

# 6<sup>th</sup> Beer and Health Symposium: *from Myths to Science*

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## **DOES BEER PLAY A SOLE ROLE IN ALCOHOL AND HEALTH SYMPHONY?**

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# THE “FRENCH PARADOX”

Fig 1 -Relation between age-standardised death rate from CHD and consumption of dairy fat in countries reporting wine consumption.

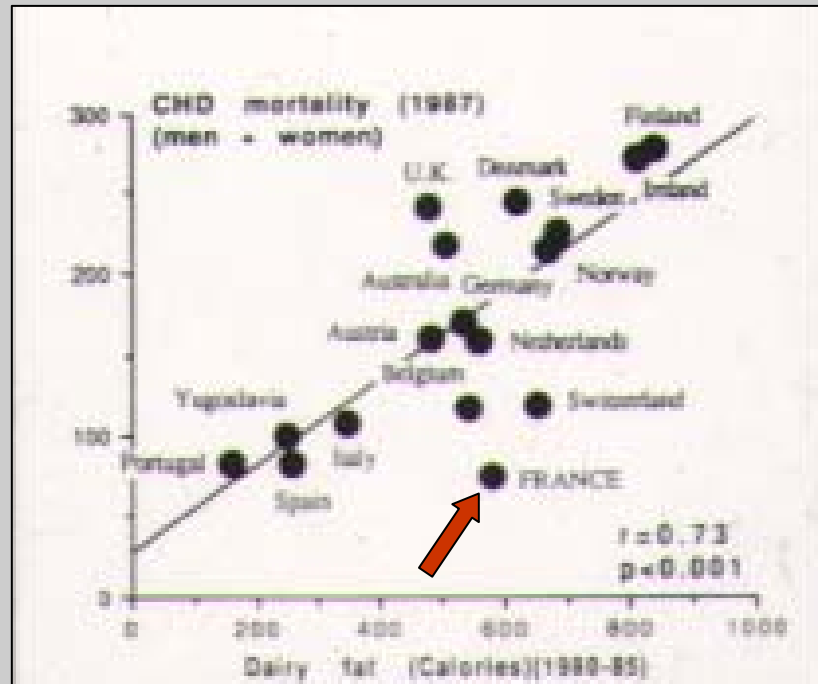
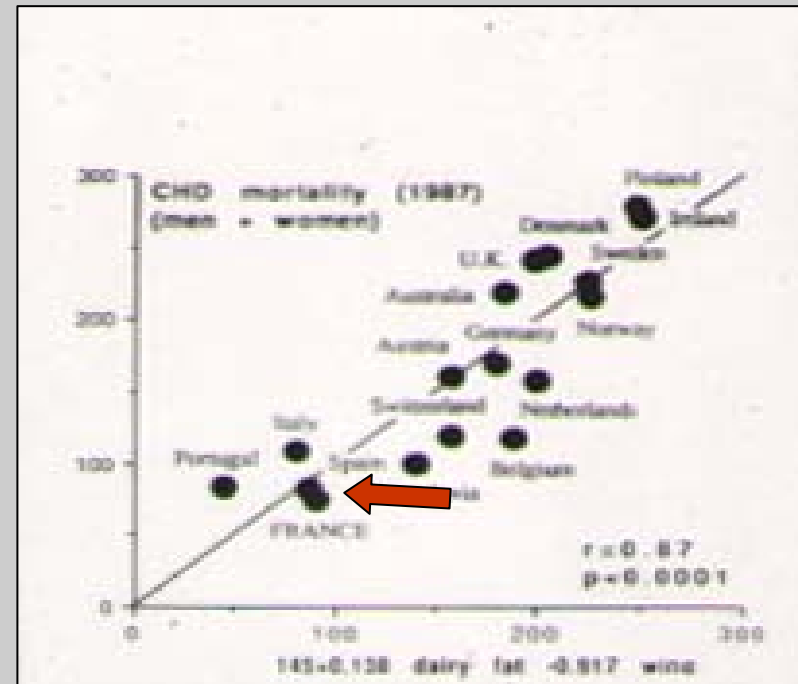


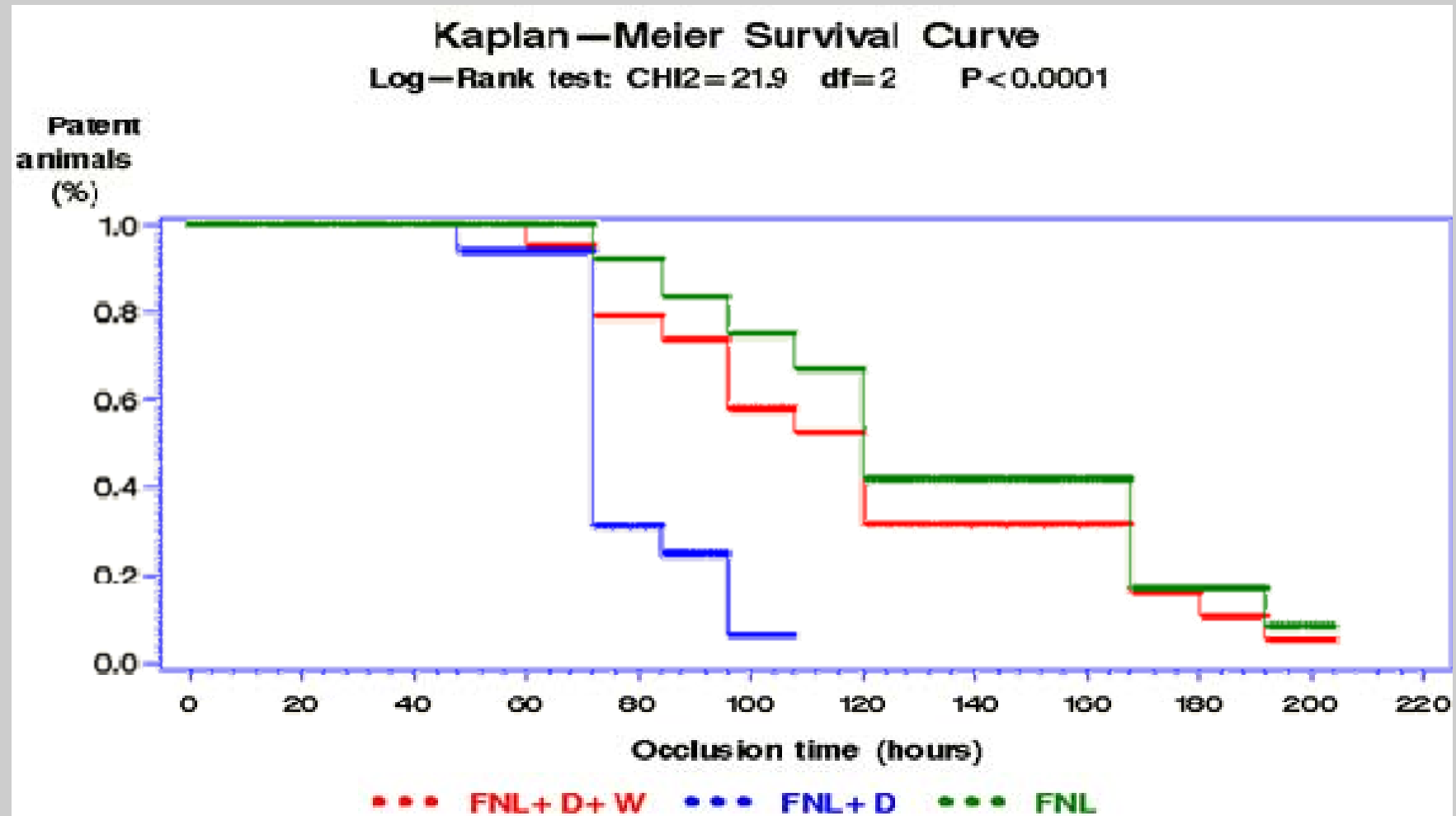
Fig 2 -Relation between age-standardised death rate from CHD and consumption of dairy fat and of wine in countries reporting wine consumption.



