

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 ^a (Exact 95% CI) |
|---------------------------|--|---|---|
| Heart disease | 120 | 140 | 24.0 (18.5–31.2) ^b |
| Stroke | 44 | 206 | 22.0 (15.6–31.0) ^b |
| Chronic pulmonary disease | 83 | 121 | 16.0 (12.1–21.0) ^b |
| Diabetes mellitus | 72 | 84 | 10.3 (7.7–13.6) ^b |
| Cancer | 38 | 89 | 9.2 (6.3–13.1) ^b |
| Connective tissue disease | 12 | 56 | 5.2 (2.7–9.3) ^b |
| Chronic kidney disease | 45 | 47 | 4.9 (3.5–6.8) ^b |
| Alcohol abuse | 57 | 39 | 4.3 (3.1–5.8) ^b |

23%

rel.risk

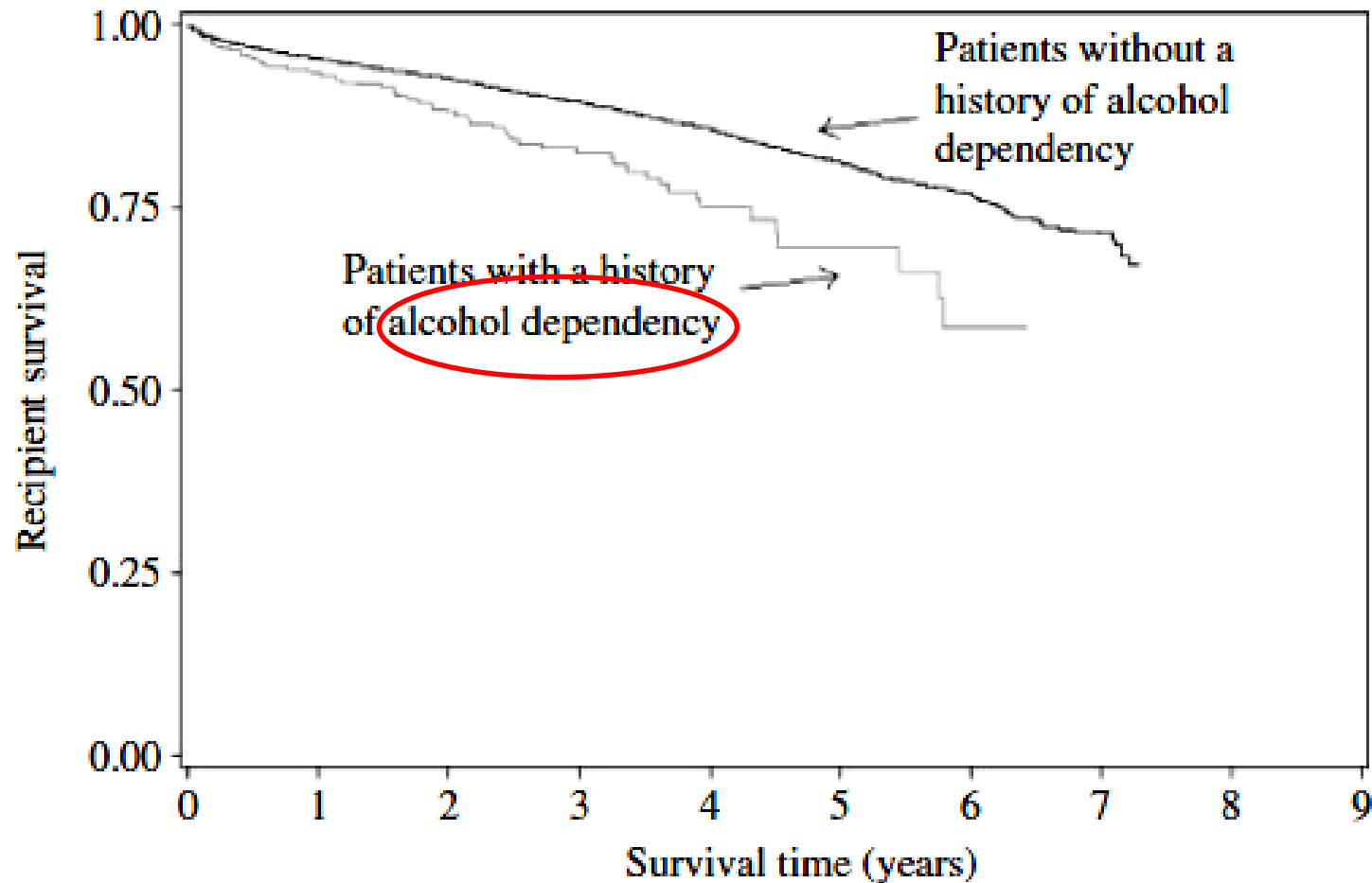


Bagshaw, Crit.Care (2005) 9:R700

Following binge drinking even bilateral renal necrosis

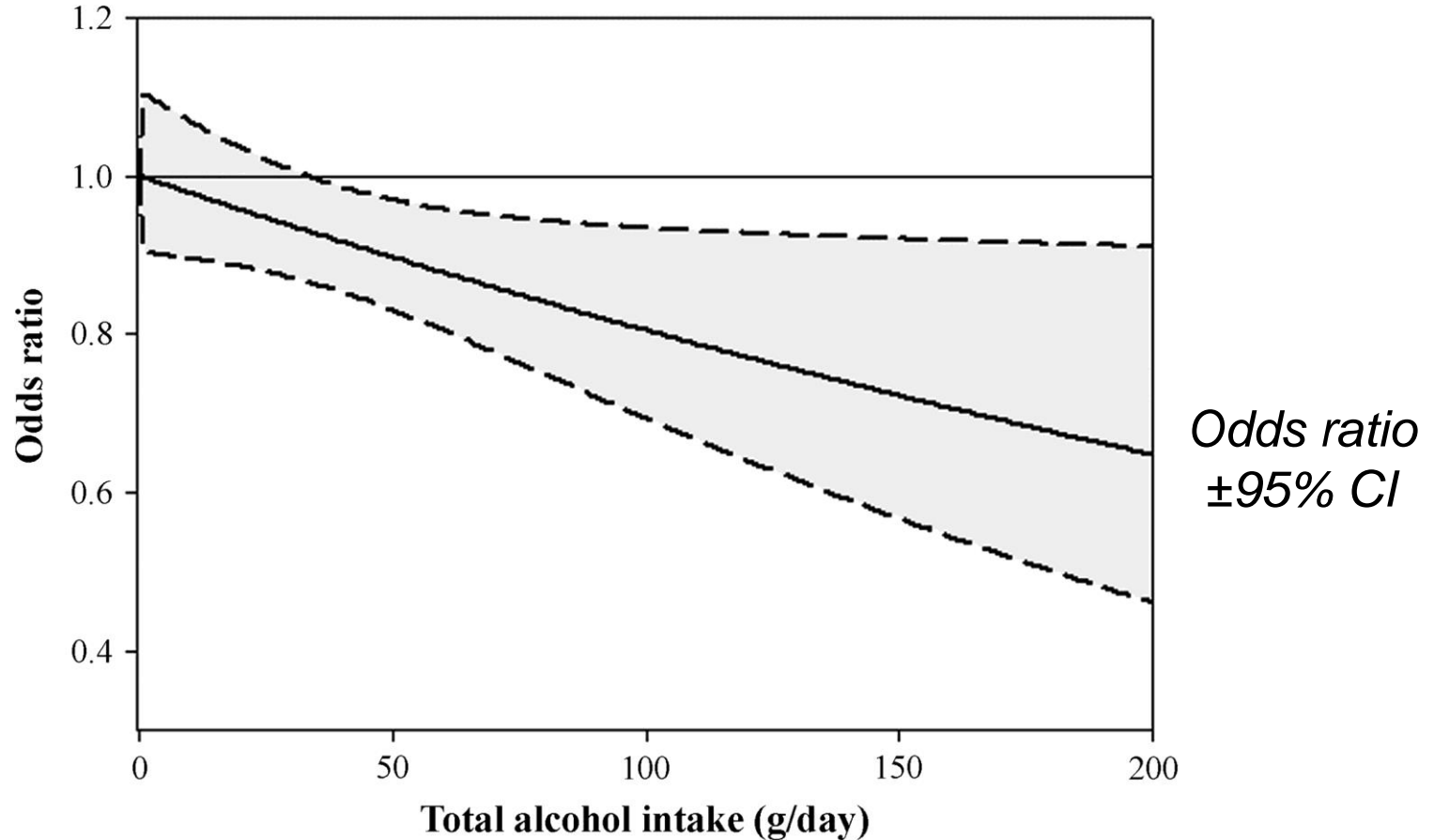
Jung, Alcohol Alcohol (2012) 47:140

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, 2nd edition
W.Saunders Co, Philadelphia :

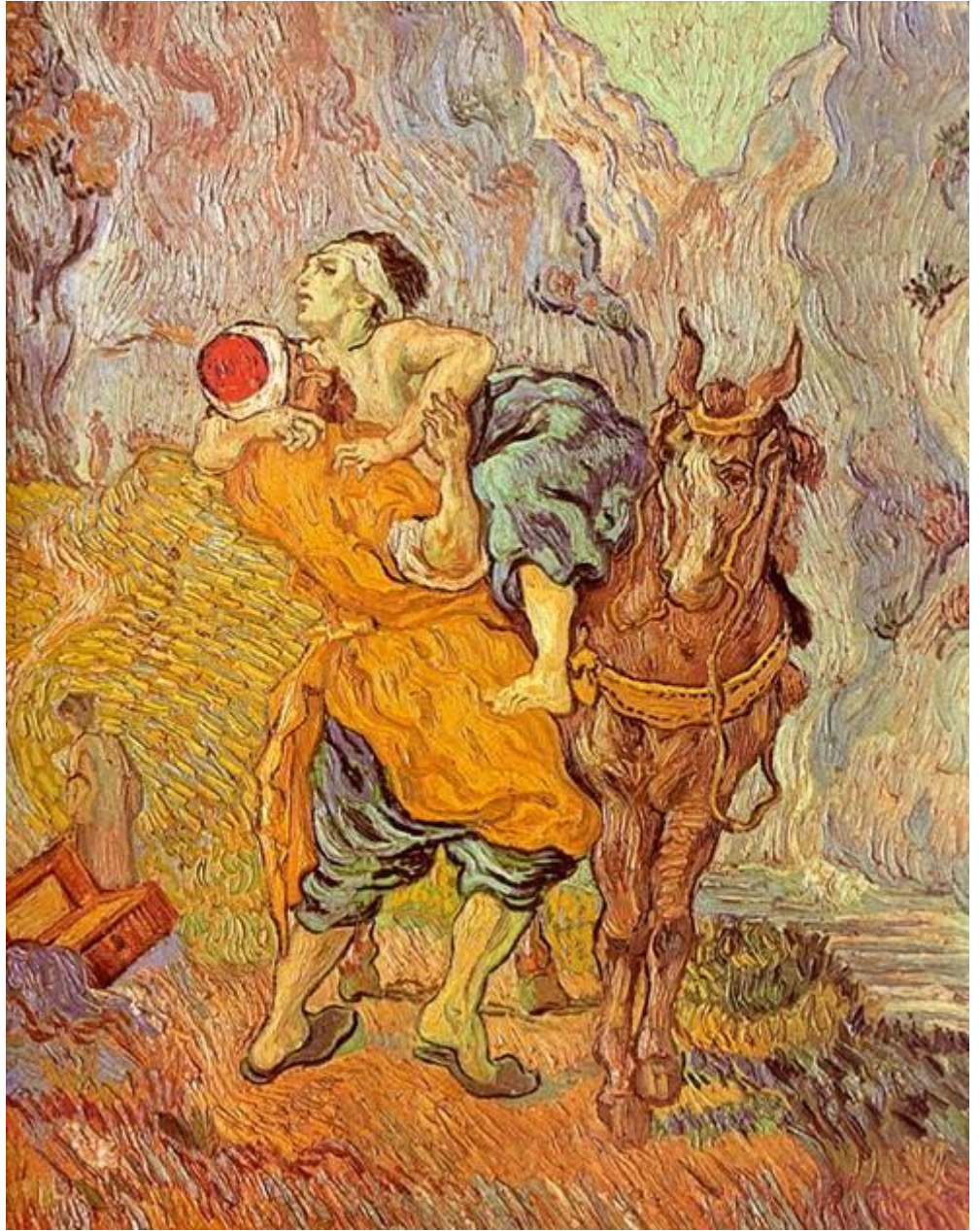
“threshold” ~ 3 drinks/day (~ 45g alcohol/day)

