



# VI Y LA DIETA MEDITERRÀNIA

**RAMON ESTRUCH**

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2018

# Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population

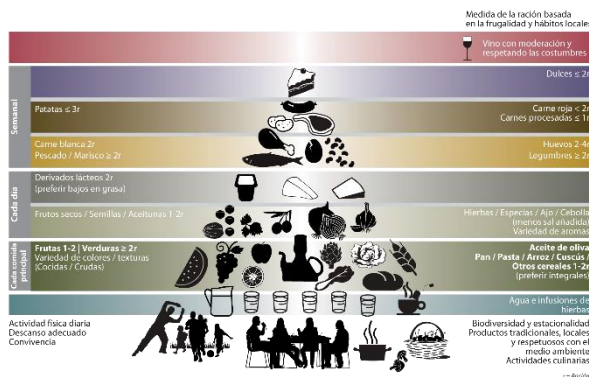
Índice de masa corporal (IMC)  
18,5-22,9 m<sup>2</sup>



No fumador  
ni exfumador



123.219 personas seguidas 35 a.



Alimentación saludable



≥ 6 h/semana

Consumo de alcohol moderado  
5-14,9 g/día

## ESPERANZA DE VIDA A LOS 50 AÑOS

SEGÚN LA ADHERENCIA A LOS ESTILOS DE VIDA SALUDABLE

**NULA**

- Mujeres: **+ 29,0 años**
- Hombres: **+ 25,5 años**

**MÁXIMA**

- Mujeres: **+ 43,1 años**
- Hombres: **+ 37,6 años**



## Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

GBD 2016 Alcohol Collaborators\*



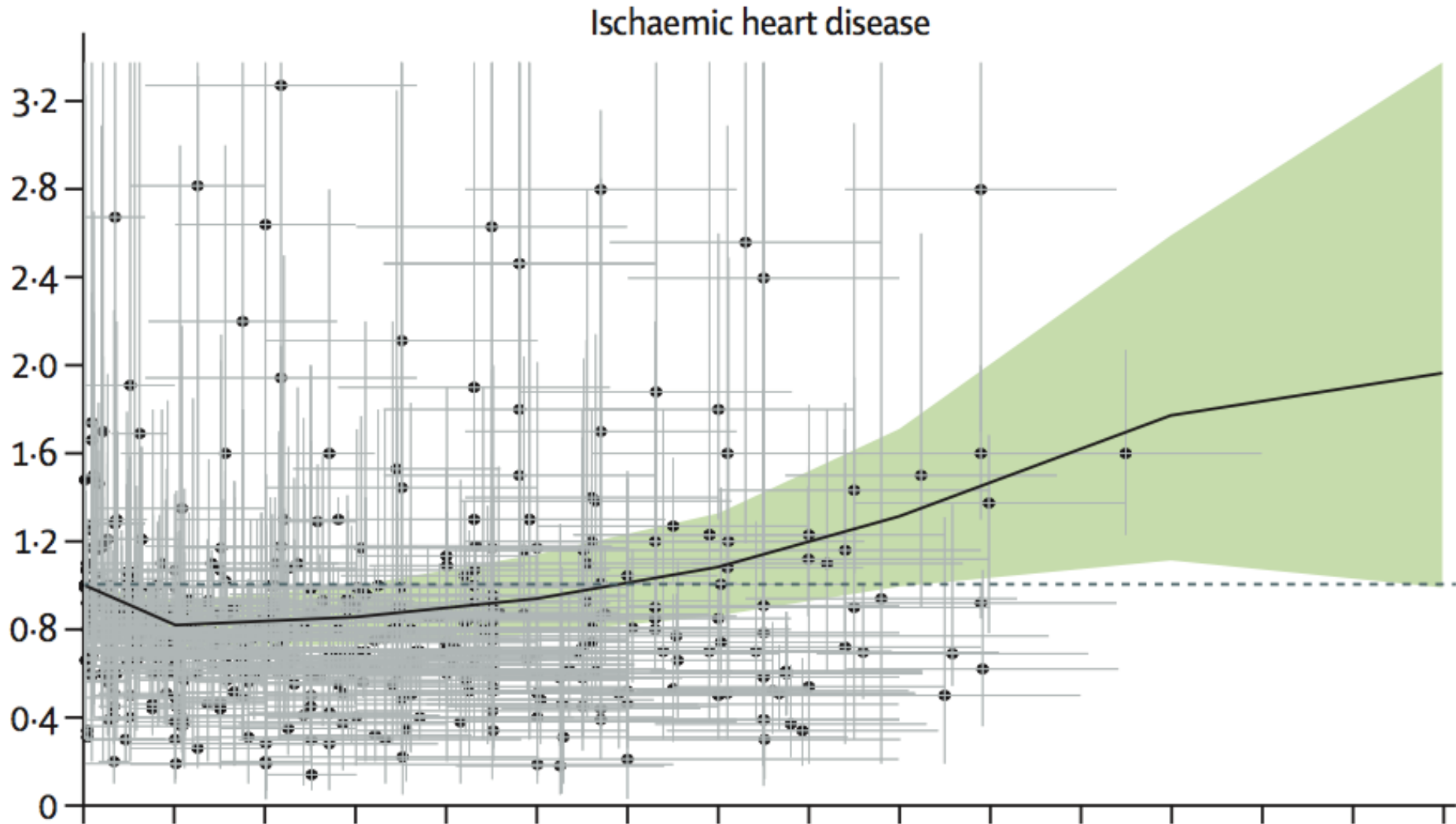
**“Interpretación** El consumo del alcohol es uno de los principales factores de riesgo de enfermedad a nivel mundial y es responsable de un empeoramiento sustancial de la salud. **Observamos que el riesgo de mortalidad por todas las causas, y por cáncer específicamente, se incrementa cuando aumentan los niveles de consumo, y el nivel de consumo que minimiza la pérdida de salud es cero.** Estos resultados sugieren que podría ser necesario revisar las políticas de control para el alcohol a nivel mundial, reenfocando nuestros esfuerzos en reducir el consumo de alcohol en la población general.”



# Lancet 2018



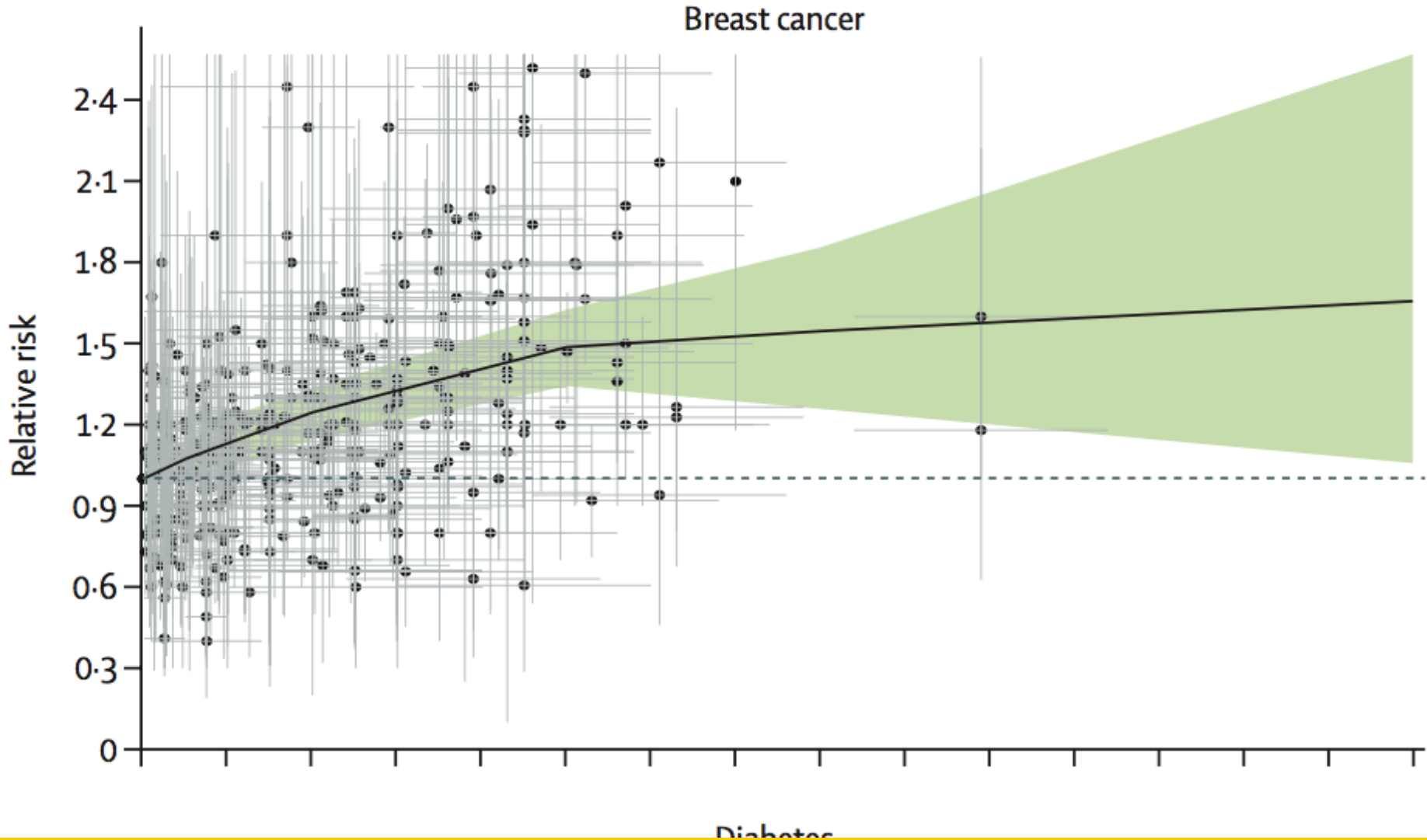
# ALCOHOL Y CARDIOPATÍA ISQUÉMICA





# ALCOHOL Y CÁNCER DE MAMA

**A** Femeninas



# DOBLE CARA DEL ALCOHOL





# MANIFESTACIONES CRÓNICAS

- Síndrome de dependencia alcohólica
- Hepatopatía alcohólica (esteatosis, fibrosis, cirrosis alcohólicas)
- Gastritis crónica. Malabsorción intestinal.
- Pancreatitis aguda y crónica
- Miocardiopatía y miopatía alcohólicas
- Demencia y Encefalopatías alcohólicas
- Polineuritis alcohólica



# **EFFECTOS TÓXICOS SOBRE EL SISTEMA CARDIOVASCULAR**

## **EFFECTOS AGUDOS**

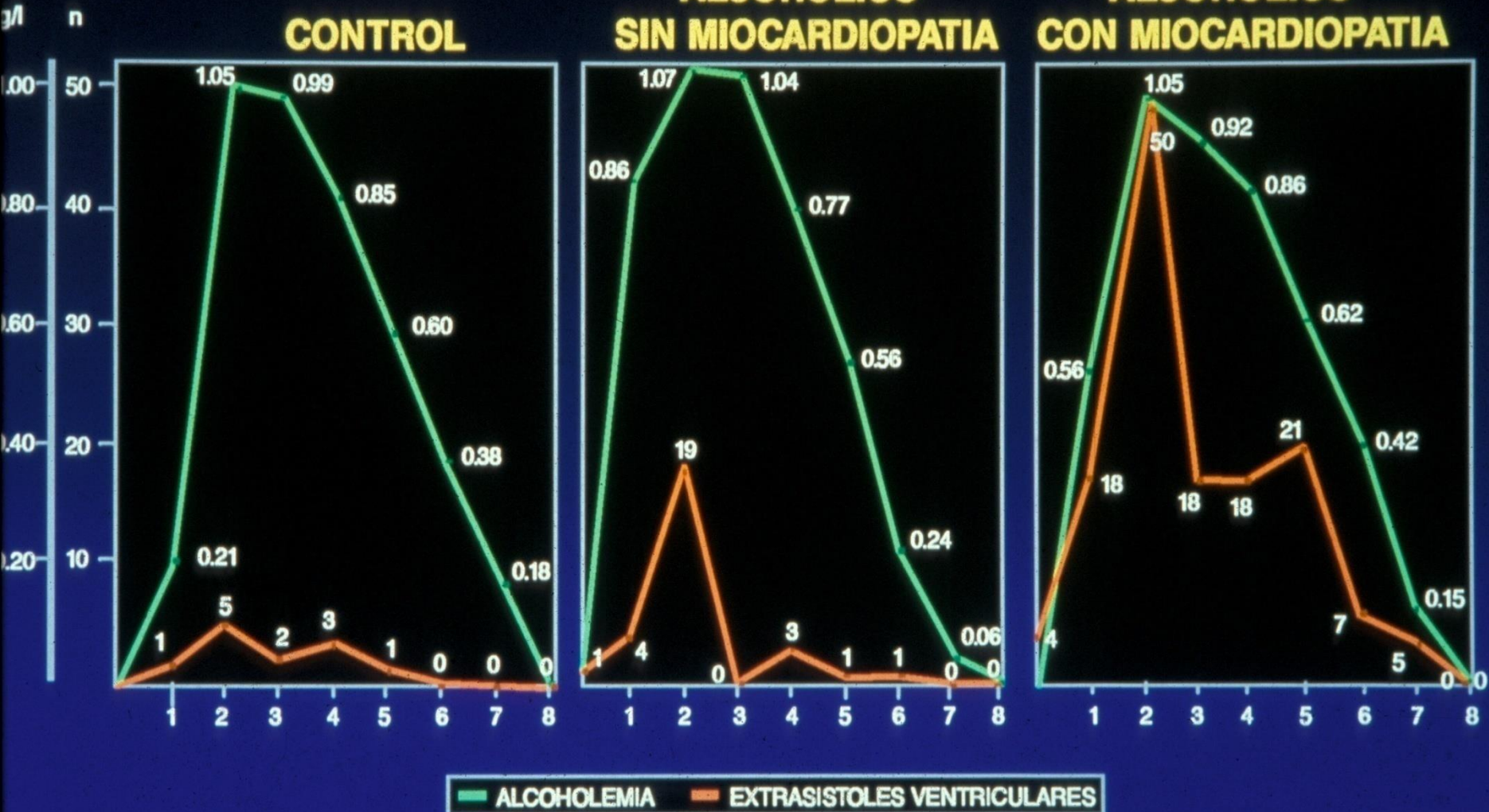
- **Arritmias cardíacas - Síndrome de corazón del fin de semana**
- **Disfunción ventricular**
- **Hipertensión arterial**
- **Muerte súbita**

