

EXPO 2015
Milano, 27 Ottobre 2015

VINO E SALUTE: PROBLEMI DI CUORE

GIOVANNI de GAETANO, MD, PhD

***IRCCS ISTITUTO NEUROLOGICO MEDITERRANEO NEUROMED
POZZILLI (Isernia)***

**DECLARATION
OF CONFLICT OF INTEREST**

***I HAVE
NO CONFLICT OF INTEREST TO DECLARE,
EXCEPT THAT I LIKE TO DRINK WINE
REGULARLY AND IN MODERATION***

IS WINE

A LIFE-SAVING
BEVERAGE?

Ο ΜΗΡΟΥ

ΟΔΥΣΣΕΙΑ.

H O M E R I

ODYSSEA,

ID EST,

DE REBUS AB VLYS-

SE GESTIS.

Βαλδερ Βασιλομυσεχία
& Μυτιλή.

Latina versum ad versum i regios apponit



E T Y T O G R A P H I A I O A N

N I S C H R I S T I N I

A T H E N A E.

1547.







Mosaic, Villa Romana del Casale,
Piazza Armerina, Sicily





THE "FRENCH PARADOX"

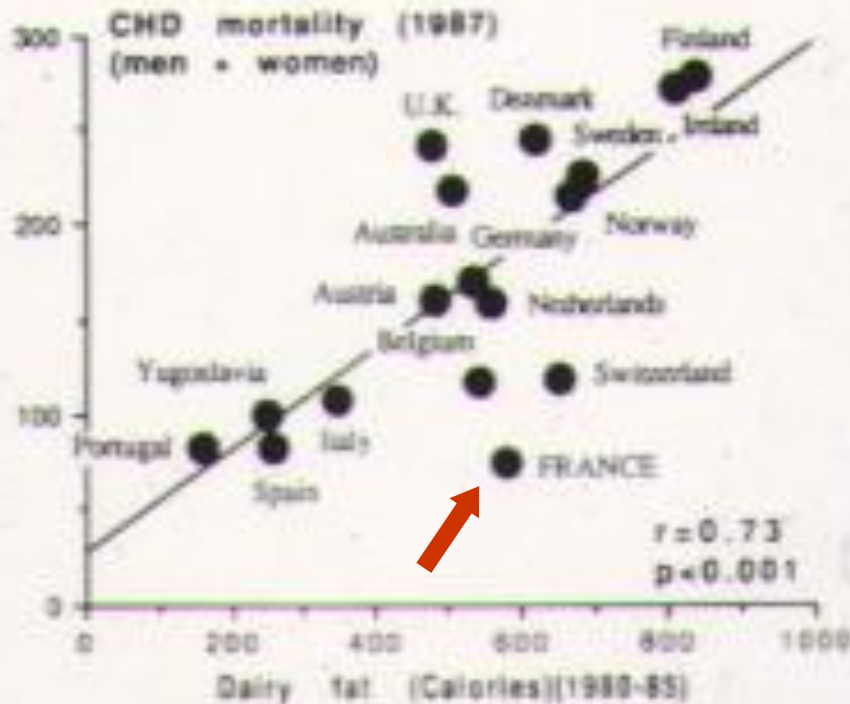


Fig 1—Relation between age-standardised death rate from CHD (mean for men and women) and consumption of dairy fat in countries reporting wine consumption.

S. Renaud and M. de Lorgeril The Lancet 1992

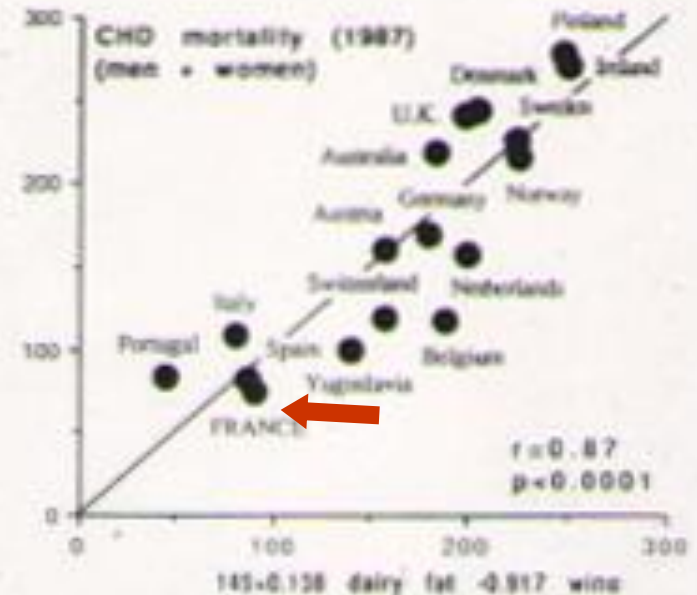
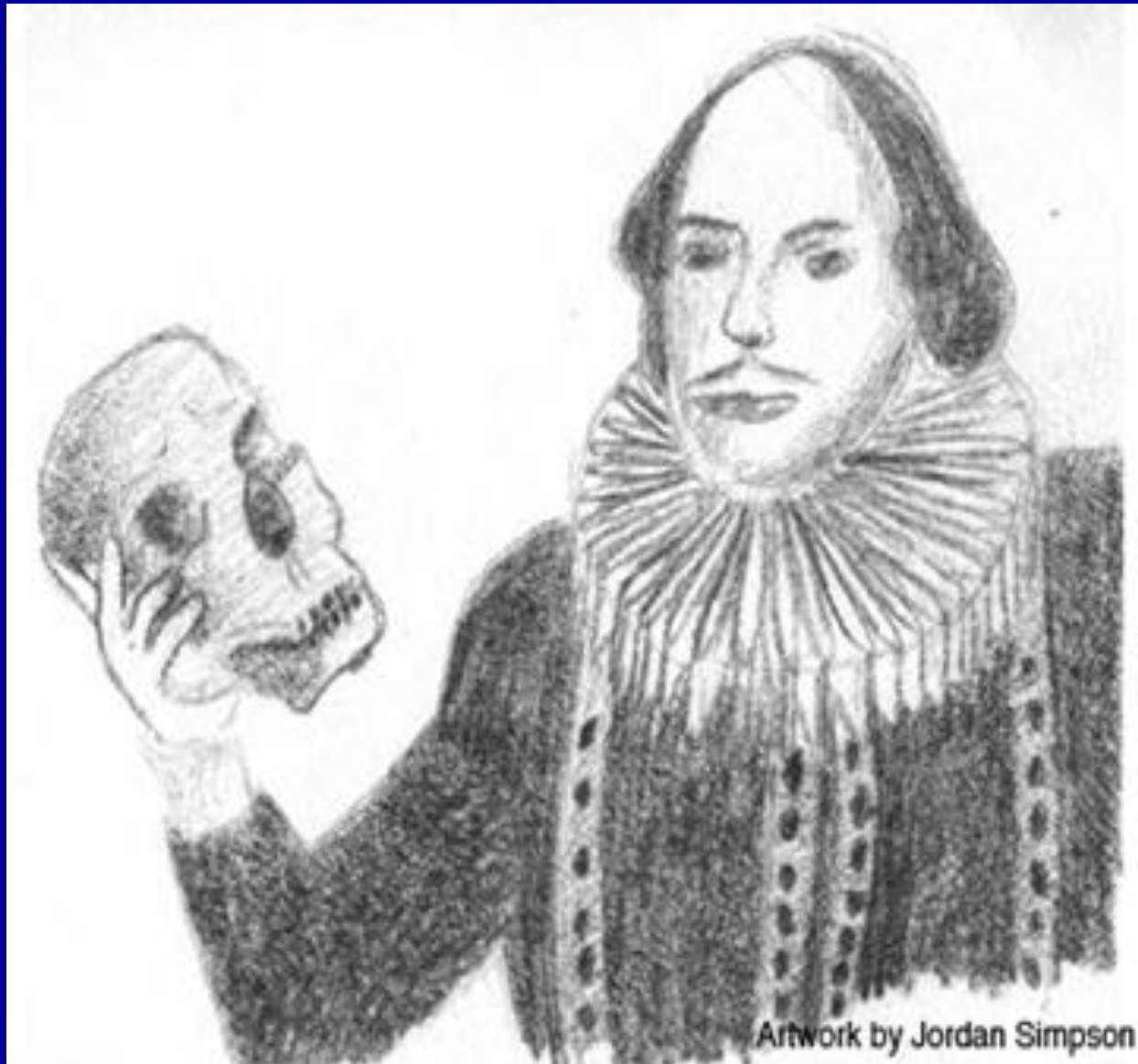


Fig 2—Relation between age-standardised death rate from CHD (mean for men and women) and consumption of dairy fat and of wine in countries reporting wine consumption.

S. Renaud and M. de Lorgeril The Lancet 1992

***THE NOVEL HAMLET
TO DRINK OR NOT TO DRINK ?***



HOW SOLID IS TODAY
THE SCIENTIFIC EVIDENCE
THAT WINE DRINKING
IS BENEFICIAL AGAINST
CARDIOVASCULAR RISK
AND ALL-CAUSE MORTALITY?



NAPOLI - SALERNO

NAPOLI - SALERNO



NAPOLI

SALERNO



RIS
P

META-ANALYSIS

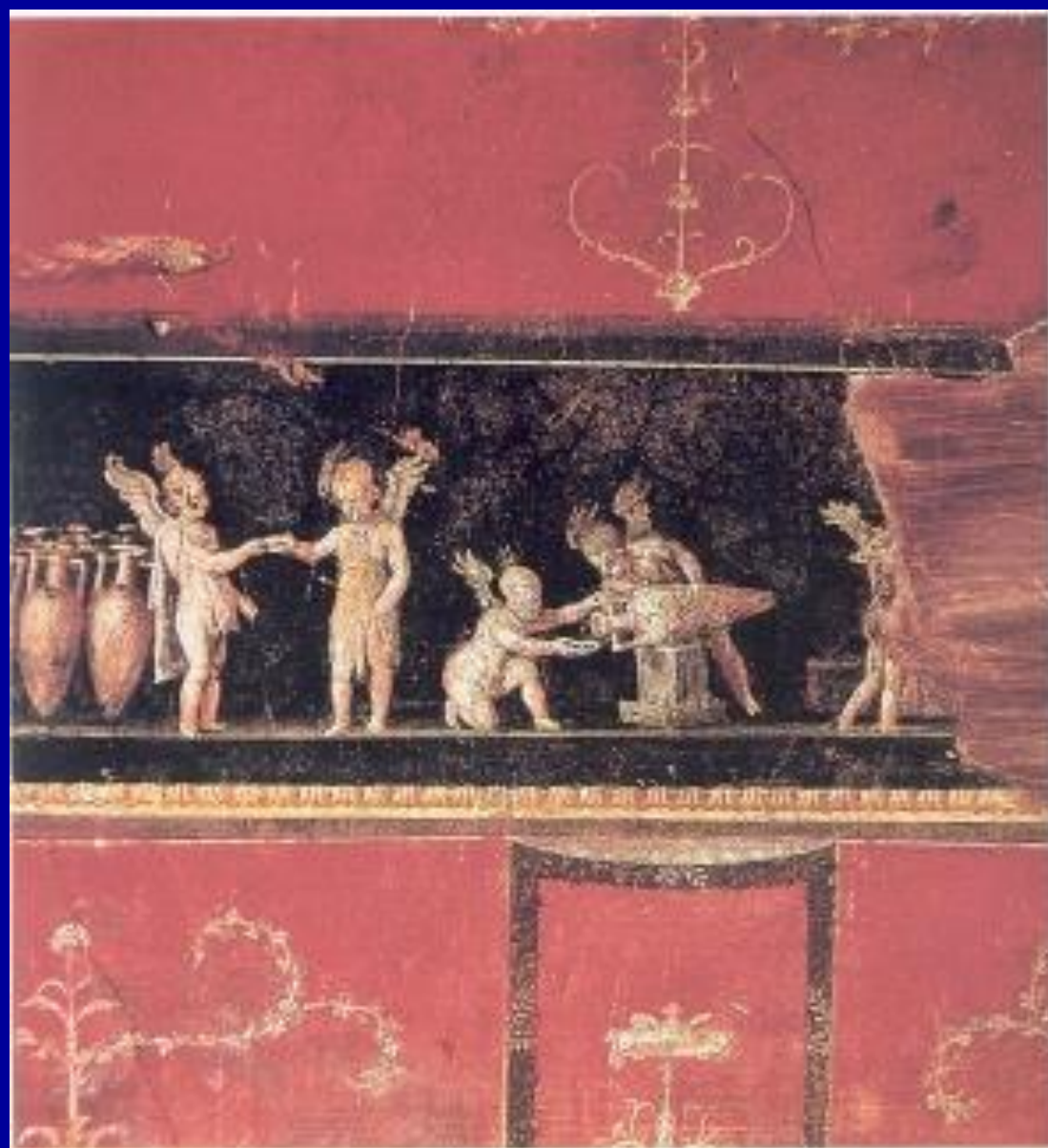
**A meta-analysis combines - as a whole –
the results of different studies
that address the same or
a set of related research hypotheses.**

**It provides a balanced view and global answers
that take into account the relative “weight”
of each single study**

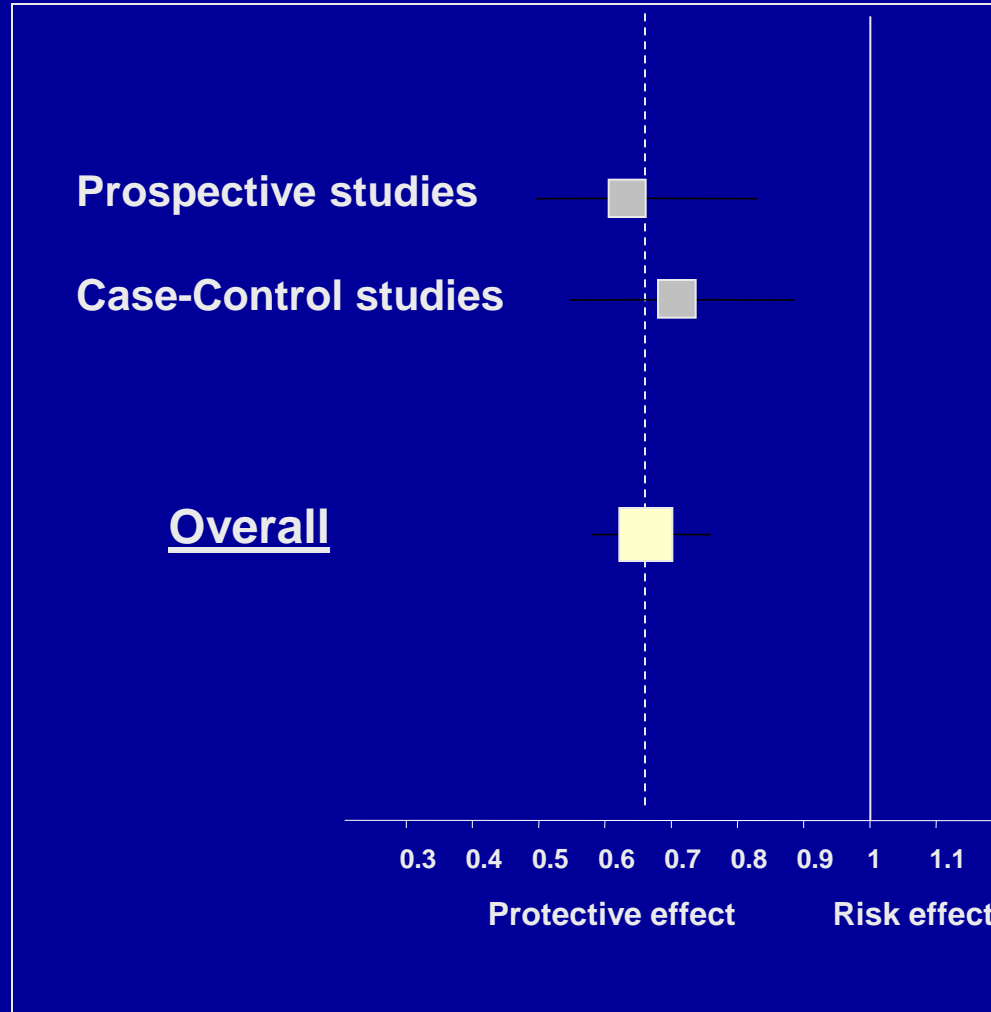


Renato Guttuso

La Vucciria, 1974.
Olio su tela, 300x300.
Universita' degli Studi di
Palermo



Odds Ratios for Vascular Disease comparing **wine** intake vs. **no wine** intake





Fotoğraf: George Steinmetz

Dev Develer

Subgroup analysis

WINE

SUBGROUP	N	RR	99%CI
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Adjustment for different types of alcoholic beverages

Not Adjusted	3	0.53	0.39-0.73
--------------	---	------	-----------

Adjusted	10	0.75	0.61-0.93
----------	----	------	-----------

Adjustment for indicators of social class level

Not Adjusted	3	0.78	0.56-1.08
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Adjusted	10	0.64	0.52-0.79
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THE DEFINITION OF REFERENCE GROUP

Subgroup analysis

WINE

SUBGROUP	N	RR	99%CI
No light or occasional drinkers in the reference group	10	0.73	0.59-0.91
No ex-drinkers in the reference group	5	0.61	0.47-0.79
With the same reference group both for wine and beer	9	0.62	0.50-0.77

HOW MUCH
WINE
SHOULD WE DRINK
TO GET
CARDIOVASCULAR
BENEFITS?

