

Fruits & Vegetables in nutritional epidemiology: cohorts, meta-analyses & trials



MA Martínez-González



RD 06/0045: Alimentación saludable en la prevención de enfermedades crónicas: Red PREDIMED

F & V in nutritional epidemiology: cohorts, meta-analyses & trials

Introduction

Cohorts & meta-analyses

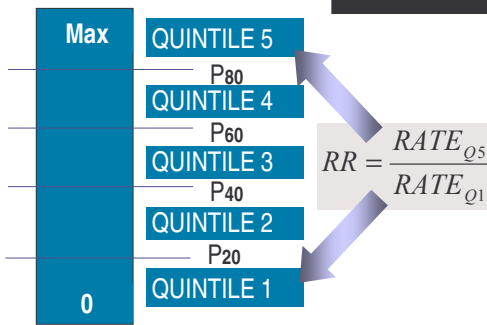
- Cancer
- CVD (CHD & stroke)
- Diabetes

Trials

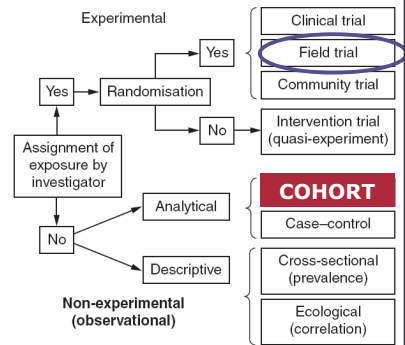
- Supplements?
- Low-fat diets?
- Whole dietary pattern approach



www.unav.es/preventiva

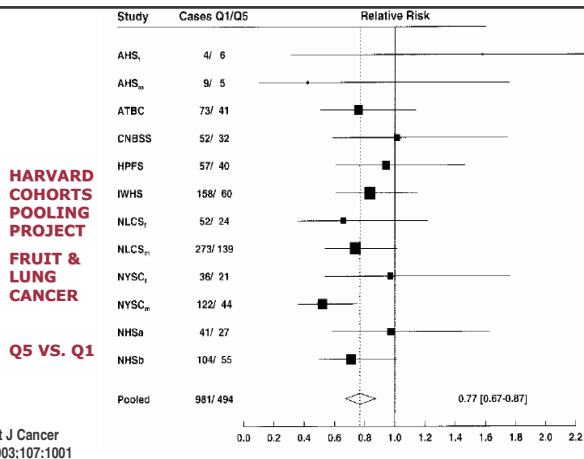


Research designs



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.

Figure 13.2 Classification of epidemiological designs.



F & V in nutritional epidemiology: cohorts, meta-analyses & trials

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Am J Clin Nutr 2003;78(suppl):559S-69S

TABLE 5

Summary results of the meta-analyses on fruit and vegetables and the risk of some cancers in case-control and cohort studies¹

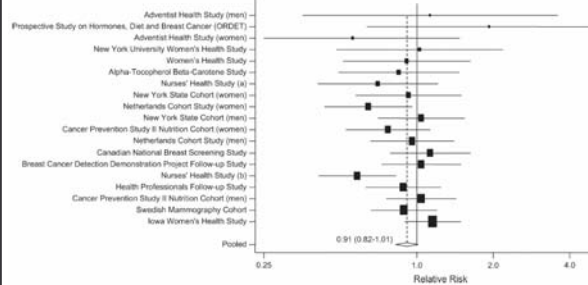
	Vegetables		Fruit	
	Case-control	Cohort	Case-control	Cohort
Mouth and pharynx	NS	?	↓	?
Larynx	NS	?	↓	?
Esophagus	↓	?	↓	?
Breast	↓	NS	NS	NS
Lung	↓	NS	↓	↓
Bladder	NS	NS	↓	↓
Stomach	↓	NS	↓	NS
Colorectum	↓	NS	↓	NS

¹ ↓, significant protective effect; NS, nonsignificant protective effect.

Pooling Project: F&V & Colon cancer

J Natl Cancer Inst 2007;99:1471

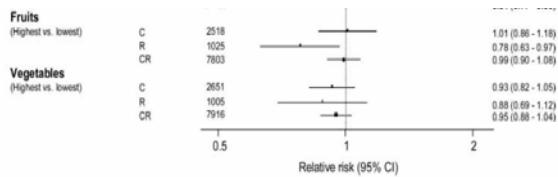
n = 756.217



Highest versus lowest quintile

Meta-analysis: 16 cohorts

Int J Cancer 2009;125:171-180



Oral cavity-pharinx, larinx & esophagus:

EPIC

Cancer Causes Control 2006;17:957-69

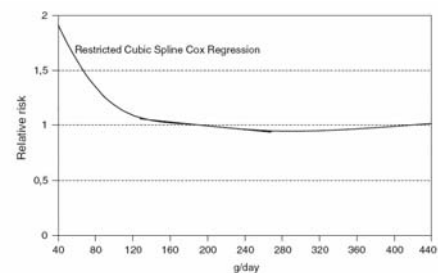


Fig. 1 Estimated relative risk of squamous cell cancer (SCC) for intake of total fruits (restricted cubic spline and linear risk functions).

