

Alcohol

*part of Western
civilization for
millenia*

social lubricant



Alcohol

(al-) kuhl arabian
guhlu assyrian }
└──────────┘

eye powder blackening the skin around the eye



antimon trisulfide
lead sulfide

bactericidal ⇨ medication for **eye diseases**

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”)

Wine

**Question of Prof. Rosivall :
are there health benefits ?**

Risks and benefits of alcohol

490,000 individuals

prospective 9 year follow-up study

Alcohol use ⇒

higher risk :

- *cirrhosis, dilated cardiomyopathy, cardiac arrhythmia, fetal alcohol syndrome, hypertension, stroke*
- *cancer (breast, mouth, esophagus, pharynx, larynx, liver)*
- *injury (e.g. traffic accidents)*

lower risk :

- less **cardiovascular death** (*lower by 30-40%*)
- less **progression of renal disease**,
- less diabetes,
- less osteoporosis,
- less cognitive impairment

Does alcohol have **adverse** health effects ?

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

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

Mark Twain (1835-1910)

Alcohol and Longevity

Raymond Pearl

(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) May31st,948-950

The rediscovery

”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

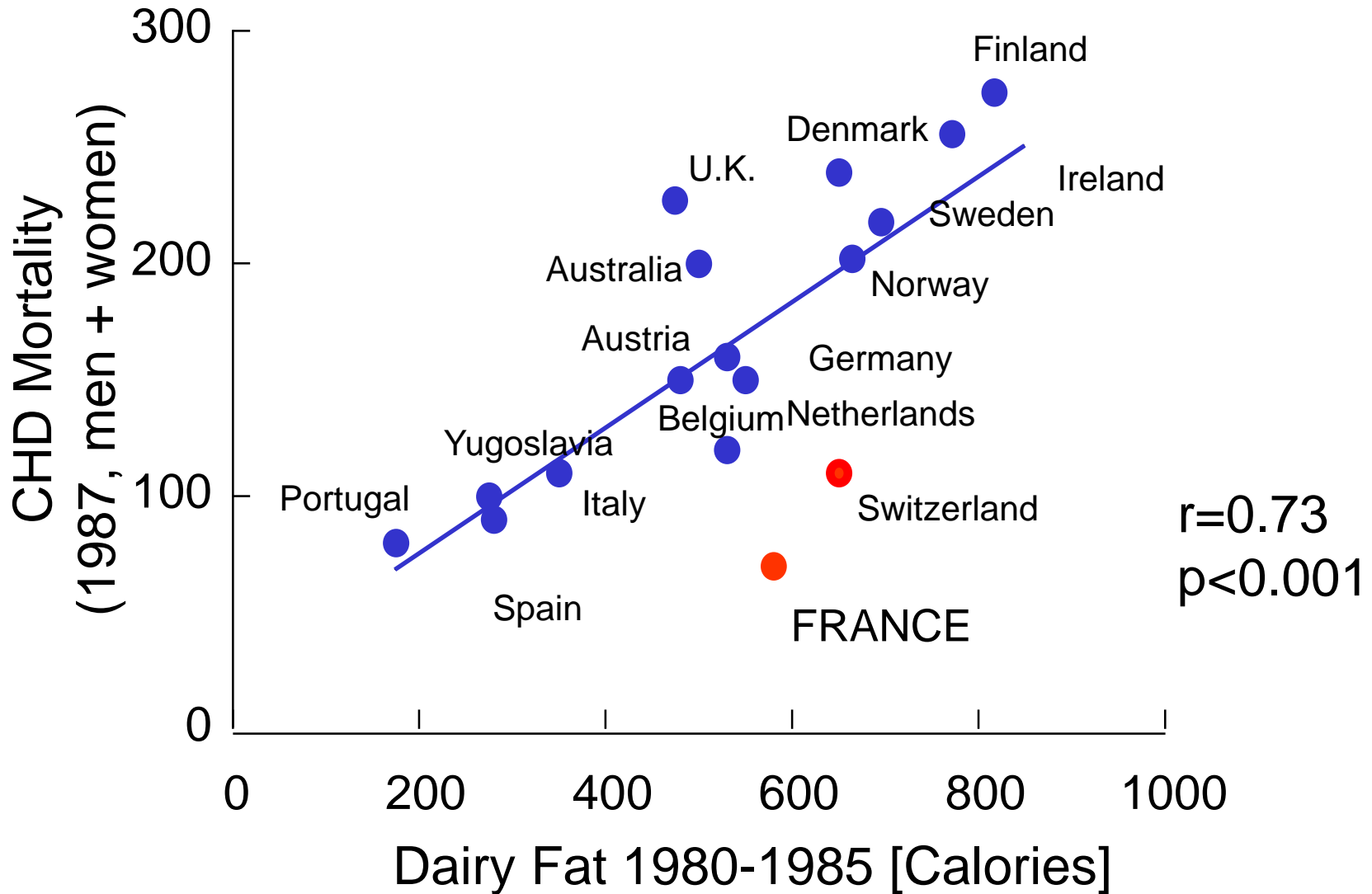
Renaud S, Lancet (1992) 339: 1523

De Lorgeril, Circulation (2002) 106: 1465

Hypothesis

Wine antagonises adverse effects of animal fat

French Paradox of coronary heart disease



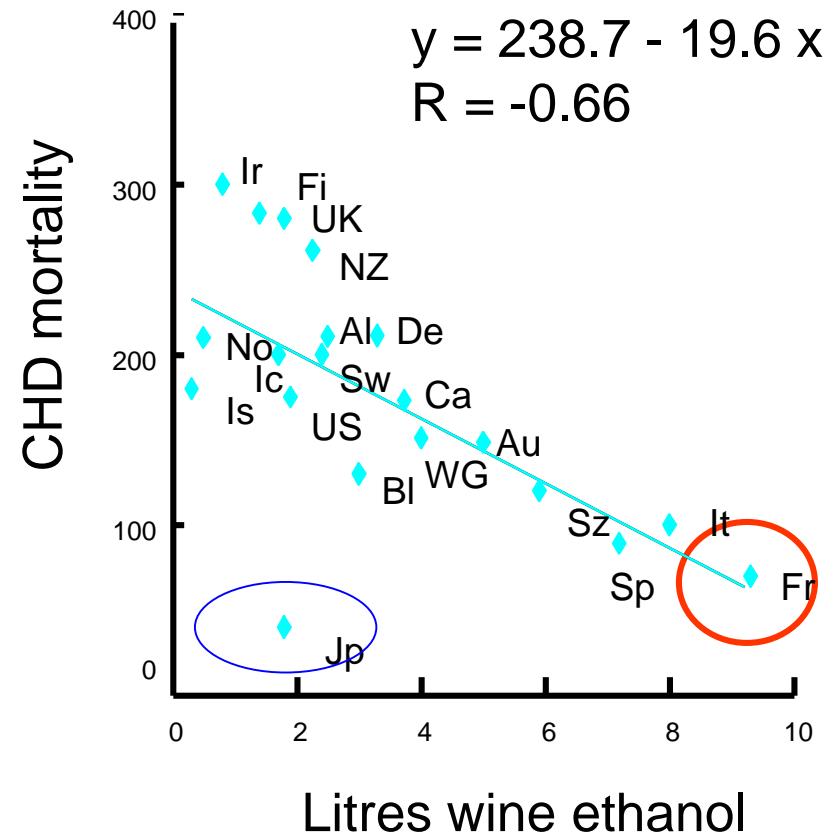
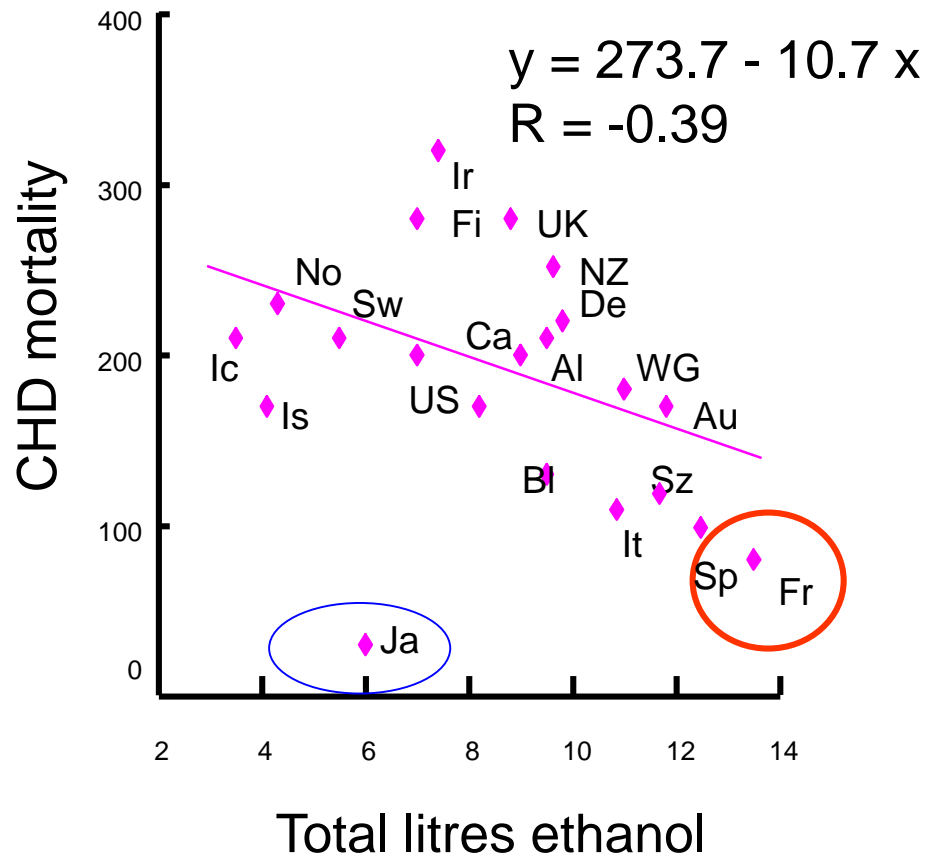
$r=0.73$
 $p<0.001$

