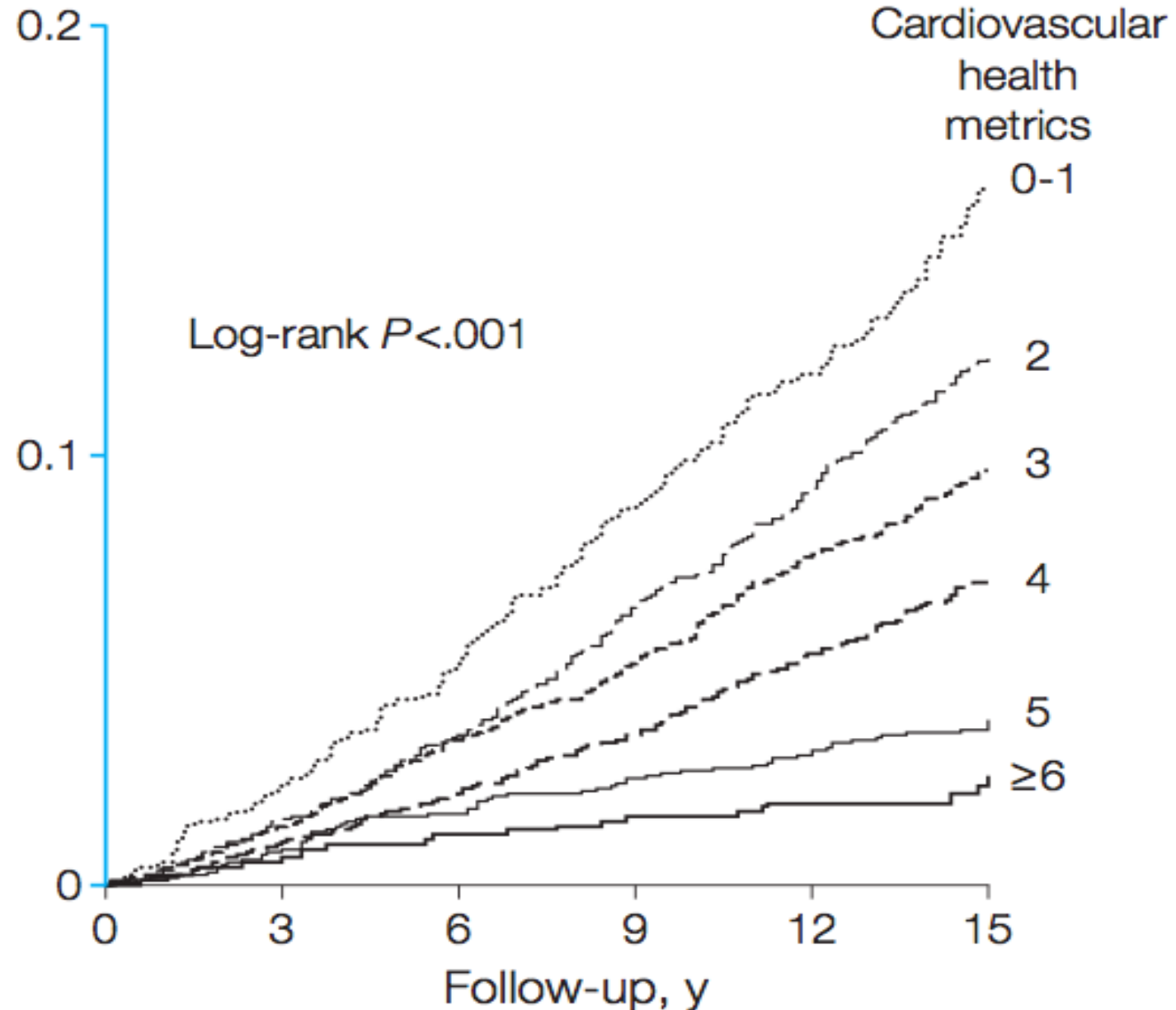


## American Heart Association's Life's Simple 7

## Cardiovascular disease mortality

Trends in Cardiovascular Health Metrics and Associations With All-Cause and CVD Mortality Among US Adults

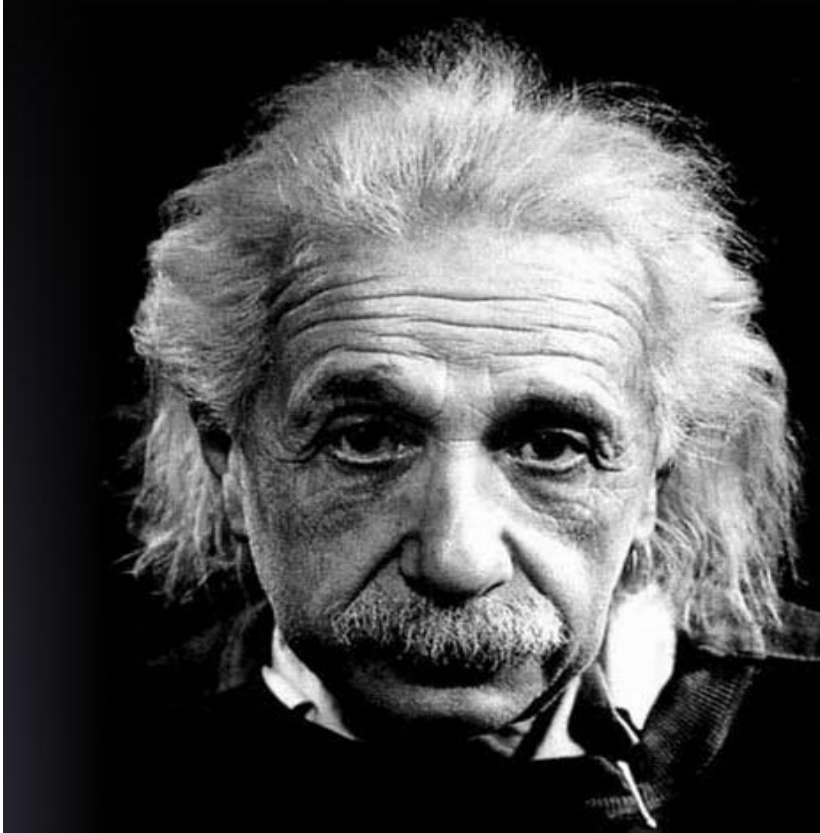
Quanhe Yang, PhD  
Mary E. Cogswell, DrPH  
W. Dana Flanders, MD, ScD  
Yuling Hong, MD, PhD  
Zefeng Zhang, MD, PhD  
Fleetwood Loustalot, FNP, PhD  
Cathleen Gillespie, MS  
Robert Merritt, BA, MA  
Frank B. Hu, MD, PhD



JAMA. 2012;307:1273-83

Albert Einstein:

- A clever person solves a problem
- A wise person avoids it



American Heart Association's Life's Simple 7:

**Defining and Setting National Goals for Cardiovascular  
Health Promotion and Disease Reduction  
The American Heart Association's Strategic Impact Goal Through 2020  
and Beyond**

*Circulation. 2010;121:586-613*

Ideal CV Health METRICS (7)

- 1.
- 2.
- 3.
- 4.
- 5.
- 6.
- 7.

# American Heart Association's Life's Simple 7: Avoiding Heart Failure and Preserving Cardiac Structure and Function

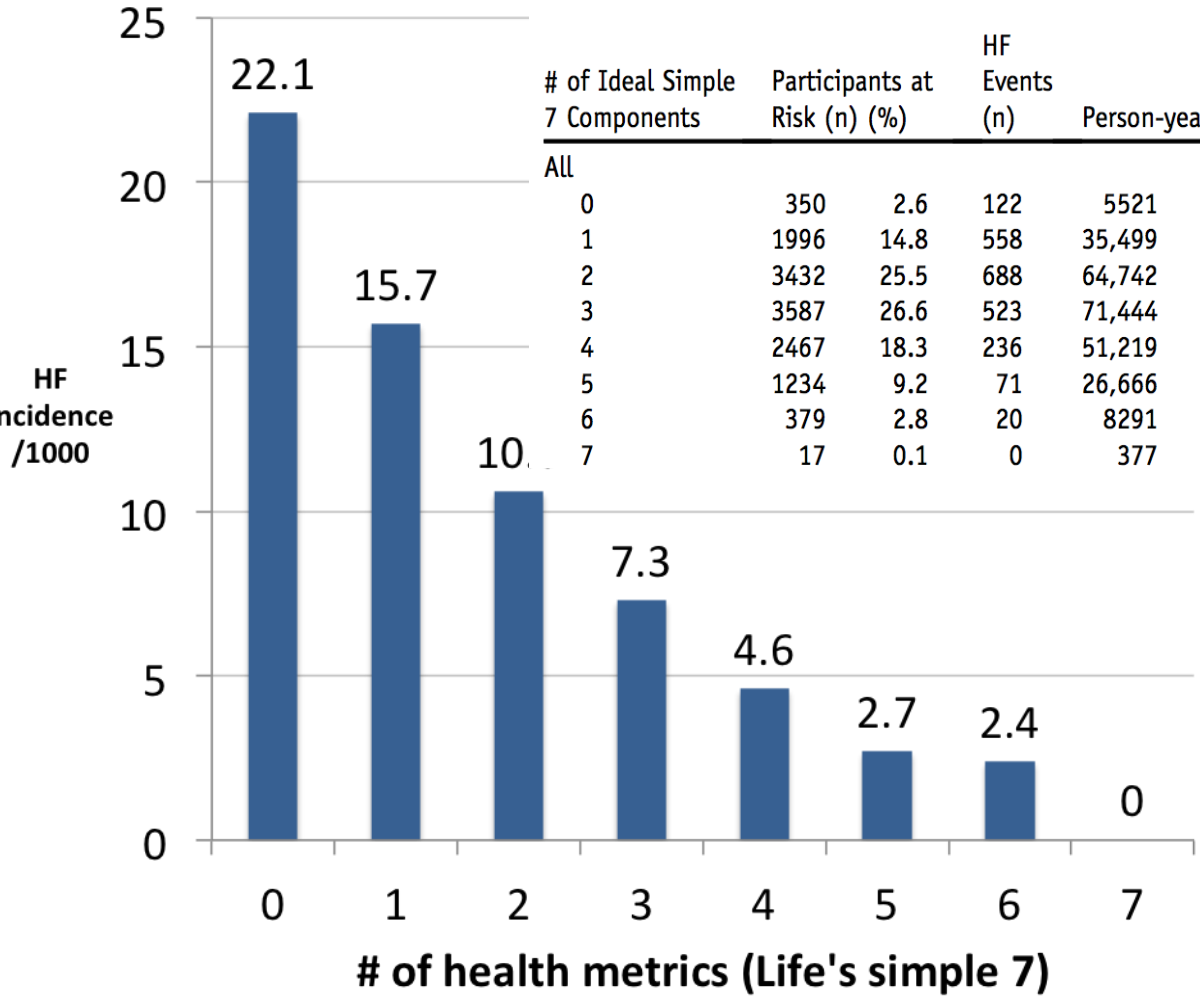


Am J Med 2015;28:970-6

Aaron R. Folsom, MD,<sup>a</sup> Amil M. Shah, MD,<sup>b</sup> Pamela L. Lutsey, PhD,<sup>a</sup> Nicholas S. Roetker, MPH,<sup>a</sup> Alvaro Alonso, MD, PhD,<sup>a</sup> Christy L. Avery, PhD,<sup>c</sup> Michael D. Miedema, MD,<sup>d</sup> Suma Konety, MD,<sup>e</sup> Patricia P. Chang, MD,<sup>f</sup> Scott D. Solomon, MD<sup>b</sup>

**Table 1** Heart Failure (HF) Incidence and Lifetime Risk in Relation to Number of Ideal AHA Life's Simple 7 Components, ARIC, 1987-2011

# of Ideal Simple 7 Components	Participants at Risk (n) (%)	HF Events (n)	Person-years	HF Incidence Rate (95% CI)*	Hazard Ratio (95% CI)†	Lifetime HF Risk (%) (95% CI)‡	Lifetime HF Risk (%), in Absence of MI (95% CI)§
All							
0	350 (2.6)	122	5521	22.1 (18.5-26.4)	1 (Ref)	45.1 (35.0-52.0)	40.7 (28.7-48.8)
1	1996 (14.8)	558	35,499	15.7 (14.5-17.1)	0.75 (0.43-0.64)	39.0 (34.9-42.1)	33.7 (29.2-37.1)
2	3432 (25.5)	688	64,742	10.6 (9.9-11.5)	0.52 (0.43-0.64)	28.0 (25.5-30.0)	24.1 (21.4-26.3)
3	3587 (26.6)	523	71,444	7.3 (6.7-8.0)	0.39 (0.31-0.48)	23.1 (20.4-25.1)	19.4 (16.7-21.5)
4	2467 (18.3)	236	51,219	4.6 (4.1-5.2)	0.27 (0.22-0.34)	16.6 (13.4-19.1)	13.2 (10.0-15.7)
5	1234 (9.2)	71	26,666	2.7 (2.1-3.4)	0.17 (0.13-0.23)		
6	379 (2.8)	20	8291	2.4 (1.6-3.7)	0.17 (0.11-0.28)	12.3 (8.8-15.2)§	10.5 (7.1-13.4)§
7	17 (0.1)	0	377	0	—		



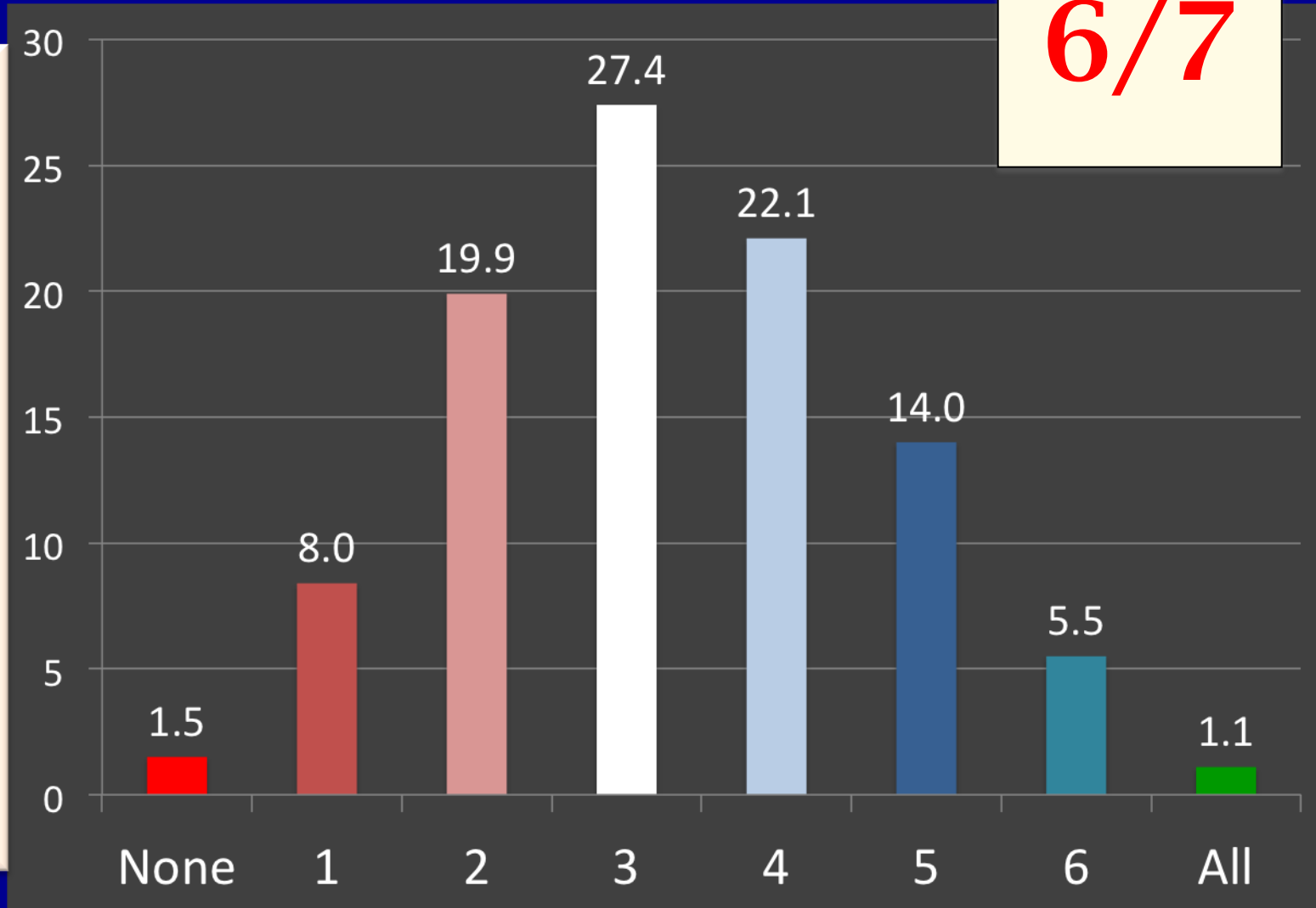
- Health METRICS**
1. Never smoking
  2. BMI < 25 kg/m<sup>2</sup>
  3. Phys. Act >149 min/wk
  4. Healthy Eating >3/5
  5. Total chol. <200 mg/dl
  6. BP < 120/80 mmHg
  7. Fasting glucose < 100