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

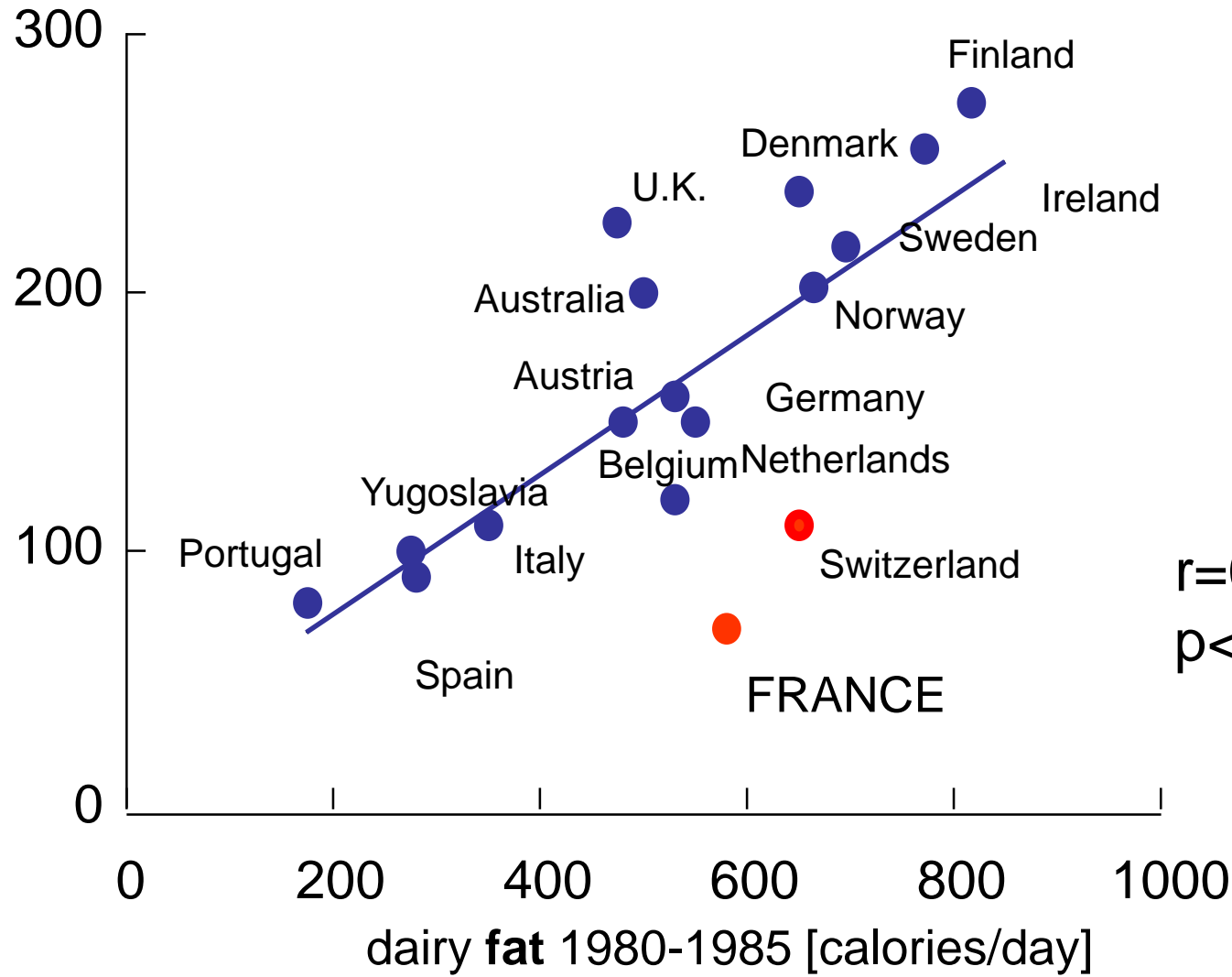
Hypothesis

Wine antagonises adverse effects of animal fat

French Paradox

of coronary heart disease

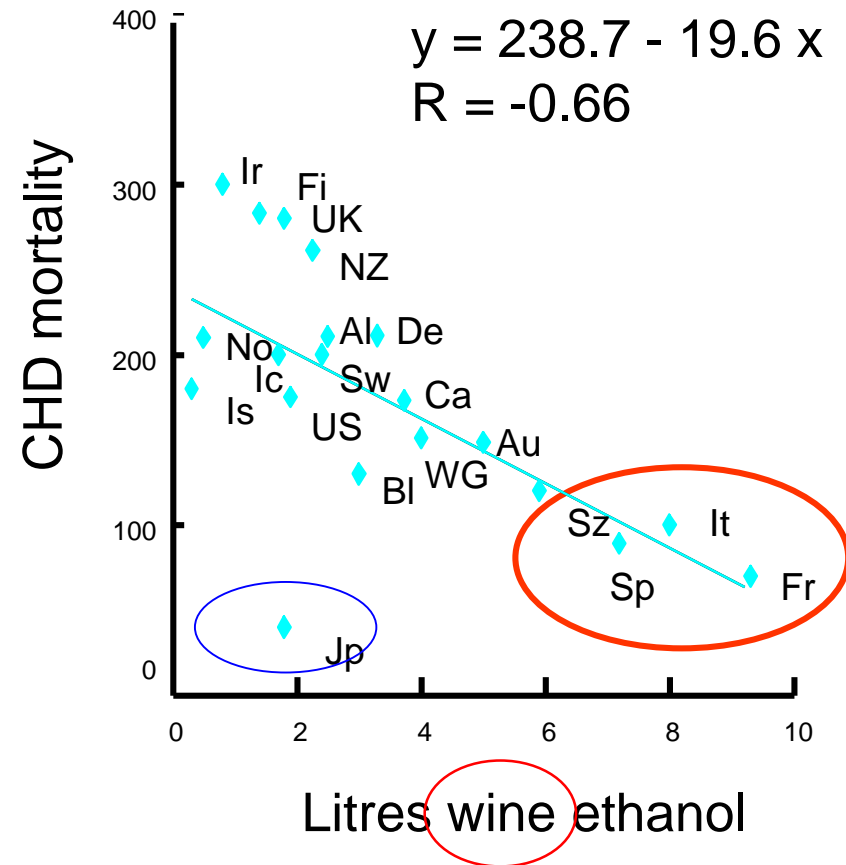
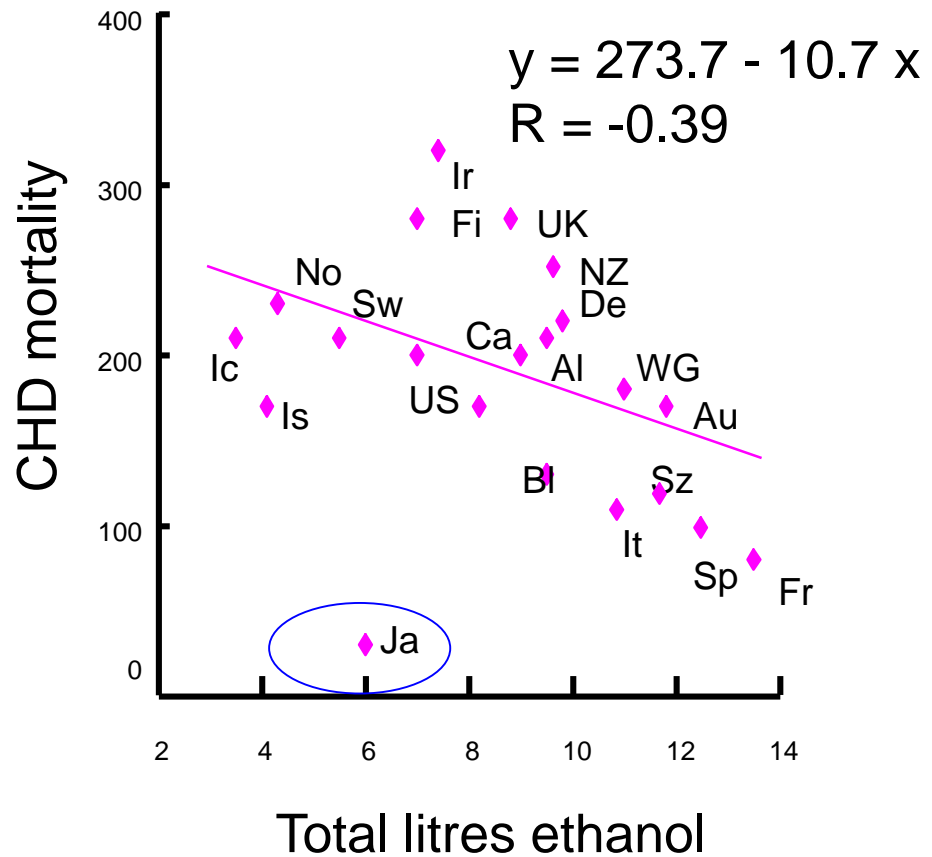
standardized rate
CHD death



$r=0.73$
 $p<0.001$

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

| | | | | |
|---------------------|-----|------|------|------|
| CV mortality | 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) ^a | 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) ^a | 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

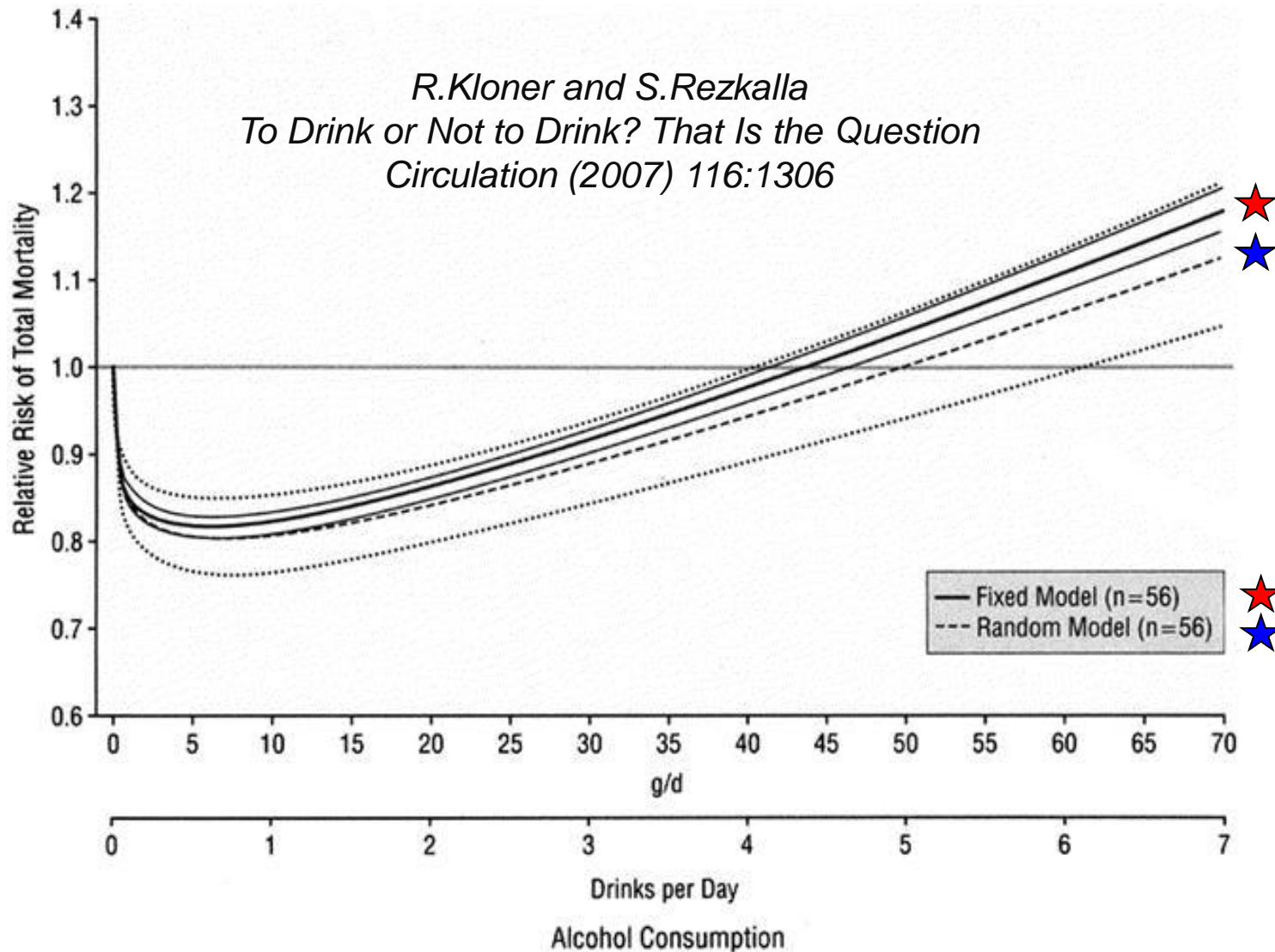
| | |
|--------------------------------|---|
| coronary heart disease | hazard ratio 0.61 (CI 0.41-0.89) |
| total cardiovascular mortality | hazard ratio 0.53 (CI 0.53-0.86) |
| all-cause mortality | hazard ratio 0.73 (CI 0.62-0.87) |

