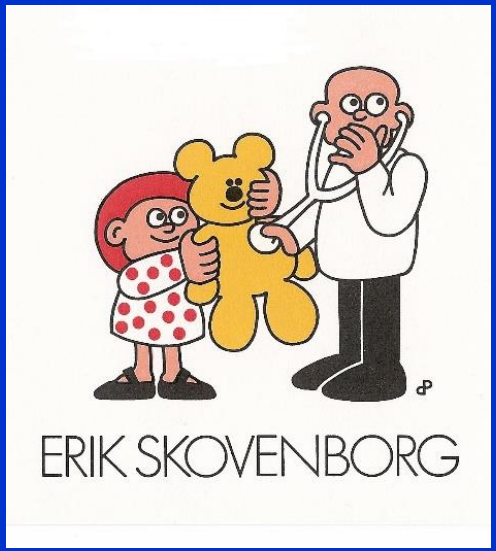
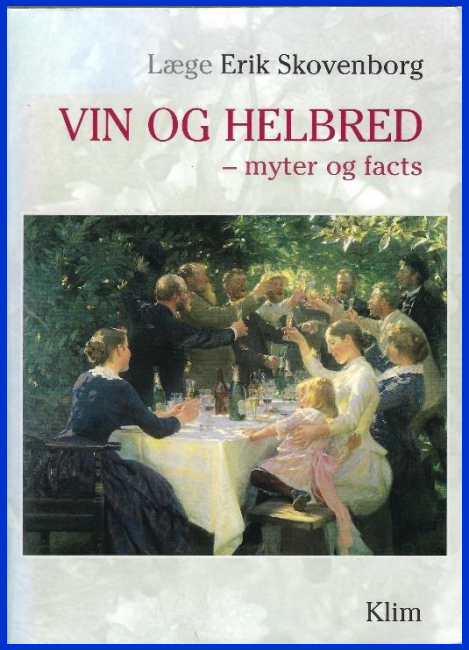
Dealing with Alcohol Drinking in the General Population: Perspective & Recommendations From a GP

Family physician for 30 years with a special interest in wine & health

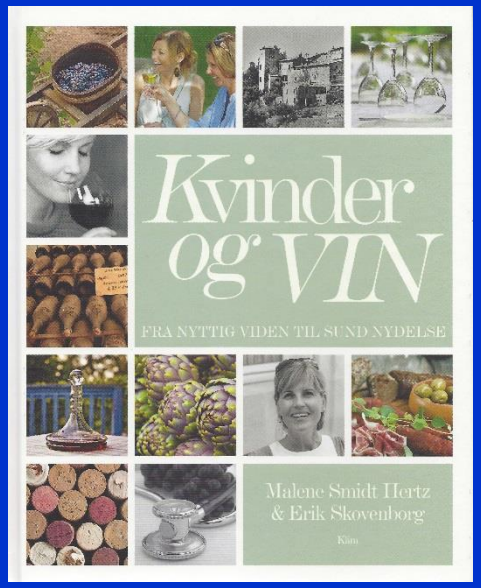


1994 co-founder of:
SCANDINAVIAN MEDICAL ALCOHOL BOARD

SCANDINAVIAN MEDICAL
S·M·A·B
ALKOHOL BOARD



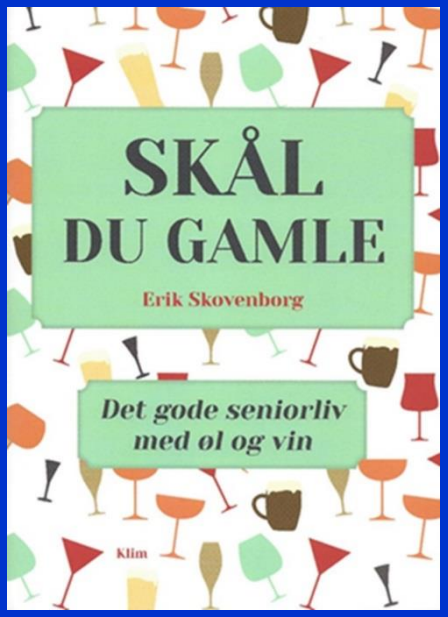
Wine and Health
- myths and facts
KLIM 2000



Women and Wine
- from helpful counsel to healthy enjoyment
KLIM 2015

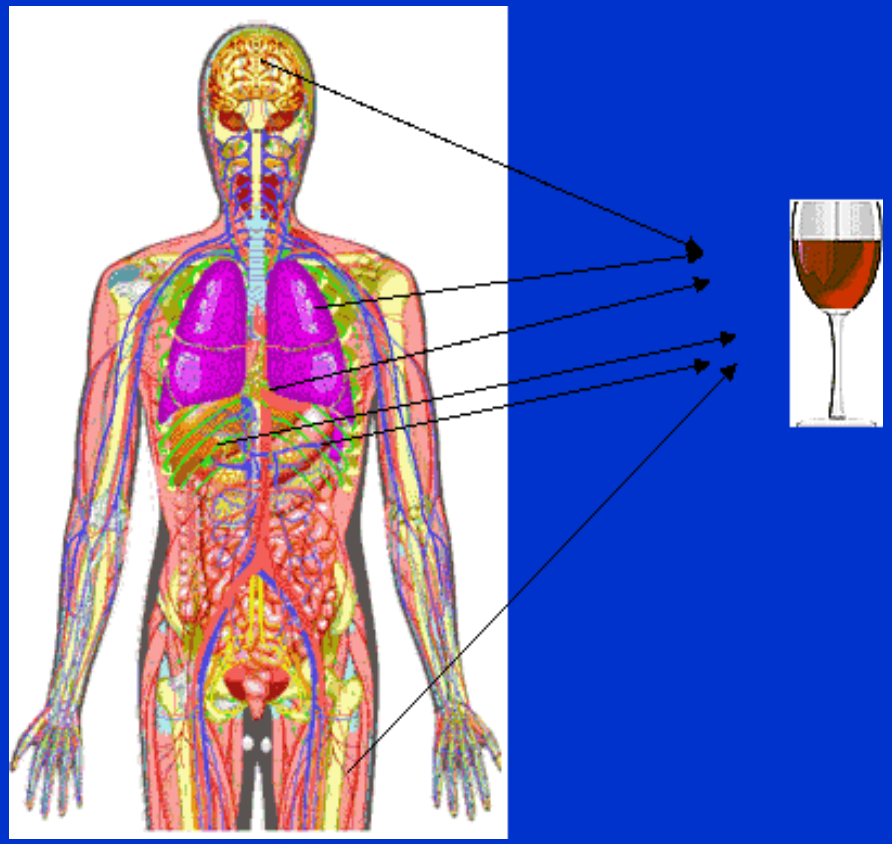
To the beer
- for joyful drinking and healthy cooking
KLIM 2016

A toast to your good health
with beer and wine in old age
KLIM 2017



1975: a young GP wondering about alcohol & health

- Wondering why most of what I was taught at the university concerned the harmful effects of heavy drinking among 5% of my patients – and almost no information about the effects of beer and wine consumption among the 95% moderate drinkers.



Few cardiac deaths in winedrinking France

THE LANCET, MAY 12, 1979

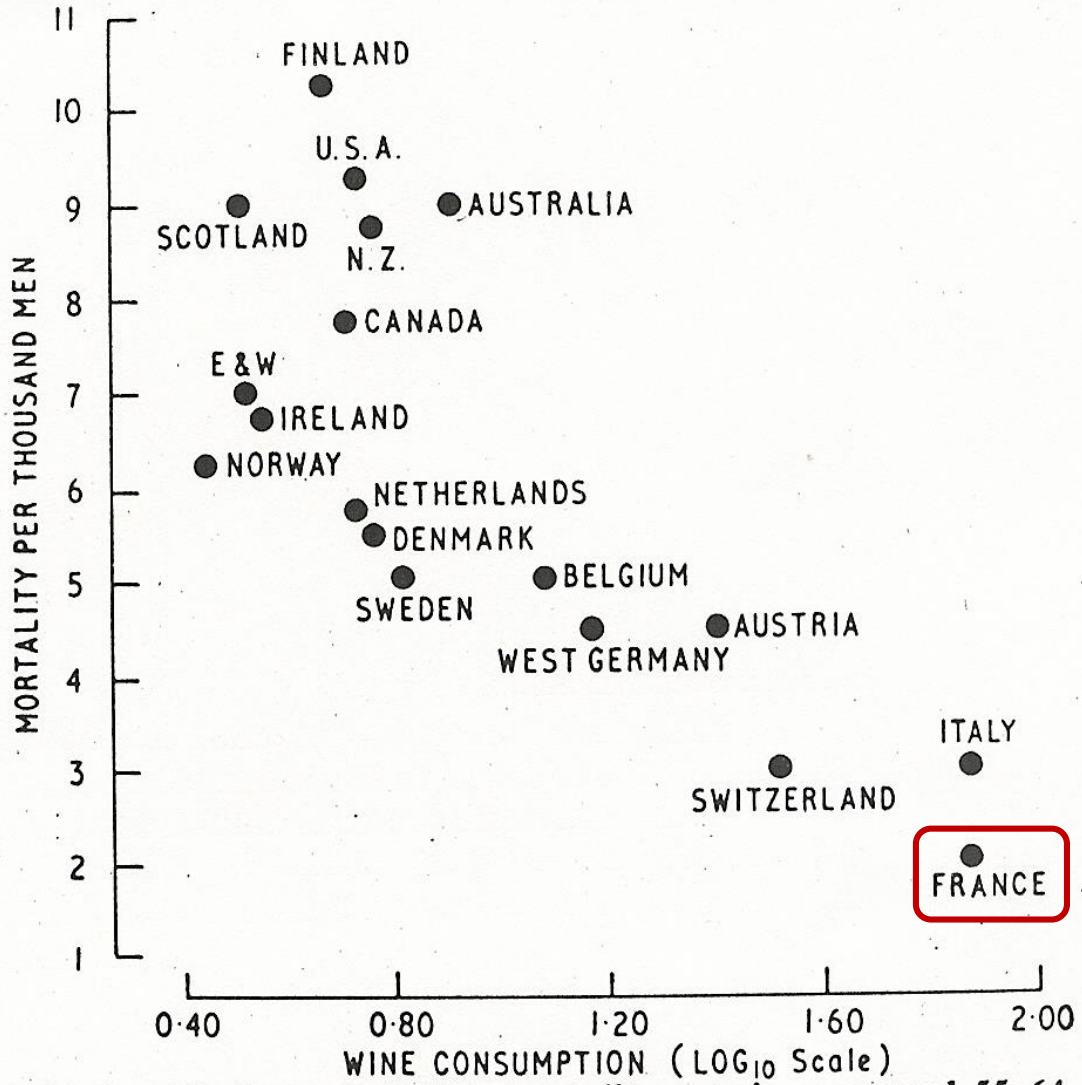
Public Health

FACTORS ASSOCIATED WITH CARDIAC MORTALITY IN DEVELOPED COUNTRIES WITH PARTICULAR REFERENCE TO THE CONSUMPTION OF WINE

A. S. ST. LEGER A. L. COCHRANE* F. MOORE

Medical Research Council Epidemiology Unit, Cardiff CF2 3AS

Summary Deaths from ischæmic heart-disease in 18 developed countries are not strongly associated with health-service factors such as doctor and nurse density. There is a negative association with gross national product per capita and a positive but inconsistent association with saturated and monounsaturated fat intake. The principal finding is a strong and specific negative association between ischæmic heart-disease deaths and alcohol consumption. This is shown to be wholly attributable to wine consumption.