Renaud, Lancet (1992) 339: 1523

**Alcohol and less cardiovascular mortality
confirmed**

**by more than 60 retrospective and
prospective epidemiological studies**

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



Health professional follow up study

50,000 men

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

Rinn et al.

Wine, beer and spirits.

Are they really horses of a different colour?

Circulation (2002) 105: 2806

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

Why U-shaped relationship?

Study 34014 young men in France 1978-1993

High alcohol intake :

cirrhosis

colorectal, gastroesophageal carcinoma

traffic accidents

but,

alcohol consumption per se **> 50 g/day** also

increased CV risk

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

How often and how much ?

**An alcoholic can be defined as a man
who drinks more than his own doctor**

A.L.Barach

Alcohol Consumption and Risk of Major Coronary Event

Drinks per day	Days per week					
	Don't drink	Rarely <1	1or2	3or4	5or6	Daily
Don't drink	1.00					
1 or 2 Units	1.01	0.99	0.93	0.75	0.36	1.20
3 or 4	0.65	0.44	0.91	0.6	0.46	0.87
5 to 8	0.80	1.13	1.00	0.46	0.50	0.83
>9		0.99	2.62	1.93	2.22	2.40
Former drinker	1.06					

Case Control Study

11511 acute myocardial infarctions

6077 controls

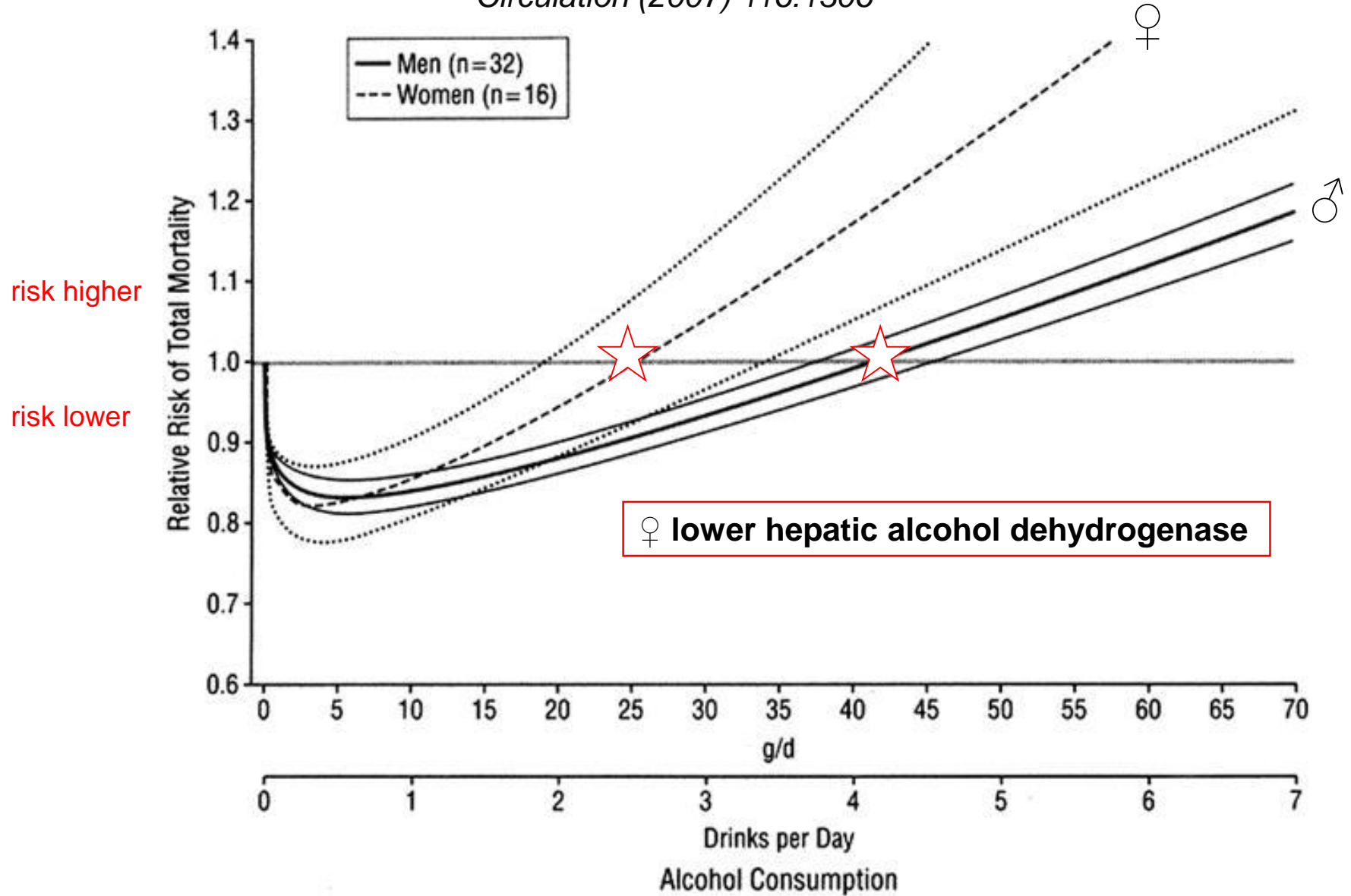
McElduff; BMJ 1997; 314: 1159

Different CV benefit from alcohol in men and women

R.Kloner and S.Rezkalla

To Drink or Not to Drink? That Is the Question

Circulation (2007) 116:1306



Benefits other than cardiovascular ?

490,000 individuals
prospective 9 year follow-up study

lower risk :

cardiovascular death lower by 30-40%, but also less
diabetes,
osteoporosis,
cognitive impairment
progression of renal disease

Alcohol and the risk to develop type 2 diabetes

Nurses health study