**Lower mortality rate of CHD in France in comparison to other European Countries, despite similar intake of high saturated fatty acid, identical smoking habits.**

**Author's explanation: Mediterranean Diet, and especially red wine, corrects the harmful effects of dietary fats.**

# THE “FRENCH PARADOX”: Red wine prevents arterial thrombosis in rats with a diet rich in cholesterol



*De Curtis.....Iacoviello L, J Thromb Haemost, 2005*

# DID THE INTEREST FOR ALCOHOL CONSUMPTION AND CVD INCREASE IN THE LAST DECADES?

## A PUBMED SEARCH :

DATE OF PUBLICATIONS	NUMBER OF STUDIES	AVERAGE NUMBER OF STUDIES PER YEAR
1970-1992	<b>222</b>	<b>10.3</b>
1992-2001	<b>495</b>	<b>52.1</b>
2002-2009	<b>896</b>	<b>119.4</b>

*\*Renaud and De Lorgeril, Lancet 1992 Jun 20;339(8808):1523-6*

IS THERE ANY SCIENTIFIC  
PROOF  
THAT ALCOHOL (wine or beer)  
IS BENEFICIAL  
TO OUR HEALTH?

# Meta-Analysis of Wine and Beer Consumption in Relation to Vascular Risk

Augusto Di Castelnuovo, MS; Serenella Rotondo, MS; Licia Iacoviello, MD, PhD;  
Maria Benedetta Donati, MD, PhD; Giovanni de Gaetano, MD, PhD

**Background**—Many epidemiological studies have evaluated whether different alcoholic beverages protect against cardiovascular disease. We performed a meta-analysis of 26 studies on the relationship between wine or beer consumption and vascular risk.

**Methods and Results**—General variance-based method and fitting models were applied to pooled data derived from 26 studies that gave a quantitative estimation of the vascular risk associated with either beverage consumption. From 13 studies involving 209 418 persons, the relative risk of vascular disease associated with wine intake was 0.68 (95% confidence interval, 0.59 to 0.77) relative to nondrinkers. There was strong evidence from 10 studies involving 176 042 persons to support a J-shaped relationship between different amounts of wine intake and vascular risk. A statistically significant inverse association was found up to a daily intake of 150 mL of wine. The overall relative risk of moderate beer consumption, which was measured in 15 studies involving 208 036 persons, was 0.78 (95% confidence interval, 0.70 to 0.86). However, no significant relationship between different amounts of beer intake and vascular risk was found after meta-analyzing 7 studies involving 136 382 persons.

**Conclusions**—These findings show evidence of a significant inverse association between light-to-moderate wine consumption and vascular risk. A similar, although smaller association was also apparent in beer consumption studies. The latter finding, however, is difficult to interpret because no meaningful relationship could be found between different amounts of beer intake and vascular risk. (*Circulation*. 2002;105:2836-2844.)

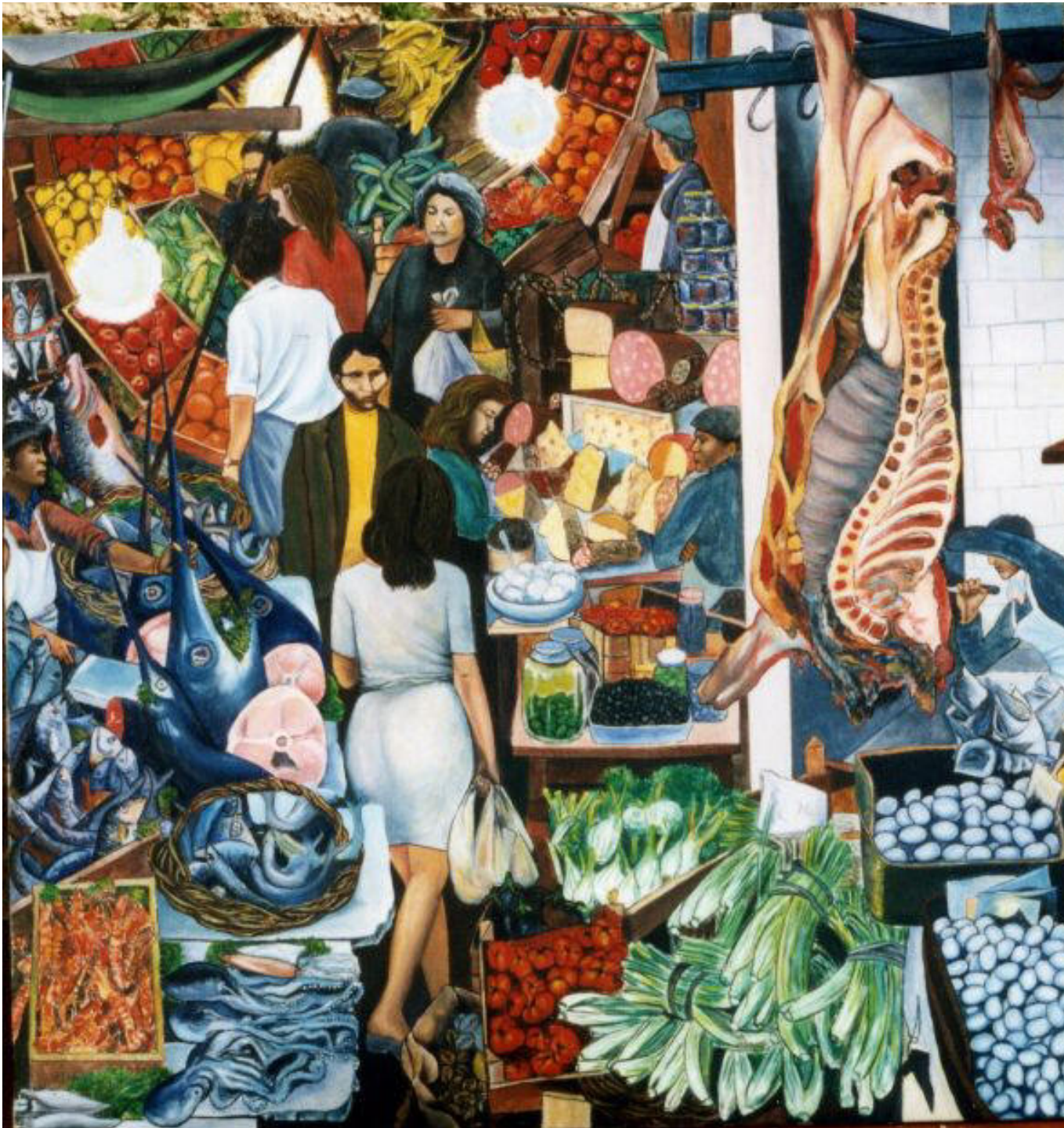
**Key Words:** cardiovascular diseases ■ wine ■ beer ■ meta-analysis