Wine consumption and different **OUTCOMES**...

Fatal and not fatal CV events:

14 Studies

9 prospective studies involving 247,141 subjects

5 case-control studies 2,621 case vs 5,086 controls

CV mortality:

5 Studies

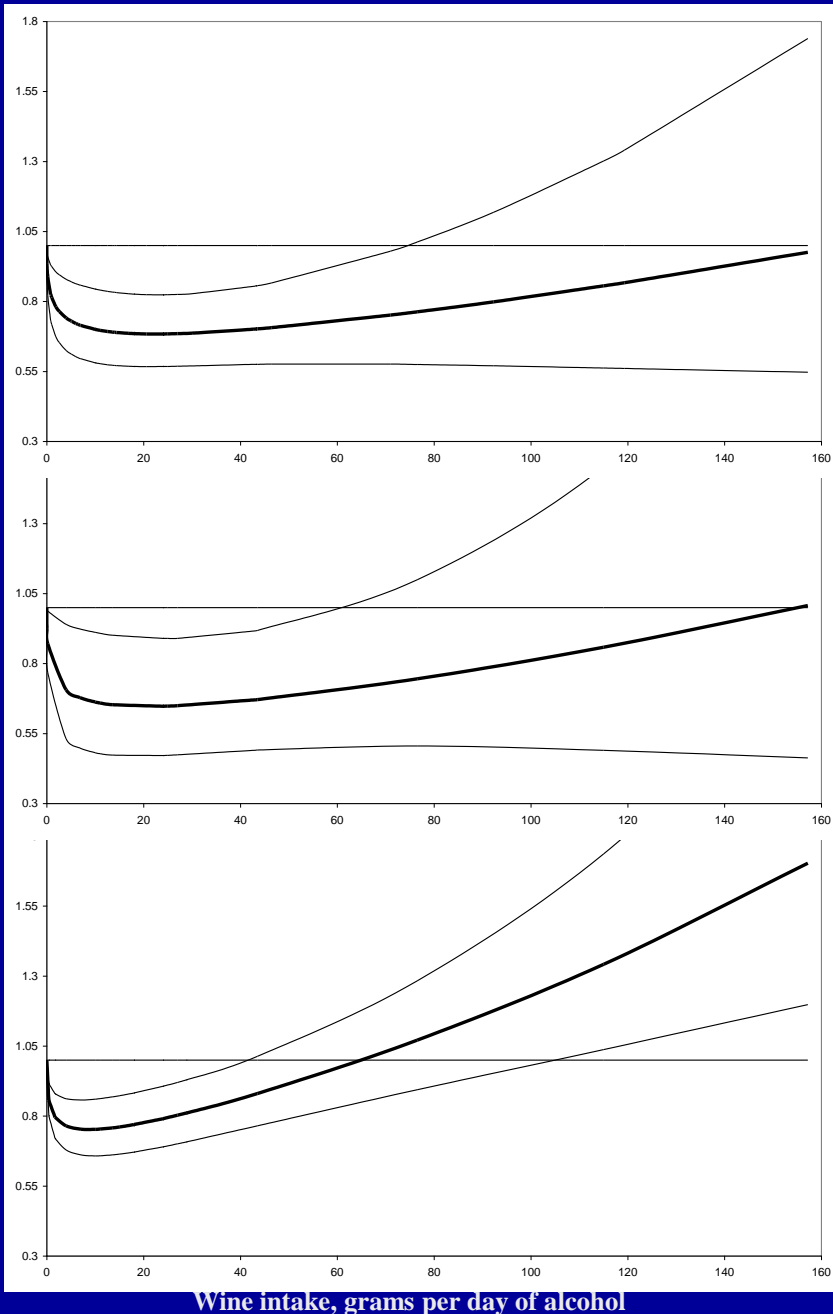
5 prospective studies involving 71,699 subjects

Total mortality:

5 Studies

5 prospective studies involving 56,696 subjects

Costanzo et al, Eur J Epidemiol, 2011



The Moli-sani Project

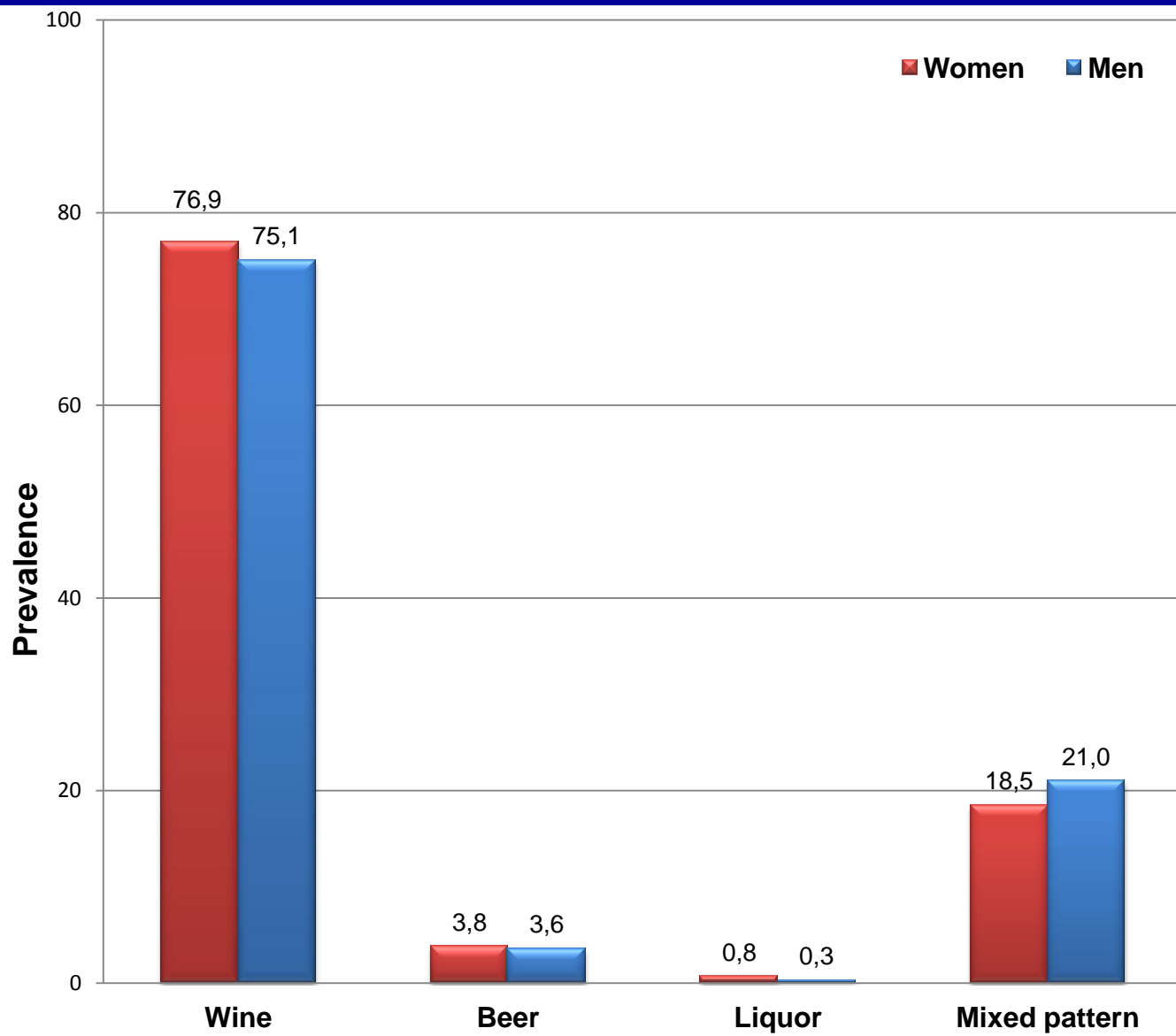


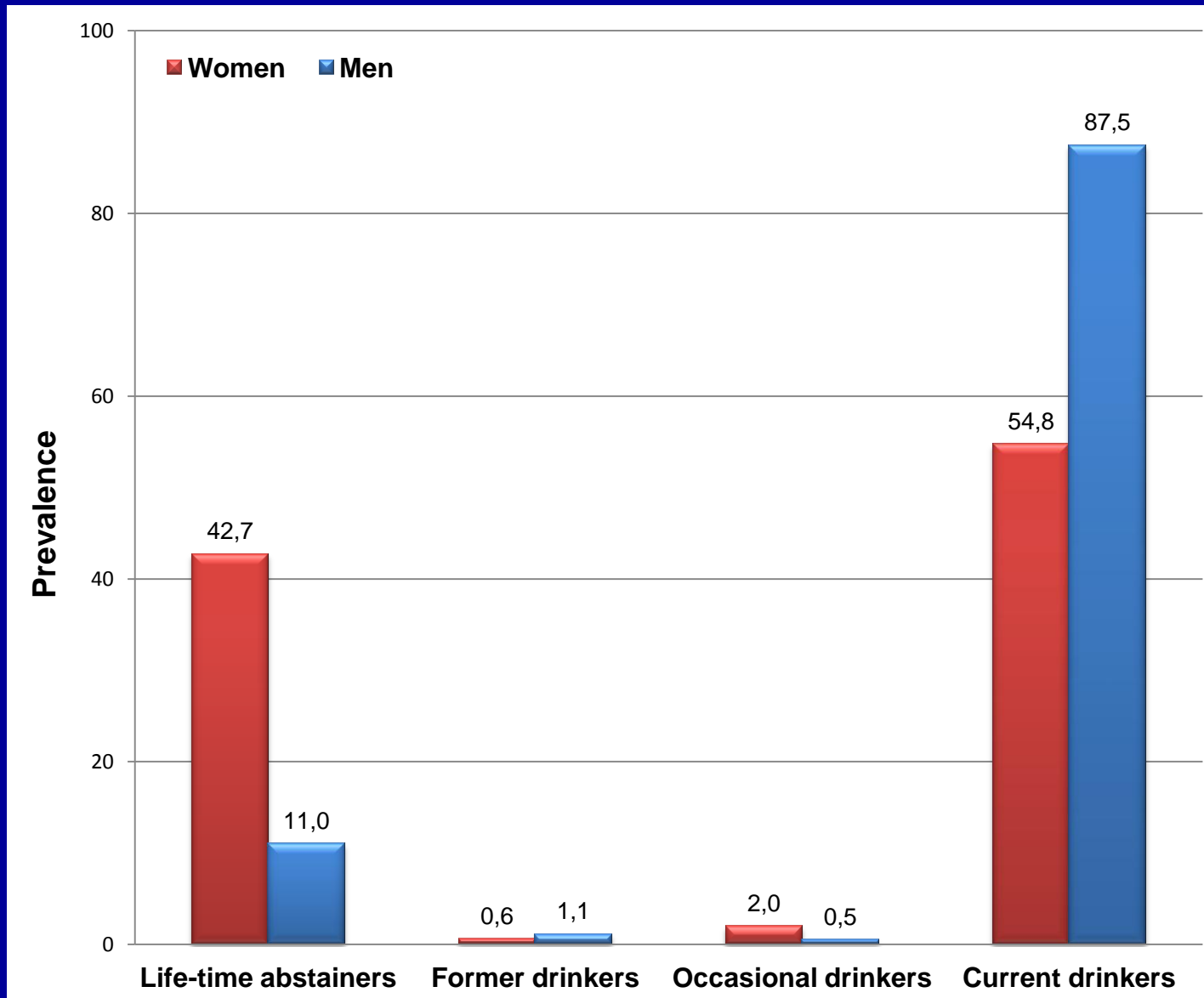
EPIDEMIOLOGICAL STUDY

- ✓ *24,325 people living in Molise*
- ✓ *Aged 35 years or more*
- ✓ *Recruitment phase: 2005-2010*
- ✓ *First follow-up: 4.5 years*
- ✓ *EPIC Questionnaire*
- ✓ *MED score*

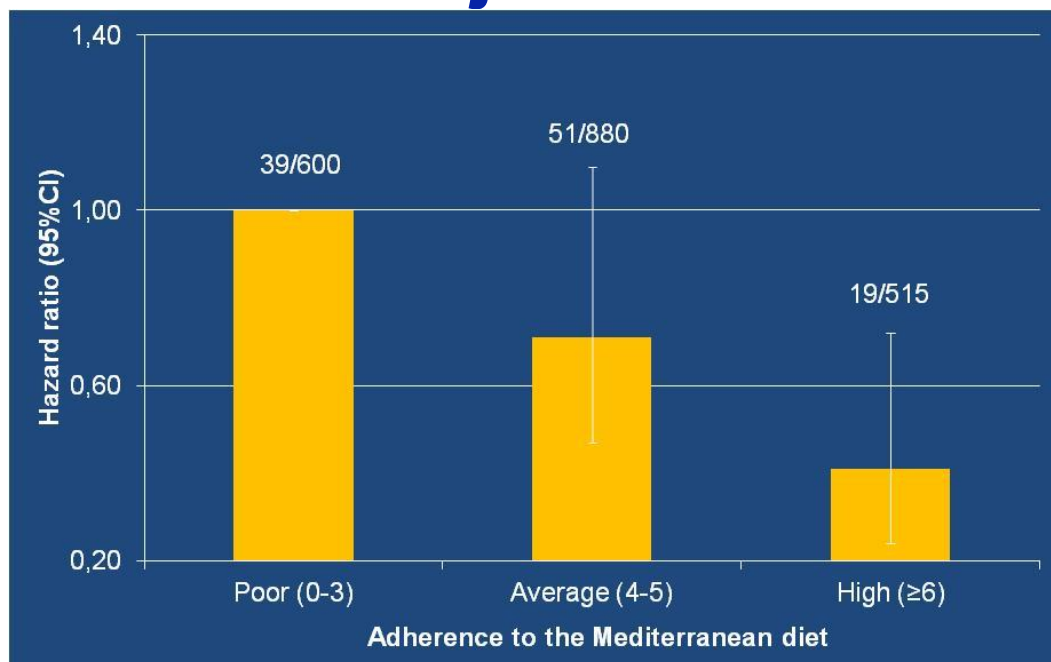
Moli-sani clinical end-points

- ✓ *Cardio-cerebrovascular disease*
- ✓ *Tumors*
- ✓ *Common intermediate phenotypes:*
 - *Metabolic syndrome*
 - *Obesity*
 - *Hypertension*
 - *Dyslipidemia*
 - *Diabetes*





Adherence to the Mediterranean diet and total mortality risk in type-2 diabetic subjects

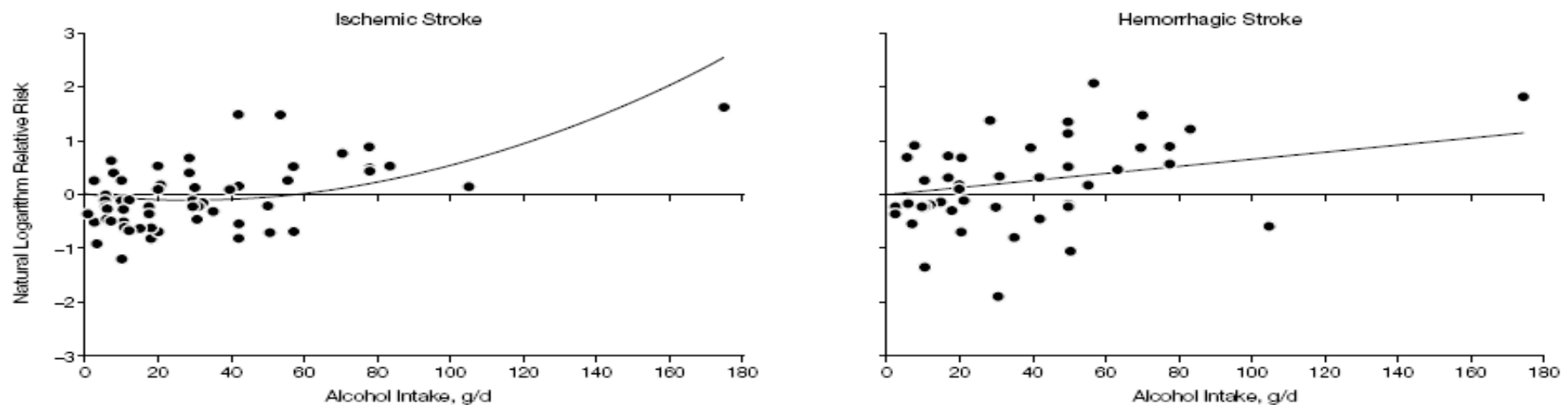


	Risk of death (95%CI)	P value	(%) Reduction total effect
Mediterranean diet score (2-point increase)	0.632 (0.494-0.803)	0.0003	-
After removal of each food item			
Moderate alcohol consumption	0.686 (0.541-0.871)	0.0020	-14.7
Dairy products (low intake)	0.681 (0.539-0.862)	0.0014	-13.4

ARE WINE'S BENEFITS
ON CARDIO-VASCULAR RISK
ALSO OBSERVED
ON CEREBRO-VASCULAR
DISEASES?

