

# Alcohol

*part of Western  
civilization*

*for millenia a  
social lubricant*



# Alcohol

(al-) kuhl  
guhlu }  
arabian  
assyrian }

**eye powder** blackening the skin around the eye



# antimon trisulfide  
# lead sulfide

bactericidal ⇒ medication for **eye diseases**

Alcohol in Europe :

**hispanoarabic** dialect ~ 1100 :  
al-kuhúl

**italian** ~ 1290 :  
alcohol (“extremely fine powder for eyes“  
called “atomi” – ultrasmall particles)

**Paracelsus** (1527) :  
alkohol vini (“the finest components of wine”)

Alcohol may **promote renal health**  
and may achieve more  
than indicated by the following silly statement:

**The kidney transforms  
good wine into insipid urine**

# Wine

*I shall try to answer the question that has been posed to me :*

**Does wine have health benefits,  
specifically does it improve renal health ?**

# **Adverse health effects of alcohol**

- *polyneuritis*
- *cirrhosis / hepatitis*
- *encephalopathy*
- *cardiomyopathy*
- *malnutrition / vitamin B1 deficiency*
- . . .

***When I read about the  
evils of drinking,  
I decided  
to give up reading***

*Mark Twain (1835-1910)*

# Does alcohol also have adverse effects on the kidney ?

*“too much of a good thing is toxic“*  
**extrarenal damage**

- polyneuritis
- cirrhosis / hepatitis
- encephalopathy
- cardiomyopathy
- malnutrition / vitamin B1 deficiency

**excessive** use of alcohol causes also **renal damage**:

- *glomerulonephritis,*
- *acute kidney injury (rhabdomyolysis),*
  - *kidney graft failure,*
  - *papillary necrosis,*
- *fetal alcohol syndrome ...*

# Alcoholics

adverse longterm outcome after postinfectious glomerulonephritis  
(*endocapillary GN with humps*)

**Table 3** Long-term renal prognosis in postinfectious GN

	At last follow-up			
	Normal renal function	Chronic renal failure	Dialysis dependency	Death
Alcoholic patients (n=17)	7	8	1	1
Non-alcoholic patients	11	0	0	0

**10/17 vs 0/11**

*Keller, Quart.J.Med.(1994) 87:97*

# **Kidney disease / glomerulonephritis – long known link to alcoholism**

## **Bright R.**

Reports of medical cases selected with a view of illustrating the symptoms and cure of diseases by a reference to morbid anatomy  
Longman, Rees, Orne, Brown and Greene eds., London, 1831

## **Frerichs F.T.**

Die Bright'sche Nierenerkrankung und deren Behandlung  
Verlag Friedrich Vieweg und Sohn, Braunschweig 1831

## **Christison R.**

On the granular degeneration of the kidney  
Edin.Med.J.(1829);32:262

## **Becquerel F.**

Traité des maladies des reins - historique de la néphrite albumineuse  
Rayer, Paris (1839)

# Alcohol abuse – higher risk of **acute kidney injury** ± *rhabdomyolysis*

Underlying condition	Number of patients with sARF (n = 240)	Annual incidence (per 100,000 population)	Relative risk <sup>a</sup> (Exact 95% CI)
Heart disease	120	140	24.0 (18.5–31.2) <sup>b</sup>
Stroke	44	206	22.0 (15.6–31.0) <sup>b</sup>
Chronic pulmonary disease	83	121	16.0 (12.1–21.0) <sup>b</sup>
Diabetes mellitus	72	84	10.3 (7.7–13.6) <sup>b</sup>
Cancer	38	89	9.2 (6.3–13.1) <sup>b</sup>
Connective tissue disease	12	56	5.2 (2.7–9.3) <sup>b</sup>
Chronic kidney disease	45	47	4.9 (3.5–6.8) <sup>b</sup>
Alcohol abuse	57	39	4.3 (3.1–5.8) <sup>b</sup>

23%

rel.risk

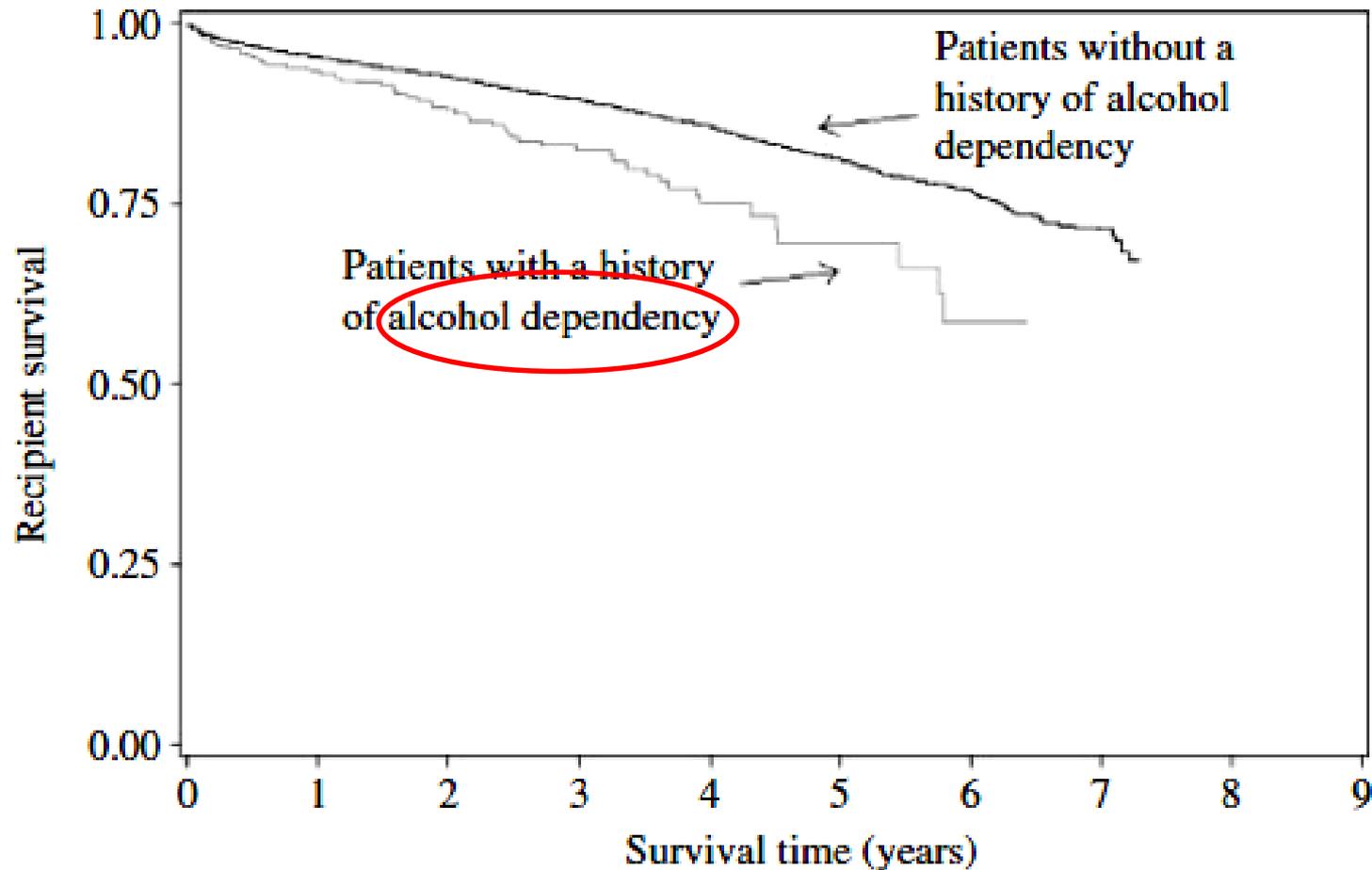


*Bagshaw, Crit.Care (2005) 9:R700*

***Following binge drinking even bilateral renal necrosis***

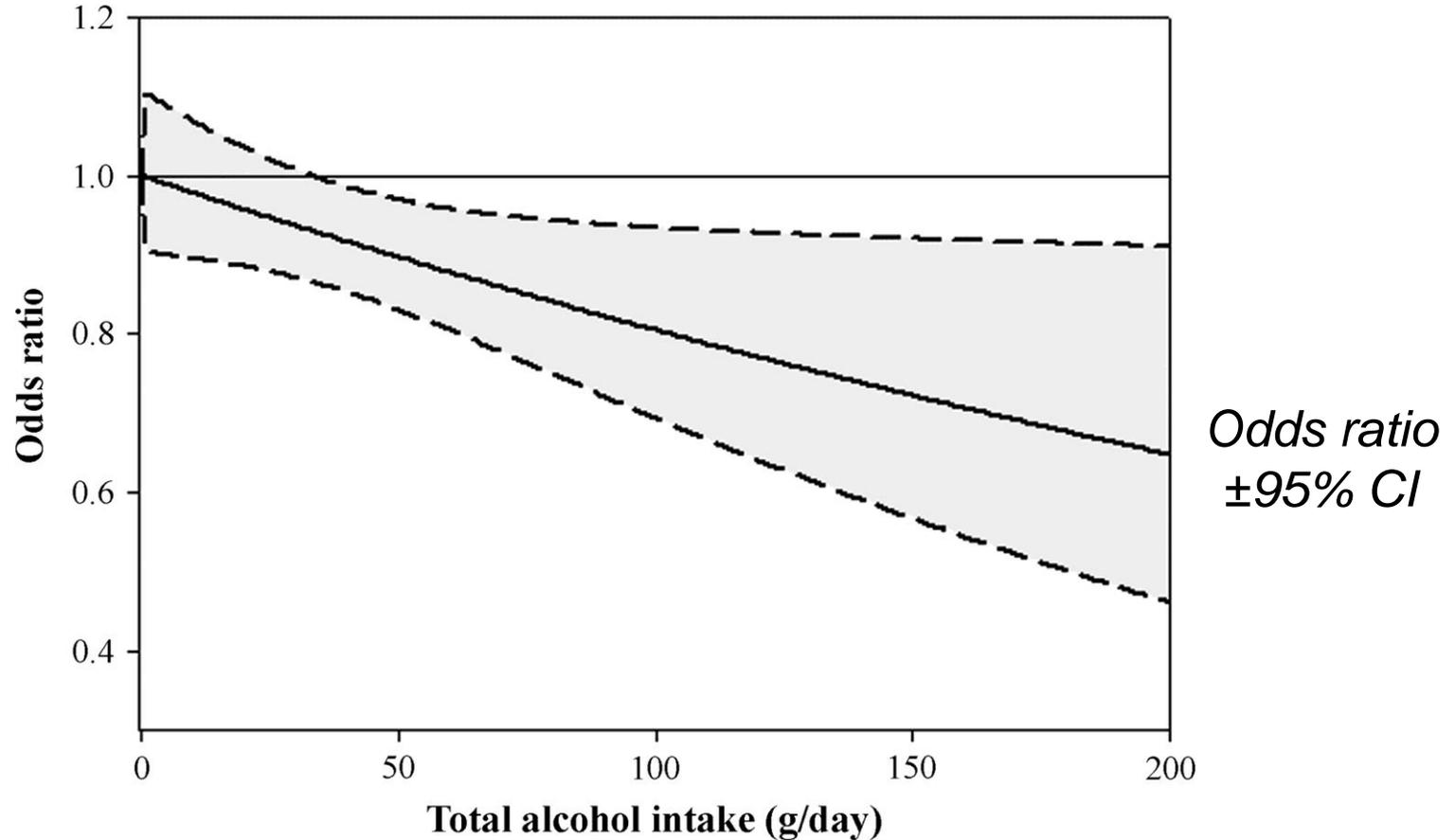
*Jung, Alcohol Alcohol (2012) 47:140*

# Alcohol dependency in patient with **kidney graft** ⇒ less graft and patient survival



# The only good news

➔ **less renal cell cancers with total alcohol intake**



*Pelucchi C , Ann Oncol (2008)19:1003*

**confirmed by:**

*Lew, Br.J.Cancer (2011) 104:537*

*Kim, Cancer Causes Control (2010) 21:2295*

*Chow, Nat.Rev.Urol.(2010) 7:245*

# Alcohol and **hypertension**

Lian C.

L'alcoolisme cause d'hypertension arterielle  
Bull.Acad.Med.(Paris) (1915) 74:525-528

“threshold” > 2 l wine per day (?)

Klatsky A.L.; Alcohol and hypertension  
in: Oparil S., Weber M.(eds.) Hypertension, 2<sup>nd</sup> edition  
W.Saunders Co, Philadelphia :

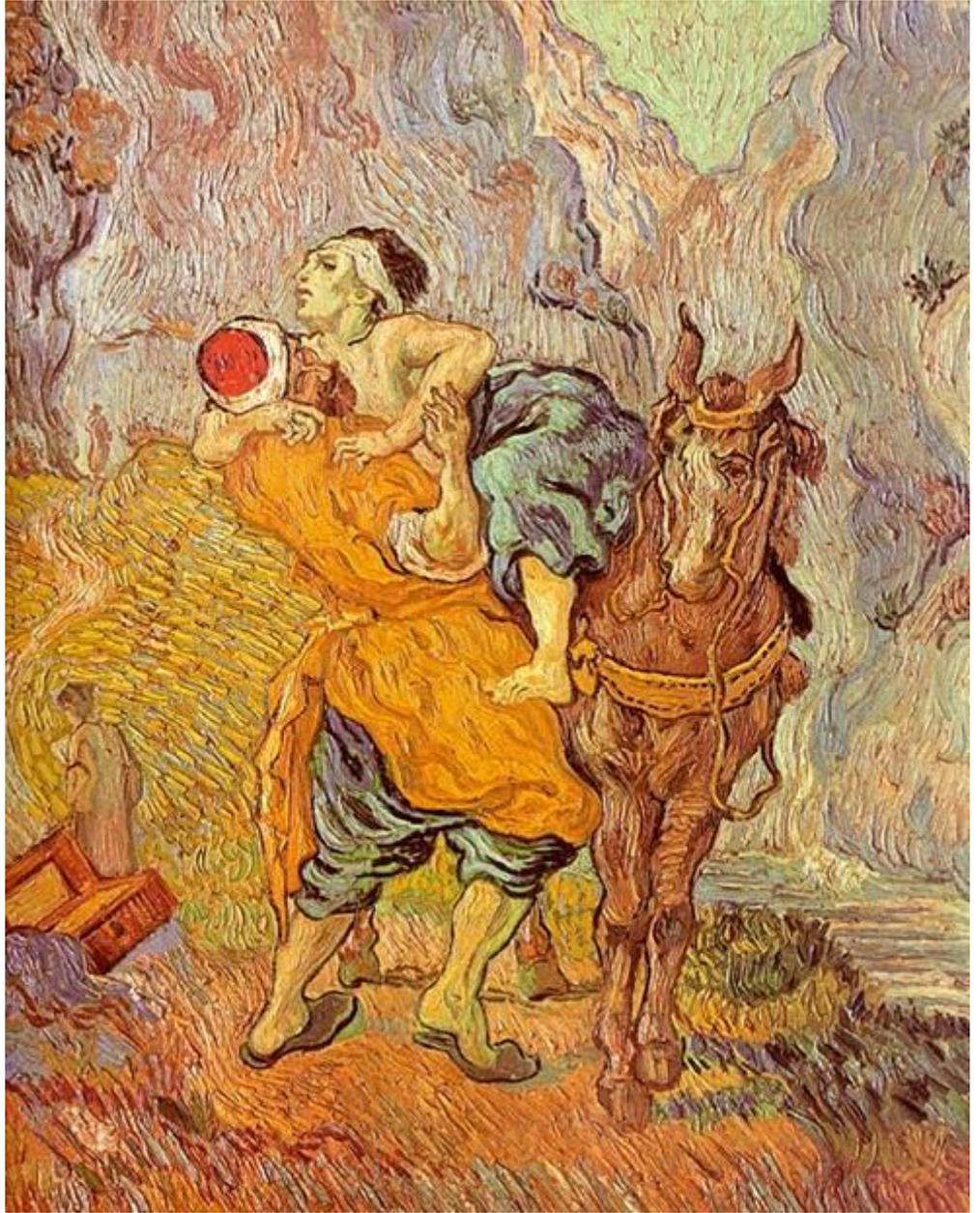
“threshold” ~ 3 drinks/day (~ 45g alcohol/day)