84,941 nurses, follow-up 1980-19963,
300 new cases of type 2 diabetes

daily alcohol consumption (g)	number of cases with type 2 diabetes	relative risk
0	1715	1.0
0.1 - 5.0	1034	0.78 (0.72-0.84)
5.1 - 10.0	189	0.56 (0.48-0.65)
>10	358	0.59 (0.52-0.66)

Hu, New Engl.J.Med. (2001) 345: 790

Moderate alcohol consumption – **lower risk of diabetes** *(Hoorn study)*

- in 1989 alcohol intake by questionnaire in 2393 subjects
 - - non-drinkers vs
 - - up to 10g/day vs
 - - 10-30 g/day vs
 - - > 30g/day
- **lowest mortality** → up to 10 g/day
- **lowest risk to develop diabetes** → up to 10 g/day
(8.0% vs 12.9% for nondrinkers)

alcohol (1-2 drinks/day)

⇒ lower risk of osteoporosis

higher alcohol consumption

⇒ more osteoporosis

Bainbridge, Osteoporosis Int. (2004) 15: 439

Moderate alcohol consumption – **less cognitive impairment**

- Nurses Health Study
Stampfer, New Engl J Med (2005) 352:245
- Gruppo Italiano di Pharmacovigilanza nell' Anziano (GIFA)
Carosella, Pharmacol.Res.(1999) 40: 287
- Hale Project (mediterranean diet and life style changes in the elderly)
Knoops, JAMA (2004) 292:1433

Moderate alcohol consumption – less dementia and Alzheimer's disease *(Metaanalysis of 23 studies)*

- **dementia** risk ratio **0.63** (95%CI 0.53-0.75)
 - **Alzheimer** risk ratio **0.57** (95%CI 0.44-0.74)
- but no significant effect:*
- **vascular dementia** risk ratio **0.82** (95%CI 0.50-1.32)

Peters, Age Ageing (2008) 37: 505



J.W.von Goethe
1749 - 1832

**Wein wirkt stärkend auf den
Geisteszustand den er vorfindet –
er macht die Dummen dümmer
und die Klugen klüger**

*(wine reinforces the state of mind
which is present –
it makes the stupid one even more stupid
but the intelligent one also more intelligent)*

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 and **progression** of renal disease – **suggestive data**