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

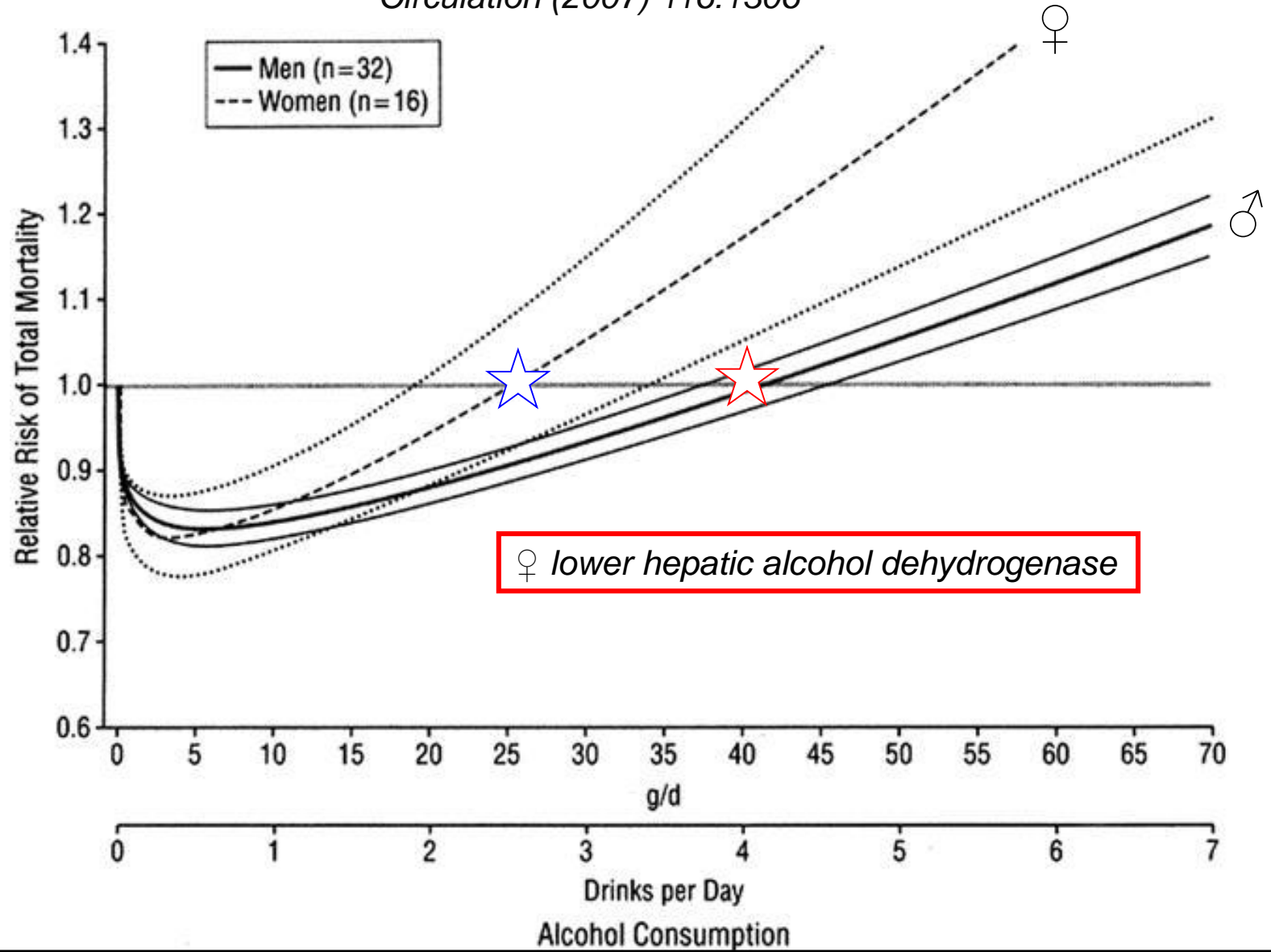


Different CV benefit from alcohol in men and women

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

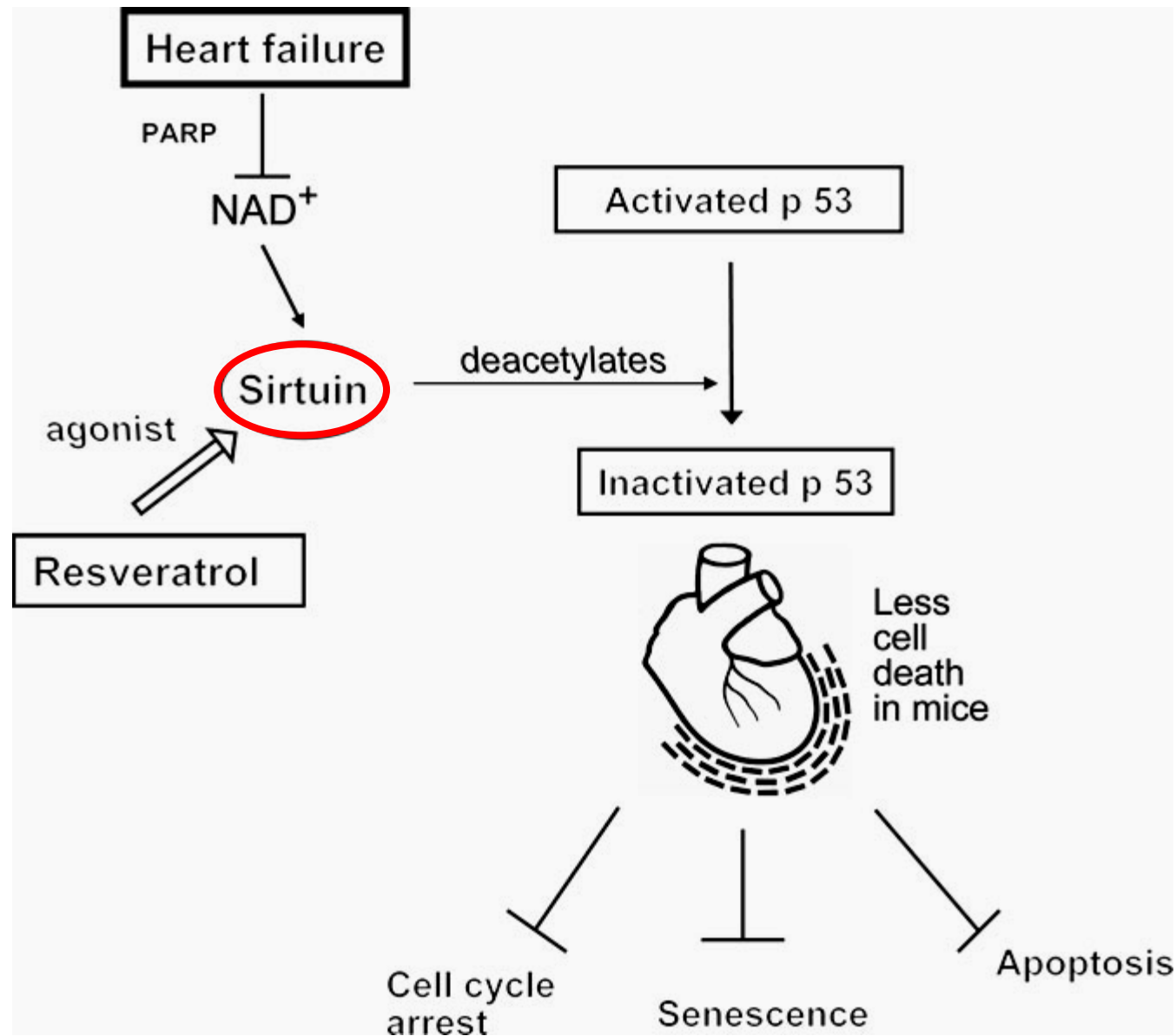
| | RR | |
|------------|-------------|---------------------|
| | 0 g alcohol | 22-32 g alcohol/day |
| smoker | 2.8 | 1.9 |
| non-smoker | 1 | 0.7 |