# **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**



## “Drinkers vs Non-Drinkers”

– 13 studies on **WINE**

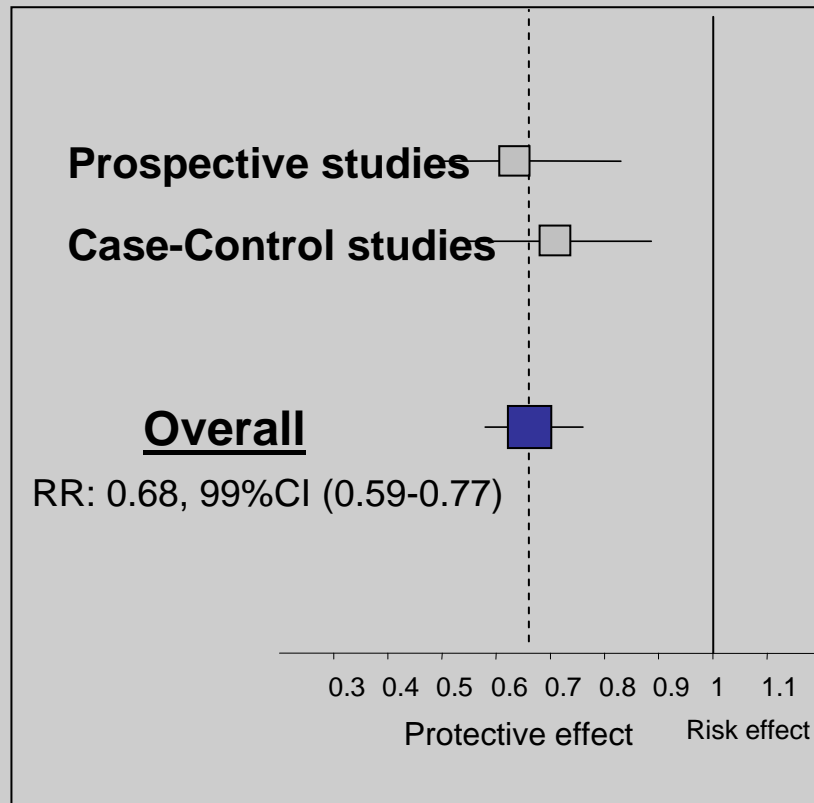
209,418 subjects

– 15 studies on **BEER**

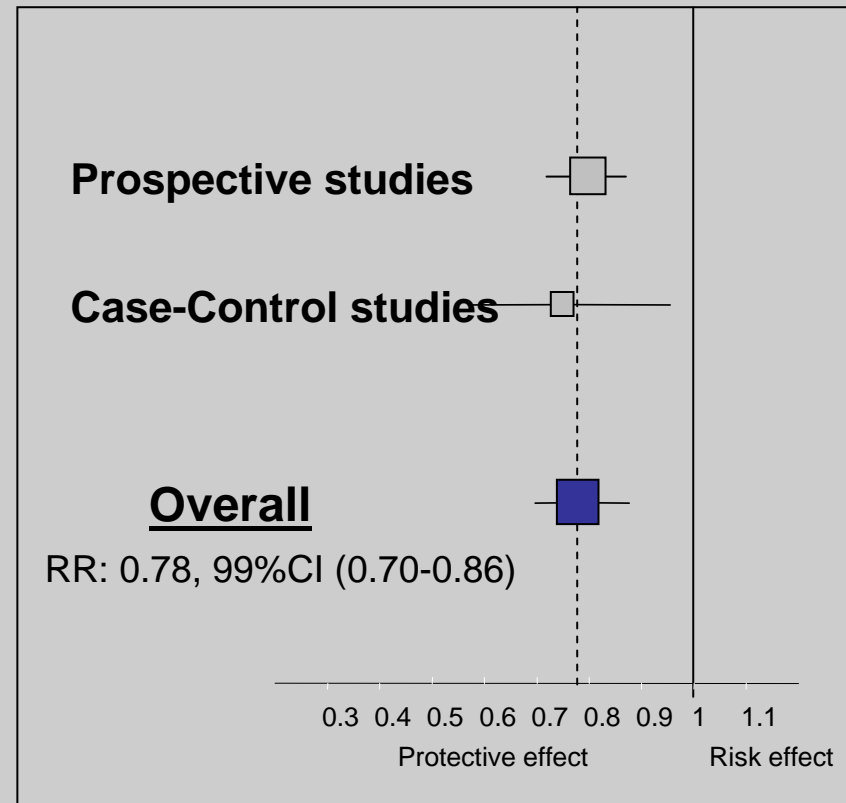
208,036 subjects

# Vascular Risk comparing

**Wine** intake vs. **no wine** intake  
13 studies reporting data for wine  
209,418 subjects



**Beer** intake vs. **no beer** intake  
15 studies reporting data for beer  
208,036 subjects



# “Drinkers versus non-drinkers”

SUBGROUP	WINE			BEER		
	N	RR	99%CI	N	RR	99%CI
<b>OVERALL</b>	13	0.68	0.59-0.77	15	0.78	0.70-0.86
<b>Type of event</b>						
<b>Coronary heart disease</b>	11	0.71	0.59-0.85	13	0.79	0.68-0.91
<b>Cerebrovascular disease</b>	2	0.43	0.24-0.78	2	0.67	0.41-1.10
<b>Non-fatal vascular events</b>	8	0.71	0.56-0.90	7	0.74	0.57-0.96
<b>Cardiovascular mortality</b>	2	0.49	0.34-0.70	3	0.76	0.55-1.05