The history of  
**beneficial** effects of alcohol  
*(wine)*

*A certain man went down from Jerusalem to Jericho and fell among thieves which stripped him of his raiment and wounded him, and departed, leaving him half dead...*

**a Samaritan... went to him, and bound up his wounds, pouring in oil and wine...**

**Luke; 10: 30-37**



**V. van Gogh**

# Medical use of alcohol

**Julius Caesar** (100-44 BC)

**Troops :** *1.5 l of wine per day with meals to prevent  
gastrointestinal infections*

*he won battles : not only by strategic skill,  
but also by healthier defecation*

**Claudius Galenus, Pergamon** (130-200 AC)

*red wine → GI disease  
adstringent (tannin rich) wine  
→ internal bleeding*



# Medical use of wine

Paracelsus

*Philippus Aurelius Theophrastus Bombastus von Hohenhain*  
(1493-1541)

”Weingeist” (Spiritus)

active ingredient of wine = alcohol

other ingredients - inert contaminants

effects of wine: **dosis facit venenum**

*(“the dose decides whether it is a poison or not”)*

# **Alcohol and Longevity**

(1926)

*New York: Alfred A. Knopf*

*“drinking alcohol in moderation  
...greater longevity than either  
abstaining or drinking heavily”*



**Raymond Pearl**

(1879-1940)

Johns Hopkins University

# Alcohol and life expectancy

Baltimore, working class population, 6000 individuals  
life table analysis

mean life time expectancy (years)

		————— drinkers —————			
age		<i>abstainers</i>	<i>moderate</i>	<i>heavy</i>	<i>moderate steady</i>
male	40 years	<u>29.91</u>	30.56	23.67	<u>32.34</u>
	60 years	<u>15.05</u>	16.81	14.41	<u>17.60</u>
female	40 years	<u>30.75</u>	33.02	17.12	<u>34.23</u>
	60 years	<u>16.71</u>	17.44	10.12	<u>18.95</u>

*Pearl R., British Medical Journal (1924) May 31st, 948-950*

Renaissance of the recognition of positive effects on health

## **”French paradox”**

- in all countries tight correlation between consumption of animal fat and coronary mortality, except

- in France and Switzerland:

coronary mortality low in relation to consumption of animal fat

*Renaud , Lancet (1992) 339: 1523*

*De Lorgeril, Circulation (2002) 106: 1465*

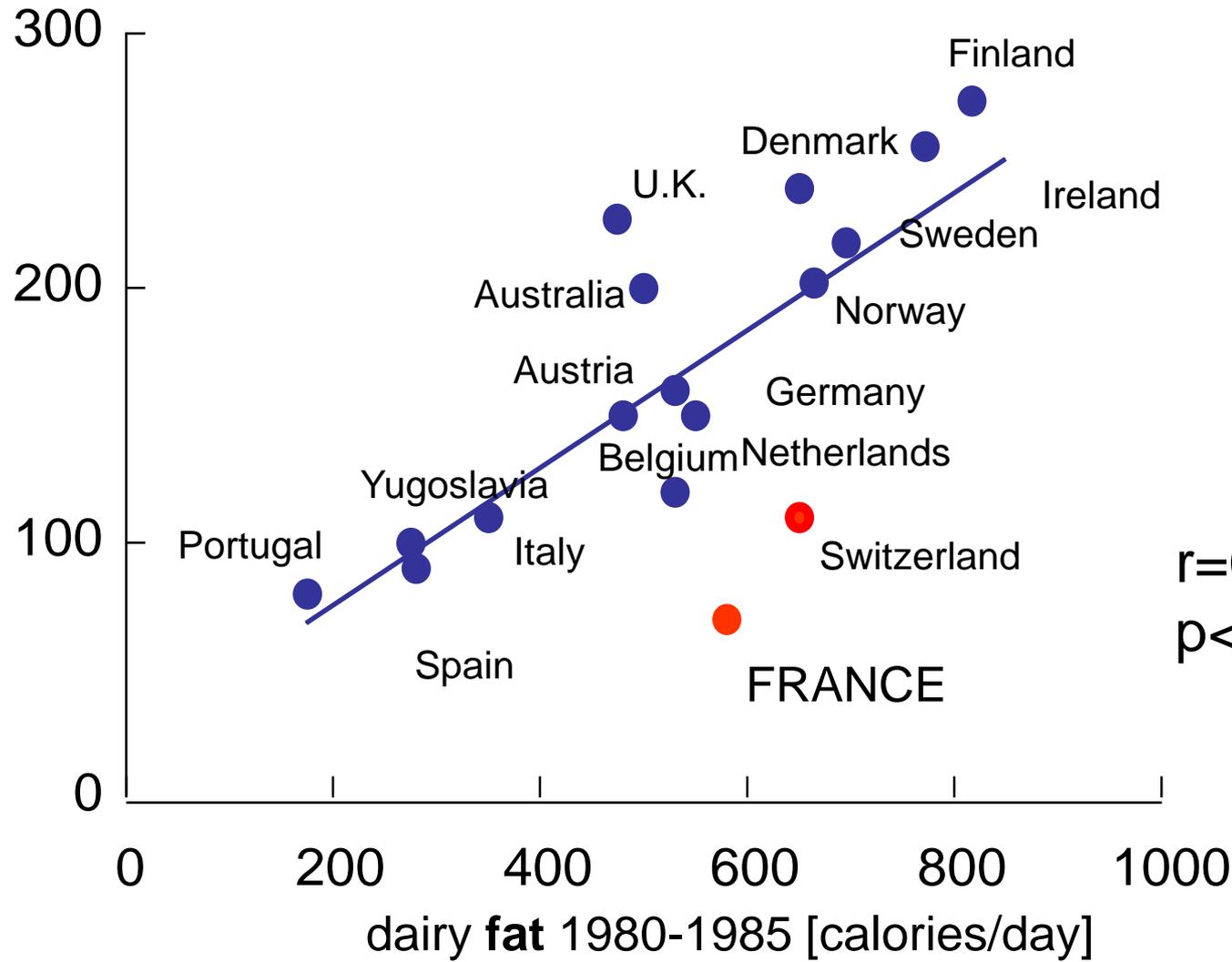
### **Hypothesis**

***Wine antagonises adverse effects of animal fat***

# French Paradox

## of coronary heart disease

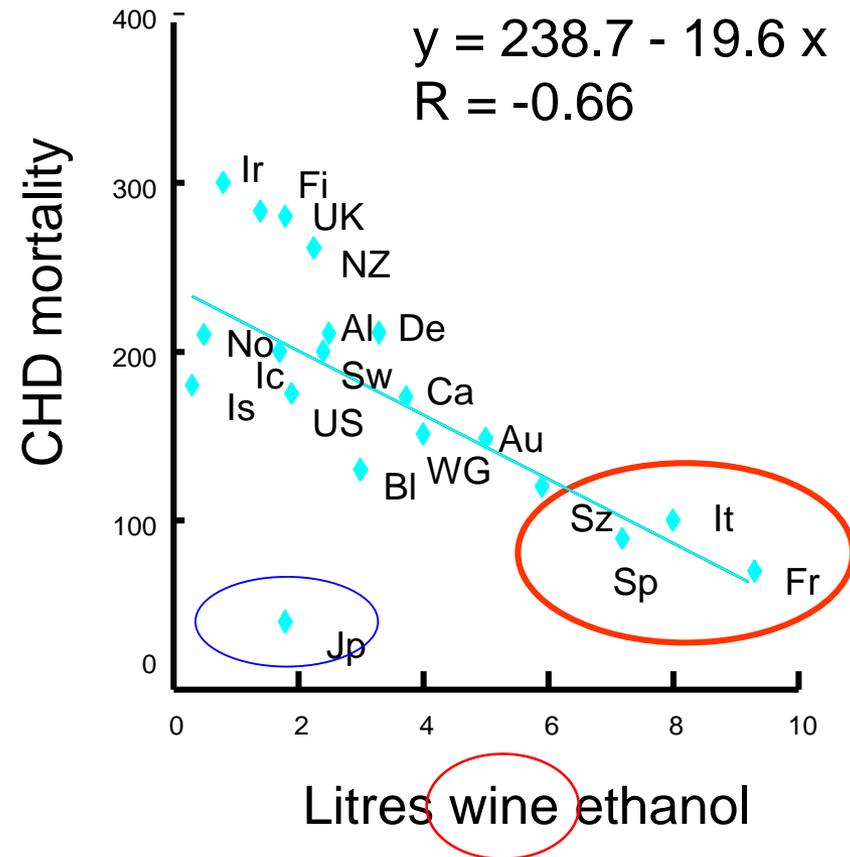
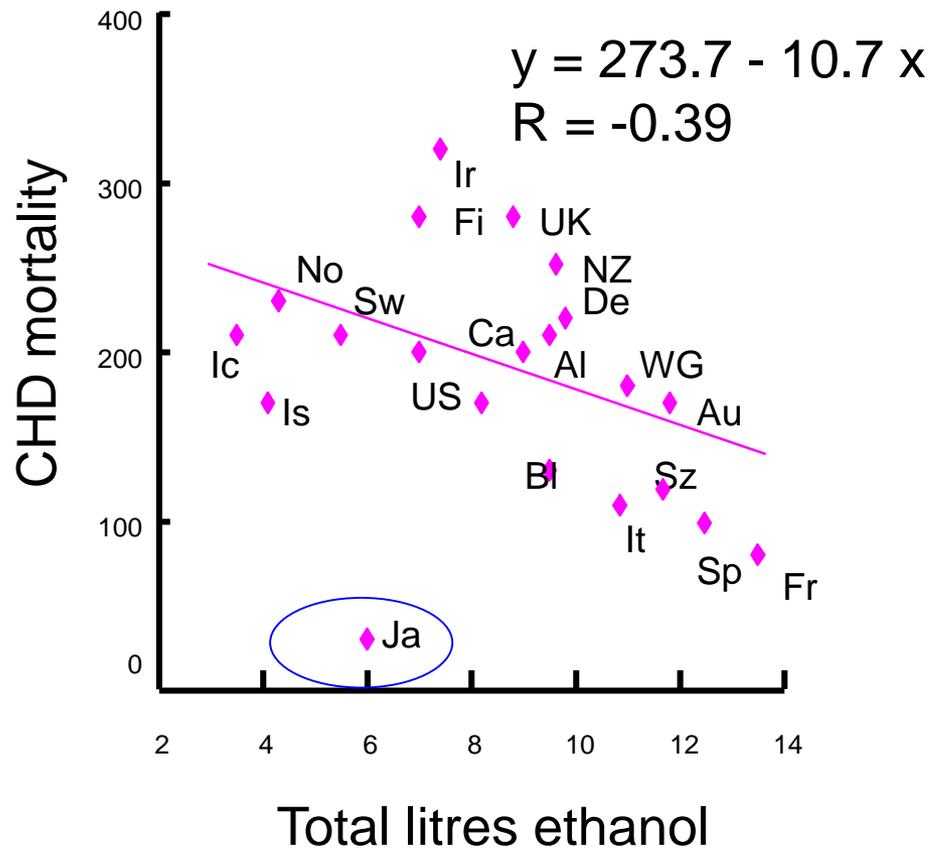
standardized rate  
CHD death



$r=0.73$   
 $p<0.001$

*Renaud, Lancet (1992) 339: 1523*

# Ethanol and wine ethanol consumption - relation to coronary heart disease mortality



# Alcohol consumption and cardiovascular death in hypertensive men *Physicians' health study*

14,125 / 88,882 hypertensives

relative risk

**alcohol consumption**

never monthly weekly daily

<b>CV mortality</b>	1.0	0.82	0.64	0.56
Overall mortality	1.0	0.86	0.72	0.73

*Malinski, Arch. Int. Med (2004) 164:623*

# Long-term alcohol consumption and risk of death and cardiovascular death

1818 doctors with **incident non-fatal MI** (*high risk*)  
 (*Health Professionals Follow-up study*)

	Long-term alcohol consumption (g/day)			
	0	0.1–9.9	10.0–29.9	≥30.0
Total deaths	168	161	97	42
Hazard ratio (95% CI) <sup>a</sup>	1.0	0.75 (0.60–0.93)	0.61 (0.47–0.79)	0.77 (0.54–1.10)
		<i>p</i> <0.03		
Cardiovascular deaths	92	81	47	23
Hazard ratio (95% CI) <sup>a</sup>	1.0	0.71 (0.52–0.96)	0.52 (0.36–0.75)	0.80 (0.50–1.29)
		<i>p</i> <0.07		