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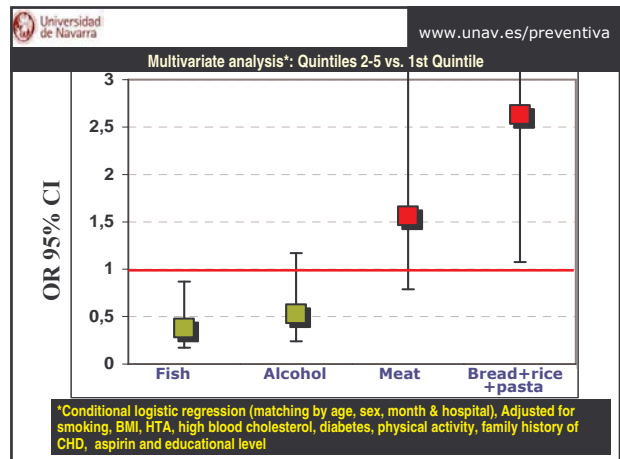
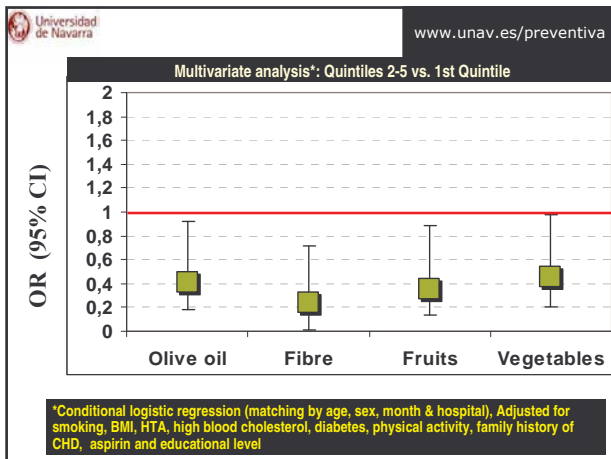
Cohorts & meta-analyses

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un Universidad de Navarra www.unav.es/preventiva

European Journal of Clinical Nutrition 2002; 56: 715-722
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www.nature.com/ejcn

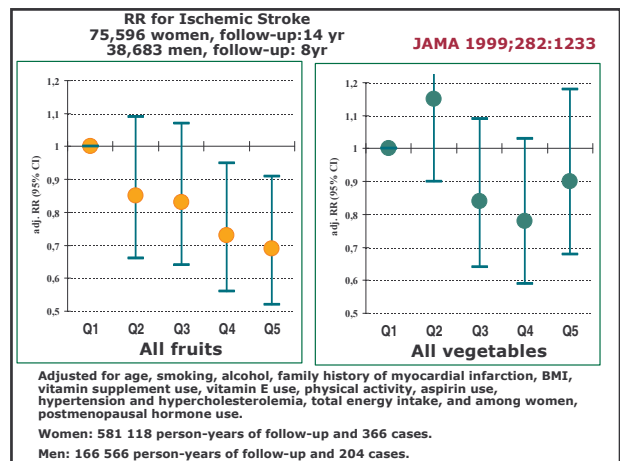
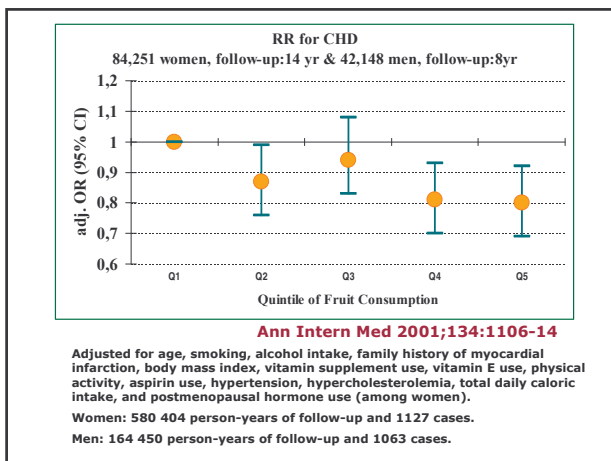
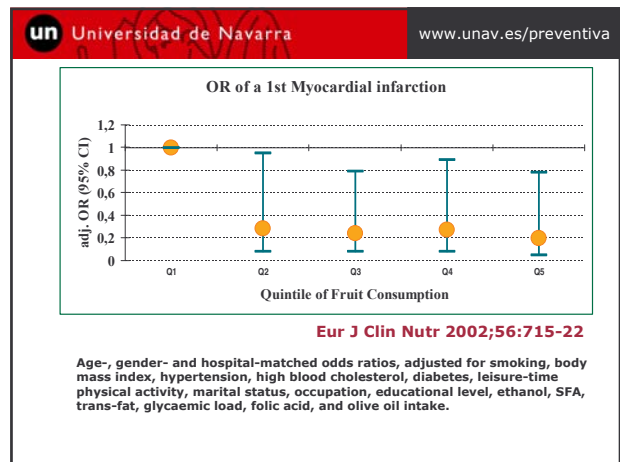
ORIGINAL COMMUNICATION