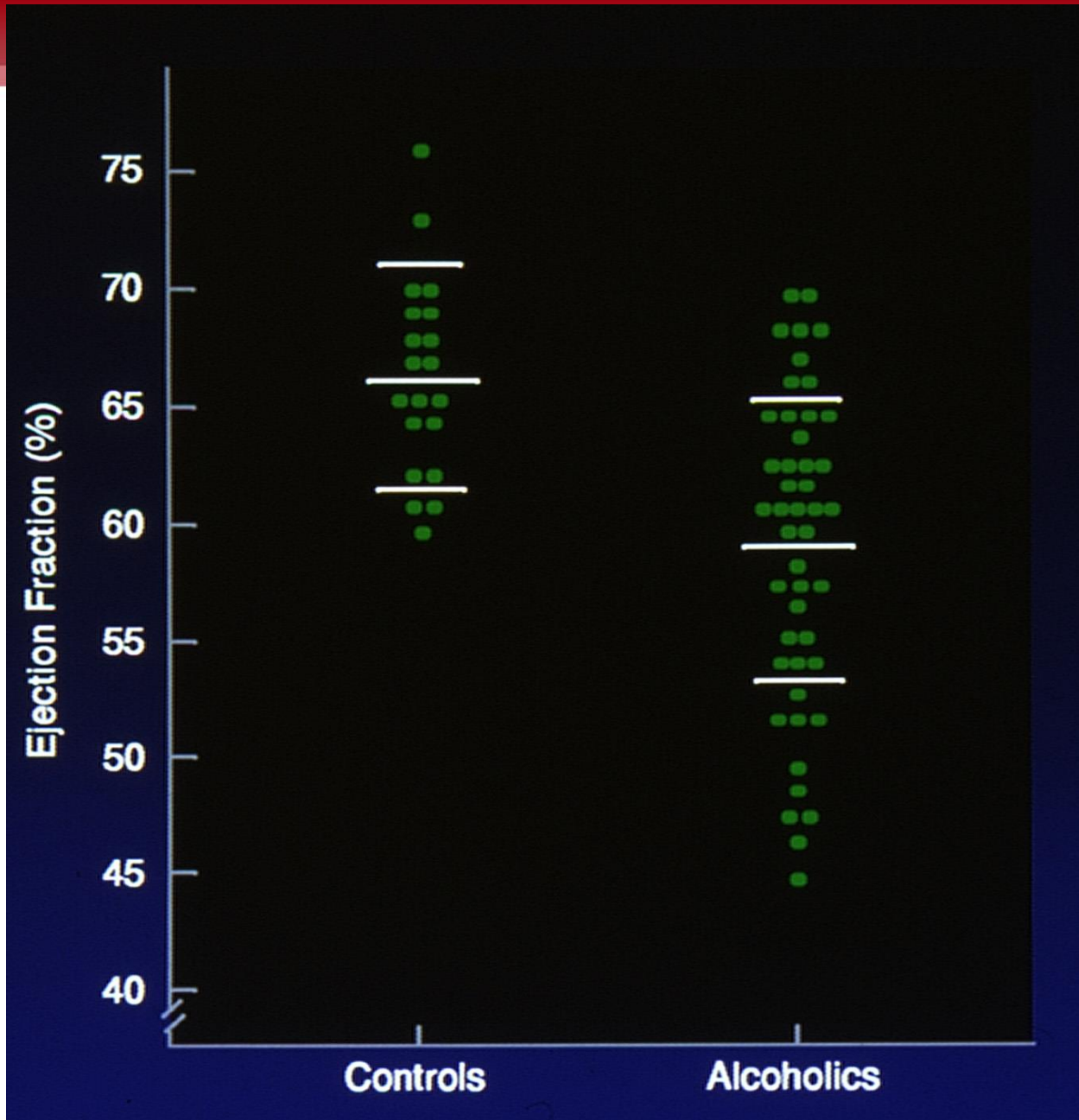
## **EFFECTOS CRÓNICOS**

- **Disfunción sistólica**
- **Disfunción diastólica**
- **Miocardopatía subclínica**
- **Miocardopatía clínica**



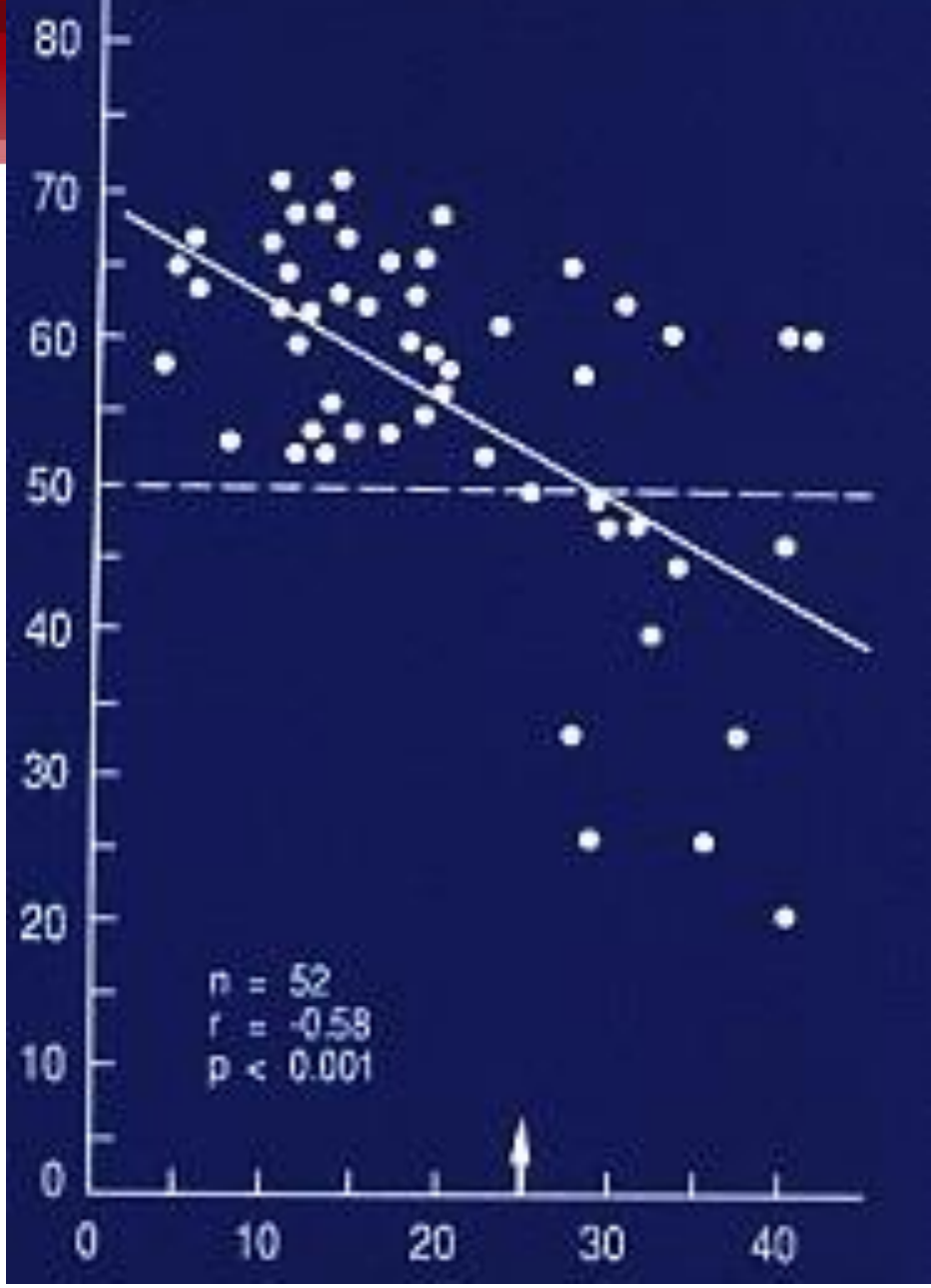
# ARRITMIAS TRAS INGESTA DE ETANOL







Ejection fraction (%)

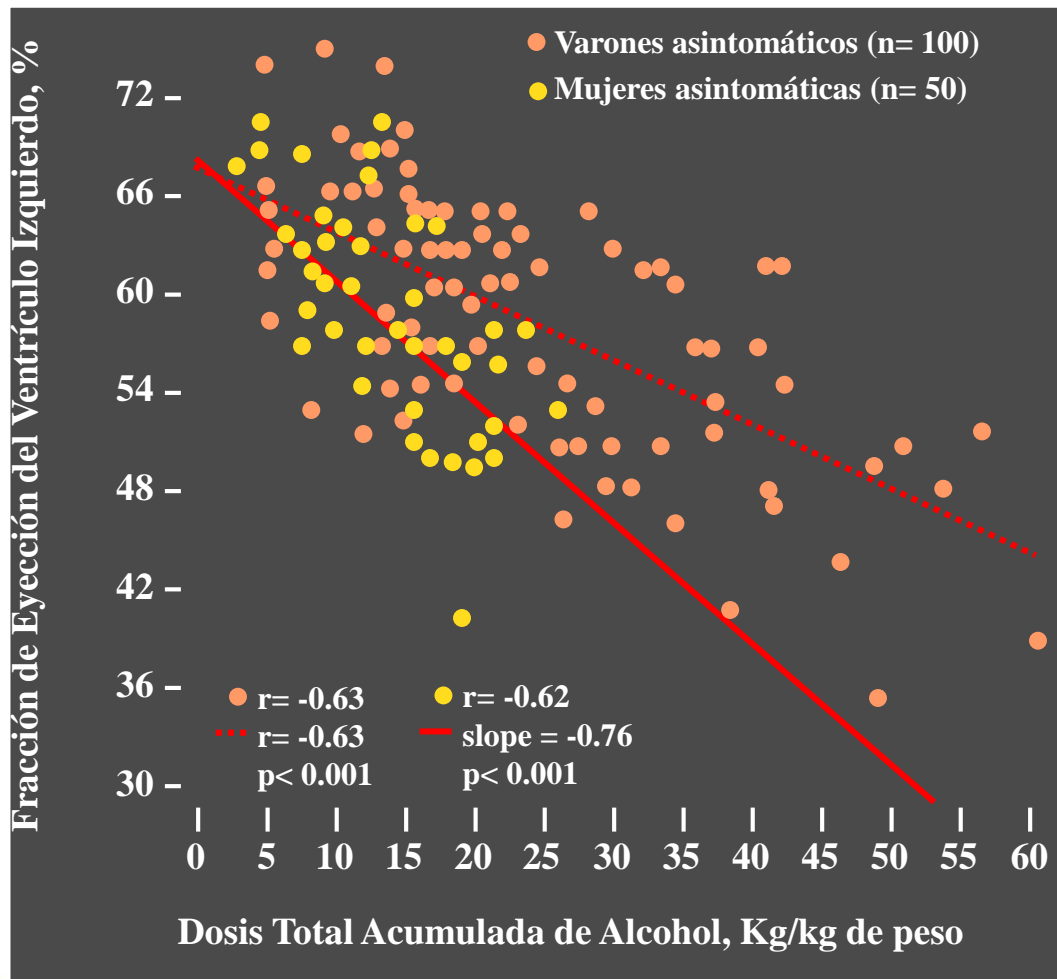


Lifetime dose of ethanol (Kg/Kg)

*N Engl J Med 1989*



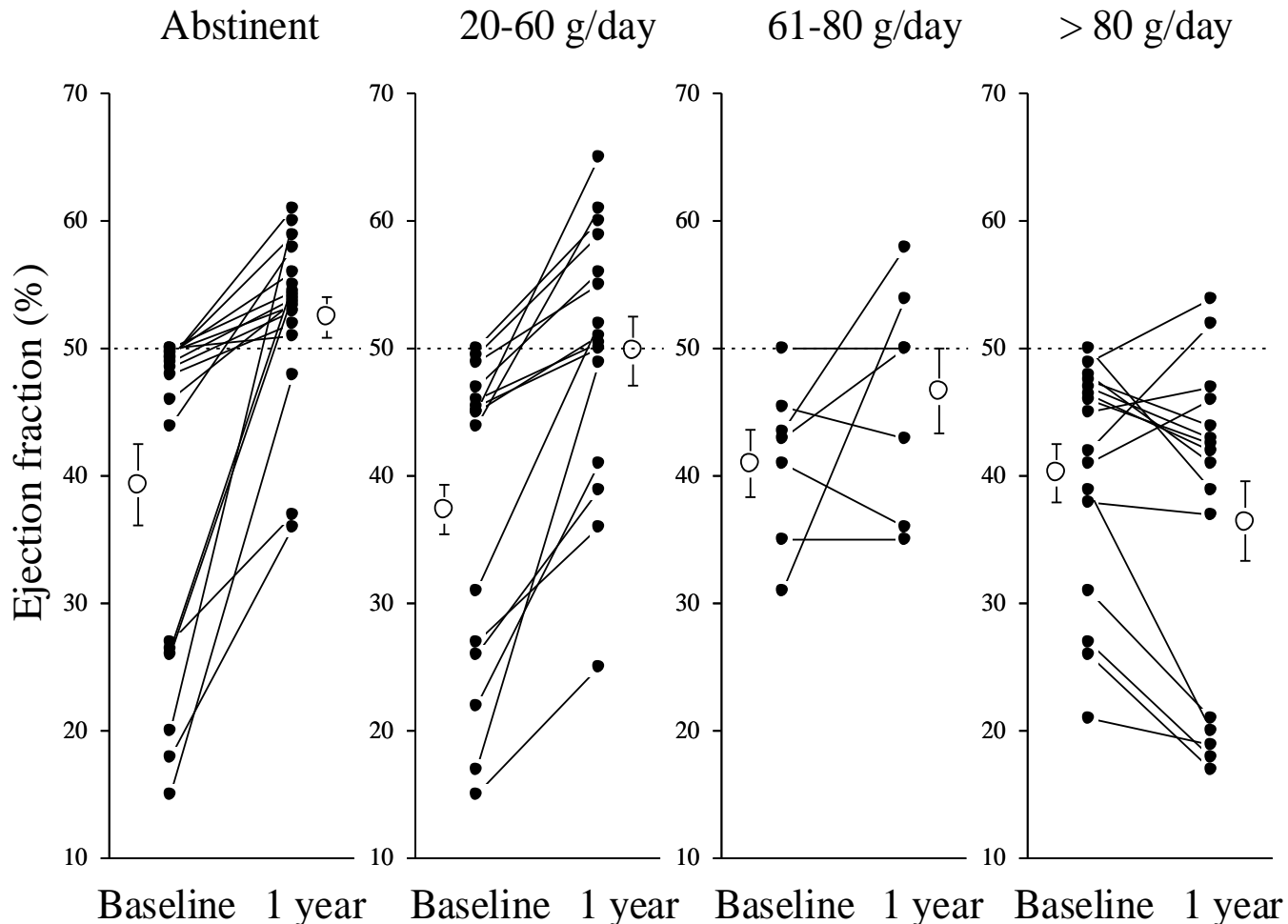
# Efectos Tóxicos sobre el Sistema Cardiovascular