6/7

7 Ideal CV

Health METRICS

1. Never smoking
2. BMI <25
3. Phys. Act >149 min/wk
4. Healthy Eating >3/5
5. Total chol. <200
6. BP <120/80
7. Fasting glucose <100



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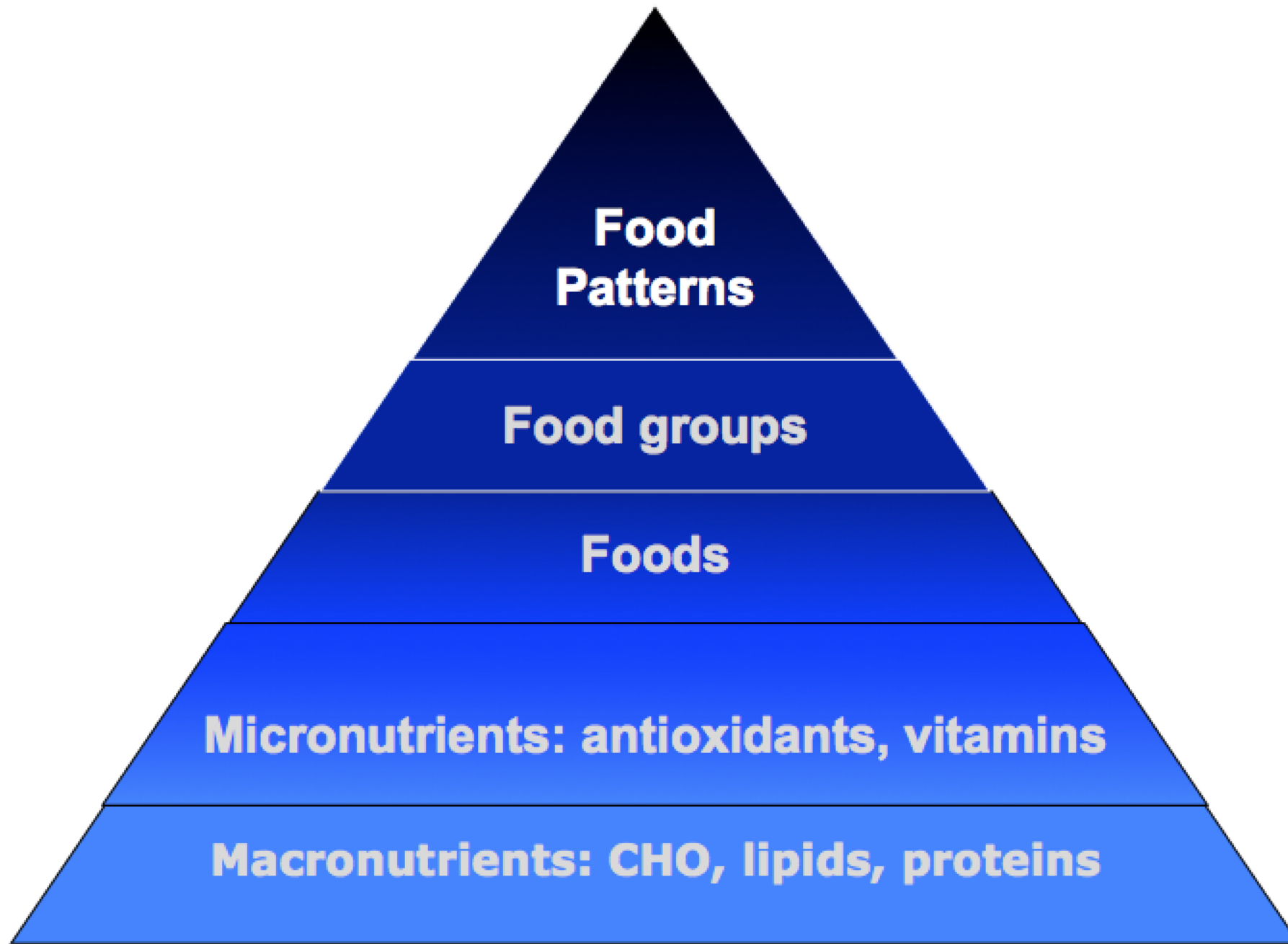
Vida simple'7

Patrones: MedDiet

PREDIMED-PLUS







# Dietary patterns: advantages

- **Interaction**

- ✓ Synergies
- ✓ Antagonisms

- **Confounding**

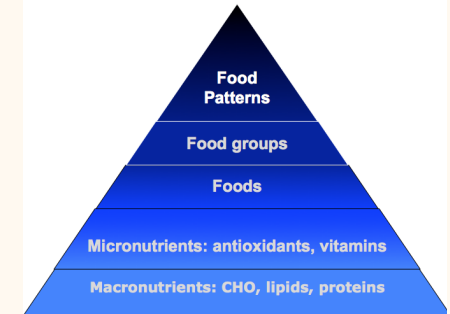
- ✓ Preempts confounding (by other dietary factors)

- **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)

## **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.

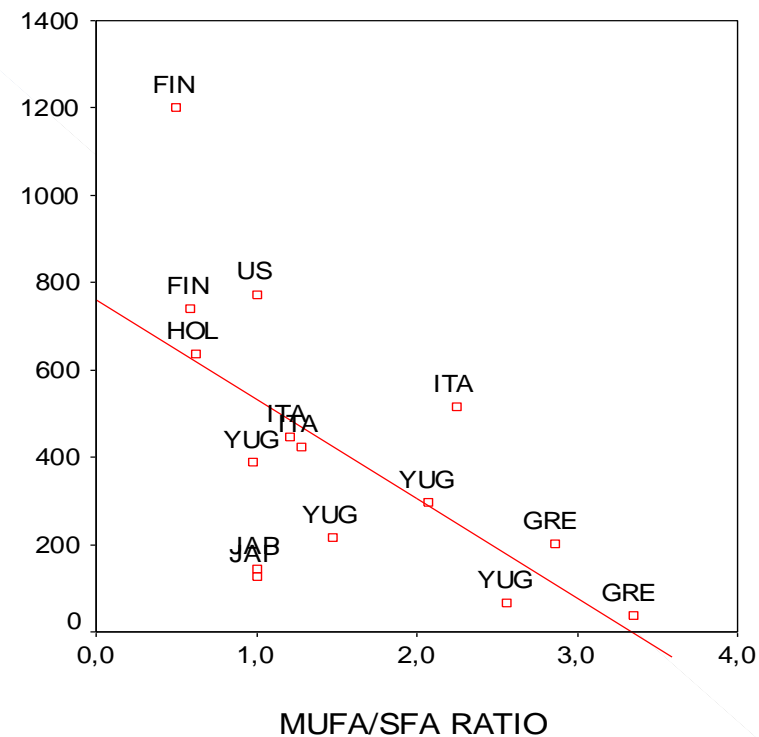
The Committee`s examination of the association between dietary patterns and various health outcomes revealed **remarkable consistency** in the findings

# 7 COUNTRIES

<i>g/d</i>	USA	The Netherlands	Greece (Crete)
<b>Fish/Seafood</b>	<b>3</b>	<b>12</b>	<b>18</b>
<b>Legumes</b>	<b>1</b>	<b>2</b>	<b>30</b>
<b>Bread</b>	<b>97</b>	<b>227</b>	<b>380</b>
<b>Fruit</b>	<b>233</b>	<b>82</b>	<b>464</b>
<b>Olive Oil</b>	<b>0</b>	<b>0</b>	<b>95</b>
<b>Meats</b>	<b>273</b>	<b>138</b>	<b>35</b>
<b>Butter</b>	<b>26</b>	<b>21</b>	<b>0</b>
<b>Margarine</b>	<b>4</b>	<b>56</b>	<b>0</b>



**Keys et al**  
**Am J Epidemiol 1986;124:903**



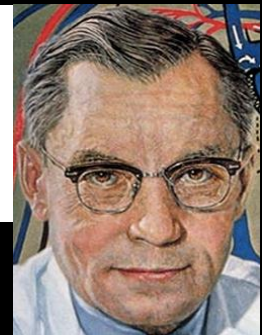
The heart of what we now consider the Mediterranean diet is mainly **vegetarian**:

- 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**

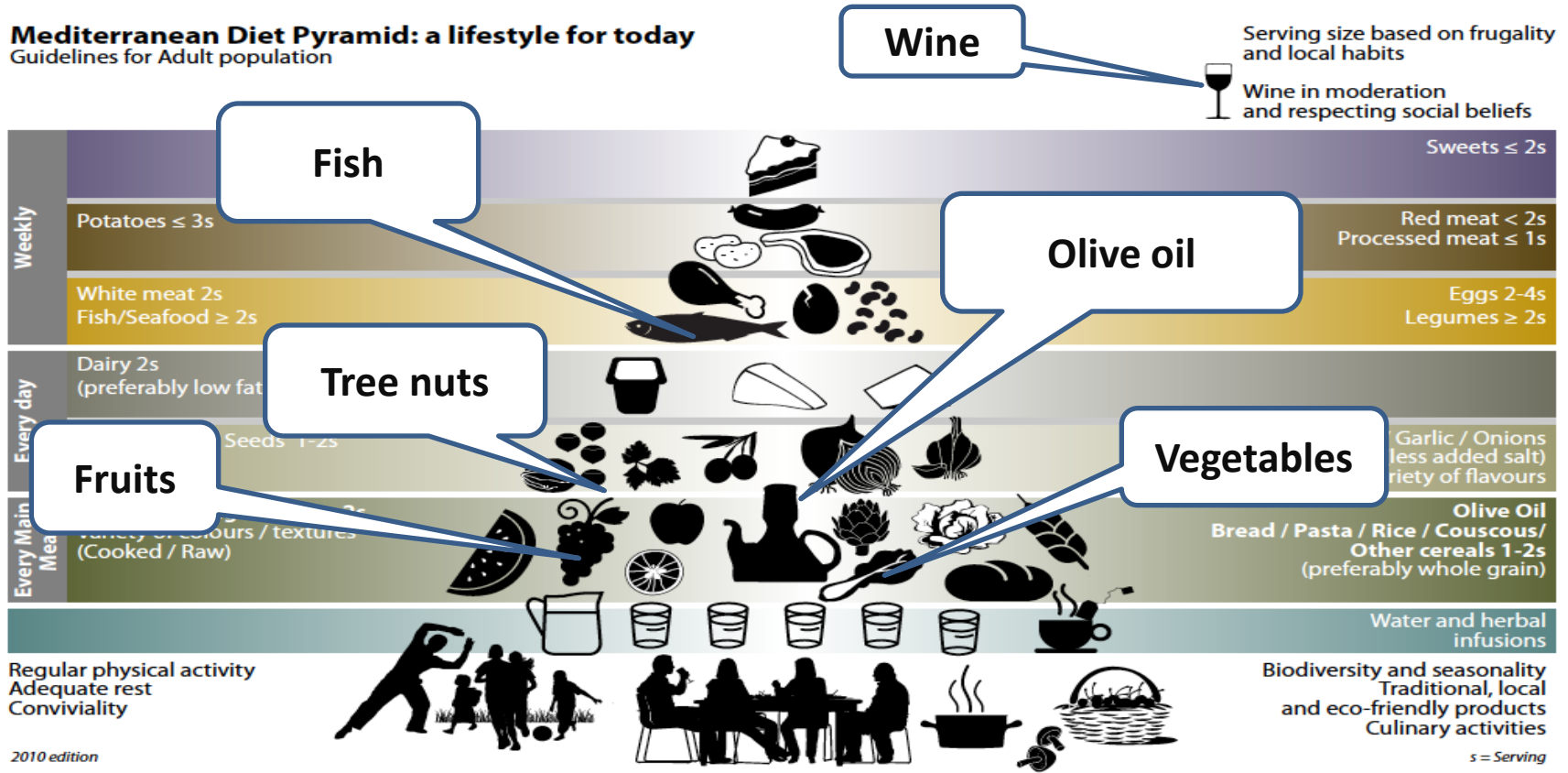
Mediterranean diet and public health: personal reflections<sup>1,2</sup>

*Ansel Keys*

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



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



Fundación  
Dieta Mediterránea

ICAF  
International Commission on the  
Anthropology of Food and Nutrition



Predimed  
Prevención con Dieta Mediterránea



[www.predimed.es](http://www.predimed.es)

# 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 $\geq$ sex-specific Median

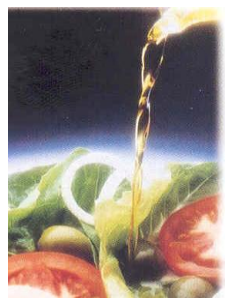
1. MUFA/SFA ratio
2. Fruits & nuts
3. Vegetables
4. Cereals
5. Legumes
6. Fish

### • 1 point if $\leq$ sex-specific Median

7. Meat/meat products
8. Dairy

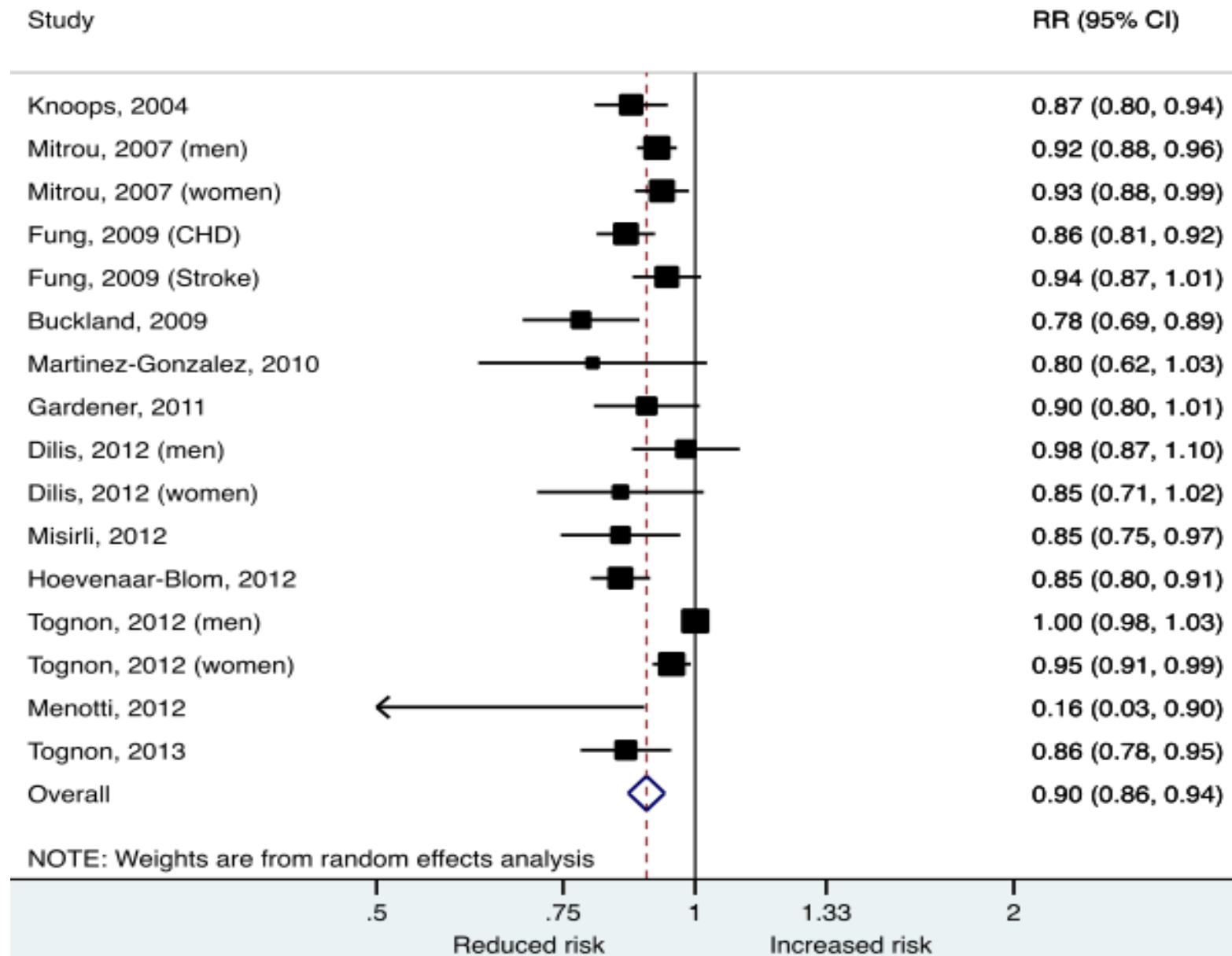
### 9. Alcohol: 1 point if

- Men: between 10-50 g/d
- Women: between 5-25 g/d



For each + 2 points

When studies using only fatal cases were removed, the heterogeneity disappeared and the risk reduction for every +2 points was 13%





# REVIEW



# Mediterranean diet and life expectancy; beyond olive oil, fruits, and vegetables

Miguel A. Martinez-Gonzalez<sup>a,b</sup> and Nerea Martin-Calvo<sup>a,b</sup>

## Mediterranean diet and life expectancy; beyond olive oil, fruits, and vegetables.

Martinez-Gonzalez MA, Martin-Calvo N.