***“The sensible drinking limit“ –  
150 years old !***

**“Anstie’s rule**

*3 drinks daily  
(~ 34g /day)*

***Anstie F.E.***

*On the uses of wine in health and disease*

*J.S.Redfield, New York N.Y.; p11-13*

***1877***

# “Drinking **half a glass of wine** increases longevity by **5 years**“

*ZUTPHEN study*  
*1373 men born 1900-1920*  
*examined until 2000*

long term **wine** consumption < half a glass per day

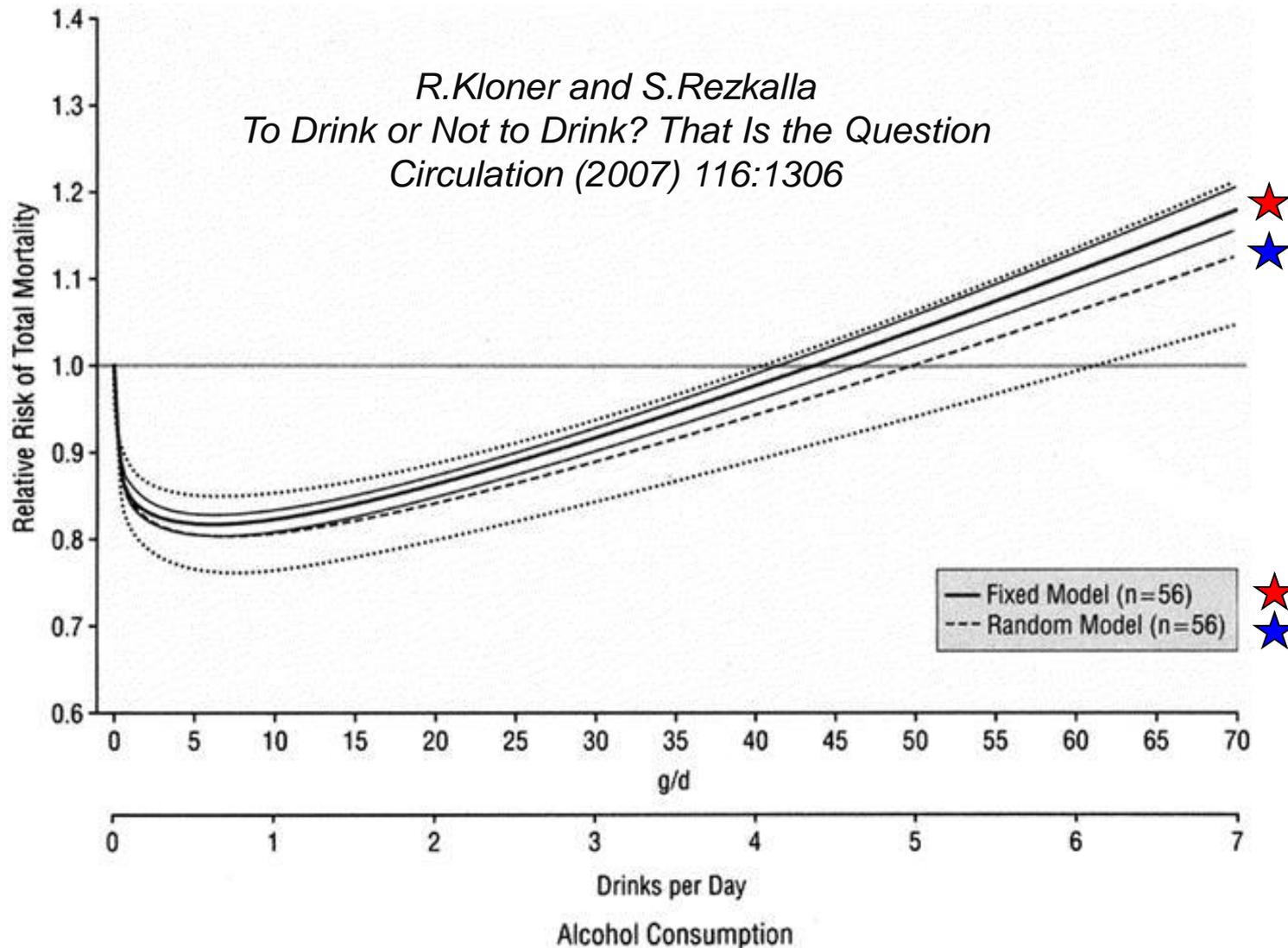
coronary heart disease	hazard ratio <b>0.61</b> (CI 0.41-0.89)
total cardiovascular mortality	hazard ratio <b>0.53</b> (CI 0.53-0.86)
all-cause mortality	hazard ratio <b>0.73</b> (CI 0.62-0.87)

**effect of wine independent** of **total alcohol** intake !!  
less than half a glass of wine / day → **life expectancy 5 years** longer

*Streppel, J Epidemiol Community Health (2009;)63:534*

**Dose response relationship**  
alcohol consumption vs all cause mortality ♂  
*U-shaped – unlike cigarette smoking or lipid abnormalities*

*R.Kloner and S.Rezkalla*  
*To Drink or Not to Drink? That Is the Question*  
*Circulation (2007) 116:1306*

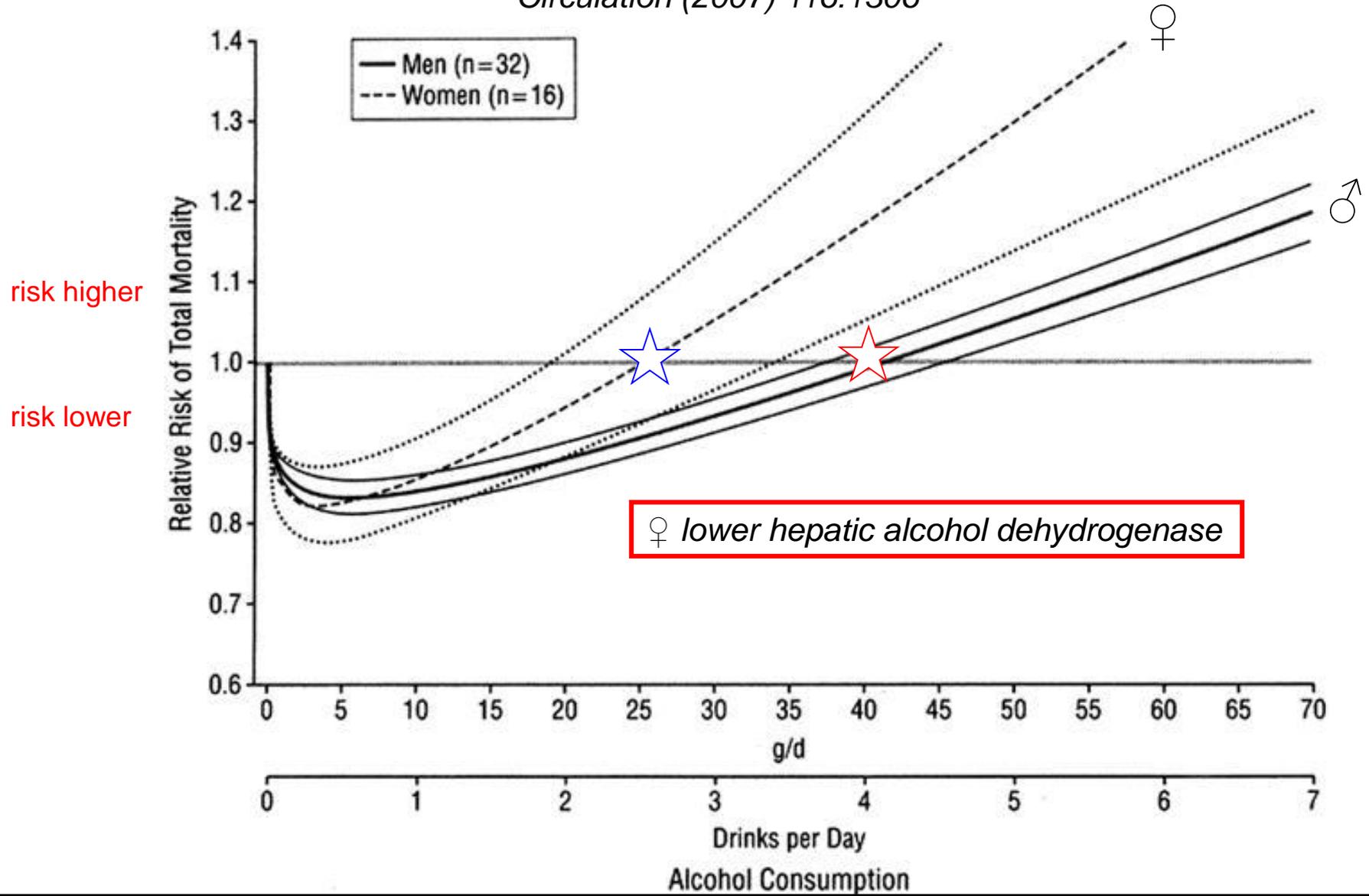


# Different CV benefit from alcohol in men and women

*Kloner and Rezkalla*

*To Drink or Not to Drink? That Is the Question*

*Circulation (2007) 116:1306*



# Risk reduction – dependent on baseline risk

→ pronounced in **smokers**, less in non-smokers

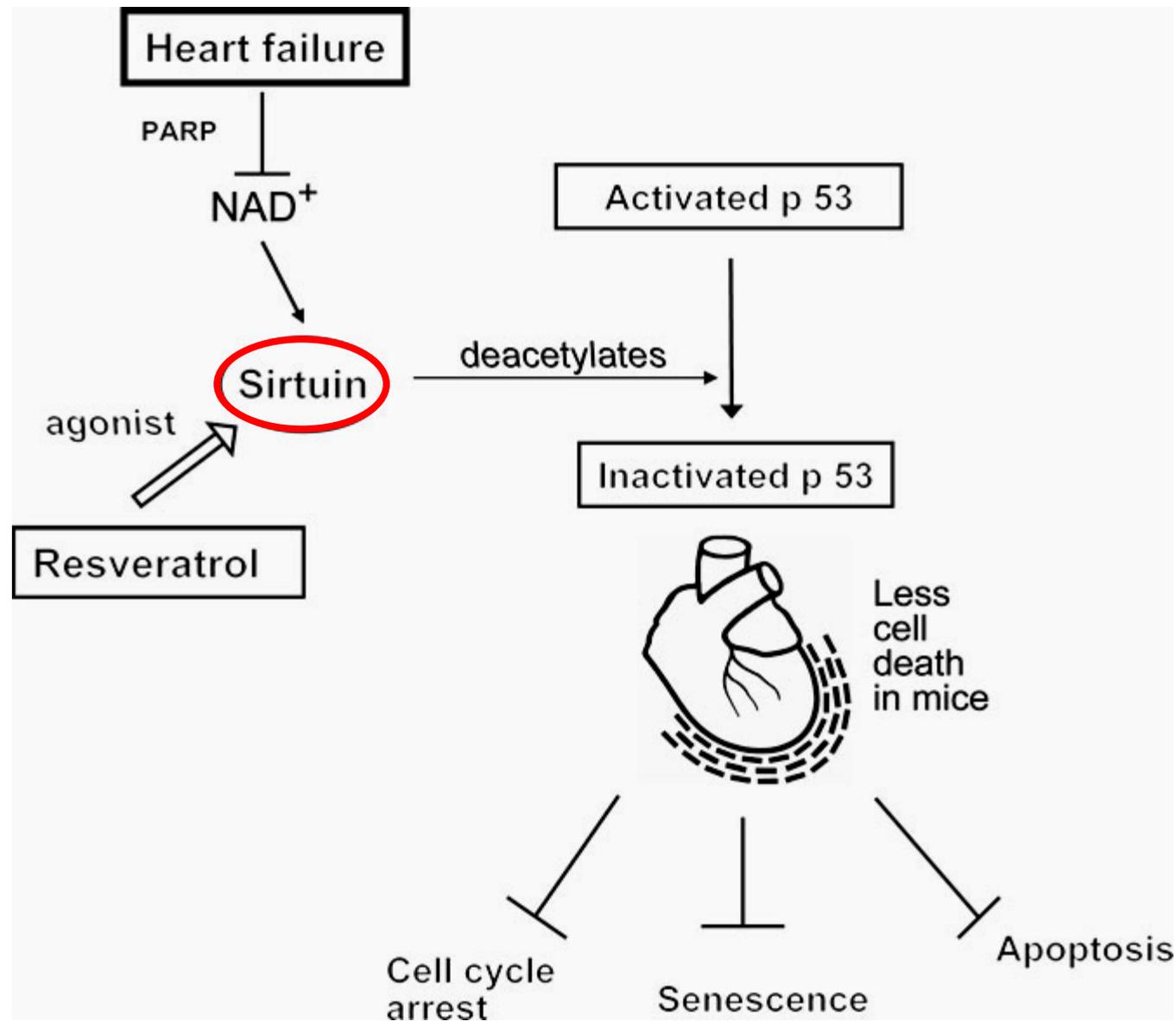
	RR	
	0 g alcohol	22-32 g alcohol/day
smoker	2.8	1.9
non-smoker	1	0.7

*Renaud*  
*Am J Clin Nutr (1992) 55: 1012*

- **any type** of moderate alcohol consumption :
  - ➔ lower all cause mortality
- **wine** ➔ more CV protection than beer
- **red wine** ➔ more CV protection than white wine