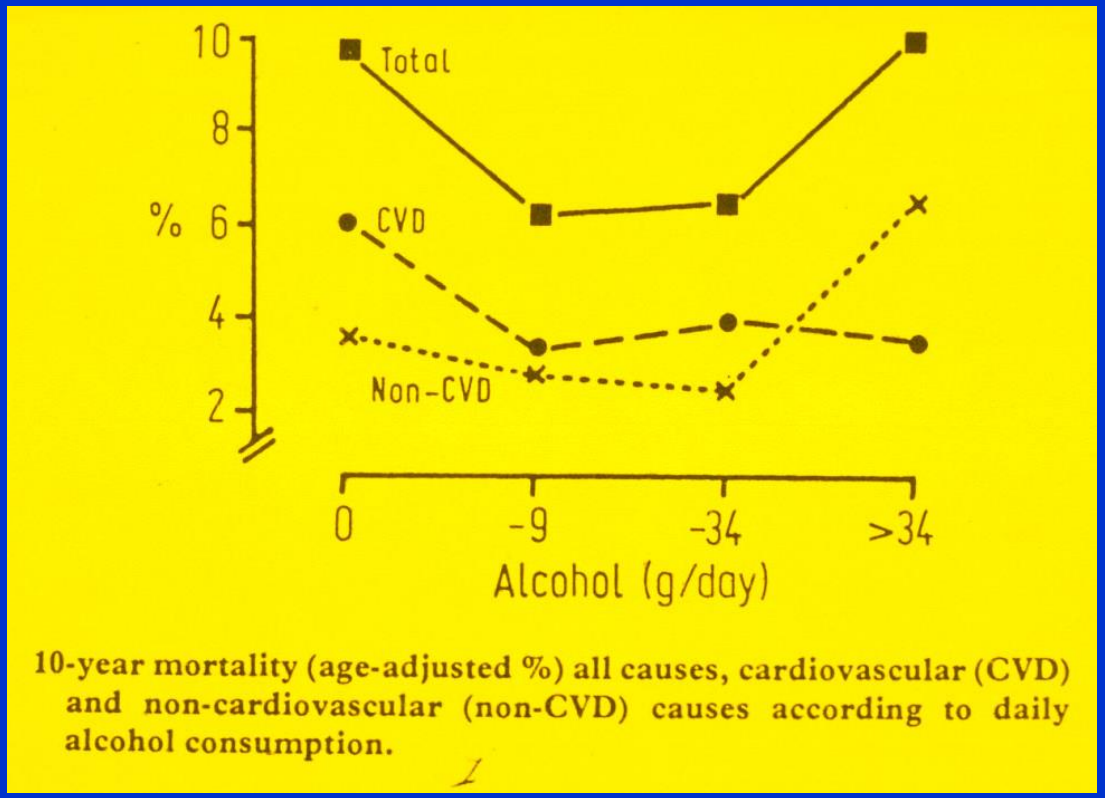


Relationship between I.H.D. mortality-rate in men aged 55–64 and wine consumption.

Classification af evidence-level

Publikationtype	Evidence	Strength
Meta-analysis of RCT	Ia	A
RCT = randomised, controlled trial	Ib	
Controlleret, non-randomised trial	IIa	B
Cohort studies	IIb	
Case-control studies	III	C
Cross-sectional studies		
Case reports / Expert opinions	IV	D

Alcohol and mortality: The U-shaped curve



10-year mortality (age-adjusted %) all causes, cardiovascular (CVD) and non-cardiovascular (non-CVD) causes according to daily alcohol consumption.

- Left downstroke:

↓ cardiovascular mortality

- U-curve nadir:

1 - 3 drinks per day
= low mortality rate

- Right upstroke:

↑ alcoholic liver disease

↑ cancer mortality

- The first U-shaped curve was found in a study of 1422 male civil servants in London (*the Whitehall Study*) investigating the relation between alcohol consumption and mortality over 10 years of follow-up. *Lancet 1981 Mar 14;1(8220 Pt 1):580-3*

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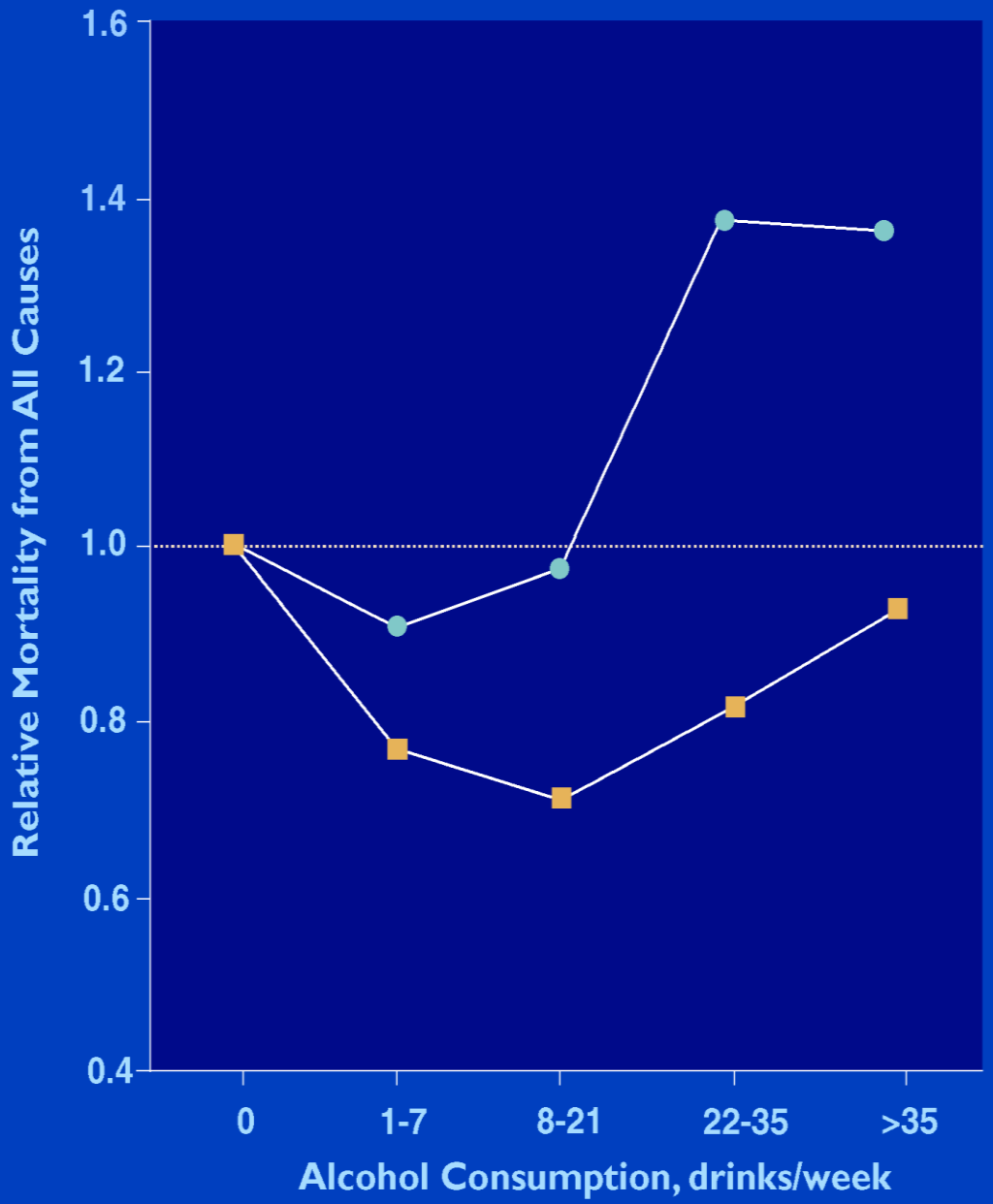
Deaths from all causes in relation to alcohol intake

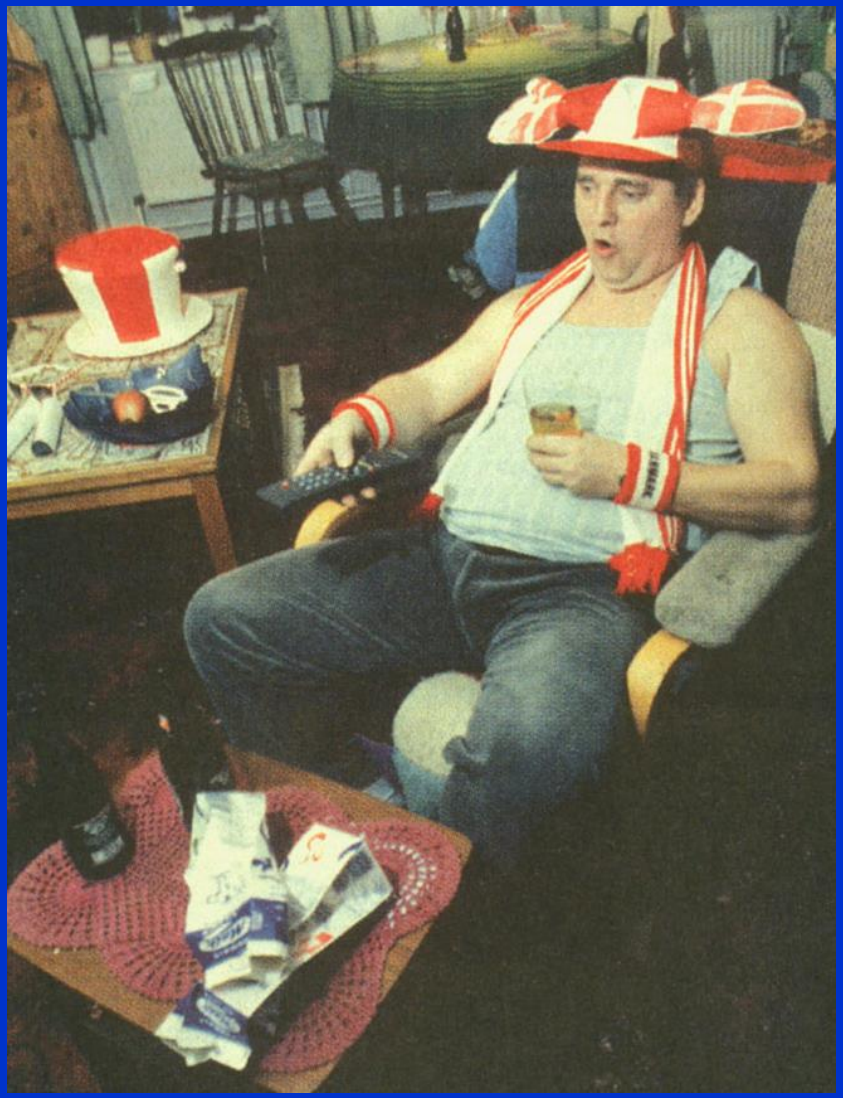
Wine drinkers: ■

Data from non-wine drinkers: ●



Grønbæk M et al. Type of alcohol consumed and mortality. Annals of Internal Medicine 2000; 133:411-19

The lifestyle of wine drinkers as compared to beer and spirits drinkers may be *a confounding factor* in the negative association between wine and mortality.