Curr Opin Clin Nutr Metab Care. 2016 Aug 23. [Epub ahead of print]

PMID: 27552476

**Table 1.** Main observational prospective studies published in 2015 and during January–May 2016 on health effects of the Mediterranean diet

Author, year (Reference)	Study	Location	Outcome (s)	Exposure	n	Follow-up	Results/observations	
Panagiotakos, 2015 [6]	ATICA	Greece	CVD	MedDiet and lifestyles	2583	10 years	MedDiet associated with lower risk of CVD (RR, 0.98; 0.93–1.01), for each additional unit in a 0–53 score, equivalent to a HR, 0.78, 0.53–1.13 for two units in a 0–9 score	
Panagiotakos, 2015 [7]	ATICA	Greece	CVD	MedDiet and mediators	2583	10 years	MedDiet associated with lower risk of CVD (RR, 0.96, 0.93–1.00), for each additional unit in a 0–53 score, equivalent to a HR, 0.60, 0.41–1.00 for two units in a 0–9 score	
Sotos-Prieto, 2015 [8*]	HFUS NHS	The United States	CVD	Several food patterns	80538	17.3 years	Improving adherence to MedDiet during the first 4 years of follow-up associated with a lower risk of CVD, HR, 0.91 (0.86–0.97)	
Harnon, 2015 [9*]	Multieethnic cohort	The United States	Mortality	Several food patterns	215782	15.5 years	MedDiet inversely associated with mortality both in men HR, 0.76 (0.73, 0.80) and in women HR, 0.78 (0.74, 0.82) for the fifth vs. first quintile	
Tektonidou, 2015 [10*]	SMC	Sweden	MI, HF stroke, HF	MedDiet	32921	10 years	MedDiet associated with lower risk of MI (RR, 0.74, 0.61–0.90), HF (RR, 0.79, 0.68–0.93), and ischemic stroke (RR, 0.78, 0.65–0.93), but not hemorrhagic stroke (RR, 0.88, 0.61–1.29)	
Tektonidou, 2016 [11*]	COSM	Sweden	HF	MedDiet	37308	10.9 years	Inverse association of the MedDiet with heart failure HR, 0.85 (0.78–0.91) for each two additional points in a 0–8 score	
Bellavia, 2016 [12]	MedDiet inversely associated with total mortality, HR, 0.81, 0.75–0.86 for high versus low adherence	COSM + SMC	Sweden	Mortality	MedDiet	71333	15 years	
Fransen, 2015 [13]	EPIC-NL	The Netherlands	QALYs	Several food patterns	33066	12.4 years	MedDiet associated with a 2-month increase in QALYs (0.63–0.6 months)	
May, 2015 [14]	EPIC-NL	The Netherlands	DALYs	MedDiet and lifestyles	33066	12.4 years	MedDiet associated with reduced DALYs –0.24 (–0.44 to –0.02)	
Menotti, 2016 [15]	Italian rural areas of Seven Countries	Italy	Mortality	MedDiet and lifestyles	1712	50 years	Inverse association of the MedDiet with all-cause mortality HR, 0.67 (0.57–0.78), CV mortality HR, 0.68 (0.54–0.86), and cancer mortality 0.54 (0.40–0.73). Life expectancy was 4.4 years longer for MedDiet	

**Table 1** (Continued)

Author, year (Reference)	Study	Location	Outcome (s)	Exposure	n	Follow-up	Results/observations
Prinelli, 2015 [16]	Lombardy cohort	Italy	Mortality	MedDiet	974	17.4 years	Inverse association of the MedDiet with mortality HR, 0.62 (0.43–0.89) for high versus low adherence
Bonaccio, 2016 [17]	Mali-Sani	Italy	Mortality	MedDiet	1995	4 years	In diabetic patients, MedDiet was inversely associated with mortality HR, 0.63 (0.49–0.81) for each two additional points in a 0–9 score
Bo, 2016 [18]	Turin study	Italy	Mortality, CVD	MedDiet	1658	12 years	High adherence to MedDiet inversely associated with all-cause mortality (HR, 0.83, 0.72–0.96), and CVD (HR, 0.79, 0.65–0.97). No association with mortality among high-risk patients
Stefler, 2015 [19]	HAPIEE	Czech Republic, Poland, Russia	Mortality, CVD	MedDiet	19333	7 years	One SD in MedDiet adherence inversely associated with all-cause death (HR, 95% CI 0.93, 0.88–0.98) and CVD (0.90, 0.81–0.99)
Hernandez-Hernandez, 2015 [20]	SUN cohort	Spain	CVD	MADP	14651	9.7 years	No significant association between the departure from the MADP and CVD, HR, 1.55 (0.58–4.16)
Martinez-Gonzalez, 2015 [21]	PREDIMED	Spain	Mortality, CVD	Empirically derived food patterns	7216	4.3 years	MedDiet (empirically identified) associated with lower risk of CV, HR fourth vs. first quartile, 0.52 (0.36–0.74) and all-cause mortality, HR, 0.53 (0.38–0.75)
Pérez-Tasigchana, 2015 [22]	UAM cohort + Seniors ENRICA cohort	Spain	Quality of life	MedDiet	4287	2.5 years	MedDiet associated with better physical quality of life, +1.34 (+0.21 to +2.47) for third vs. first tertile but no association with mental quality of life according to SF-12
Stewart, 2016 [23*]	STABILITY (patients with stable CHD)	39 countries	CVD	MedDiet	15482	3.7 years	MedDiet associated with lower CVD HR, 0.95 (0.91–0.98), for each additional unit in a 0–24 score, equivalent to a HR, 0.76, 0.61–0.90 for two units in a 0–9 score, but only if more than 12 points in the 0–24 score
Lau, 2015 [24]	Patients with stable CHD	Hong Kong	BP variability stroke	MedDiet	274	77 months	Lower variability in BP, lower SBP and lower incidence of stroke, HR, 0.48 (0.24–0.94) associated with better adherence to MedDiet

Study	Location	Outcome(s)	Exposure	n	follow-up	Results/observations	
Harmon, 2015	Multi-ethnic cohort	US	Mortality	Several food patterns	215782	15.5 y	MedDiet <b>inversely associated with mortality</b> both in men HR, 0.76 (0.73, 0.80) and in women HR, 0.78 (0.74, 0.82) for the 5th vs. 1st quintile
Martinez-Gonzalez, 2015	PREDIMED	Spain	Mortality, CVD	Empirically-derived food patterns	7216	4.3 y	MedDiet (empirically identified) associated with lower risk of CV, HR 4th vs. 1st quartile, 0.52 (0.36-0.74) and all-cause mortality, HR, 0.53 (0.38-0.75)
Panagiotakos, 2015	ATTICA	Greece	CVD	MedDiet and lifestyles	2583	10 y	MedDiet associated with <b>lower risk of CVD</b> (RR, 0.98, 0.95-1.01), for each additional unit in a 0-55 score, equivalent to a HR, 0.78, 0.53-1.13 for 2 units in a 0 to 9 score
Sotos-Prieto, 2015	HPFUS NHS	US	CVD	Several food patterns	80538	17.3 y	Improving adherence to MedDiet during the first 4 y of follow-up associated with a <b>lower risk of CVD</b> , HR, 0.91 (0.86-0.97)
Stefler, 2015	HAPIEE	Czech Rep., Poland, Russia	Mortality, CVD	MedDiet	19333	7 y	One standard deviation (SD) in MedDiet adherence <b>inversely associated with all-cause death</b> (HR, 95 % CI 0.93, 0.88-0.98) and CVD (0.90, 0.81-0.99)

Author, year	Study	Location	Outcome(s)	Exposure	n	follow-up	Results/observations
Prinelli, 2015	Lombardy cohort	Italy	Mortality	MedDiet	974	17.4 y	Inverse association of the MedDiet with mortality HR, 0.62 (0.43-0.89) for high versus low adherence
Bo, 2016	Turin study	Italy	Mortality, CVD	MedDiet	1658	12 y	High adherence to MedDiet inversely associated with all-cause mortality (HR, 0.83, 0.72–0.96), and CVD (HR, 0.79, 0.65–0.97). No association with mortality among high risk subjects
Bonaccio, 2016	Moli-Sani	Italy	Mortality	MedDiet	1995	4 y	In diabetics, MedDiet was inversely associated with mortality HR, 0.63 (0.49–0.81) for each 2 additional points in a 0 to 9 score
Bellavia, 2016	COSM+SMC	Sweden	Mortality	MedDiet	71333	15 y	MedDiet inversely associated with total mortality, HR, 0.81, 0.75-0.86 for high versus low adherence
Tektonidis, 2015	SMC	Sweden	MI, stroke, HF	MedDiet	32921	10 y	MedDiet associated with lower risk of MI (RR, 0.74, 0.61-0.90), Heart failure (RR, 0.79, 0.68-0.93) and ischemic stroke (RR: 0.78, 0.65-0.93), but not hemorrhagic stroke (RR: 0.88, 0.61-1.29).
Tektonidis, 2016	COSM	Sweden	Heart failure	MedDiet	37308	10.9 y	Inverse association of the MedDiet with heart failure HR, 0.85 (0.78-0.91) for each 2 additional points in a 0 to 8 score
Stewart, 2016	STABILITY (patients with stable CHD)	39 countries	CVD	MedDiet	15482	3.7 y	MedDiet associated with lower CVD HR, 0.95, 0.91-0.98), for each additional unit in a 0-24 score, equivalent to a HR, 0.76, 0.61-0.90 for 2 units in a 0 to 9 score, but only if >12 points in the 0-24 score

## Research designs

Source: Martínez JA, Martínez-González 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.

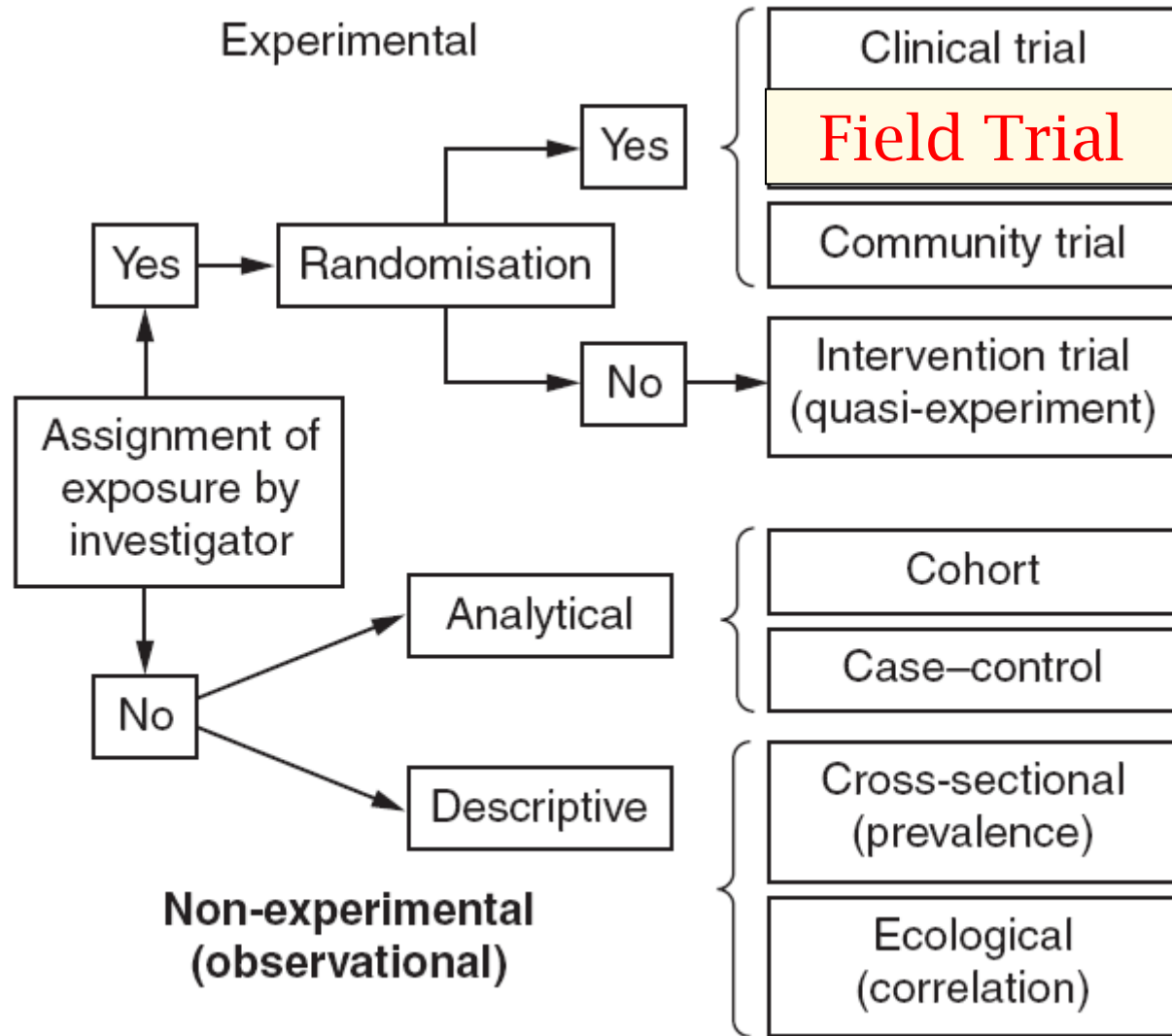


Figure 13.2 Classification of epidemiological designs.

# U.S. Dietary Guidelines: An Evidence-Free Zone

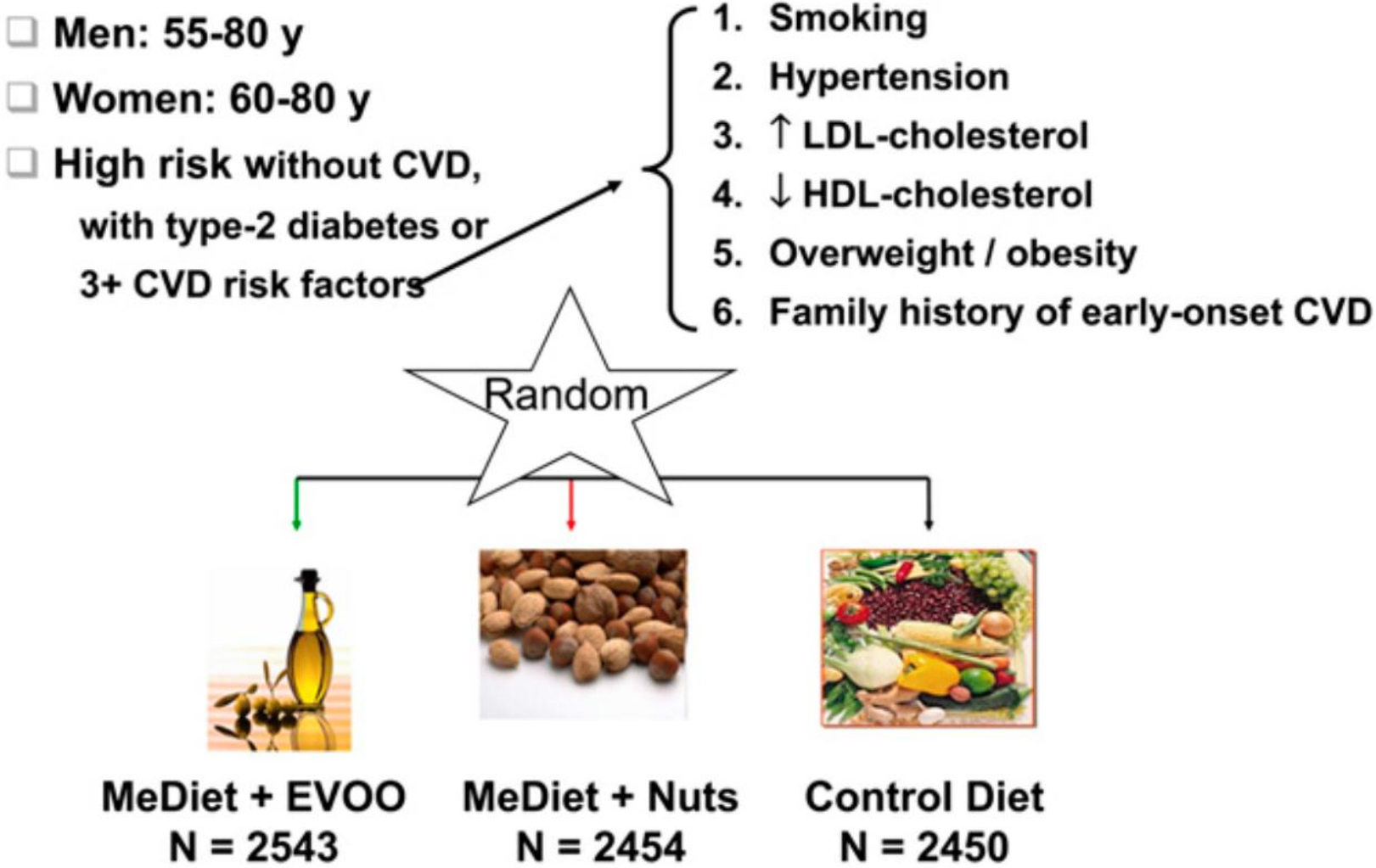
Steven E. Nissen, MD

The lack of high-quality RCTs has left dietary advice to cult-like advocates, often with opposite recommendations. One group advises virtually complete elimination of carbohydrates from the diet, whereas others promote a virtually fat-free diet. A search of online bookstores and Web sites reveals an unlimited choice of diets, all with extraordinary claims for incredible weight loss and health benefits.

rated fats, 0.70 (CI, 0.54 to 0.92) for  $\omega$ -6 polyunsaturated fats, and 1.16 (CI, 1.06 to 1.27) for trans fats. Of course, this analysis shares the same limitations of the observational research it summarizes.