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

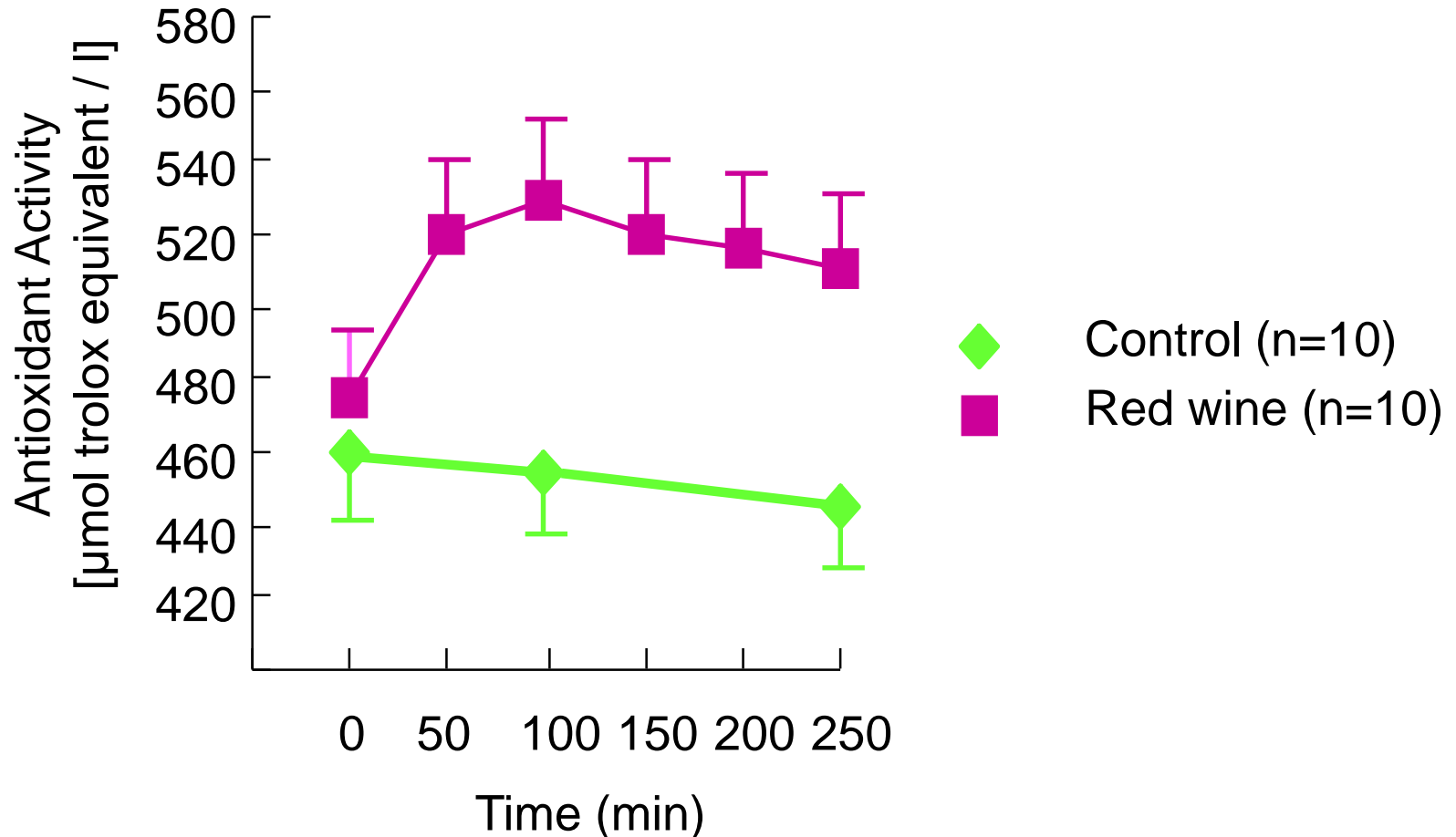
Opie, Eur.Heart J.(2007) 28:1683

Mechanisms of cardioprotection by alcohol in heart failure



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

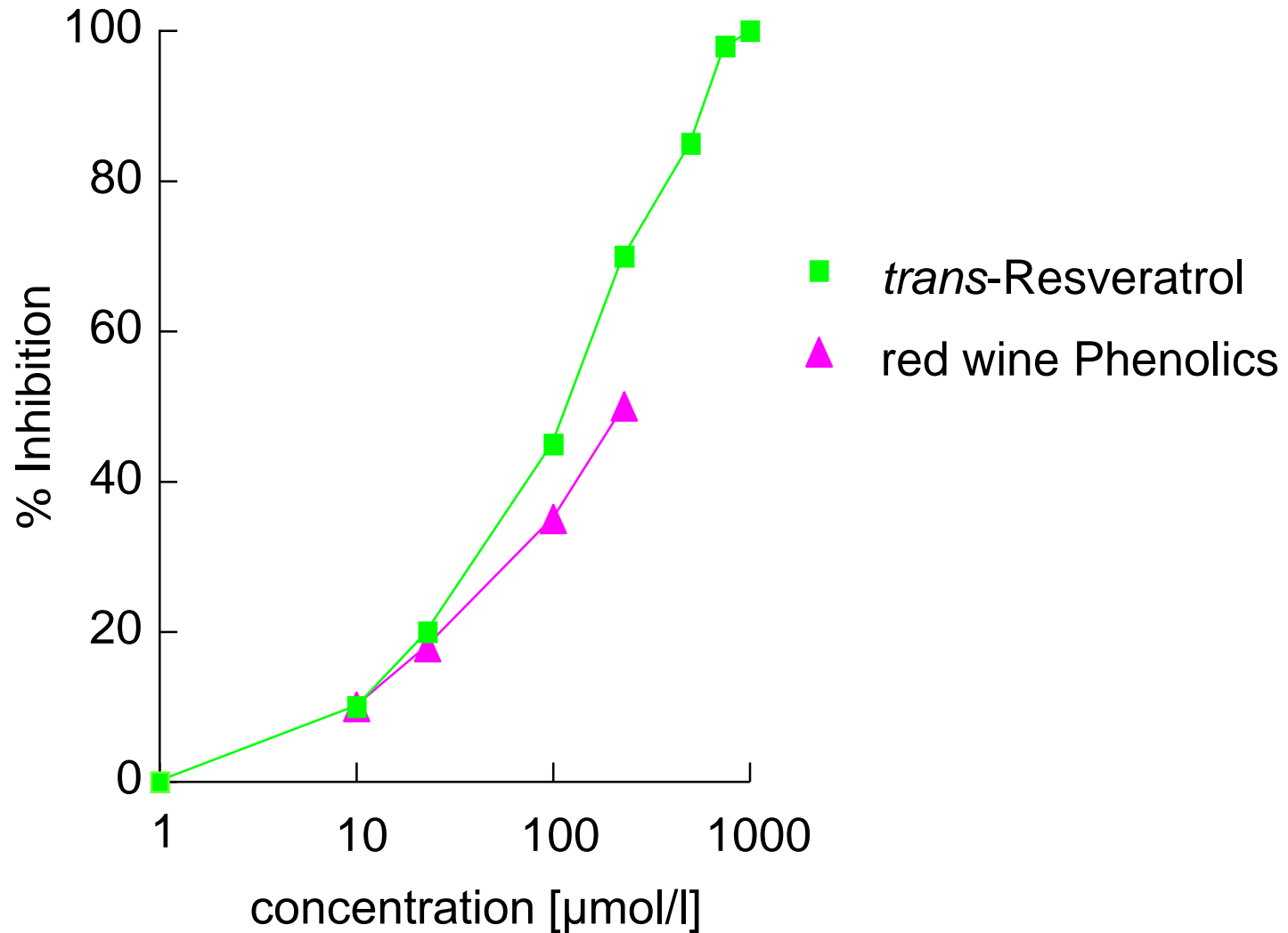
Impact of Red Wine on Serum Antioxidant Activity in Healthy Volunteers



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

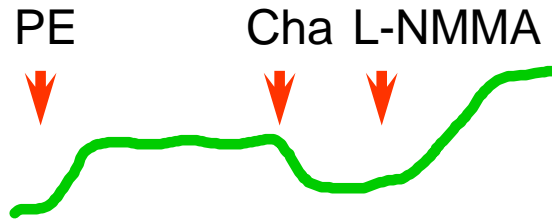
Leikert, Circulation (2002) 106: 1614

Human Coronary Artery

Effects of Red and White Wine

red

Chateuneuf
du Pape
(+endothelium)



Chateauneuf
du Pape
(- endothelium)

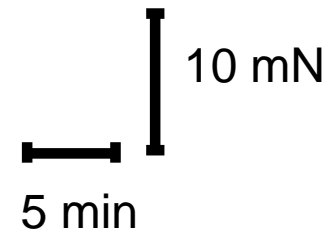
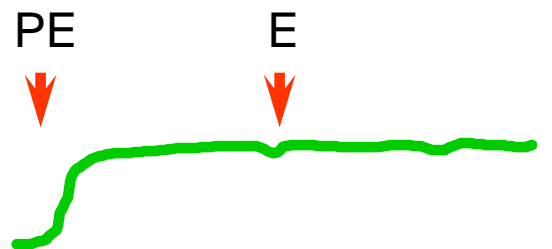


white

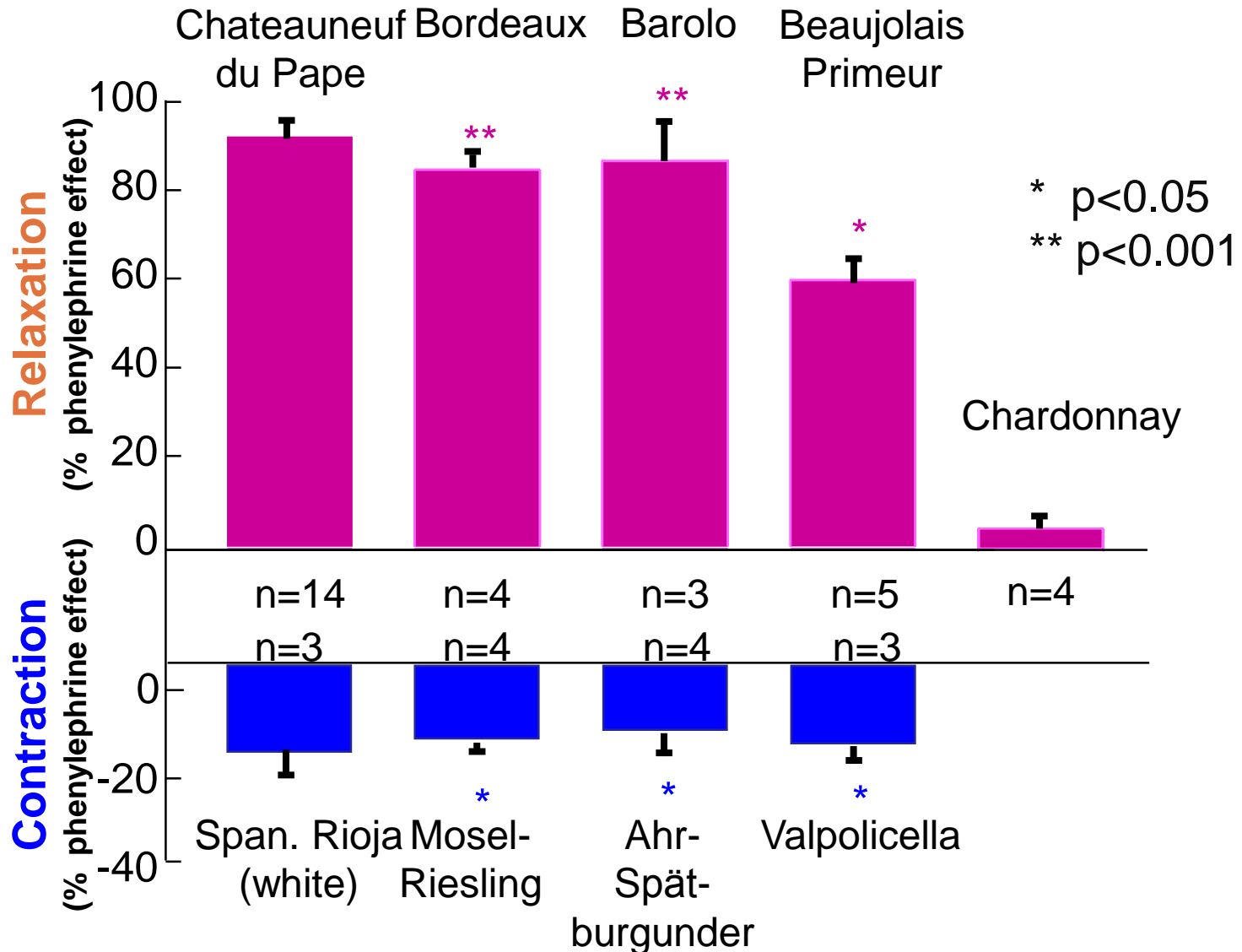
Mosel-
Riesling



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 ²) | 87 | 108 | 124 | 93 |

longitudinal arm 117 patients

odds ratio

| | | |
|-------------------|-----|------------------|
| abstainers | 1.0 | |
| light drinkers | 0.4 | <i>p</i> < 0.024 |
| moderate drinkers | 0.1 | <i>p</i> < 0.002 |
| heavy drinkers | 2.3 | <i>p</i> < 0.492 |

Alcohol consumption and course of IgA-glomerulonephritis

| estimated daily alcohol consumption | | | |
|---|---|--|---|
|  |  |  1-3x |  |
| abstinence | little | moderate | high |

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**

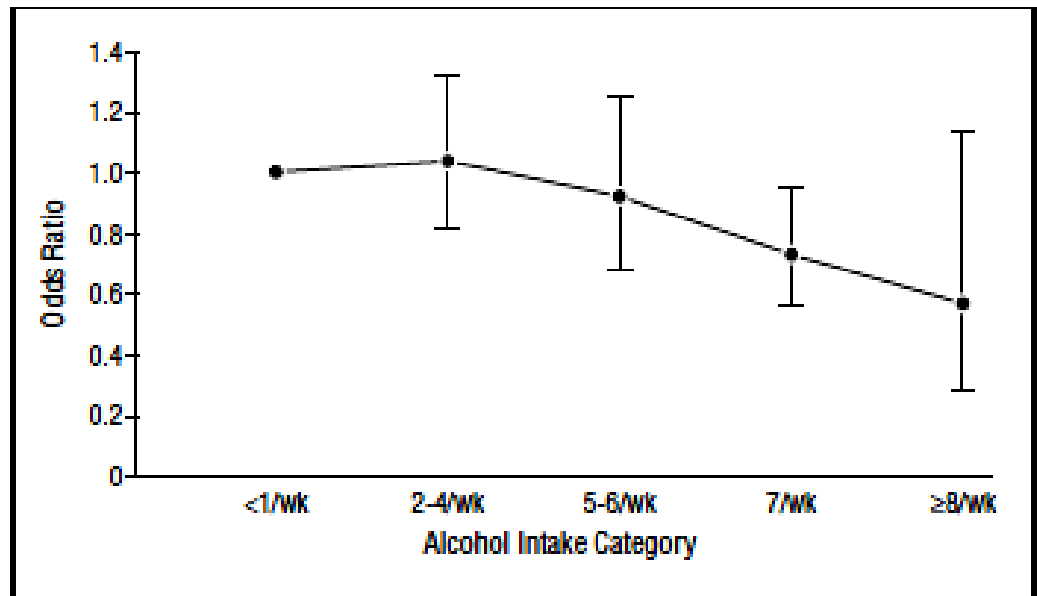
(endpoint : S-creatinine > 1.5mg/dl)