Food buying habits of people who buy wine or beer: study

BMJ 2006;332:519-22

Ditte Johansen, Karina Friis, Erik Skovenborg, Morten Grønbæk

Abstract

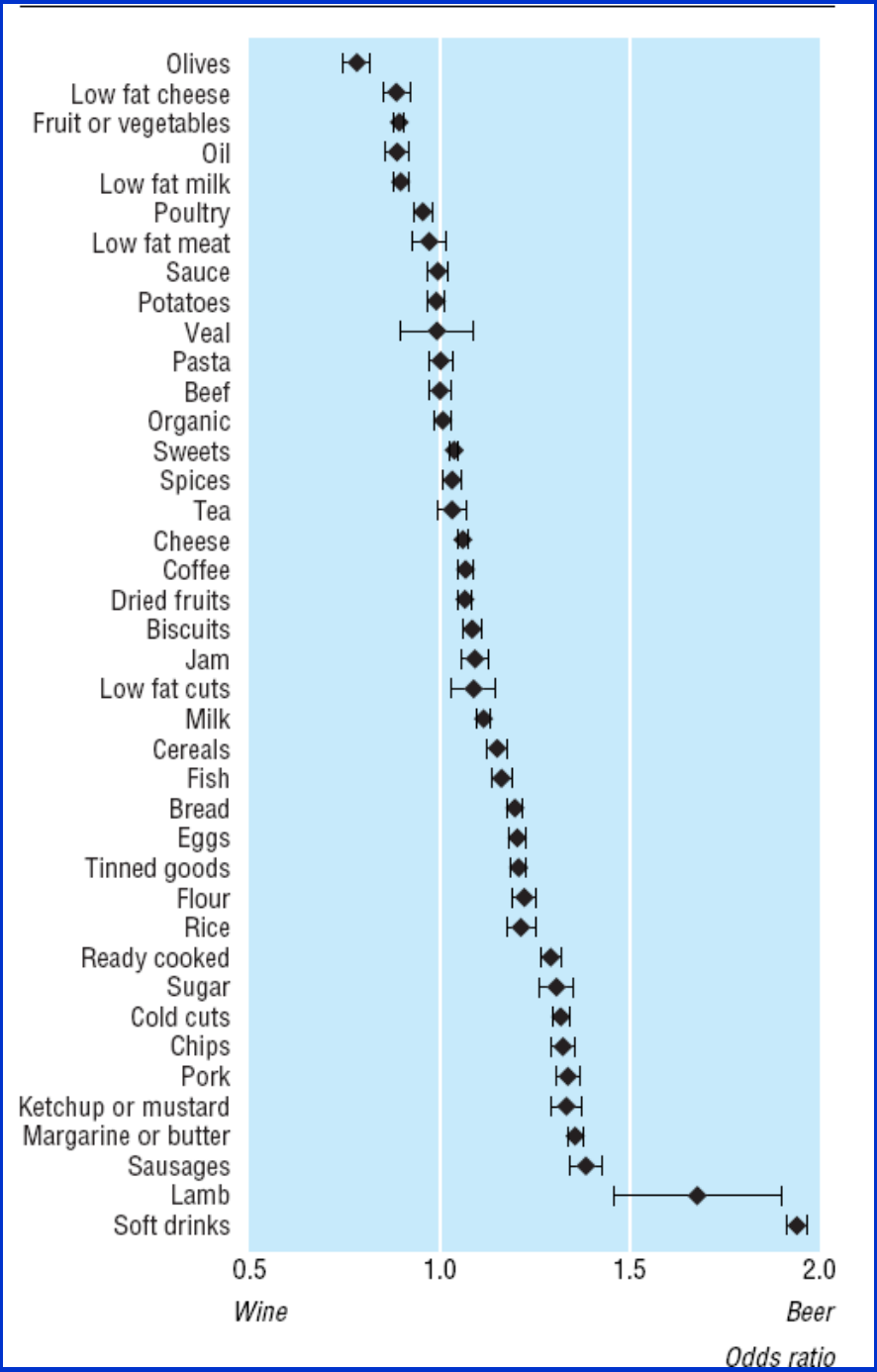
Objective To investigate whether people who buy wine buy healthier food items than those who buy beer.
Design Cross sectional study.
Setting Supermarkets in Denmark.
Data Information on number, type of item, and total charge from 3.5 million transactions over a period of six months.
Results Wine buyers bought more olives, fruit and vegetables, poultry, cooking oil, and low fat cheese, milk, and meat than beer buyers. Beer buyers bought more ready cooked dishes, sugar, cold cuts, chips, pork, butter or margarine, sausages, lamb, and soft drinks than wine buyers.
Conclusions Wine buyers made more purchases of healthy food items than people who buy beer.

Methods

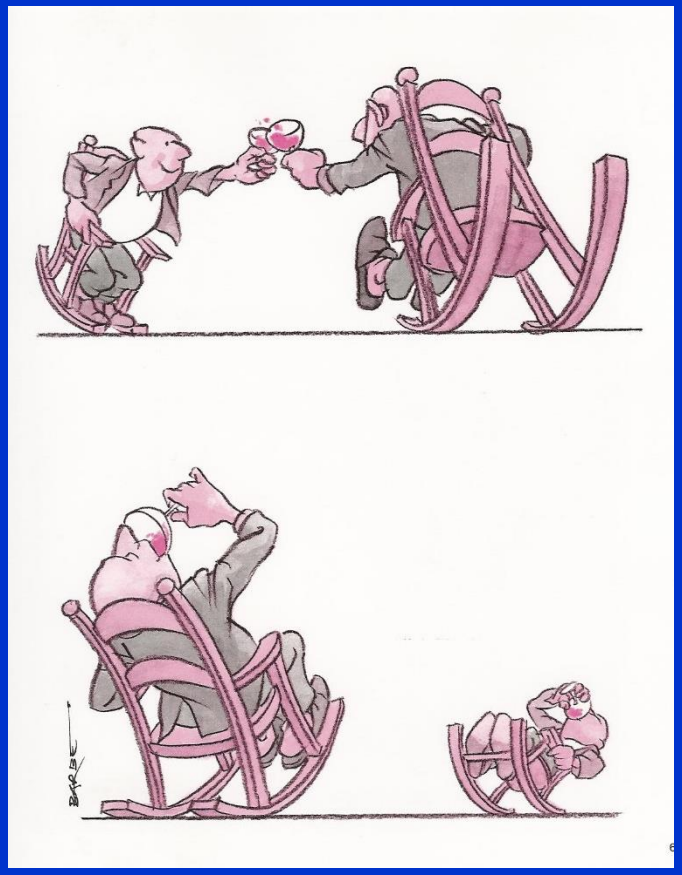
Data were taken from approxim
chosen at random from 98 c
supermarket chains—16 Bilka and
six months (from September 20
Supermarked, which collects the
provided us with details of which i
and price of the items, and the to
transaction. The data cannot b
consumers.

Because spirits are bought in a
markets and are not found on rec
only data relating to beer and win
"wine only," "beer only," "mixed,"
items were divided into 40 catego
were dichotomised: 1 if a custome

- Results:
- Wine buyers bought more olives, fruit and vegetables, poultry, cooking oil, and low fat cheese, milk, and meat than beer buyers.
- Beer buyers bought more ready cooked dishes, sugar, cold cuts, chips, pork, butter or margarine, sausages, lamb, and soft drinks than wine buyers.
- Conclusions: Wine buyers made more purchases of healthy food items than people who buy beer.



Moderate alcohol consumption is associated with reduced risk of dementia: *causal effect* or *reverse causation?*



Will drinking wine decrease your risk of dementia?

Or do you stop drinking because you forgot how to open the bottle?

To drink or not to drink?

- Association in observational studies does not prove causation.

- To prove causation we would need to do *a randomised, controlled double-blind study* with a group of high-risk men as trial subjects casting and drawing lots whether to be included in the intervention (drinking) group or the control (non-drinking) group.

A Sisyphean task

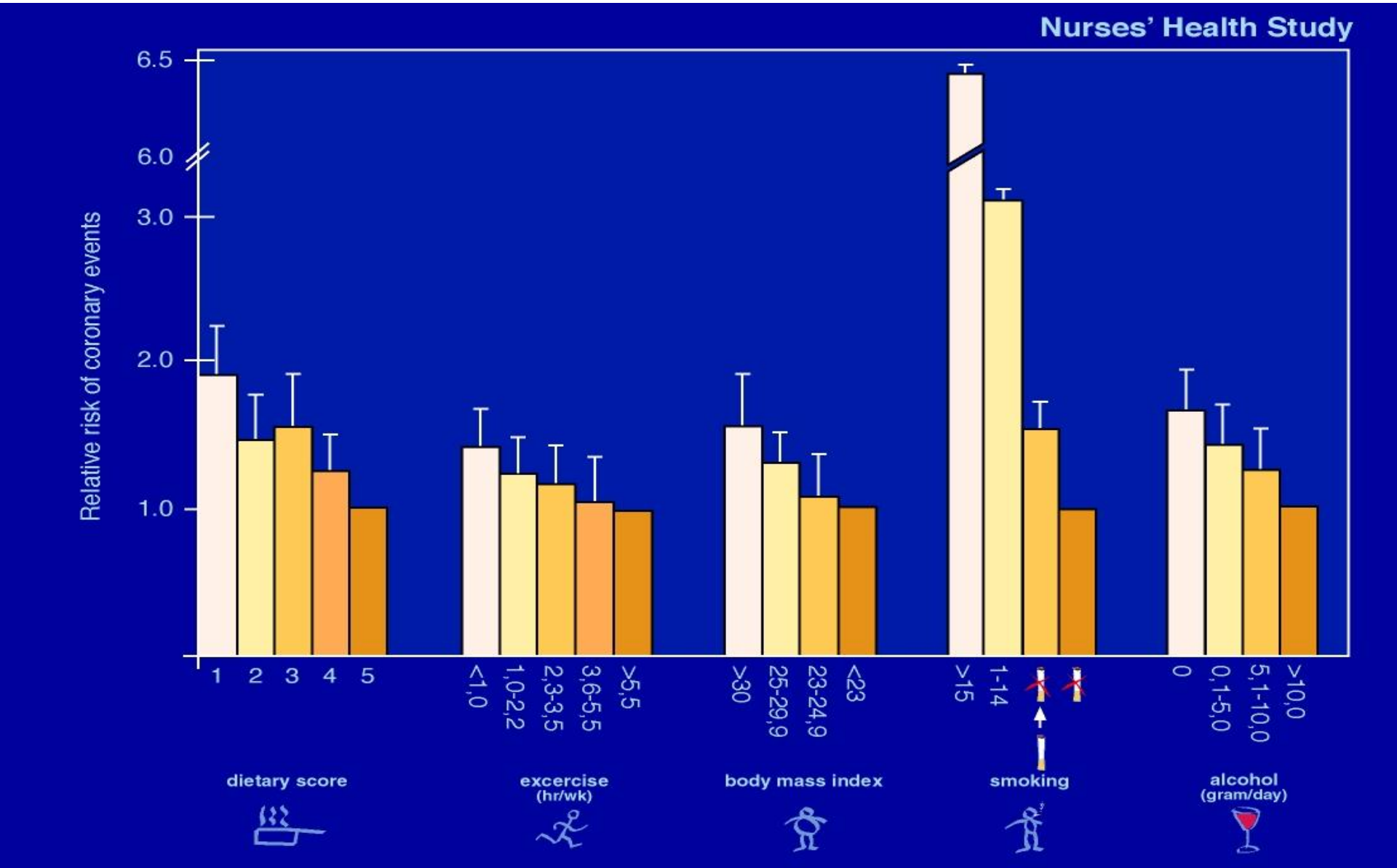
- Problems of the highly sought after RCT:
- Funding: Almost 75% of U.S. clinical trials in medicine are paid for by private companies, however, fears have been voiced that funding by the alcohol industry might influence the study's design or interpretation. *Eur J Public Health 2018; 28: 664–673.*
- Feasibility: RCT of lifestyle interventions are difficult, complex and subject to important issues, such as patient preference and non-adherence, that may threaten the internal and external validity of studies. *Int J Epidemiol 2015;44:2006-19.*
- External validity: RCT of men diagnosed with / in high risk of CHD have limited external validity: the generalizability of study results to healthy middle-aged men and women might not rise above the level of the educated guess. *BMC Fam Pract. 2017;18:113.*

- Any randomized controlled study would need to be large, in the order of at least 7500 patients, and would need to be conducted over at least 4 years.
- The drinking cohort must be very compliant. Liver function tests would need to be performed.