**JAMA 1995**



# INFLUENCE OF ETHANOL ON LV-EF CHANGES



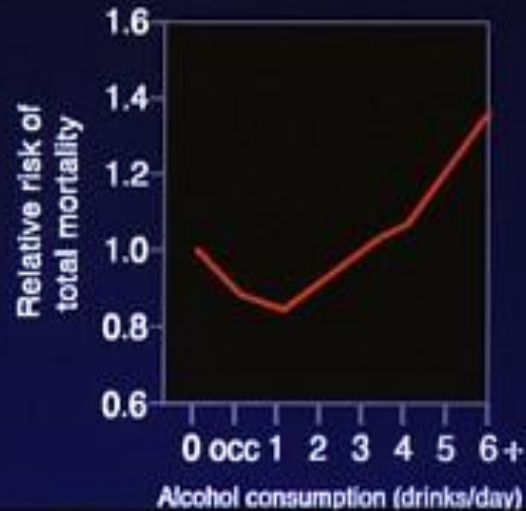
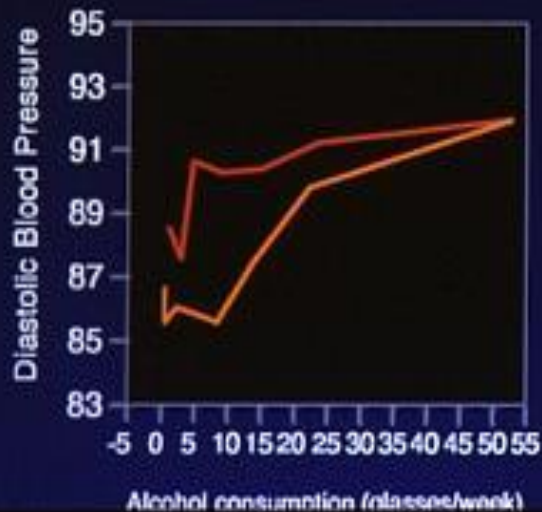
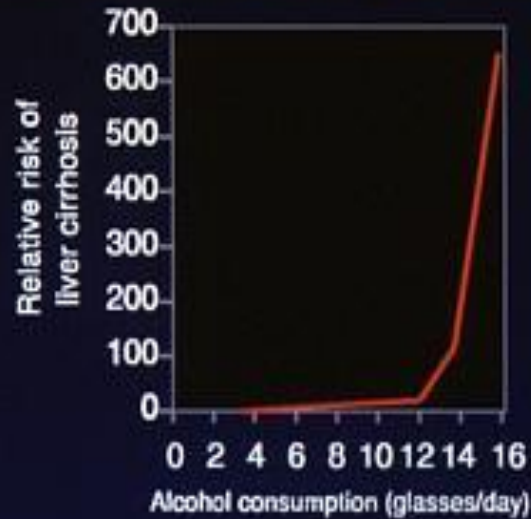
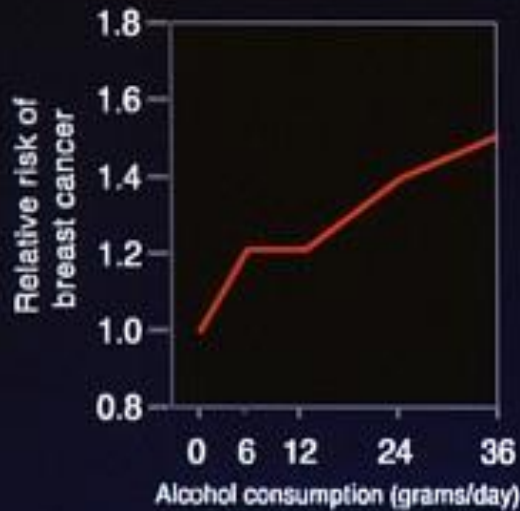


# LA CARA POSITIVA

**CONSUMO MODERADO DE VINO**

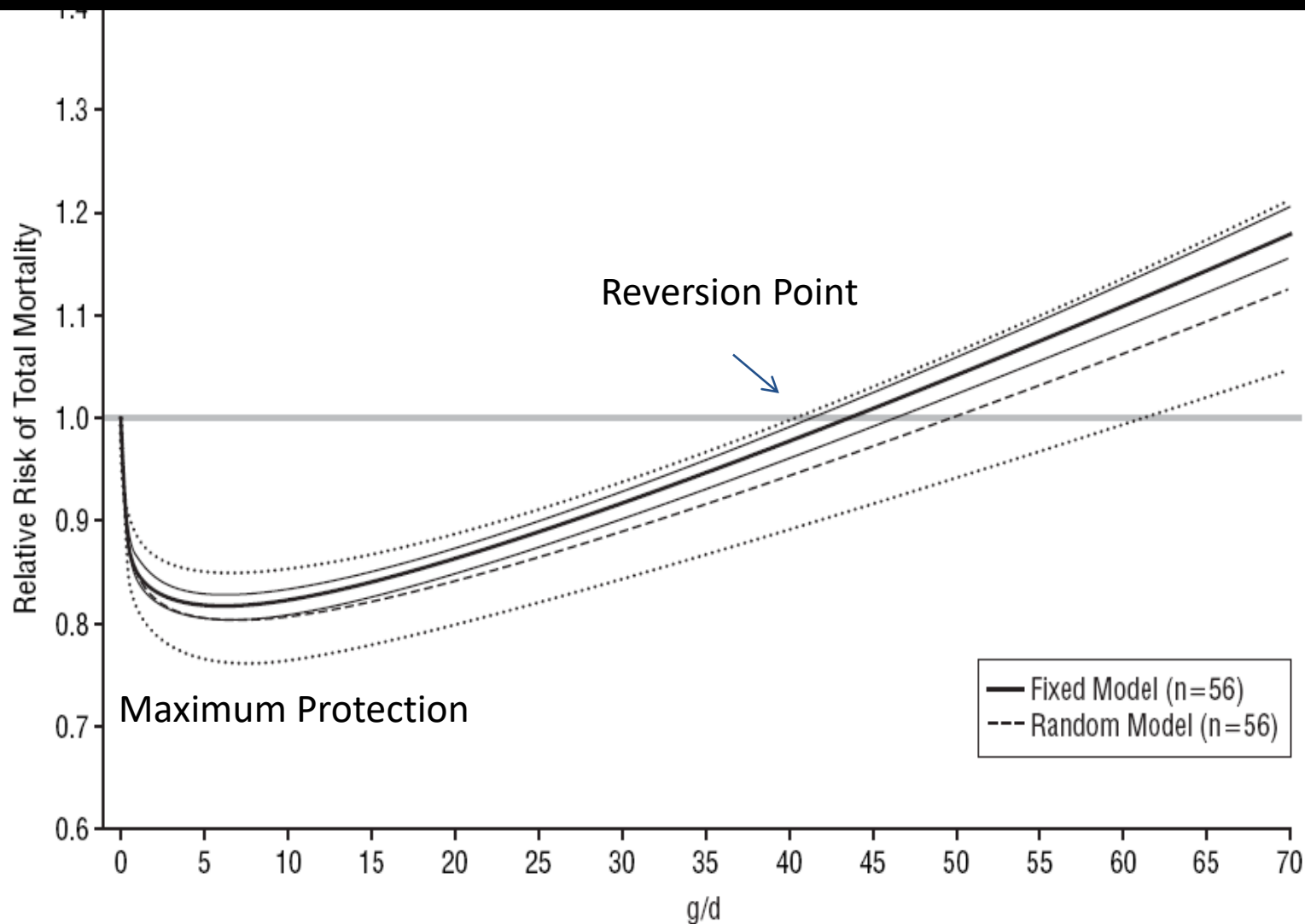
# DOSE-RESPONSE RELATIONSHIP

## ALCOHOL INTAKE vs ALCOHOL-RELATED OUTCOMES



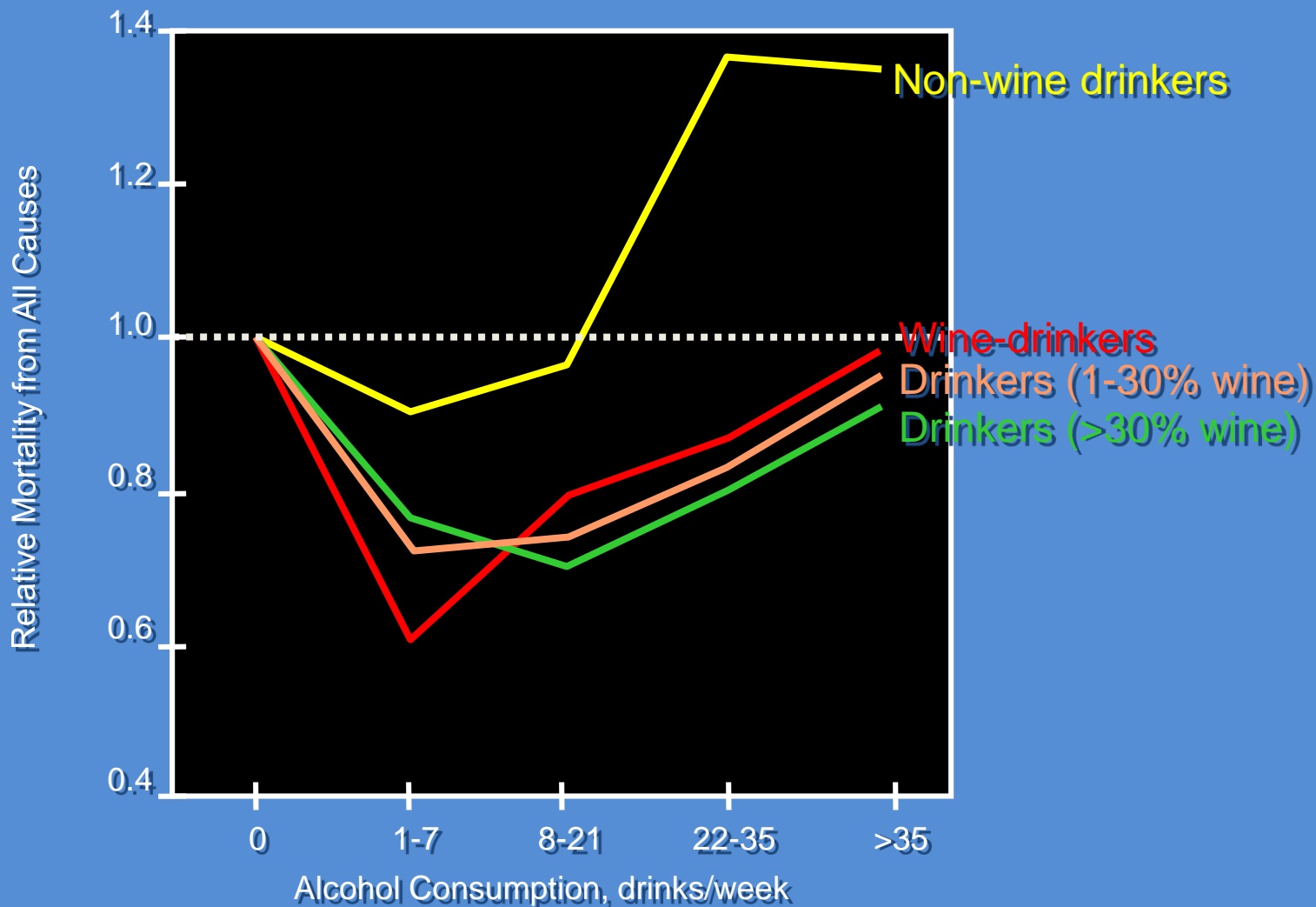


# ALCOHOL CONSUMPTION AND MORTALITY FOR ANY CAUSE



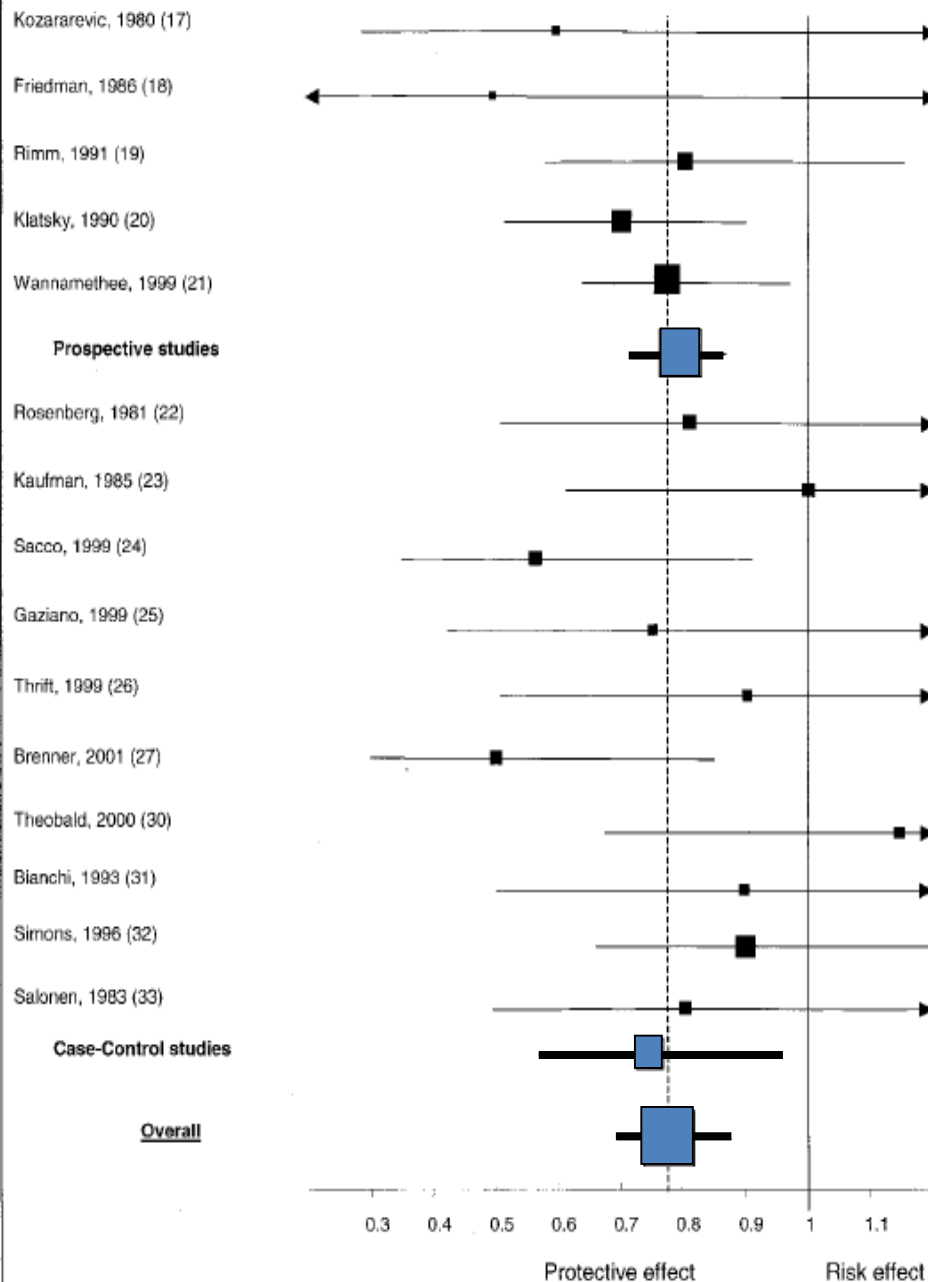
Thirty-four studies provided 56 independent dose-response curves for a total of 1,015,835 subjects and 94,533 deaths from any cause. The association with a lower mortality was apparent up to 42 g/d and the lowest mortality was seen at 6 g/d, (RR, 0.81 [CI, 0.80-0.83]).