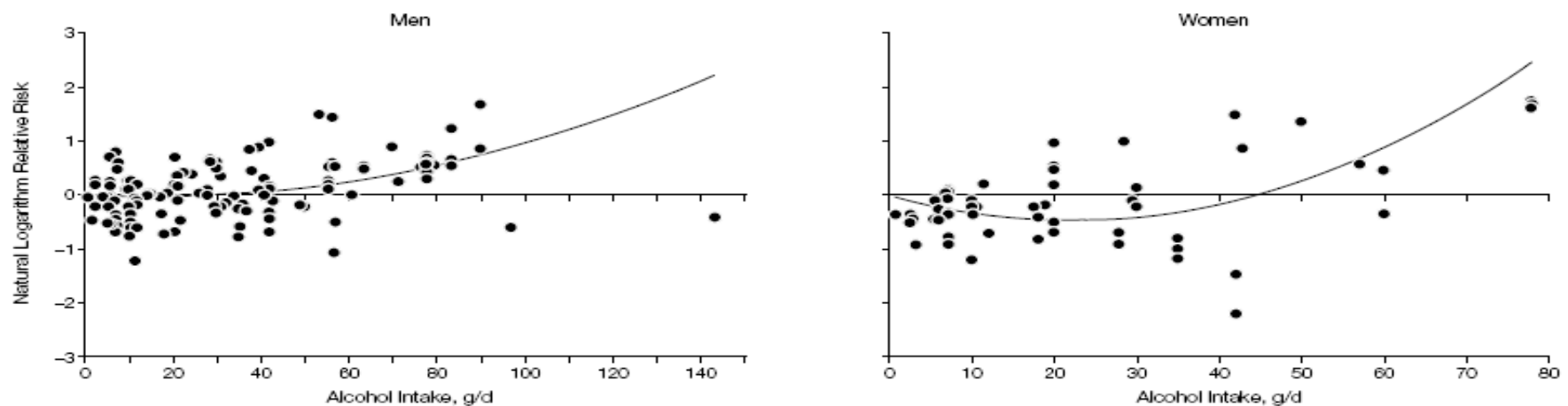
Alcohol Consumption and Risk of Stroke

Figure 1. Scatterplot of Log Relative Risk and Meta-Regression Curve of Stroke Associated With Alcohol Consumption by Subtypes of Stroke



Most studies provided more than 1 relative risk estimate for multiple levels of alcohol consumption.

Figure 2. Scatterplot of Log Relative Risk and Meta-Regression Curve of Stroke Associated With Alcohol Consumption by Sex



Most studies provided more than 1 relative risk estimate for multiple levels of alcohol consumption.

IS
THE AMOUNT OF WINE
ONLY IMPORTANT
OR
THE WAY
IT IS CONSUMED TOO?

Does drinking pattern modify the effect of alcohol on the risk of coronary heart disease? Evidence from a meta-analysis

V Bagnardi,^{1,2} W Zatonski,³ L Scotti,^{1,4} C La Vecchia,^{4,5} G Corrao¹

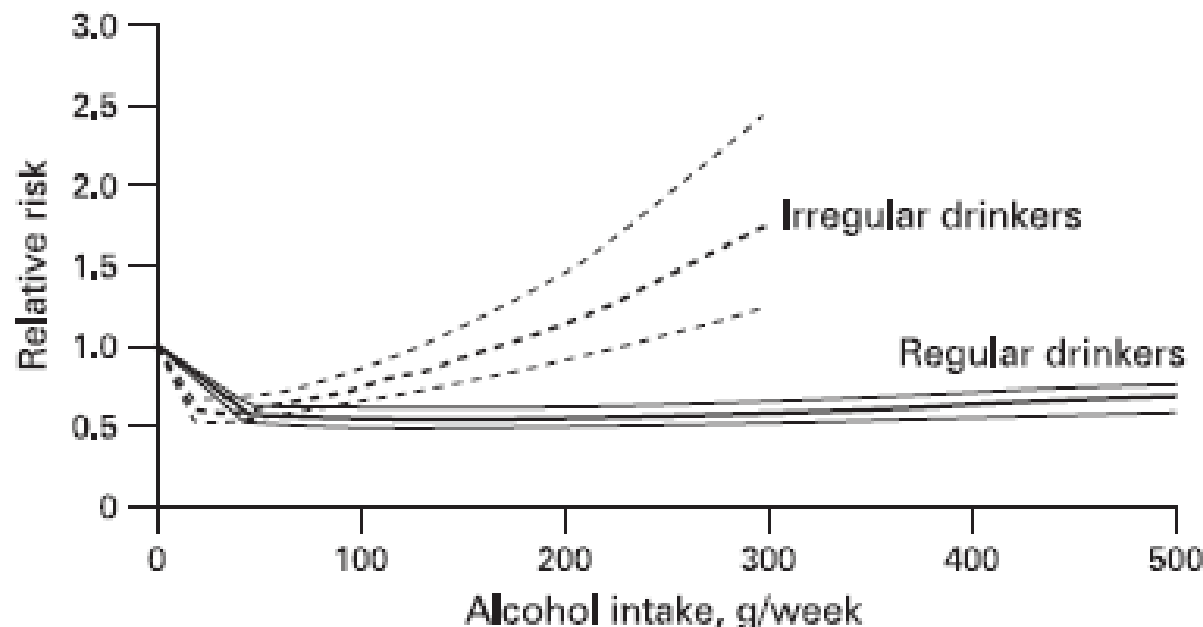


Figure 2 Meta-regression of dose-response relation between weekly alcohol intake and relative risk (and the corresponding 95% confidence bands) of coronary heart disease in regular and irregular drinkers.



IS
WINE

PROTECTIVE
AT ALL AGES?

RELATION BETWEEN ALL CAUSE MORTALITY AND ALCOHOL CONSUMPTION, BY AGE AND SEX

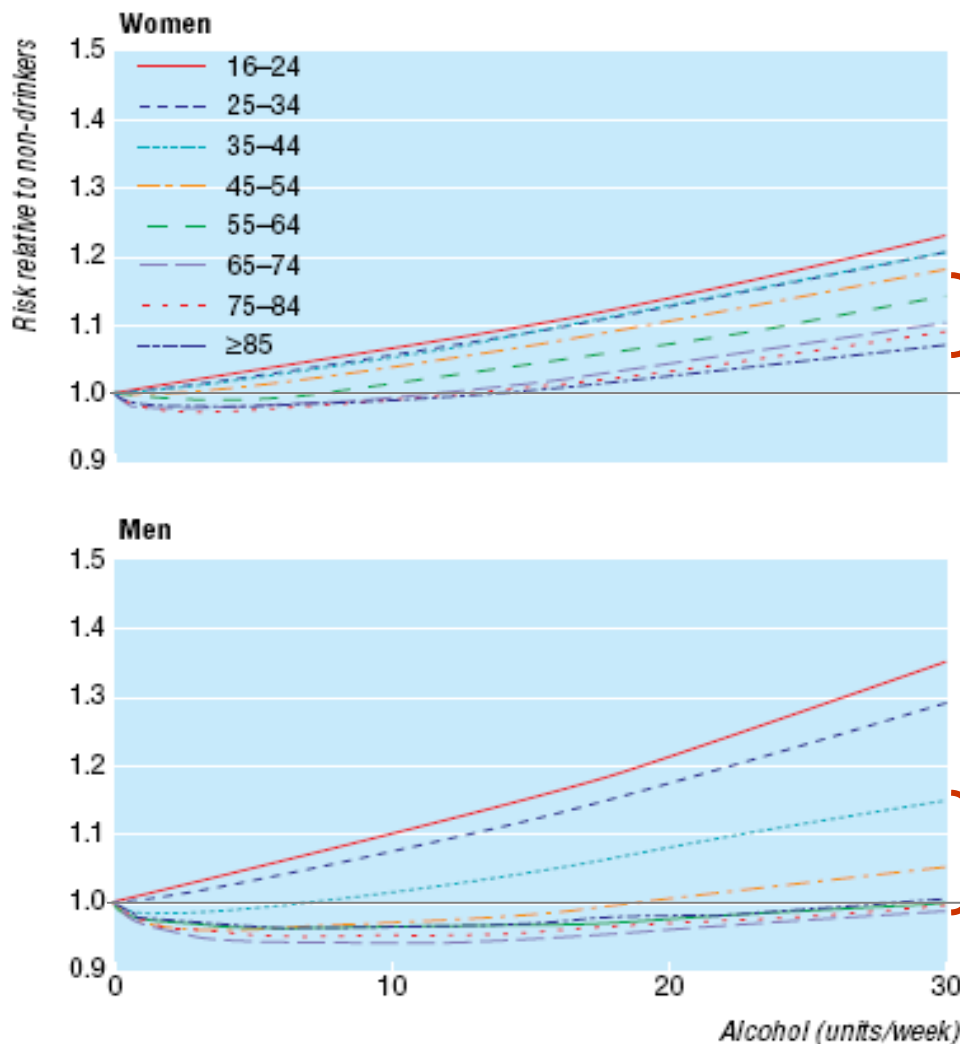


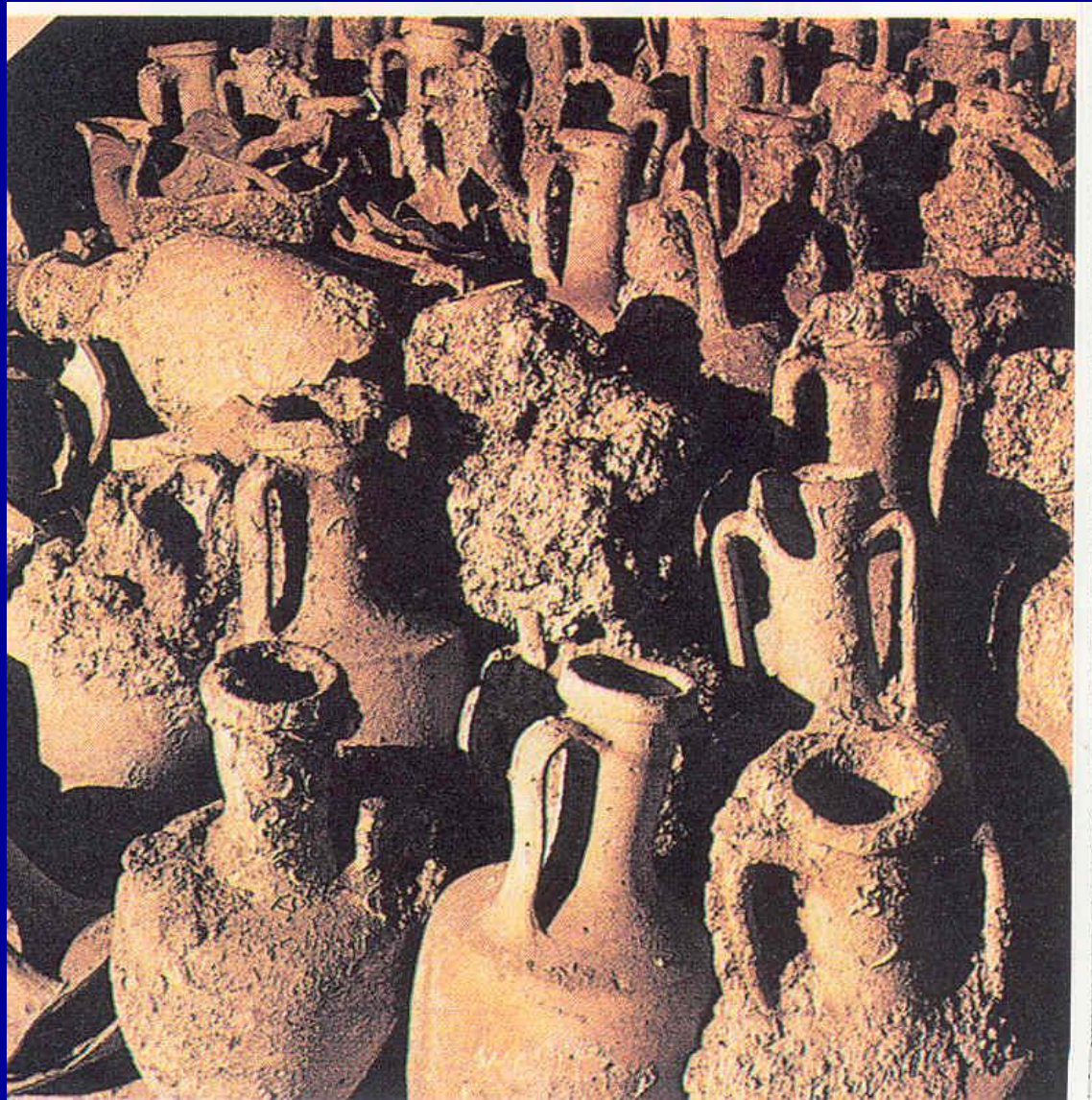
Fig 4 Risk of all cause mortality (relative to non-drinkers) by level of alcohol consumption in women and men

Women:

Positive relation up to age 35-44,
but U shape appears from age 45-54.

Men:

Below 35 years the curve is steeper
than it is in women,
but U shape appears at age 35-44.



IS WINE CONSUMPTION
EFFECTIVE

IN THE SECONDARY
PREVENTION

OF CARDIOVASCULAR
DISEASE?

QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Alcohol Consumption and Mortality in Patients With Cardiovascular Disease

A Meta-Analysis

Simona Costanzo, SCD, Augusto Di Castelnuovo, SCD, Maria Benedetta Donati, MD, PhD,
Licia Iacoviello, MD, PhD, Giovanni de Gaetano, MD, PhD

Campobasso, Italy

Objectives

The purpose of this study was to quantify the relation between alcohol consumption and cardiovascular and total mortality in patients with a history of cardiovascular events.

Background

Regular, moderate alcohol consumption by healthy people is associated with lower cardiovascular and all-cause mortality. No extensive meta-analysis is presently available on the possible association of alcohol consumption with secondary events in patients with cardiovascular disease.

Methods

Articles were retrieved through October 2009 by search in PubMed and EMBASE. Fifty-four publications were identified, but only 8 were selected for our analyses, including 16,351 patients with a history of cardiovascular disease. Secondary events were cardiovascular or all-cause mortality. All selected studies were prospective. Data were pooled with a weighted, least-squares regression analysis of second-order fractional polynomial models.

Results

The meta-analysis on cardiovascular mortality showed a J-shaped pooled curve with a significant maximal protection (average 22%) by alcohol at approximately 26 g/day. In the meta-analysis on mortality for any cause, J-shaped pooled curves were observed in the overall analysis (average maximal protection of 18% in the range of 5 to 10 g/day) and in all subgroups according to either the type of patients or the characteristics of the studies.

Conclusions

In patients with cardiovascular disease, light to moderate alcohol consumption (5 to 25 g/day) was significantly associated with a lower incidence of cardiovascular and all-cause mortality. (J Am Coll Cardiol 2010;55:1339-47) © 2010 by the American College of Cardiology Foundation

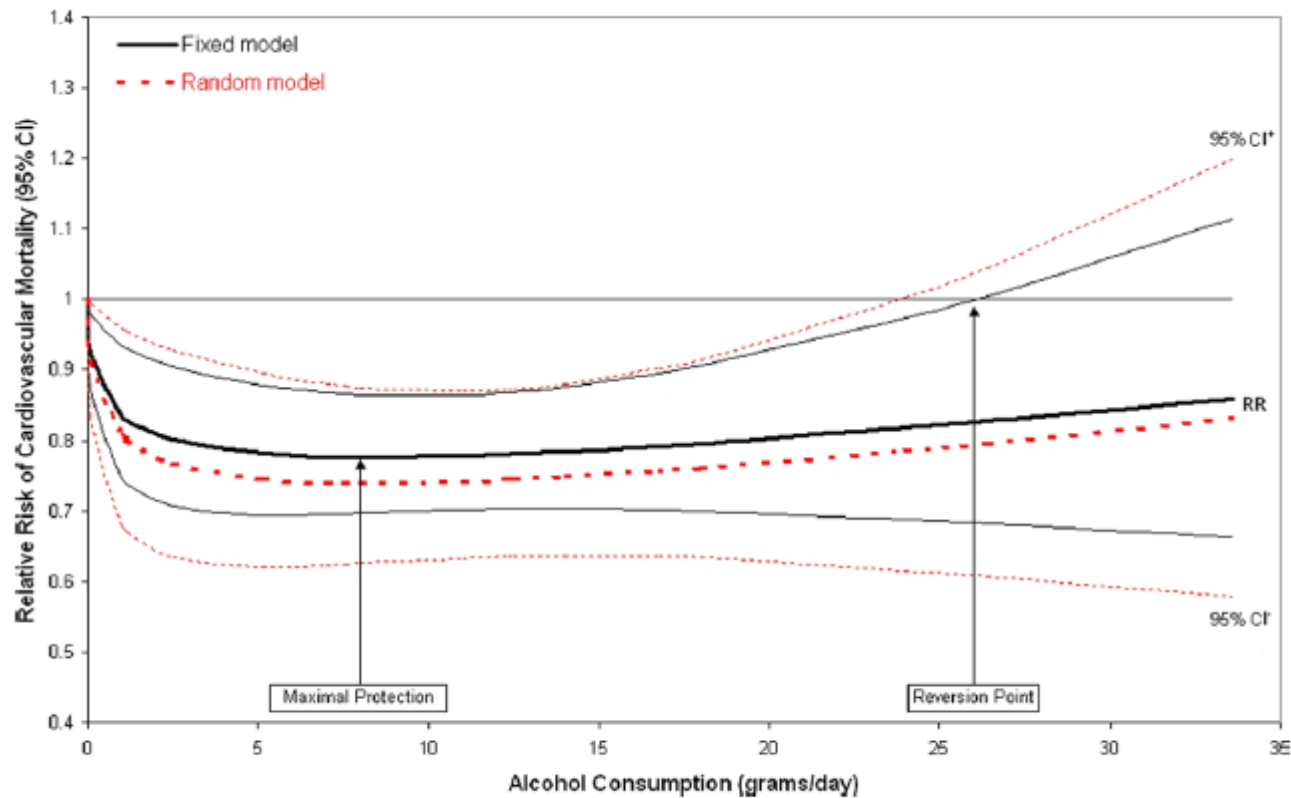


Figure 3 Alcohol Consumption In Relation to Cardiovascular Mortality In Cardiovascular Disease Patients