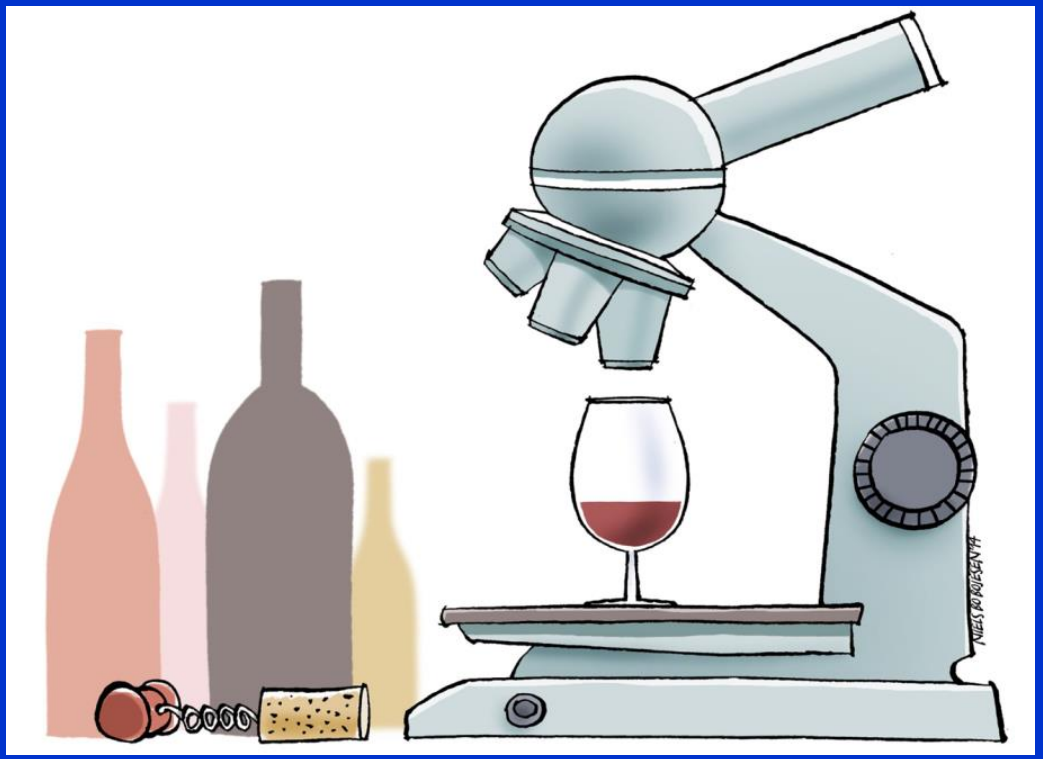
- Clinical monitoring would need to be of the highest quality. Methods would be needed to ensure that the drinking group had started drinking.
- Methods would be needed to ensure that the control group had not started drinking.

Circulation 2007;116:1306-17

Most likely the golden RCT will never be done; the best lifestyle evidence will continue to originate from major observational population studies such as the large *Nurses' Health Study*.



Should the abscence of conclusive RCT evidence on wine & health discourage the GP from informing patients about the potential beneficial effect of light-to-moderate alcohol consumption?



Wine & Health Information under attack

- ”Health experts agree…if you don’t drink now, there’s no reason to start… If you are concerned about coronary disease, there are better ways to lower your risk than consuming alcohol.”
- ”Light to moderate drinking is associated with increased likelihood of motor vehicle accidents, alcohol-medication interactions, fetal effects, hemorrhagic stroke, a shift to heavy drinking with attendant complications and, possibly, breast and colon cancer.” *Gordis E, Dufour M. NIAAA letter 1995 to CBS’s 60 Minutes.*
- ”Considering that the study by Millwood et al cast doubts about the net protective effects of moderate drinking and the 2016 Global Burden of Disease Study showed harms at all levels of alcohol use, further trials would be unethical. We further advocate that the term ”harmful use” should no longer be used.”

Comment: Lancet April 4, 2019. http://dx.doi.org/10.1016/S0140-6736(18)32214-1

- Levels of evidence supporting primary care practice:
- Primary care physicians should be aware that only a minority of recommendations (18%) are based on grade A high-quality, patient-oriented evidence. 34% of recommendations were grade B and 49% were grade C. *Evid Based Med 2017;22:88-92.*
- Levels of evidence supporting Cardiology Guidelines:
- Across 26 current ACC/AHA guidelines 248 recommendations (8.5%) were classified as grade A, 1465 (50.0%) as grade B, and 1217 (41.5%) as grade C. *JAMA 2019;321:1069-1080.*
- Levels of evidence supporting Cancer Guidelines:
- Of the 1,023 recommendations found in the 10 guidelines, the proportions of category I, IIA, IIB, and III EC were 6%, 83%, 10%, and 1%, respectively. *J Clin Oncol 2011;29:186-91.*
- Conclusion: The evidence levels supporting advice on lifestyle in general (& advice on light-to-moderate alcohol consumption in particular) are second to none.

What's relevant and important is the scientific evidence collected over the years from various populations with various scientific methods – and not the sensational new discovery!

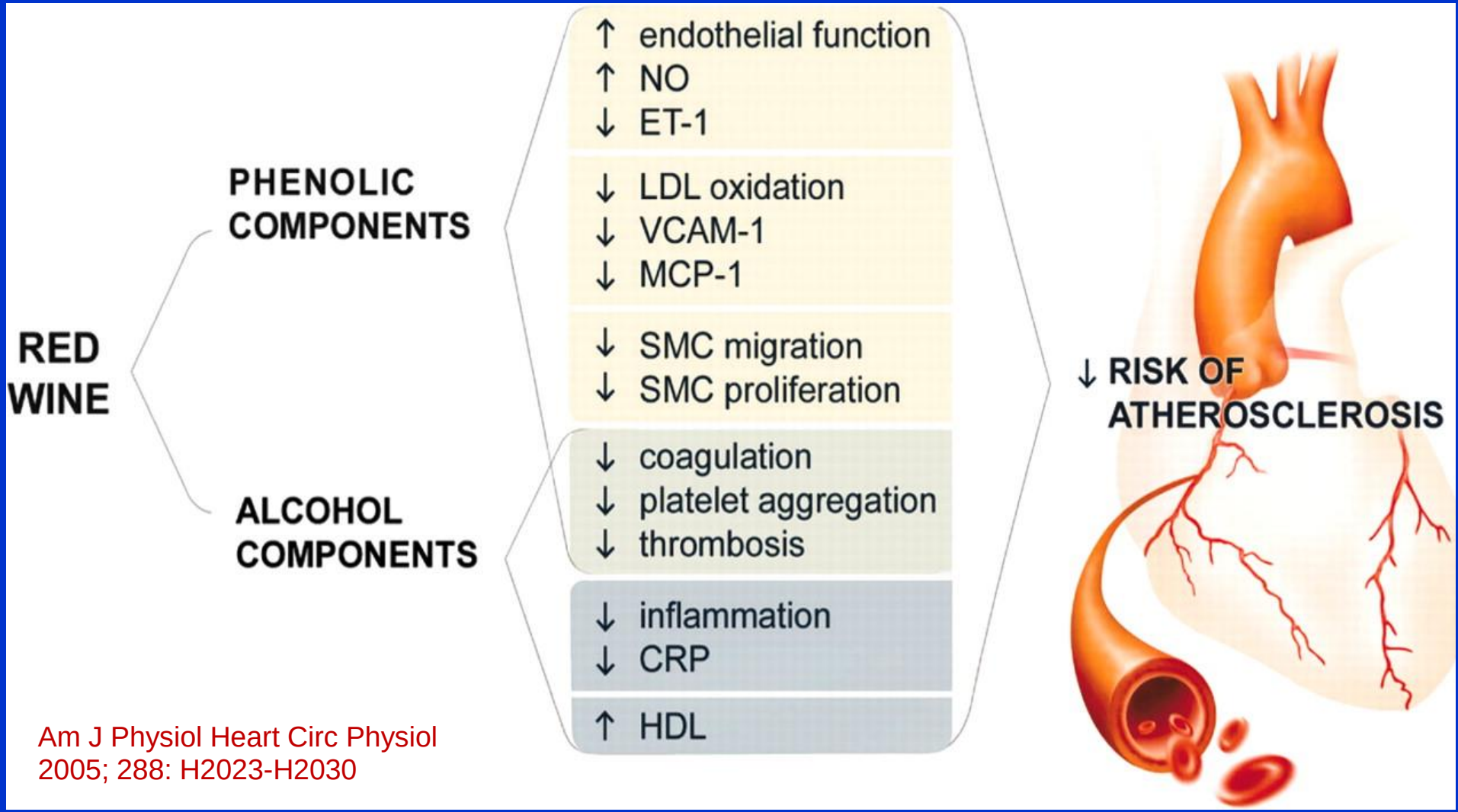
- The association of alcohol and cardiovascular health is compatible with existing theory and knowledge of the process of atherosclerosis.

- The effect of alcohol consumption on several factors of the biological pathways of atherosclerosis support the plausibility of the causal nature of the negative association between moderate alcohol consumption and risk of cardiovascular disease:
- 10-15% increase of HDL-c level
- 0.2 g/L decrease of Fibrinogen level
- 0,6 mg/L increase of Adiponectin level

Nutrition Research 2019;63:42-50.

Hills Criteria of Causation outlines the minimal conditions needed to establish a causal relationship between two items.

Red wine polyphenols may reduce the risk of arterio-sclerosis, decrease platelet aggregation and thrombosis and also counteract the harmful effects of *free radicals*



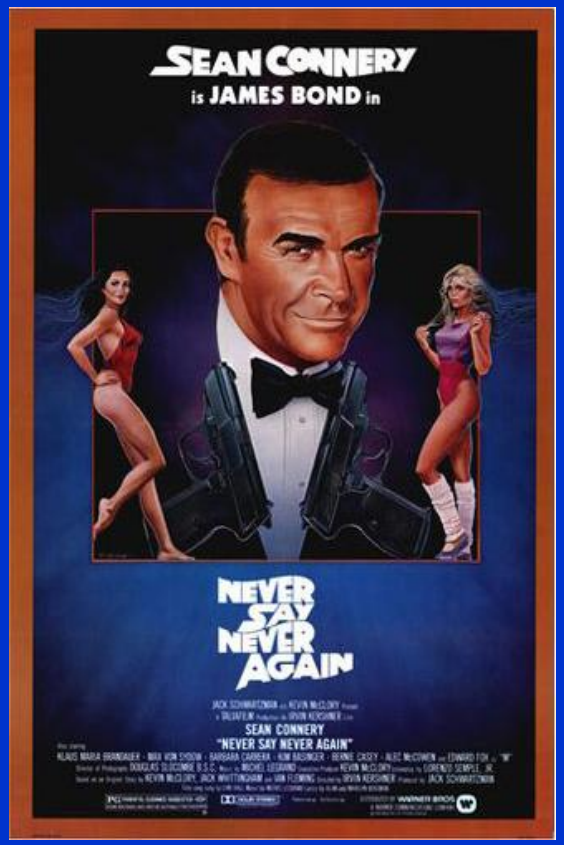
Am J Physiol Heart Circ Physiol 2005; 288: H2023-H2030

Feeling that Bond is slipping, M orders him to enroll in a health clinic in order to "eliminate all those free radicals and get back into shape”.