Fortunately, a large (7447 participants) high-quality RCT was finally published in 2013, the PREDIMED (Prevencción con Dieta Mediterránea) study, conducted in Spain, comparing the Mediterranean diet with the conventional AHA-style, low-fat diet in participants at risk for coronary disease (10). The multivariable-adjusted hazard ratios for coronary disease were 0.70 (CI, 0.54 to 0.92) for the group assigned to a diet enriched with extra-virgin olive oil and 0.72 (CI, 0.54 to 0.96) for the group assigned to a diet enriched with nuts, both compared with the low-fat diet.

How do we proceed in the pursuit of scientific understanding about the relationship between diet and coronary disease? It is time for careful RCTs testing various dietary interventions—studies unlikely to be industry-funded. Federal agencies, such as the National Institutes of Health and Centers for Disease Control and Prevention, must fund and help conduct such trials. The successful completion of the PREDIMED Study, funded by the Spanish government, proves that such studies



Ros et al.  
Adv Nutr.  
2014;5:330S-6S

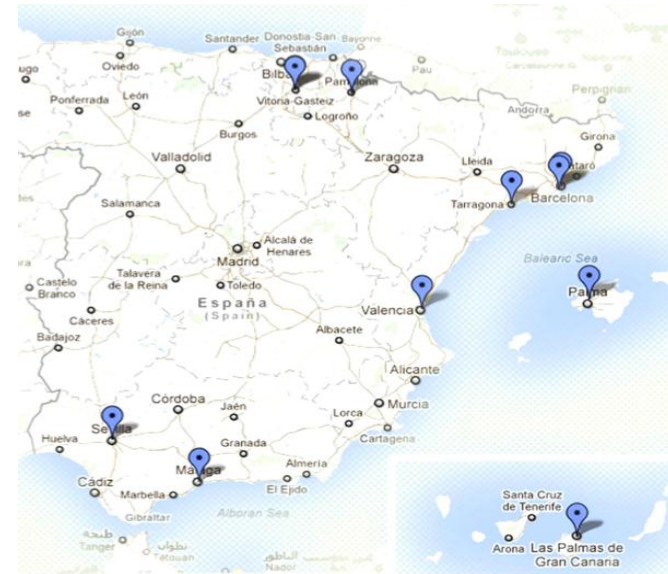
**FIGURE 1** Design of the PREDIMED (Prevención con Dieta Mediterránea) study. CVD, cardiovascular disease; EVOO, extra-virgin olive oil; MeDiet, Mediterranean diet.

# Predimed

Prevención con Dieta Mediterránea

1. Clinic (Barcelona)- Ramón Estruch  Clinic Lipids- Emilio Ros 
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 
8. Son Espases (Mallorca)- Miquel Fiol / D. Romaguera   

9. U. Las Palmas- Lluís Serra-Majem 
10. H. Belvitge (Barcelona)- Xavier Pintó 
11. U. Navarra / Osasunbidea – Miguel A. Martínez-González 



**n = 7,447**

	<b>Mediet + VOO (n= 2543)</b>	<b>MeDiet + Nuts (n=2454)</b>	<b>Control (n=2450)</b>
Age (SD)	67 (6)	67 (6)	67 (6)
Women (%)	59	54	60
Diabetes (%)	50	47	48
Hypertension (%)	82	82	84
Current smokers (%)	14	15	14
High cholest. (%)	72	73	72
BMI (SD)	30 (4)	30 (4)	30 (4)
Waist (SD)	100 (10)	100 (11)	101 (11)



- |   |                            |
|---|----------------------------|
| 1. Do you use olive oil as the principal source of fat for cooking?   | Yes                        |
| 2. How much olive oil do you consume per day (including that used in frying, salads, meals eaten away from home, etc.)?           | $\geq 4$ Tbsp <sup>5</sup> |
| 3. How many servings of vegetables do you consume per day? Count garnish and side servings as 1/2 point; a full serving is 200 g. | $\geq 2$                   |
| 4. How many pieces of fruit (including fresh-squeezed juice) do you consume per day?  | $\geq 3$                   |
| 5. How many servings of red meat, hamburger, or sausages do you consume per day? A full serving is 100–150 g.                     | $< 1$                      |
| 6. How many servings (12 g) of butter, margarine, or cream do you consume per day?  | $< 1$                      |
| 7. How many carbonated and/or sugar-sweetened beverages do you consume per day?   | $< 1$                      |

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

- |  |               |
|--|---------------|
| 8. Do you drink wine? How much do you consume per week?  | $\geq 7$ cups |
| 9. How many servings (150 g) of pulses do you consume per week?  | $\geq 3$      |
| 10. How many servings of fish/seafood do you consume per week?<br>(100–150 g of fish, 4–5 pieces or 200 g of seafood)  | $\geq 3$      |
| 11. How many times do you consume commercial (not homemade) pastry such as cookies or cake per week?   | $< 2$         |
| 12. How many times do you consume nuts per week? (1 serving = 30 g)  | $\geq 3$      |
| 13. Do you prefer to eat chicken, turkey or rabbit instead of beef, pork, hamburgers, or sausages?   | Yes           |
| 14. How many times per week do you consume boiled vegetables, pasta, rice, or other dishes with a sauce of tomato, garlic, onion, or leeks sautéed in olive oil? | $\geq 2$      |

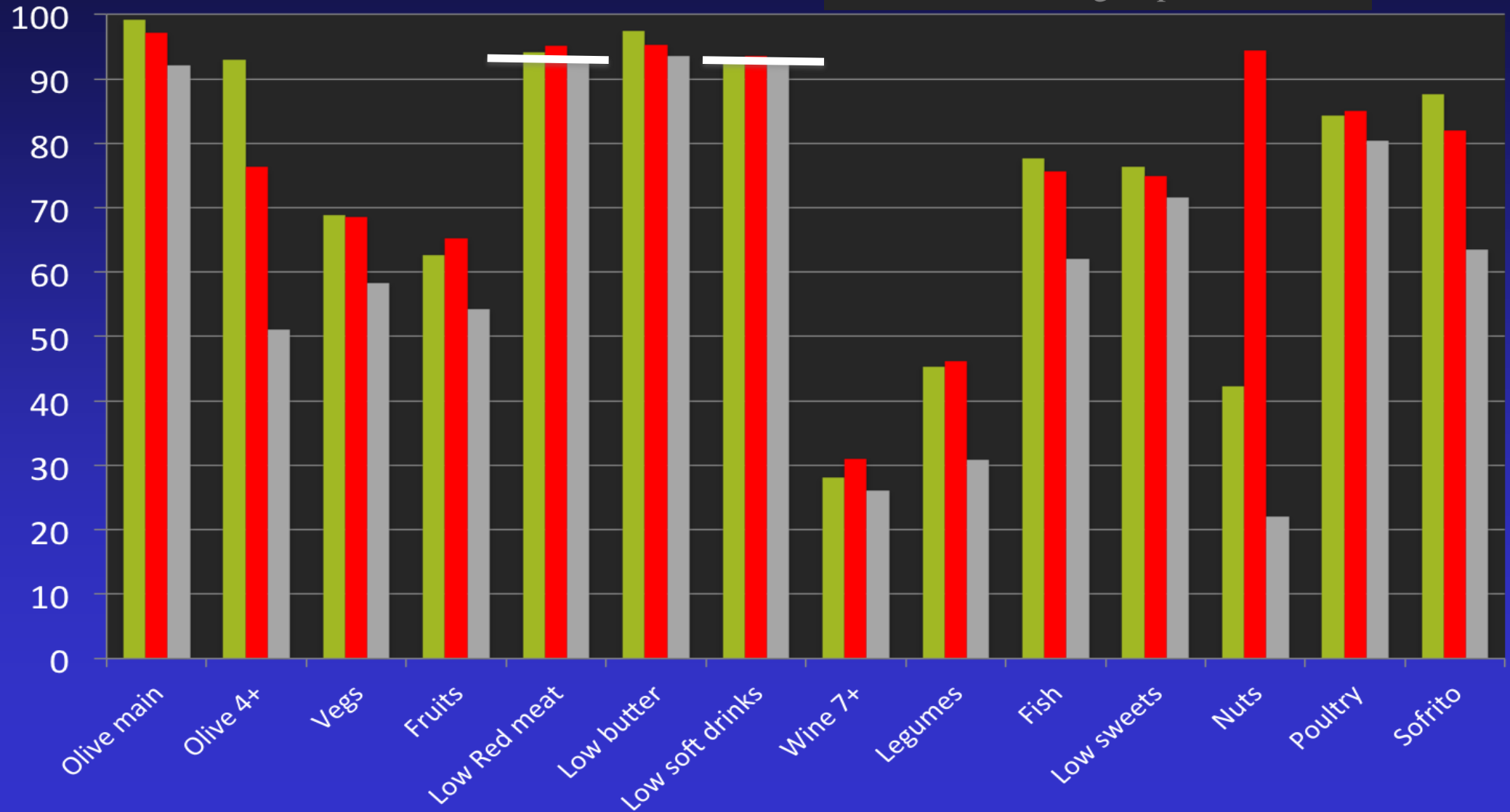
**Sofrito**

# 3-yr attainments (%) for each of the 14 items

MedDiet + Virgin olive oil

MedDiet + mixed nuts

Control group



# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

APRIL 4, 2013

VOL. 368 NO. 14

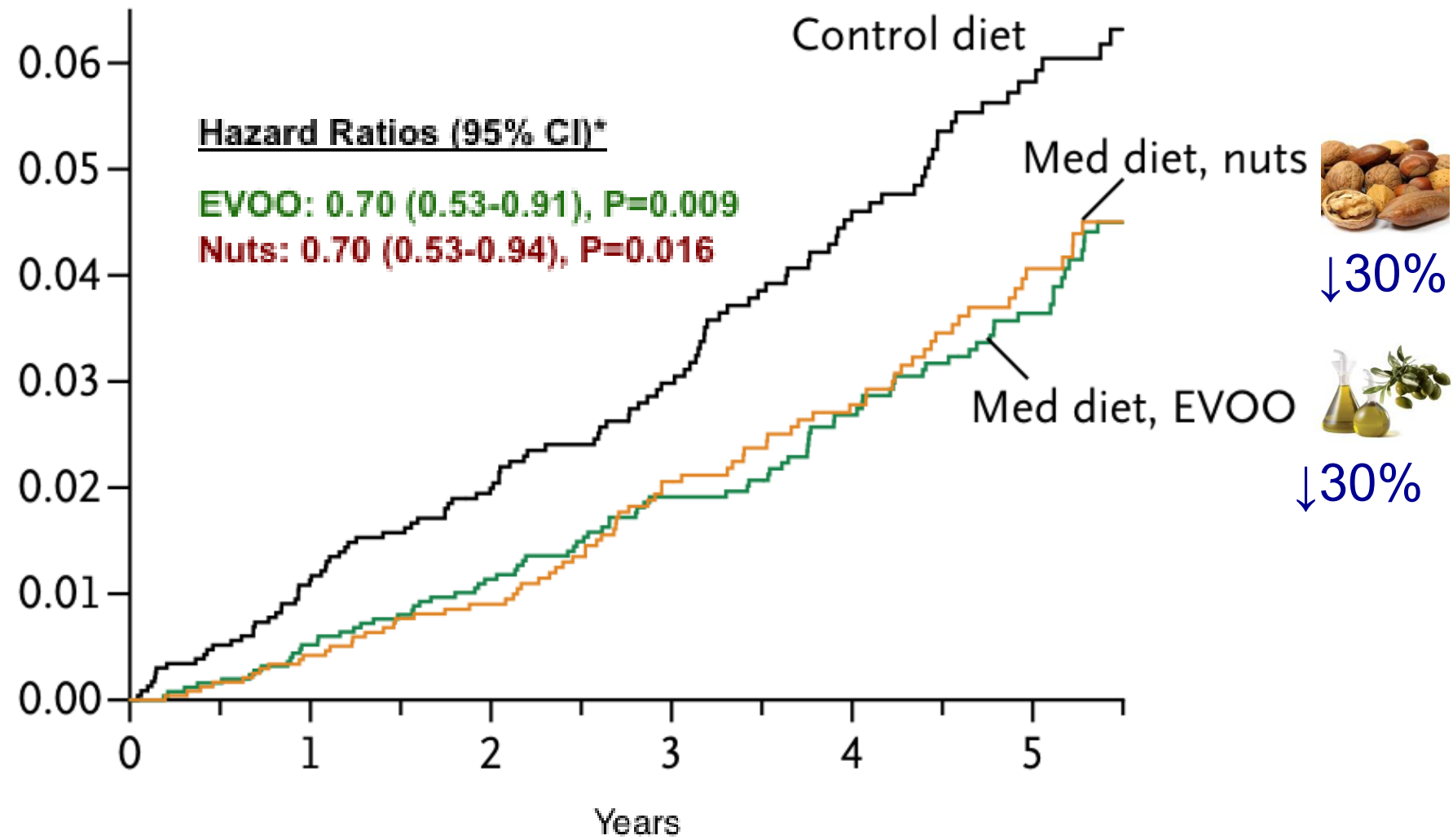
## Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

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\*

Stopped for early evidence of benefit  
after 4.8-y median follow-up

# PREDIMED RCT– Primary end-point (MI, stroke or CV death)

[www.predimed.es](http://www.predimed.es)



**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

**5** How many servings of red meat do you consume per day? (1 serving = 100-150 grams)



Less than 1.



1 or more.

**11** How many times per week do you consume commercial sweets or pastries (not homemade), like cakes, cookies or biscuits?



Less than 3.



More than 3.