# RELATIVE RISK FOR DEATH FROM ALL CAUSES IN RELATION TO TOTAL ALCOHOL INTAKE



Relative risk is set at a 1.0 among non drinkers (<1 drinks/week)

Ann Intern Med 2000



# Meta-analysis: Consumption of different alcoholic beverages and vascular risk

## Reduction of vascular risk

- **Wine: -32%**
- **Beer: -22%**

# Possible Mechanisms of Beneficial Effects of Moderate Consumption of Alcohol

## Prevention of arterial lesions

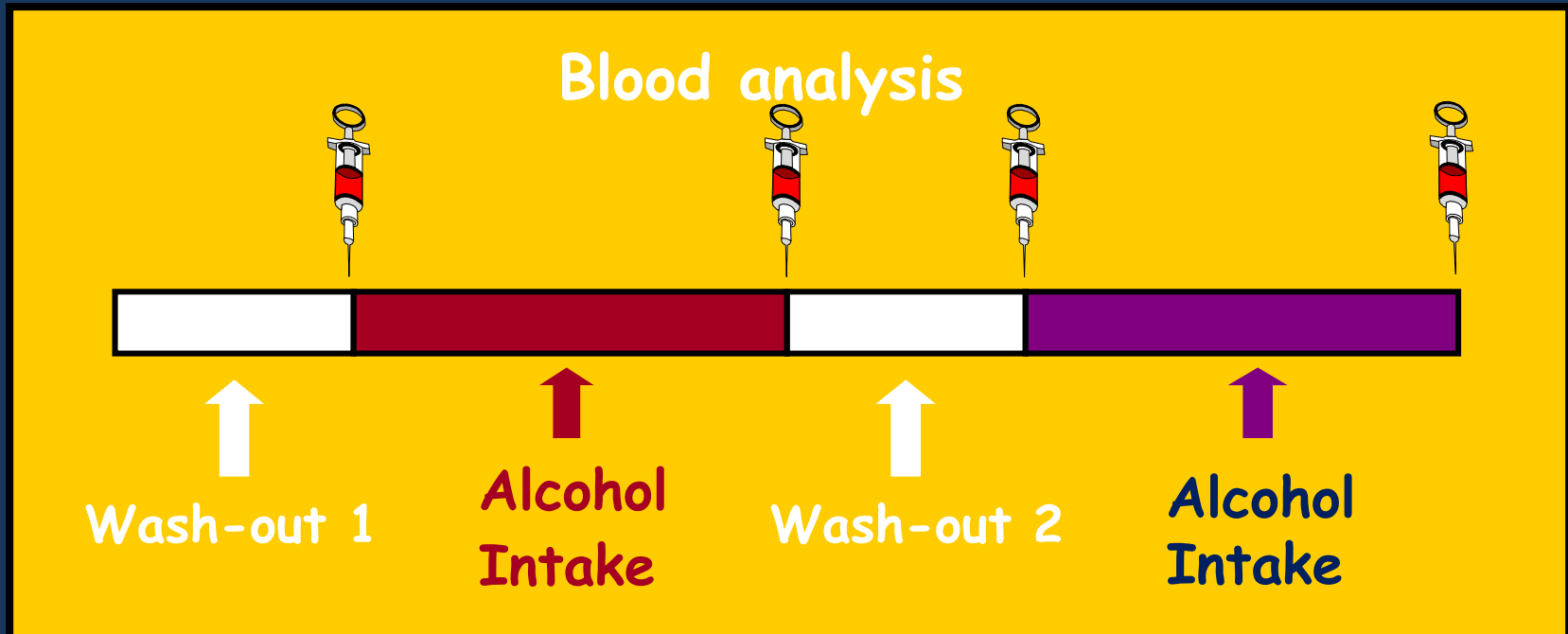
- Increase in HDL-cholesterol
- Reduction in the oxidation of LDL- cholesterol particles
- Changes in the endothelium of arterial wall
- Improving insulin sensitivity or others

## Prevention of arterial thrombosis

- Reduction of platelet aggregation
- Inhibition of clot formation
- Activation of fibrinolytic system

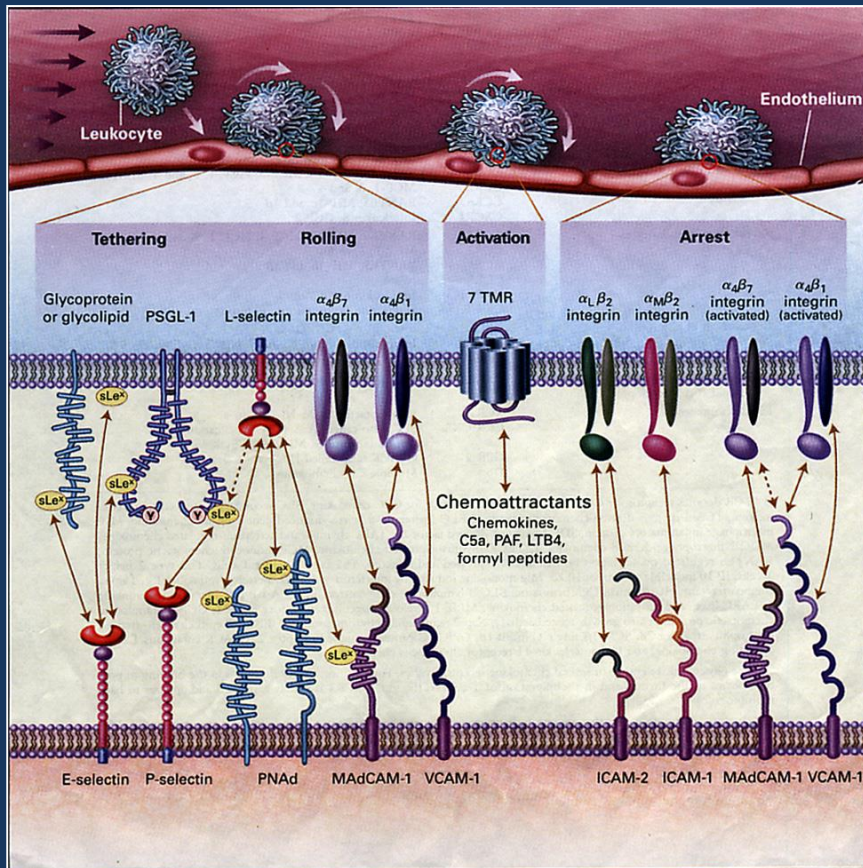
# Methodology

**Design: Randomized prospective cross-over clinical trials**



- Consumption of 20 (women) - 30 (men) g/day of alcohol
- Comparisons: Polyphenol-rich alcoholic beverage vs polyphenol-poor alcoholic beverage.

# LYMPHOCYTE AND MONOCYTE ADHESION MOLECULES AND CHEMOKINES



- LYMPHOCYTE FUNCTION-ASSOCIATED ANTIGEN – 1 (LFA-1)
- MAC – 1
- VERY LATE ACTIVATION ANTIGEN – 4 (VLA-4)
- CD40 , CD45
- SYALIL-LEWIS
- MONOCYTE CHEMOTACTIC PEPTIDE -1 (MCP-1)

# Adhesion Molecules Analysis in Lymphocytes and Monocytes

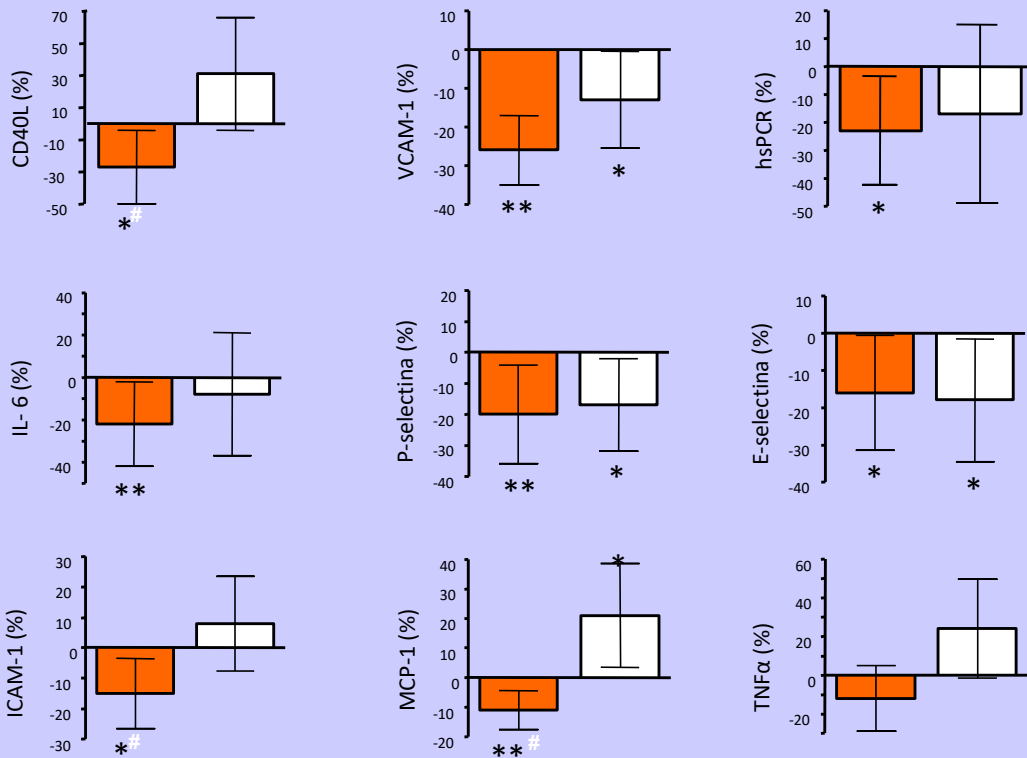
	Alcohol - PP		Alcohol + PP	
	Before	After	Before	After
<b>T lymphocytes</b>				
LFA <sub>1</sub> (MFI)	126.3 ± 47.8	135.7 ± 40.6	139.4 ± 34.7	142.7 ± 26.4
VLA <sub>4</sub> (MFI)	32.0 ± 8.3	33.9 ± 9.8	36.2 ± 7.5	31.2 ± 7.5
<b>Monocytes</b>				
LFA <sub>1</sub> (MFI)	192.8 ± 89.4	255.4 ± 117.4	187.5 ± 44.2	136.6 ± 44.2
Mac <sub>1</sub> (MFI)	88.4 ± 45.6	97.9 ± 65.8	78.0 ± 37.0	57.2 ± 27.9
VLA <sub>4</sub> (MFI)	41.4 ± 17.1	53.4 ± 28.9	44.1 ± 21.3	29.7 ± 10.6
MCP <sub>1</sub> (MFI)	27.9 ± 24.5	24.7 ± 16.1	31.4 ± 20.7	17.0 ± 10.4

P ≤ 0.05

P ≤ 0.001



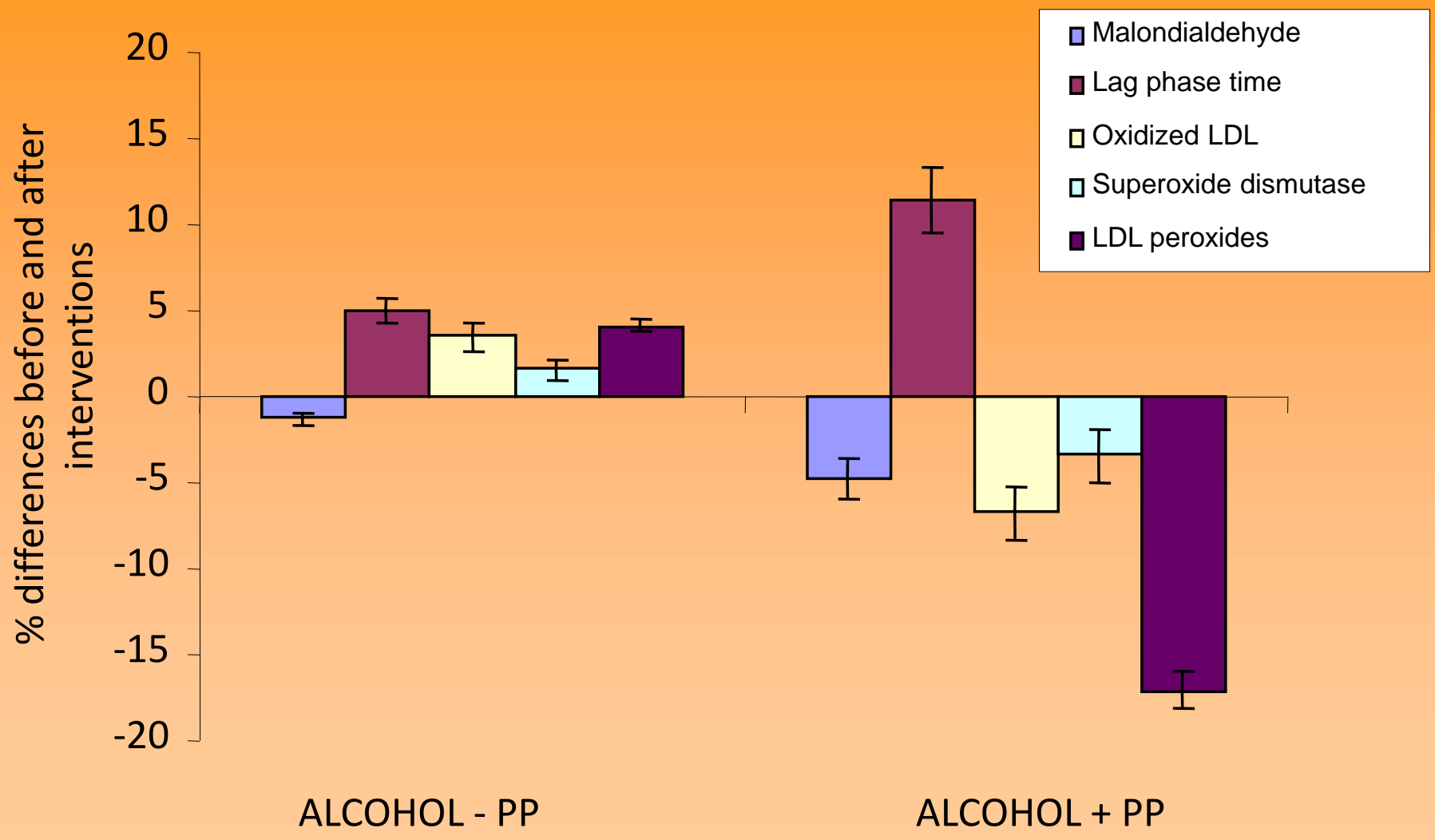
# Changes in adhesion molecules and other inflammatory markers