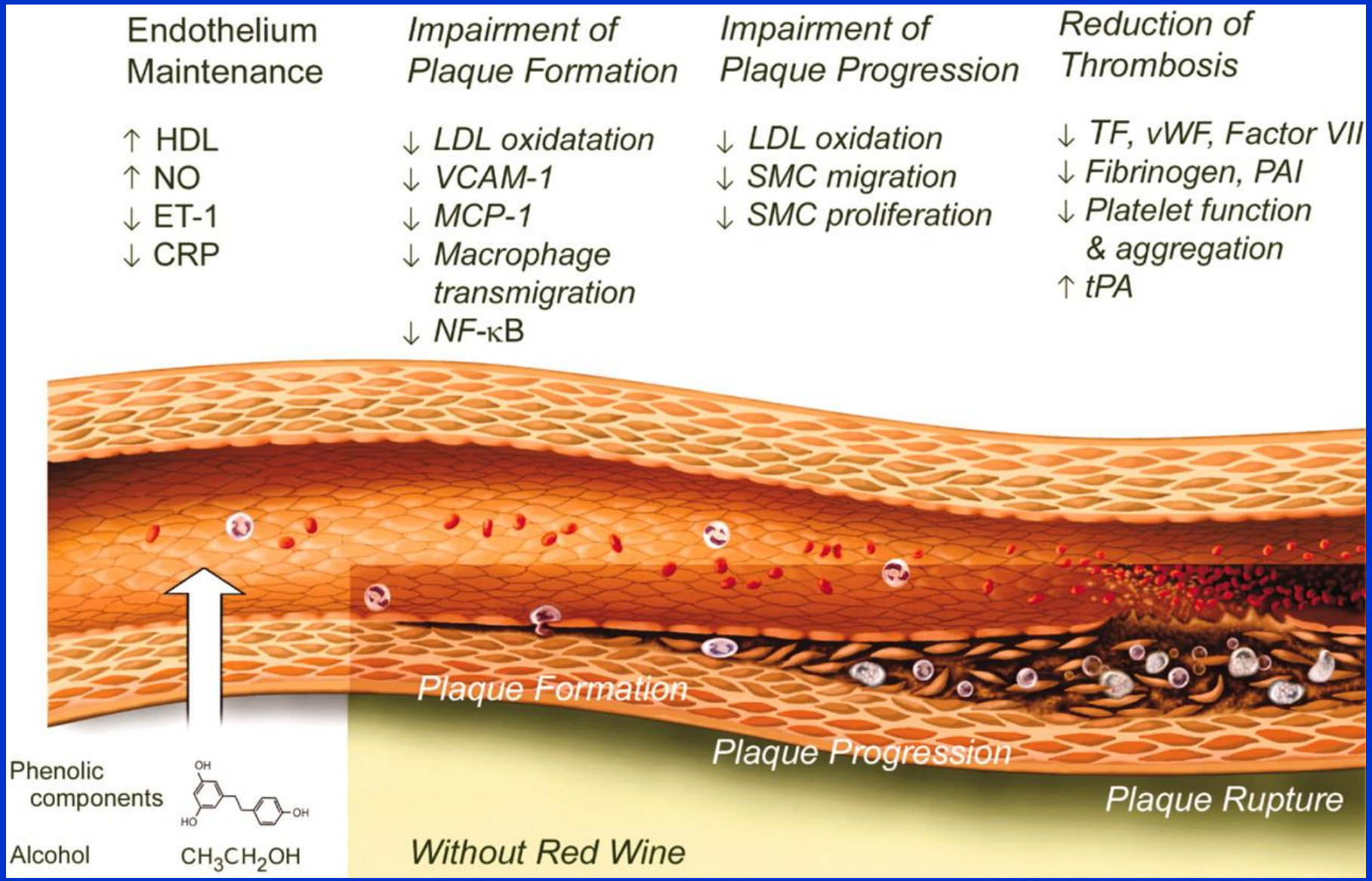
Bond: “Free radicals?”

M explains: “Toxins that destroy the brain and the body. Too much white bread, red meat, and too many dry Martinis.”

Bond: “I’ll cut down on the bread!”



Results from in vitro investigations and small clinical trials suggest that red wine polyphenols may also reduce the risk of thrombosis



Szmitko, P. E. Am J Physiol Heart Circ Physiol 2005; 288: H2023-H2030

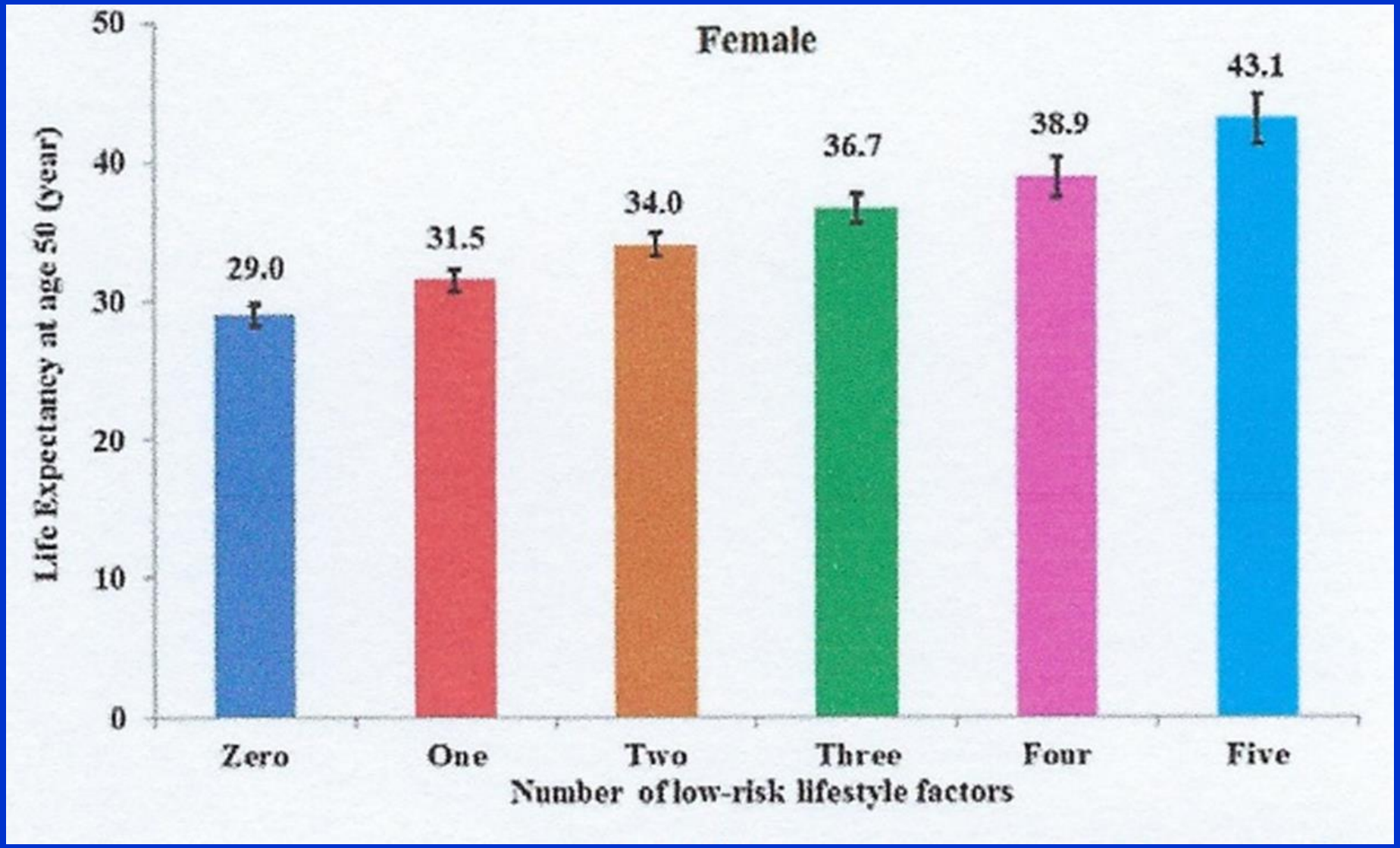
Impact of Healthy Lifestyle Factors

- Using data from:
  Nurses' Health Study (1980-2014; n=78 865).
  Health Professionals Follow-up Study (1986-2014, n=44 354)
  five low-risk lifestyle factors were defined:

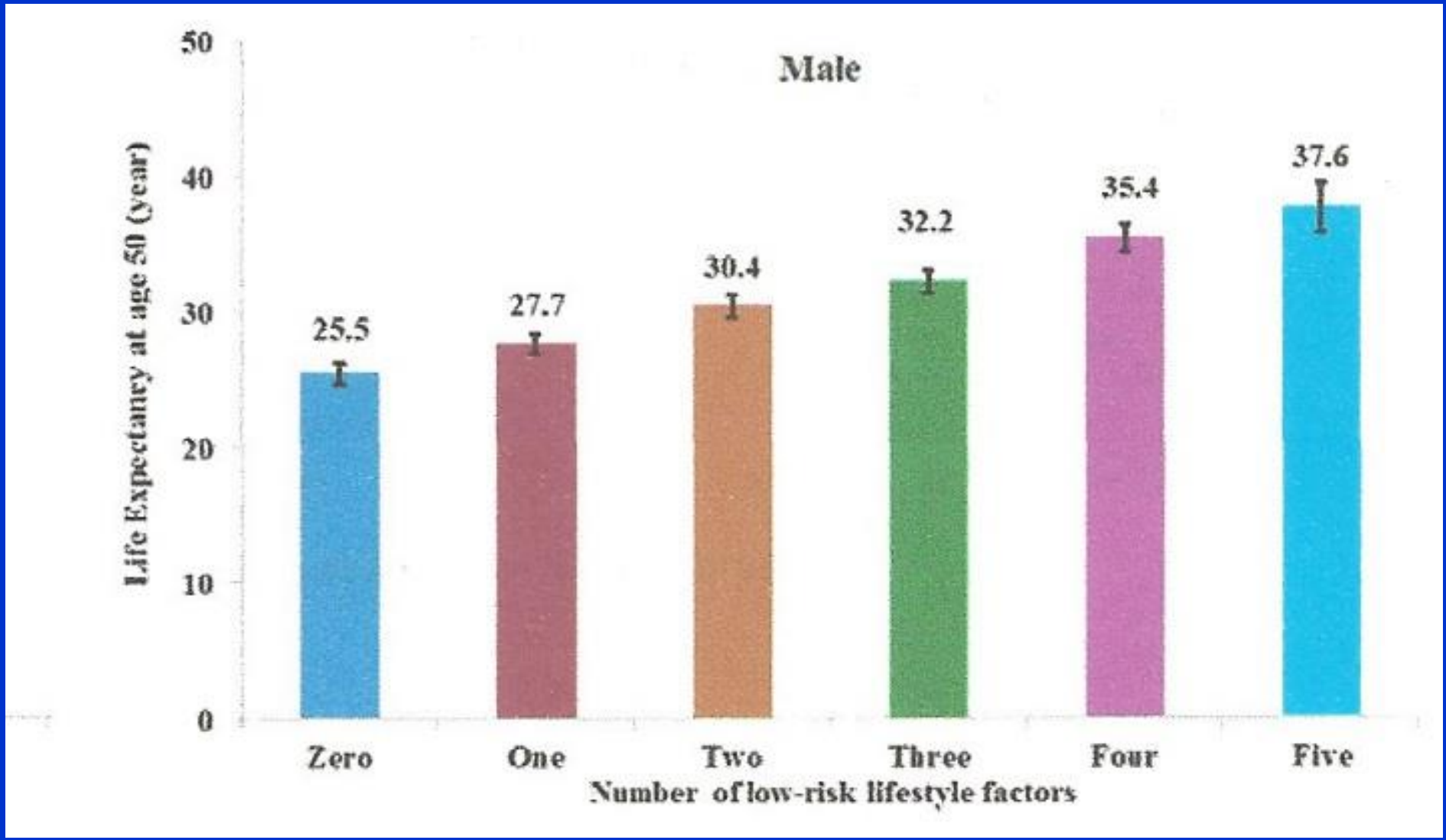
1. Never smoking
2. Body mass index of 18.5 to 24.9 kg/m^2
3. A high diet quality score (upper 40%)
4. ≥30 minutes/d of moderate to vigorous physical activity
5. A moderate alcohol intake: ♀ 5-15 g/day; ♂ 3-30 g/day.