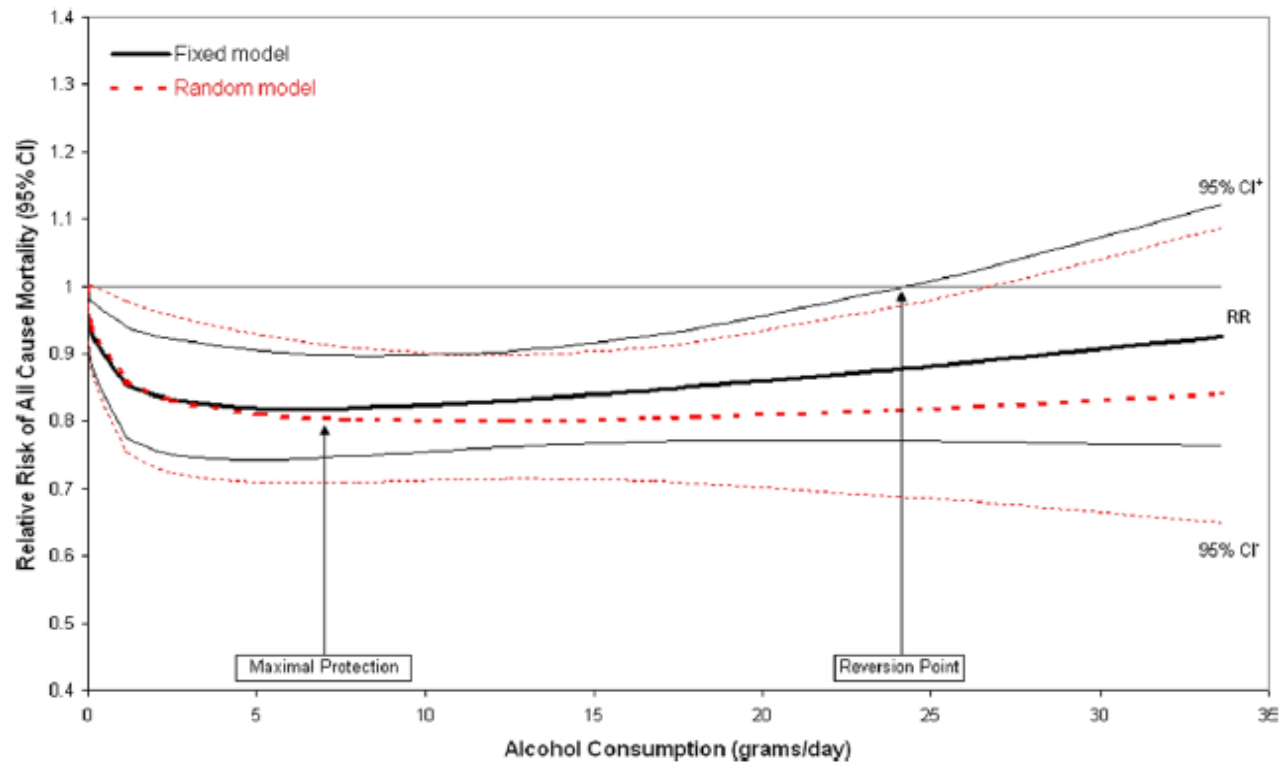
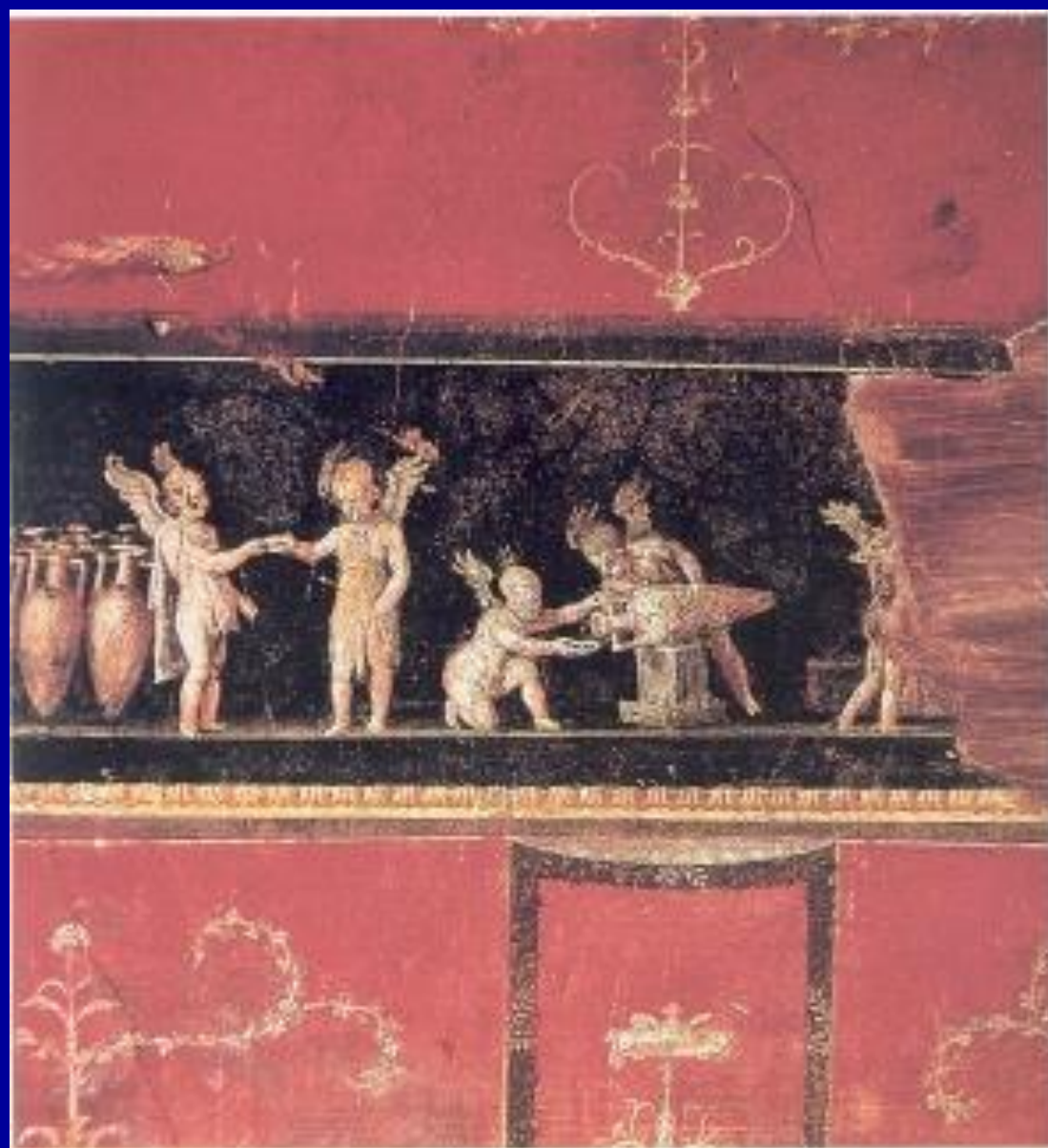


Figure 4 Alcohol Consumption In Relation to All-Cause Mortality in Cardiovascular Disease Patients



BUT FINALLY
ONE WOULD LIKE
TO KNOW WHETHER
DRINKING WINE
IN MODERATION
DOES PROTECT AGAINST
CARDIOVASCULAR DEATH
or MORTALITY
FOR ANY CAUSE

WHAT IS THE EFFECT
OF MODERATE
WINE CONSUMPTION
ON CARDIOVASCULAR
MORTALITY?

Wine consumption and different OUTCOMES...

Fatal and not fatal CV events:

14 Studies

9 prospective studies involving 247,141 subjects

5 case-control studies 2,621 case vs 5,086 controls

CV mortality:

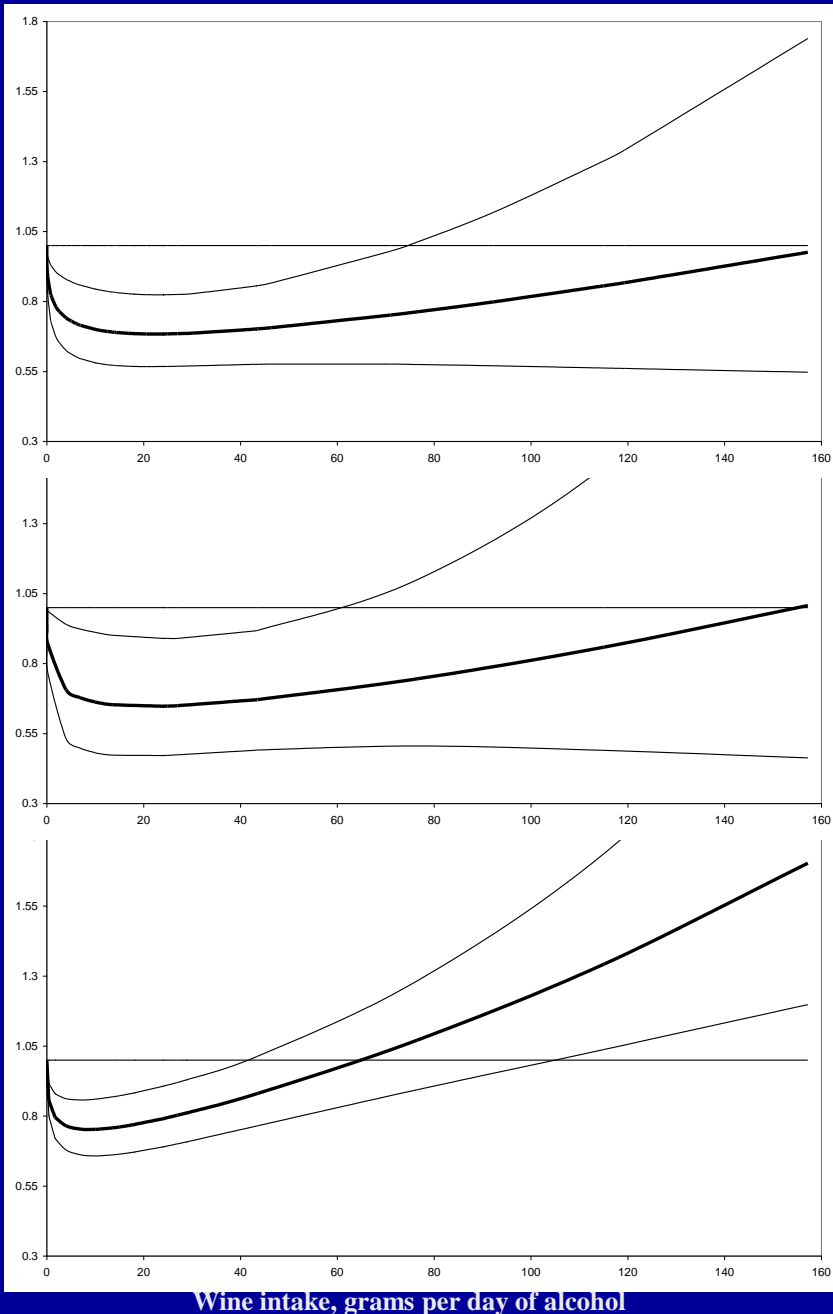
5 Studies

5 prospective studies involving 71,699 subjects

Total mortality:

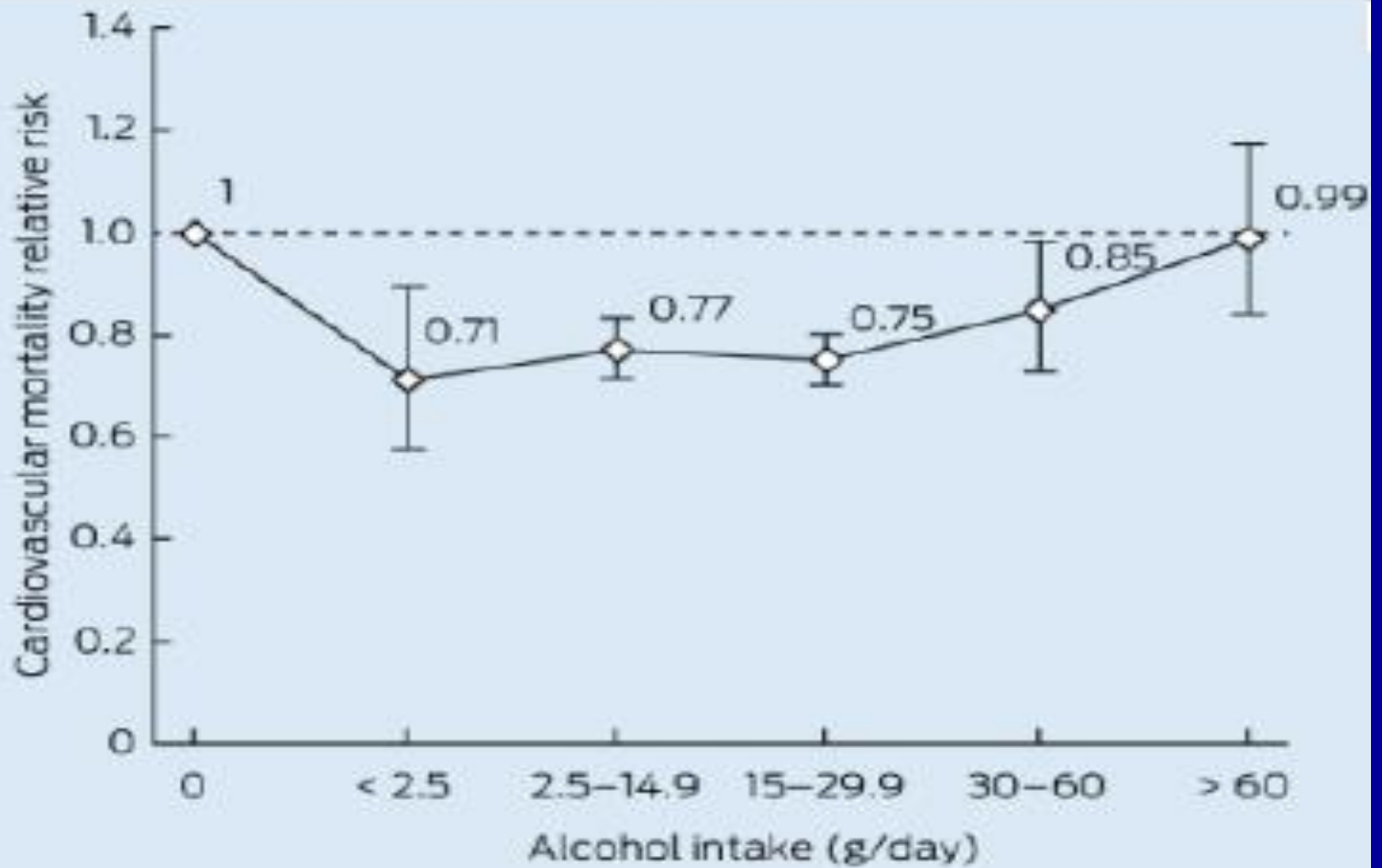
5 Studies

5 prospective studies involving 56,696 subjects



Costanzo et al, Eur J Epidemiol, 2011

Box 2 – Meta-analysis showing the J-shaped relationship between cardiovascular mortality and alcohol intake based on 84 studies involving over a million people



Thompson, Med J Aust (2013)

WHAT IS THE EFFECT
OF MODERATE
WINE CONSUMPTION
ON TOTAL MORTALITY?

Mortality associated with moderate intakes of wine, beer, or spirits

Morten Grønþæk, Allan Deis, Thorkild I A Sørensen, Ulrik Becker, Peter Schnohr, Gorm Jensen

Abstract

Objective—To examine the association between intake of different types of alcoholic drinks and mortality.

Design—Prospective population study with base-line assessment of alcohol intake, smoking habit, income, education, and body mass index, and 10-12 years' follow up of mortality.

We assessed the effects of different types of alcoholic drinks on the risk of death from all causes and from cardiovascular and cerebrovascular disease, while taking into account sex, age, socioeconomic conditions, smoking habits, and body mass index.