*Di Castelnuovo et al, Circulation 2002*

**METANALYSIS OF TOTAL CORONARY  
HEART DISEASE EVENTS:  
PREVENTION BY ASPIRIN  
OR WINE OR BEER INTAKE**

<b>INTAKE</b>	<b>Odds Ratio</b>	<b>(C.I.)</b>
<b>ASPIRIN</b>	<b>0.72</b>	<b>(0.60 - 0.87)</b>
<b>WINE</b>	<b>0.71</b>	<b>(0.59 - 0.85)</b>
<b>BEER</b>	<b>0.79</b>	<b>(0.68-0.91)</b>

*Hayden et al., Ann Int Med 2002; Di Castelnuovo et al., Circulation 2002*



Fotoğraf: George Steinmetz

Dev Develer

# Subgroup analysis

SUBGROUP	WINE			BEER		
	N	RR	99%CI	N	RR	99%CI
<b>Adjustment</b> for different types of alcoholic beverages						
Not Adjusted	3	<b>0.53</b>	0.39-0.73	4	0.79	0.62-1.01
<b>Adjusted</b>	<b>10</b>	<b>0.75</b>	<b>0.61-0.93</b>	<b>11</b>	<b>0.77</b>	<b>0.65-0.92</b>
<b>Adjustment</b> for indicators of social class level						
Not Adjusted	3	0.78	0.56-1.08	3	0.68	0.41-1.14
Adjusted	10	<b>0.64</b>	0.52-0.79	12	<b>0.78</b>	0.68-0.91

# THE DEFINITION OF REFERENCE GROUP

## Subgroup analysis

SUBGROUP	WINE			BEER		
	N	RR	99%CI	N	RR	99%CI
No light or occasional drinkers in the reference group	10	<b>0.73</b>	0.59-0.91	11	<b>0.80</b>	0.66-0.97
No ex-drinkers in the reference group	5	<b>0.61</b>	0.47-0.79	5	<b>0.77</b>	0.63-0.94
With the same reference group both for wine and beer	9	<b>0.62</b>	0.50-0.77	9	<b>0.72</b>	0.59-0.88

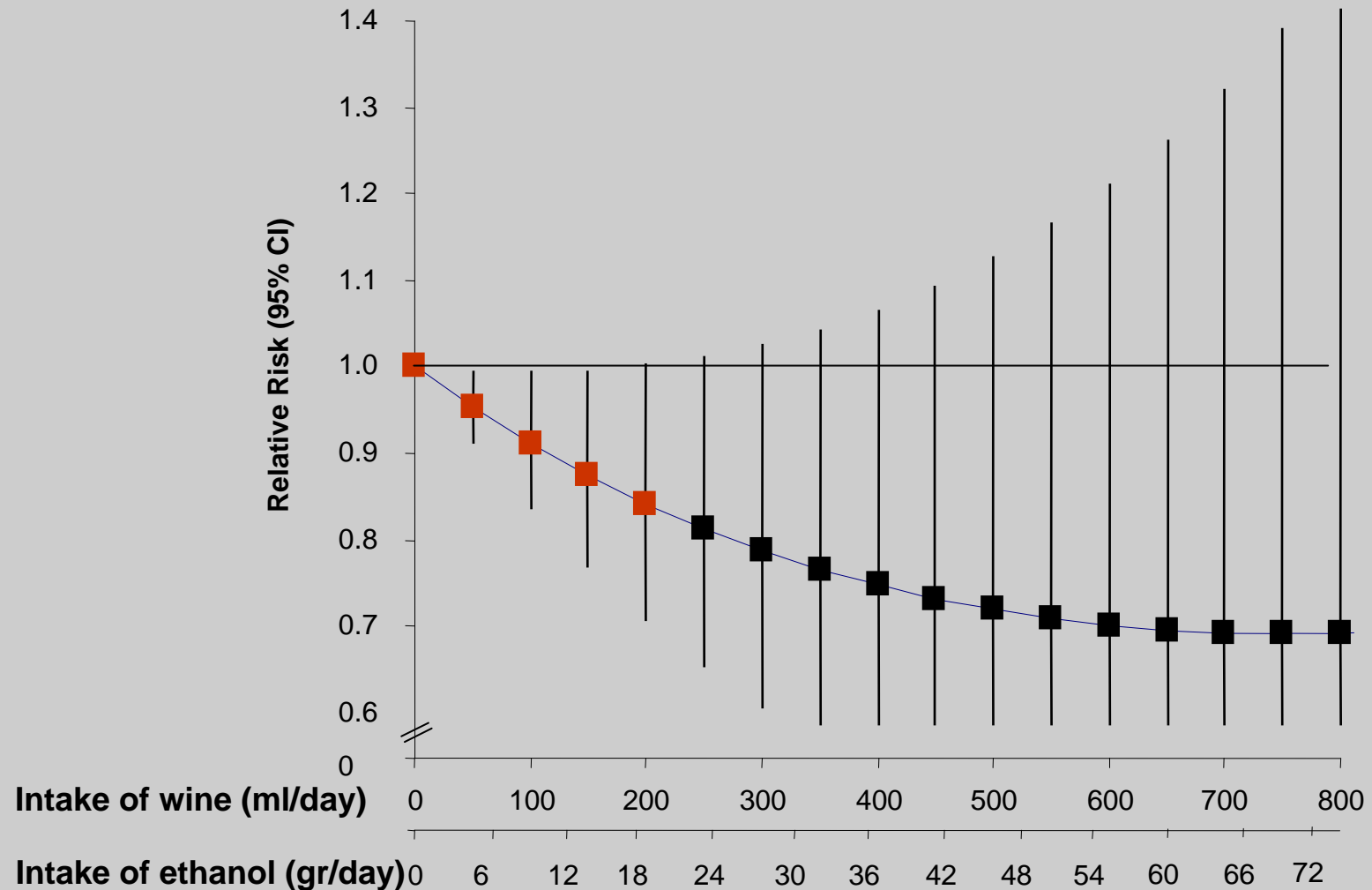
HOW MUCH  
WINE OR BEER  
CAN WE DRINK  
TO GET A BENEFICIAL  
EFFECT ON OUR HEALTH?