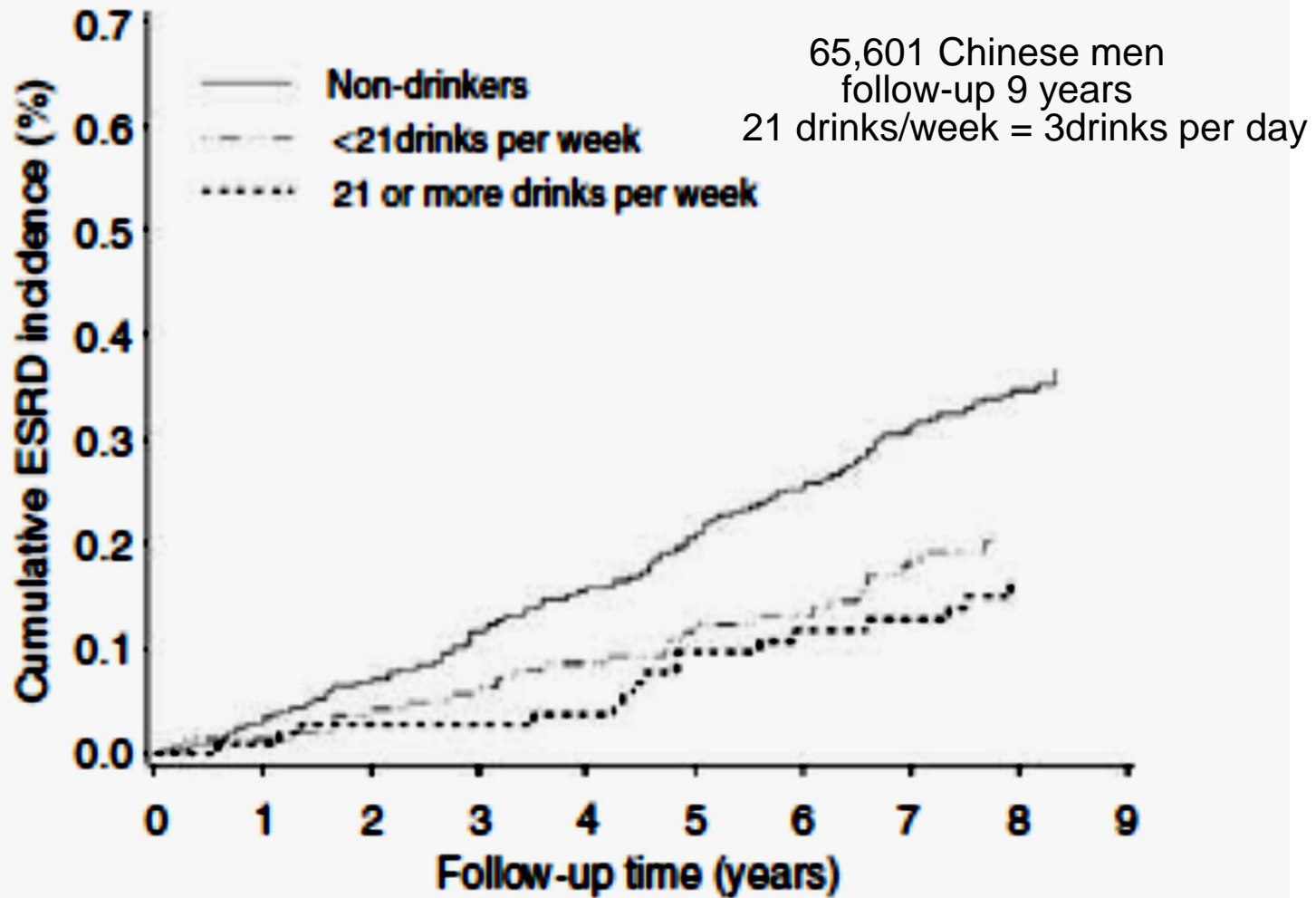
**decline of renal function and alcohol
prospective 11 year study in 1658 nurses**

	<i>odds ratio > 25 % decrease GFR</i>	
	<i>normotensive</i>	<i>hypertensive</i>
<i>0 - 4.9 g/day</i>	<i>0.98</i>	<i>0.98</i>
<i>5 -14</i>	<i>0.83</i>	<i>0.62</i>
<i>15 -60</i>	<i>0.81</i>	<i>0.53</i>