**PREDIMED**  
DATE EL GUSTO  
DE COMER SANO

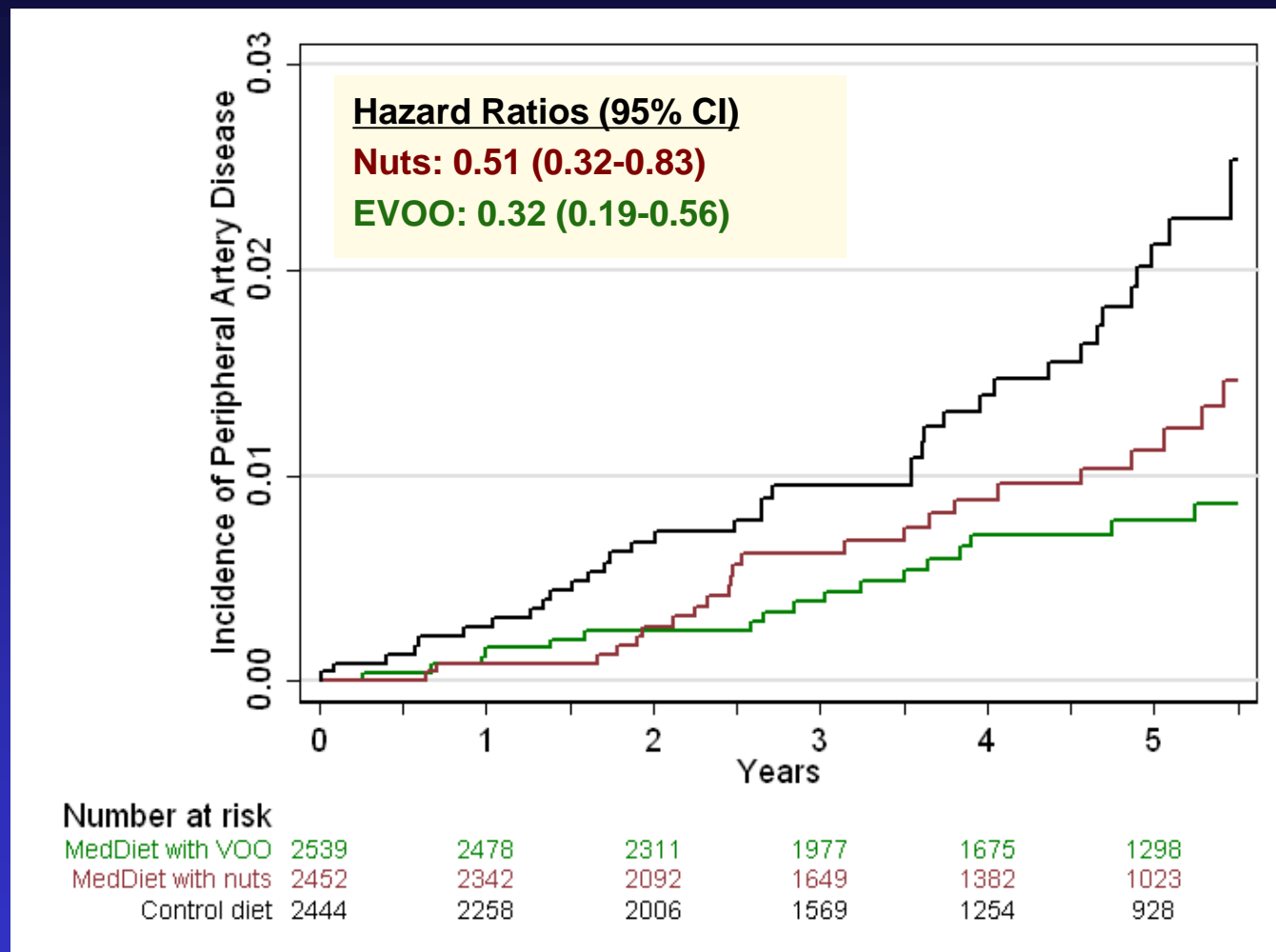
ANA SÁNCHEZ-TAINTA  
BEATRIZ SAN JULIÁN  
MIGUEL ÁNGEL MARTÍNEZ-GONZÁLEZ



**EUNSA**

# PREDIMED RCT– Peripheral Artery Disease

N = 89 cases  
Follow-up 4.8 y



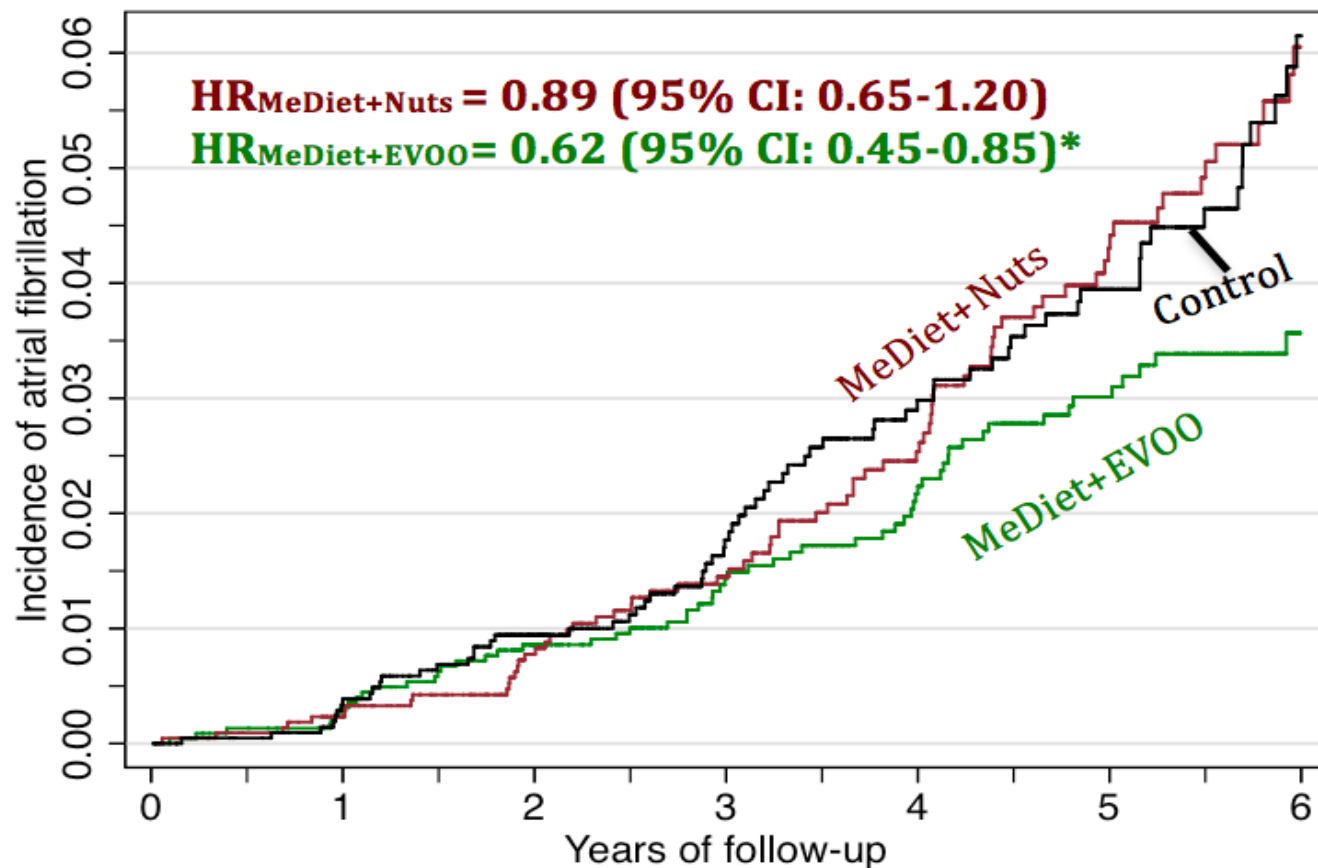
↓49%

↓68%

Ruiz-Canela M, et al. JAMA 2014;311:415-7.



# PREDIMED RCT – Atrial Fibrillation



↓11%



↓38%

253 cases  
Follow-up 4.7 y

Number at risk

g = MeDiet+EVOO	2292	2234	2097	1798	1511	1144	496
g = MeDiet+Nuts	2210	2113	1899	1499	1244	903	387
g = Control	2203	2044	1837	1438	1152	851	358

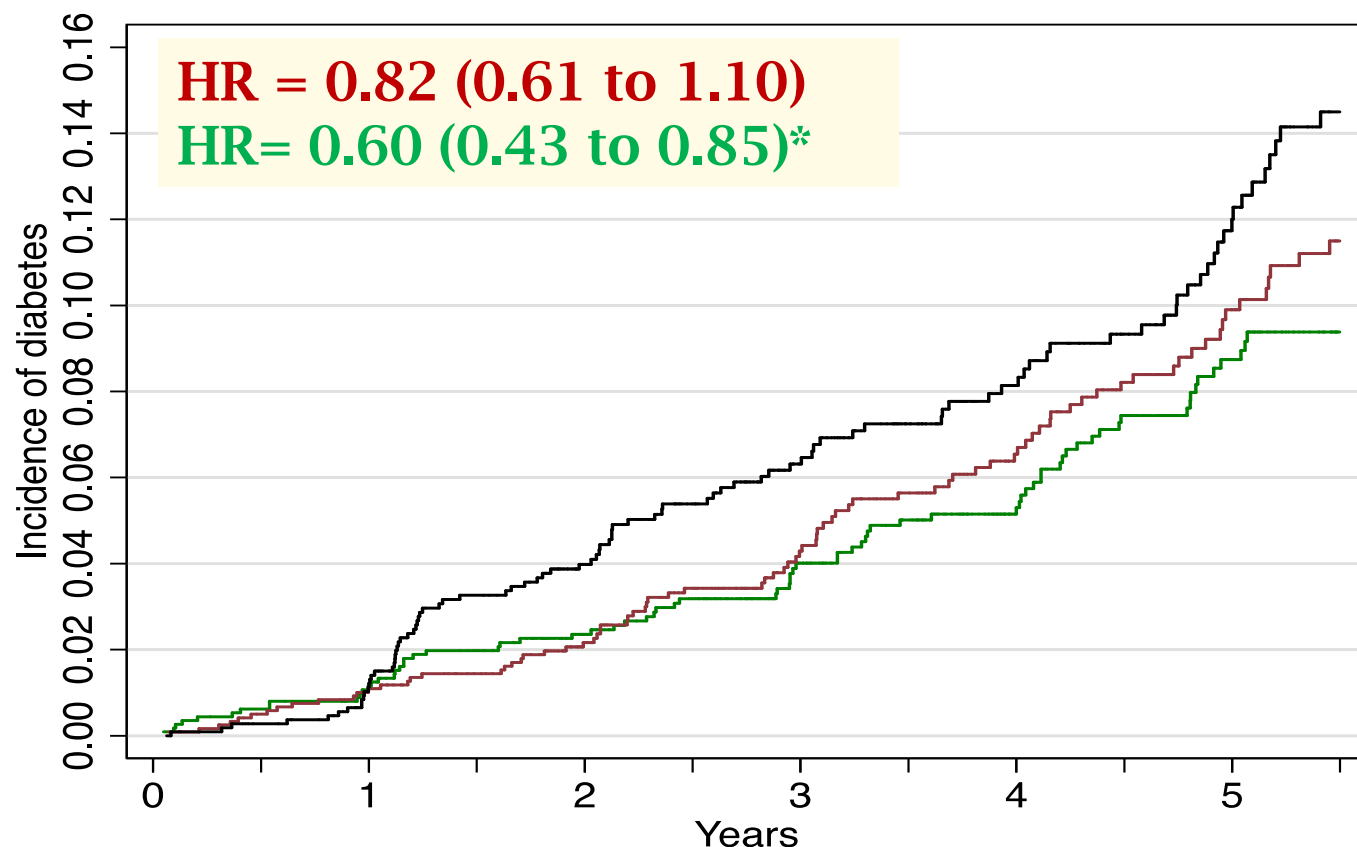
Martínez-González MA, et al. Circulation 2014;130:18-26

# Prevention of Diabetes With Mediterranean Diets

## A Subgroup Analysis of a Randomized Trial

Jordi Salas-Salvadó, MD, PhD\*; Mònica Bulló, PhD; Ramón Estruch, MD, PhD; Emilio Ros, MD, PhD; Maria-Isabel Covas, DPharm; Núria Ibarrola-Jurado, RD, PhD; Dolores Corella, DPharm, PhD; Fernando Arós, MD, PhD; Enrique Gómez-Gracia, MD, PhD; Valentina Ruiz-Gutiérrez, PhD; Dora Romaguera, MD, PhD; José Lapetra, MD, PhD; Rosa Maria Lamuela-Raventós, DPharm, PhD; Lluís Serra-Majem, MD, PhD; Xavier Pintó, MD, PhD; Josep Basora, MD, PhD; Miguel Angel Muñoz, MD, PhD; José V. Sorlí, MD, PhD; and Miguel A. Martínez-González, MD, PhD\*

N = 273 cases  
Follow-up 4.1 y



### 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

↓18%



↓40%



# Behavioral and Dietary Risk Factors for Noncommunicable Diseases

N Engl J Med 2013;369:954-64.

Majid Ezzati, Ph.D., and Elio Riboli, M.D.

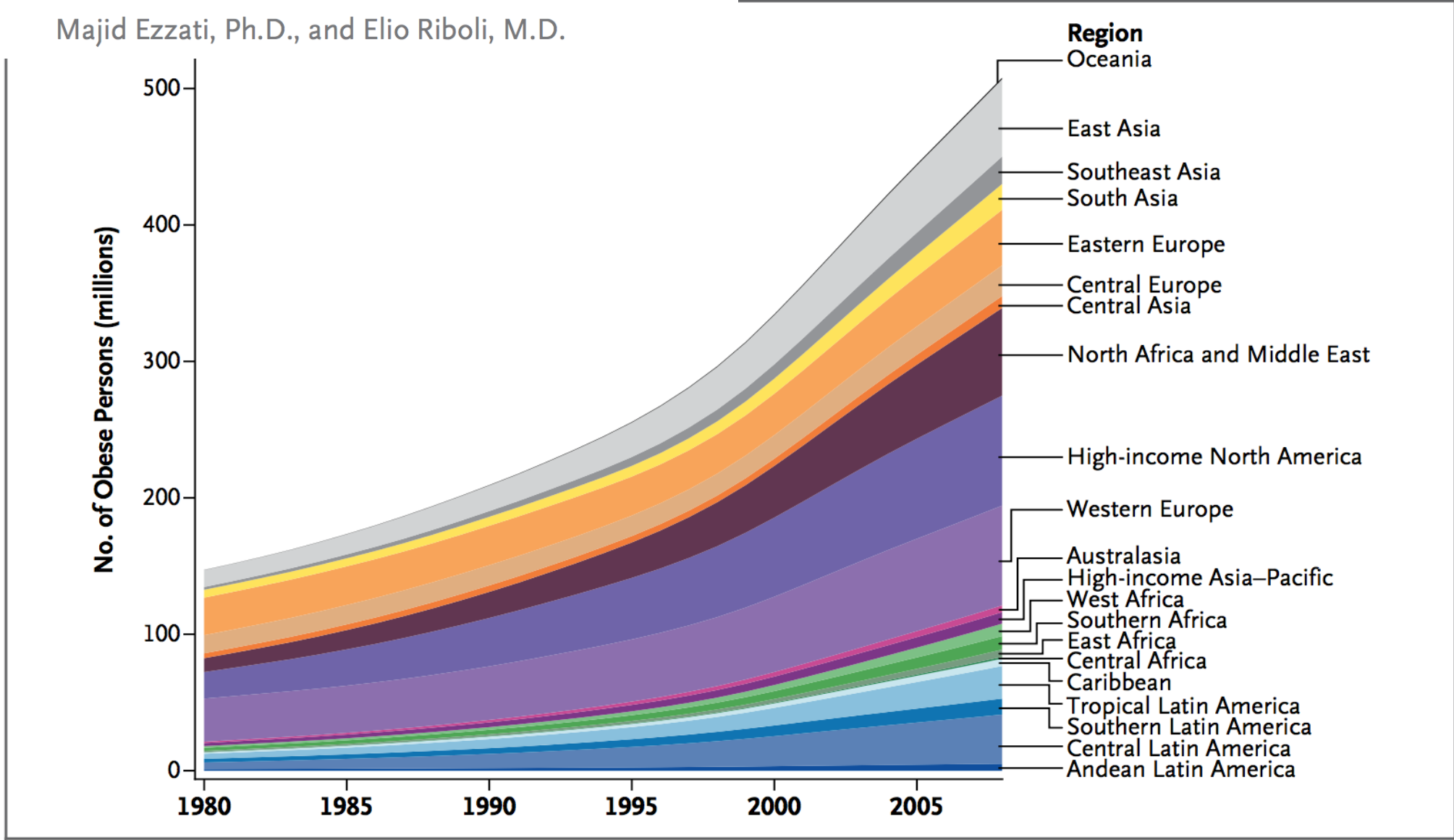


Figure 4. Trends in the Number of Obese Persons, According to Region.

# Effect of a high-fat Mediterranean diet on bodyweight and waist circumference: a prespecified secondary outcomes analysis of the PREDIMED randomised controlled trial

Ramon Estruch\*, Miguel Angel Martínez-González, Dolores Corella, Jordi Salas-Salvadó, Montserrat Fitó, Gemma Chiva-Blanch, Miquel Fiol, Enrique Gómez-Gracia, Fernando Arós, José Lapetra, Lluís Serra-Majem, Xavier Pintó, Pilar Buil-Cosiales, José V Sorlí, Miguel A Muñoz, Josep Basora-Gallisá, Rosa María Lamuela-Raventós, Mercè Serra-Mir, Emilio Ros\*, for the PREDIMED Study Investigators†

Participants in all three groups reduced their body weight.

Compared to the control group, adjusted differences in 5-year changes in **body weight (kg)**:

- MedDiet + EVOO: **-0.43** (95% CI, **-0.86 to -0.01**) kg
- MedDiet +nuts: **-0.08** (95% CI, **-0.50 to +0.35**) kg



Diff. in 5-y changes in **waist circumference (cm)**:

- MedDiet + EVOO: **-0.55** (95% CI, **-1.16 to -0.06**) cm
- MedDiet +nuts: **-0.94** (95% CI, **-1.60 to -0.27**) cm



*Lancet Diab Endocrinol 2016 Aug;4(8):666-76.*

# MedDiet: a high-quality diet

The shortest way to reach nutritional goals is to adopt Mediterranean food choices: evidence from computer-generated personalized diets<sup>1-3</sup>

Matthieu Maillot, Carine Issa, Florent Vieux, Denis Lairon, and Nicole Darmon

Am J Clin Nutr 2011;94:1127-37.