## **“Dose-Response” meta-analysis**

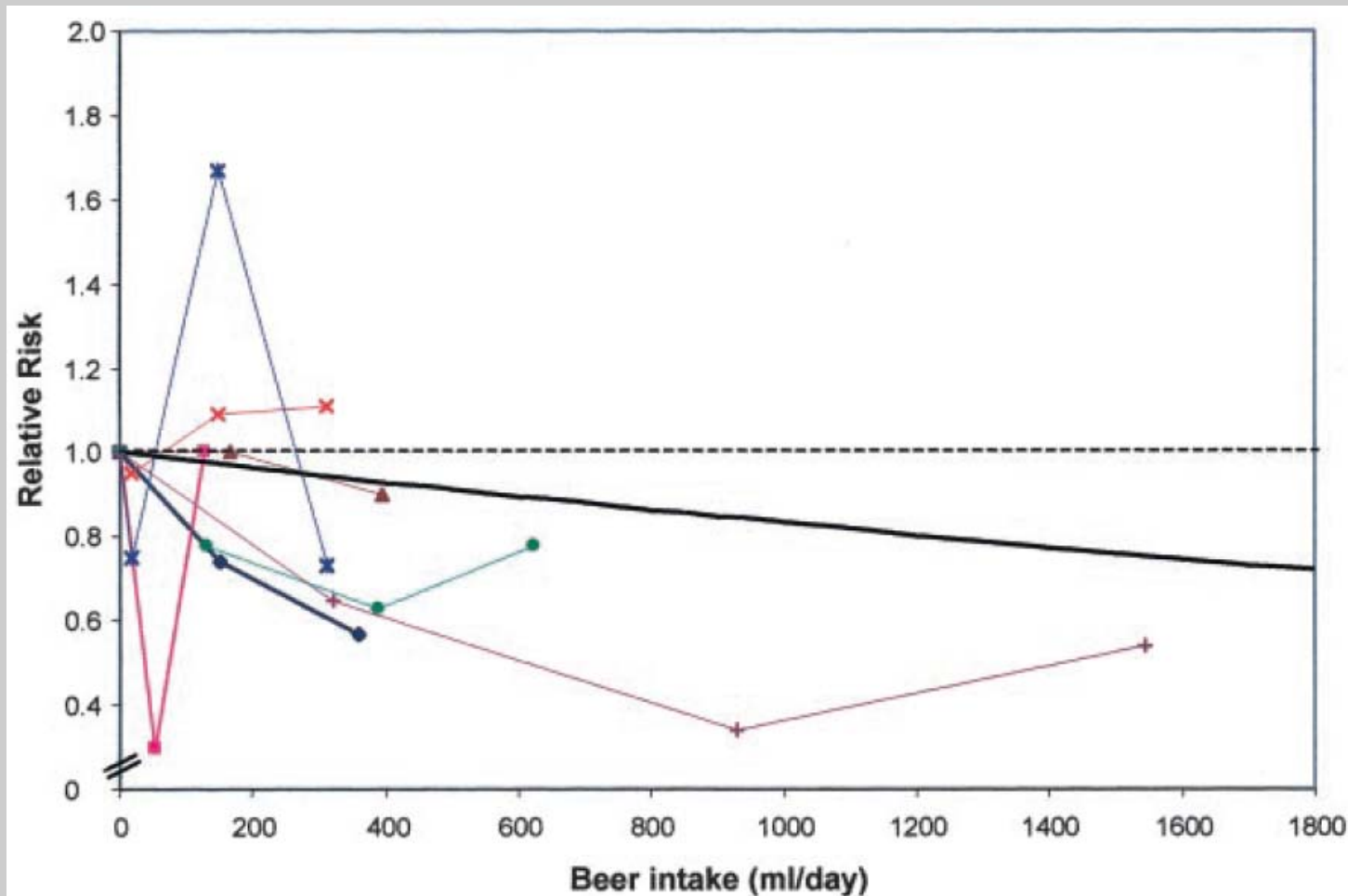
- 10 studies reporting trend analysis for WINE  
176,042 subjects**
- 7 studies reporting trend analysis for BEER  
136,382 subjects**

# Best fitting model for **wine** effect using dose-response curves from 7 prospective studies



**STATISTICAL SIGNIFICANCE REACHED UP TO 150 mL/day WINE INTAKE**

# BEER EFFECT DOSE-RESPONSE CURVES FROM 7 STUDIES



**NO CORRELATION BETWEEN THE AMOUNT OF DAILY BEER CONSUMPTION  
AND CARDIOVASCULAR RISK**

# **Meta-Analysis of Wine and Beer Consumption in Relation to Vascular Risk**

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## **2002 → 2011 UPDATE**

### **WHY?**

**MORE PUBLISHED STUDIES ON WINE AND BEER CONSUMPTION  
IN RELATION TO CVD EVENTS AND MORTALITY**

**NEW STATISTICAL METHODS THAT EXPLAIN BETTER  
THE NON-LINEAR RELATION BETWEEN  
DOSE OF BEVERAGES (WINE OR BEER) AND OUTCOMES**

# DATA EXTRACTION

The **amount of a drink of alcohol** (gr/day) was taken as quantified by each autor whenever possible.

## **1 drink of alcohol**

**= 10 grams of ethanol**

**= 130 ml of wine (10°)**

**= 250 ml of beer (5°)**

**= 40 ml of spirits (32°)**

DOES DRINKING ALCOHOL  
IS ALWAYS BENEFICIAL  
TO OUR HEALTH?

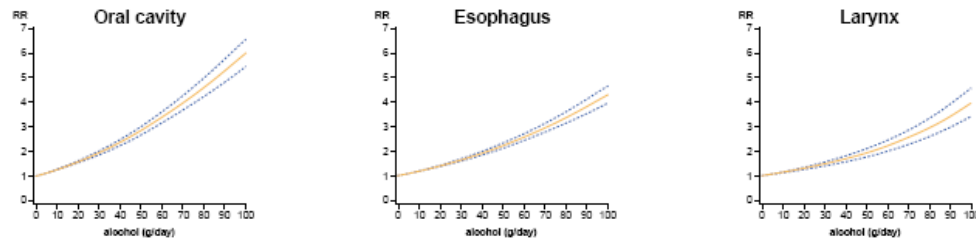
The case of cancer.

# Alcohol Consumption and the Risk of Cancer

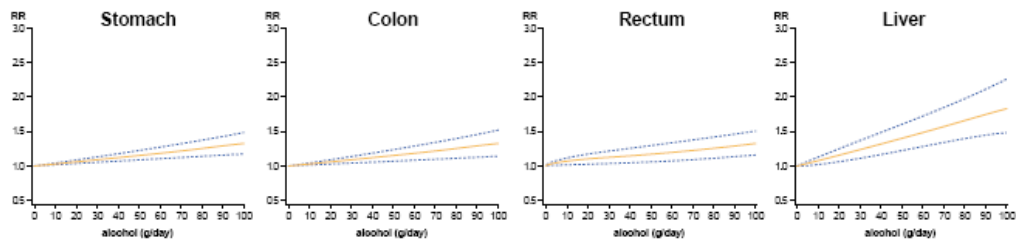
## *A Meta-Analysis*

VINCENZO BAGNARDI, MS.C., MARTA BLANGIARDO, MS.C.,  
CARLO LA VECCHIA, M.D., AND GIOVANNI CORRAO, PH.D.