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/1.73m²
alcohol consumption by questionnaire

odds ratio of CKD

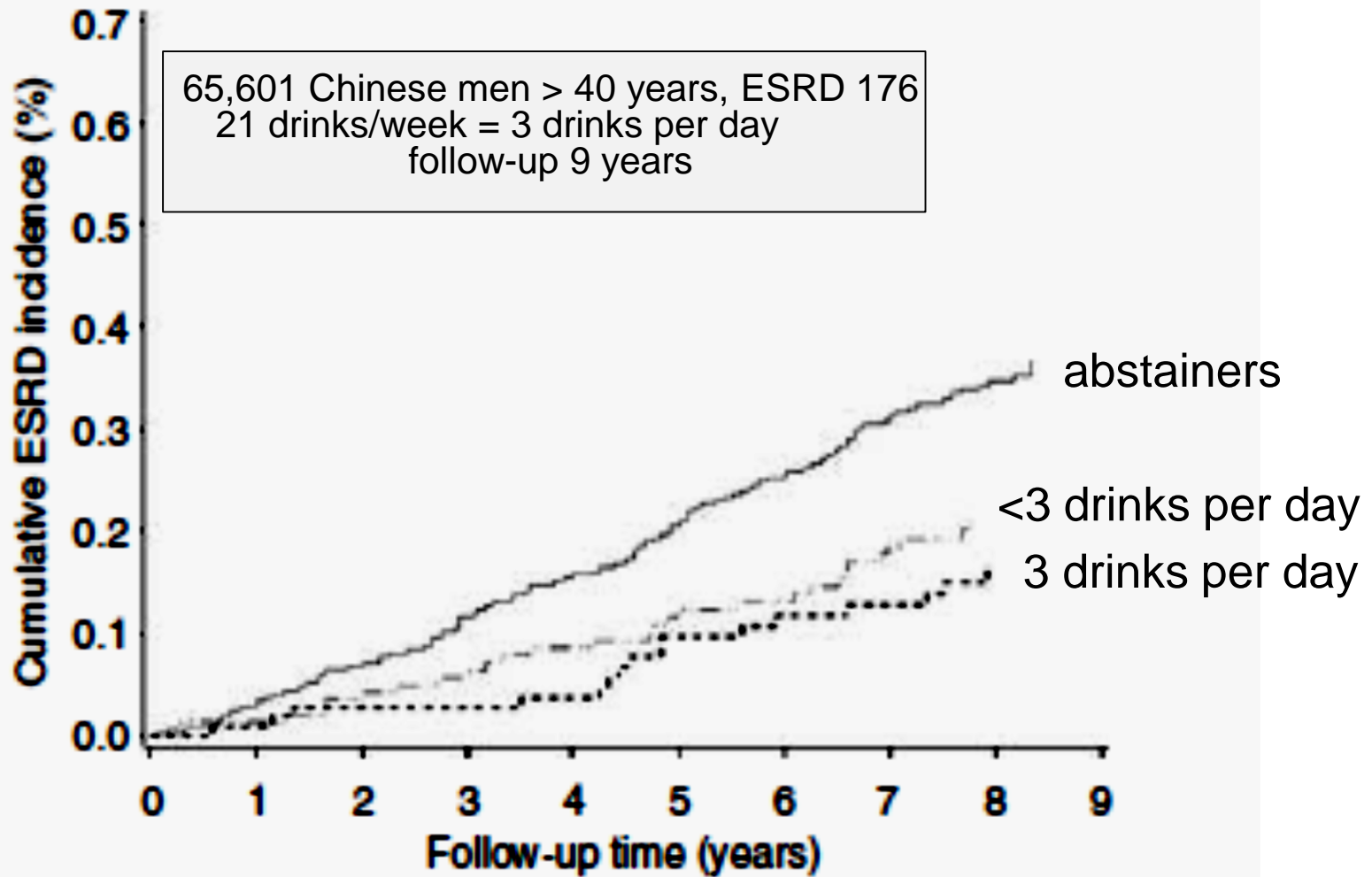
| | |
|-----------------|-------------------------------|
| nondrinkers | 1.0 |
| 1-2 drinks/week | 0.76 (95%CI 0.60-0.95) |
| 3-4“ | 0.74 (95%CI 0.59-0.93) |
| 5-6“ | 0.79 (95%CI 0.64-0.97) |
| daily | 0.60 (95%CI 0.51-0.79) |

(p=0.001 for trend)

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

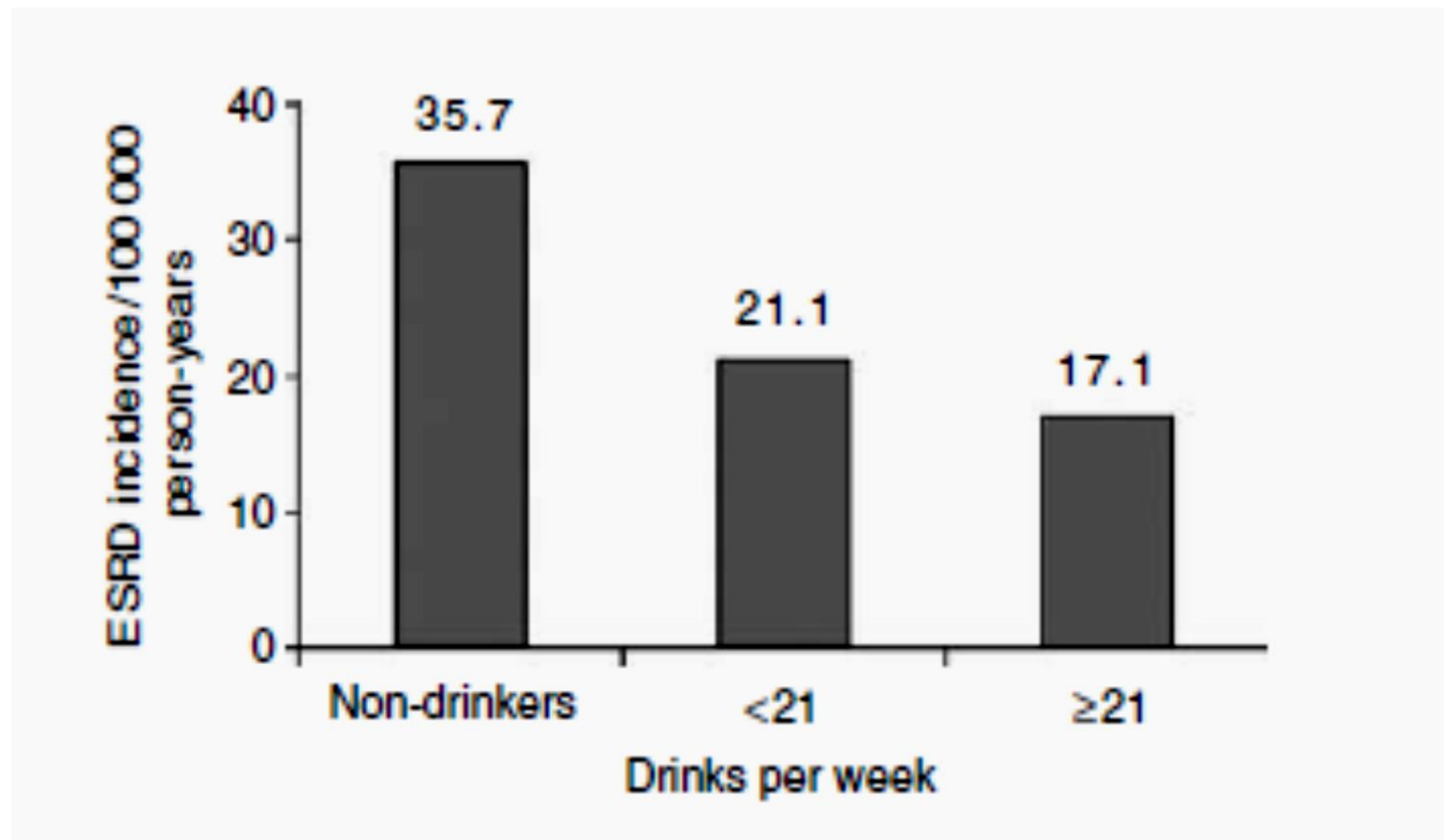
Alcohol and **endstage renal disease** :

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 |
| alcohol intake (yes/no) | 0.72 (0.42-1.24) | 0.66 (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**

**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)**

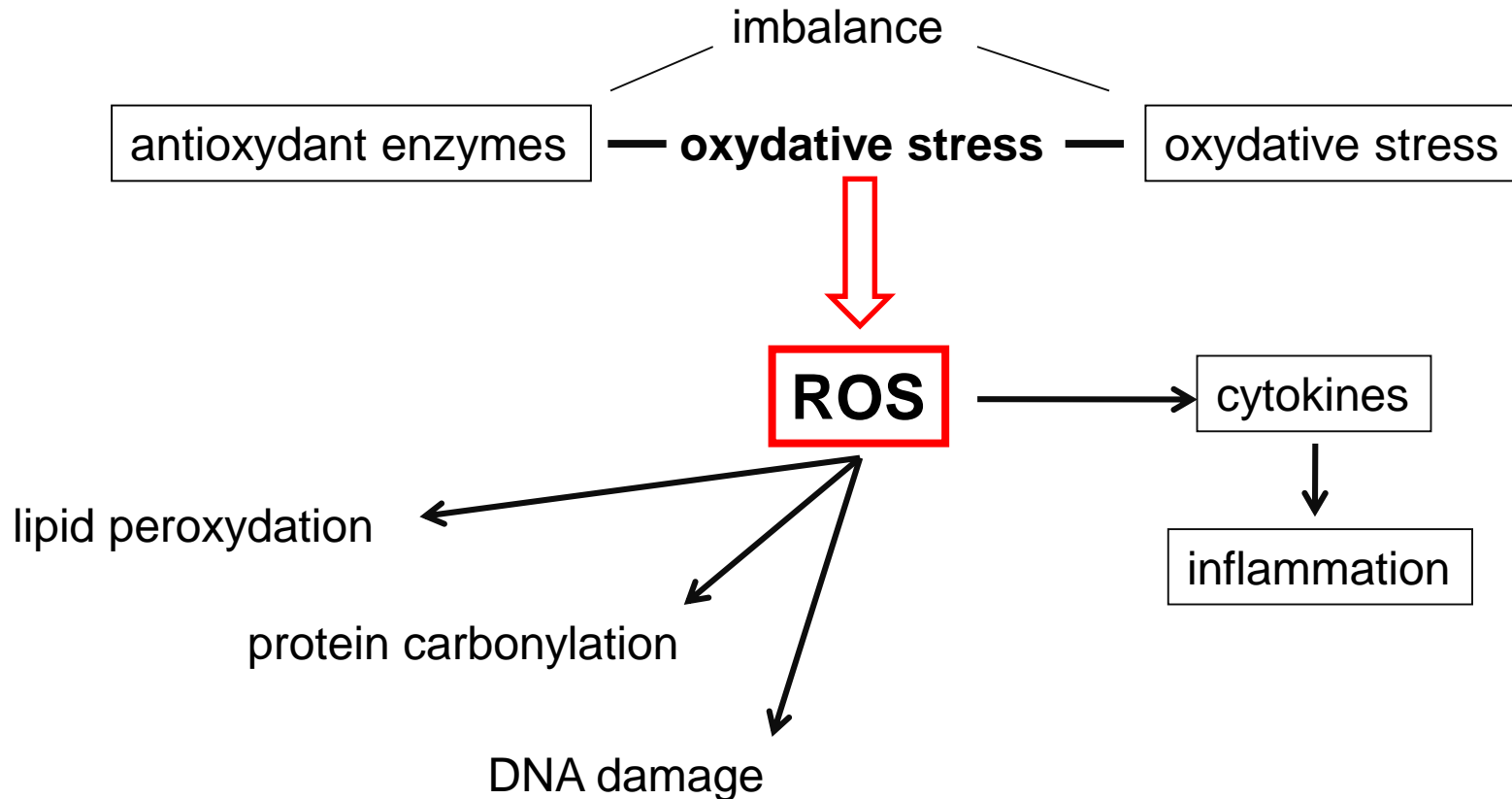
⇒ benefit from moderate consumption of red **wine**
via **increased antioxidant defense**

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)