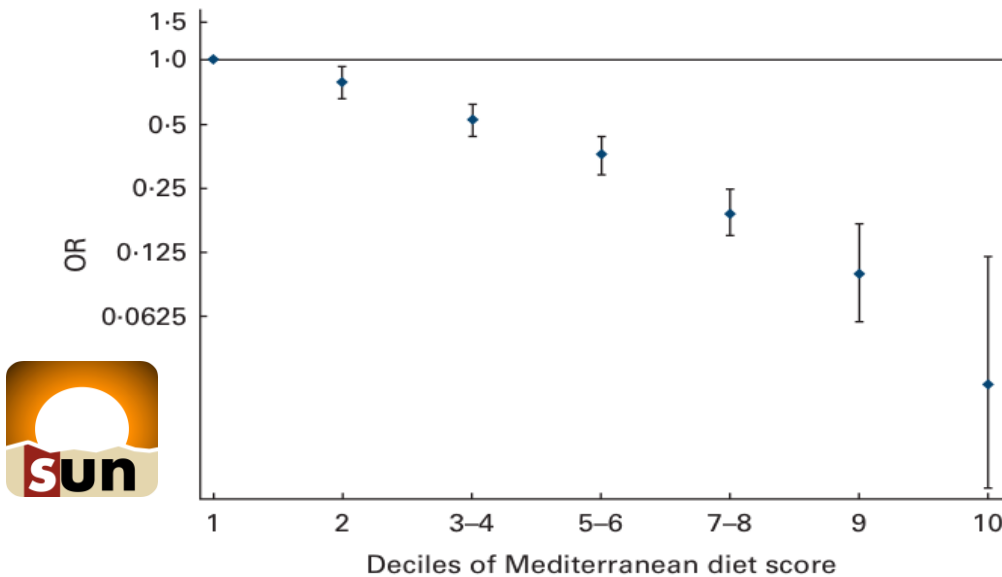
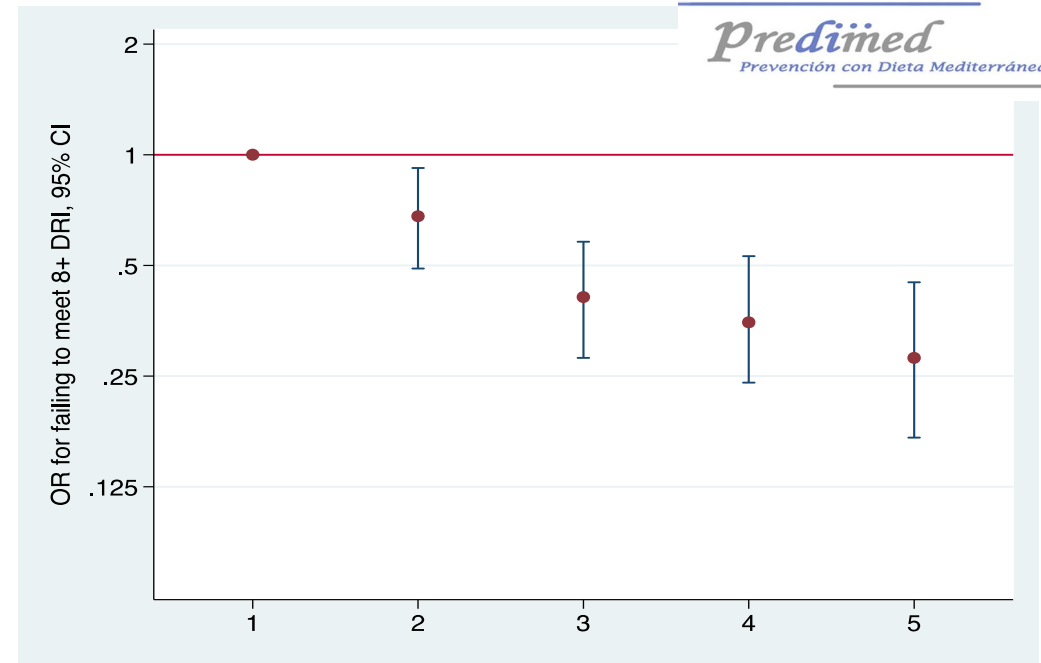


Fig. 2. Risk of failing to meet  $\geq 4$  dietary recommended intakes according to deciles of Mediterranean diet score in 16841 participants of the Seguimiento Universidad de Navarra (SUN) Project using the probabilistic approach.

Br J Nutr 2014;111:2000-9



Eur J Nutr 2016;55:93-10

**Epidemiol. descriptiva**

**Factores de riesgo**

**Vida simple'7**

**Patrones: MedDiet**

**PREDIMED-PLUS**



# Epidemiol. descriptiva

Factores de riesgo

Vida simple'7

Patrones: MedDiet

**PREDIMED-PLUS**



## Lo que NO hicimos en PREDIMED

- Si tiene sobrepeso, pierda **peso**
- Coma menos de **todo**
- Practique/incremente su **actividad física**



ORIGINAL ARTICLE

# Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

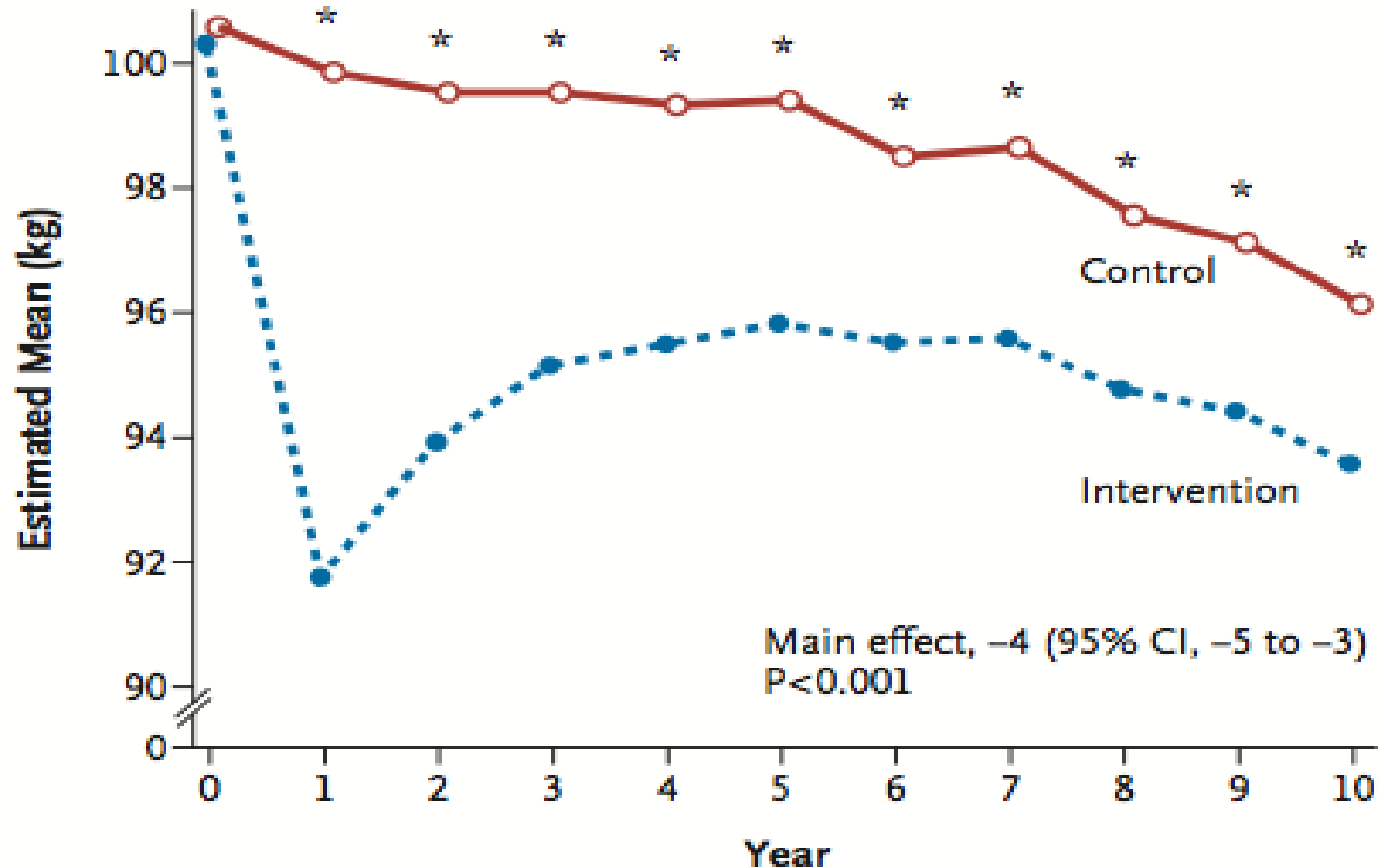
The Look AHEAD Research Group\*

n = 5145 - all diabetics  
BMI:  $\geq 25$   
Max. follow-up: 13.5 yr  
recruitment: 2001-2004

Interv. = 1.83  
Control = 1.92  
(events per 100 p-years)

HR = **0.95** (0.83 to 1.09) P=0.51

**A Weight**



# Futility

no difference in the number of **cardiovascular events** was noted between the two groups after 9.6 years (median F-U).

## DIABETES

### Looking back at Look AHEAD —giving lifestyle a chance

*Nat Rev Cardiol. 2013;10:1846*

Jean-Pierre Després and Paul Poirier

**Box 1** | Questions on current paradigms in preventive cardiology raised by the Look AHEAD trial

- Is the traditional method of assessing obesity (using BMI) useful in CVD risk assessment?
- Is weight loss the best target to reduce CVD risk in patients with type 2 diabetes mellitus, or should the focus be on reducing visceral adiposity or ectopic fat deposits such as liver fat?
- Should we focus on caloric restriction or put more emphasis on **improving nutritional quality?**
- Should we design the physical activity and exercise component of lifestyle intervention programmes to optimally improve cardiorespiratory fitness, which is a key marker of participation in vigorous physical activities?
- Do patients with type 2 diabetes need to do more physical activity and exercise in order to reduce their risk of CVD risk than individuals without diabetes?

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.

Miguel A. Martínez-González, M.D., Ph.D.  
University of Navarra, Pamplona, Spain  
[mamartinez@unav.es](mailto:mamartinez@unav.es)

**CORRESPONDENCE**

Jordi Salas-Salvadó, M.D., Ph.D.  
Rovira i Virgili University, Reus, Spain

**Intensive Lifestyle Intervention in Type 2 Diabetes**

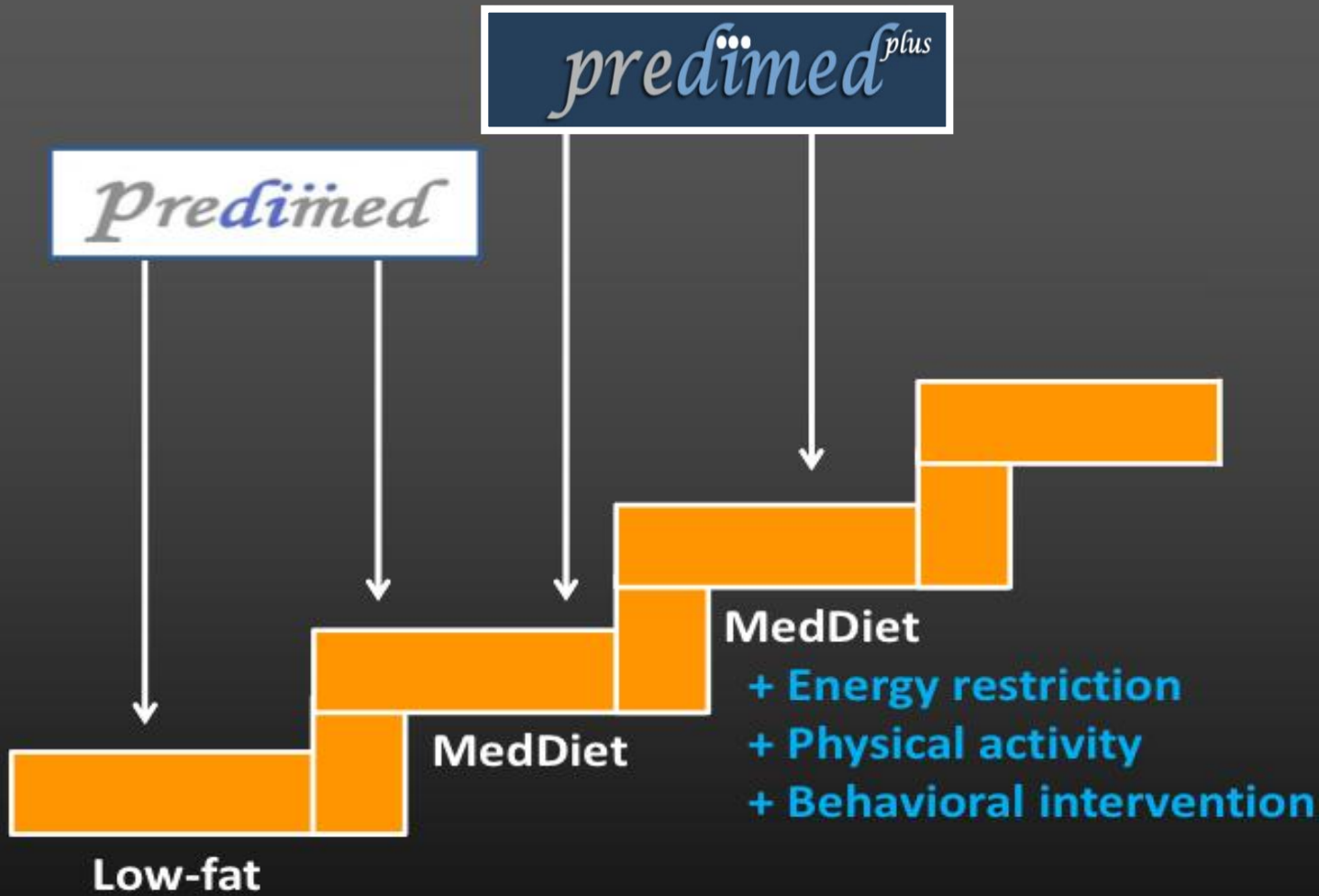
N Engl J Med 2013; 369:2356-2359 | [December 12, 2013](#) | DOI: 10.1056/NEJMc1312802

Ramon Estruch, M.D., Ph.D.  
Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y Nutrición,  
Barcelona, Spain

 @MAM\_UNAV  
 @predimedplus

# PREDIMED-PLUS DESIGN

*predimed<sup>plus</sup>*



**Weight loss → long-term maintenance → ↓ CVD**



# PREDIMED-PLUS DESIGN

*predimed*<sup>plus</sup>

*predimed*<sup>plus</sup>

← → ↻ 🏠 <https://erc.europa.eu/long-term-effects-energy-restricted-mediterranean-diet-mortality-and-cardiovascular-disease-predimed> 🔍 ☆ 🛑 🗄 :  
Aplicaciones 📍 Google Maps 📁 Dropbox 📁 GOOGLE DRIVE 📧 GMAIL 📘 FACEBOOK 🐦 Twitter 📄 PubMed 📄 JCR 📄 Google Académico... 📄 Asignat » 📁 Otros marcadores

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## Long-term effects of an energy-restricted Mediterranean diet on mortality and cardiovascular disease: the PREDIMED PLUS Study

### • Project details:



**Researcher (PI):** Miguel ángel Martínez González

**Host institution:** University Of Navarra, Spain

**Project:** Long-term effects of an energy-restricted Mediterranean diet on mortality and cardiovascular disease: the PREDIMED PLUS Study, (PREDIMED PLUS)

**ERC call:** Advanced Grant , ERC-2013-ADG, panel LS7

**Max ERC funding:** 2,078,970 €

**Duration:** Start date: 2014-05-01, End date: 2019-04-30



@MAM\_UNAV

@predimedplus

n = 6000

Eligible participants

**Eligibility criteria:**  
55-75 yr (60-75 women)  
BMI: 27-40 kg/m<sup>2</sup>  
Meeting ≥ 3 MetS criteria  
< 25% diabetics



n = 3000

n = 3000

**Intensive weight-loss lifestyle intervention**

**Usual care (MedDiet)**

Energy-restricted Mediterranean diet  
+  
Physical activity  
+  
Behavioral intervention



[www.predimedplus.com](http://www.predimedplus.com)

**1<sup>ary</sup> end-point:**

**AMI, non-fatal stroke or CV mortality**

# The 11 centres of PREDIMED-1

1. Clinic (Barcelona)- Ramón Estruch  Clinic Lipids- Emilio Ros 
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 
8. Son Espases (Mallorca)- Miquel Fiol / D. Romaguera   