 **chronic kidney disease –
potential benefit from alcohol**

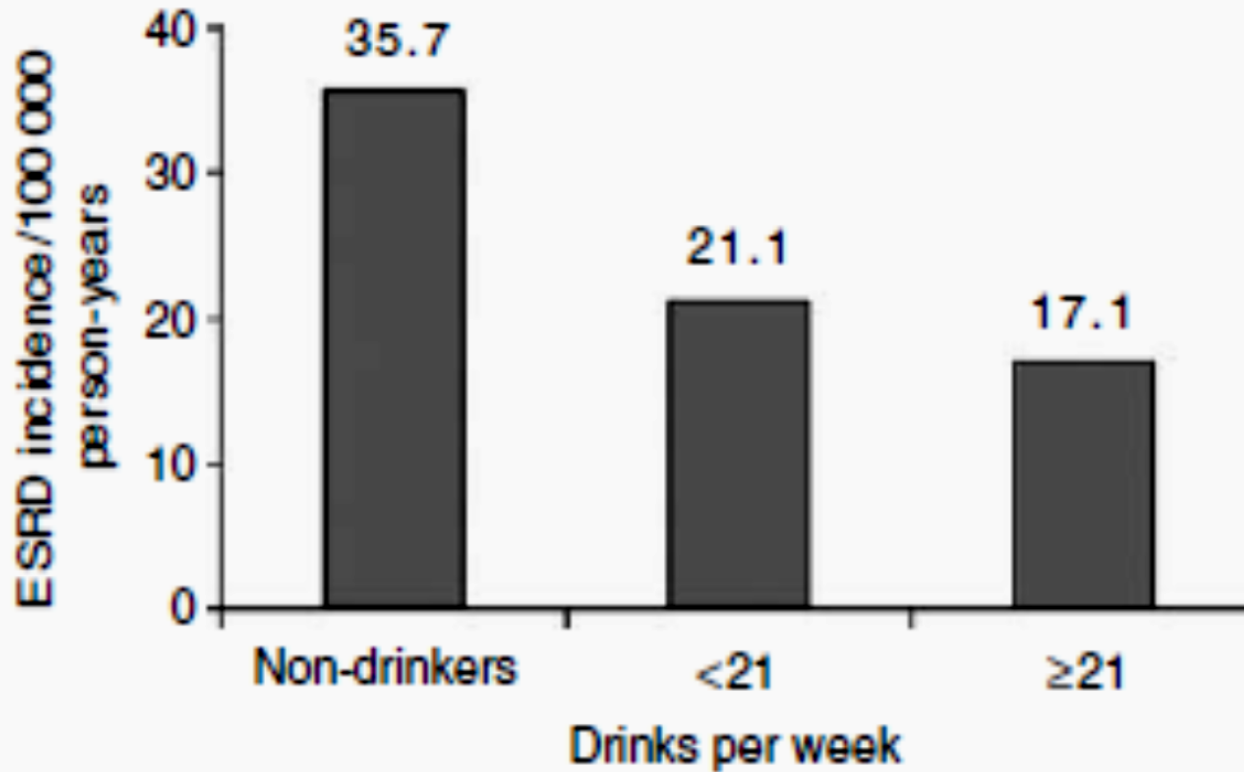
Knight, Nephrol.Dial.Transplant. (2003) 18:1549

Alcohol and endstage renal disease – definite data



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

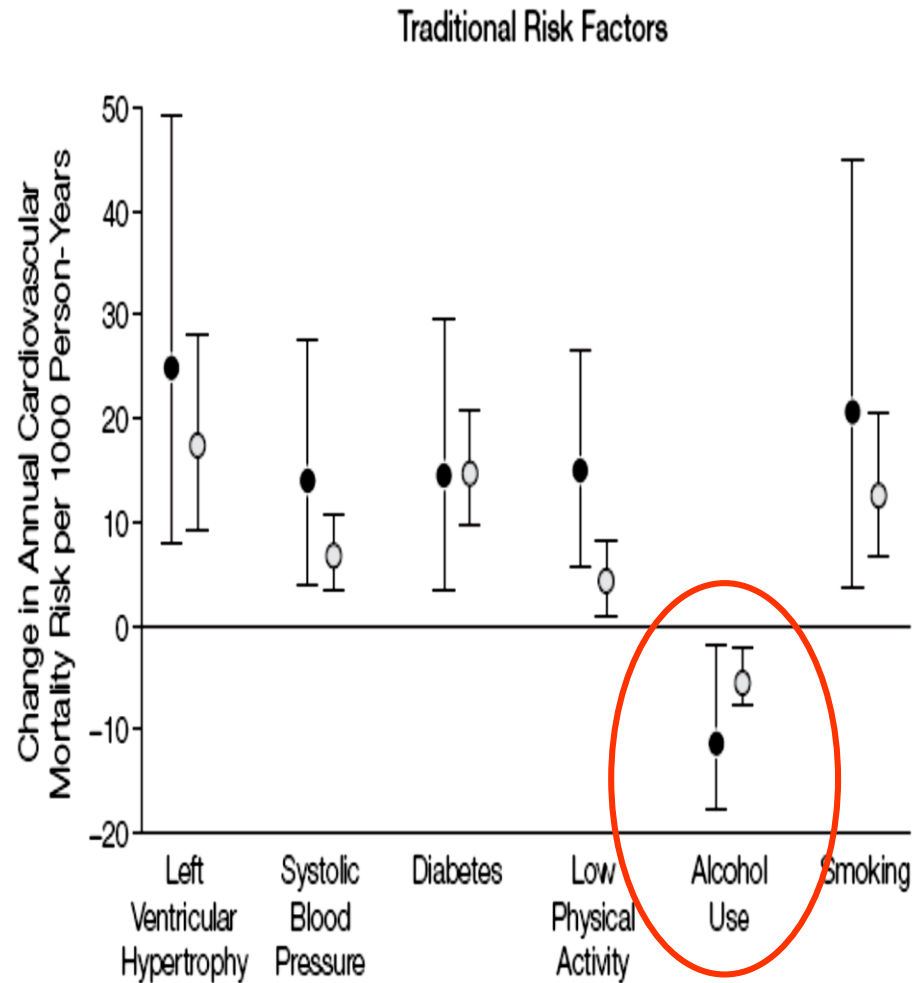
Incidence of all-cause endstage renal disease (per 100,000 person years standardized by age) dose-response relationship



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

In chronic kidney disease

not only impact on progression, but also on **CV risk**



Shlipak, JAMA (2005) 293:1737

Are all alcoholic drinks created equal?