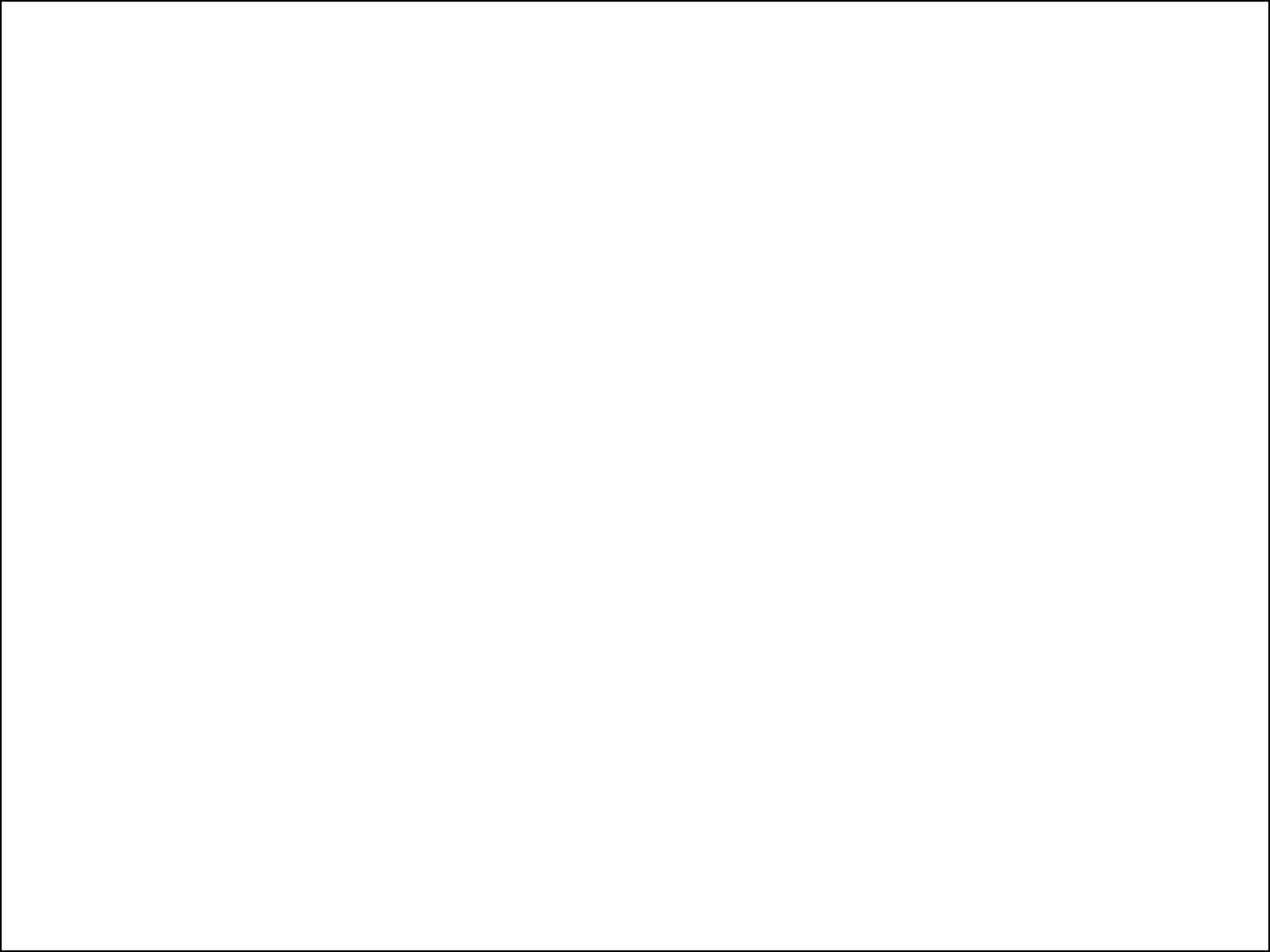
***Centuries ago our ancestors knew already
the health benefits of alcohol
as reflected by the toasts***

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

***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

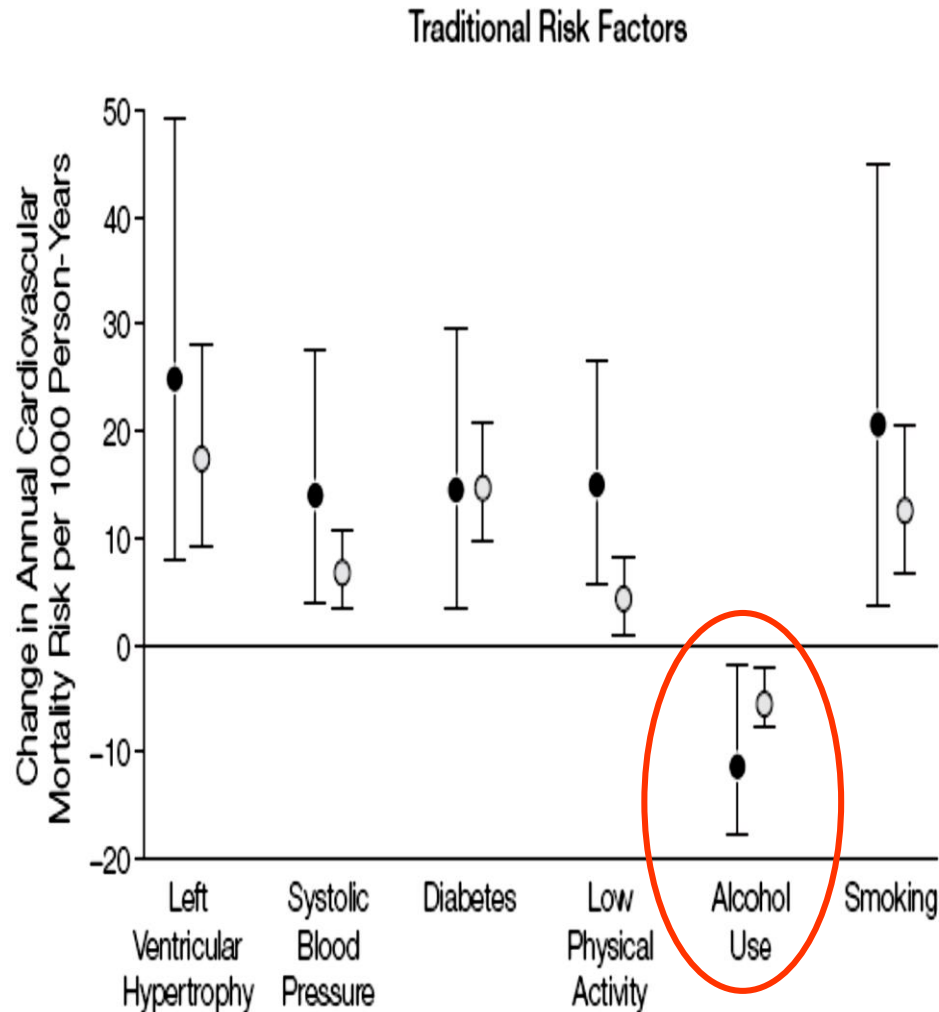
< 60g/day 0.63 0.85 0.74 0.77

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> | |

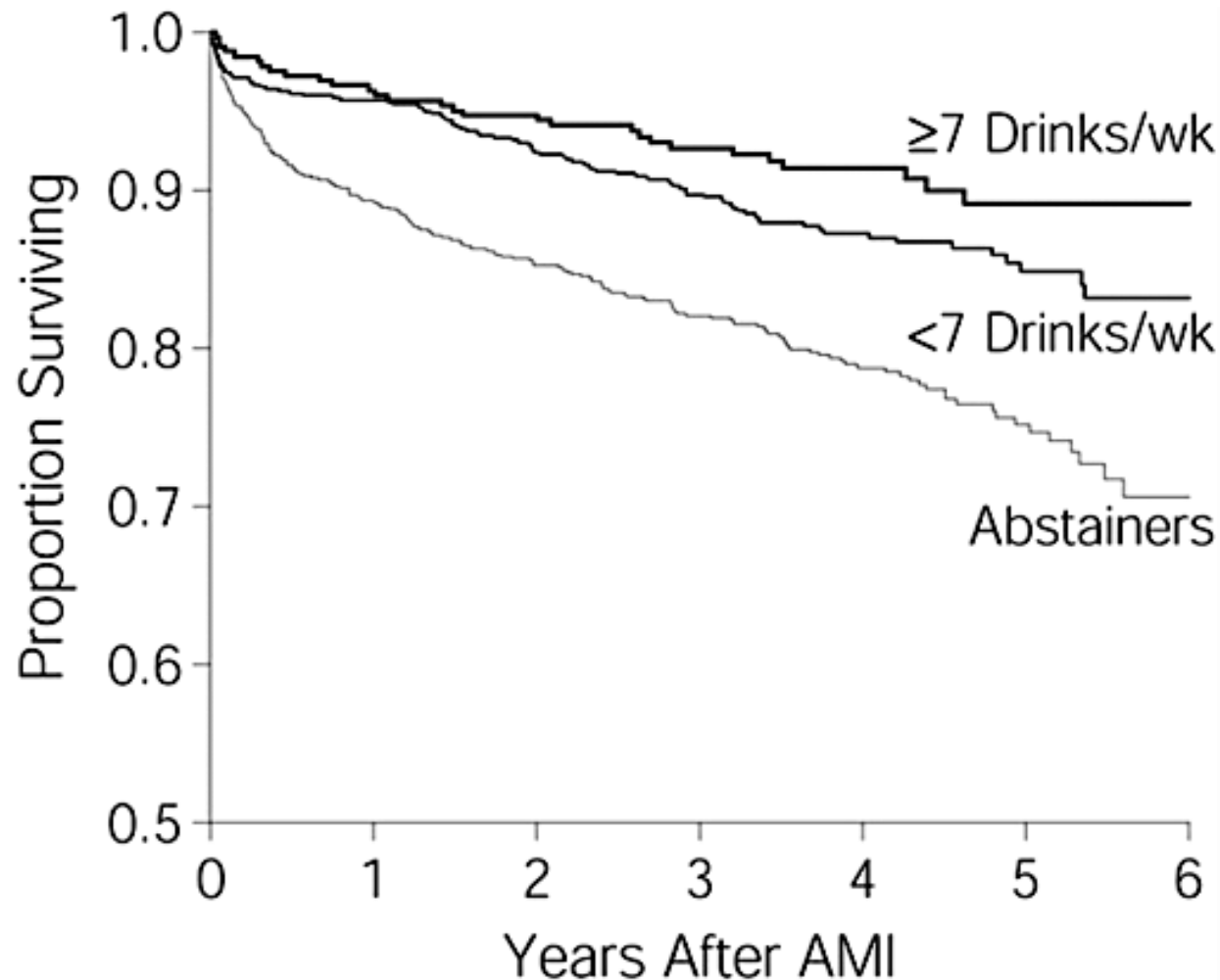
 **moderate alcohol consumption – no substantial adverse effect
on renal function in women during 11 year follow-up**