Subjects and methods

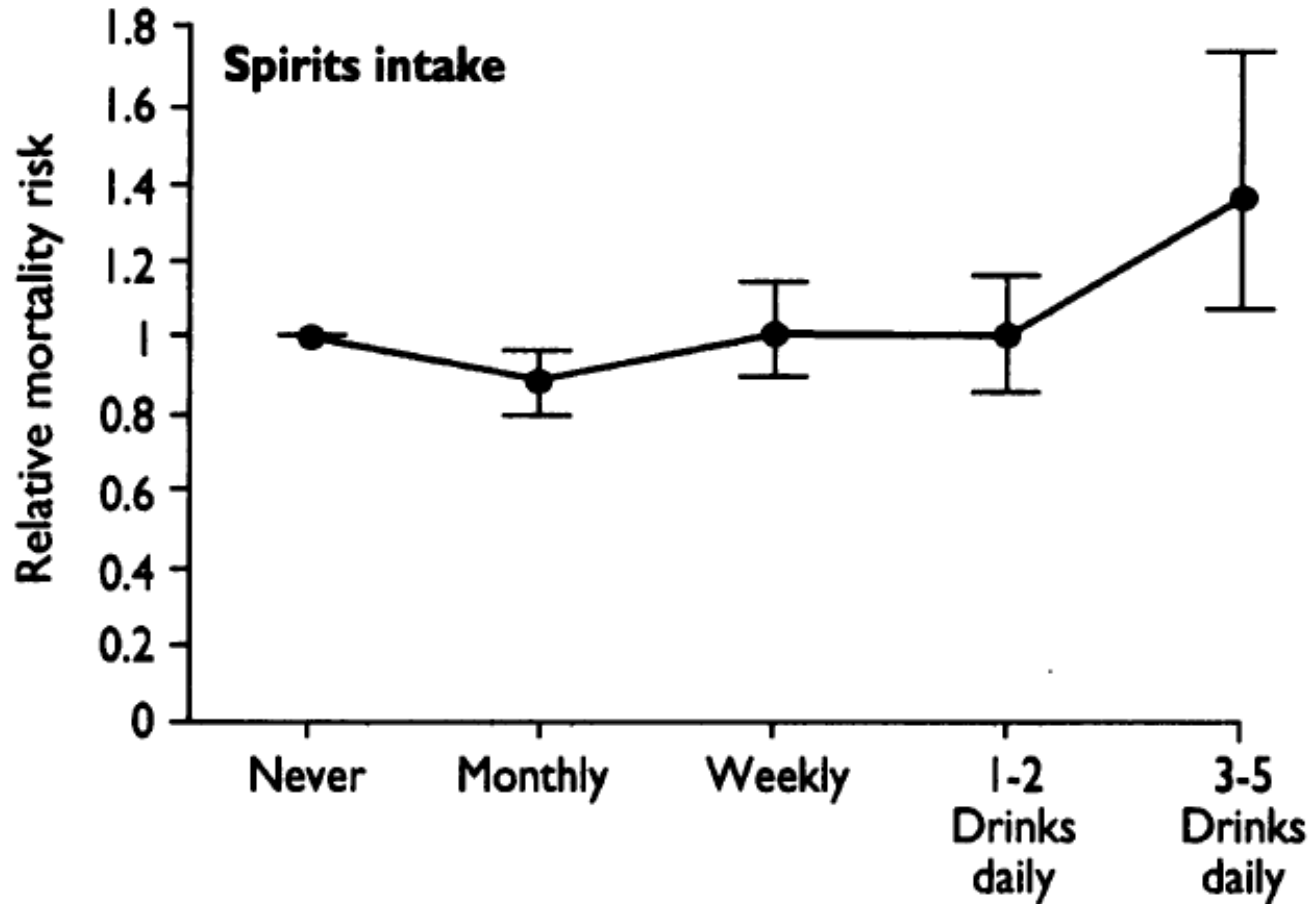
Lo studio ha preso in considerazione oltre 20.000 cittadini arruolati dalla popolazione generale e seguiti per oltre 10 anni.

I soggetti appartenevano a 4 tipologie di consumo:

- **astemi** (N.5910);
- bevitori prevalentemente di **birra** (N. 5767)
- bevitori prevalentemente di **superalcoolici** (3574) e
- bevitori prevalentemente di **vino** (9092)

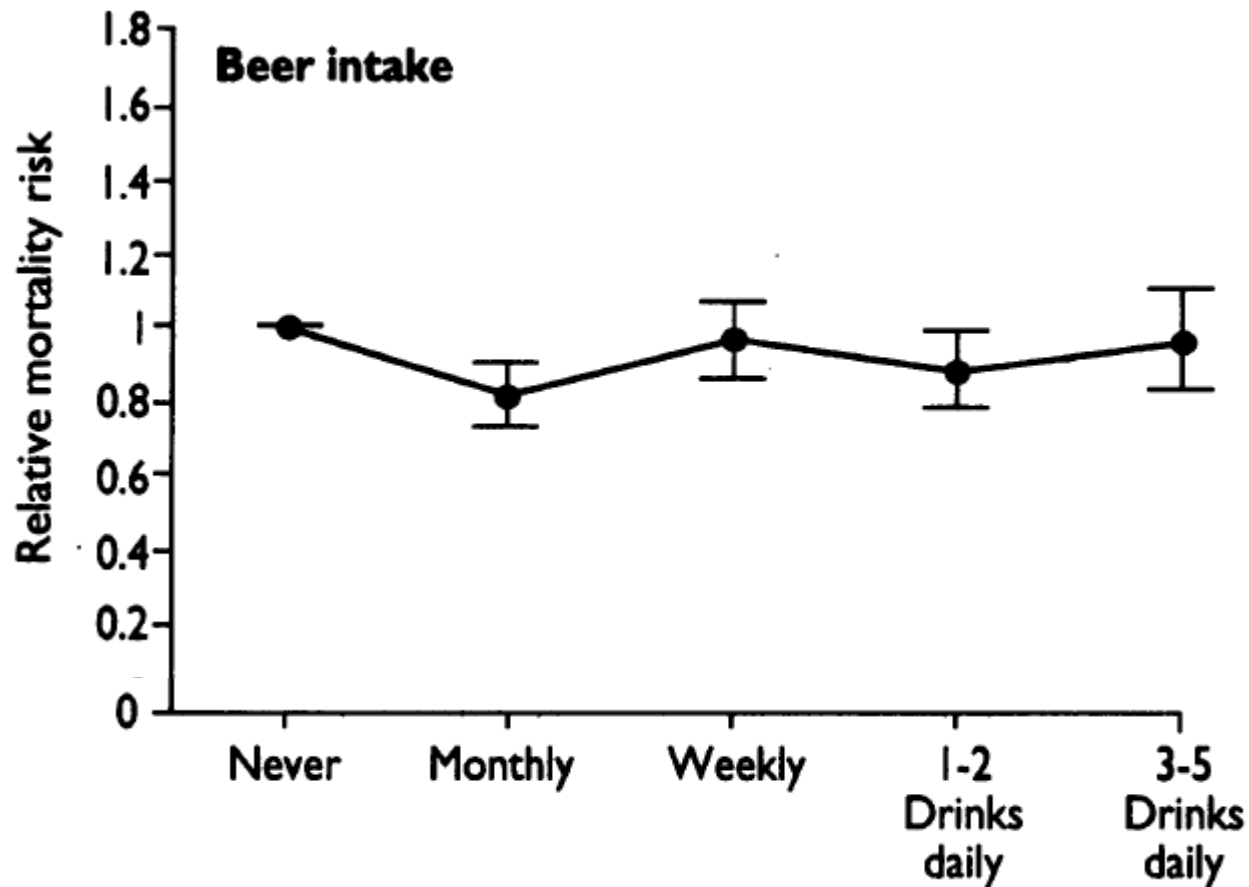
Copenhagen City Heart Study

Gronbaek M et al. *BMJ* 1995;310:1165-1169



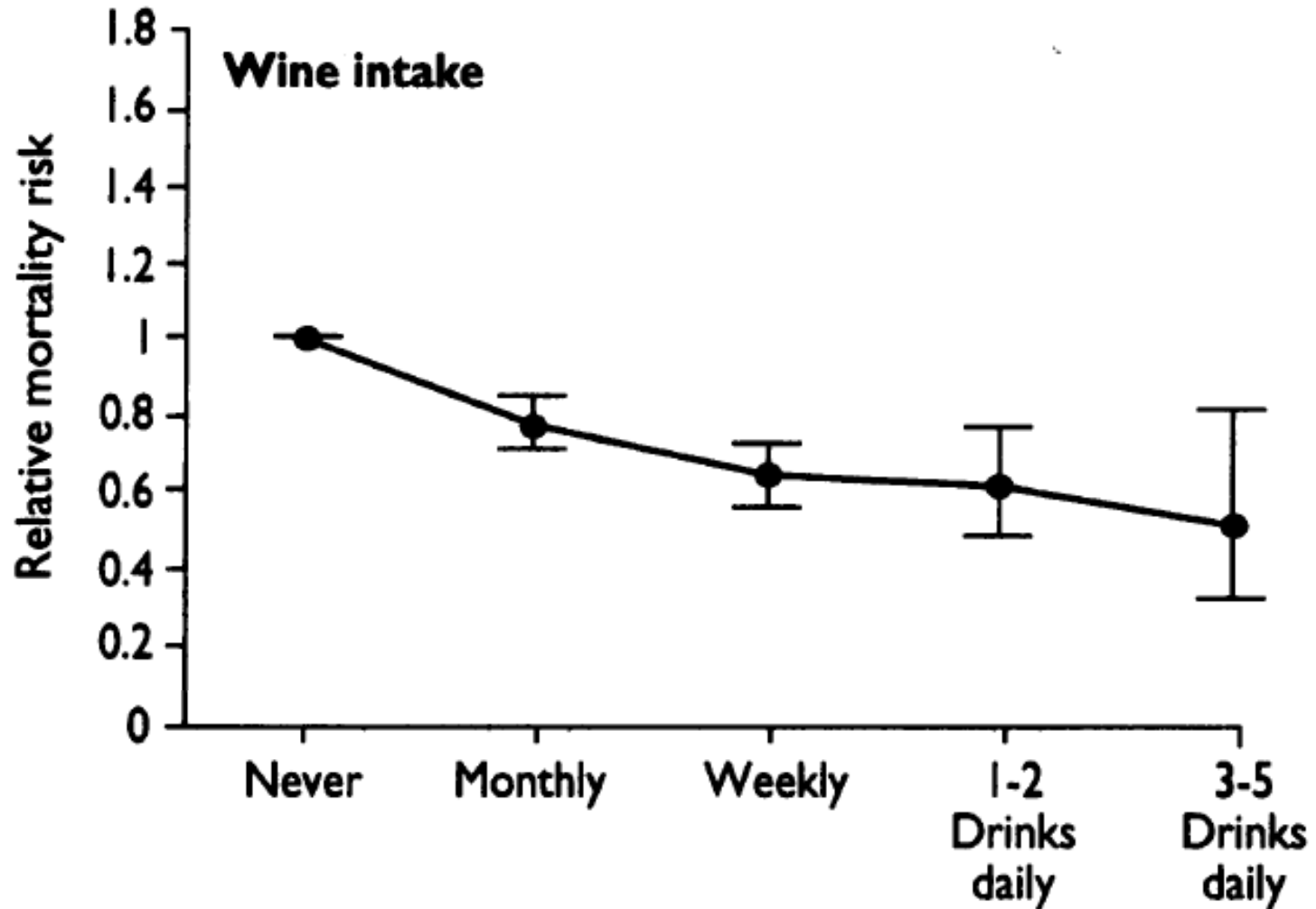
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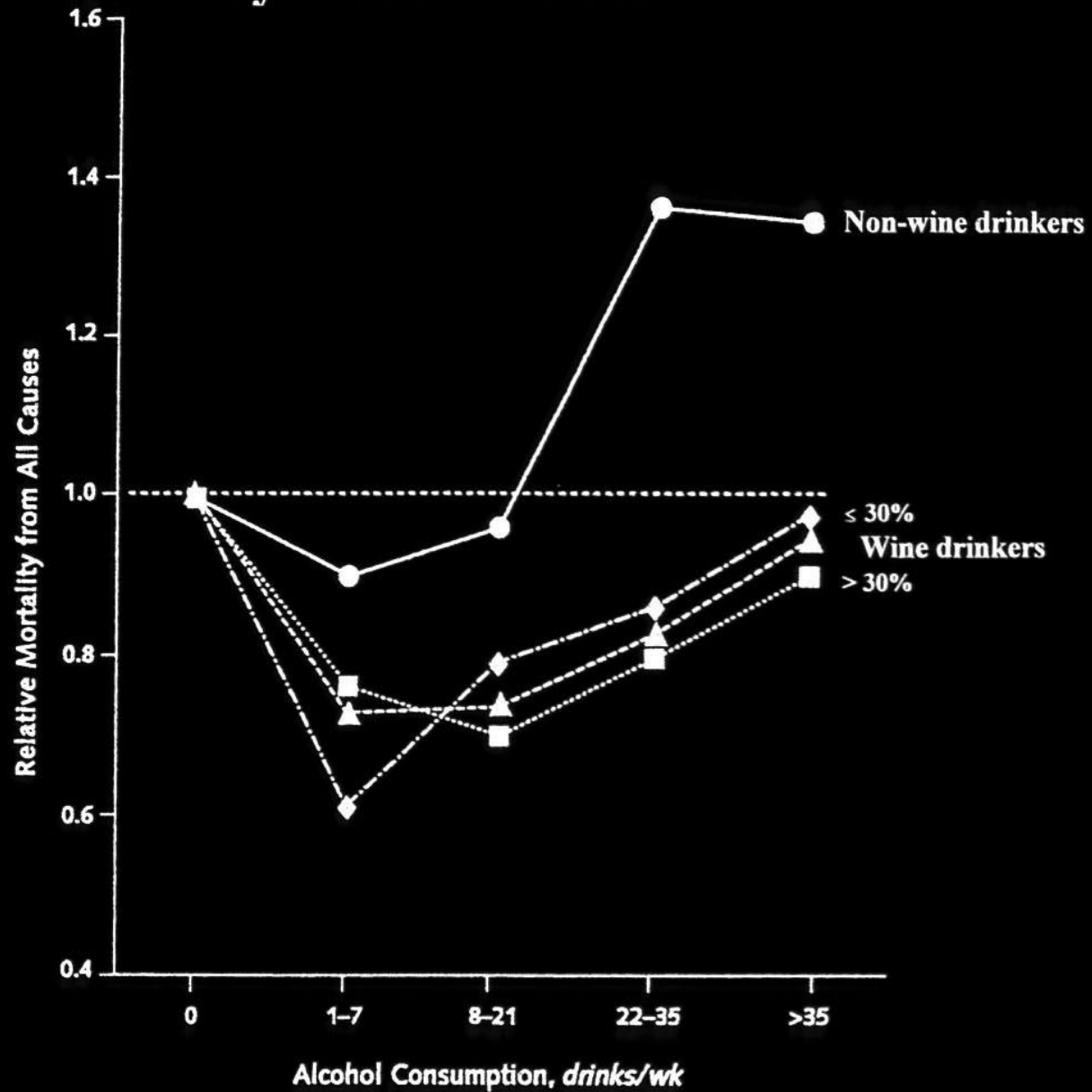


Type of Alcohol Consumed and Mortality from All Causes, Coronary Heart Disease, and Cancer

Morten Grønbaek, MD, DrMedSci; Ulrik Becker, MD, DrMedSci; Ditte Johansen, MSc; Adam Gottschau, MSc, PhD; Peter Schnohr, MD; Hans Ole Hein, MD; Gorm Jensen, MD, DrMedSci; and Thorkild I.A. Sørensen, MD, DrMedSci

© 2000 American College of Physicians–American Society of Internal Medicine

All-Cause Mortality by Intake of Alcohol



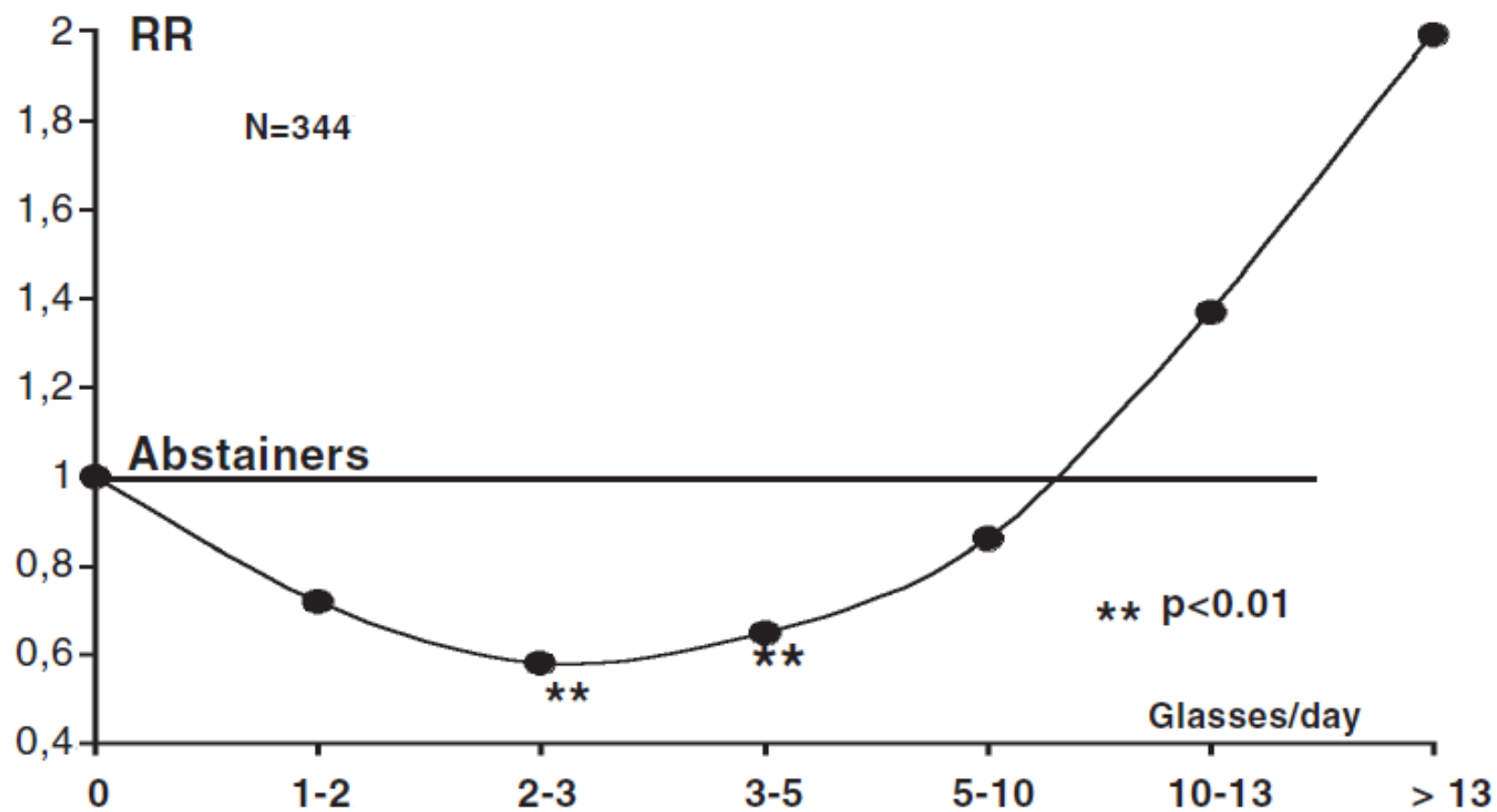
Alcohol and Mortality from All Causes

SERGE RENAUD¹, DOMINIQUE LANZMANN-PETITHORY¹, RENÉ GUEGUEN² and
PASCALE CONARD²

¹Emile Roux Hospital, Public Assistance of Paris Hospitals France

²Center of Preventive Medicine, Nancy, France

Lo studio di Renaud merita un cenno particolare per
l'elevata dimensione della casistica, pari a 36.000
soggetti di sesso maschile



Wine consumption and different OUTCOMES...