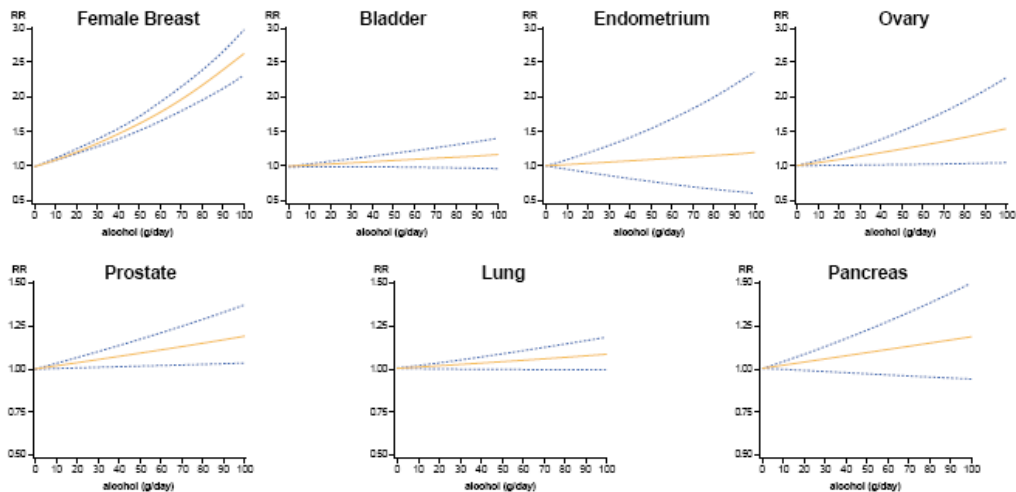
### A. Neoplasms of the Upper-Aerodigestive Tract



### B. Neoplasms of the Lower Digestive Tract



### C. Other Neoplasms



# A meta-analysis on alcohol drinking and esophageal and gastric cardia adenocarcinoma risk

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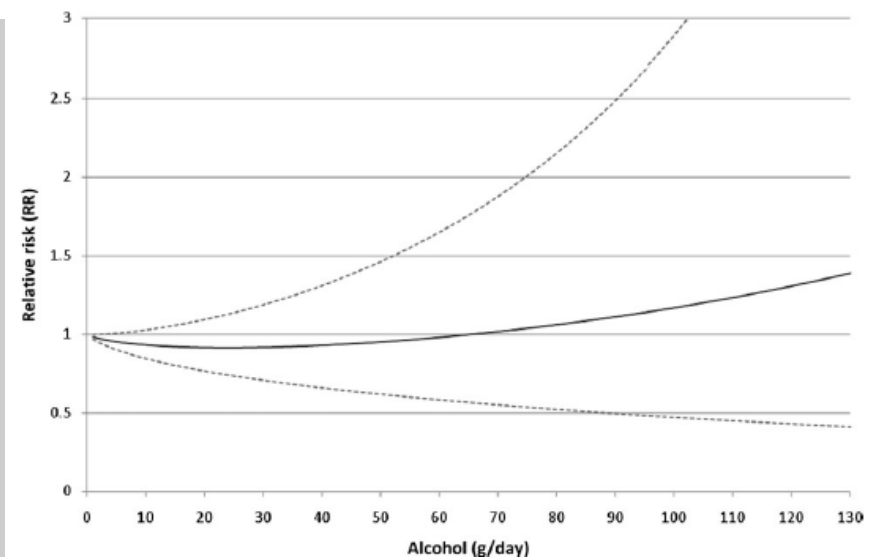
Received 14 January 2011; revised 25 February 2011; accepted 2 March 2011

**Background:** In order to provide a precise quantification of the association between alcohol drinking and esophageal and gastric cardia adenocarcinoma risk, we conducted a meta-analysis of available data.

**Patients and methods:** We identified 20 case-control and 4 cohort studies, including a total of 5500 cases. We derived meta-analytic estimates using random-effects models, taking into account correlation between estimates, and we carried out a dose-risk analysis using nonlinear random-effects meta-regression models.

**Results:** The relative risk (RR) for drinkers versus nondrinkers was 0.96 [95% confidence interval (CI) 0.85–1.09] overall, 0.87 (95% CI 0.74–1.01) for esophageal adenocarcinoma and 0.89 (95% CI 0.76–1.03) for gastric cardia adenocarcinoma. Compared with nondrinkers, the pooled RRs were 0.86 for light ( $\leq 1$  drink per day), 0.90 for moderate (1 to  $< 4$  drinks per day), and 1.16 for heavy ( $\geq 4$  drinks per day) alcohol drinking. The dose-risk model found a minimum at 25 g/day, and the curve was  $< 1$  up to 70 g/day.

**Conclusions:** This meta-analysis provides definite evidence of an absence of association between alcohol drinking and esophageal and gastric cardia adenocarcinoma risk, even at higher doses of consumption.





# A meta-analysis on alcohol drinking and gastric cancer risk

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<sup>1</sup>Department of Epidemiology, Mario Negri Institute for Pharmacological Research, Milan; <sup>2</sup>Department of Statistics, University of Milano-Bicocca, Milan; <sup>3</sup>Division of Epidemiology and Biostatistics, European Institute of Oncology, Milan; <sup>4</sup>Department of Clinical Medicine and Prevention, Centre of Biostatistics for Clinical Epidemiology, University of Milano-Bicocca, Monza, Italy; <sup>5</sup>International Agency for Research on Cancer, Lyon, France; <sup>6</sup>Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran; <sup>7</sup>Section of Medical Statistics, Department of Occupational Health, University of Milan, Milan, Italy; <sup>8</sup>International Prevention Research Institute, Lyon, France; <sup>9</sup>The Tisch Cancer Institute, Mount Sinai School of Medicine, New York, USA

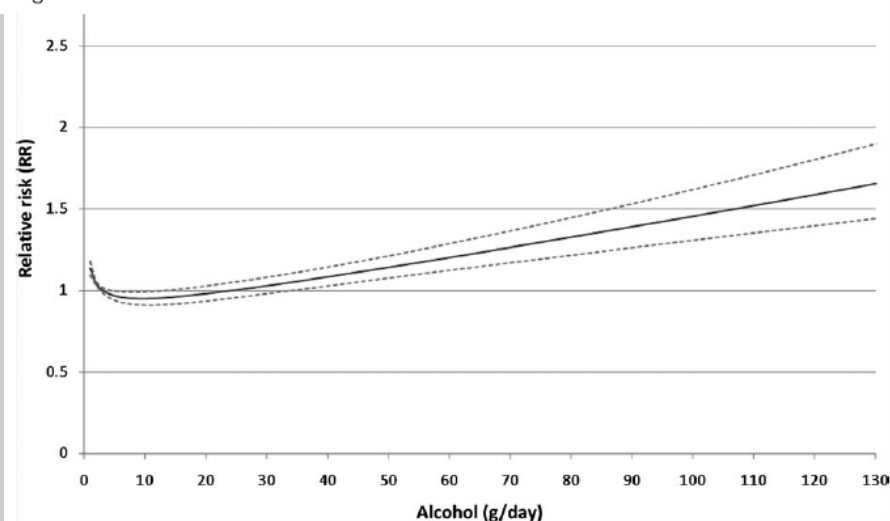
Received 14 January 2011; revised 21 February 2011; accepted 2 March 2011

**Background:** Whether an association between alcohol drinking and gastric cancer risk exists is an open question. In order to provide a definite quantification of the association between alcohol drinking and gastric cancer risk, we conducted a meta-analysis of available data.