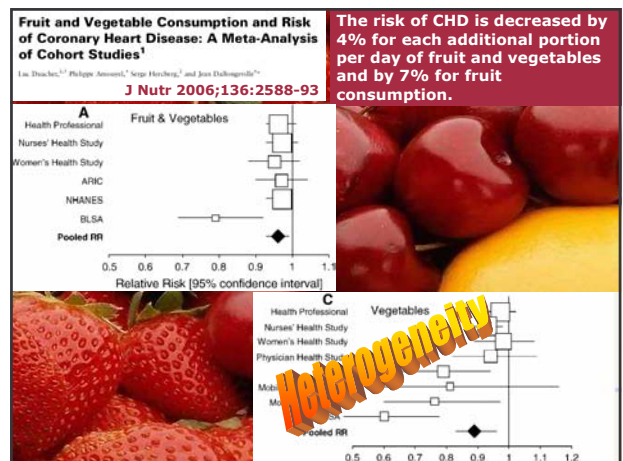
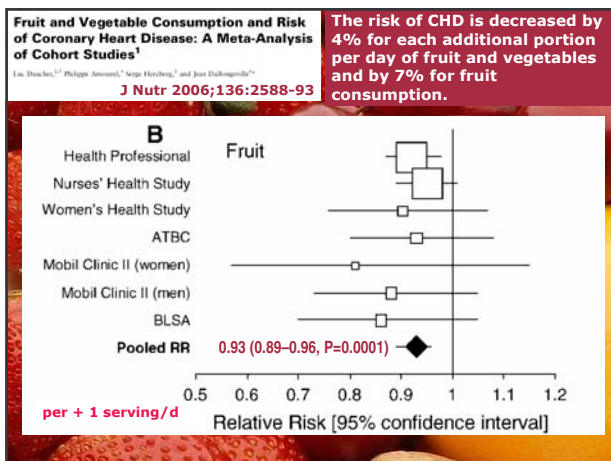
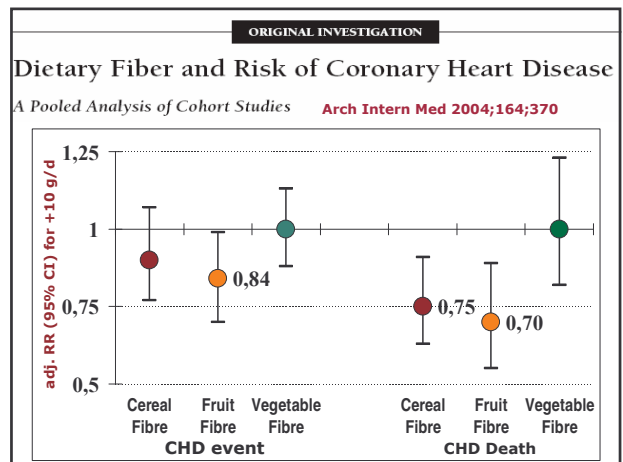
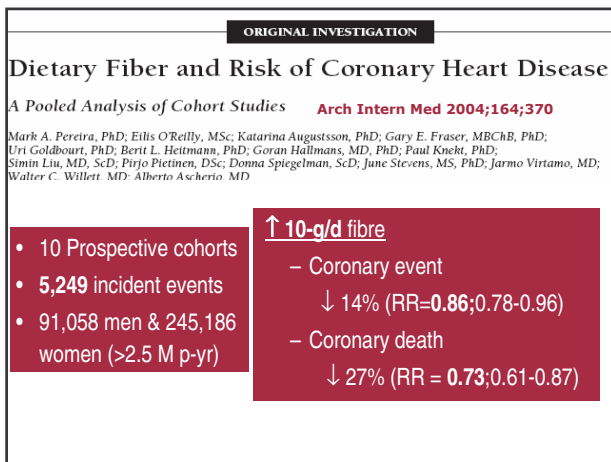
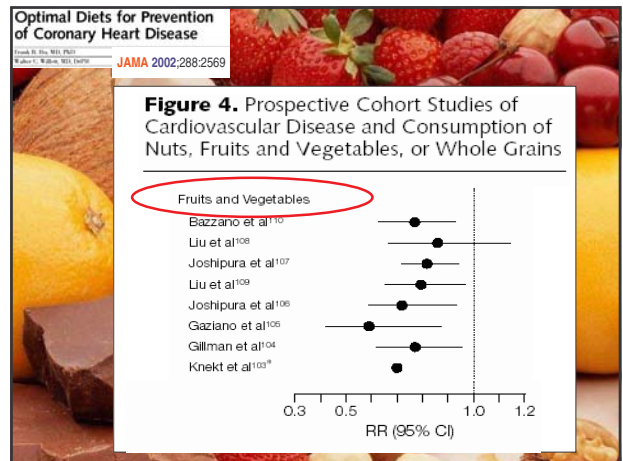
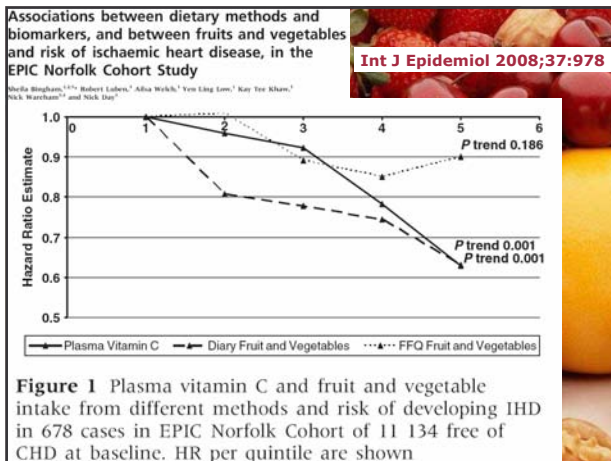
Role of fibre and fruit in the Mediterranean diet to protect against myocardial infarction: a case-control study in Spain