\* $P < 0.05$   
 \*\* $P < 0.01$   
 #  $P < 0.05$

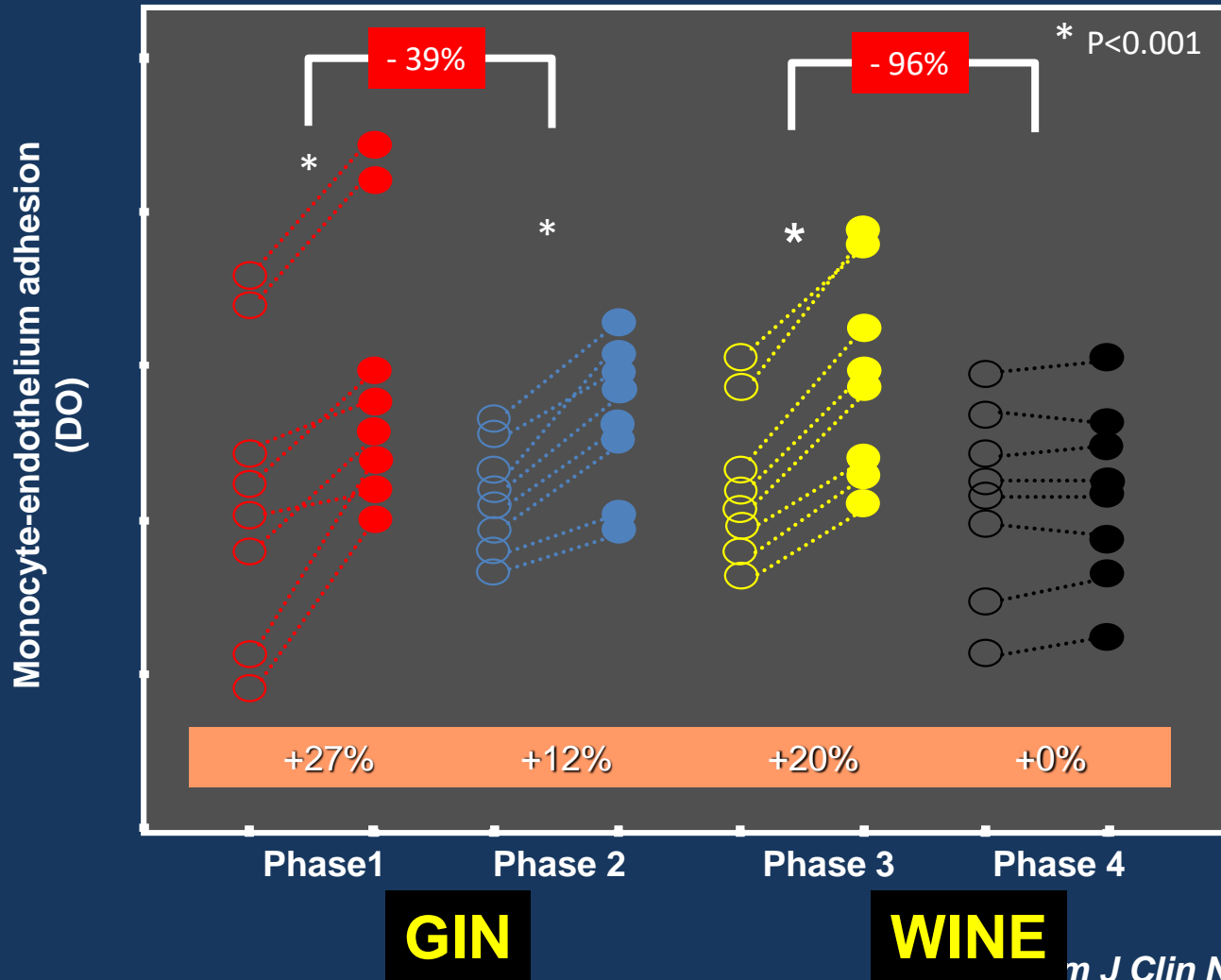
Alcohol - PP  
 Alcohol + PP

# EFFECTS OF ALCOHOLIC BEVERAGES WITH AND WITHOUT POLYPHENOLS ON OXIDATIVE STRESS

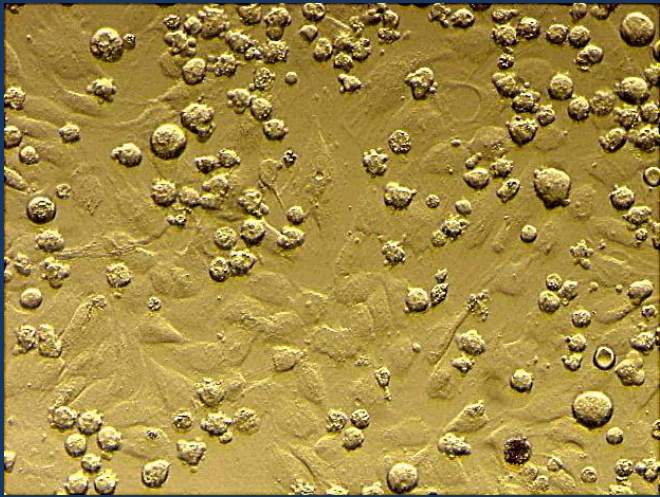


# Alcohol and Arteriosclerosis

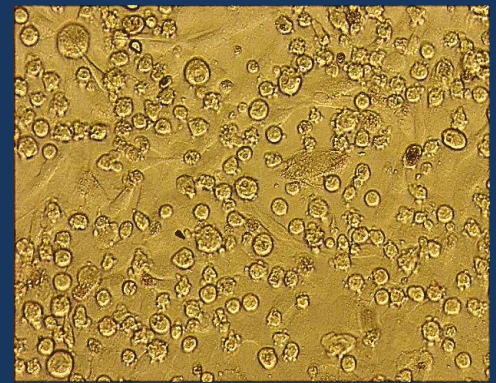
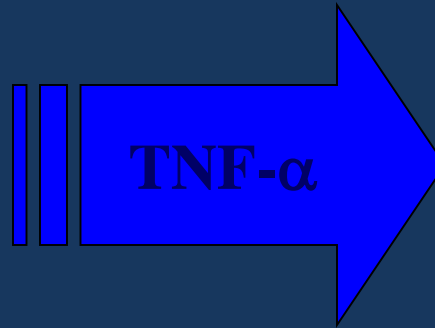
Values of monocyty adhesion to an endothelial line in basal conditions and following stimulation with TNF- $\alpha$



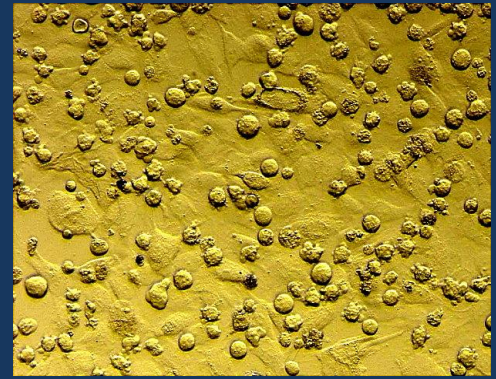
# ASSAY OF MONOCYTE- ENDOTHELIAL ADHESION (endothelial line Ea.Hy926)



**BASELINE**



**WASH-OUT**



**GIN**



**RED WINE**

# STUDY DESIGN

- Open
- Crossover
- Randomized



Volunteers

WASH OUT  
15 days

## Interventions:

- RW: 272mL red wine (30g OH)
- DRW: 272mL dealcoholized red wine
- G: 100mL gin (30g OH)

1<sup>st</sup> INTERVENTION 2<sup>nd</sup> INTERVENTION 3<sup>rd</sup> INTERVENTION



28 days



28 days



28 days

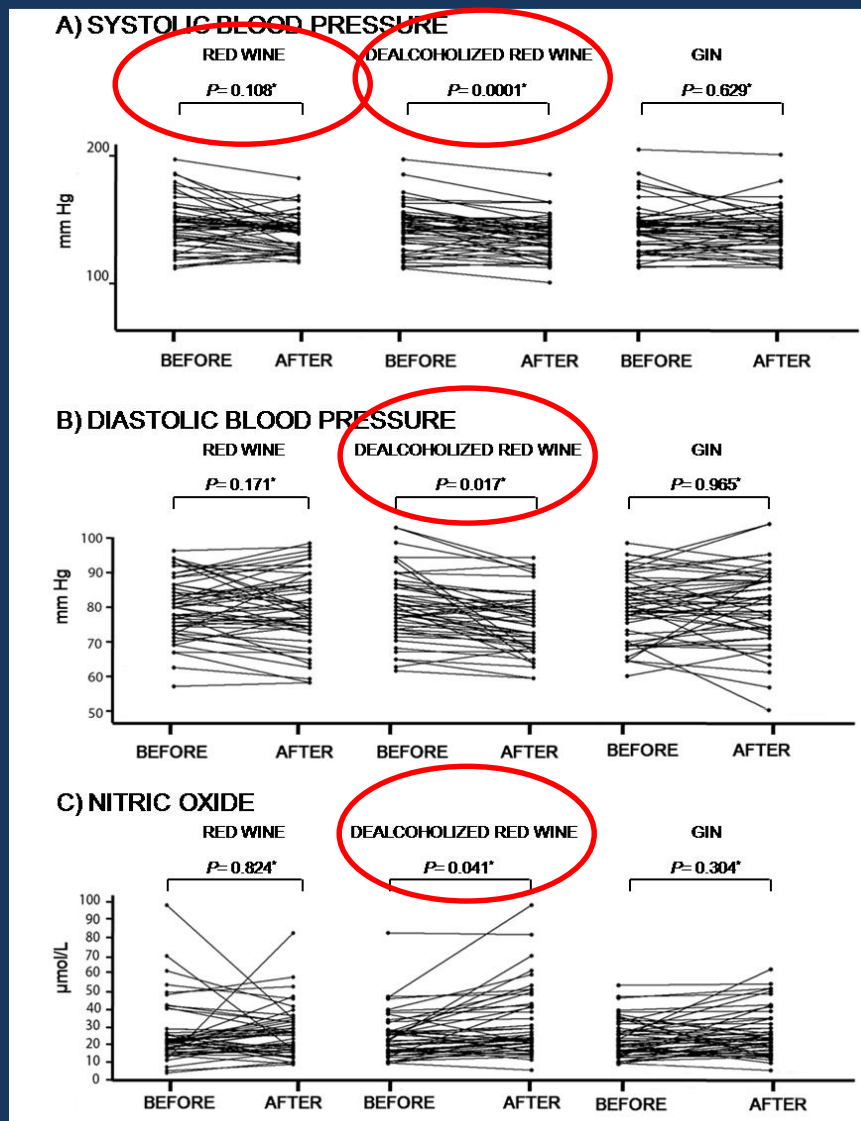
Baseline  
Samples

1<sup>st</sup> Intervention  
Samples

2<sup>nd</sup> Intervention  
Samples

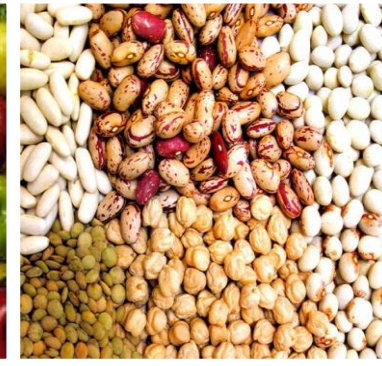
3<sup>rd</sup> Intervention  
Samples

# EFFECTS OF WINE POLYPHENOL ON BLOOD PRESSURE (I)





# Efectos de la Dieta Mediterránea en la Prevención Primaria de la Enfermedad Cardiovascular (Estudio PREDIMED)







# Sample Size and Randomization



7,447 participantes



Dieta Mediterránea  
Aceite Oliva Virgen Extra  
(1L/semana)

n=2.543



Dieta Mediterránea  
Frutos Secos  
(30g/día)

n=2.454



Dieta Baja en Grasa  
“American Heart  
Association guidelines”

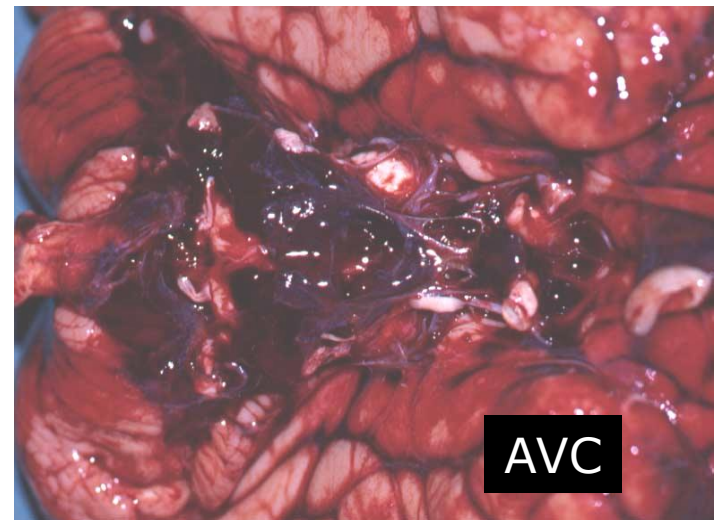
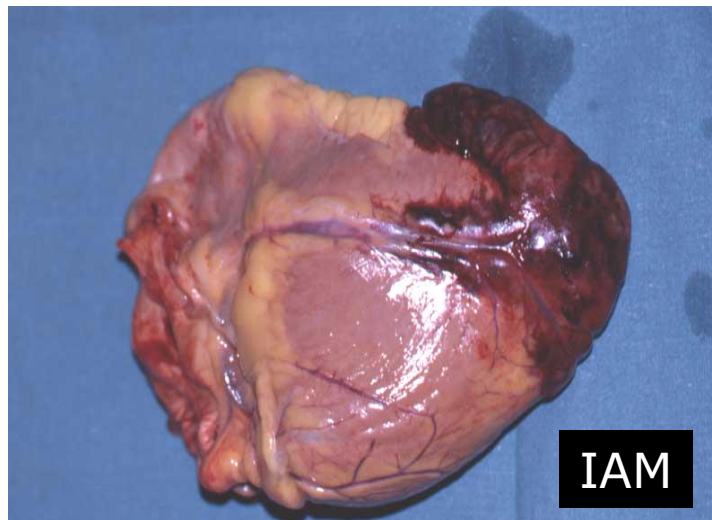
n=2.450