- Hazard ratios for mortality in adults with 5 compared with zero low-risk factors were 0.26 (95% CI 0.22-0.31) for all-cause mortality, 0.35 (95% CI 0.27-0.45) for cancer mortality, 0.18 (95% CI 0.12-0.26) for cvd mortality. *Circulation 2018;138:345-355*

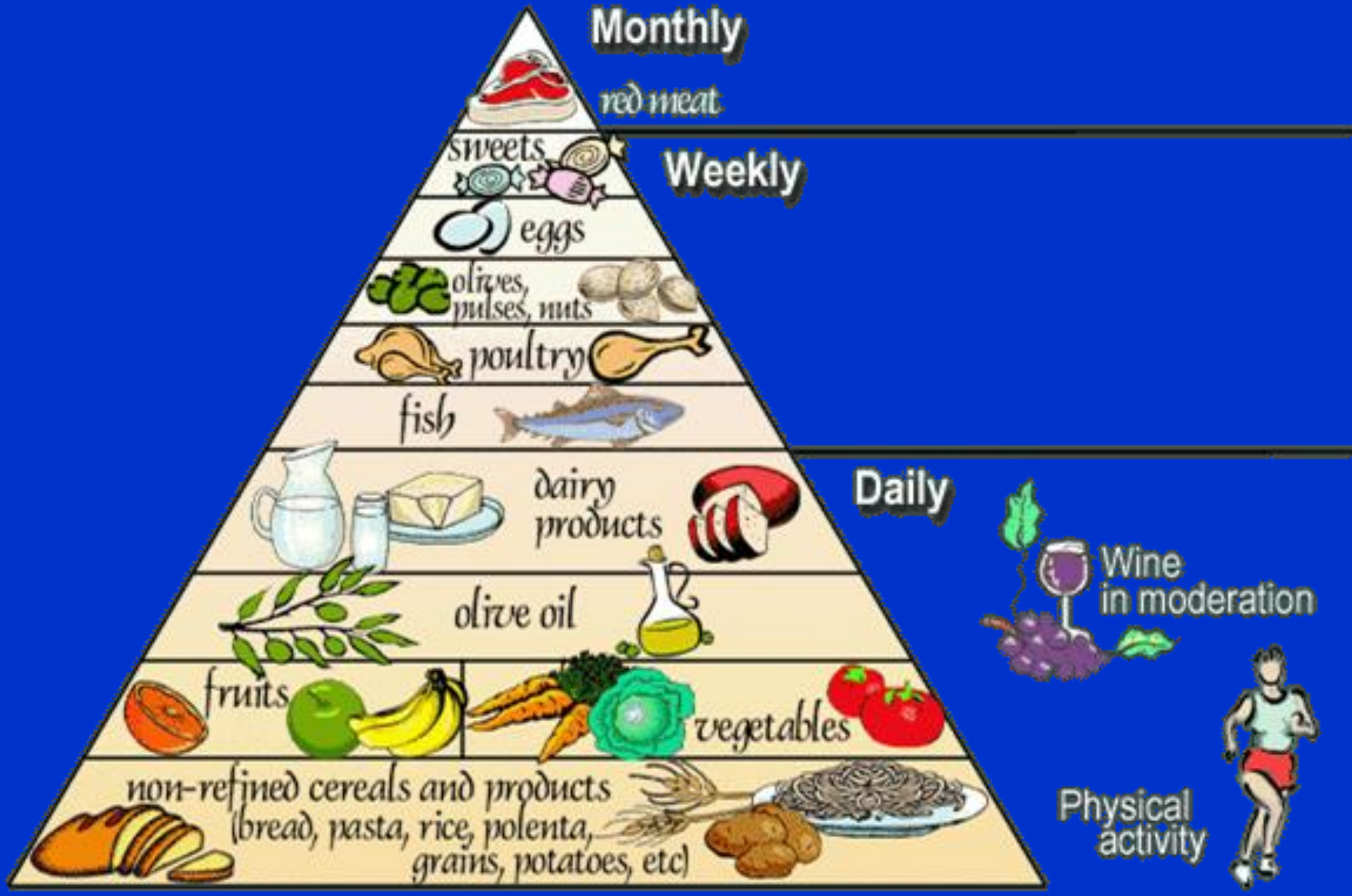
- The projected life expectancy at age 50 years was on average 14.1 years (95% CI 11.8-16.2) longer among females with 5 low-risk factors compared with those with zero low-risk factors.



- The projected life expectancy at age 50 years was on average 12.1 years (95% CI 10.1-14.2) longer among males with 5 low-risk factors compared with those with zero low-risk factors.



PYRAMID OF MEDITERRANEAN DIET



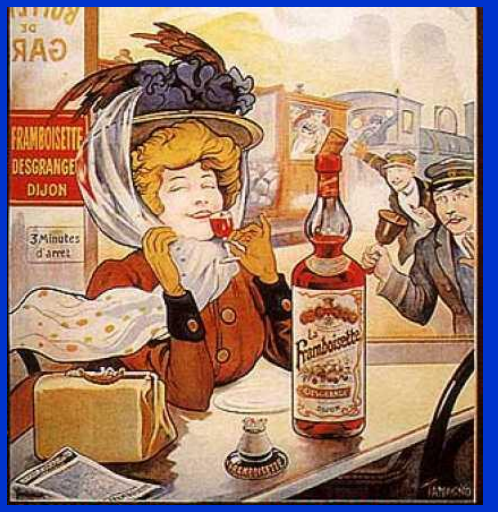
The anatomy of the Mediterranean Diet

Table 4 | Mortality ratios associated with two unit increment* in Mediterranean diet score (MDS) and after alternate subtraction of each of its dietary components

Dietary variable	Mortality ratio† (95% CI)	P value	Reduction in apparent effect (%)‡
MDS overall	0.864 (0.802 to 0.932)	<0.001	0
MDS minus vegetables	0.886 (0.822 to 0.955)	0.002	16.2
MDS minus legumes	0.877 (0.815 to 0.944)	<0.001	9.7
MDS minus fruit and nuts	0.879 (0.818 to 0.946)	0.001	11.2
MDS minus cereals	0.872 (0.814 to 0.935)	<0.001	6.1
MDS minus monounsaturated/saturated lipids (ratio)	0.878 (0.806 to 0.957)	0.003	10.6
MDS minus dairy products	0.870 (0.806 to 0.939)	<0.001	4.5
MDS minus meat and meat products	0.887 (0.825 to 0.953)	0.001	16.6
MDS minus ethanol	0.896 (0.835 to 0.962)	0.002	23.5

- The Greek EPIC Study found a higher Mediterranean diet score associated with a significant reduction in total mortality.
- The contribution of the Mediterranean Diet components: Moderate alcohol consumption: 23,5%. Less red meat: 16,6%. A lot of vegetables: 16,2%. Plenty of fruit and nuts: 11,2%. Olive oil for cooking: 10,6%. More legumes: 9,7%. Only small effects of cereals and dairy products. *BMJ 2009;338:b2337*

Sensible drinking (men should not regularly drink more than 3-4 units a day, and women 2-3 units a day) is associated with:



- 25% lower risk of cardiovascular disease mortality
- 13% lower risk of all cause mortality
- 30% lower risk of type 2 diabetes
- 23% lower risk of all forms of dementia
- 33 (wine) - 41% (beer) lower risk of kidney stone
- 32% lower risk of gallstones
- 22 - 31% lower risk of rheumatoid arthritis
- 20% lower risk of hip fracture
- 29% higher risk of mouth and throat cancer (mainly in smokers)
- 7 - 12% higher risk of breast cancer per unit (mainly in women with low (<300 µg/d) folate intake)

- ”It is correct and ethical for a MD to inform his/her patients about the results of many observational studies suggesting a beneficial effect of moderate alcohol consumption (especially red wine). We believe that a doctor should simply inform but not formally advise (nor of course ”prescribe”) nondrinking patients to start consume alcohol (wine) in moderation for heath reasons only.” *Giovanni de Gaetano, MD, PhD*

- ”Medical practitioners have a ”solemn duty” to tell the truth about alcohol consumption, as they understand it, to all their patients. I have always found it easier to deal with individuals than to make statements, that are applicable to entire populations. I find it much more satisfactory, and I am on surer ground, when I have an individual person in my office who wants to know how much he or she should drink.”

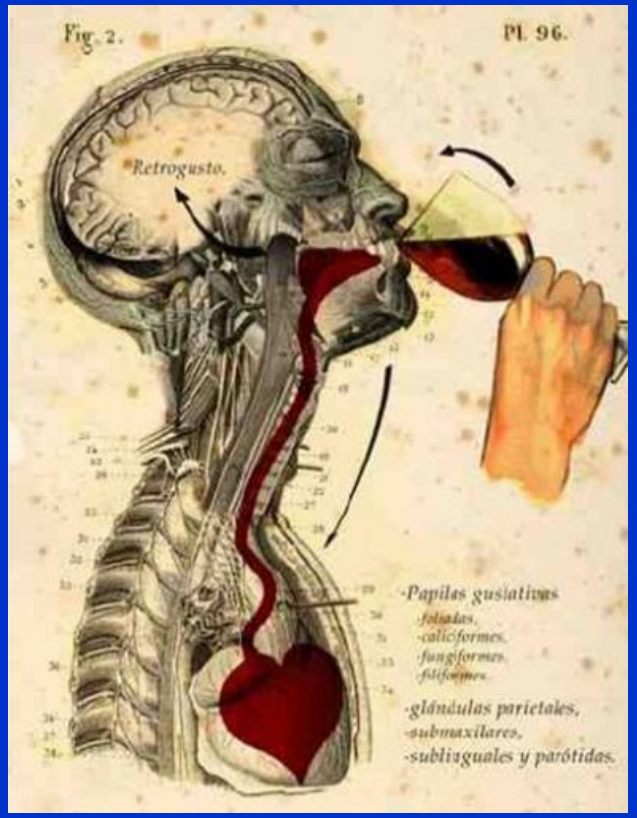
  Arthur L. Klatsky, MD

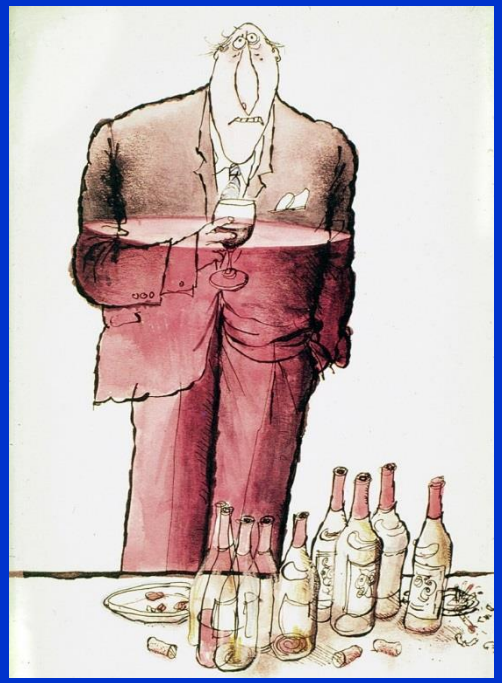
  Investigator at the Kaiser Permanente Northern California Division of Research

Healthy/prudent drinking patterns

- The blood alcohol content (BAC) and the health effects of alcohol intake depends on several different factors:

- The drinker: sex, age, physique, usual alcohol intake.
- Average volume of alcohol consumption: light to moderate intake / heavy drinking.
- Drinking habits: drinking with meals / drinking without food.
- Drinking pattern: steady drinking most days / binge drinking.
- The drink: beer / wine / spirits / carbon dioxide gas (CO_2).