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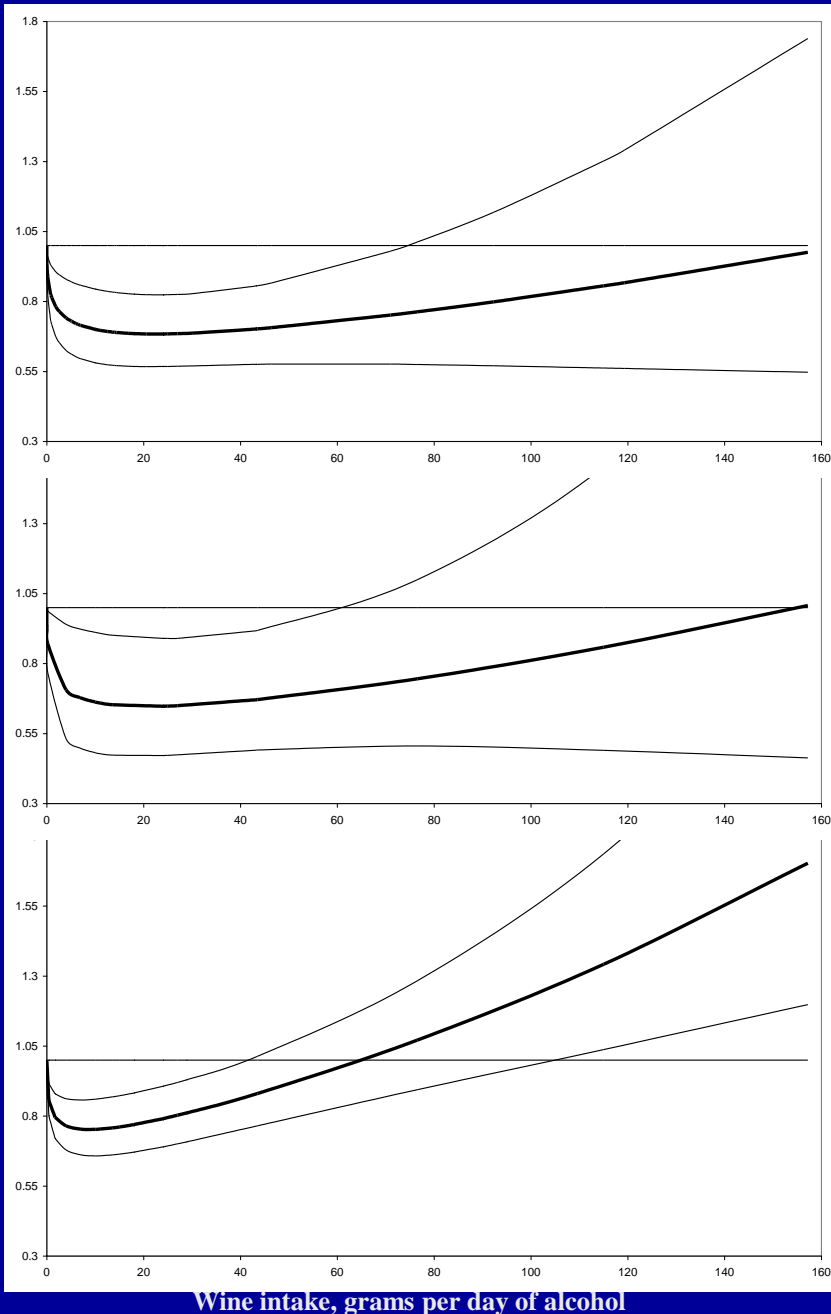
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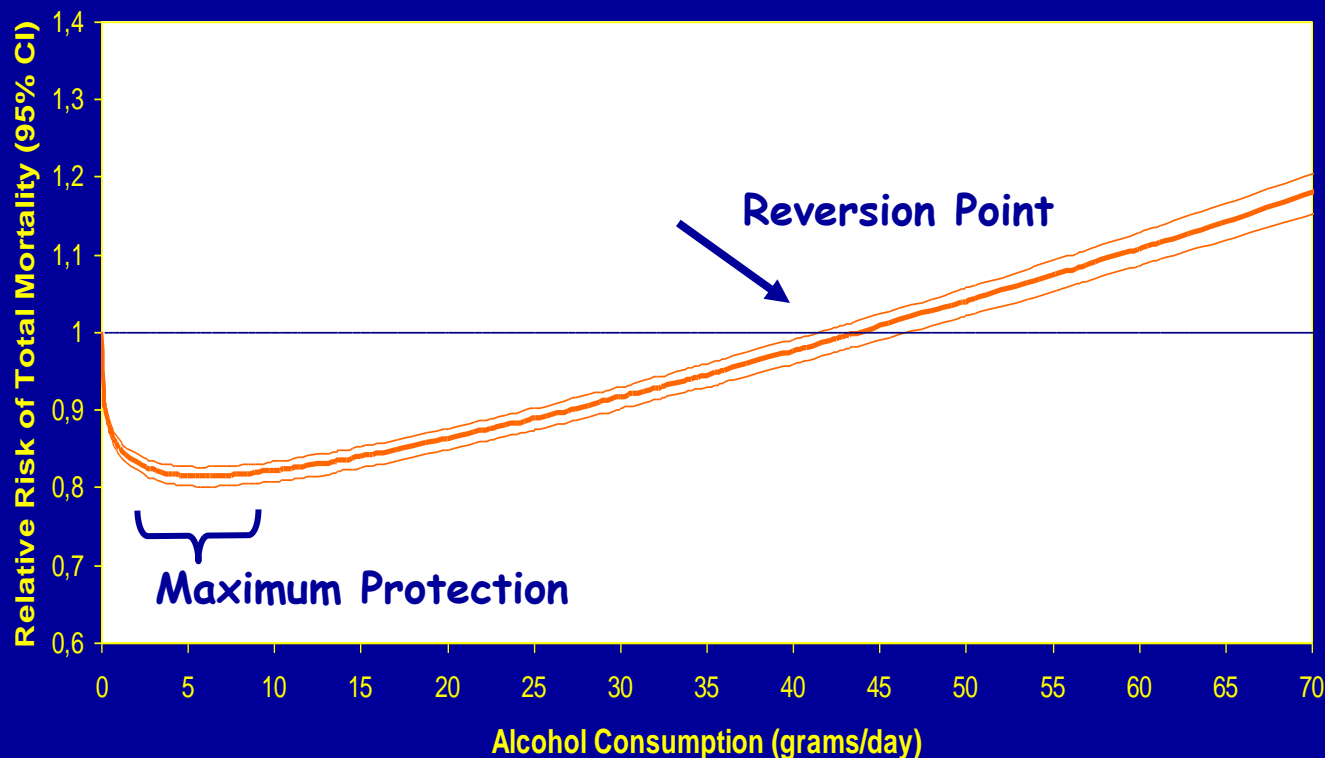
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Costanzo et al, Eur J Epidemiol, 2011

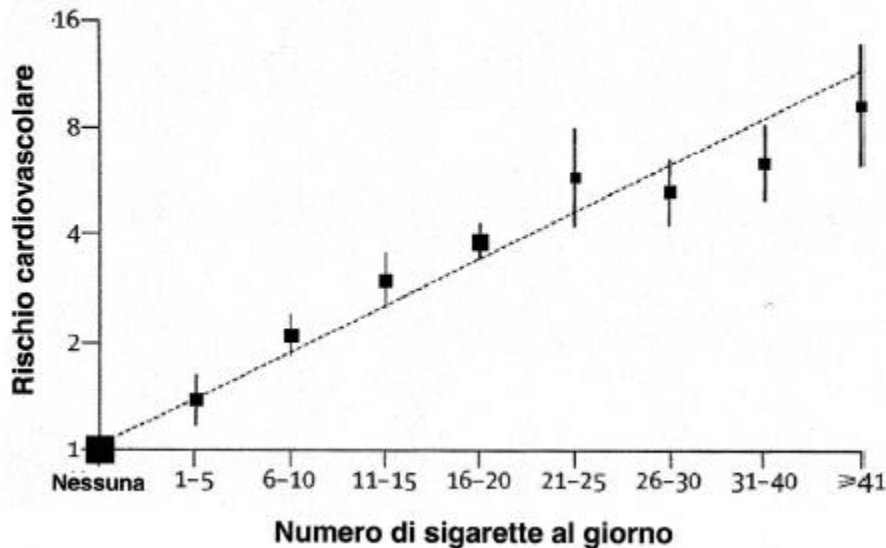
ALL STUDIES (1,015,835 SUBJECTS and 94,533 DEATHS)



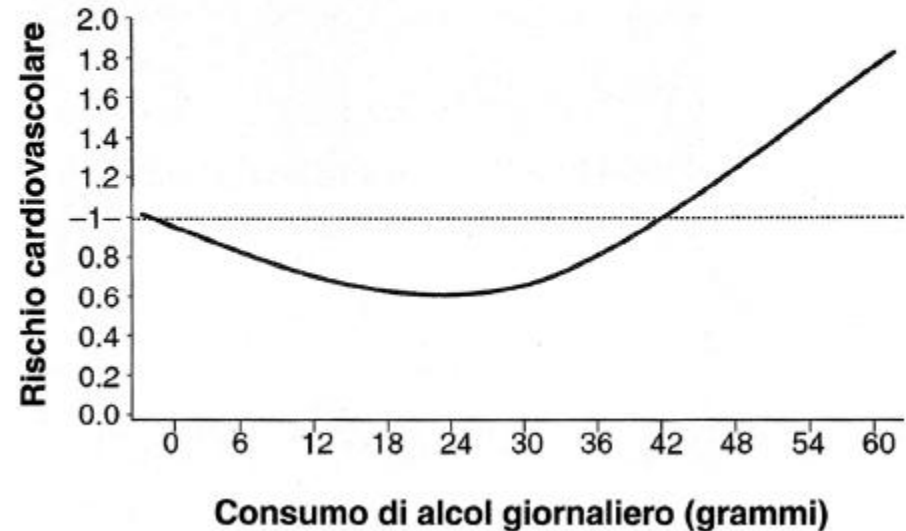
MAX PROTECTION: RR= 0.81 (0.80-0.83) → ALCOHOL INTAKE = 6 gr/day

REVERSION POINT: → ALCOHOL INTAKE = 42 gr/day

Cardiovascular risk, smoking or wine consumption



The INTERHEART study. Lancet, 2004



Di Castelnuovo et al. Arch Intern Med., 2006

There is no protection by moderate smoking!!!

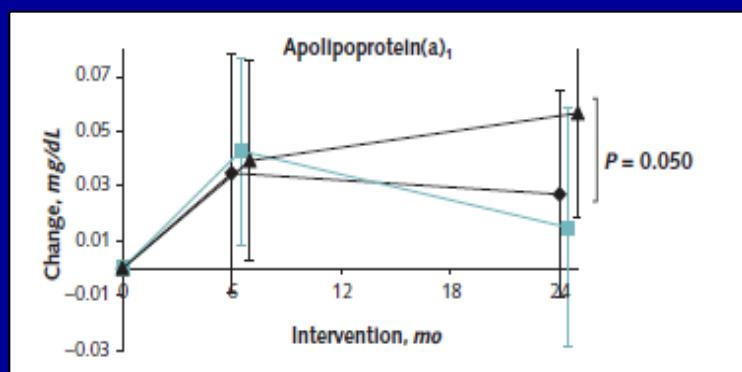
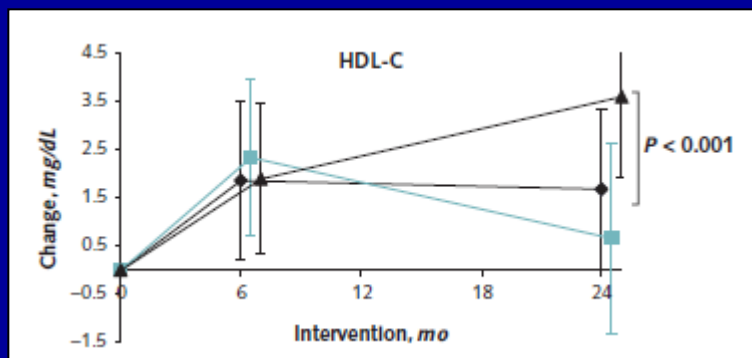


LAST BUT NOT LEAST...

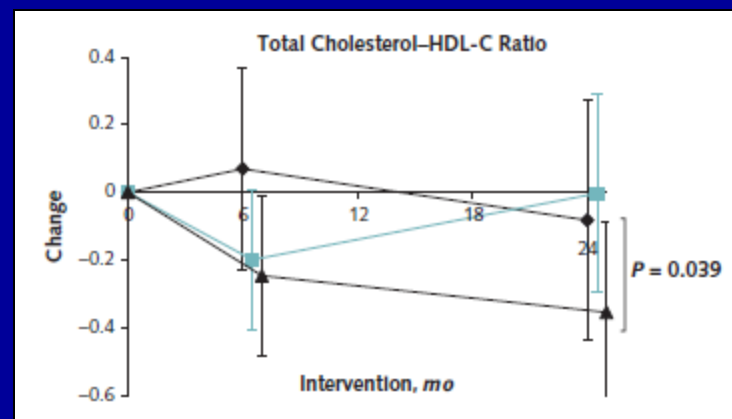
Effects of Initiating Moderate Alcohol Intake on Cardiometabolic Risk in Adults With Type 2 Diabetes

A 2-Year Randomized, Controlled Trial

Yftach Gepner, MPH*; Rachel Golan, RD, PhD*; Ilana Harman-Boehm, MD; Yaakov Henkin, MD; Dan Schwarzfuchs, MD; Ilan Shelef, MD; Ronen Durst, MD; Julia Kovsky, MSc; Arkady Bolotin, PhD; Eran Leitersdorf, MD; Shoshana Shpitzen, MA; Shai Balag, MD; Elad Shemesh, MD; Shula Witkow, RD, MPH; Osnat Tangi-Rosental, BA†; Yoash Chassidim, PhD; Idit F. Liberty, MD; Benjamin Sarusi, MSc; Sivan Ben-Avraham, RD, MPH; Anders Helander, PhD; Uta Ceglarek, PhD; Michael Stumvoll, MD; Matthias Blüher, MD; Joachim Thiery, MD; Assaf Rudich, MD, PhD; Meir J. Stampfer, MD, DrPH; and Iris Shai, RD, PhD



—◆— Water —■— White wine —▲— Red wine



EDITORS' NOTES

Context

The long-term benefits and risks of moderate alcohol intake among patients with type 2 diabetes mellitus (T2DM) are unclear.

Contribution

Alcohol-abstaining patients with T2DM were randomly assigned to 150 mL (5 ounces) of red wine, white wine, or mineral water with dinner for 2 years. Primary study outcomes included lipid and glycemic control measures.

Caution

The trial did not include a grape juice control group.

Implication

Moderate alcohol intake, particularly red wine, among patients with T2DM was associated with decreased cardiometabolic risks and no significant adverse events. Genetic typing for alcohol dehydrogenase may identify patients who may benefit clinically from moderate alcohol consumption.