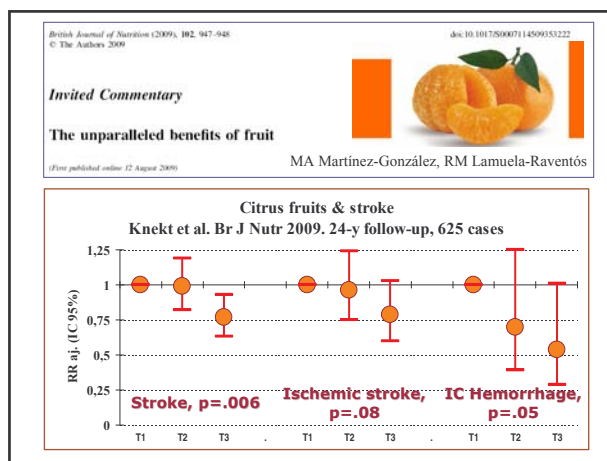
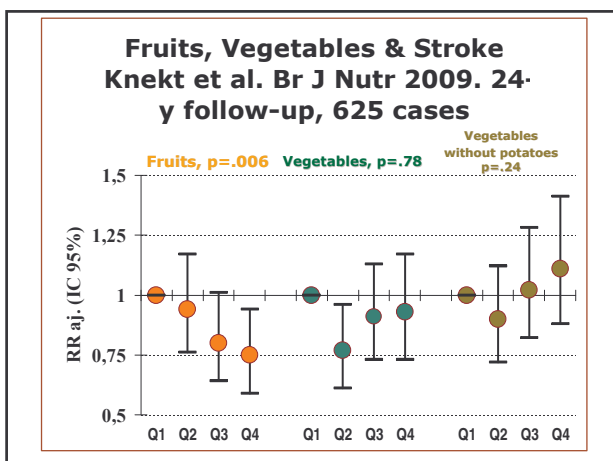
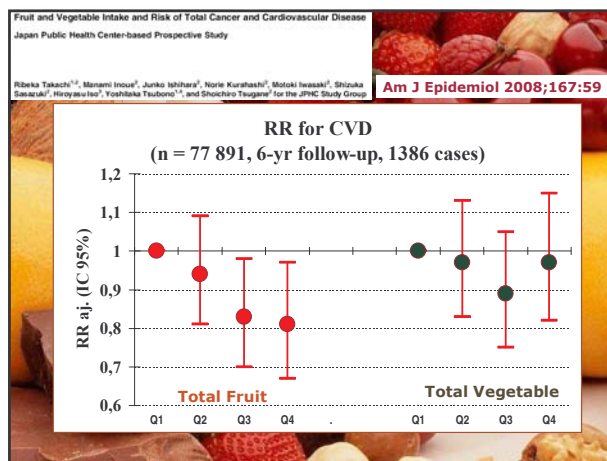
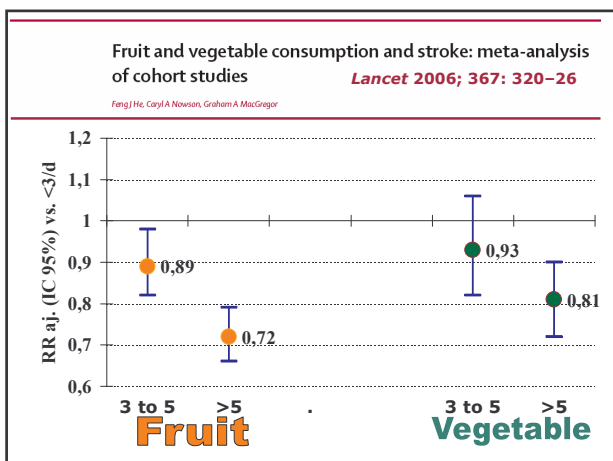
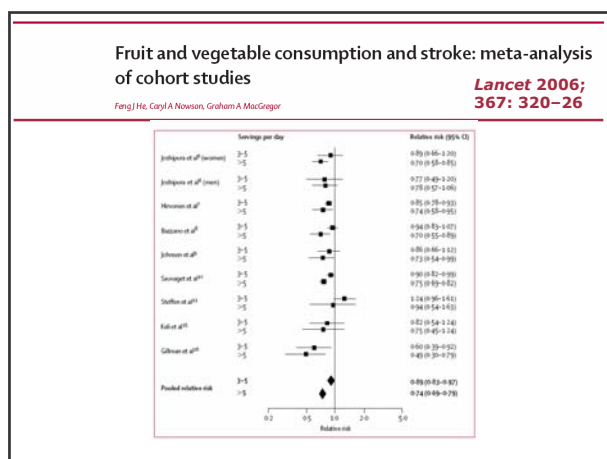
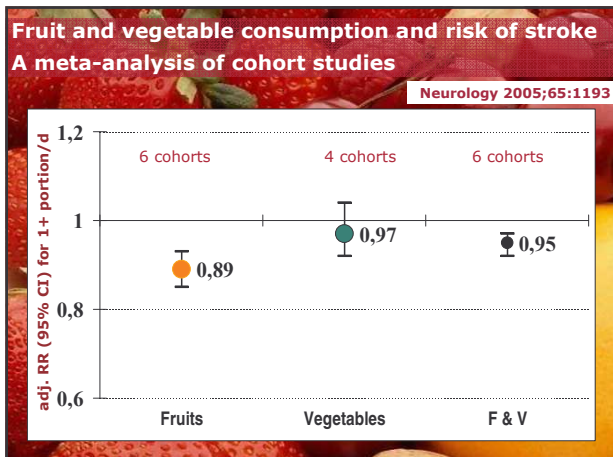
MA Martínez-González^{1*}, E Fernández-Jarne^{1,2}, E Martínez-Losa^{1,3}, M Prado-Santamaría^{1,3}, C Brugarolas-Brufau^{1,3} and M Serrano-Martínez^{1,3}

¹Department of Epidemiology and Public Health, University of Navarre, Pamplona, Spain; ²Department of Cardiology, University Clinic of Navarre, Navarre, Spain; and ³Navarre Primary Care Health Services, Navarre, Spain