Alcohol vs wine:

Inverse correlation any alcohol consumption and
coronary mortality ($r = - 0.39$)
better correlation wine consumption and
coronary mortality ($r = 0.66$)

Criqui and Ringel

Does diet or alcohol explain the French paradox

Lancet (1994) 344: 1719

⇒ alcohol coronary protection
constituents of **wine additional coronary protection**

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*



smore effective than alternative alcoholics
outrage in Bavaria – beer the liquid bread of Bavarians

alcohol – coronary protection

wine – additional coronary protection

metaanalysis

200,000 subjects

beer consumption risk reduction - 20%

wine consumption risk reduction - 32%

Di Castelnuovo

Circulation (2002) 105: 2836

confirmed :

Klatsky

Am.J.Epidemiol (2003) 158: 585

- **moderate consumption of any type of alcohol** → **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

The polyphenol **Resveratrol** (*in red wine*)

Cardioprotection

- **decreased arterial damage**
 - *ANGII* ↓
 - *platelet aggregation* ↓
 - *NO* ↑
- **anti-ischemic effect**
 - *prosurvival pathways*
[antisenescence factor **sirtuin** (p53)]
 - *insulin sensitivity* ↑
 - *LDL oxydation* ↓
 - *HDL* ↑
 - *antiinflammatory effects*
 - ...

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

Effects of wine on **endothelial cells**

Red wine, but not wodka,
increases coronary flow reserve

Shimada, Lancet (1999) 354: 1002

Small amounts of alcohol increase postischemic forearm
blood flow in CHD patients specifically
(nitrate as control negative)

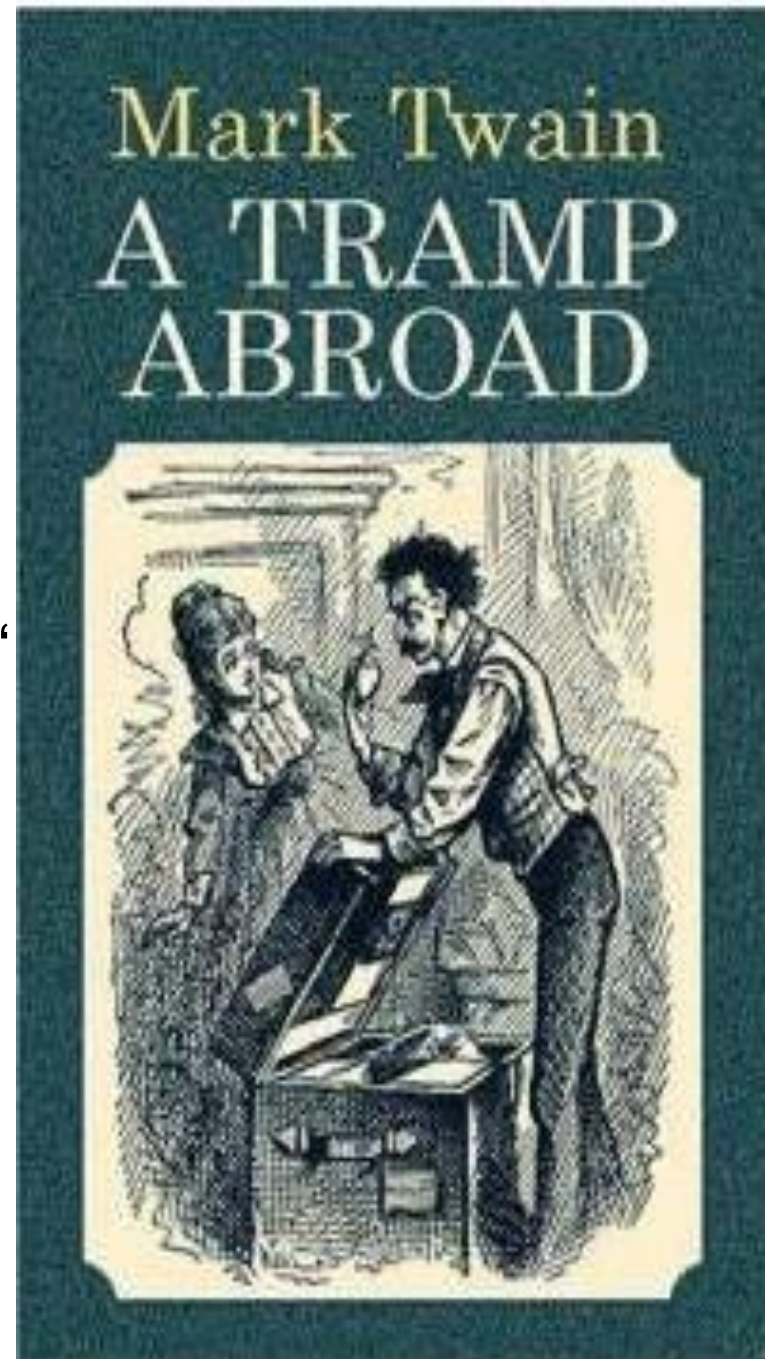
Teragawa , Atherosclerosis (2002) 165: 145