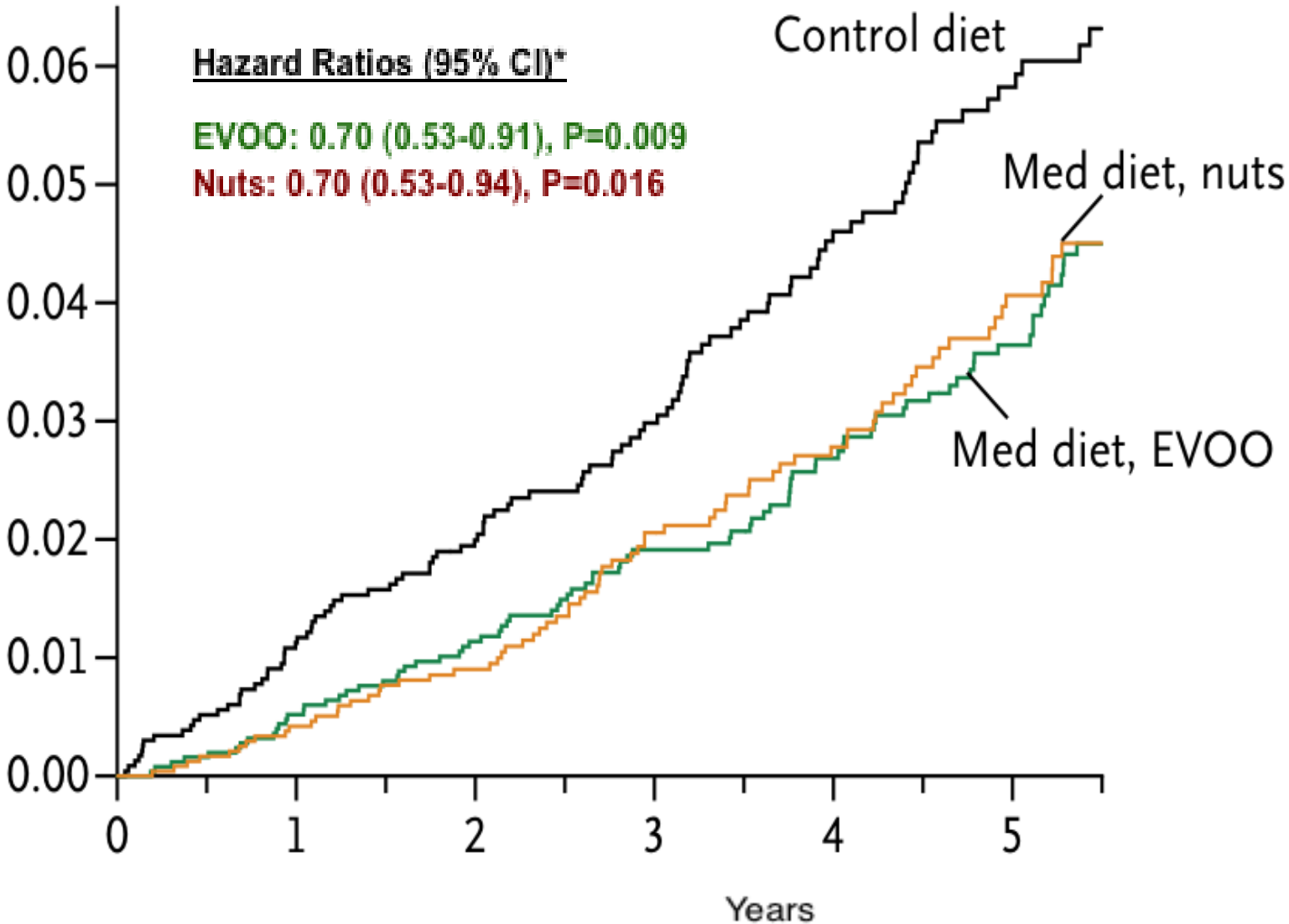


# Variables Finales

## VARIABLES PRIMARIAS

**Muerte Cardiovascular**  
**Infarto Agudo de Miocardio**  
**Accidente Vascular Cerebral**





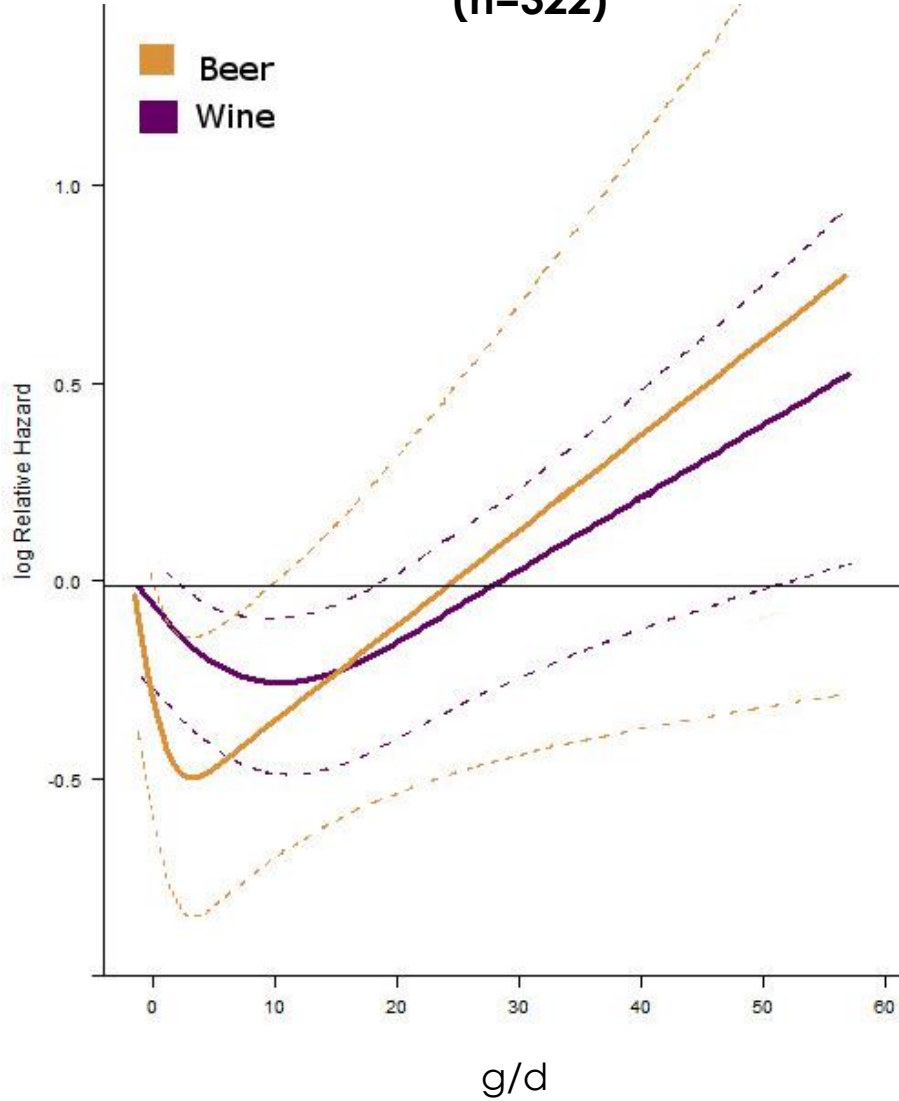
**Number at risk**

Control group	2450	2268	2020	1583	1268	946
MeDiet+EVOO	2543	2486	2320	1987	1687	1310
MeDiet+Nuts	2454	2343	2093	1657	1389	1031