Eur J Clin Nutr 2002;56:715-22







Br J Nutr 2009;102:1075

- An inverse association was found between **fruit** consumption and the incidence of cerebrovascular diseases, ischaemic stroke and intracerebral haemorrhage.
- The adjusted relative risks (RR) between the highest and lowest quartiles of intake of **any** cerebrovascular disease, **ischaemic** stroke and intracerebral haemorrhage were
 - ✓ 0.75 (95 % CI 0.59, 0.94)
 - ✓ 0.73 (95 % CI 0.54, 1.00)
 - ✓ 0.47 (95 % CI 0.24, 0.92)
- These associations were primarily due to the consumption of **citrus fruits** and occurred only in men.
- Total consumption of vegetables or cereals was not associated with the cerebrovascular disease incidence.

The SUN cohort

Published by Oxford University Press on behalf of the International Epidemiological Association International Journal of Epidemiology 2006;35:1417-1422
© The Author 2006. All rights reserved. Advance Access publication 22 October 2006 doi:10.1093/ije/dyl224

COHORT PROFILE

Cohort profile: The 'Seguimiento Universidad de Navarra' (SUN) study *Int J Epidemiol* 2006;35:1417.

Maria Seguí-Gómez*, Carmen de la Fuente, Zenaida Vázquez, Jokin de Irala and Miguel A. Martínez-González

Public Health Nutrition: 9:1417-1422

DOI: 10.1079/PHN.2005935

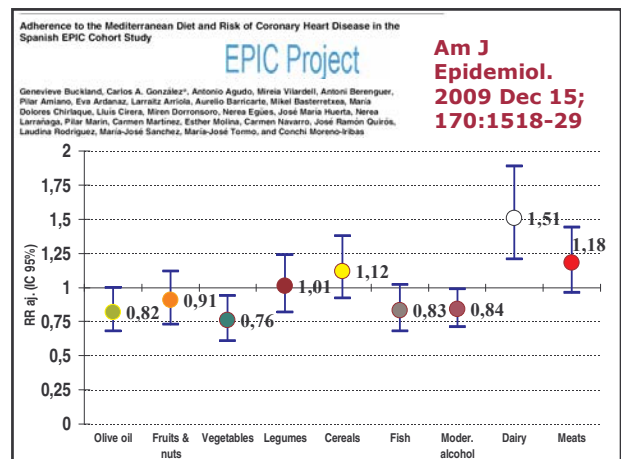
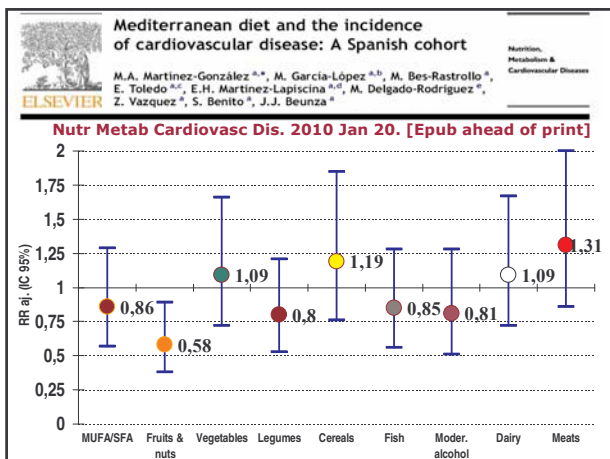
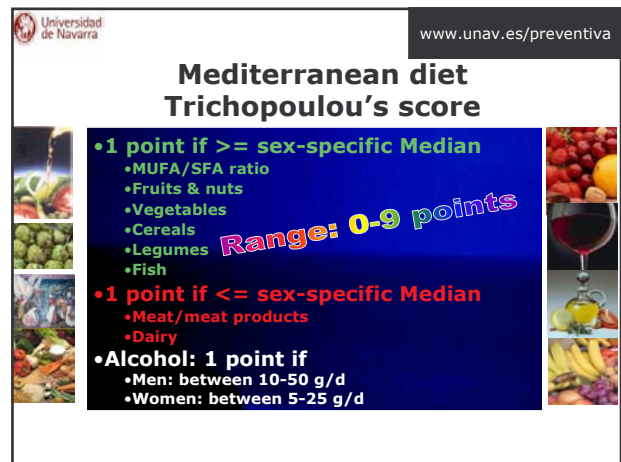
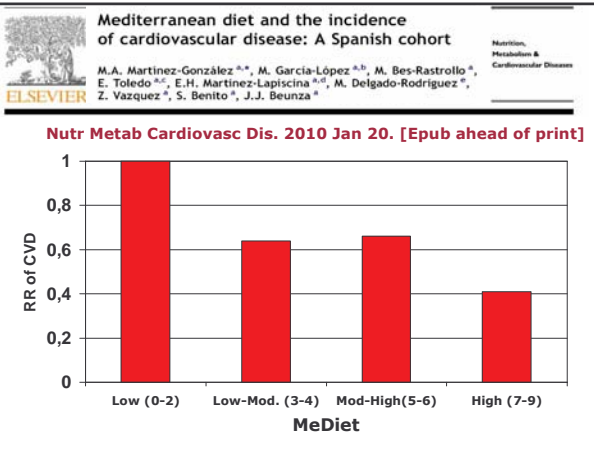
The SUN cohort study (Seguimiento University of Navarra)