9. U. Las Palmas- Lluís Serra-Majem 
10. H. Belvitge (Barcelona)- Xavier Pintó 
11. U. Navarra / Osasunbidea – Miguel A. Martínez-González 

plus  
predimed



## 12 New Centers

Univ. Navarra (Nutrition)– J. Alfredo Martínez



Univ. Mallorca (Phys. Activity)– J. A. Tur



Univ. Córdoba (Internal Med.)– J. López-Miranda



Hosp. Virgen Victoria Málaga (Endocrin.)– F. Tinahones



Hosp. Clinic Barcelona (Endocrin.)– Josep Vidal



Univ. M. Hernandez, Alicante (Epidemiology)- J. Vioque



Univ. Granada (Epidemiology)– A. Bueno



F. Jiménez-Díaz Madrid (Endocrin.)– Clotilde Vázquez



Univ. Jaén (Epidemiology)- M. Delgado-Rodríguez



IMDEA Madrid (Nutrition)– J.M. Ordovás



H.C. San Carlos Madrid (Endocrin.)– M.A. Rubio

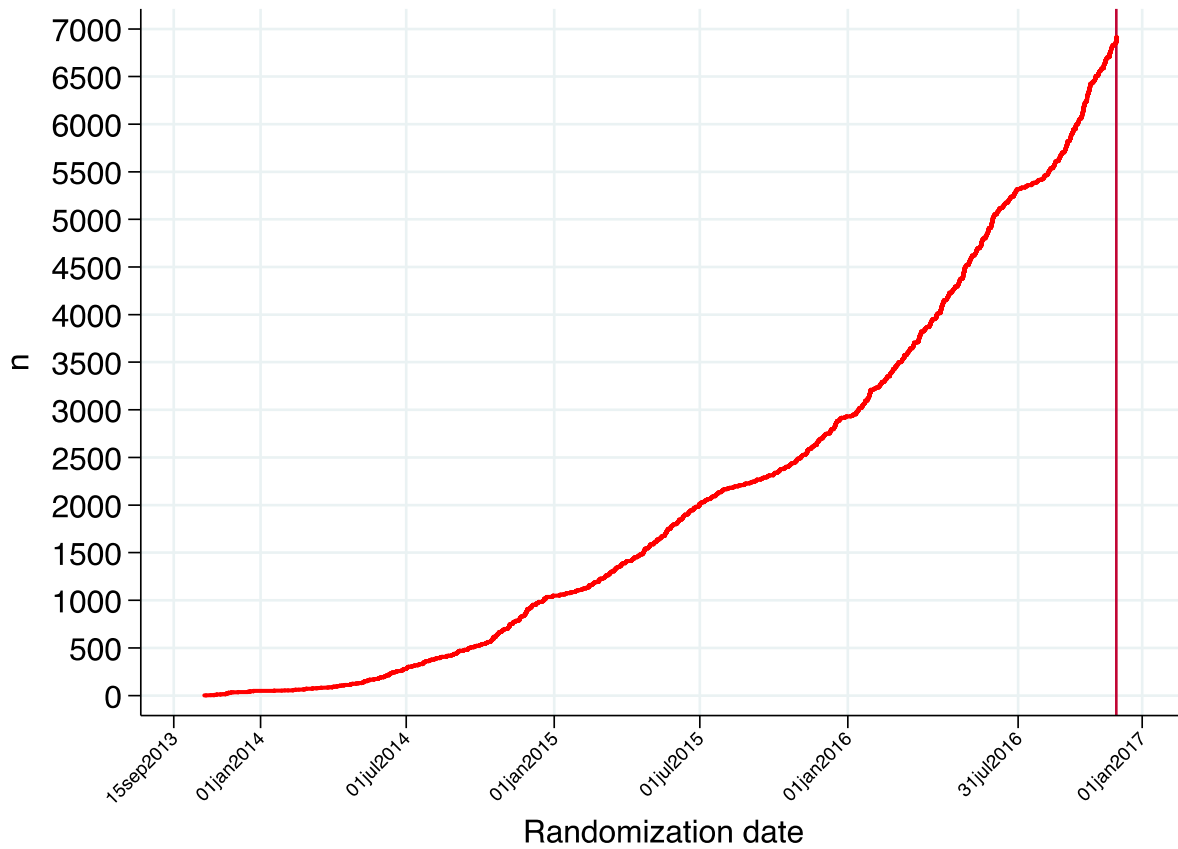


Univ. León (Primary Care)– Vicente Martín





# Randomized participants (completed Nov 30, 2016)



**Nov 30/2016: 6913**

Data presented as mean value ( $\pm$ SD) or percentage.

Variable	Intervention (n=3035)	Control (n=3069)
Age (y)	65 (5)	65 (5)
% Female	48%	48%
Baseline weight (kg)	87 (13)	87 (13)
Baseline waist (cm)	108 (9)	108 (10)
Baseline BMI (kg/m <sup>2</sup> )	32.5 (3.4)	32.6 (3.5)
% Hypertension	84%	83%
% Diabetes	29%	28%
% Family history of premature CHD	16%	18%
LDL (mg/dl)	123 (35)	124 (35)
HDL (mg/dl)	48 (13)	48 (12)
Triglycerides (mg/dl)	170 (92)	169 (80)
Glucose (mg/dl)	116 (33)	115 (30)
Systolic Blood pressure (mmHg)	140 (17)	140 (17)
Diastolic Blood pressure (mmHg)	81 (10)	81 (10)

# 17-item screener

negotiated goals for the intervention group

1. *¿Usa usted el aceite de oliva virgen extra como principal grasa para cocinar?:*
2. *¿Cuántas raciones de verdura u hortalizas consume al día?: (las guarniciones o acompañamientos= 1/2 ración) 1 ración= 200 g.*
3. *¿Cuántas piezas de fruta (incluyendo zumo natural) consume al día?:*
4. *¿Cuántas raciones de carnes rojas, hamburguesas, salchichas, jamón o embutidos consume a la semana?: (ración= 100 - 150 g.)*
5. *¿Cuántas raciones de mantequilla, margarina o nata consume a la semana?: (porción individual=12 g.)*
6. *¿Cuántas bebidas azucaradas (refrescos, colas, tónicas, bitter, zumos de frutas con azúcar añadido) consume a la semana?:*
7. *¿Cuántas raciones de legumbres consume a la semana?: (1 plato o ración de 150 g.)*
8. *¿Cuántas raciones de pescado o mariscos consume a la semana?: (1 plato, pieza o ración= 100 - 150 g. de pescado o 4 - 5 piezas o 200 g. de marisco)*

## Energy-restricted MedDiet

1. Olive oil main culinary fat
2. Vegetables  $\geq 2$  /d
3. Fruits  $\geq 3$  /d
4. Red/processed meats  $\leq 1$  /wk
5. Butter, margarine, cream  $< 1$ /wk
6. Sugary beverages  $< 1$  /wk
7. Legumes  $\geq 3$  /wk
8. Fish / seafood  $\geq 3$  /wk

# 17-item screener

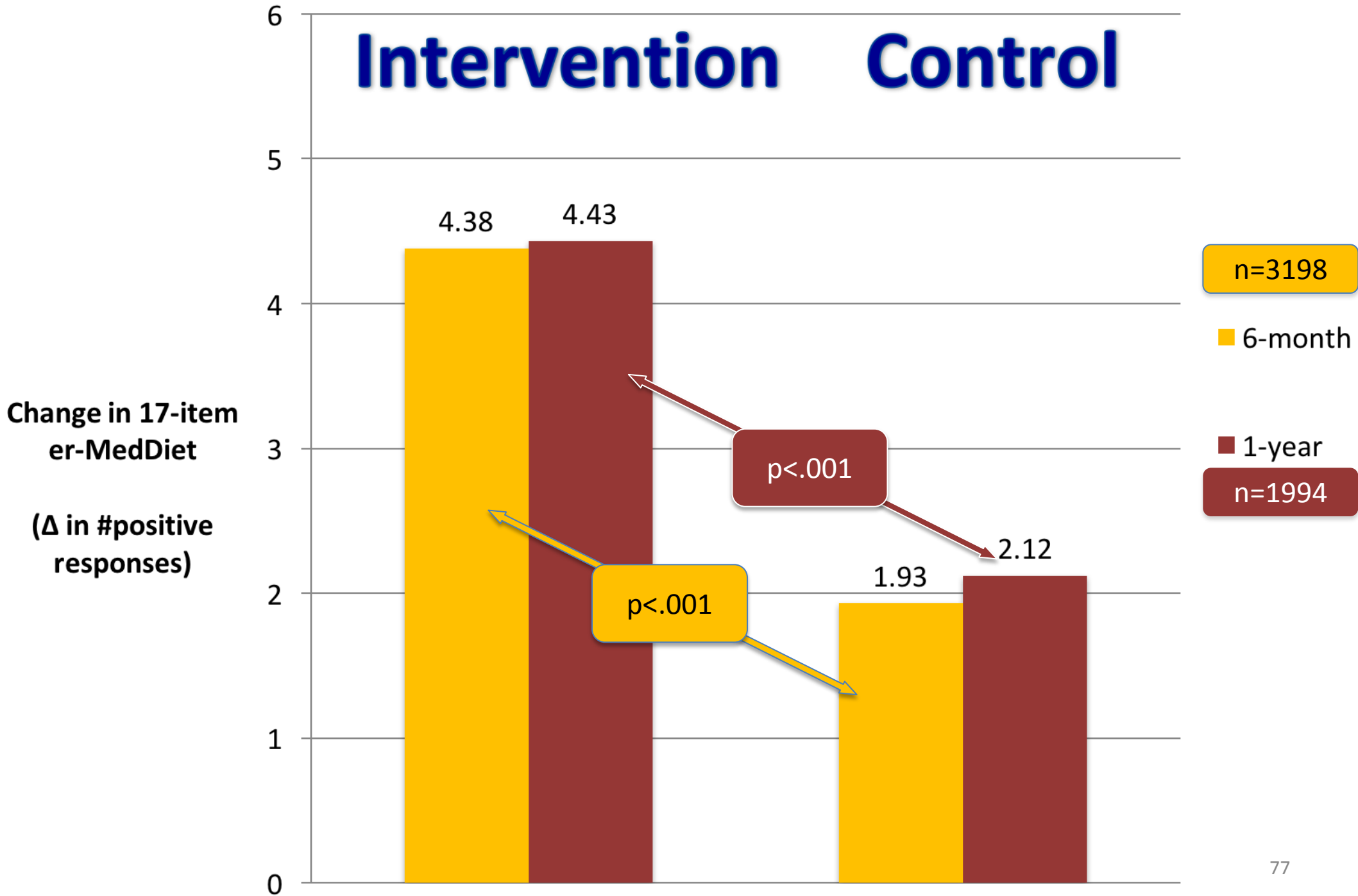
negotiated goals for the intervention group

## Energy-restricted MedDiet

9. *¿Cuántas veces consume repostería tal como galletas, flanes, dulces o pasteles a la semana?:*
10. *¿Cuántas veces consume frutos secos a la semana?: (ración 30 g.)*
11. *¿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.)*
12. *¿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)?:*
13. *¿Añade usted azúcar a las bebidas (café, té)?:*
14. *¿Cuántas raciones de pan blanco consume al día?: (1 ración=75g.)*
15. *¿Cuántas raciones de cereales y alimentos integrales (pan, arroz, pasta) consume a la semana?:*
16. *¿Cuántas raciones de pan, arroz y/o pasta refinados consume a la semana?:*
17. *¿Bebe usted vino? ¿Cuánto consume a la semana?*

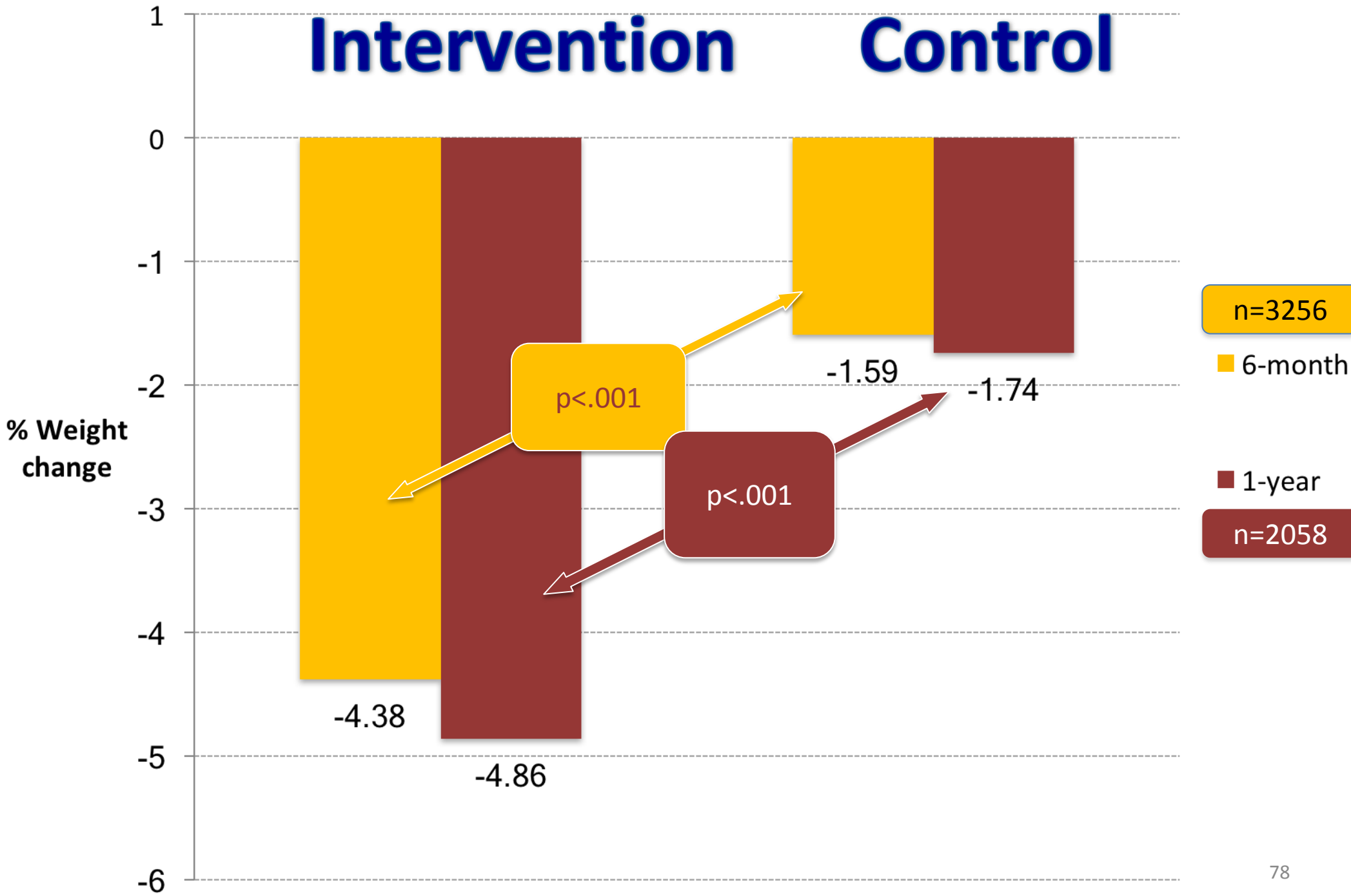
9. Bakery, cookies, sweets < 3 /wk
10. Tree nuts  $\geq$  3 /wk
11. Poultry > red-processed meats
12. Sofrito  $\geq$  2 /wk
13. Not adding sugar to beverages
14. White bread  $\leq$  1 /d
15. Whole grains  $\geq$  5 /wk
16. Refined grains-rice-pasta < 3 /wk
17. Wine glasses:           men 2-3 /d  
  women 1-2 /d