**Patients and methods:** We carried out a PubMed search of articles published up to June 2010 and identified 44 case-control and 15 cohort studies, including a total of 34 557 gastric cancer cases. We derived meta-analytic estimates using random-effects models, taking into account correlation between estimates. We carried out a dose-risk analysis using nonlinear random-effects meta-regression models.

**Results:** Compared with nondrinkers, the pooled relative risk (RR) was 1.07 [95% confidence interval (CI) 1.01–1.13] for alcohol drinkers and 1.20 (95% CI 1.01–1.44) for heavy alcohol drinkers ( $\geq 4$  drinks per day). The pooled estimates were apparently higher for gastric noncardia (RR for heavy drinkers = 1.17, 95% CI 0.78–1.75) than for gastric cardia (RR = 0.99, 95% CI 0.67–1.47) adenocarcinoma. The dose-risk model estimated a RR of 0.95 (95% CI 0.91–0.99) for 10 g/day and 1.14 (95% CI 1.08–1.21) for 50 g/day.

**Conclusions:** This meta-analysis provides definite evidence of a lack of association between moderate alcohol drinking and gastric cancer risk. There was, however, a positive association with heavy alcohol drinking.



# Population attributable risk of tobacco and alcohol for upper aerodigestive tract cancer

D. Anantharaman et al./Oral Oncology 47 (2011) 725–731

## S U M M A R Y

Tobacco and alcohol are major risk factors for upper aerodigestive tract (UADT) cancer and significant variation is observed in UADT cancer rates across Europe. We have estimated the proportion of UADT cancer burden explained by tobacco and alcohol and how this varies with the incidence rates across Europe, cancer sub-site, gender and age. This should help estimate the minimum residual burden of other risk factors to UADT cancer, including human papillomavirus. We analysed 1981 UADT cancer cases and 1993 controls from the ARCAGE multi-centre study. We estimated the population attributable risk (PAR) of tobacco alone, alcohol alone and their joint effect. Tobacco and alcohol together explained 73% of UADT cancer burden of which nearly 29% was explained by smoking alone, less than 1% due to alcohol on its own and 44% by the joint effect of tobacco and alcohol. Tobacco and alcohol together explained a larger proportion of hypopharyngeal/laryngeal cancer (PAR = 85%) than oropharyngeal (PAR = 74%), esophageal (PAR = 67%) and oral cancer (PAR = 61%). Tobacco and alcohol together explain only about half of the total UADT cancer burden among women. Geographically, tobacco and alcohol explained a larger proportion of UADT cancer in central (PAR = 84%) than southern (PAR = 72%) and western Europe (PAR = 67%). While the majority of the UADT cancers in Europe are due to tobacco or the joint effect of tobacco and alcohol, our results support a significant role for other risk factors in particular, for oral and oropharyngeal cancers and also for UADT cancers in southern and western Europe.

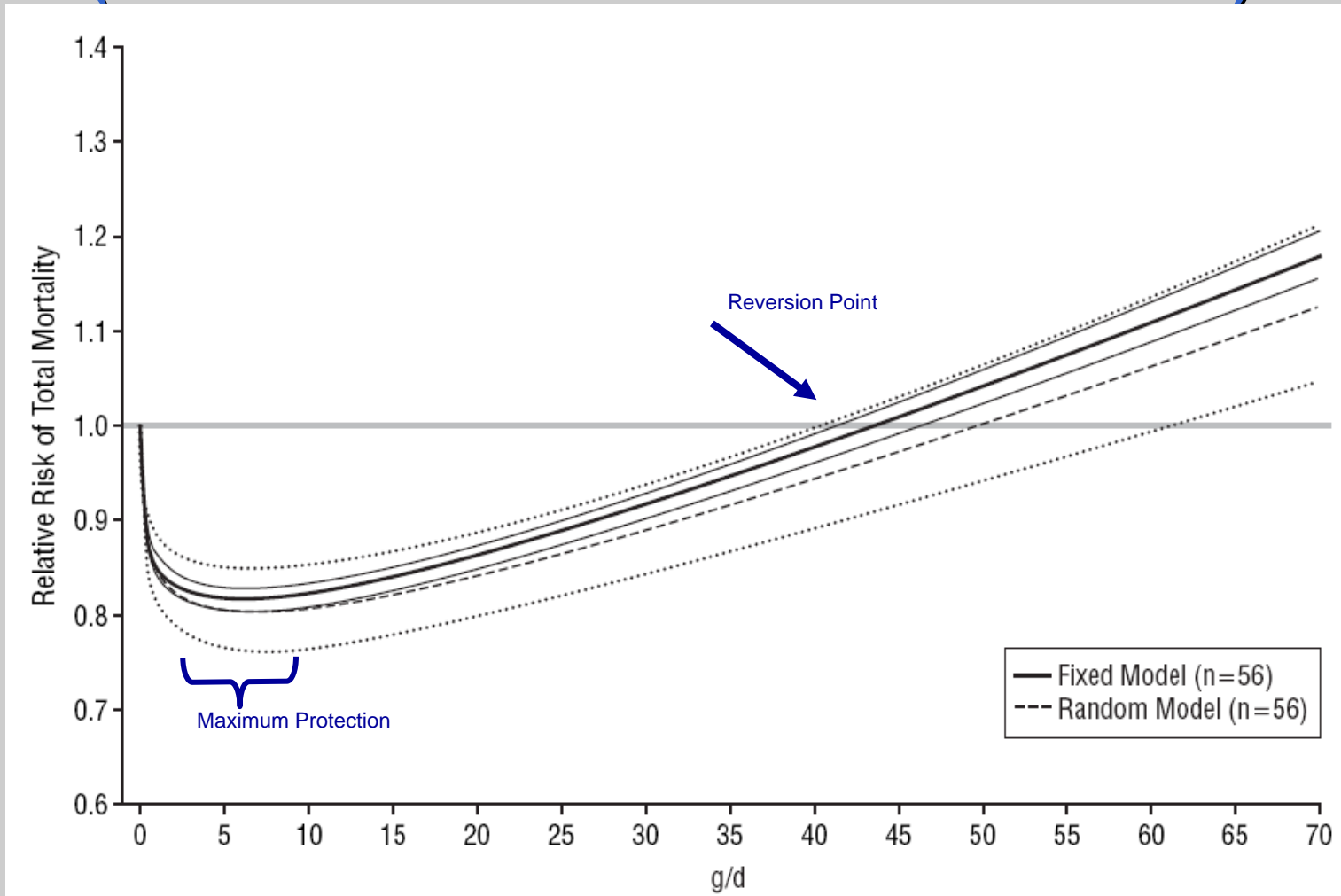
**Table 2**

Tobacco and alcohol associated risk and attributable fractions for upper aerodigestive tract (UADT) cancer.