Miguel Ángel Martínez-González*

Department of Preventive Medicine and Public Health, Facultad de Medicina, Clínica Universitaria, Universidad de Navarra, Irunlarrea 1, 31080 Pamplona, Spain

Public Health Nutr 2006;9:127

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F & V in nutritional epidemiology: cohorts, meta-analyses & trials

Introduction

Cohorts & meta-analyses

- Cancer
- CVD (CHD & stroke)
- Diabetes

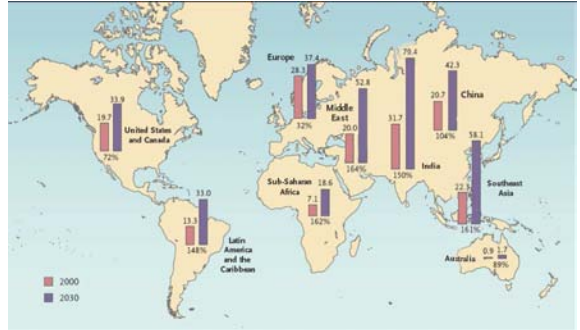
Trials

- Supplements?
- Low-fat diets?
- Whole dietary pattern approach



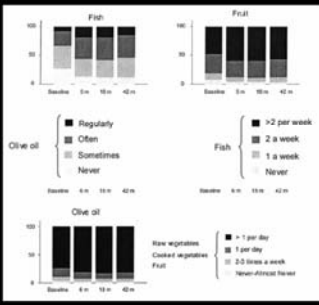
Millions of cases of diabetes in 2000 and Projections for 2030

(N Engl J Med 2007;356:214)

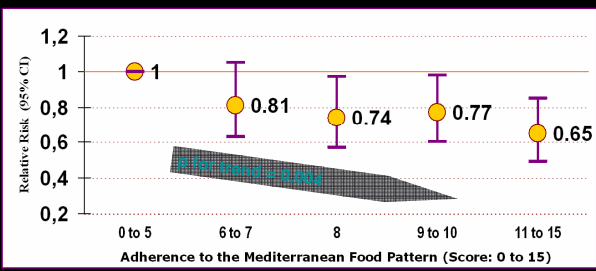


GISSI-Prevenzione study (Lancet 2007;370:667-75)

- 8 291 survivors of AMI
- Simple questionnaire
- 5-item score (0-3 points for each)
 - Fish
 - Fruit
 - Cooked vegetables
 - Raw vegetables
 - Olive oil
- Score: 0 to 15
- Mean follow-up: 3.2 yr
- 998 participants developed new-onset diabetes



GISSI-Prevenzione study (Lancet 2007;370:667-75)



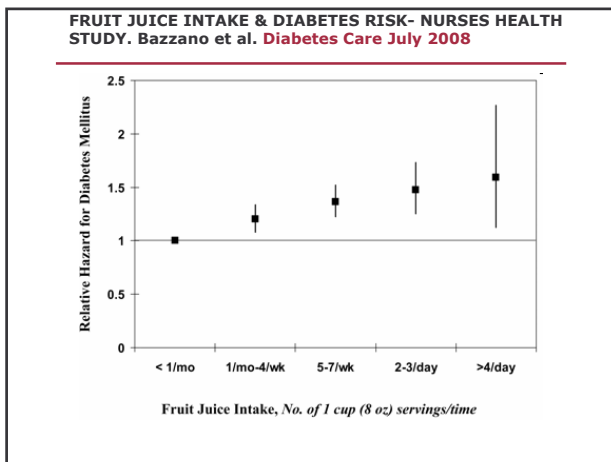
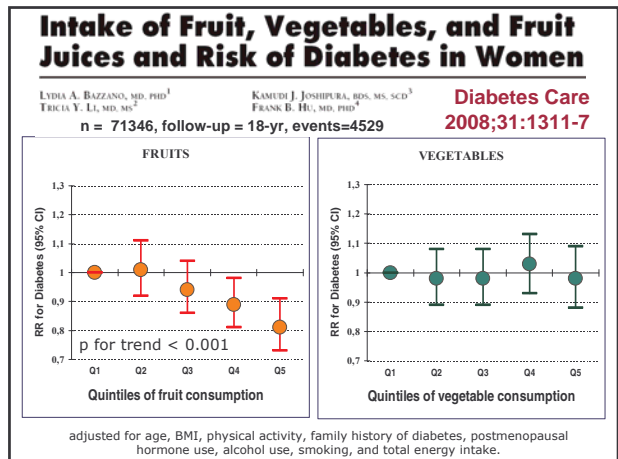
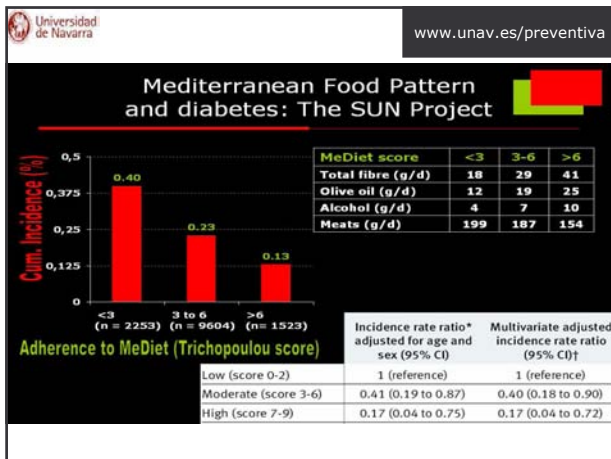
*Adjusted for age, sex, smoking, time from AMI to enrollment, treatment assignment, BMI, physical activity, stress testing, NYHA class, angina class, history of hypertension, another prior AMI, use of medication, consumption of cheese, wine and coffee.