# Intervention Control

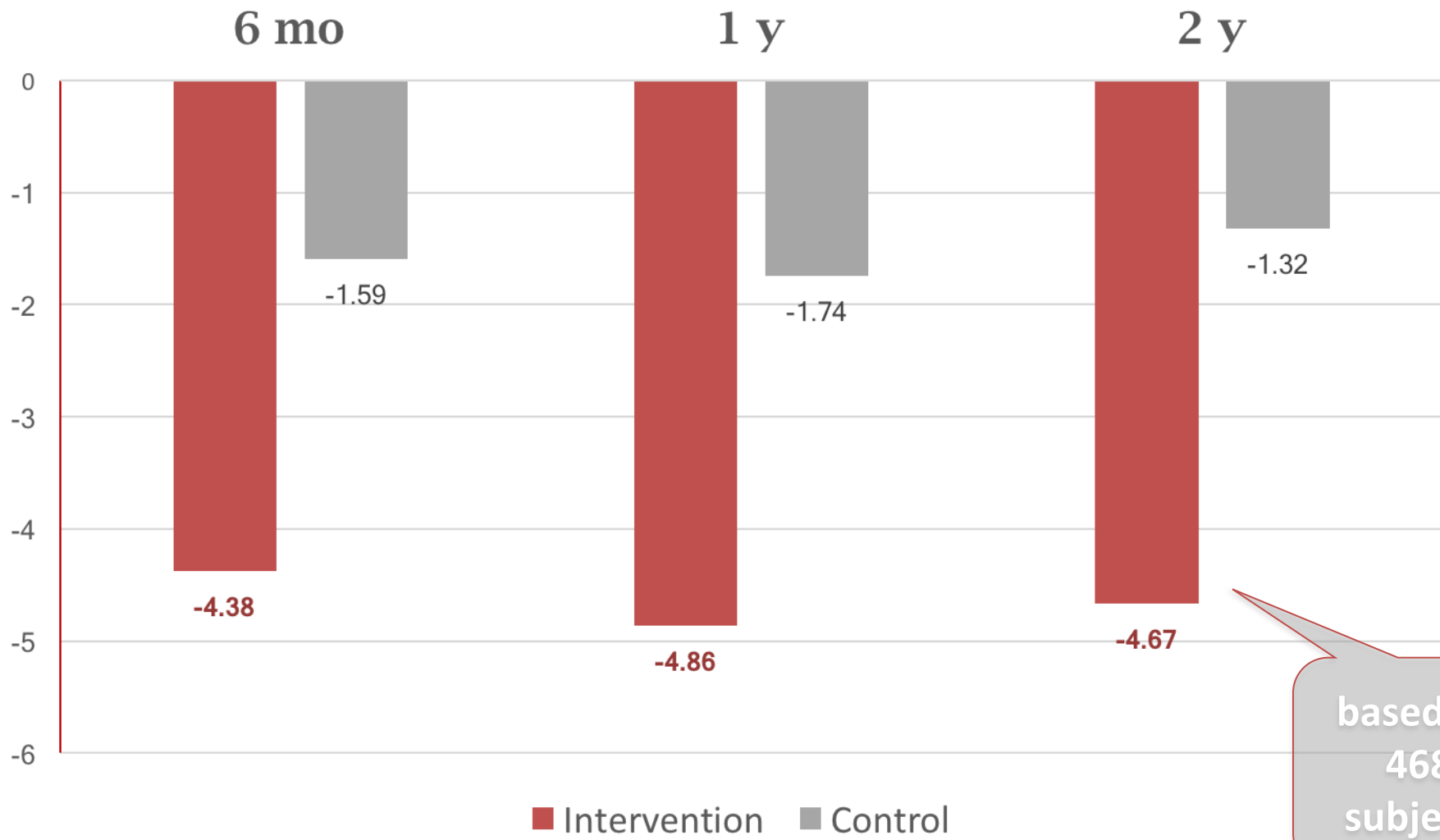


# Intervention

# Control



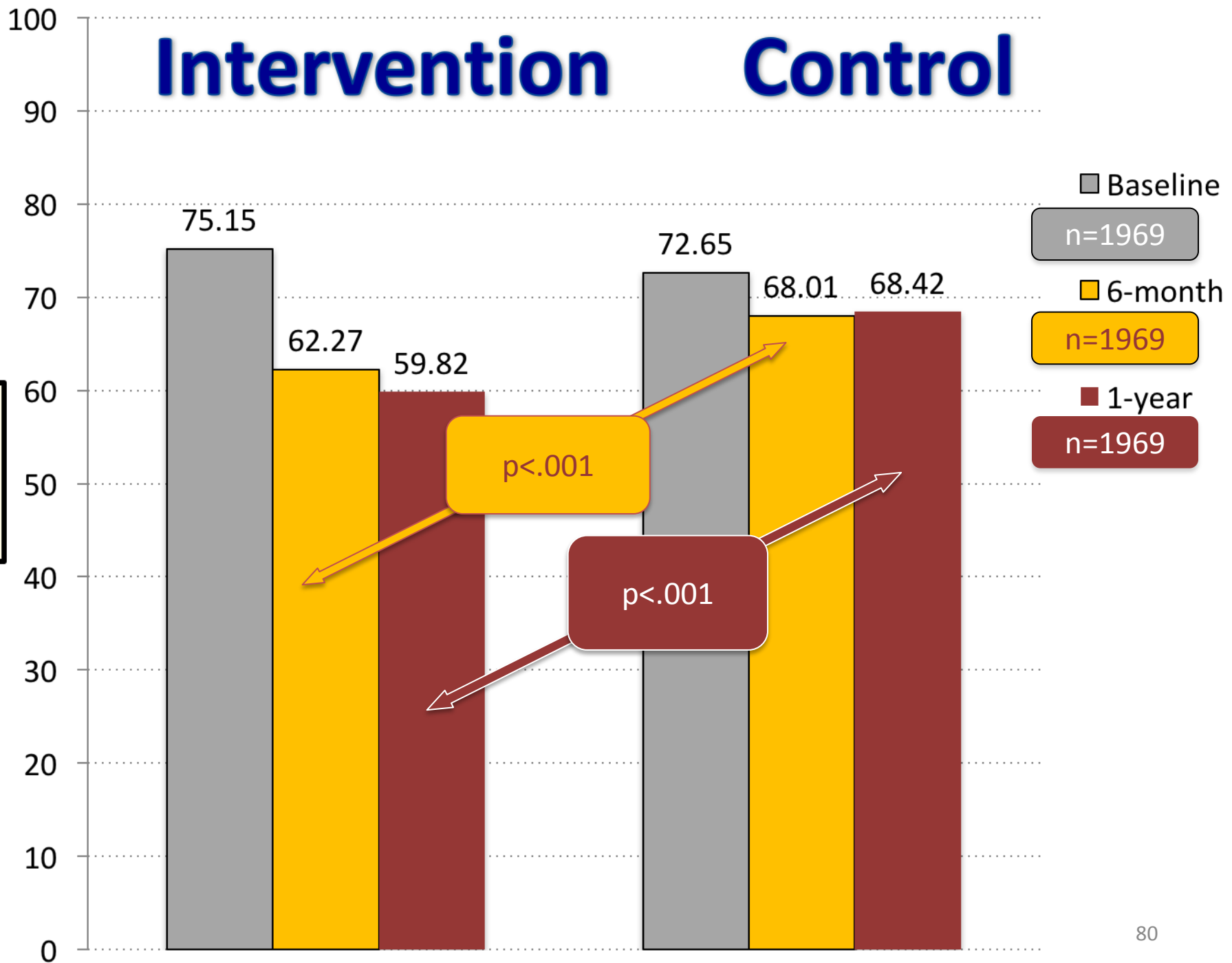
**% weight change versus baseline**



based on  
468  
subjects

# Intervention

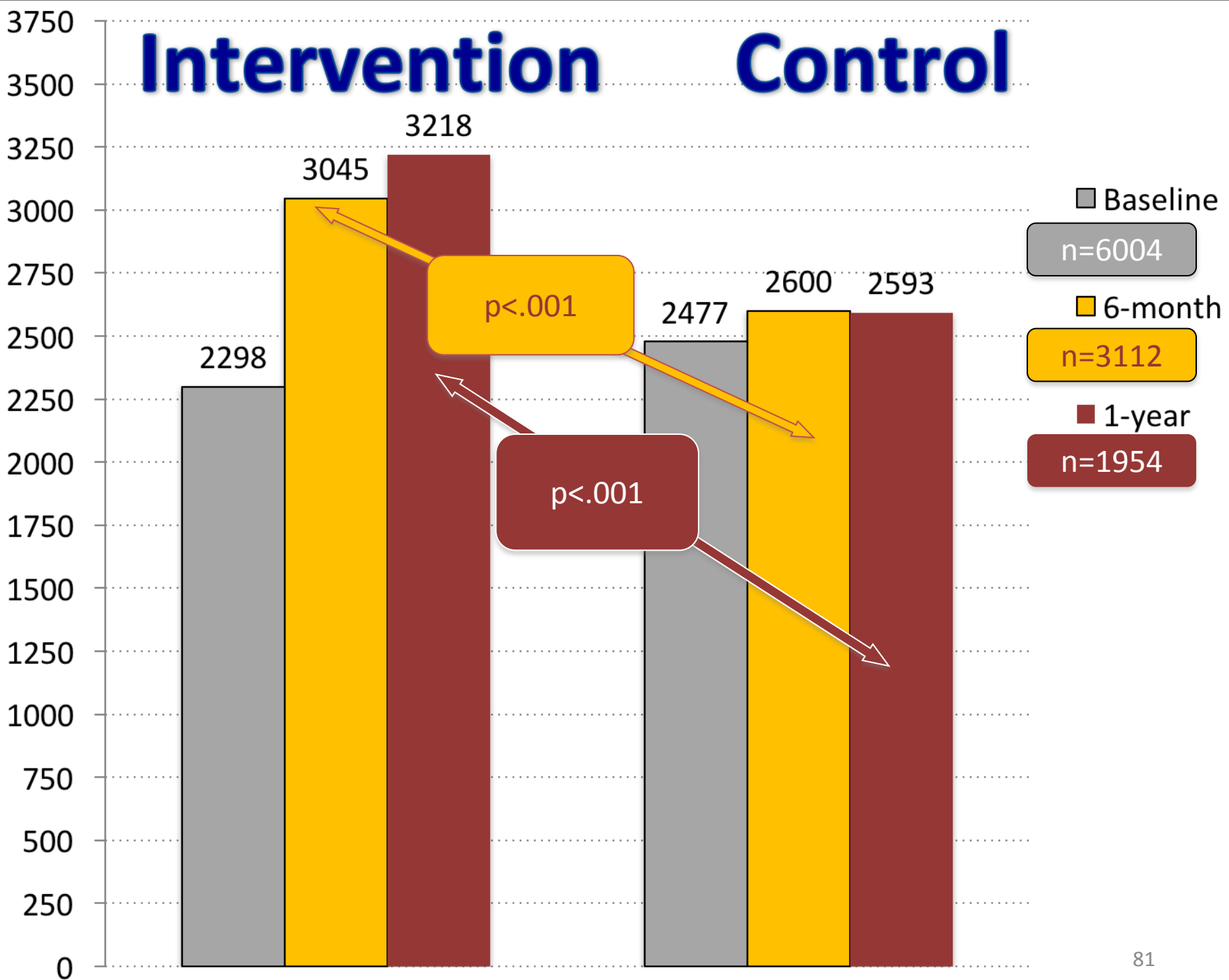
# Control





# Intervention

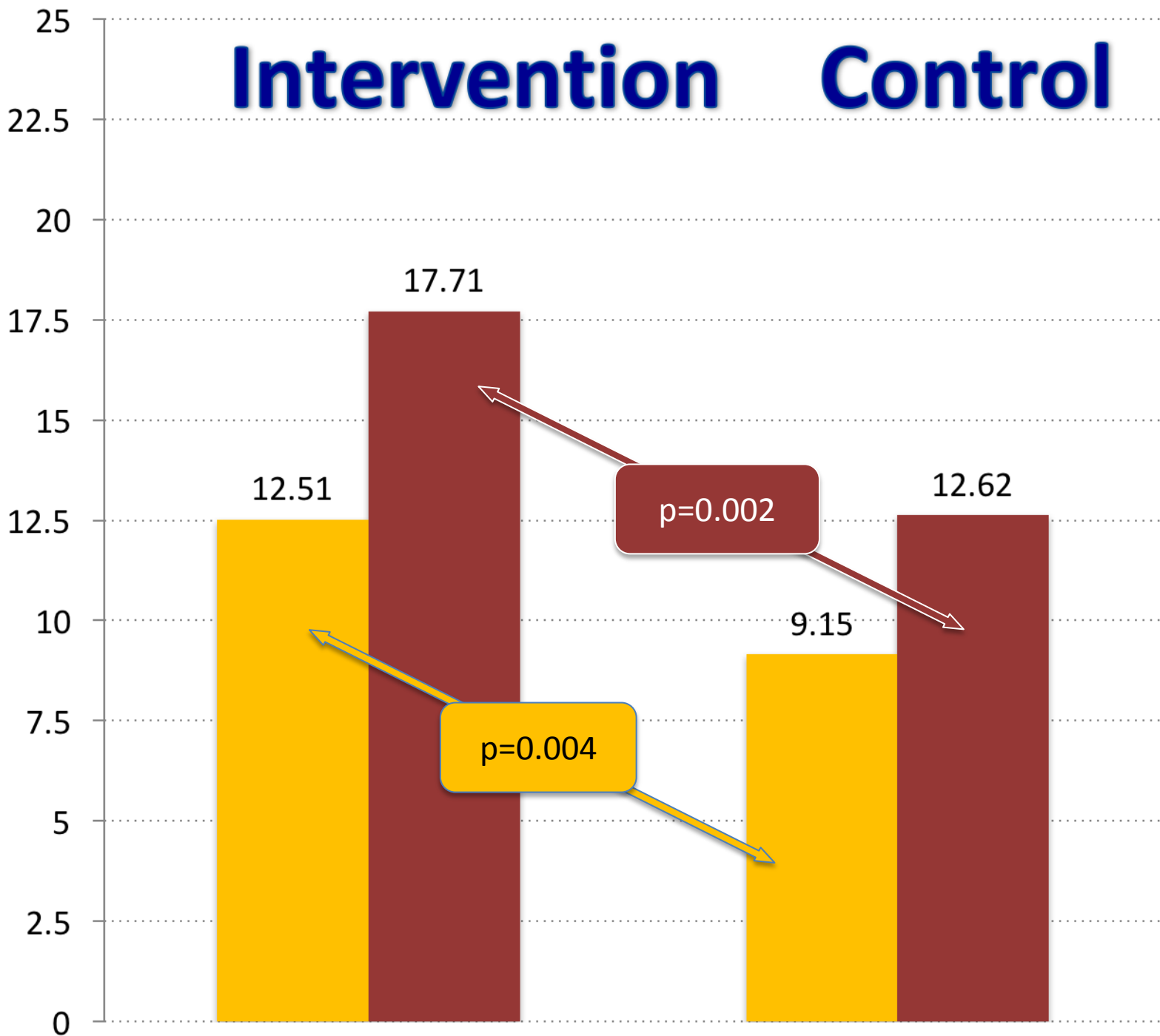
# Control



**LTPA**  
**METs-min/d**  
(Minnesota questionnaire)

# Intervention Control

**% Relative Change in CHAIR FITNESS TEST**



n=2975

6-month

1-year

n=1824

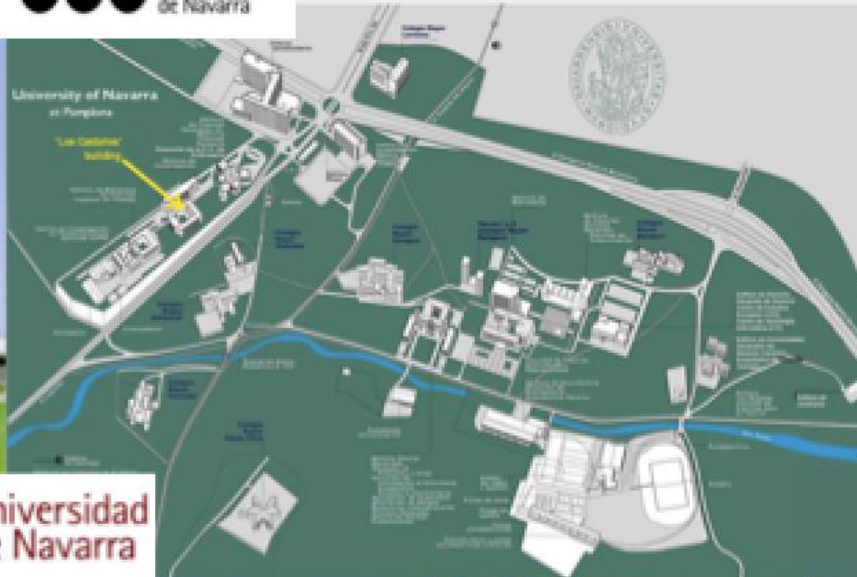
# En resumen...

- Las enfermedades que **más matan** a la humanidad son **altamente prevenibles**
  - la vida es simple'7
- Patrón **nutricional**: implicado en **6/7 métricas**
- No hay otro patrón con una **evidencia** tan fuerte en prevención CV como **MedDiet**
- MedDiet **14 items**: evaluar+predecir+*feedback*
- er-MedDiet: probablemente la opción más inteligente para combatir **obesidad, DMT2 y ECV** (las pandemias del siglo XXI)

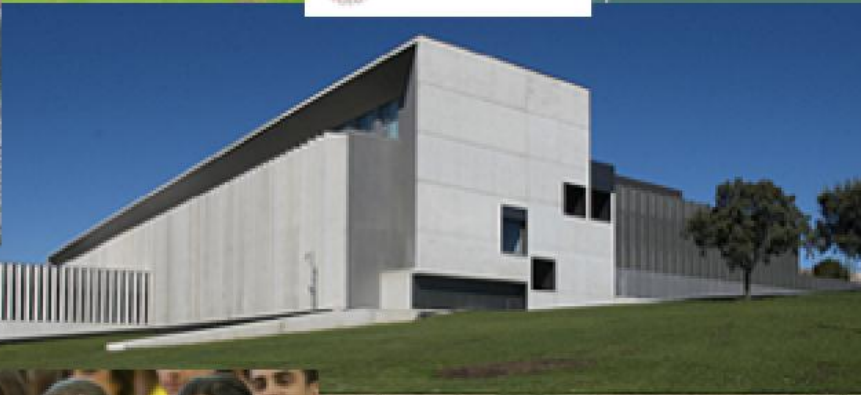
¡Muchas gracias!  
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