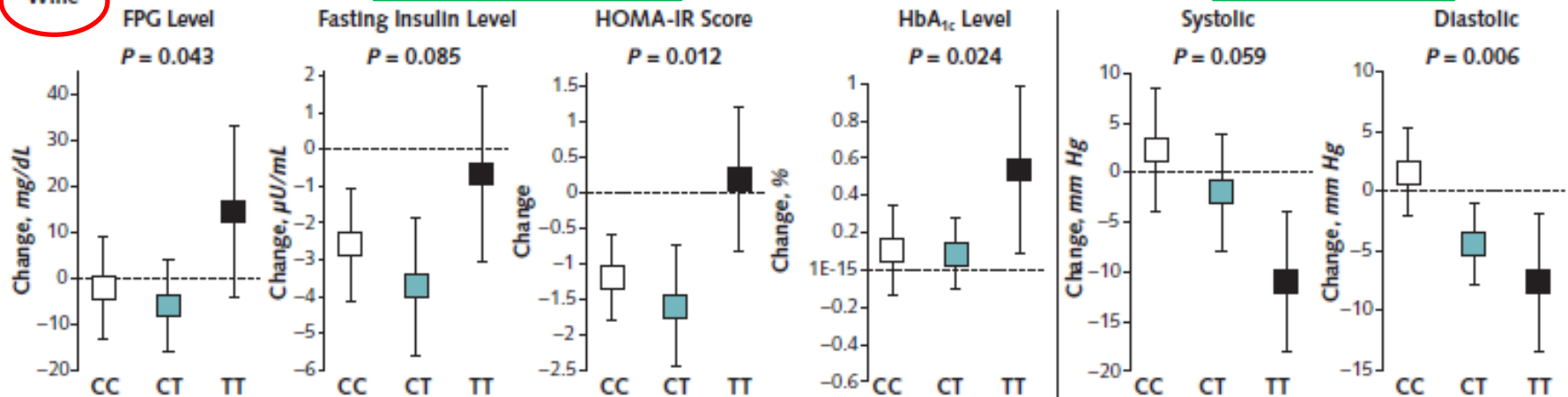
Annals Intern Med, 2015

Effect of long-term consumption of 150 mL mineral water, white wine or red wine per day on glycemic control and BP variables in type 2 diabetes mellitus according to genetic variations in ADH1B

Glycemic Control Biomarkers

Blood Pressure

Wine



Water

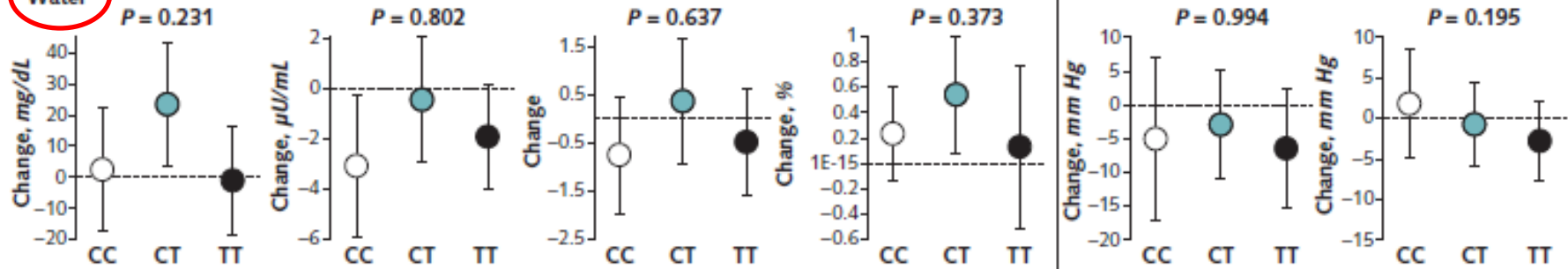
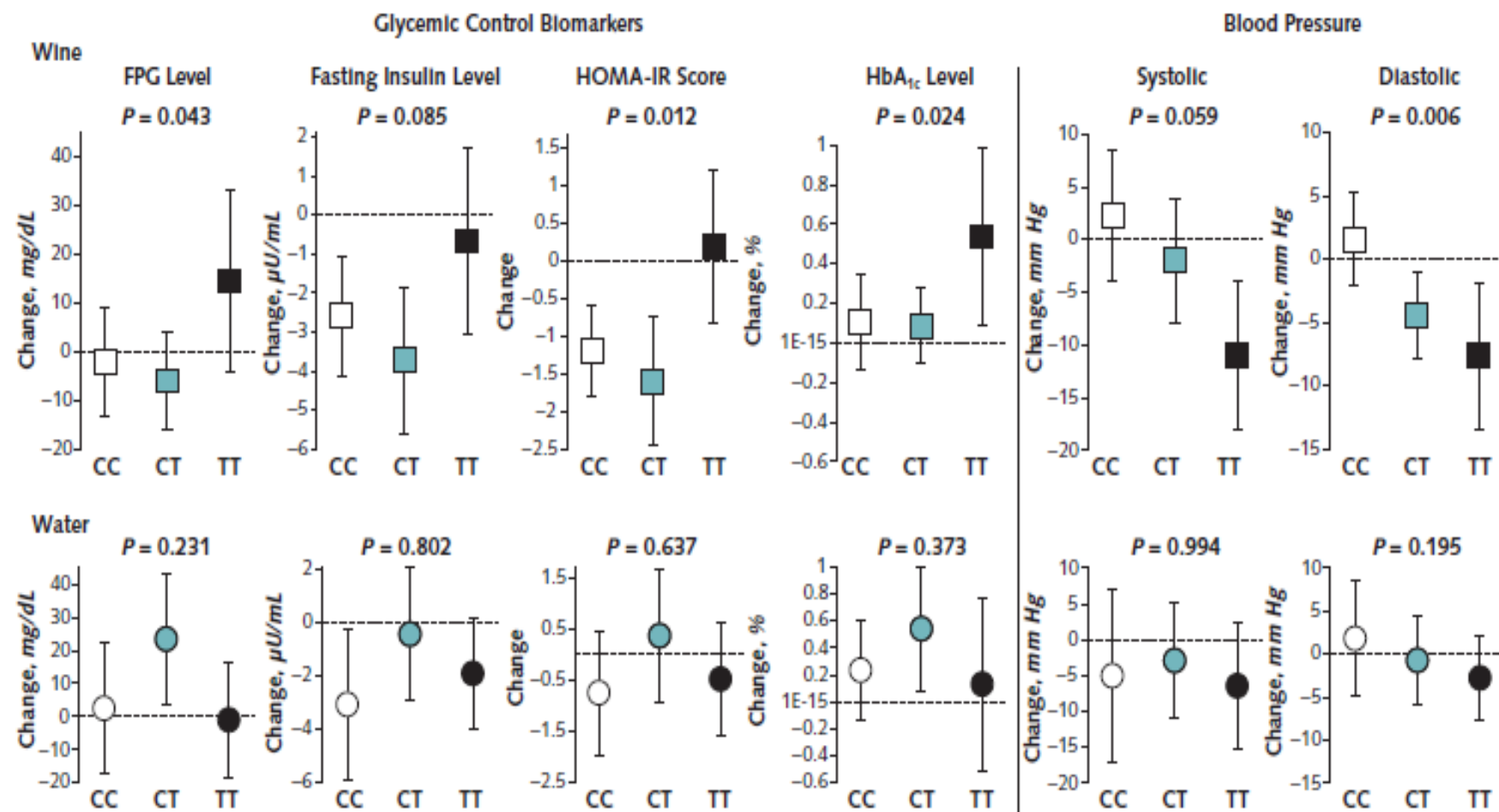


Figure 3. Effect of long-term consumption of 150 mL of mineral water, white wine, or red wine per day on glycemic control and BP variables in type 2 diabetes mellitus according to genetic variation in *ADH1B*.



The P values are for the comparison of the combined genotypes CC (*ADH1B**1 homozygotes; slow alcohol metabolism) and CT (heterozygotes) group versus the TT (*ADH1B**2 homozygotes; fast alcohol metabolism) genotype group. Variables are mean changes; bars indicate 95% CIs, and the between-group analyses for differences are for 2 y. A total of 173 participants with available DNA samples completed the 2-y trial—103 in the combined wine group and 70 in the water group. To convert FPG values to mmol/L, multiply by 0.0555. FPG = fasting plasma glucose; HbA_{1c} = hemoglobin A_{1c}; HOMA-IR = homeostatic model assessment of insulin resistance.



ELSEVIER

Atherosclerosis 175 (2004) 117–123

ATHEROSCLEROSIS

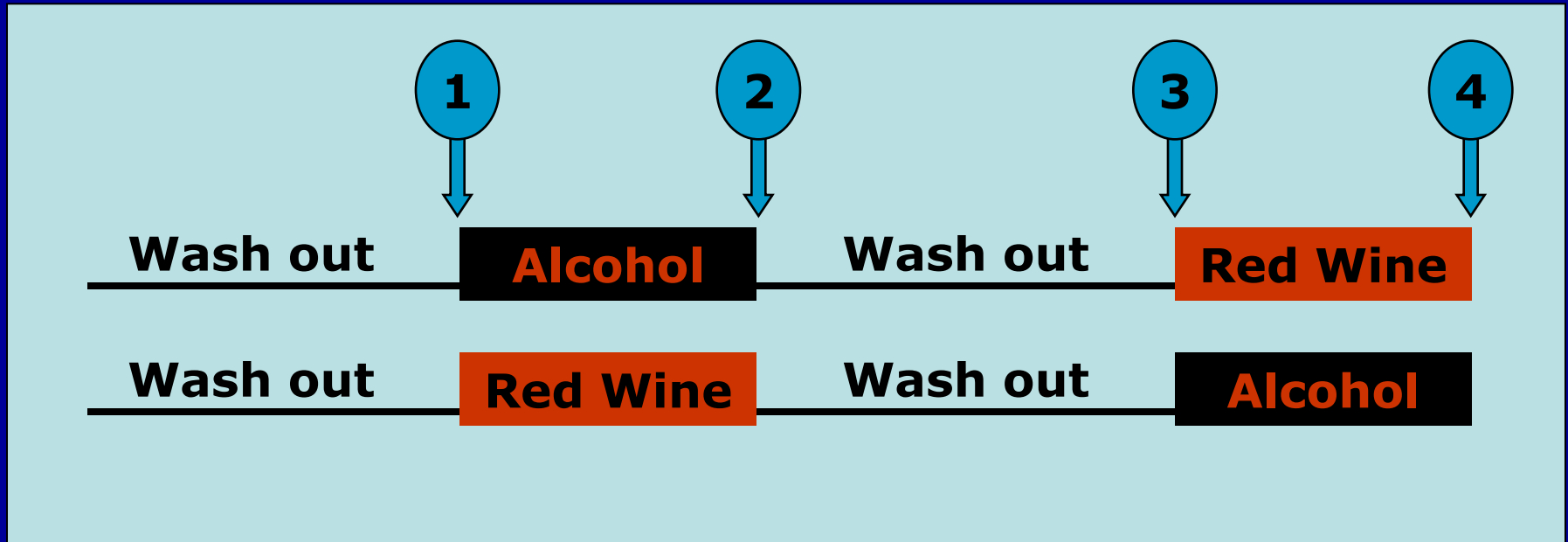
www.elsevier.com/locate/atherosclerosis

Different effects of red wine and gin consumption on inflammatory biomarkers of atherosclerosis: a prospective randomized crossover trial

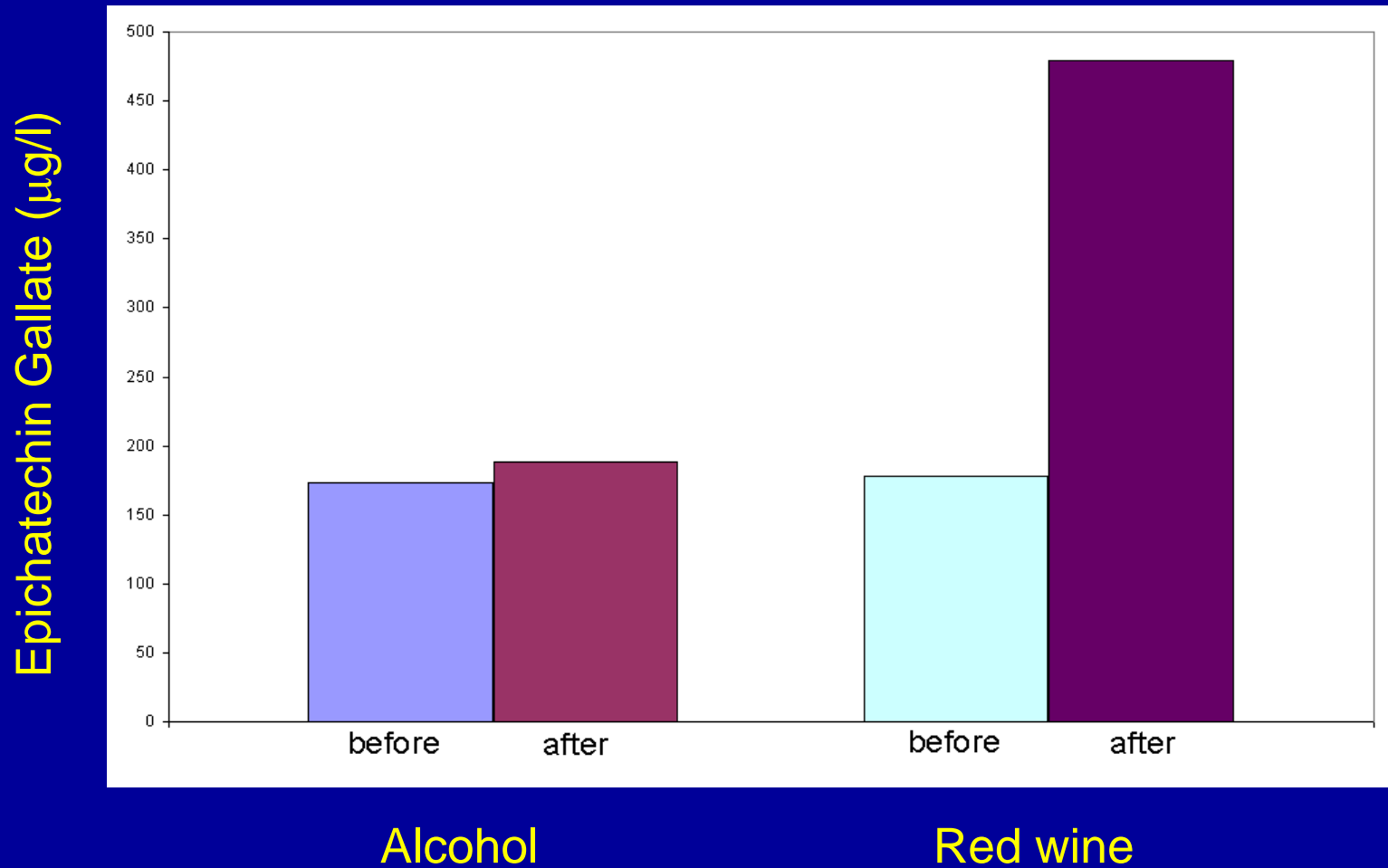
Effects of wine on inflammatory markers

Ramon Estruch^a, Emilio Sacanella^a, Eva Badia^a, Emilia Antúnez^a, José Maria Nicolás^a,
Joaquim Fernández-Solá^a, Domenico Rotilio^b, Giovanni de Gaetano^c, Emanuel Rubin^{d,*},
Alvaro Urbano-Márquez^a

A controlled, prospective, randomized, cross-over study in 40 healthy Spanish volunteers