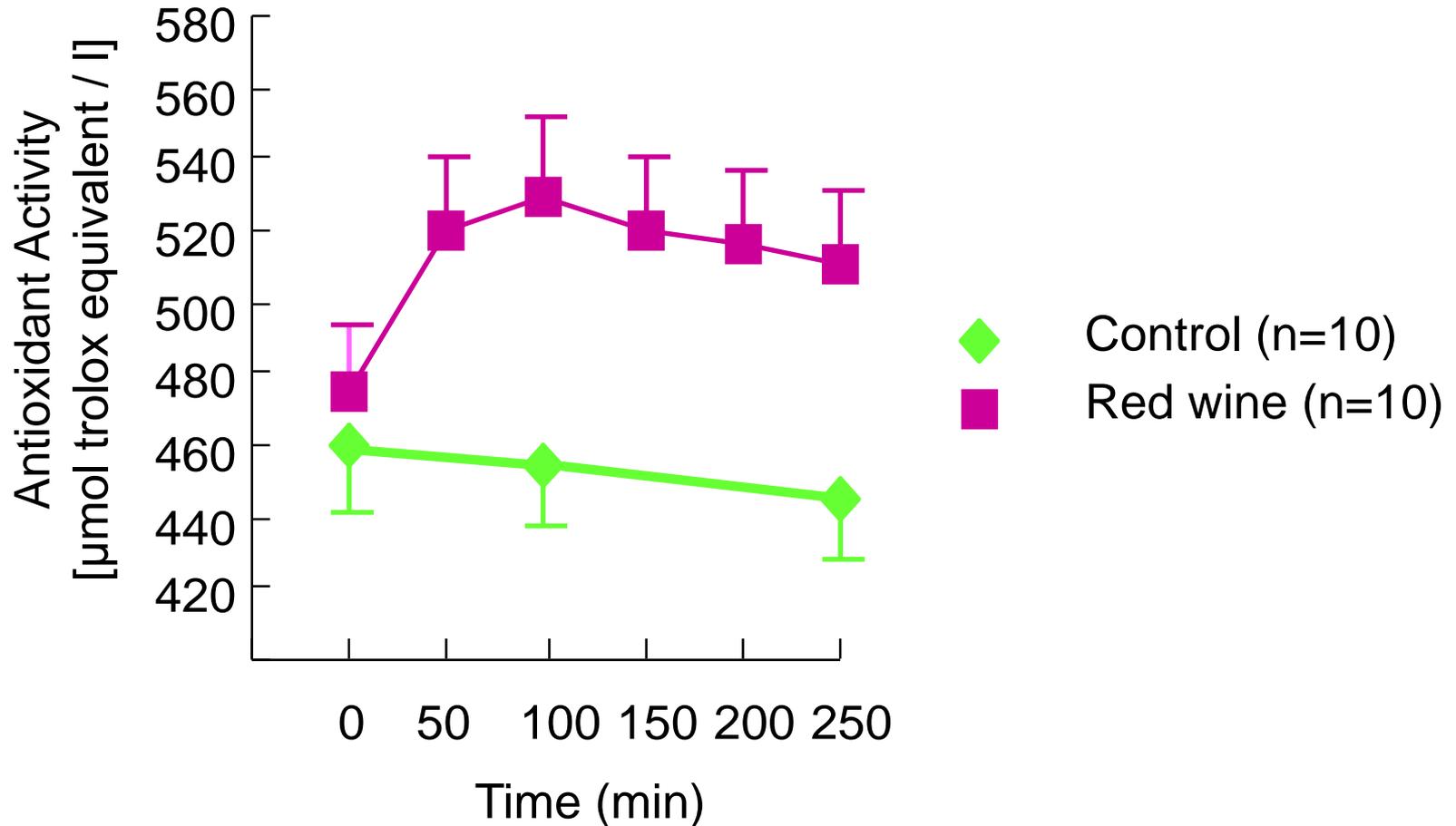
*Opie, Eur.Heart J.(2007) 28:1683*

# Mechanisms of cardioprotection by alcohol in heart failure



Opie, *European Heart J.*(2007) 28:1683

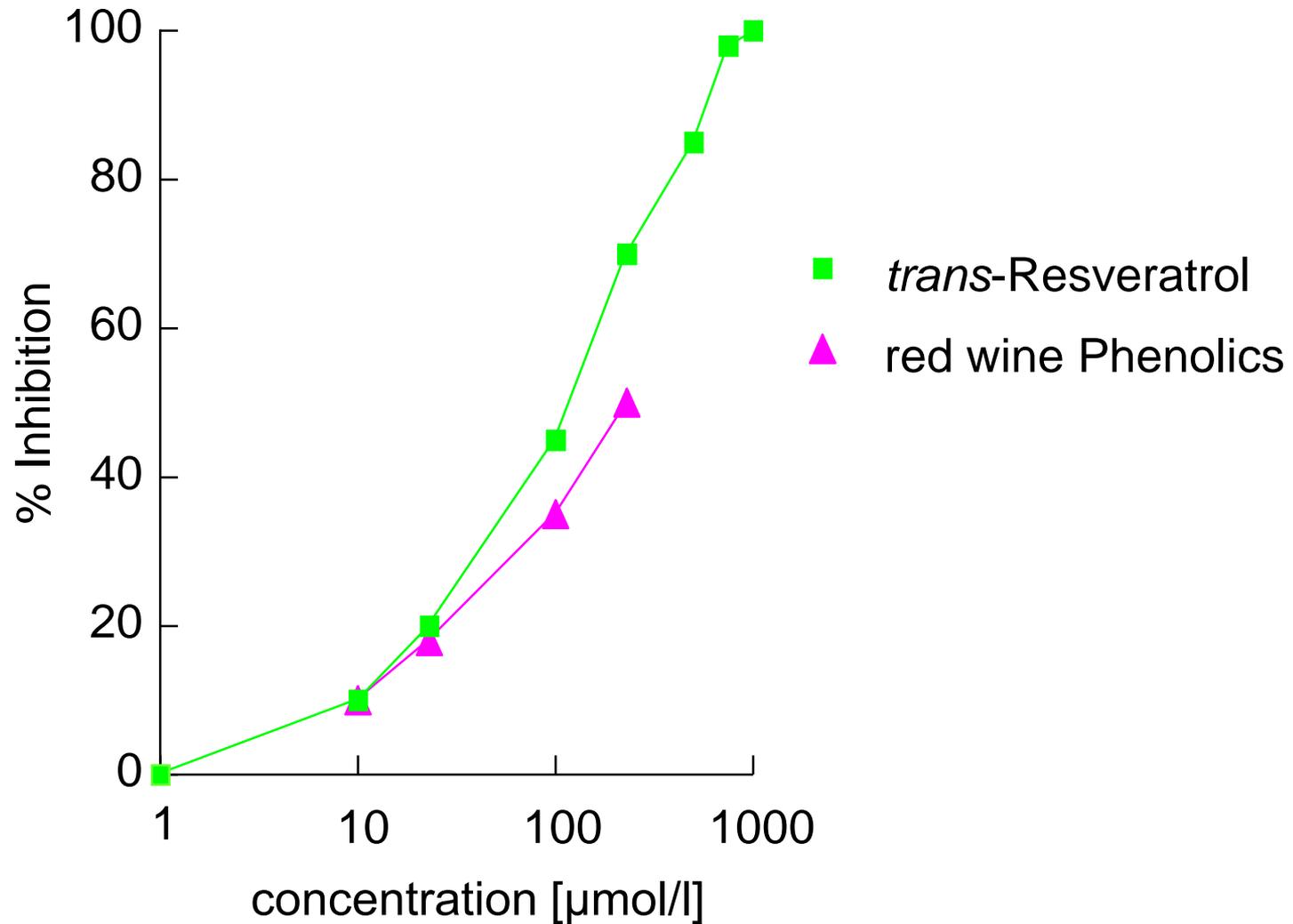
# Impact of Red Wine on Serum Antioxidant Activity in Healthy Volunteers



Standard meal alone or with 5.7 ml Bordeaux / kg

Maxwell, Lancet (1994) 344: 193

# Inhibition of ADP-induced platelet aggregation in vitro



*Pace-Asciak, Clin Chem Acta (1996)246:183*

# Effects of wine on **endothelial cells**

red wine phenols (resveratrol) increase expression  
and activity of endothelial NO synthase

- nitric oxide generation ↑
- shear stress induced vasodilatation ↑
- adhesion of mononuclear cells/platelets

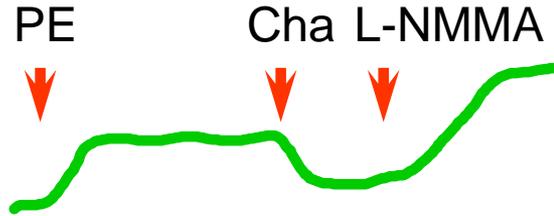
*Leikert, Circulation (2002) 106: 1614*

# Human Coronary Artery

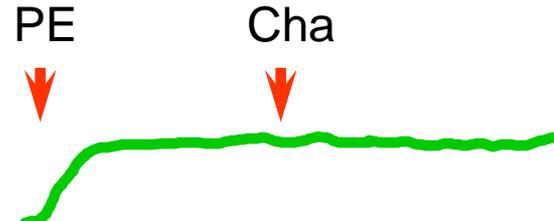
## Effects of Red and White Wine

red

Chateuneuf  
du Pape  
(+endothelium)



Chateauneuf  
du Pape  
(- endothelium)

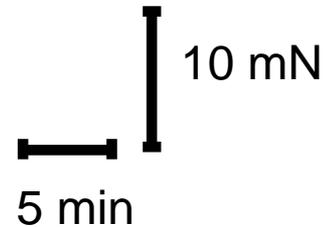
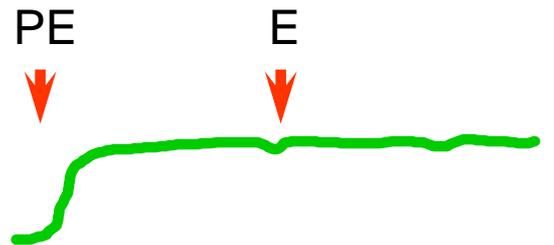


white

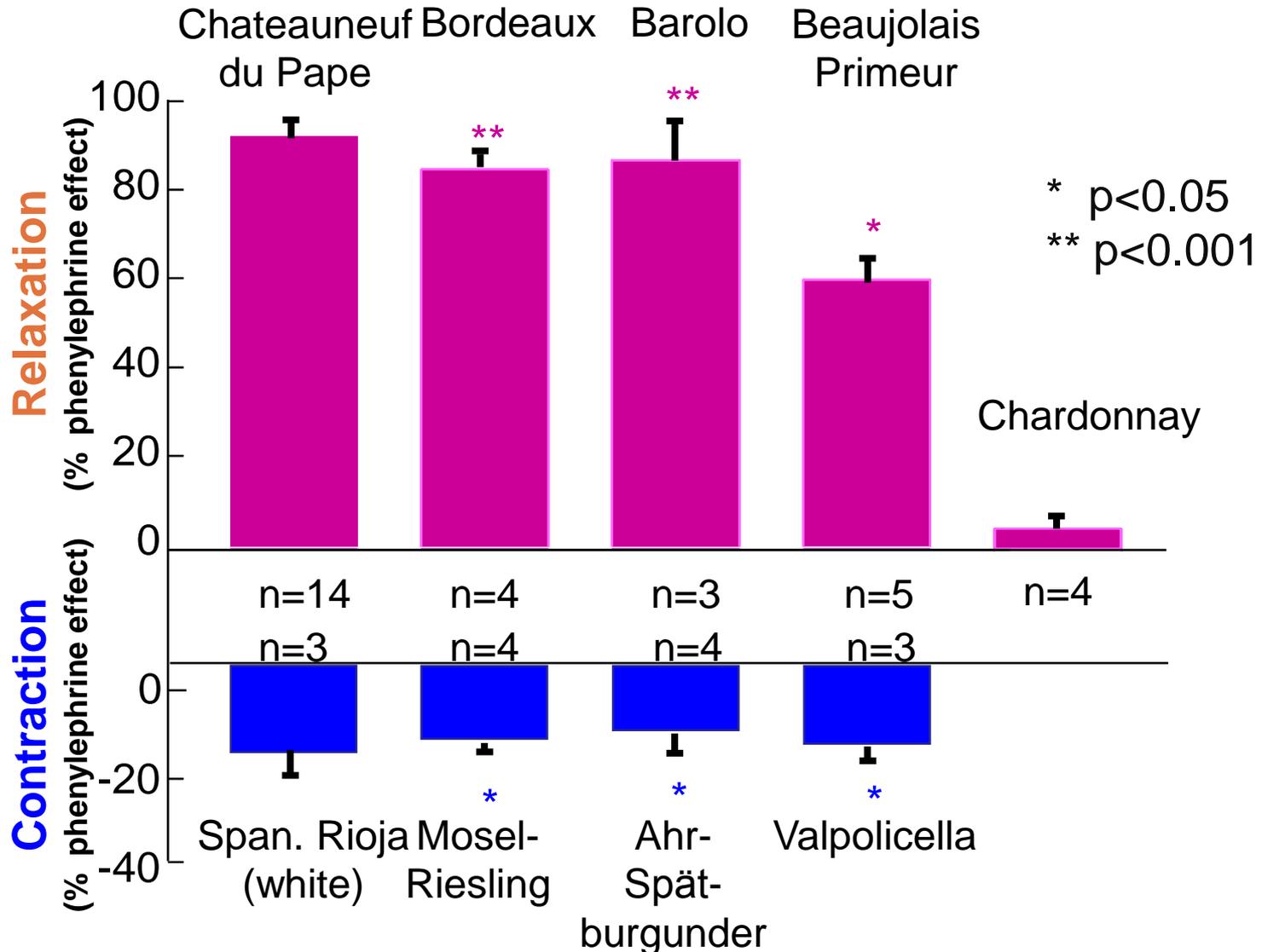
Mosel-  
Riesling



Ethanol



# Vascular Effects of Red and White Wine



Flesch, Am J Physiol (1998) 275: H1183



**„Rotwein ist für alte Knaben  
eine von den besten Gaben.“**

*“For elderly gentlemen  
red wine is one of the best gifts ”*



*Wilhelm Busch  
(1832-1908)*

# Wine

*Question of Prof. Rosivall*

***Does wine have **renal** health benefits ?***

# Finnish study : alcohol consumption and kidney function in **IgA glomerulonephritis**

cross-sectional arm 158 patients

	abstainers	light drinkers	moderate drinkers	heavy drinkers
proteinuria (g/24h)	0.21	0.28	0.39	0.78
creatinine clearance (ml/min/1.73m <sup>2</sup> )	87	108	124	93

longitudinal arm 117 patients

odds ratio

abstainers	1.0	
light drinkers	0.4	$p < 0.024$
moderate drinkers	0.1	$p < 0.002$
heavy drinkers	2.3	$p < 0.492$

# Alcohol consumption and course of IgA-glomerulonephritis

estimated daily alcohol consumption			
		 1-3x	
<b>abstinence</b>	<b>little</b>	<b>moderate</b>	<b>high</b>

*Predicting less progression:*

**women:**



**men:**



*Kaartinen, Nephron Clin Pract (2009)112:c86–c93*

Methodological concerns :

*How were the investigators able to find Finns without alcohol consumption?*

# Alcohol consumption and **new onset renal dysfunction**

(endpoint : S-creatinine > 1.5mg/dl)

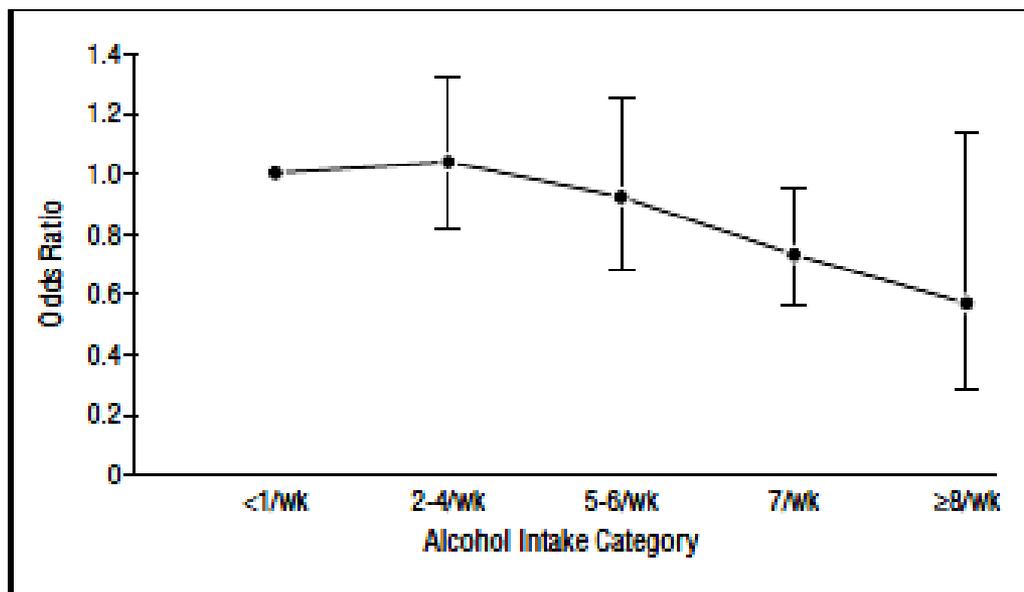
**the definite proof**

*prospective study in 11,023 healthy men with 14 years follow-up*

**Alcohol consumption  
category**

*OR (95%CI)*

≤1/wk	1.00
2-4/wk	1.00 (0.77-1.31)
5-6/wk	0.88 (0.62-1.23)
≥7/wk	0.75 (0.57-0.98)
<i>P</i> for trend	.03