Description	Cases	Controls	OR* (95% CI)	PAR (95% CI) <sup>†</sup>
<i>Overall</i>				
Never users	177	603	Reference	
Tobacco alone	781	834	3.54 (2.89–4.33)	28.7 (26.2–30.9)
Alcohol alone	36	110	1.31 (0.85–1.99)	0.4 (–0.3–0.9)
Joint effect	954	412	9.64 (7.70–12.08)	43.9 (42.6–44.9)
Total			$\Psi = 2.08$ (1.33–3.23) <sup>†</sup>	73.1 (68.5–76.7)

BUT, AT LAST,  
IF WE REGULARLY DRINK  
ALCOHOL  
IN MODERATION  
WILL OUR MORTALITY RISK  
BE REDUCED  
INDEPENDENTLY FROM  
ANY CAUSE OF DEATH?

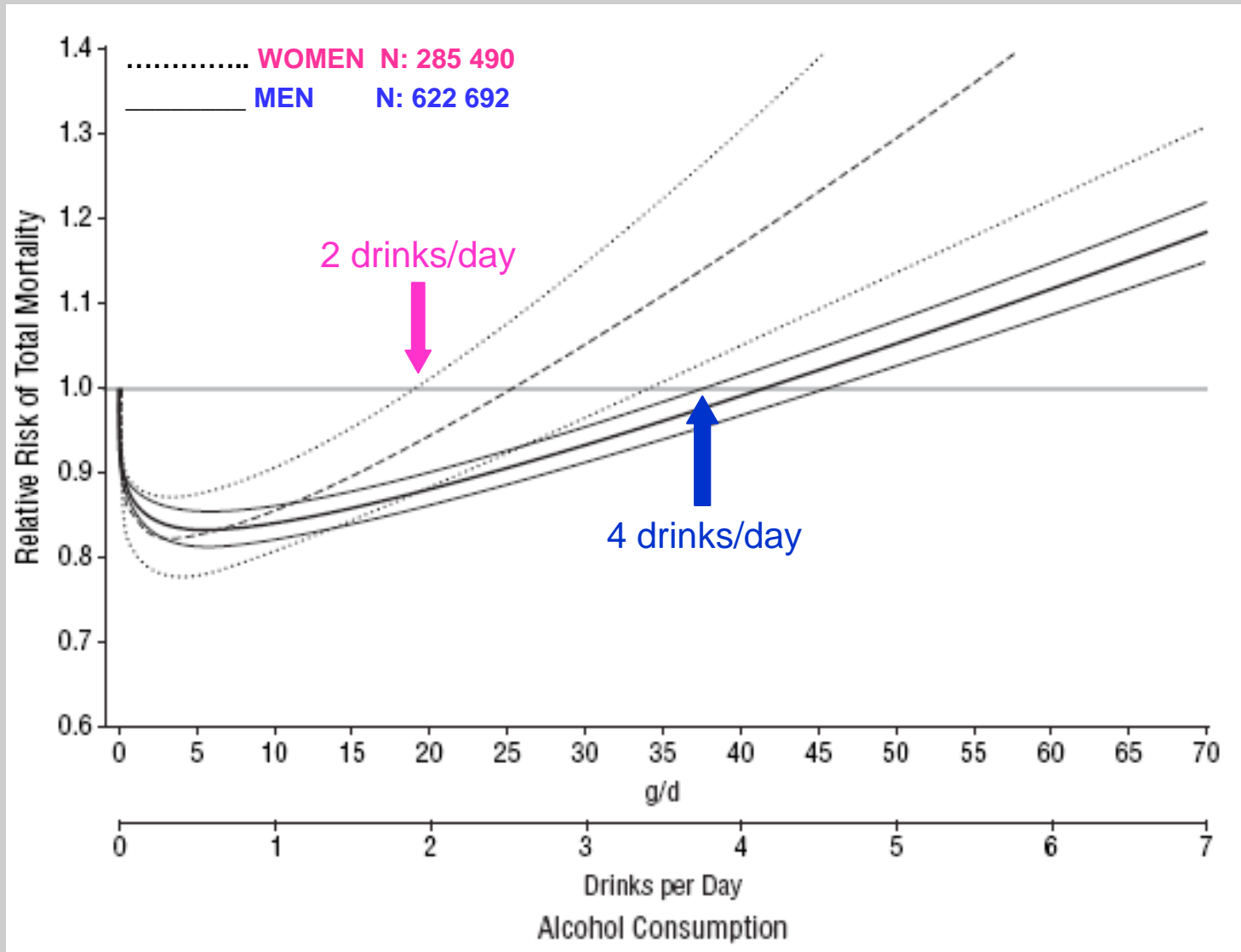
# ALL STUDIES (1 015 835 SUBJECTS and 94 533 DEATHS)



**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)



# ALCOHOL, AGE AND MORTALITY

Adjusted relative risk of death according to baseline age,  
Northern California, 1978-1985

Age (years)	1-2 drinks/day Vs. never drinkers
	RR (95% CI)
< 30	1.34 (0.95-1.89)
30-39	1.24 (0.93-1.64)
40-49	1.05 (0.85-1.30)
50-59	0.83 (0.73-0.95)
60-69	0.86 (0.77-0.95)
≥70	0.88 (0.79-0.98)

***“Reduction of total mortality risk  
only among persons aged 50 or more years”.***

# **CONCLUSIONS**

## **...to drink or not to drink?**

**THESE META-ANALYSES .....**

**CONFIRM THE HAZARDS OF EXCESS DRINKING**

**INDICATE THE EXISTENCE OF POTENTIAL WINDOWS OF  
WINE OR BEER INTAKE**

**WHICH MAY CONFER**

**A NET BENEFICIAL EFFECT OF DRINKING,**

**AT LEAST IN TERMS OF FATAL AND NON-FATAL  
VASCULAR EVENTS**

**IN APPARENTLY HEALTHY POPULATION**

From the public health viewpoint,  
the only easy rules are

**Heavy drinkers** would be better off to reduce drinking or abstain

**Light to moderate drinkers,**  
should be warned to avoid heavy drinking

**Abstainers** should be informed that regular and moderate alcohol consumption, would put them at a level of cardiovascular or mortality risk substantially lower than avoiding drinking.







**Vincent van Gogh**, *The Drinkers, or the Four Ages of Man*, 1890. Art Institute of Chicago.