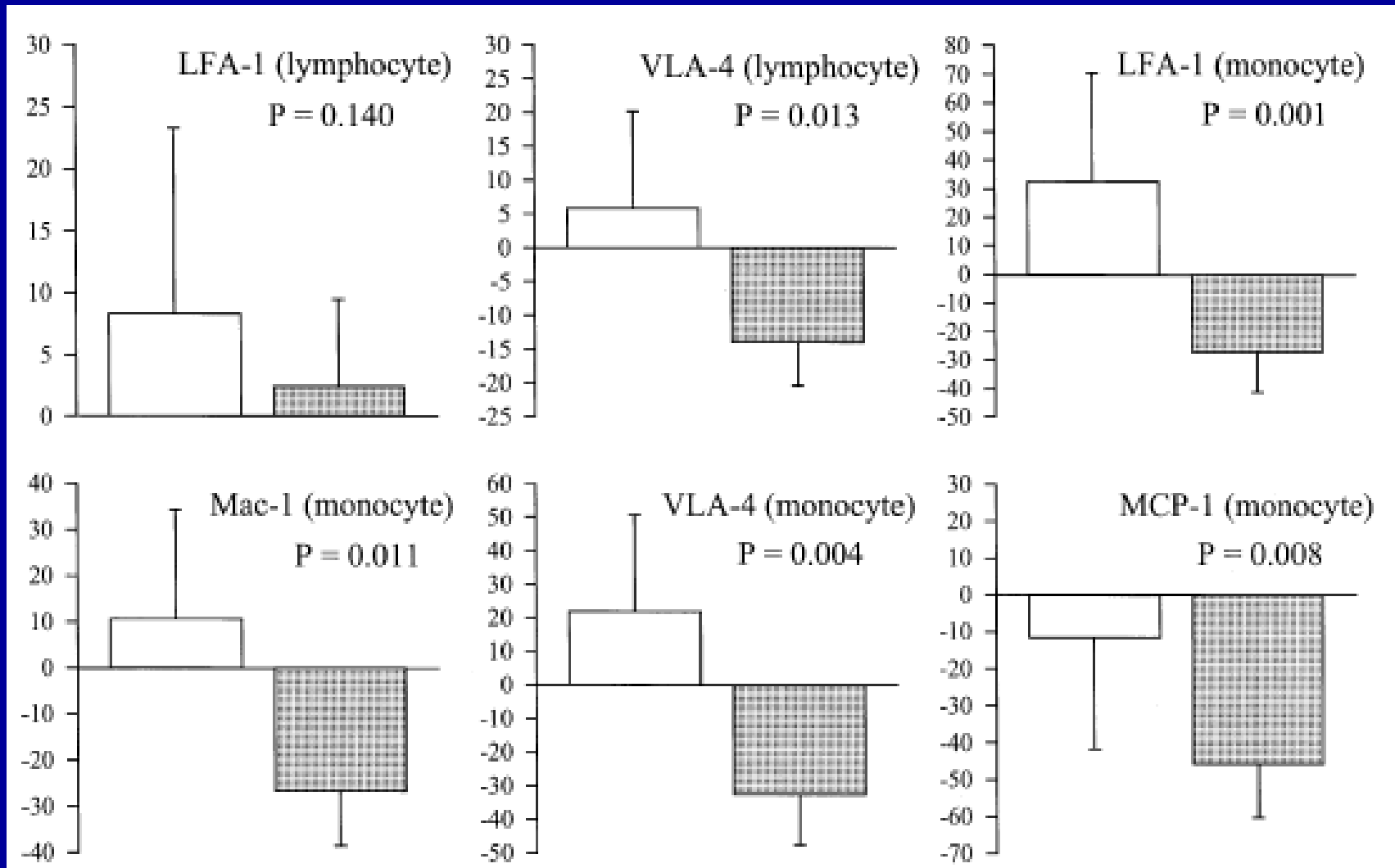


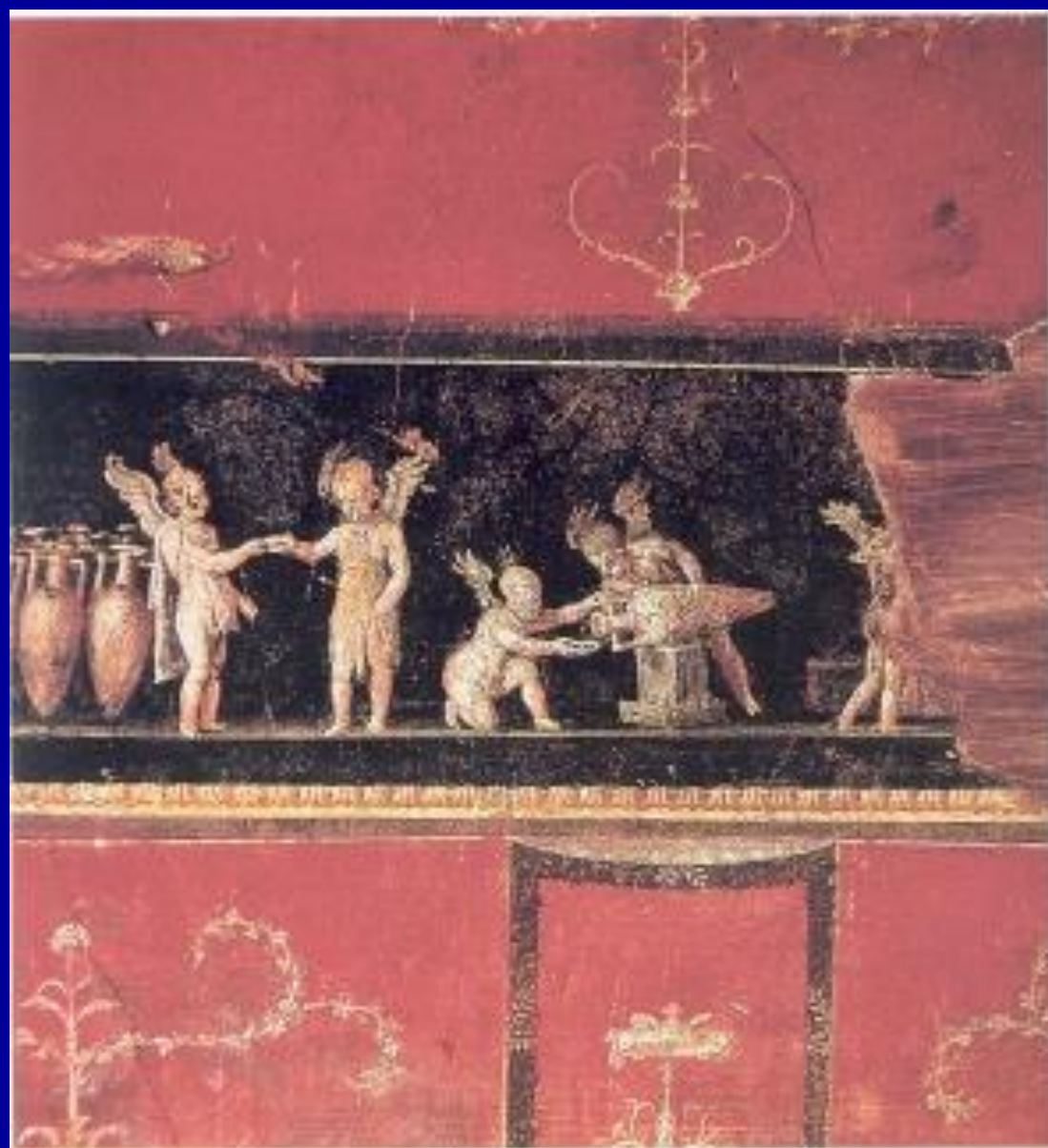
Effects on blood polyphenol levels



Estruch et al, Atherosclerosis, 2004

EFFECTS OF RED WINE OR ALCOHOL ON CELL ADHESION MOLECULES

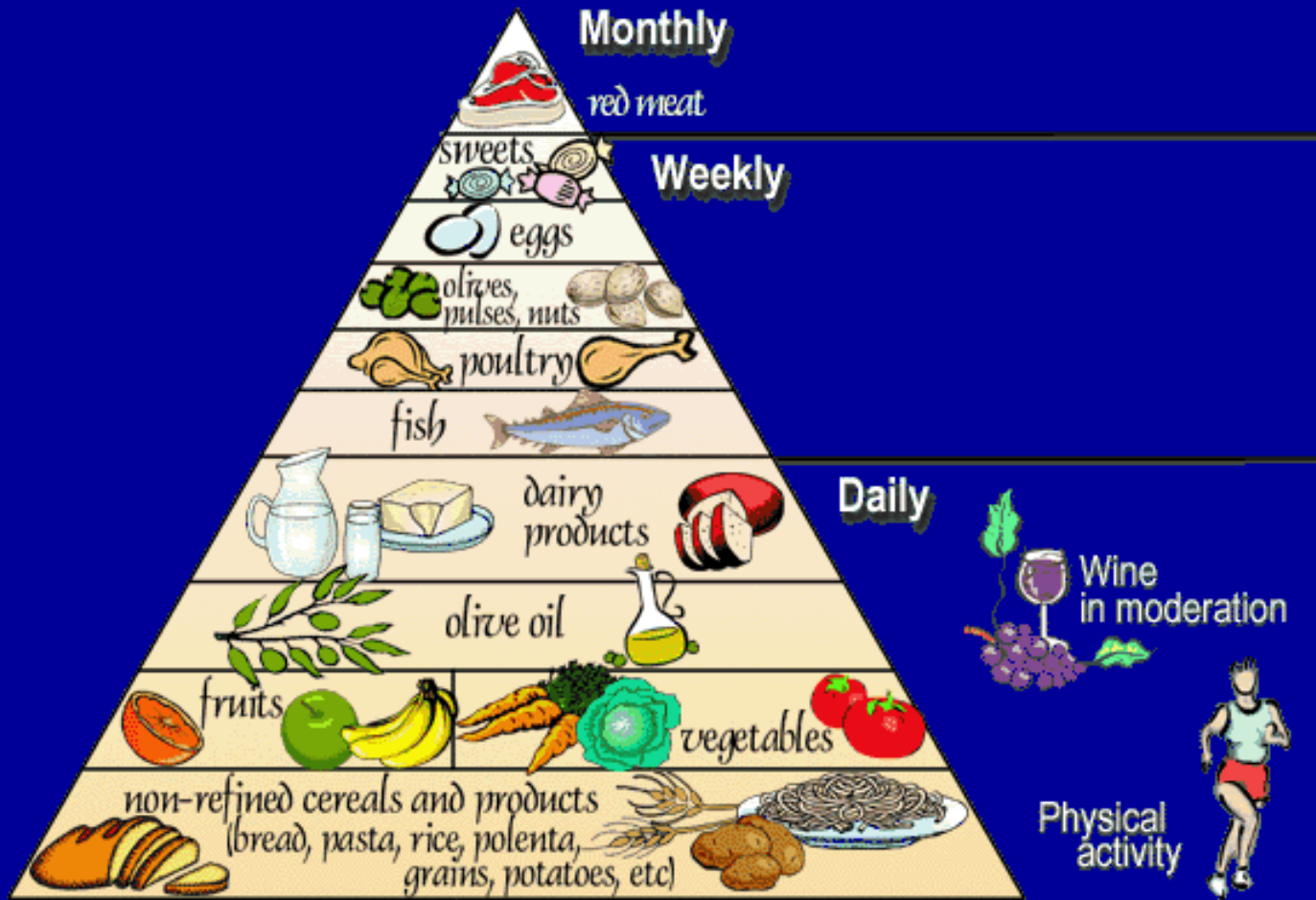




BERE VINO
MODERATAMENTE
NEL CONTESTO
DI UNA ALIMENTAZIONE
EQUILIBRATA

IMPORTANZA DELLA
"DIETA MEDITERRANEA"

PYRAMID OF THE MEDITERRANEAN DIET





Dipartimento di Epidemiologia e Prevenzione IRCCS NEUROMED, Pozzilli (IS)

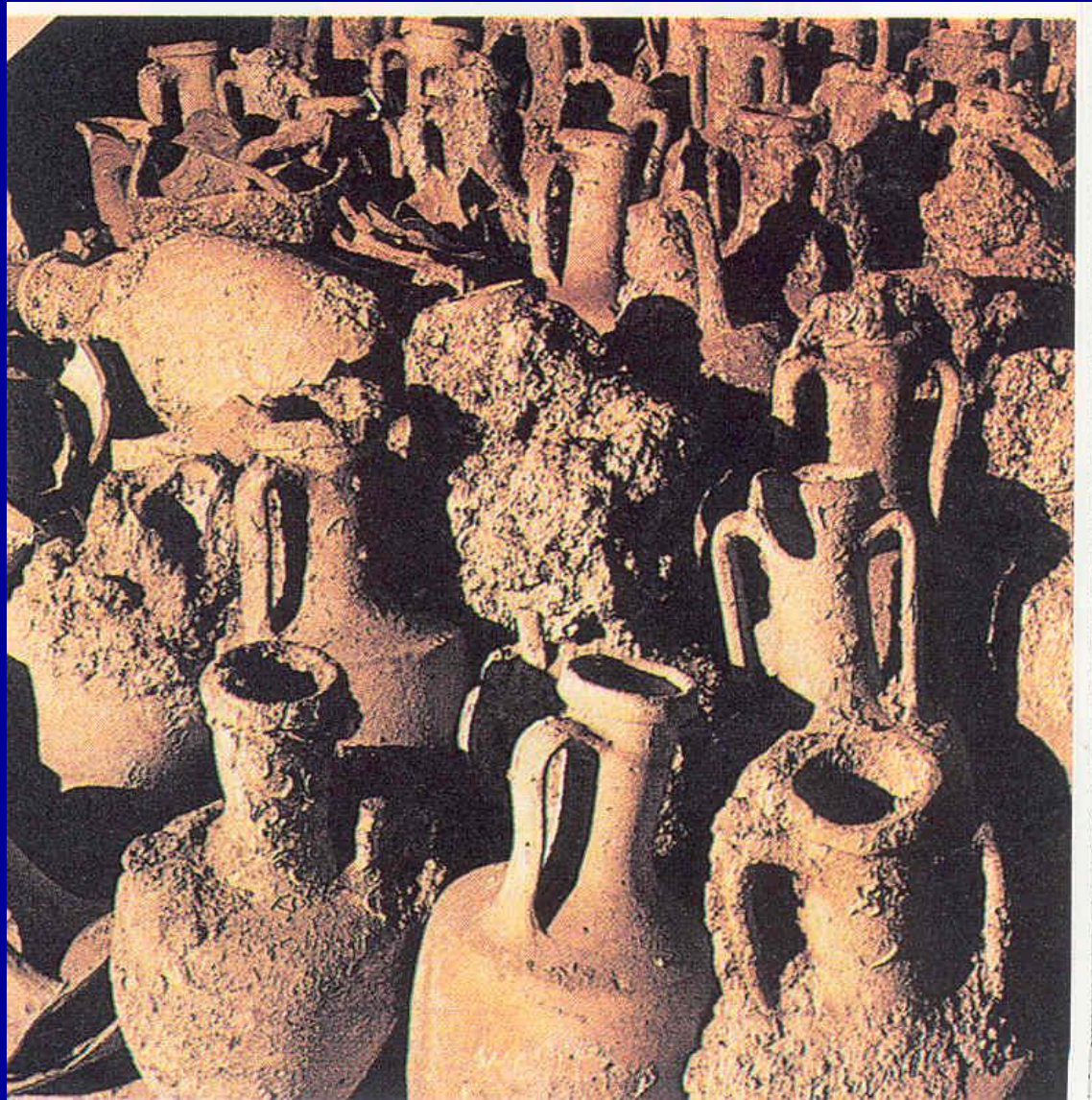




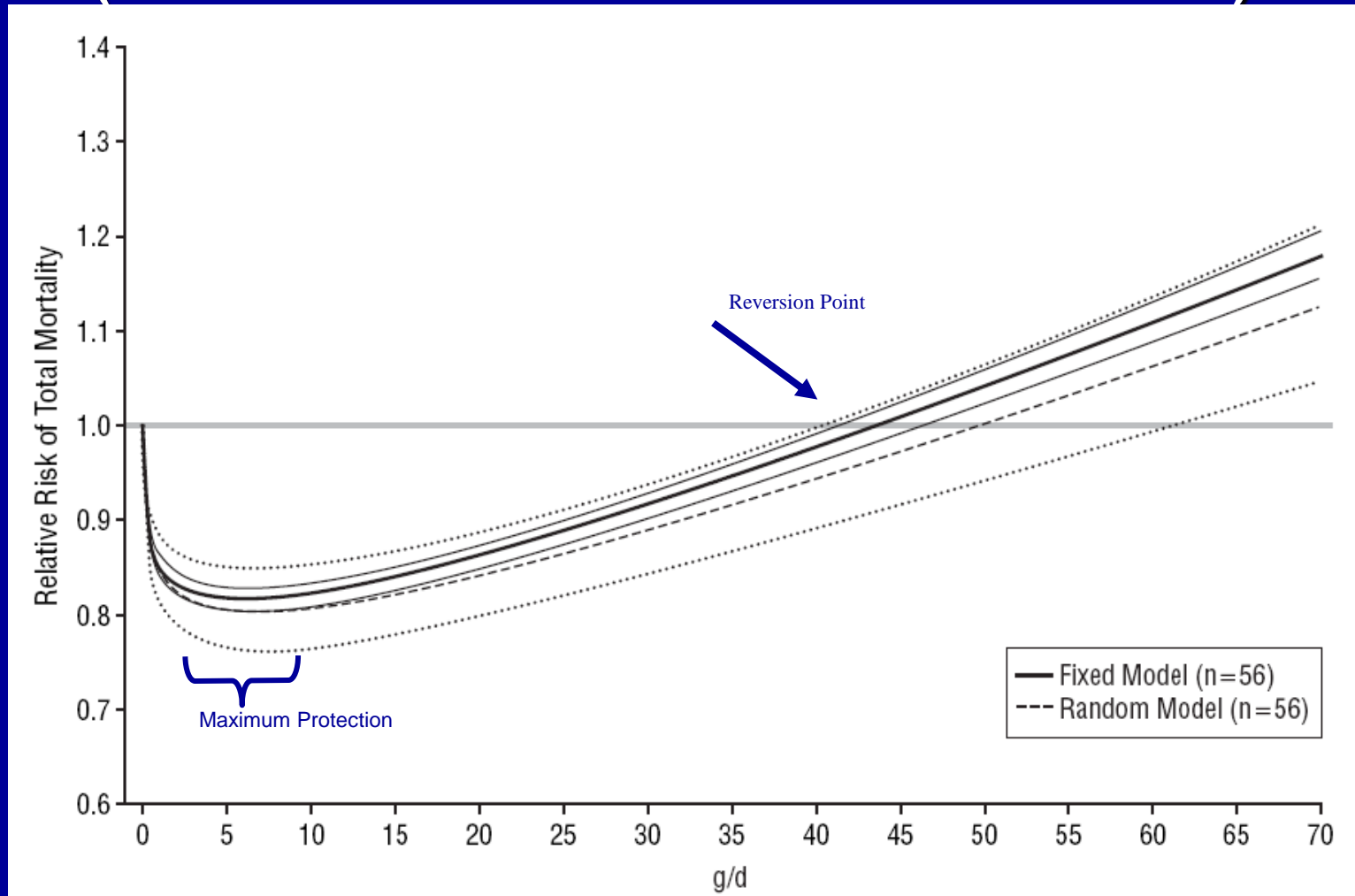


IRCCS NEUROMED
Parco Scientifico
Pozzilli (Isernia)





ALL STUDIES (1 015 835 SUBJECTS and 94 533 DEATHS)



MAX PROTECTION: RR= 0.81 (0.80-0.83) → ALCOHOL INTAKE = 6 gr/day

REVERSION POINT: → ALCOHOL INTAKE = 42 gr/day

SEX DIFFERENCES (WOMEN 285 490 ; MEN 622 692)