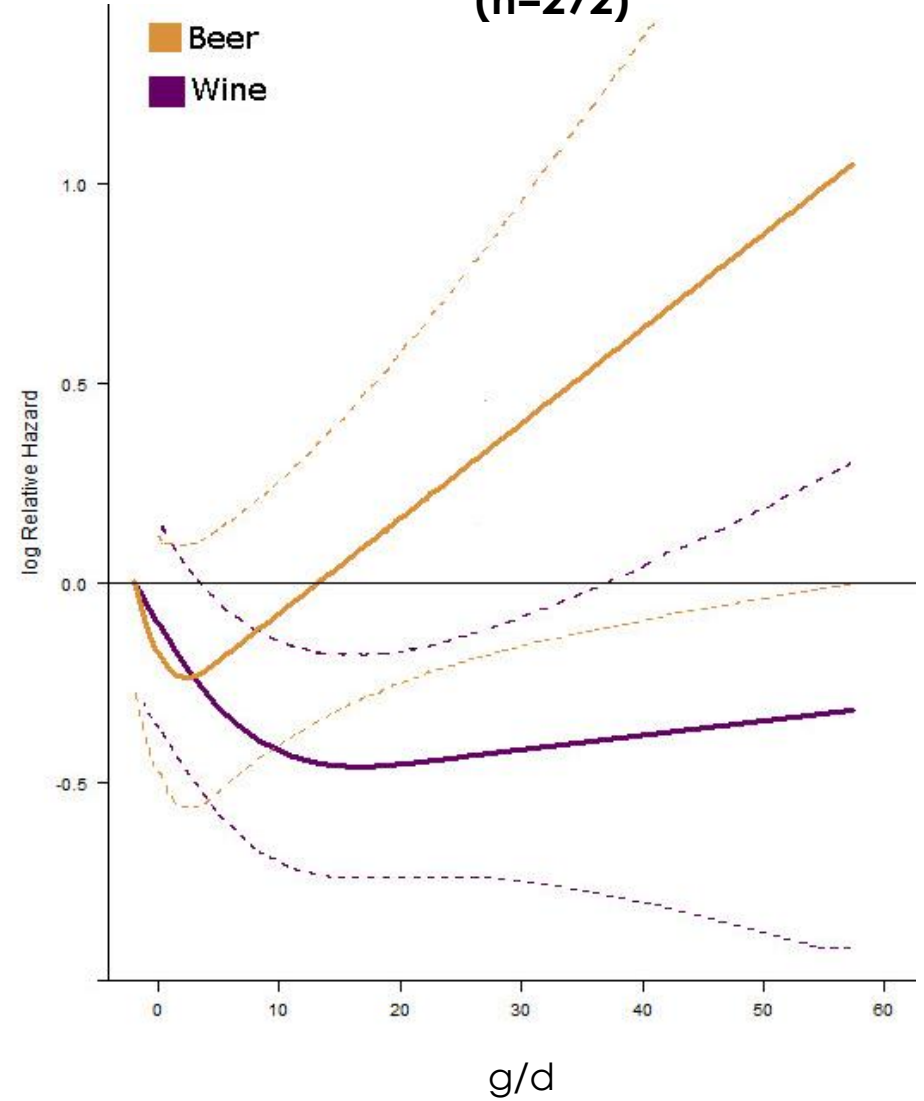


# EFFECTOS DEL VINO SOBRE LAS VARIABLES FINALES

## Total mortality (n=322)

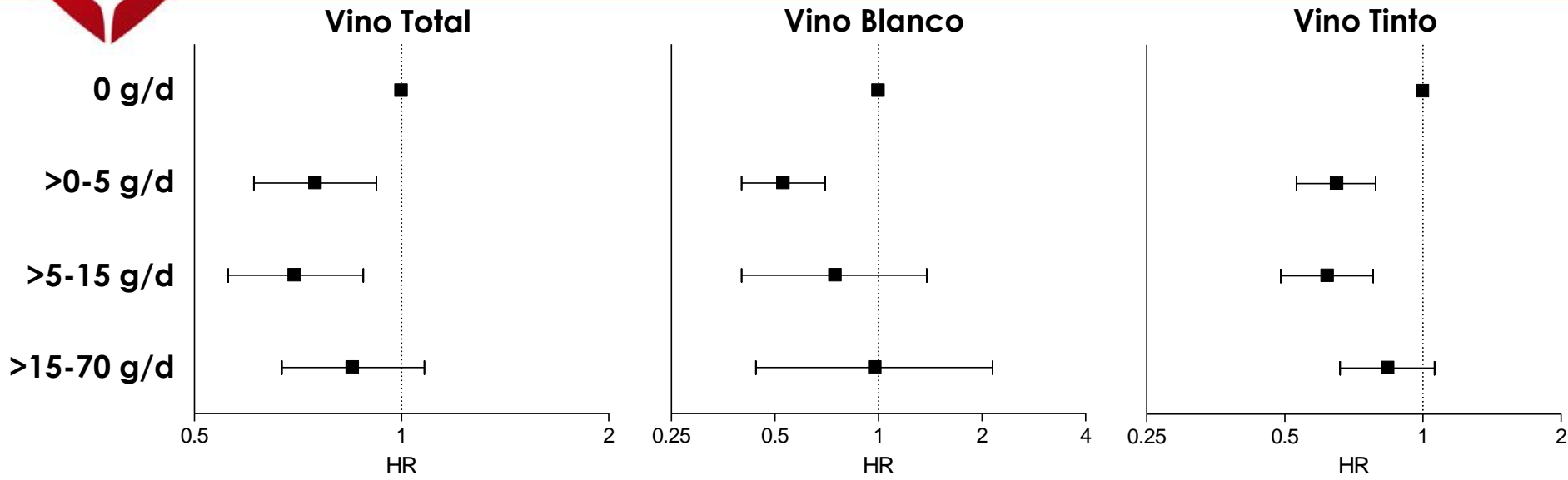


## Cardiovascular event (n=272)



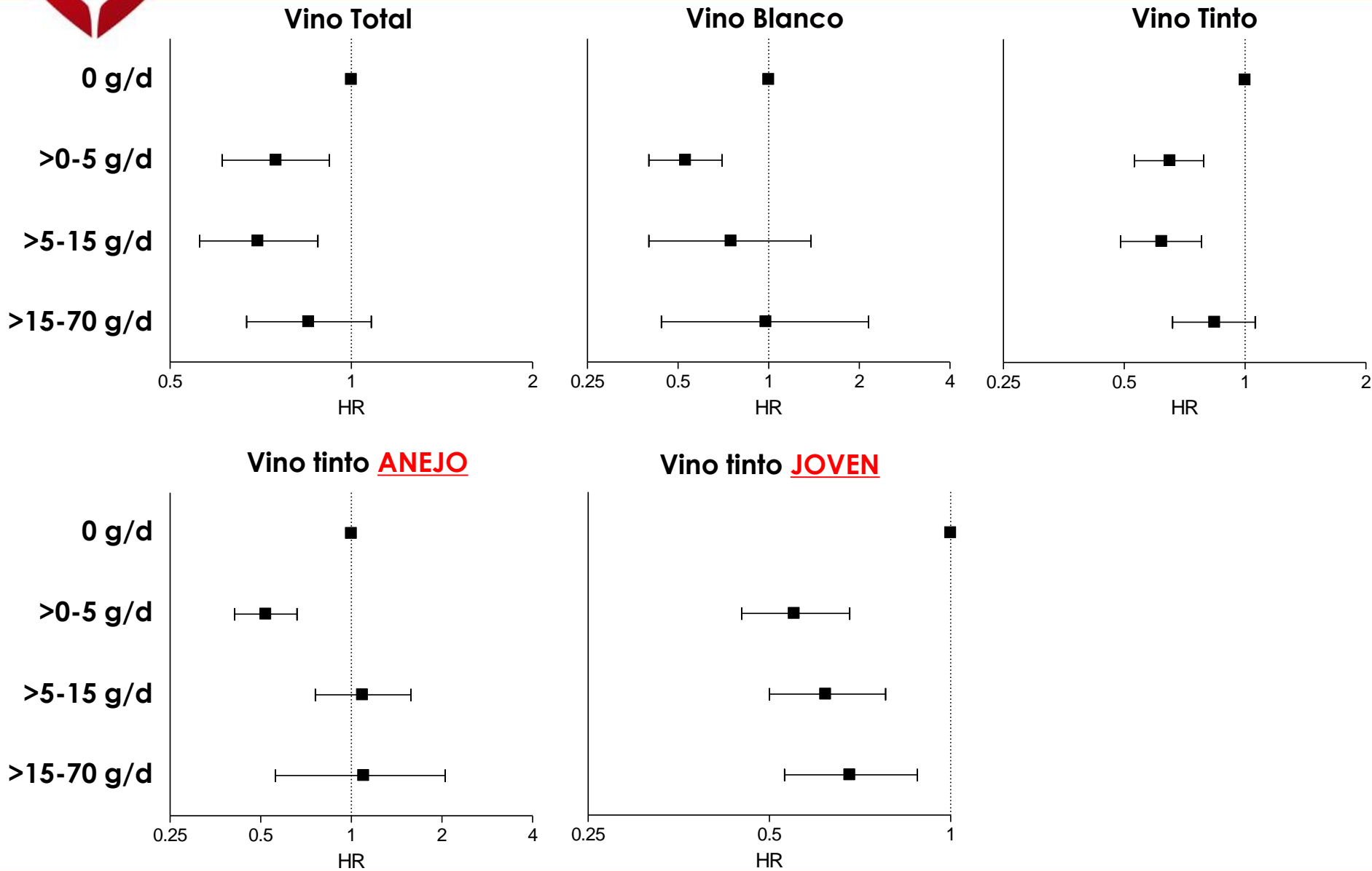


# TODOS LOS VINOS SON IGUALES ? EF. MORTALIDAD TOTAL





# TODOS LOS VINOS SON IGUALES ? EF. MORTALIDAD TOTAL

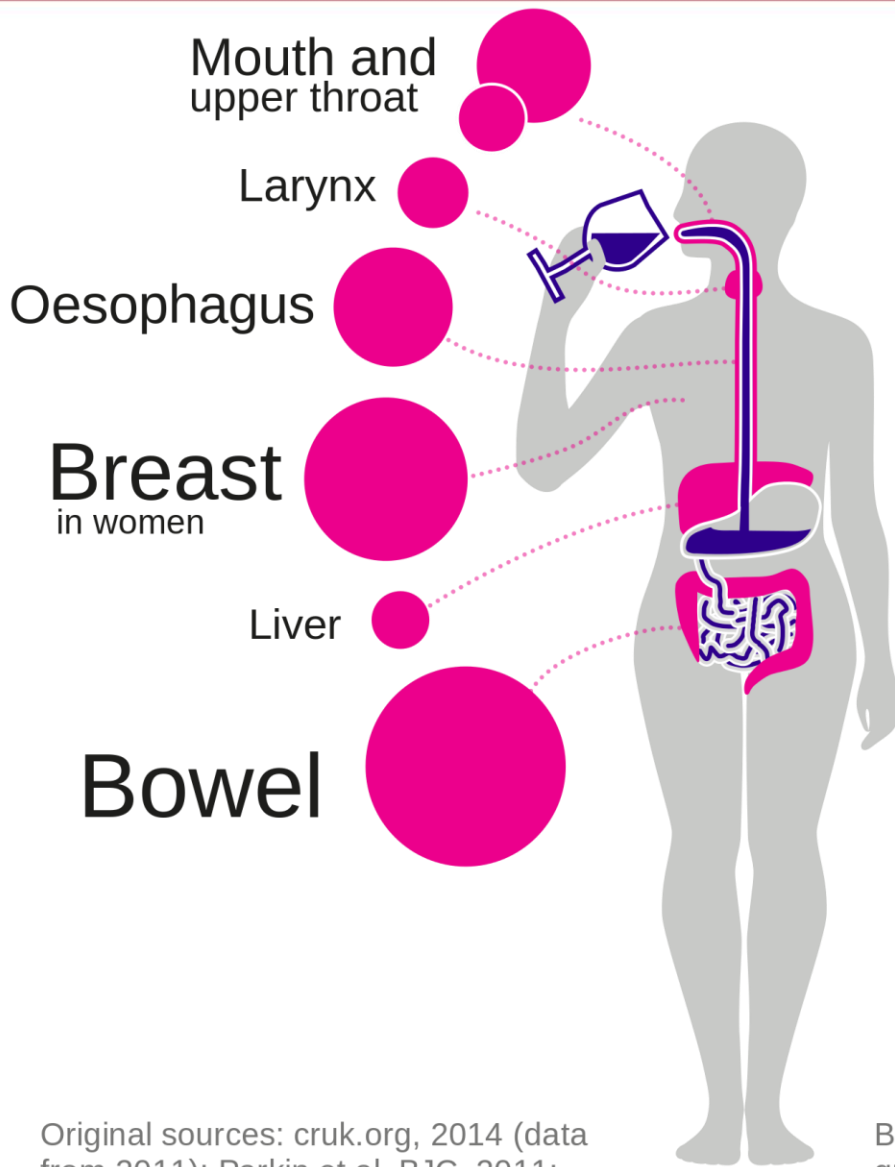




# ALCOHOL Y CÁNCER



# ALCOHOL: CAUSA DE 7 TIPOS DE CÁNCER



## 4 WAYS ALCOHOL CAUSES CANCER

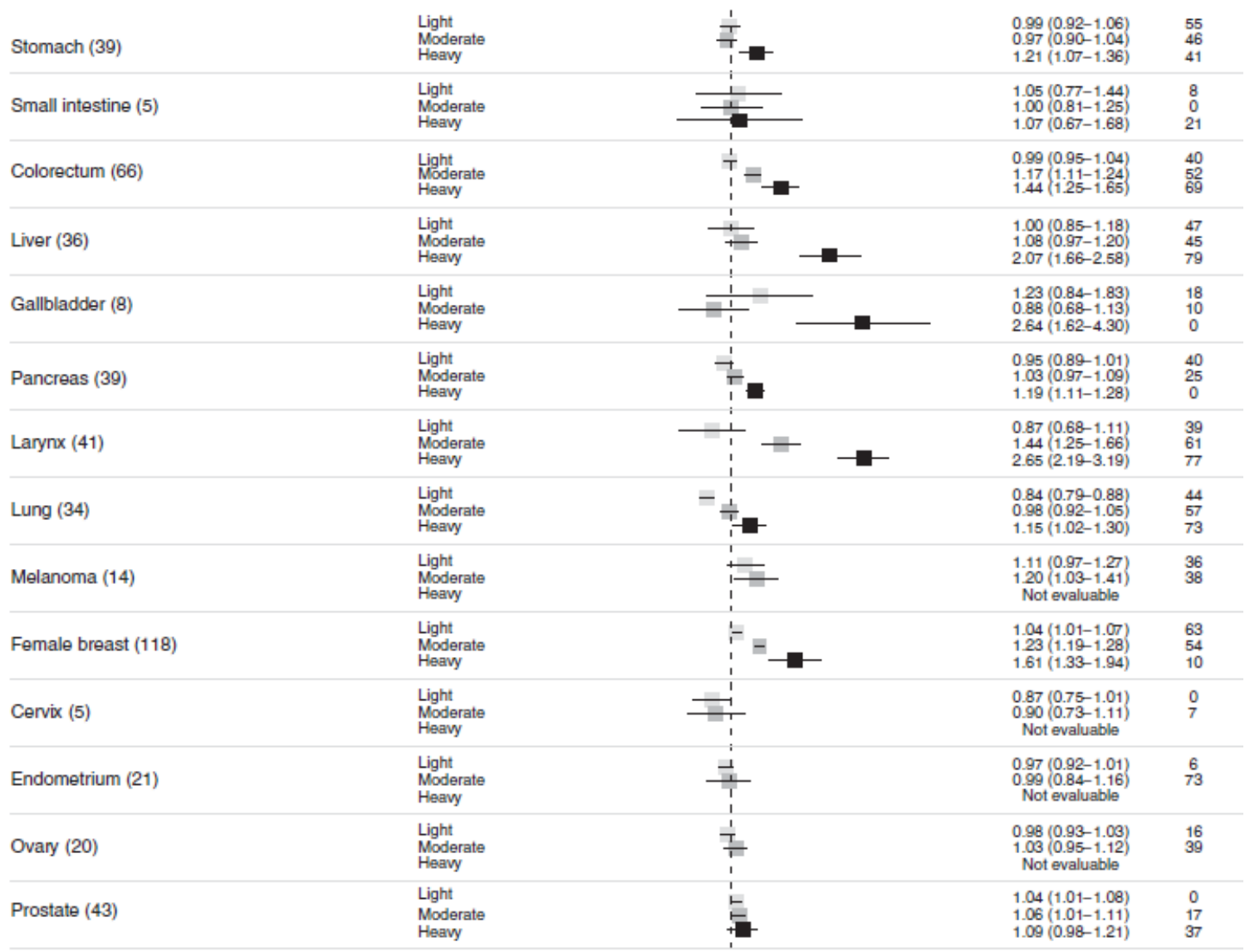
- Damages cells
- Increases damage from tobacco
- Affects hormones linked to breast cancer
- Breaks down into cancer-causing chemicals

Original sources: cruk.org, 2014 (data from 2011); Parkin et al, BJC, 2011;

Based on a Cancer Research UK graphic published in 2014



# META-ANALYSIS DE ALCOHOL Y CANCER





# CONSUMO MEDIO SEMANAL DE VINO/ALCOHOL



Cancer Causes Control (2016) 27:1049–1058  
DOI 10.1007/s10552-016-0778-6

ORIGINAL PAPER

## CONSUMO Diario vs. Semanal

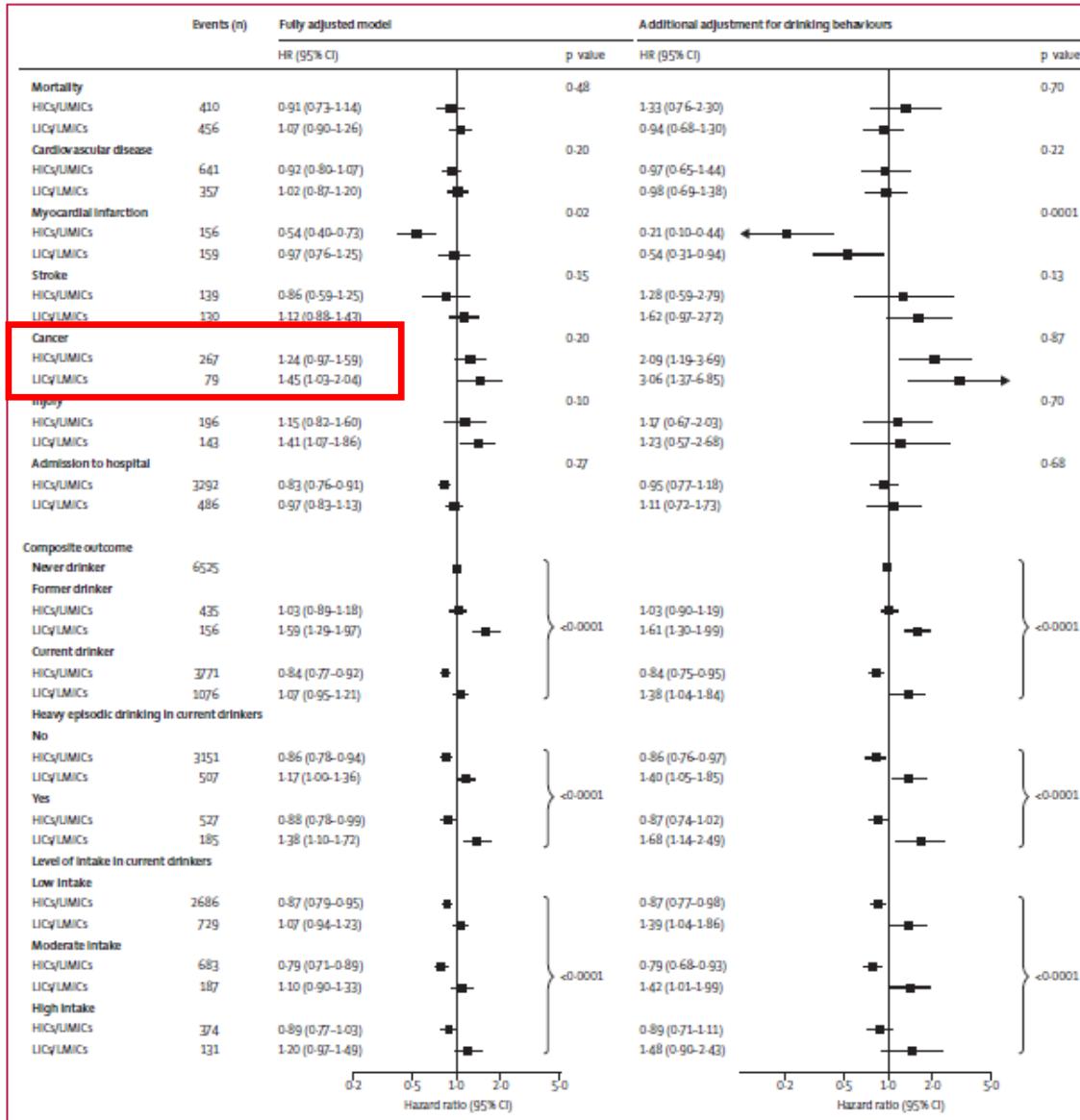
### Alcohol intake, drinking patterns, and prostate cancer risk and mortality: a 30-year prospective cohort study of Finnish twins