*effect independent of hypertension, diabetes, cholesterolemia*

*Schaeffner, Arch.Intern.Med.(2005) 165:1048*

# Association between frequency of drinking alcohol and prevalence of CKD in men confirmation

9,196 men; age 57.9±5.1 years; health check-up  
CKD : eGFR < 60 ml/min/1.73m<sup>2</sup>  
alcohol consumption by questionnaire

odds ratio of CKD

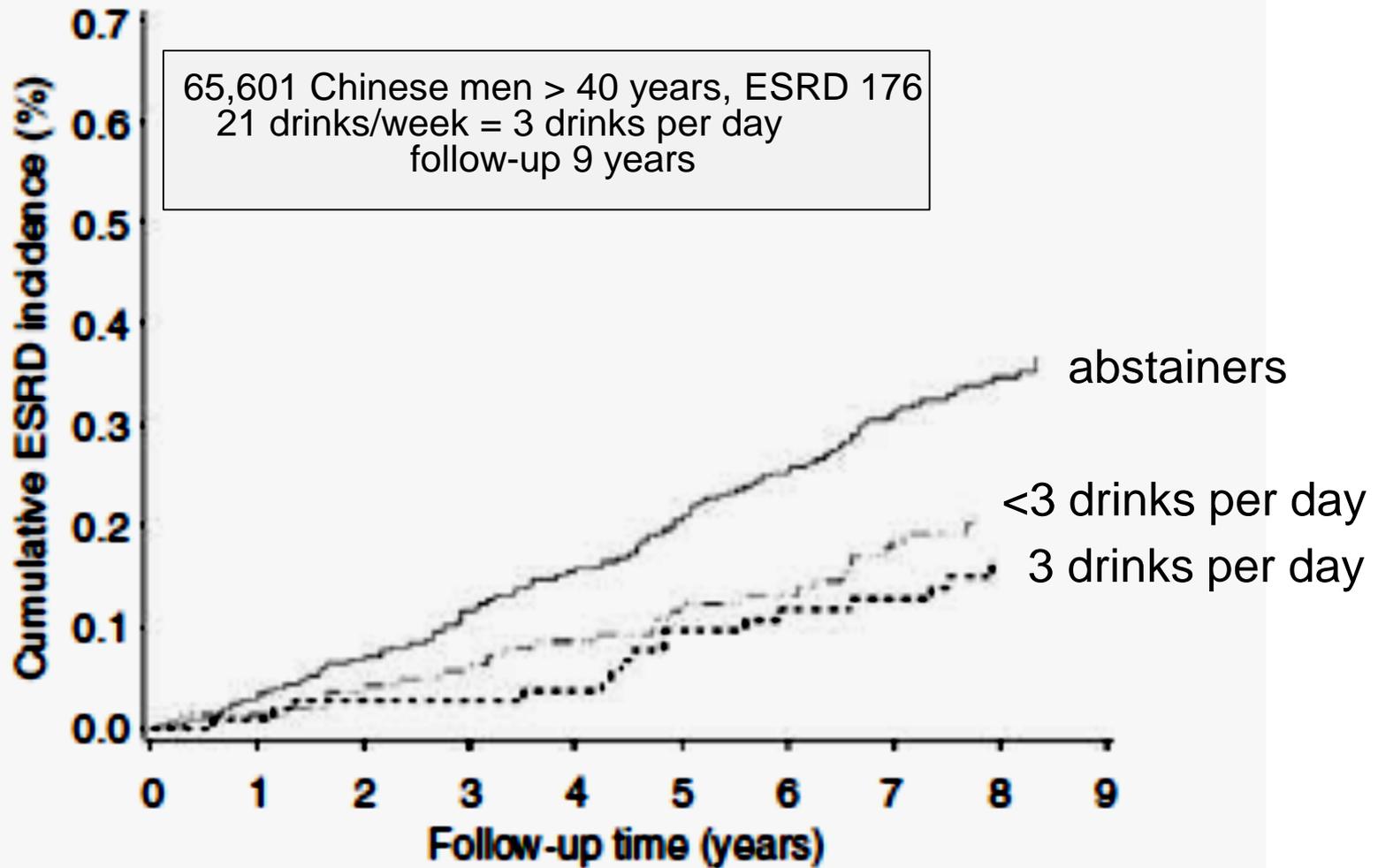
nondrinkers	1.0
1-2 drinks/week	0.76 (95%CI 0.60-0.95)
3-4“	0.74 (95%CI 0.59-0.93)
5-6“	0.79 (95%CI 0.64-0.97)
<b>daily</b>	<b>0.60</b> (95%CI 0.51-0.79)

*(p=0.001 for trend)*

*Funakoshi, Environ.Health Prev.Med.(2012) 17:199*

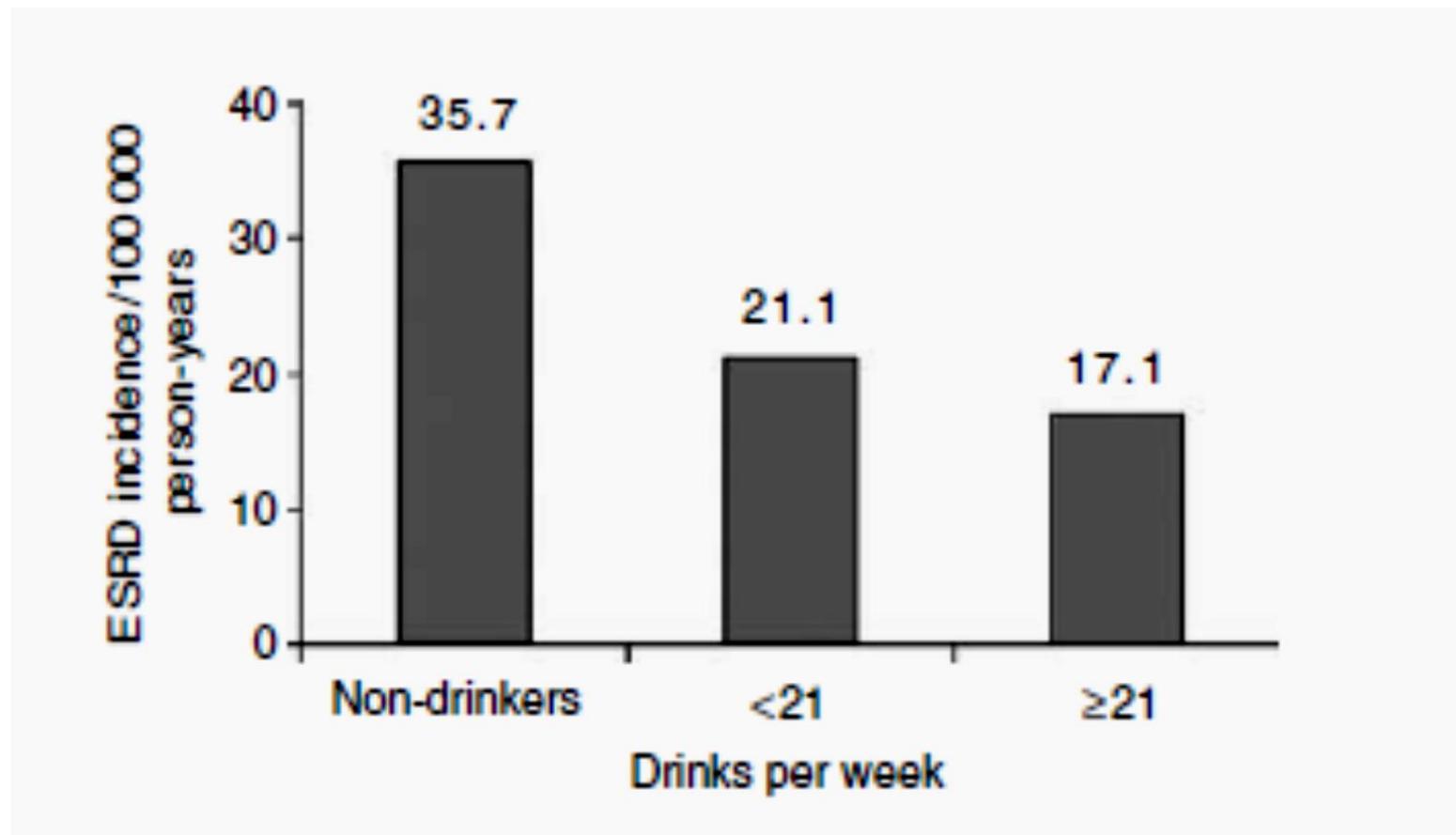
# Alcohol and **endstage renal disease** :

*the definite proof of longterm benefit ESRD*



*Reynolds, Kid.Internat.(2008) 73:870*

# Incidence of all-cause endstage renal disease dose dependent (per 100,000 person years standardized by age)



*Reynolds, Kid.Internat.(2008) 73:870*

# Alcohol and **glomerular** as well as **arteriolar changes** *autopsy-based population survey*

(Hisayama study 1962-1994)

**Age adjusted odds ratio ( $\pm 95\%CI$ )**

male  
*n=458*

**Glomerulosclerosis    Arteriolar Hyalinosis**

pulse pressure ( $\Delta 10\text{mmHg}$ )	1.17	1.28
Glucose intolerance	2.43	2.06
BMI	0.99	1.01
<b>alcohol intake</b> (yes/no)	<b>0.72</b> (0.42-1.24)	<b>0.66</b> (0.39-1.11)

same findings in females

Multivariate analysis:  
age and proteinuria were significant independent risk factors for glomerulosclerosis,  
and **alcohol had protective effects**

*Kubo, Kidn.Internat.(2003) 63:1508*

**Long-term alcohol consumption independent risk factor  
of **hypertension development**  
(*Kailuan study; China*)**

32,389 male coal miners free of hypertension

alcoholic intake (g)

**0**; 1-24; 25-49; 50-99; 100-149; **>150**

cumulative incidence of hypertension (%)

**25.0**; 28.8; 30.1 ; 37.1; 40.1; **42.5**

*Peng M., Wu S., Jiang X., Jin C., Zhang W.,  
Kailuan Cardiovascular survey group  
J.Hypertension (2013) 31:2342*

# Hypothesis

kidney rich in polyunsaturated fatty acids  
**vulnerable** to damage by **reactive oxygen species (ROS)**

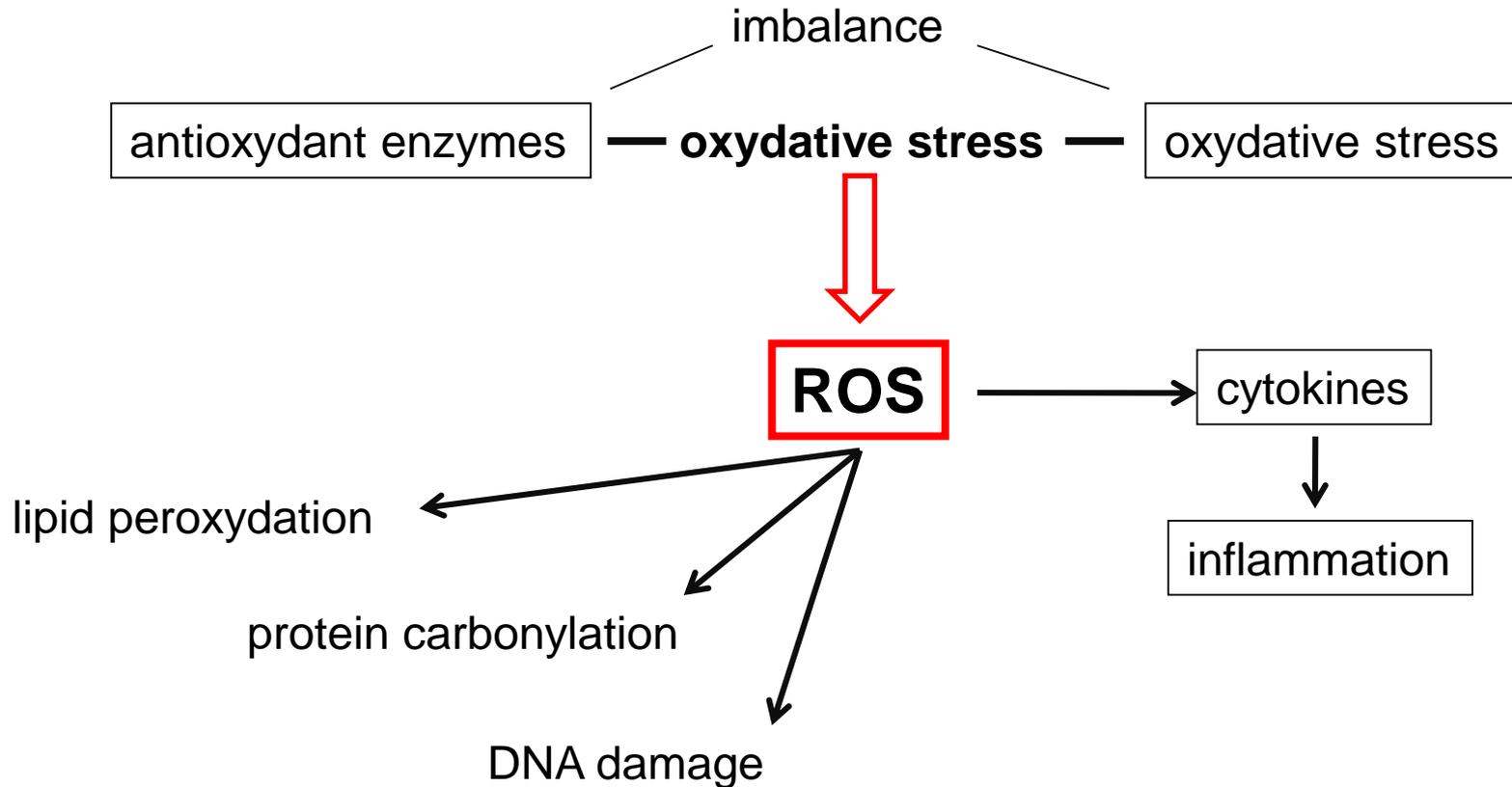
⇒ benefit from moderate consumption of red **wine**  
via **increased antioxidant defense**

# **polyphenols** → *ROS scavengers and metal chelators*

# **ethanol** → *increased activity of antioxidant enzymes*

# Polyphenols counteract oxydative damage in kidney

(based on glycerol injection rhabomyolysis model of acute renal failure)



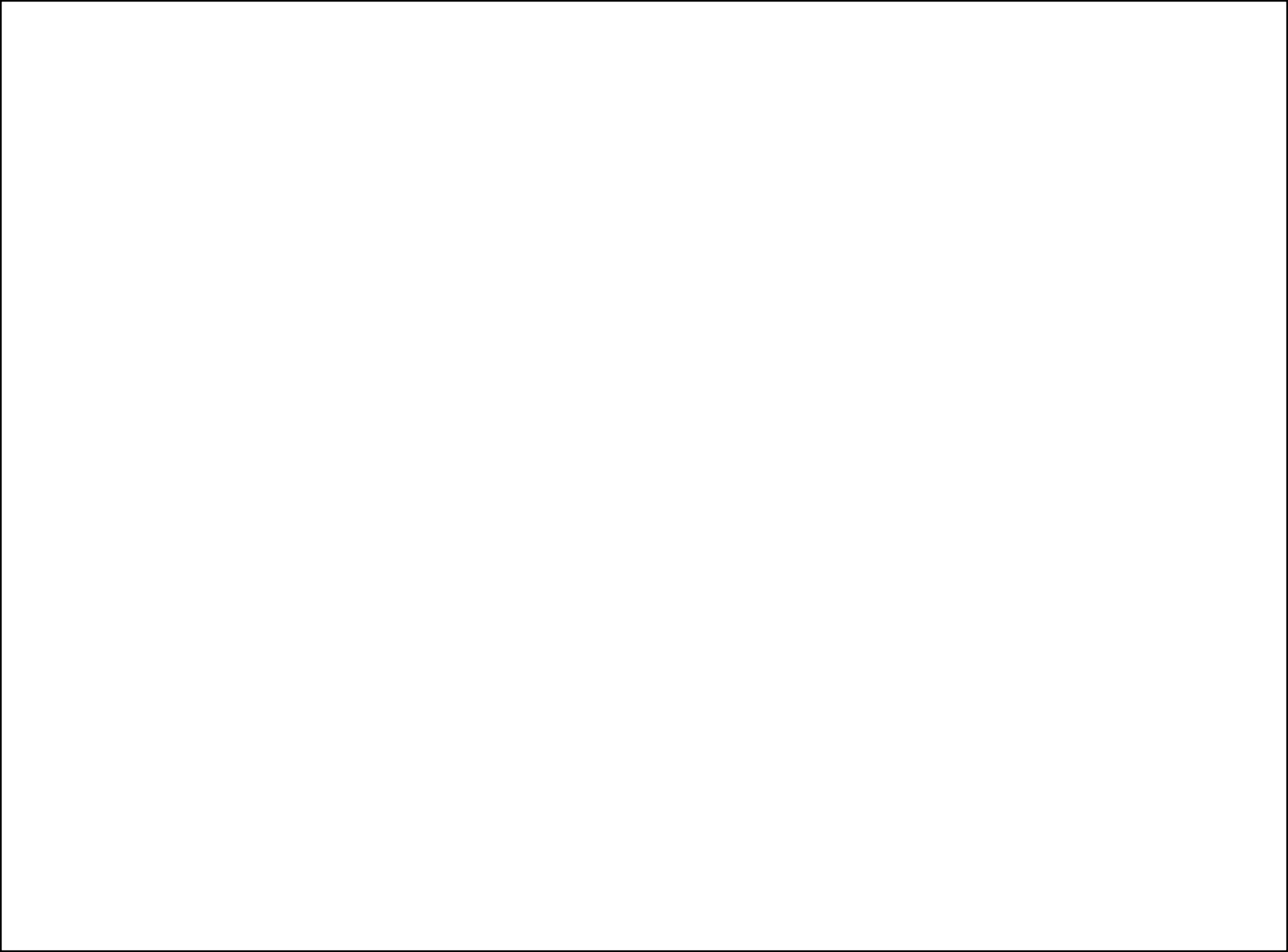
***Centuries ago our ancestors knew already  
the health benefits of alcohol  
as reflected by the toasts***

german	Prosit ! zum Wohl !
english	cheers !
estonian	terviseks !
finnish	terveydeksi !
greek	για μας !
polish	na zdrowie !
french	santé !
italian	salute !
spanish	salud !
hungarian	egészségére