www.unav.es/preventiva
RESEARCH
SUN
Adherence to Mediterranean diet and risk of developing diabetes: prospective cohort study
 M Á Martínez-González, professor of epidemiology and chair,¹ C de la Fuente-Arrillaga, research assistant,¹ J M Nunez-Cordoba, research fellow,^{2,3} F J Basterra-Gortari, research fellow,^{3,4} J J Beunza, assistant professor,¹ Z Vazquez, research assistant,⁵ S Benito, research assistant,⁶ A Tortosa, research fellow,¹ M Bes-Rastrollo, assistant professor¹
 Department of Preventive Medicine and Public Health, Medical School-Clinica Universitaria, University of Navarra, Pamplona, Spain
ABSTRACT
 Objective To assess the relation between adherence to a Mediterranean diet and the incidence of diabetes among initially healthy participants.
 diabetes. Many studies have shown that the Mediterranean food pattern has a role in prevention of cardiovascular disease.¹⁻⁶ The similarity of some risk factors and some etiological and mechanistic evidence
BMJ 2008;336:1348-51

www.unav.es/preventiva
Mediterranean Food Pattern and diabetes: The SUN Project

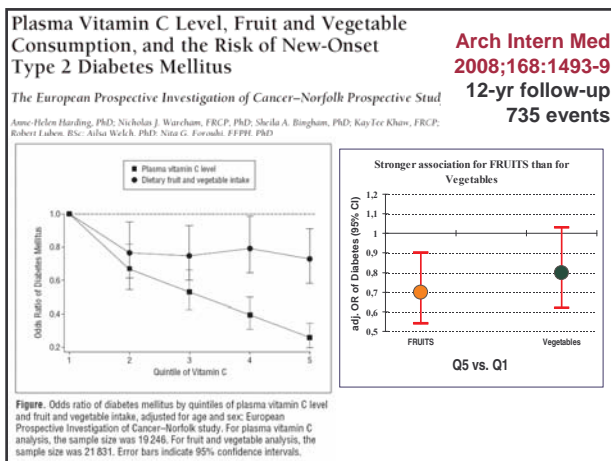
Adherence MeDiET (Trichopoulos score)	Cumulative Incidence (%)
<3 (n = 2253)	0.40
3 to 6 (n = 9604)	0.23
>6 (n = 1523)	0.13

MeDiET score	<3	3-6	>6
Total fibre (g/d)	18	29	41
Olive oil (g/d)	12	19	25
Alcohol (g/d)	4	7	10
Meats (g/d)	199	187	154



Dietary patterns and the risk of diabetes

Study	Protection	Risk
Van Dam, 2002 US	--	Red & processed meats, sweets & desserts, French fries, refined grains, high-fat dairy
Fung, 2004 US	--	Red & processed meats, sweets & desserts, french fries, refined grains
Montonen, 2005 Finland	fruits and vegetables	Butter, potatoes, high-fat milk, red & processed meats
Heidemann, 2005 Germany	fresh fruits	Soft drinks, beer, red & processed meats, poultry, refined breads, legumes
Hodge, 2007 Australia	salads, cooked vegetables, whole grains	Red meats, fried fish, processed meats, fat-cooked potatoes
Zhang, 2007 US	fruit, green leafy vegetables, poultry, fish	Red meat, processed meats



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Logo: MINISTERIO DE CIENCIA E INNOVACION, Fondo Europeo de Desarrollo Regional, Universidad de Navarra

Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention

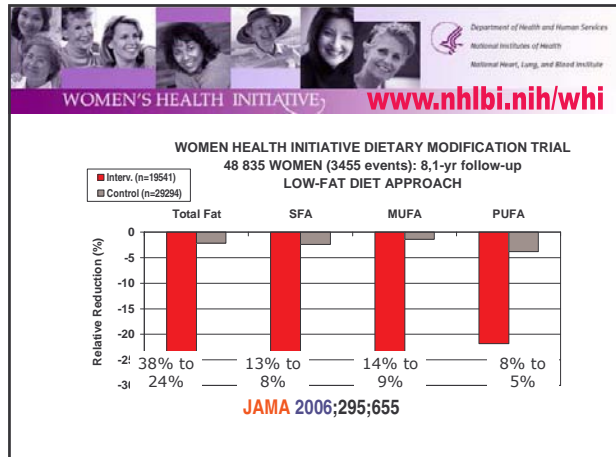
Systematic Review and Meta-analysis

Data Synthesis When all low- and high-bias risk trials of antioxidant supplements were pooled together there was no significant effect on mortality (RR, 1.02; 95% CI, 0.98-1.06). Multivariate meta-regression analyses showed that low-bias risk trials (RR, 1.16; 95% CI, 1.05-1.29) and selenium (RR, 0.998; 95% CI, 0.997-0.9995) were significantly associated with mortality. In 47 low-bias trials with 180 938 participants, the antioxidant supplements significantly increased mortality (RR, 1.05; 95% CI, 1.02-1.08). In low-bias risk trials, after exclusion of selenium trials, beta carotene (RR, 1.07; 95% CI, 1.02-1.11), vitamin A (RR, 1.16; 95% CI, 1.10-1.24), and vitamin E (RR, 1.04; 95% CI, 1.01-1.07), singly or combined, significantly increased mortality. Vitamin C and selenium had no significant effect on mortality.