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

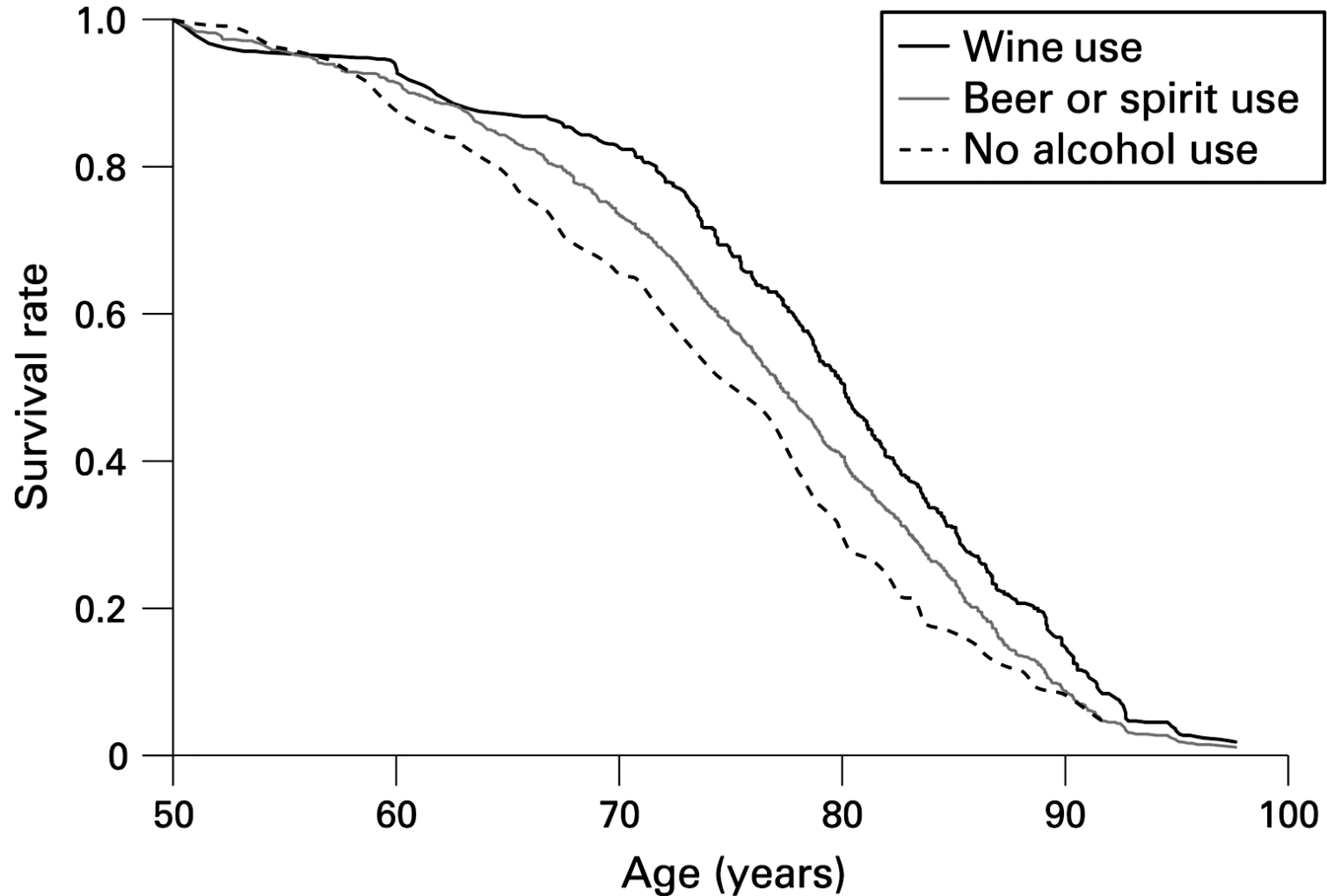
but,

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) | 0.4 | 2.6 | 11.1 | 24.1 |
| Age adjust.rel risk (95%) (<i>multivariate</i>) | 1 | 0.91 (0.62-1.3) | 0.94 (0.64-1.38) | 0.53 (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/1.73m²
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 Menon¹, Ronit Katz², Kenneth Mukamal³, Bryan Kestenbaum⁴, Ian H. de Boer⁴, David S. Siscovick⁵, Mark J. Sarnak¹ and Michael G. Shlipak⁶

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)

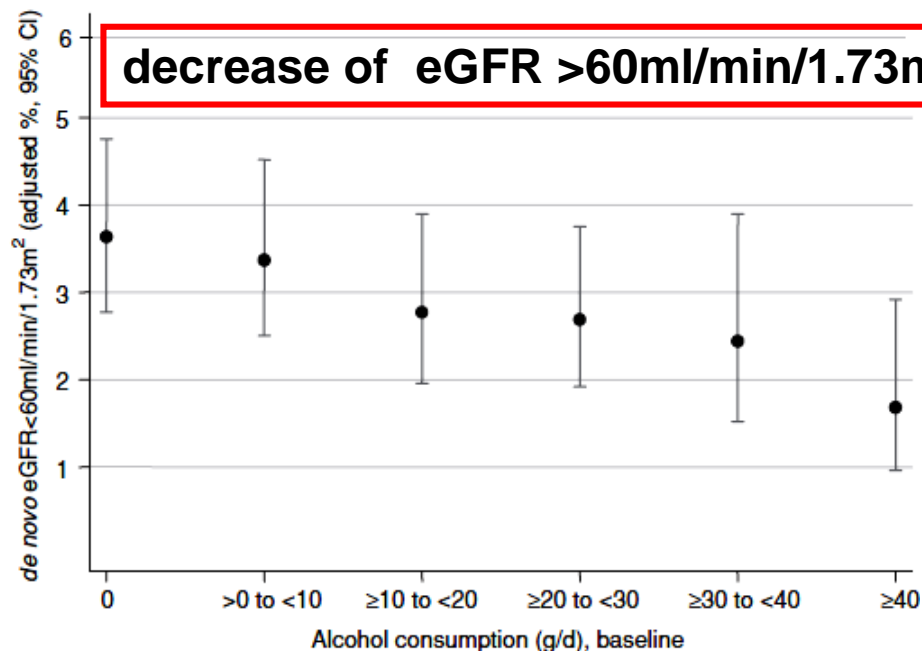
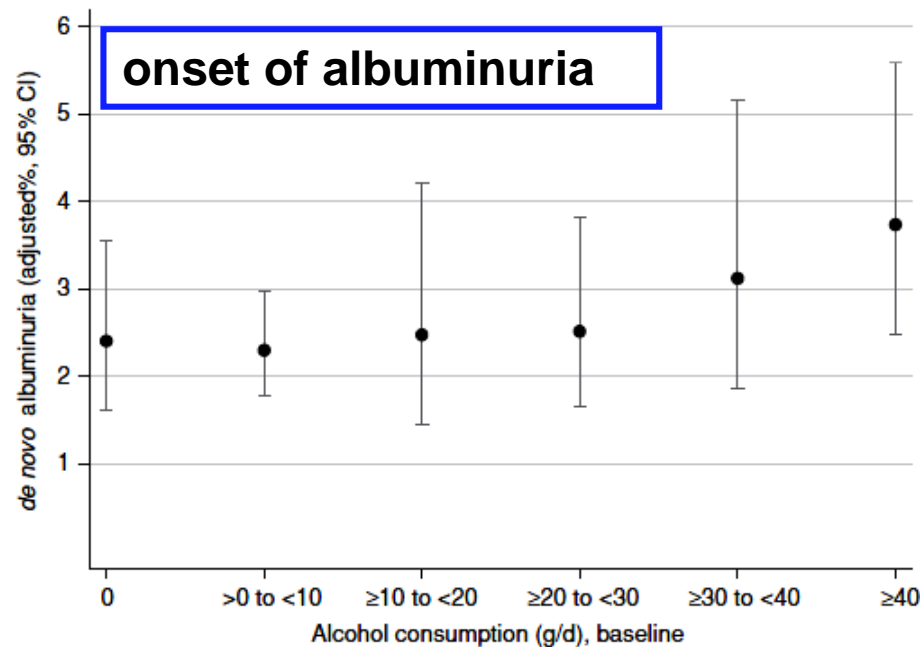
| | |
|--------------------|------------------|
| former alcohol use | 1.18 |
| < 1drink | 1.20 |
| 1-6 | |
| 7-13 | 1.10 |
| >14 | 0.89 (0.61-1.13) |

Alcohol consumption

onset of **albuminuria** and
loss of **GFR** < 60 ml/min/1.73m²

- 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 | 0.86 (0.78-0.95) p<0.002 |
| | | >20g/day | 1.04 (0.86-1.25) NS |
| | ♀ | < 20g/day | 0.85 (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 | 0.92 (0.86-0.98) $p < 0.0065$ |
| | | >20g/day | 0.93 (0.79-1.10) NS |
| | ♀ | < 20g/day | 0.91 (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) ^a | 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) ^a | 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

A lcohol 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

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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 ± 5.1 years; health check-up
CKD eGFR < 60 ml/min/1.73m²
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 Menon¹, Ronit Katz², Kenneth Mukamal³, Bryan Kestenbaum⁴, Ian H. de Boer⁴, David S. Siscovick⁵, Mark J. Sarnak¹ and Michael G. Shlipak⁶

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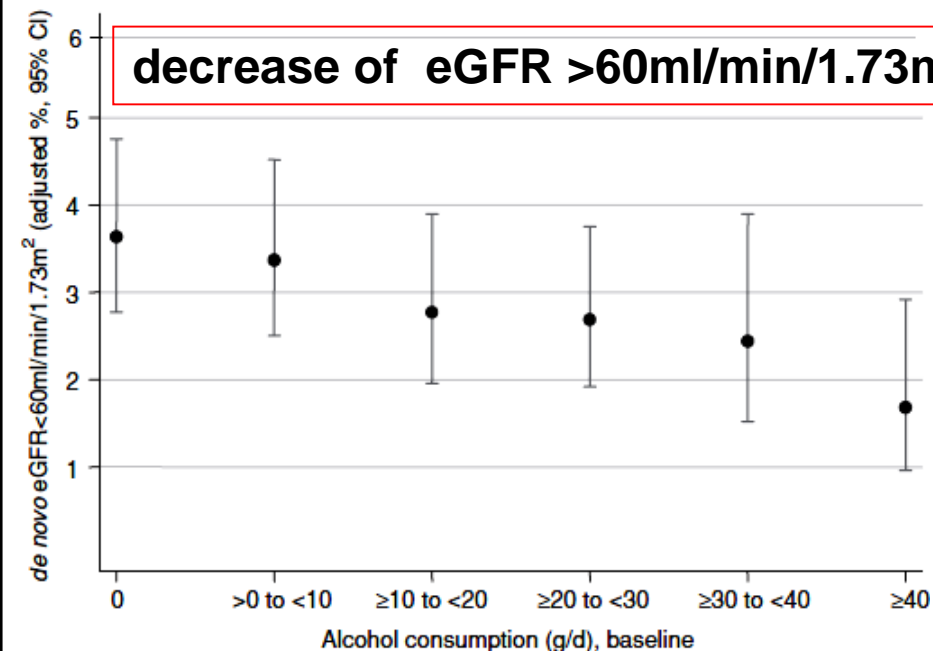
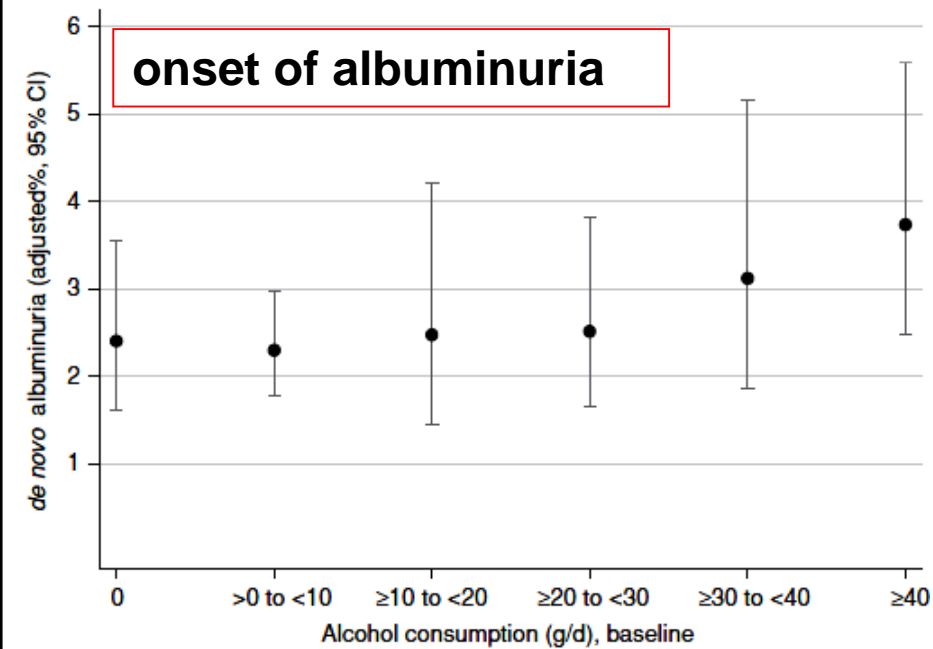
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Alcohol consumption

onset of albuminuria and
loss of GFR < 60 ml/min/1.73m²

- AUSDIAB study
- 6259 adults
 - 14 years follow-up
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*White,
Nephrol.Dial.Transplant.(2009) 24: 2464*