***to your / our  
wellbeing***

***to your / our  
health***





# Potential explanation

## Moderate wine drinkers

⇒ lower hypertension-related all cause mortality  
(no benefit for beer drinkers)

rel.risk all cause mortality  
(compared to abstainers)

systolic BP quartiles

mmHg            116                    129                    139                    158

wine drinking

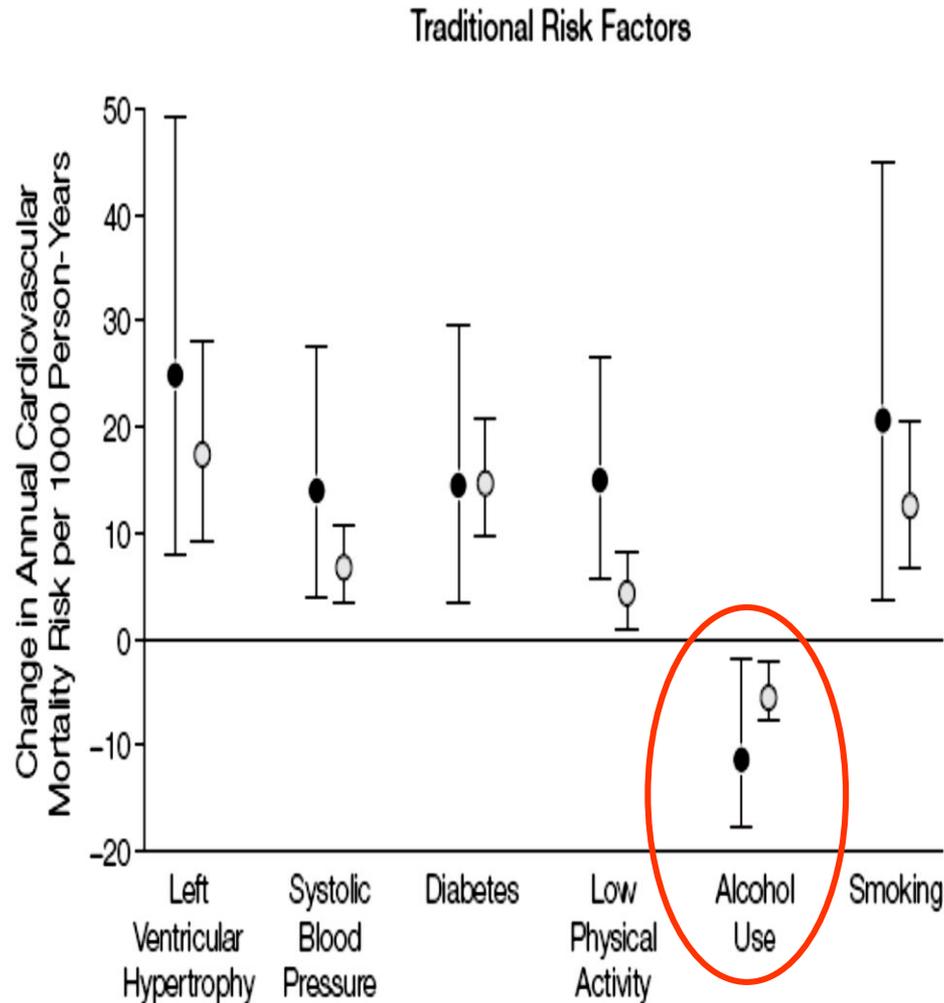
< 60g/day            0.63                    0.85                    0.74                    0.77

*p*<                    0.001                    NS                    0.007                    0.02

>60g/day            0.97                    1.27                    0.95                    1.21

NS

# Chronic Kidney Disease – not only less progression, but also **lower CV risk** in patients with chronic kidney disease



*Shlipak, JAMA (2005) 293:1737*

# Alcohol and age dependent loss of renal function

**Decline of renal function and alcohol consumption:  
prospective 11 year study in 1658 nurses  
no known primary kidney disease**

*compared to nurses with no alcohol consumption  
odds ratio to develop 10 year risk of > 25 % decrease GFR*

	<i>normotensive</i>	<i>hypertensive</i>
--	---------------------	---------------------

<i>0 - 4.9 g/day</i>	<i>0.98</i>	<i>0.98</i>	} small sample size not significant
<i>5 -14</i>	<i>0.83</i>	<i>0.62</i>	
<i>15 -60</i>	<i>0.81</i>	<i>0.53</i>	

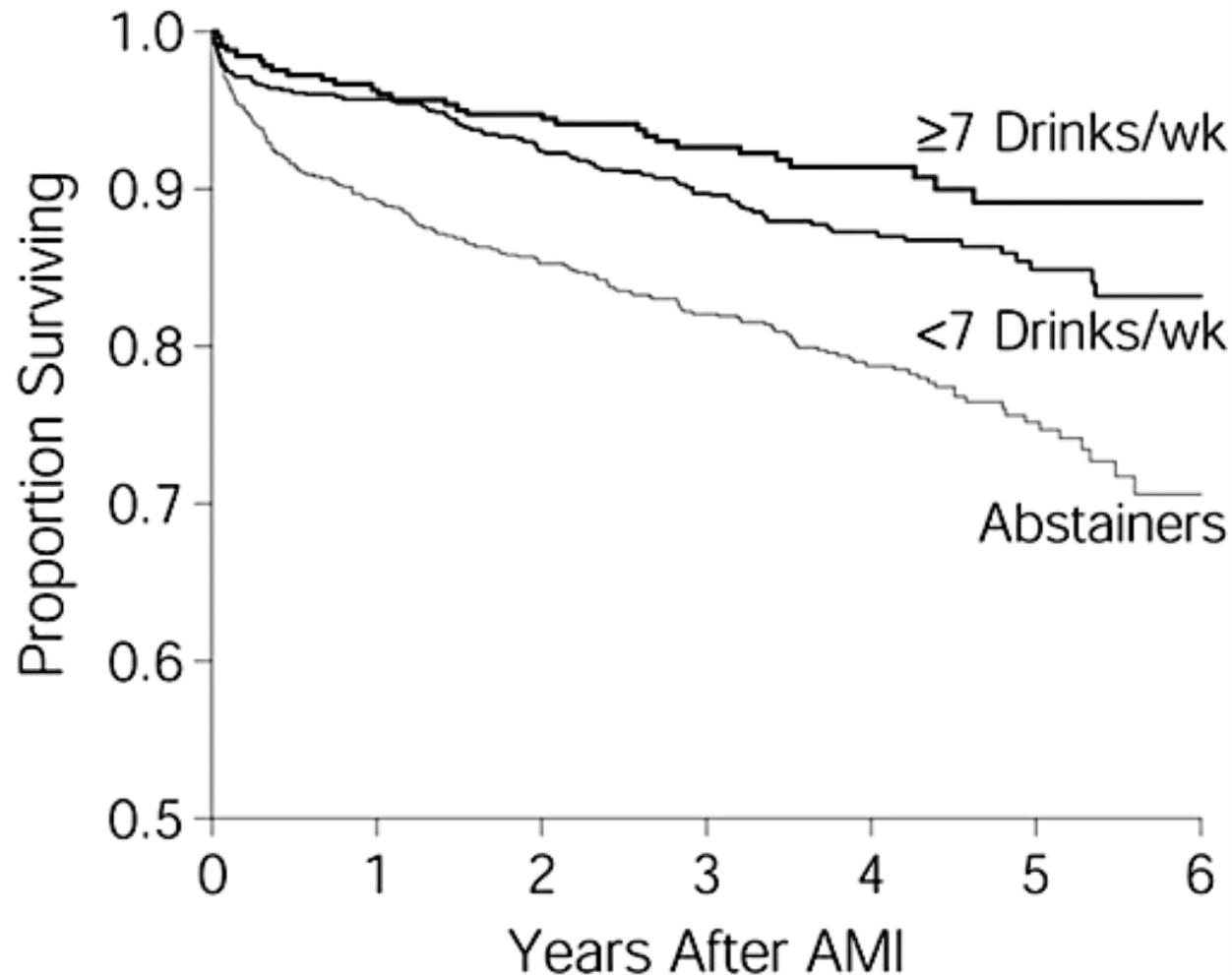
 **moderate alcohol consumption – no substantial adverse effect  
on renal function in women during 11 year follow-up**

*Knight, Nephrol.Dial.Transplant. (2003) 18:1549*

# Prolongation of lifespan

- **SIRT1** (Sirtuin)  
class II histone deacetylase,  
increased by Resveratrol
- p66 **Shc** gene ⇒  
less reactive oxygen species

# Benefit from **alcohol** consumption following **myocardial infarction**



*Mukamal, JAMA (2001) 285: 1965*

# Women and alcohol

Higher blood alcohol levels

Higher risk of mammary carcinoma

Impact on CV risk dependent on age (**menopausal** state)

prospective study of 45,709 nurses

alcohol:

- increased CV risk in young women with low baseline CV risk, even at low alcohol intake
  - **decreased CV risk** only at **age  $\geq$  50 years**

*Fuchs , N Engl J Med (1995) 332: 1245*

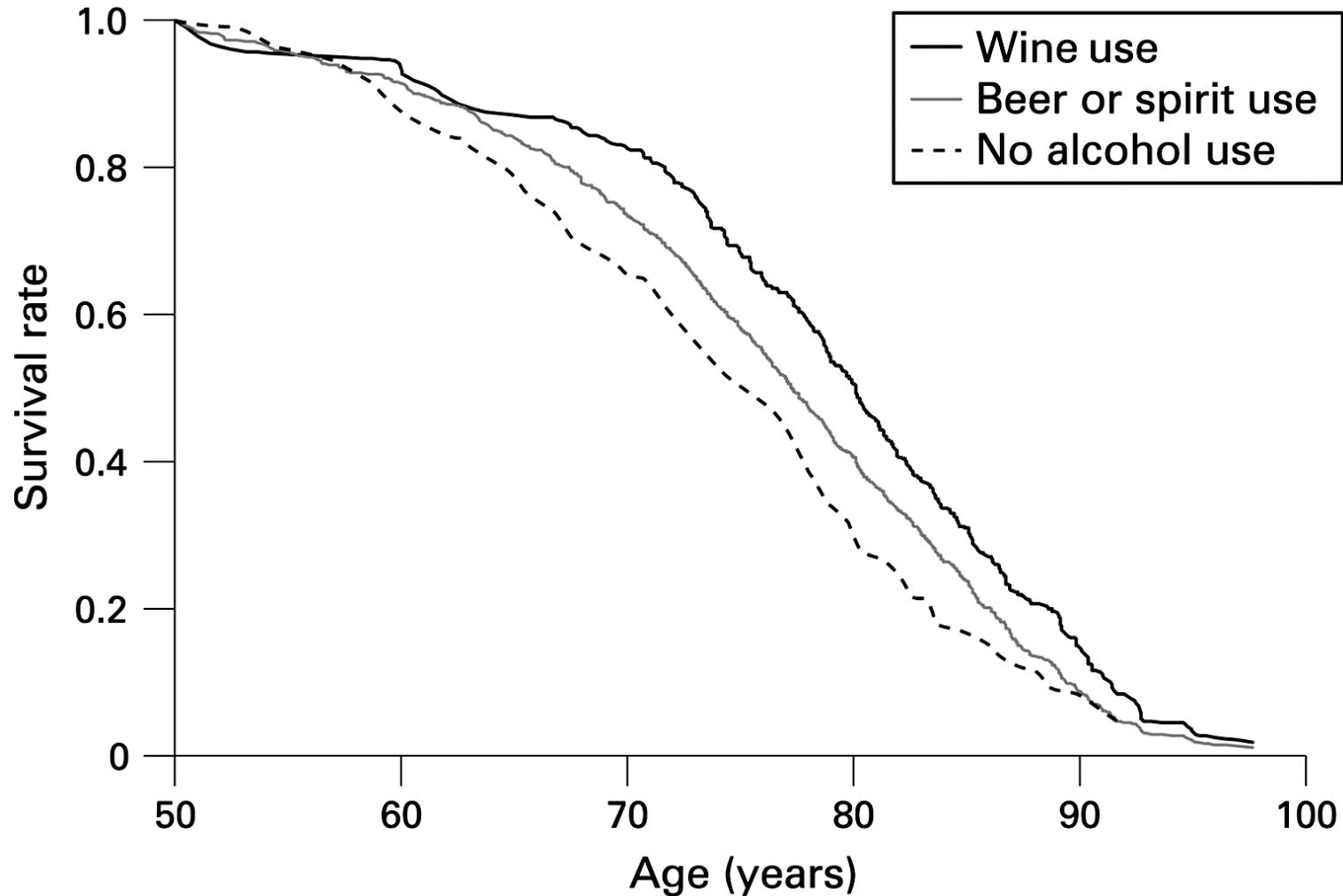
but,

even **young** (30 y) women at **high CV risk** (e.g. type 2 diabetes)  
26% **risk reduction** with alcohol (0.1-4.9 g/day)

*Solomon, Circulation (2000) 102: 494*

# “Drinking half a glass of wine increases longevity by 5 years”

*ZUTPHEN study; 1373 men born 1900-1920*



*Streppel, J Epidemiol Community Health (2009;)63:534*

# Health professional follow up study

**50,000 men**

**→ 5-30 g alcohol per day  
reduction of CV mortality by ~ 25%**

*Rimm et al.*

*Wine, beer and spirits.*

*Are they really horses of a different colour?*

*Circulation (2002) 105: 2806*

# **Alcohol and cardiovascular mortality**

**confirmed by > 60 retrospective and  
prospective epidemiological studies**

**Completely ignored and forgotten  
during the years of prohibition**

*“weil nicht sein kann was nicht sein darf“*

*it is impossible that something can exist if it is forbidden*

# Regimen Sanitatis Salernitani

*Arnoldo de Villanueva*

1235-1311



“... during meals drink wine happily  
*little but often...*”

“...avoid harming the body: *never*  
drink *between meals...*”

*Ursini,*

*Ann.NY Acad Sci (2002) 957:200*

*School of Salerno*

# Medical use of alcohol

**Hippokrates** of Kos (439-377 BC)

**Wine**

*Tranquilizer*

*Analgesic*

*Diuretic*

*Antidiarrhoic*

*Treatment of wounds*

**New Testament**

*(Luke 10; 30-37) The Good Samaritan*

# Alcohol intake and **renal cell cancer** : a metaanalysis

20 case-control studies, 3 cohort studies,  
1 **pooled analysis** of cohort studies

Combined **rel. risk** of renal cell cancer **0.76** (CI 0.68-0.85)