French red wine
more cardioprotection
than German red wine

Wallerath, J. Am. Coll. Cardiol. (2003) 41:471

“The Germans are exceedingly fond of Rhine wines ... one tells them from vinegar by the label“

Mark Twain
A Tramp Abroad
1880



Effects of wine on endothelial cells

In **isolated** human **coronary arteries**

red wine (Châteauneuf du Pape),

but not white wine (Mosel Riesling) or ethanol

→ endothelial cell dependent vasodilatation,

effect **NO-dependent** (inhibited by L-NMMA)

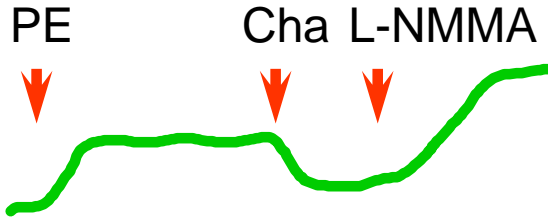
Flesch, Am J Physiol (1998) 275: H1183

Human Coronary Artery

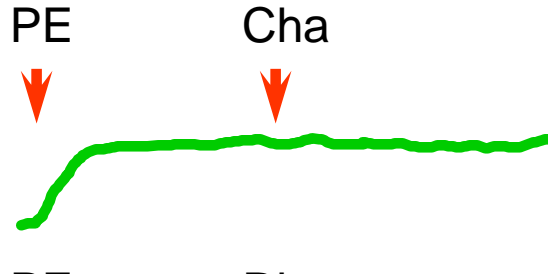
Effects of Red and White Wine

red

Chateuneuf
du Pape

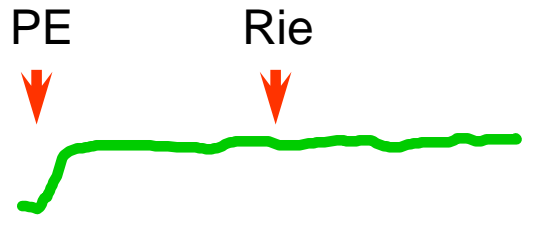


Chateauneuf
du Pape
(- endothelium)

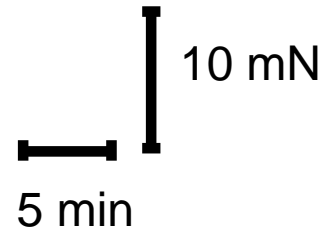
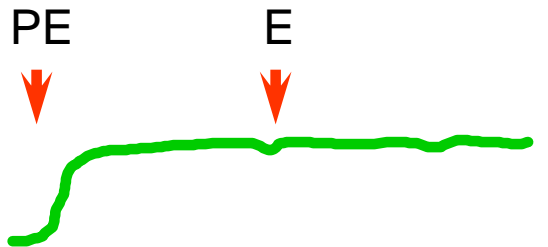


white

Mosel-
Riesling



Ethanol





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

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



*Wilhelm Busch
(1832-1908)*

**No one should talk longer in public
than he is prepared to make love in private**

*Francois La Rochefoucauld,
Prince de Marcillac
1613-1680*



Toasts pointing to benefits of alcohol

german Prosit !
 zum Wohl !
english cheers !
estonian terviseks !
finnish terveydexi !
greek για μας !
polish na zdrowie !

french santé !
italian salute !
spanish salud !

hungarian egészségére

*to your / our
wellbeing*

*to your / our
health*

enjoy the
wine
tasting



Risks and benefits of alcohol

490,000 individuals
prospective 9 year follow-up study

Alcohol use lower risk of :

- **cardiovascular death** (*lower by 30-40%*)
- **progression of renal disease,**
- diabetes,
- osteoporosis,
- cognitive impairment
- ...