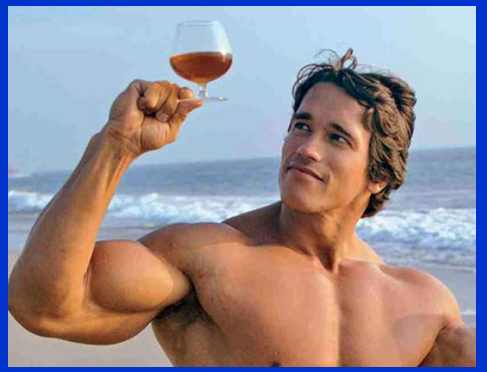




Blood Alcohol Content (BAC) & Total Body Water

- BAC is the concentration of alcohol in blood measured as mass per volume.
- When drinking the same number of drinks the person with more Body Water will get a lower Blood Alcohol Content.

- Due to low water content (10%) of fat in female breasts and buttocks and a high muscle water content (75%) a man has an excess of about 10 liters of body water compared to a woman of same age and weight and accordingly his BAC will be markedly lower with a comparable alcohol intake.



Total Body Water in men fra 20 to 89 years of age:

- 20-29 years: 45,6 liters
- 30-39 years: 47,5 liters
- 40-49 years: 45,7 liters
- 50-59 years: 46,9 liters
- 60-69 years: 44,8 liters
- 70-79 years: 44,1 liters
- 80-89 years: 42,5 liters

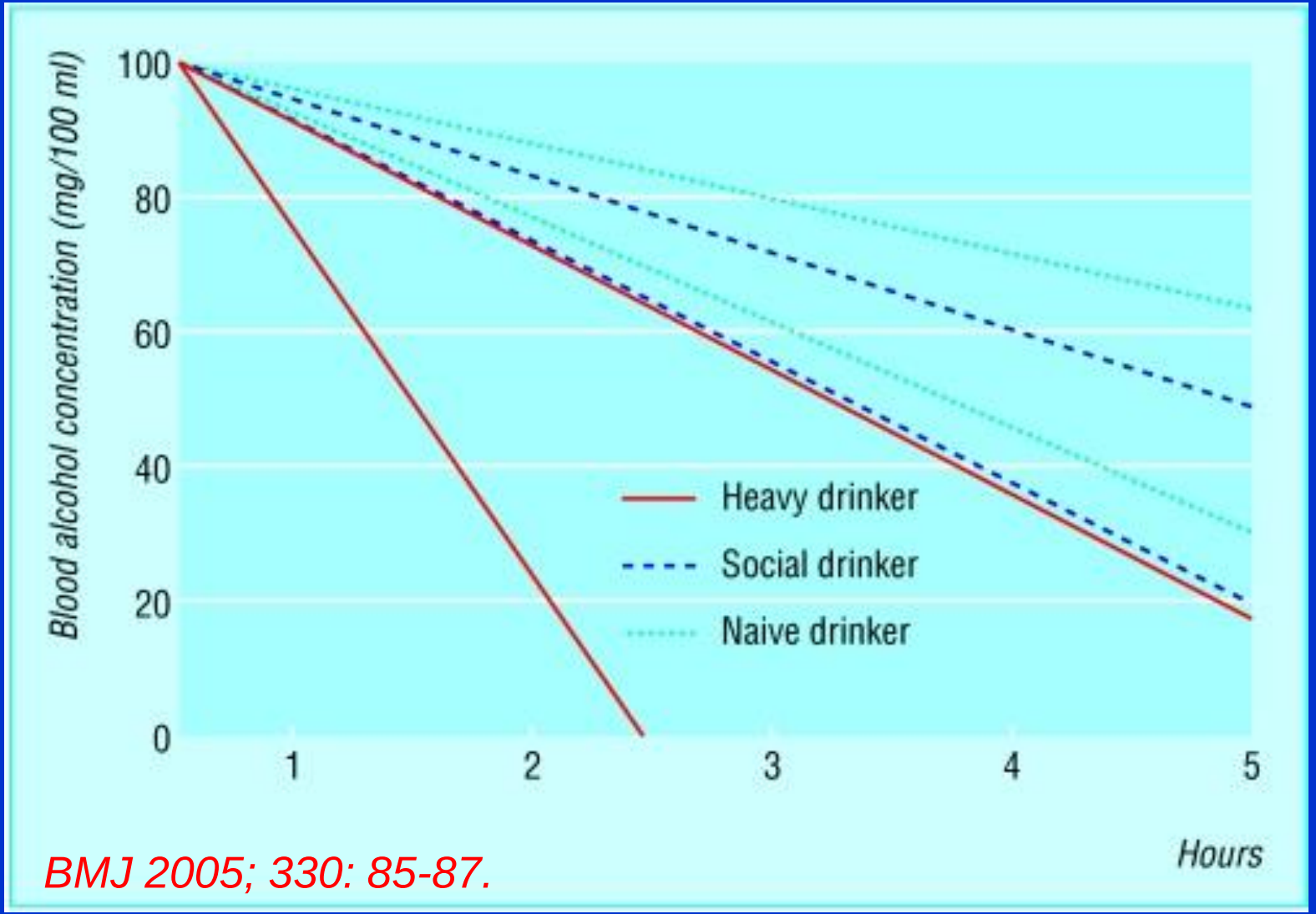
Kidney International 2001;59:2250-58

Total Body Water in women from 20 to 89 years of age:

- 20-29 years: 32,0 liters
- 30-39 years: 33,2 liters
- 40-49 years: 33,0 liters
- 50-59 years: 32,9 liters
- 60-69 years: 31,4 liters
- 70-79 years: 30,9 liters
- 80-89 years: 30,2 liters

Kidney International 2001;59:2250-58

Rate of decrease of concentrations of alcohol in the blood in heavy, social, and naïve drinkers. The two lines represent maximum and minimum rates for each category.



BMJ 2005; 330: 85-87.

Healthy/prudent drinking patterns

- The blood alcohol content (BAC) and the health effects of alcohol intake depends on several different factors:

- The drinker: sex, age, physique, usual alcohol intake.
- Average volume of alcohol consumption: light to moderate intake / heavy drinking.
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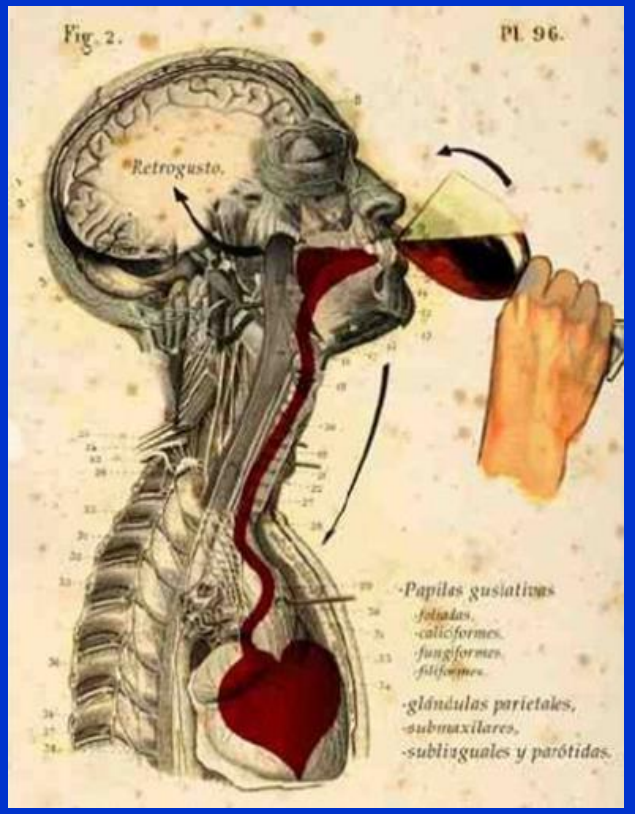


- The development of a valid global guideline is virtually impossible due to societies with various drinking habits and drinking patterns and varying degrees of under-reporting: the common quantity-frequency measure generally captures only about 50% of alcohol sales.
- A search of official definitions of standard drinks & consumption guidelines on government websites (57 countries) found a remarkable lack of agreement about what constitutes harmful or excessive alcohol consumption with no consensus about the ratios of consumption guidelines for men and women.

  Drug and Alcohol Review 2013;32:11-18.
- Information from governmental agencies in 37 countries reveled wide variation in standard drink definition: 8 to 20 g. Significant variability was also evident for low-risk drinking guidelines, ranging from 10-42 g per day for women and 10-56 g per day for men to 98-140 g per week for women and 150-280 g per week for men. *Addiction 2016:111:1293-1298.*

Summary

Morten N. Grønbæk, Lars Iversen, Jørn Olsen, Povl Ulrik Becker, Finn Hardt & Thorkild I. A. Sørensen:

Sensible drinking limits.

Ugeskr Læger 1997; 159: 5939-45.

A large number of prospective population studies from many countries have described a J- or U-shaped relation between alcohol intake and mortality. Both heavy drinkers and abstainers are at a higher risk of dying from all causes than individuals with light to moderate alcohol intake. This makes information to the public about sensible drinking limits more complex than, eg, that concerning smoking.

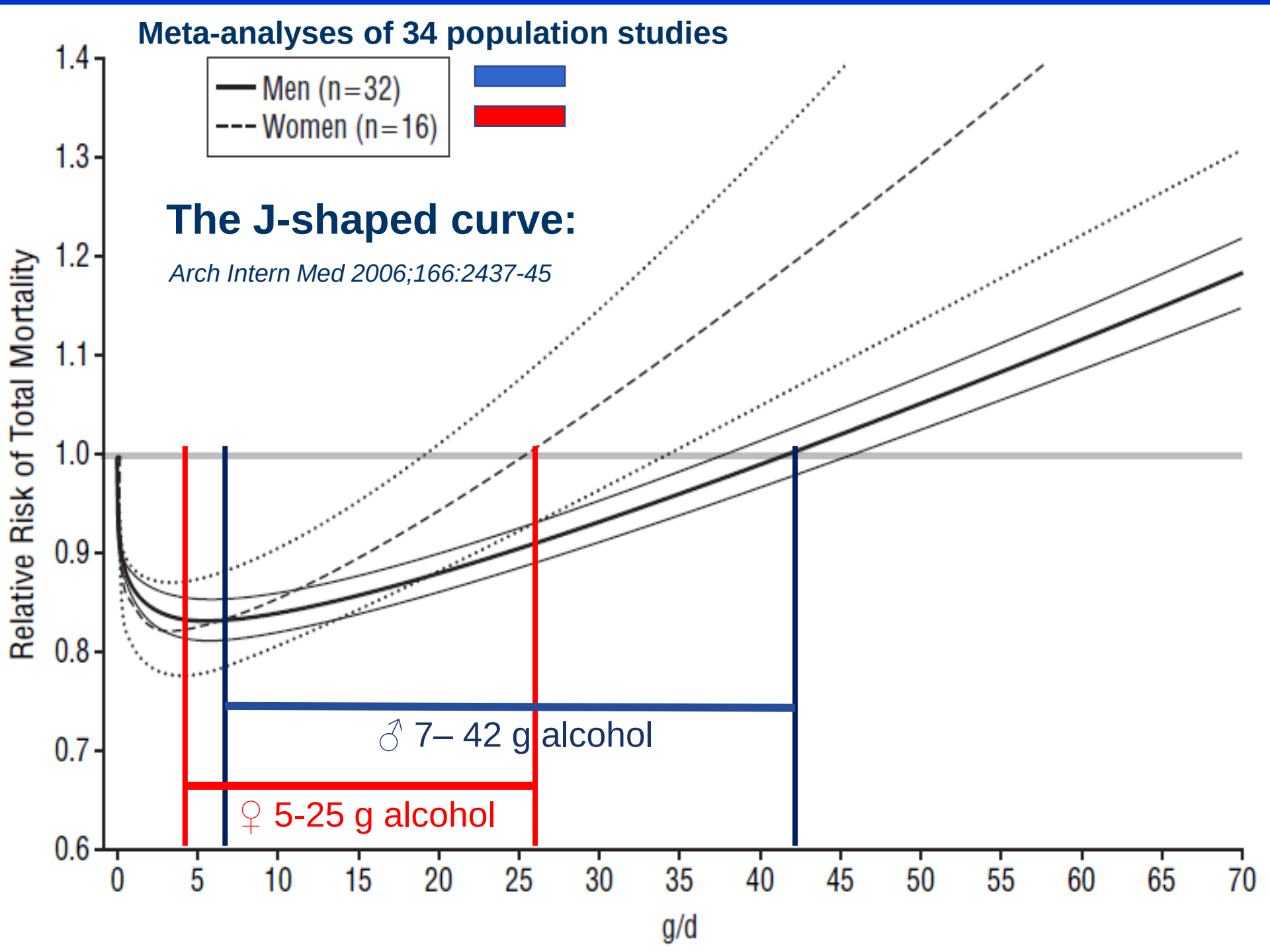
The present paper aims at identifying upper thresholds for harmless alcohol intake. The review is mainly based on epidemiological evidence concerning somatic morbidity and mortality.