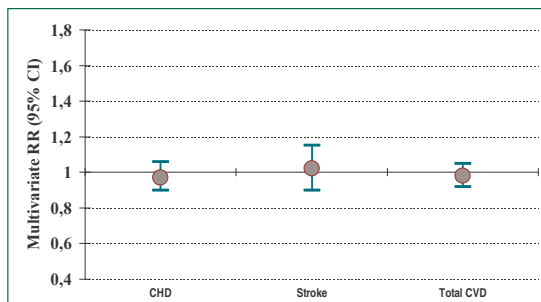
Conclusions Treatment with beta carotene, vitamin A, and vitamin E may increase mortality. The potential roles of vitamin C and selenium on mortality need further study.

JAMA. 2007;297:842-857

www.jama.com



WOMEN HEALTH INITIATIVE DIETARY MODIFICATION TRIAL
48 835 WOMEN (3455 events): 8,1-yr follow-up
LOW-FAT DIET APPROACH



JAMA 2006;295:655

PREDIMED

RD 06/0045 www.predimed.es

Fondo Europeo de Desarrollo Regional
Una manera de hacer Europa

Predimed
Prevención con Dieta Mediterránea

PREDIMED TRIAL: DESIGN

- Men: 55-80 yr
- Women: 60-80 yr
- High CV risk without CVD
- type 2 diabetics
- 3+ risk factors

Random

- Mediet + Virgin Olive Oil
- Mediet + Nuts
- Control Low-fat

AMERICAN HEART ASSOCIATION
Lipids and Life

Fondo Europeo de Desarrollo Regional
Una manera de hacer Europa

Predimed
Prevención con Dieta Mediterránea

PREDIMED Participants

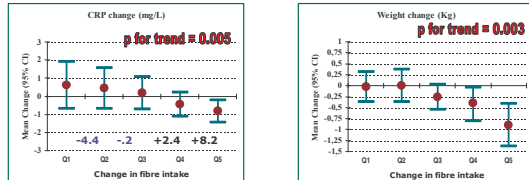
	Mediet + VOO (n= 2487)	MeDiet + Nuts (n=2396)	Control (n=2349)
Age (SD)	67 (6)	67 (6)	67 (6)
Women (%)	57	54	58
Diabetes (%)	50	47	48
Hypertension (%)	82	82	84
Current smokers (%)	14	15	14
High cholest. (%)	72	73	72
BMI (SD)	30 (4)	30 (4)	30 (4)
Waist (SD)	100 (10)	100 (10)	101 (11)
MeDiet 0-14 p (SD)	8.7 (2)	8.7 (2)	8.3 (2)

Predimed.org (www.predimed.es)

Annals of Internal Medicine Ann Intern Med 2006;145:1-11 | ARTICLE

Effects of a Mediterranean-Style Diet on Cardiovascular Risk Factors A Randomized Trial

Ramon Estruch, MD, PhD; Miguel Angel Martínez-González, MD, PhD; Dolores Corella, PhD; Jordi Salas-Salvadó, MD, PhD; Valentina Ruiz-Gutierrez, PhD; Maria Isabel Covas, PhD; Miguel Fiol, MD, PhD; Enrique Gómez-Gracia, MD, PhD; Mari Carmen López-Sabater, PhD; Ernest Vinuela, MD, PhD; Fernando Azúa, MD, PhD; Manuel Conde, MD, PhD; Carlos Lahoz, MD, PhD; José Lapetra, MD, PhD; Guillermo Sáez, MD, PhD; and Emilio Ros, MD, PhD, for the PREDIMED Study Investigators*

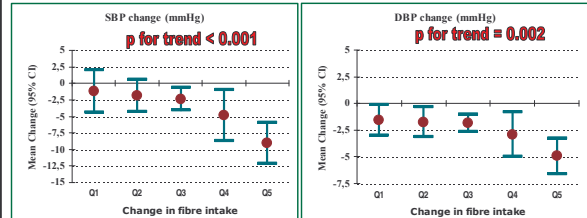


Predimed.org (www.predimed.es)

J Epidemiol
Community
Health
2009;63:582
-588.

Effects of dietary fibre intake on risk factors for cardiovascular disease in subjects at high risk

R Estruch,^{1,2} M A Martínez-González,³ D Corella,^{2,4} J Basora-Gallissá,⁵ V Ruiz-Gutiérrez,⁶ M I Covas,^{2,7} M Fiol,^{2,8} E Gómez-Gracia,⁹ M C López-Sabater,¹⁰ R Escoda,¹ M A Pena,¹¹ J Díez-Espino,³ C Lahoz,¹² J Lapetra,^{2,13} G Sáez,¹⁴ E Ros,^{2,15} on behalf of the PREDIMED Study Investigators



www.predimed.org www.predimed.es Modification of dietary habits

Current Research

RESEARCH Journal of the American Dietetic Association

A Large Randomized Individual and Group Intervention Conducted by Registered Dietitians Increased Adherence to Mediterranean-Type Diets: The PREDIMED Study

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

Mediterranean type diets increase adherence through dietitian intervention

www.predimed.es

RD 06/0045 *Predimed*
Prevención con Dieta Mediterránea

Universidad de Navarra Departamento de Medicina Preventiva y Salud Pública

MINISTERIO DE CIENCIA E INNOVACIÓN

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Conclusions

- Most prospective studies suggest a protection by **F & V** against CVD, hypertension and diabetes
- Stronger protection by **fruits** than **vegetables**?
- Randomised trials are needed
 - Whole dietary patterns, not supplements
 - Low-fat approach is misleading
 - Best approach: cohorts + trials
 - Spain: EPIC + SUN + PREDIMED