An inverse correlation was observed

*# in men and women*

*# for each specific type of alcoholic beverages (beer, wine, liquor)*

*# in case-control and in cohort studies*

*# in each specific type of alcoholic beverage (beer, wine, liquor)*

*Song, Brit.J..Cancer (2012) 106:1881*

# Alcohol drinking and lower renal cancer risk in a cohort of Finnish smokers

total alcohol intake and type of alcoholic beverages  
29,133 Finnish alcohol consuming smokers;  
50-69 years, 8 year follow-up

Alcohol intake category	1	2	3	4
Alcohol (g/day)	<b>0.4</b>	<b>2.6</b>	<b>11.1</b>	<b>24.1</b>
Age adjust.rel risk (95%) ( <i>multivariate</i> )	1	0.91 (0.62-1.3)	0.94 (0.64-1.38)	<b>0.53</b> (0.34-0.83)

*Mahabir, Cancer Epidemiol.Biomarkers Prev. (2005) 14: 170*

*early death from noncancer causes ?*

# Alcohol increases blood pressure

## Paris Gendarmes



⇒ *cardiovascular and renal benefit despite higher blood pressure ?*

# Frequency of drinking alcohol and CKD in men

9196 men age 57.9±5.1 years  
CKD : eGFR < 60 ml/min/1.73m<sup>2</sup>  
Alcohol drinking by questionnaire

	nondrinkers	1-2/week	3-4/week	5-6/week	daily
odds ratio CKD	1.0	0.76	0.74	0.79	0.60

*multivariable, adjusted*

*Funakoshi, Environ.Health Prev.Med.(2012) 17:199*

**Moderate alcohol consumption –  
*enhances vaccine induced responses  
in rhesus macaques***

*Modified Vaccinia Ankara (MVA)  
vaccination at baseline; subsequently open-access to 4% ethanol  
after 7 months second vaccination  
animals with blood ethanol concentrations >80 mg/dl  
# lower CD4 and CD8 T cell proliferation  
# lower response to MVA booster  
compared to animals with blood alcohol <80 mg/dl*

*Messaoudi, Vaccine (2014) 32:54*

**Extra benefit in high risk populations ?**

**Dose response relationship ?**

**All alcoholic beverages created equal ?**

# Alcohol consumption and kidney function decline in the elderly

Alcohol and Kidney Disease

Vandana Menon<sup>1</sup>, Ronit Katz<sup>2</sup>, Kenneth Mukamal<sup>3</sup>, Bryan Kestenbaum<sup>4</sup>, Ian H. de Boer<sup>4</sup>, David S. Siscovick<sup>5</sup>, Mark J. Sarnak<sup>1</sup> and Michael G. Shlipak<sup>6</sup>

*Nephrol.Dial.Transplant.(2010) 25:3301*

4343 subjects > 65 years Cardiovascular Health Study  
primary outcome eGFR loss > 3 ml/min/year  
follow-up 5.6 years

## odds ratio

no alcohol (reference)

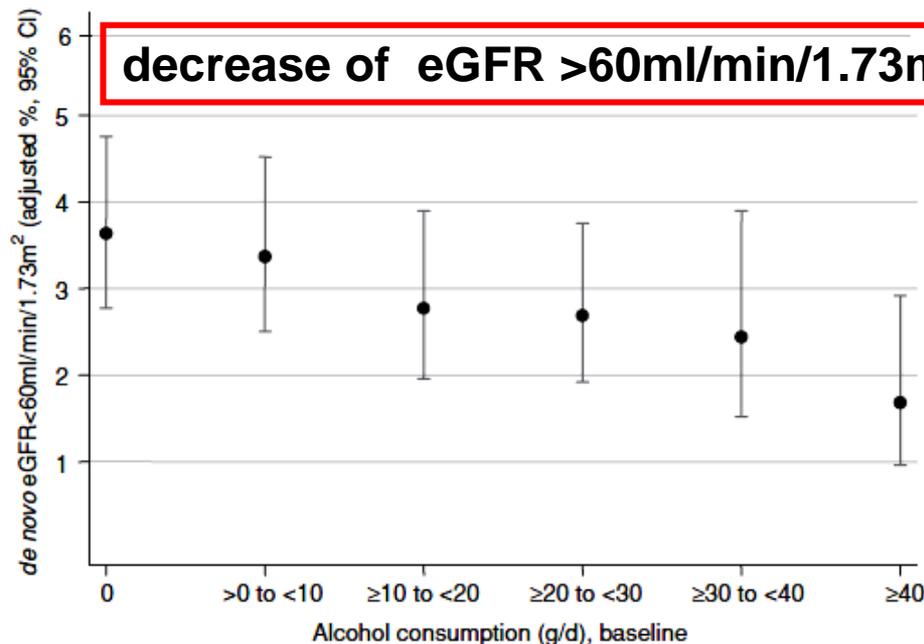
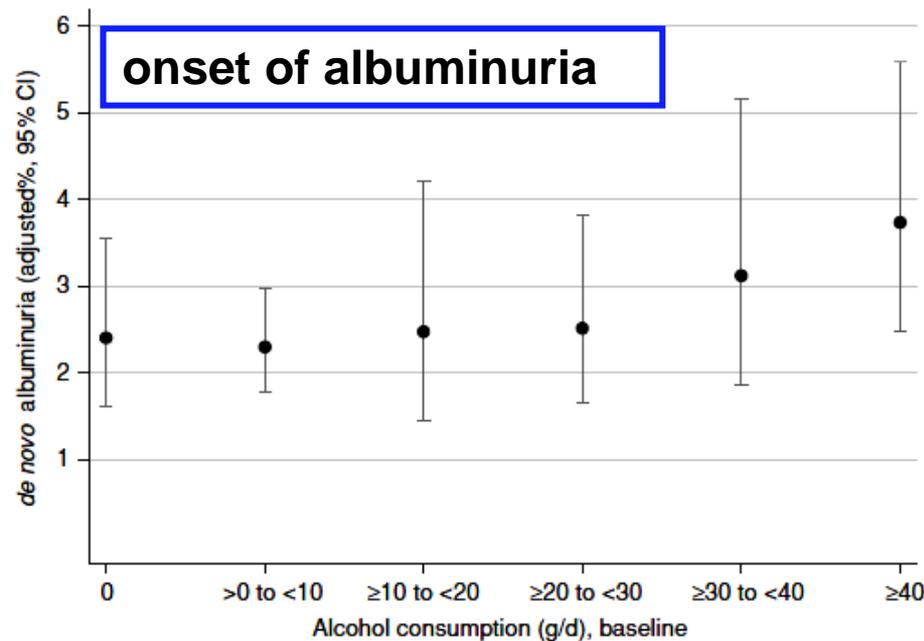
former alcohol use	1.18
< 1drink	1.20
1-6	
7-13	1.10
>14	0.89 (0.61-1.13)

# Alcohol consumption

onset of **albuminuria** and  
loss of **GFR** < 60 ml/min/1.73m<sup>2</sup>

- AUSDIAB study
- 6259 adults
  - 14 years follow-up
  - self-identification of alcohol consumption

*White,  
Nephrol.Dial.Transplant.(2009) 24: 2464*



# Alcohol consumption and risk of CKD

## Japanese 10 year study in a community based population

123,764 individuals (41012 male, 82752 female)

within 10 years de novo:

CKD I or II 4307 individuals (2048 ♂, 2259 ♀)

CKD III or higher 19411 individuals (4257 ♂, 15154 ♀)

*predictors:*

*age, GFR, hematuria, hypertension, diabetes,  
s-lipids, obesity, smoking, alcohol*

### CKD I or II

hazard ratio	♂	ethanol < 20g/day	<b>0.86</b> (0.78-0.95) p<0.002
		>20g/day	1.04 (0.86-1.25) NS
	♀	< 20g/day	<b>0.85</b> (0.63-1.02) p<0.069
		> 20g/day	1.05 (0.26-4.24) NS

*Yamagata, Kidn, Internat. (2007) 71:159*

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s-lipids, obesity, smoking, alcohol*

### CKD III or higher

hazard ratio	♂	ethanol < 20g/day	<b>0.92</b> (0.86-0.98) $p < 0.0065$
		> 20g/day	0.93 (0.79-1.10) NS
	♀	< 20g/day	<b>0.91</b> (0.83-1.00) $p < 0.04$
		> 20g/day	0.59 (0.22-1.56) NS

*Yamagata, Kidn, Internat. (2007) 71:159*

# Alcohol consumption and renal cell cancer

## 2 Italian multicentric case-control studies

1115 incident, histologically confirmed cases (1985-2004) vs  
2582 controls hospitalized with acute non-neoplastic conditions

compared to nondrinkers odds ratio of renal cell cancer was:

OR **0.87** (CI 0.73-1.04) for up to 4 drinks per day

**0.76** (CI 0.59-0.99) „ 4-8 drinks per day

**0.70** (CI 0.5-0.97) „ > 8 drinks per day

no differences between wine, beer and spirits compared to  
abstainers

# Decreasing risk of renal cell cancer with alcoholic beverages

Case-control study in Swedish adults  
855 cases vs 1204 controls

**compared to nondrinkers :  
ethanol intake >620g/month**

***significantly decreased risk of renal cell carcinoma :***  
**odds ratio 0.6** (95%CI 0.4-1.0; *p value for trend =0.0*)

Risk decreased 30-40%  
with drinking > 2 glasses per week

- red wine (OR 0.6)
- white wine (OR 0.7)
- beer (OR 0.6)

# **Inverse association between alcohol intake and risk of renal cell cancer**

*(analysis of 12 prospective studies)*

12 prospective studies including 530,469 ♂ and 229,575 ♀  
follow-up times 7-20 years  
validated food-frequency questionnaires at baseline

1430 cases (711 ♀; 719 ♂) of incident renal cell cancer  
incidence rate nondrinkers 23 ; drinkers 15  
*per 100,000 person years*

Compared with nondrinking alcohol consumption (>15g/day)  
decreased risk :

pooled multivariable RR = 0.72 (95%CI 0.60-0.86;p<0.01)

*no significant difference between genders*

*no significant difference between beer vs wine vs liquor p=0.40)*

*Lee, J.Natl.Cancer Inst.(2007) 16:801*

Long-term **alcohol consumption** and risk for **death** and cardiovascular death  
 1818 doctors with incident non-fatal MI  
 (*Health Professionals Follow-up study*)

	Long-term alcohol consumption (g/day)			
	0	0.1–9.9	10.0–29.9	≥30.0
Total deaths	168	161	97	42
Hazard ratio (95% CI) <sup>a</sup>	1.0	0.75 (0.60–0.93)	0.61 (0.47–0.79)	0.77 (0.54–1.10)
		<i>p</i> <0.03		
Cardiovascular deaths	92	81	47	23
Hazard ratio (95% CI) <sup>a</sup>	1.0	0.71 (0.52–0.96)	0.52 (0.36–0.75)	0.80 (0.50–1.29)
		<i>p</i> <0.07		

# Factors impacting on renal glomerular changes

## Autopsy-based population survey

*(Hisayama study 1962-1994)*

### Age adjusted odds ratio ( $\pm 95\%CI$ )

male <i>n=458</i>	Glomerulosclerosis	Arteriolar Hyalinosis
pulse pressure ( $\Delta 10\text{mmHg}$ )	1.17	1.28
Glucose intolerance	2.43	2.06
BMI	0.99	1.01
alcohol intake (yes/no)	0.72 (0.42-1.24)	0.66 (0.39-1.11)
female <i>n=381</i>		
pulse pressure ( $\Delta 10\text{mmHg}$ )	1.28	1.17
Glucose intolerance	1.60	1.63
BMI	1.01	1.04
alcohol intake (yes/no)	0.21 (0.05-0.92)	1.94 (0.73-5.18)

multivariate analysis age and proteinuria were significant independent risk factors for glomerulosclerosis and alcohol had protective effect

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*Yamagata, Kidn, Internat. (2007) 71:159*

# Association between frequency of drinking alcohol and CKD in men

9,196 men; age  $57.9 \pm 5.1$  years; health check-up  
CKD eGFR  $< 60$  ml/min/1.73m<sup>2</sup>  
alcohol consumption by questionnaire

## odds ratio of CKD

nondrinkers	1.0
1-2 drinks/week	0.76 (95%CI 0.60-0.95)
3-4“	0.74 (95%CI 0.59-0.93)
5-6“	0.79 (95%CI 0.64-0.97)
daily	0.60 (95%CI 0.51-0.79)

inverse trend across increasing frequency of drinking alcohol  
( $p=0.001$  for trend)

# Alcohol consumption and kidney function decline in the elderly

Alcohol and Kidney Disease

Vandana Menon<sup>1</sup>, Ronit Katz<sup>2</sup>, Kenneth Mukamal<sup>3</sup>, Bryan Kestenbaum<sup>4</sup>, Ian H. de Boer<sup>4</sup>, David S. Siscovick<sup>5</sup>, Mark J. Sarnak<sup>1</sup> and Michael G. Shlipak<sup>6</sup>