Barbra A. Dickerman<sup>1</sup> · Sarah Coseo Markt<sup>1</sup> · Markku Koskenvuo<sup>2</sup> ·  
Eero Pukkala<sup>3,4</sup> · Lorelei A. Mucci<sup>1</sup> · Jaakko Kaprio<sup>2,5,6</sup>

**Table 2** Average weekly alcohol consumption category (average of 1975 and 1981), binge drinking status (1981), and prostate cancer risk and mortality (HR, 95 % CI), Older Finnish Twin Cohort, 1981–2012

	Person-years	Prostate cancer incidence				Prostate cancer-specific mortality					
		No. events	Age-adjusted		Fully adjusted <sup>a</sup>		No. events	Age-adjusted		Fully adjusted <sup>a</sup>	
			HR	95 % CI	HR	95 % CI		HR	95 % CI	HR	95 % CI
<b>Alcohol consumption category<sup>b</sup></b>											
Light drinkers	89,453	185	1.00 (ref)		1.00 (ref)		33	1.00 (ref)		1.00 (ref)	
Abstainers <sup>c</sup>	18,993	56	1.21	0.90, 1.62	1.27	0.94, 1.71	17	<b>1.95</b>	<b>1.10, 3.48</b>	<b>1.90</b>	<b>1.04, 3.47</b>
Moderate drinkers	135,646	266	<b>1.26</b>	<b>1.05, 1.52</b>	1.20	0.99, 1.46	45	1.24	0.79, 1.93	1.22	0.76, 1.97
Heavy drinkers	45,250	94	<b>1.55</b>	<b>1.21, 1.99</b>	<b>1.46</b>	<b>1.12, 1.91</b>	15	1.47	0.79, 2.73	1.32	0.66, 2.62
<b>Binge drinking status<sup>d</sup></b>											
No	145,568	326	1.00 (ref)		1.00 (ref)		60	1.00 (ref)		1.00 (ref)	
Yes	122,088	206	<b>1.35</b>	<b>1.12, 1.61</b>	<b>1.28</b>	<b>1.06, 1.55</b>	27	1.01	0.63, 1.60	0.87	0.52, 1.45

# CURRENT DRINKING AND OUTCOMES BY INCOME REGION



## Alcohol consumption and cardiovascular disease, cancer, injury, admission to hospital, and mortality: a prospective cohort study



Andrew Smyth, Koon K Teo, Sumathy Rangarajan, Martin O'Donnell, Xiaohu Zhang, Punam Rana, Danyil P Loong, Gilles Dagenais, Pamela Seaton, Amika Koenigsmann, Aletta E Schutte, Patricia Lopez-Jaramilla, Ayetkin Uguz, Japhat Chijambwa, Rafael Diaz, Scott Lear, Alvaro Avanzun, Rajesh Kumar, Viswanathan Mohan, Andray Saibu, Li Wei, Wang Yang, Bo Jian, Martin Mukherjee, Salim Yusuf, on behalf of the PURE Investigators\*

**NIVEL SOCIO-ECONÓMICO**

Figure 3: Association between current drinking and outcomes by income region



**MAL REGISTRO (*UNDER-REPORTING*) DEL ALCOHOL** puede aumentar el riesgo de ciertos cánceres con un consumo “moderado” de bebidas alcohólicas.

**EFFECTOS MIXTOS** de consumo bajo y moderado con un consumo excesivo o el abuso, que no permite delimitar las diferencias en los efectos sobre la salud.

**EFFECTOS DIFERENTES** según el **TIPO DE BEBIDA ALCOHÓLICA** consumida. Efectos diferentes si el consumo es preferentemente de vino, cerveza o destilados.

Importancia del **PATRON DE CONSUMO**: consumo moderado regular vs. consumo excesivo (‘binge’).



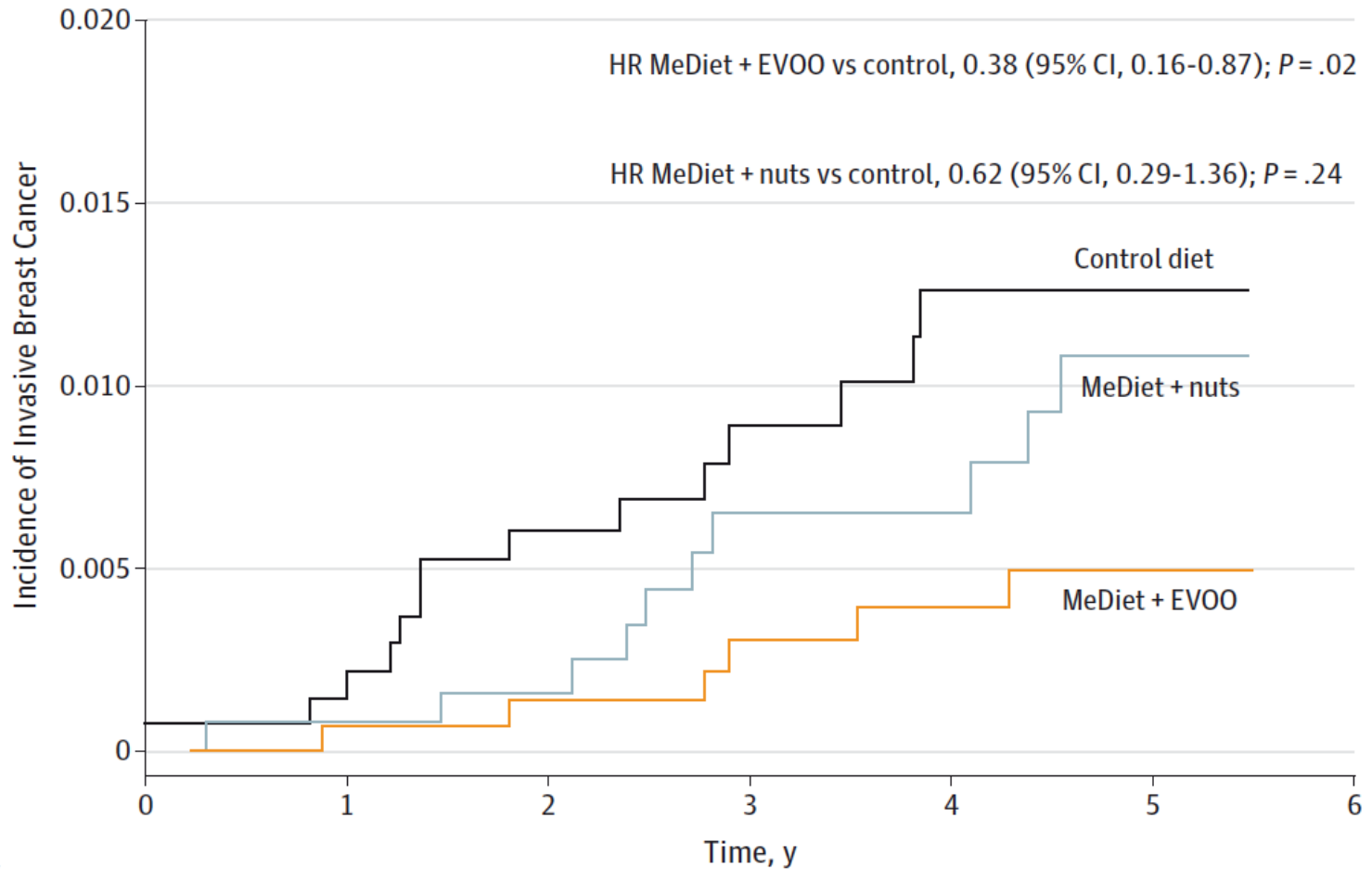
# **ESTUDIO PREDIMED**

**EFFECTOS DE UNA INTERVENCIÓN CON DIETA  
MEDITERRÁNEA SOBRE LA INCIDENCIA DE CÁNCER**

**EFFECTOS SOBRE EL CÁNCER DE MAMA**



Figure 1. Incidence of Invasive Breast Cancer, According to the Intervention Group



No. at risk

MeDiet + EVOO	1476	1463	1369	1184	1013	785
MeDiet + nuts	1285	1271	1117	879	741	532
Control diet	1391	1353	1209	940	759	573



# CONSUMO DE VINO Y MORTALIDAD POR CÁNCER

Stratified analysis of mortality. Hazard ratios of mortality (95% confidence intervals) according to the type of death and daily alcohol intake and dietary intervention

Groups according to alcohol intake (g/d)	n, cases	WINE				p for interaction
		0	>0-5	>5-15	>15-70	
<b>Cardiovascular death</b>						0.74
Mediterranean Diet	4786, 53	1.00 (ref.)	0.89(0.41-1.92)	0.62(0.25-1.51)	0.36(0.11-1.19)	
Control	2368, 26	1.00 (ref.)	0.69(0.18-2.54)	1(0.26-3.79)	0.57(0.10-3.39)	
<b>Cancer death</b>						0.03
Mediterranean Diet	4786, 93	1.00 (ref.)	0.60(0.32-1.11)	0.52(0.25-1.06)	0.54(0.32-0.99)	
Control	2368, 34	1.00 (ref.)	2.13(0.75-6.45)	2.09(0.62-6.99)	1.90(0.45-7.98)	
<b>Death from other causes</b>						<0.01
Mediterranean Diet	4786, 68	1.00 (ref.)	0.44(0.22-0.89)	0.73(0.35-1.46)	0.44(0.15-1.28)	
Control	2368, 65	1.00 (ref.)	1.85(0.64-5.30)	0,89(0.24-3.28)	1.40(0.35-5.65)	

## **NEGATIVE EFFECTS**



- Alcohol Dependence Syndrome
- Liver Cirrhosis
- Dilated Cardiomyopathy
- Encephalopathies
- Polineuropathy, Myopathy
- Fetal Alcohol Syndrome
- Accidents and Violence

## **POSITIVE EFFECTS**



- Overall Mortality
- Cardiovascular Disease
- Cancer
- Alzheimer Disease
- Gall and Kidney Stones
- Non-insulin dependent Diabetes
- Rheumatoid Arthritis

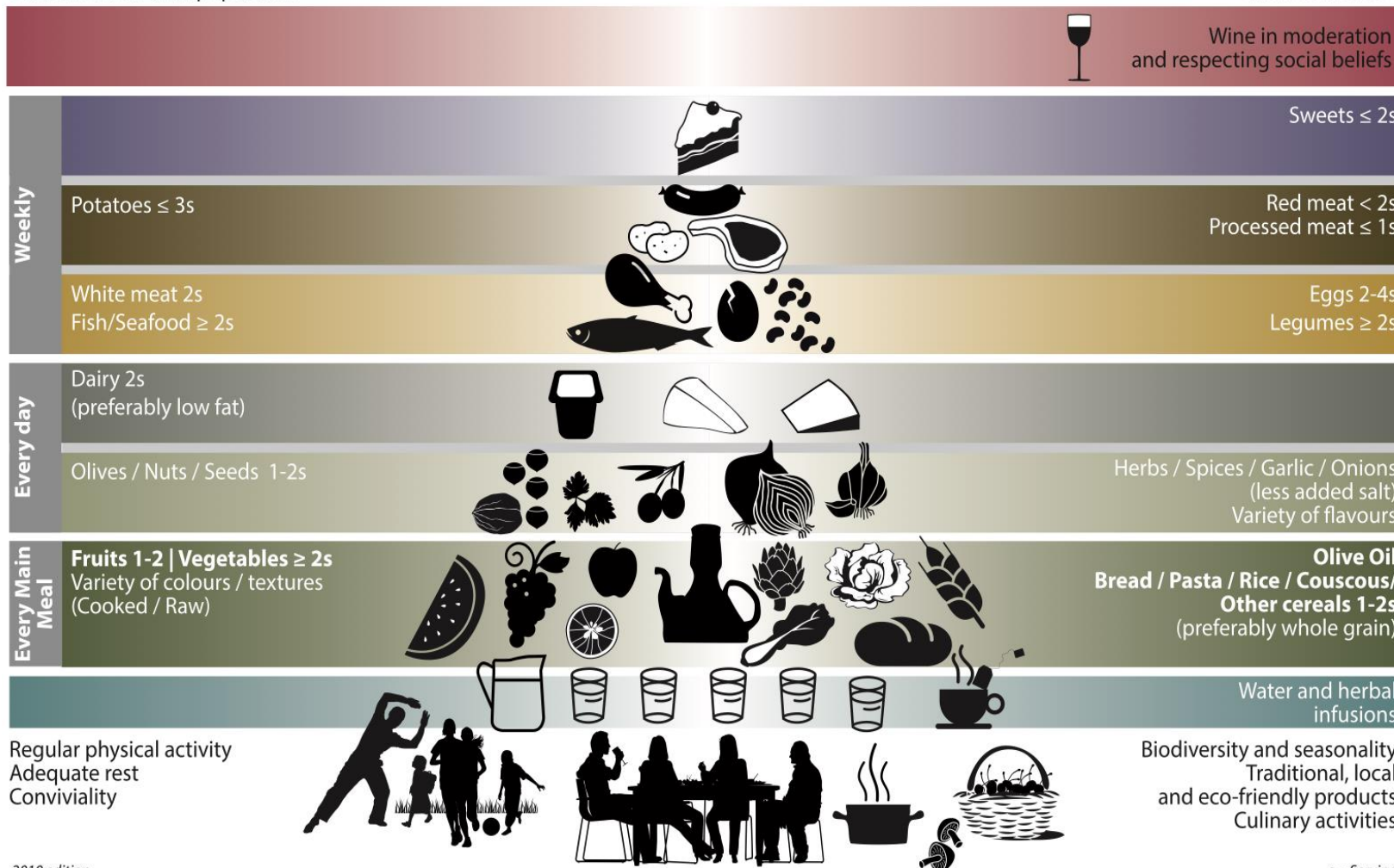


# MEJOR OPCIÓN

## Mediterranean Diet Pyramid: a lifestyle for today

Guidelines for Adult population

Serving size based on frugality and local habits



Regular physical activity  
Adequate rest  
Conviviality

Biodiversity and seasonality  
Traditional, local and eco-friendly products  
Culinary activities

2010 edition

s = Serving

© 2010 Fundación Dieta Mediterránea  
The use and promotion of this pyramid is recommended without any restriction





**MOLTES GRACIES!**