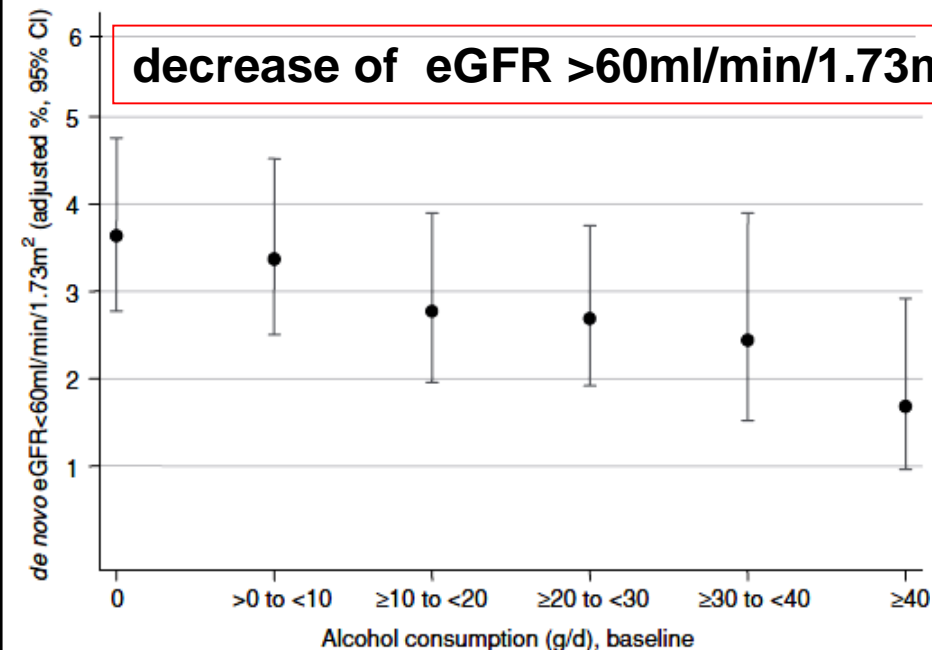
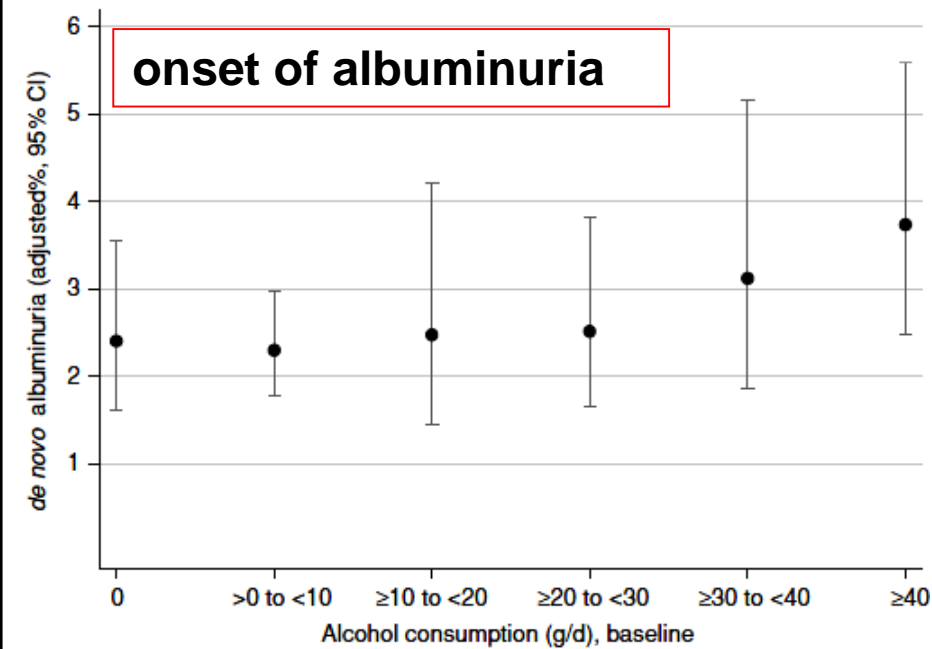


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Nephrol.Dial.Transplant.(2009) 24: 2464*



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

Chih-Chun Chang¹, Chieh-Yu Chang¹, Yang-Tzu Wu¹, Jiung-Pang Huang¹, Tzung-Hai Yen² and Li-Man Hung^{1*}

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 |

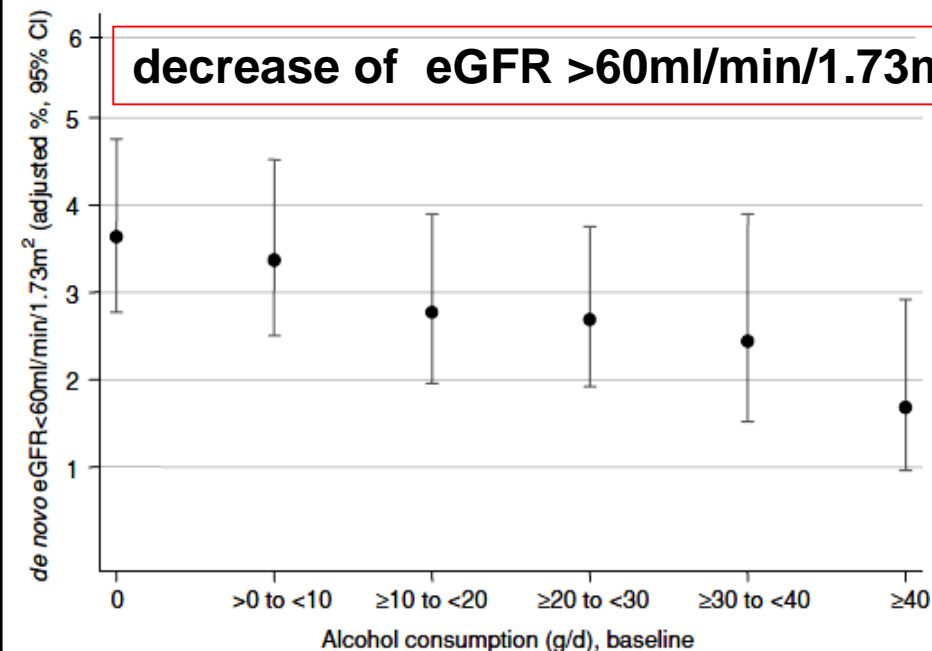
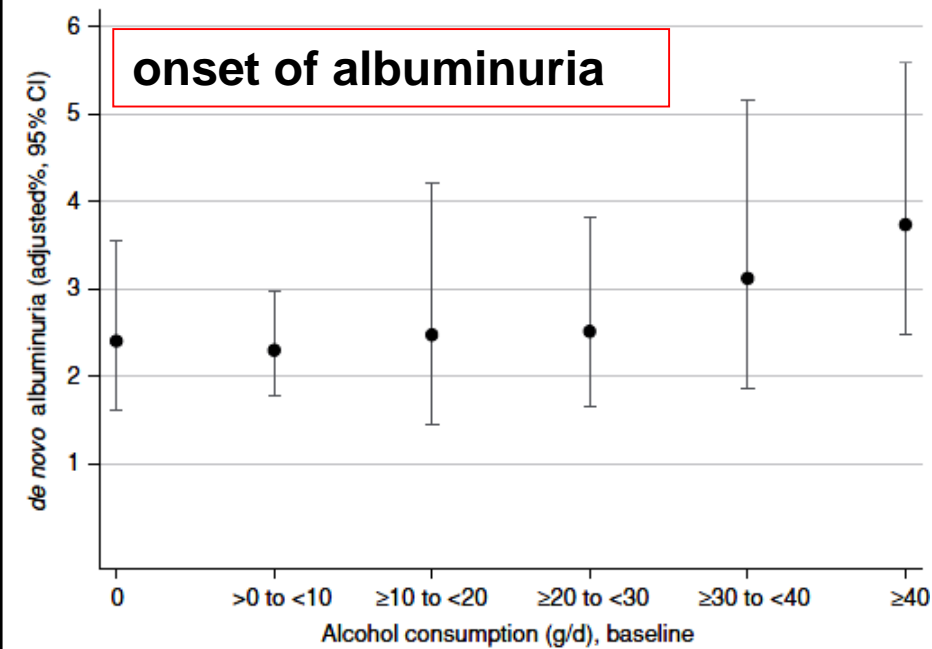
Lewis New Engl J Med (2001) 345:851

Alcohol consumption

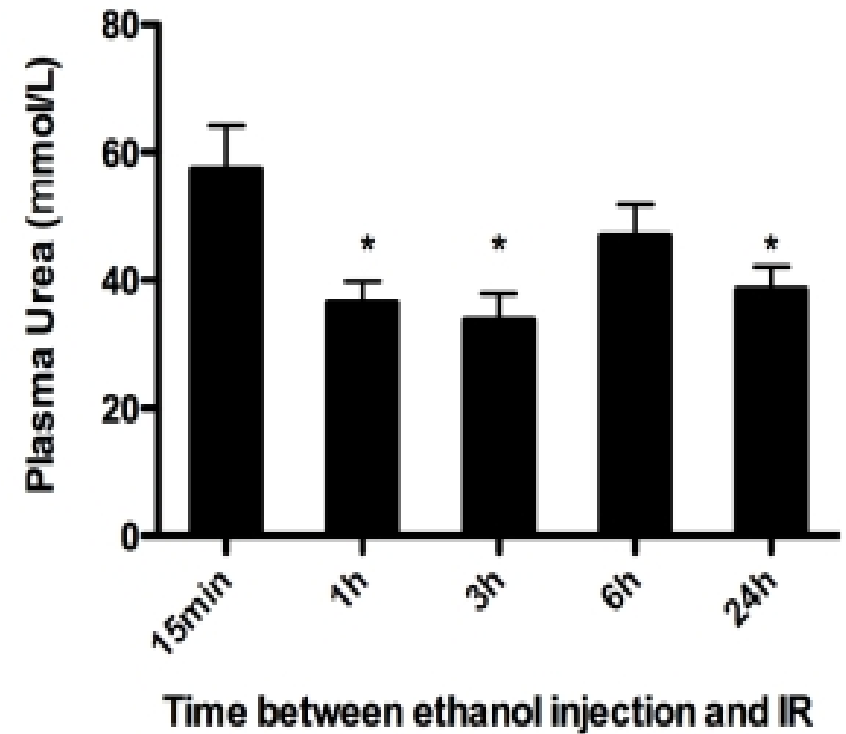
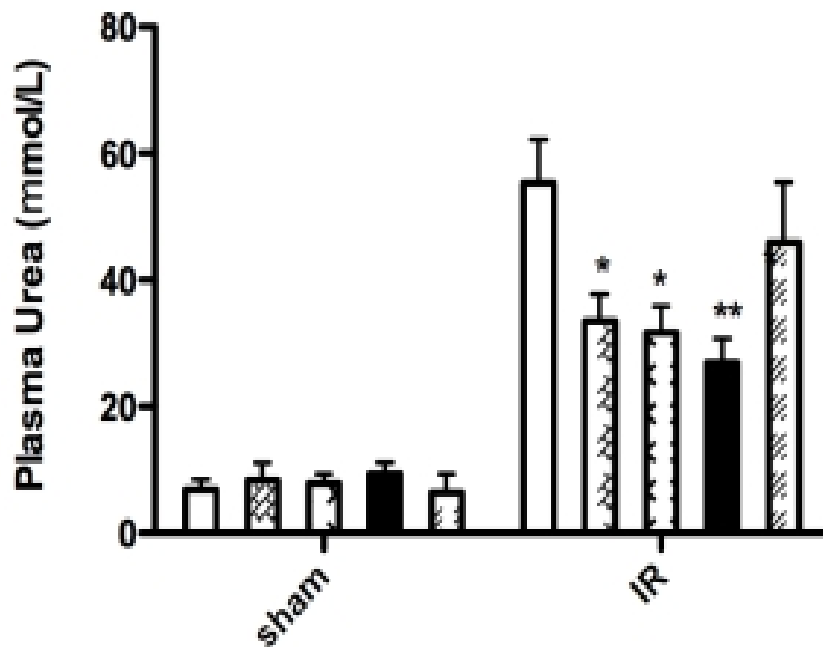
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Preconditioning with “physiological“ levels of ethanol *protects in animal experiments the kidney against ischemia/reperfusion (IR) injury*



“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)

| | |
|----------------------------------|---|
| cerebrovascular mortality | hazard ratio 0.43 (CI 0.26-0.70) |
| cardiovascular mortality | hazard ratio 0.70 (CI 0.55-0.89) |
| all-cause mortality | hazard ratio 0.75 (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