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follow-up 5.6 years

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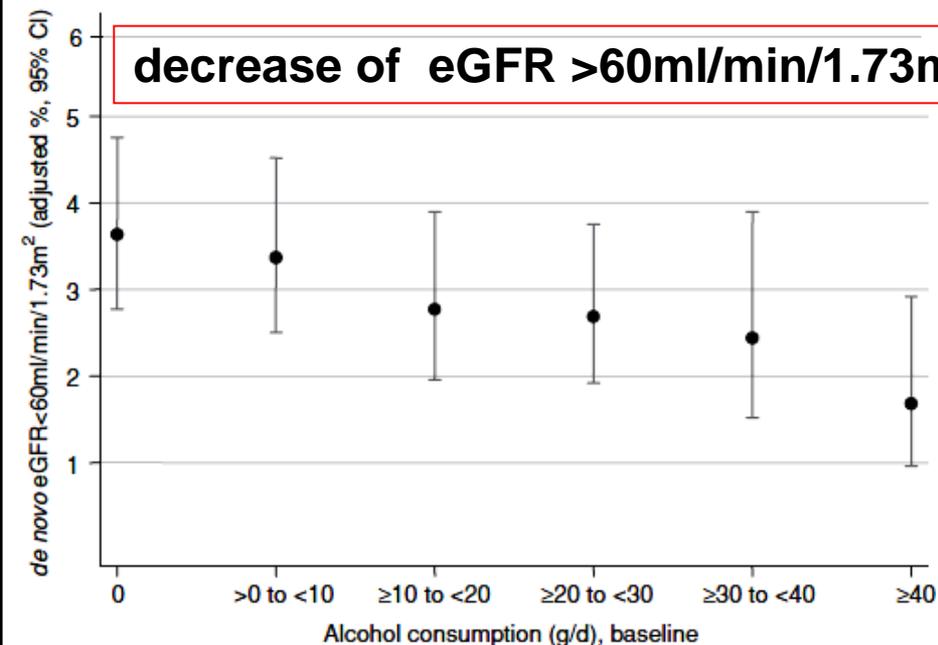
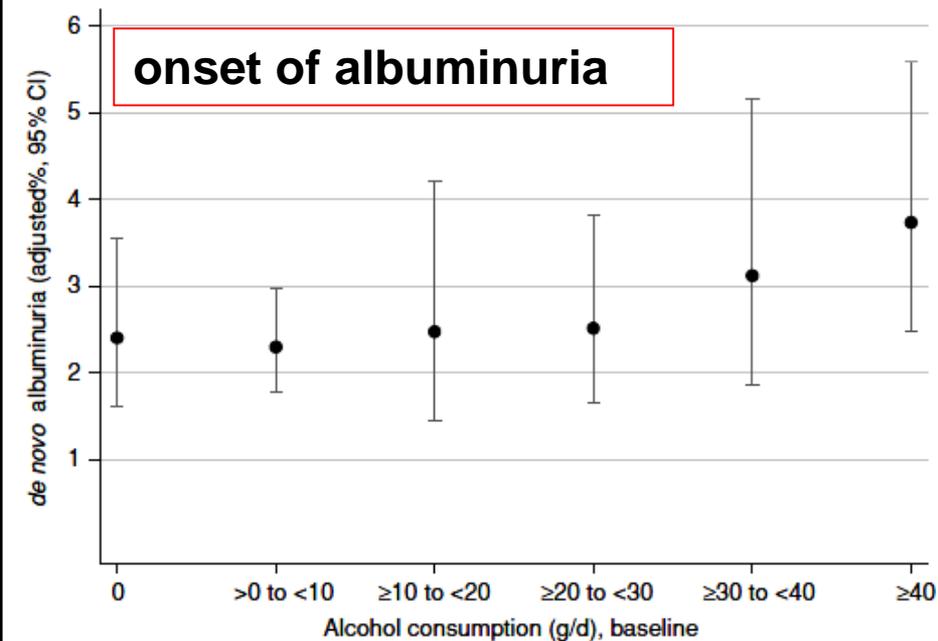
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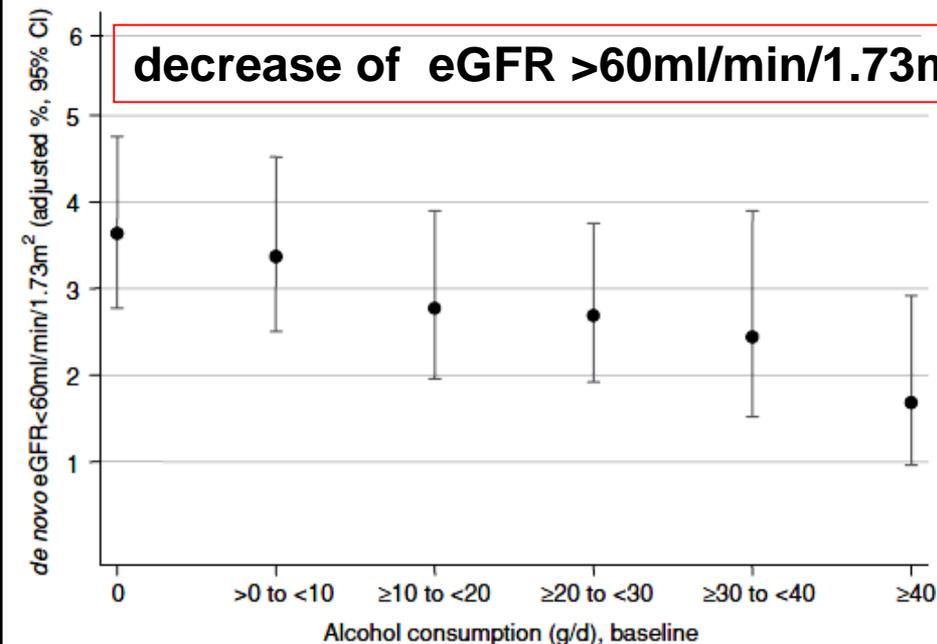
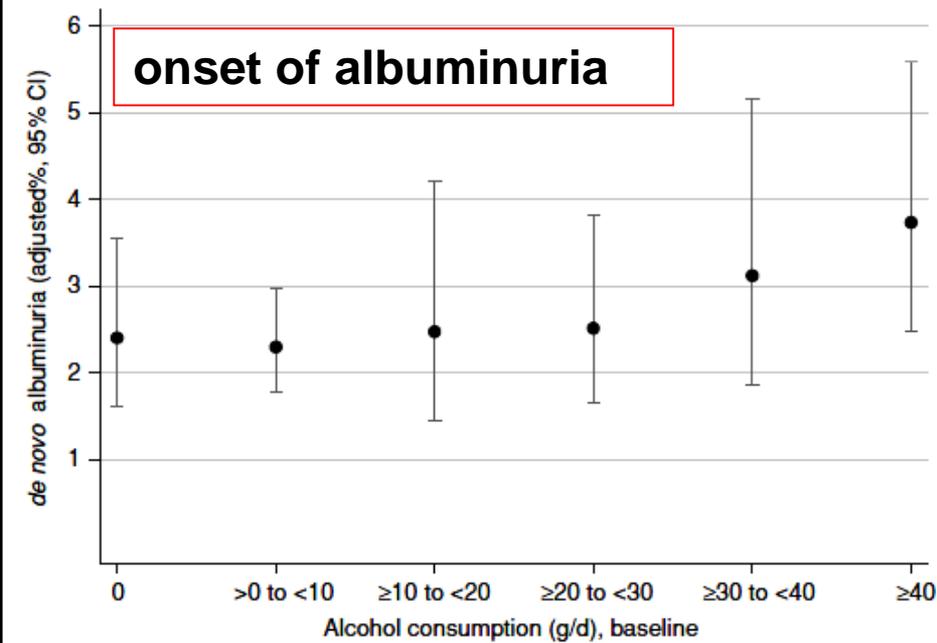


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# Resveratrol retards progression of diabetic nephropathy through modulations of oxidative stress, proinflammatory cytokines, and AMP-activated protein kinase

Chih-Chun Chang<sup>1</sup>, Chieh-Yu Chang<sup>1</sup>, Yang-Tzu Wu<sup>1</sup>, Jiung-Pang Huang<sup>1</sup>, Tzung-Hai Yen<sup>2</sup> and Li-Man Hung<sup>1\*</sup>

*J.Biomed.Sci.(2011) 28:47*

**Alcohol may be man's worst enemy,  
but the bible says love your enemy.**

*Frank Sinatra*  
*1915-1998*

# Alcohol consumption and blood pressure

(*French Nutrition and Health Study*)  
 (Individuals 18-70 years)



Der Alkohol ist des Menschen grösster Feind,  
doch in der Bibel steht geschrieben:  
„Du sollst die Feinde lieben“

*Frank Sinatra*  
*1915-1998*

# IDNT study – alcohol consumption and risk of **progression** of **diabetic** nephropathy

	renal endpoint (n=462)	no renal endpoint (n=1253)
alcohol consumption: yes	23 %	28 %
p (univariate analysis)		0.02

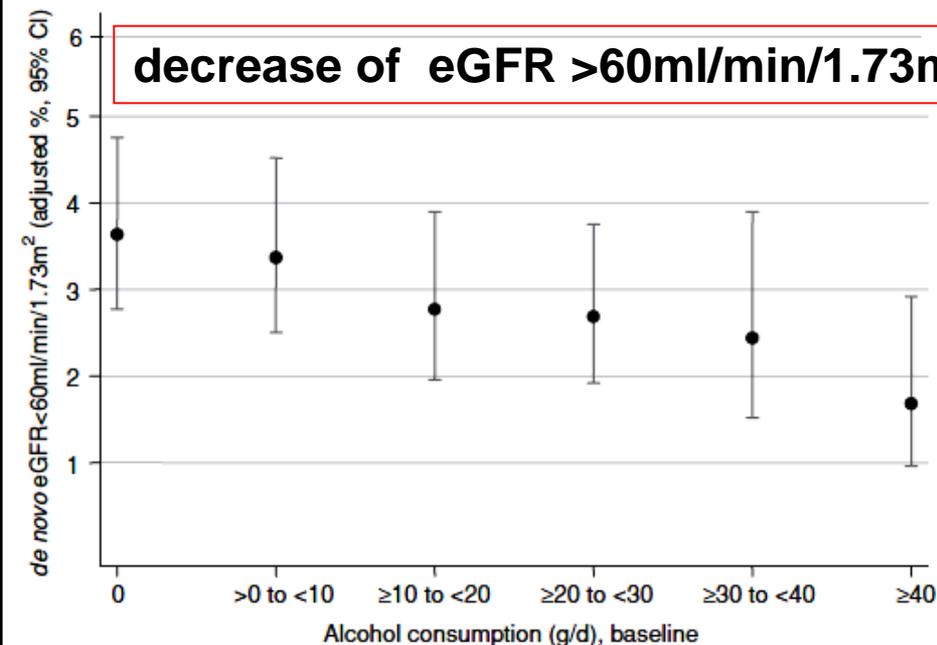
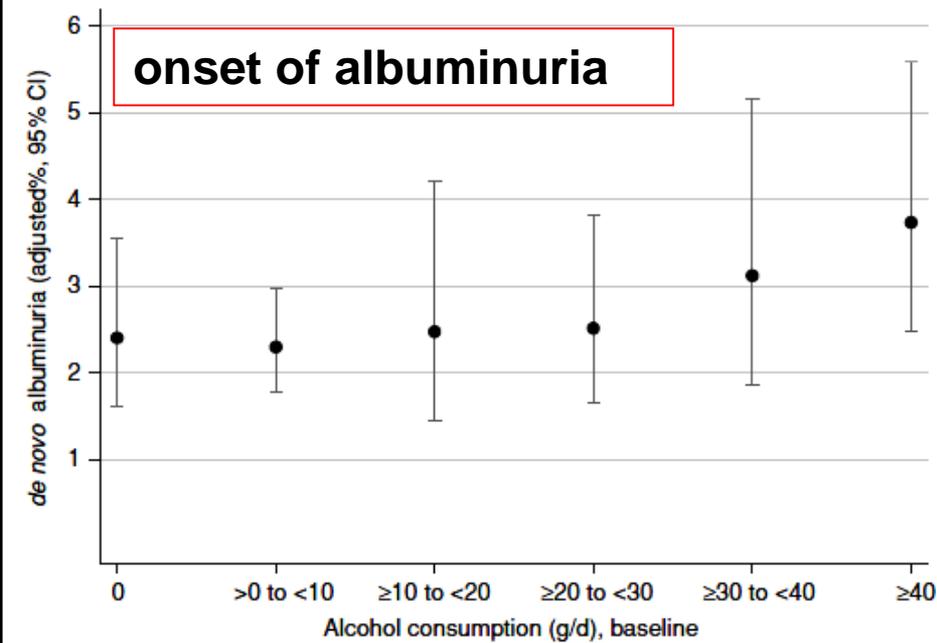
*Lewis New Engl J Med (2001) 345:851*

# Alcohol consumption

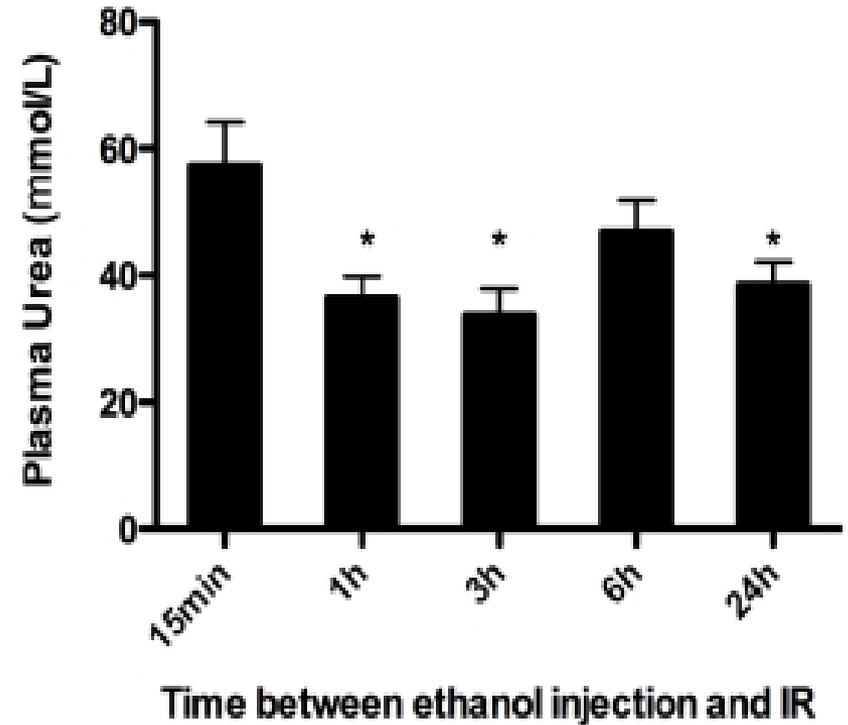
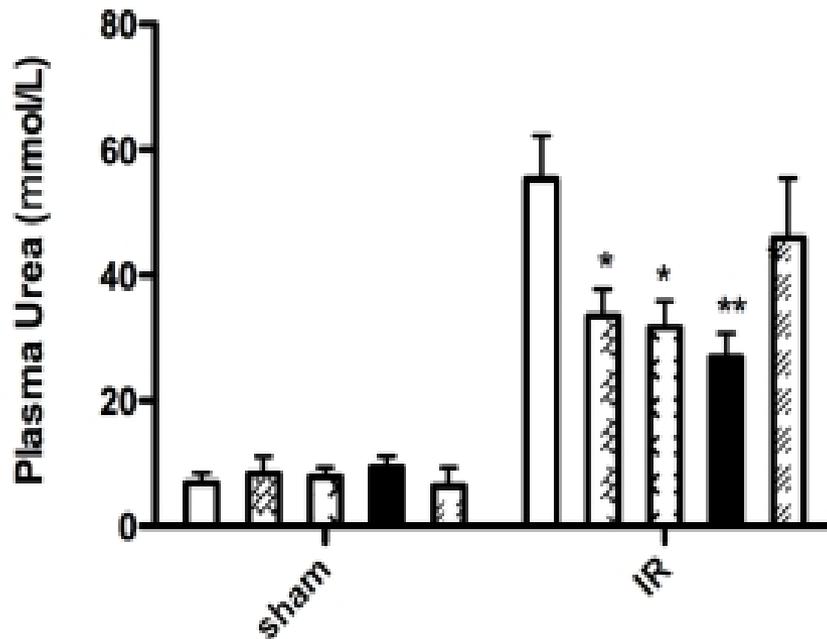
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**Preconditioning** with “physiological“ levels of ethanol *protects in animal experiments the kidney against ischemia/reperfusion (IR) injury*



# “Drinking **half a glass of wine** increases longevity by **5 years**“

*ZUTPHEN study  
1373 men born 1900-1920  
examined until 2000*

long term light **alcohol** consumption (< 20g/day)

<b>cerebrovascular mortality</b>	<b>hazard ratio 0.43</b> (CI 0.26-0.70)
<b>cardiovascular mortality</b>	<b>hazard ratio 0.70</b> (CI 0.55-0.89)
<b>all-cause mortality</b>	<b>hazard ratio 0.75</b> (CI 0.63-0.91)

*Streppel,, J Epidemiol Community Health (2009;)63:534*

# **Alcohol and progression of nondiabetic renal disease**

## **negative epidemiological data**

- presence of chronic kidney disease  
alcohol no increased risk (except moonshine; Pb)

*Vupputuri, Ann Epidem.(2003) 13:712*

- alcohol not related to chronic kidney  
disease in 9082 US adults (NHANES II)

*Stengel, Epidemiology (2003) 14:479*

**Drinking alcohol**  
**evolution of albuminuria vs eGFR**  
*individuals with no primary kidney disease*

6259 Australian adults < 65 years, prospective 5 year follow-up

males : selfreported consumption < 3g vs > 3g alcohol/day

**new onset of:**

**albuminuria** (*albumin/creatinine*)    **OR 1.87** (CI 0.99-3.52)    ?

**eGFR<60 ml/min**                      **OR 0.34** (CI 0.22-0.59)    ★

*White, Nephrol.Dial.Transplant.(2009) 24:2464*