It is concluded that the present Danish recommendations – 14 drinks per week for women and 21 drinks per week for men – should be maintained. It is emphasized that these limits apply to adults who are at no risk of dependency and that they do not apply to pregnant women. Information about a potentially beneficial effect of a moderate alcohol intake should be reserved for individuals already at risk of coronary events.

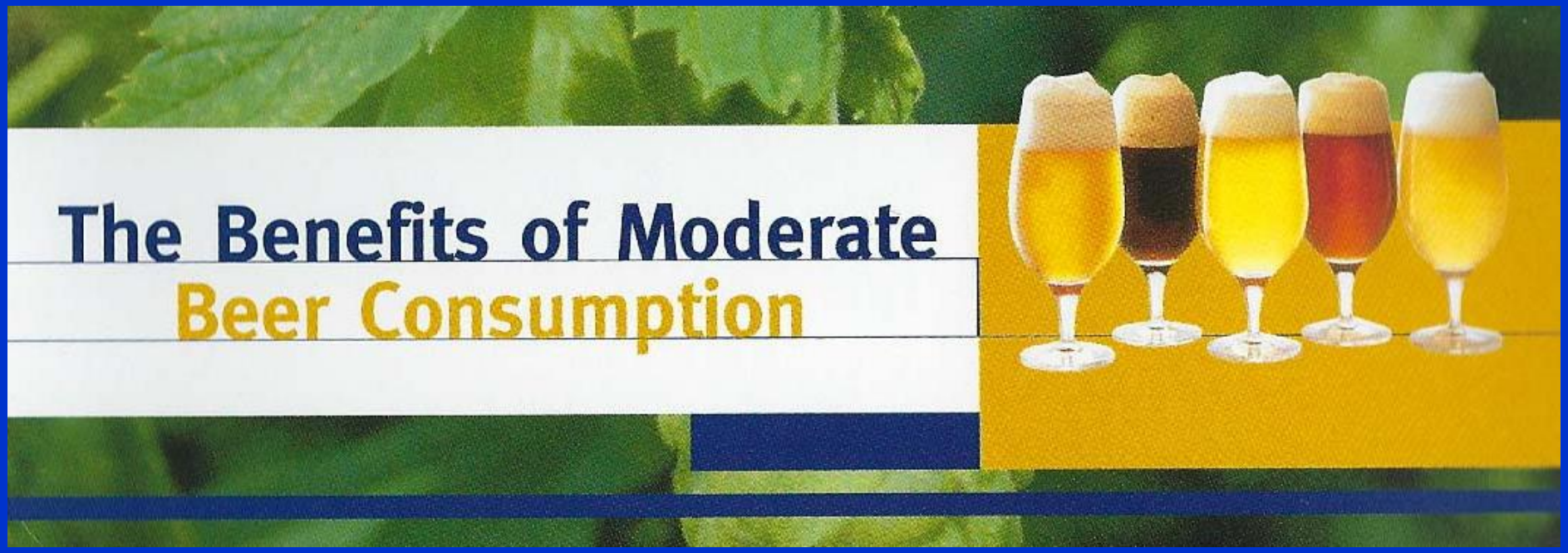
Sensible Danish drinking limits 1990-2010

- 14 drinks per week for women
- 21 drinks per week for men.

Meta-analyses of 34 population studies



Beer and Health Symposium 2001

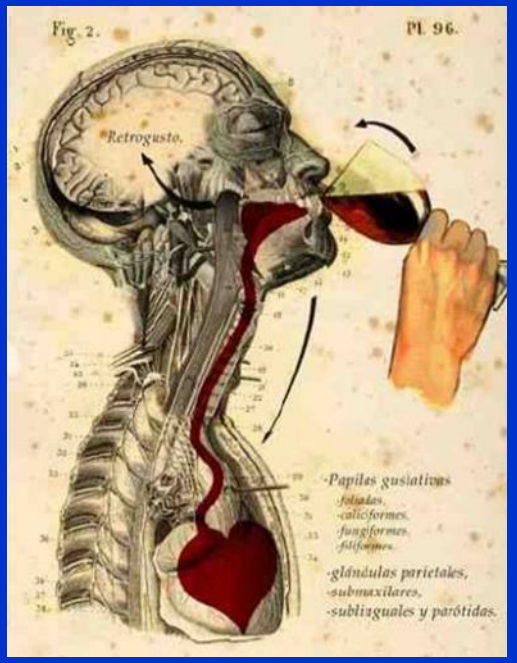


Dr Skovenborg, speaking at the symposium, defined moderation in the following terms. "To drink moderately is to drink within the limits set by your health, the society in which you live and your obligations towards your family and friends: 1 – 3 drinks a day for most men". "Women are more sensitive to alcohol so they are advised to drink less than men: 1 to 2 drinks a day."

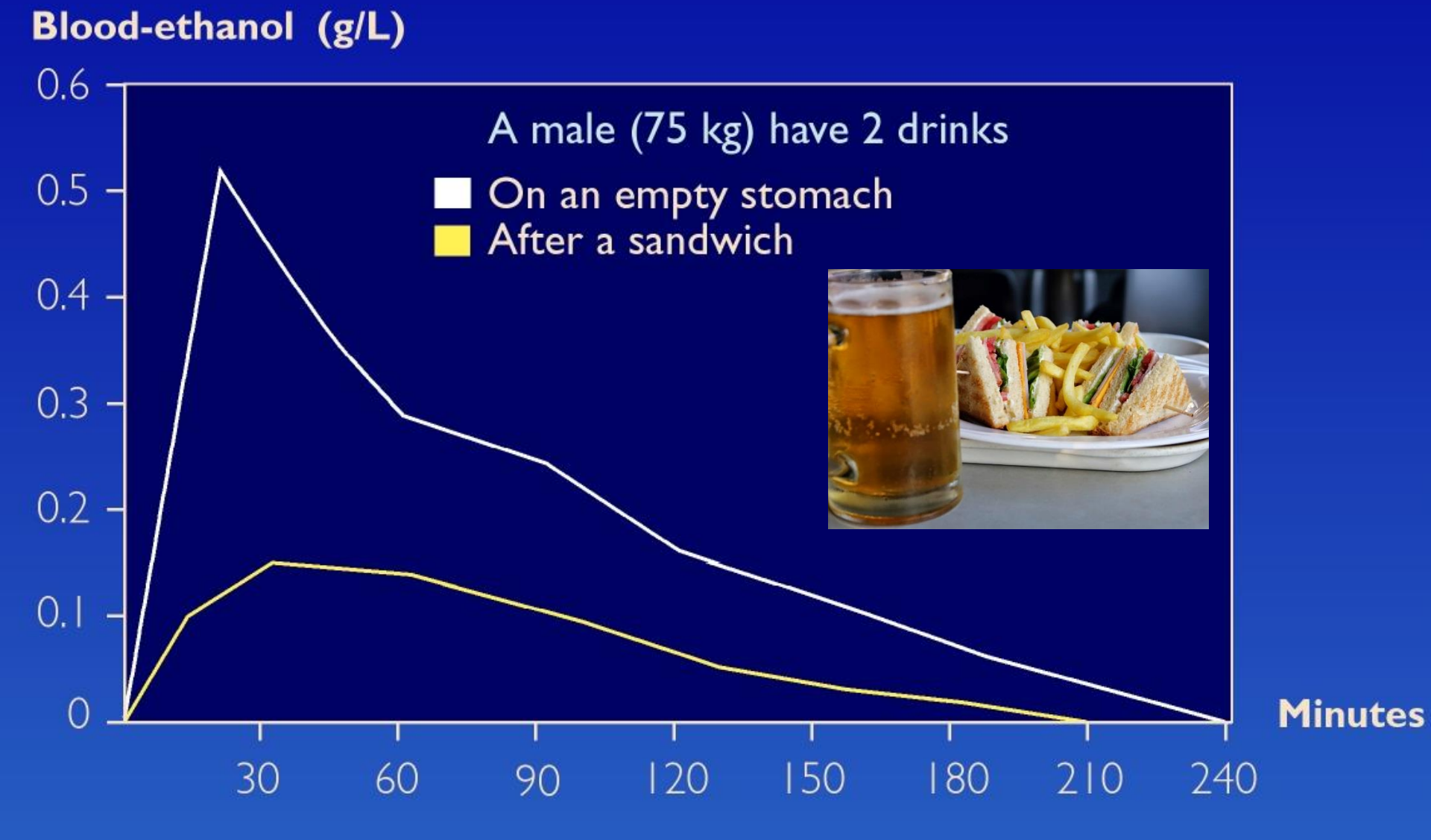
Healthy/prudent drinking patterns

- The blood alcohol content (BAC) and the health effects of alcohol intake depends on several different factors:

- The drinker: sex, age, physique, usual alcohol intake.
- Average volume of alcohol consumption: light to moderate intake / heavy drinking.
- Drinking habits: drinking with meals / drinking without food.
- Drinking pattern: steady drinking most days / binge drinking.
- The drink: beer / wine / spirits / carbon dioxide gas (CO_2).

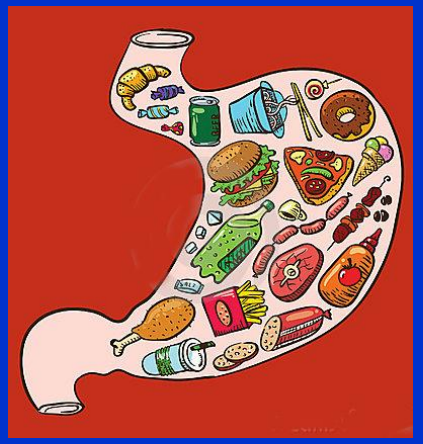


The intake of alcohol with food increases gastric and hepatic First Pass Metabolism of ethanol with a considerably lower BAC:
2 drinks with food: 15 mg/100 ml vs 53 mg/100 ml when fasting.



Food-induced lowering of blood-ethanol

- Food in the stomach before drinking not only leads to a lowering of the peak BAC and diminishes the feelings of intoxication, but also boosts the rate of ethanol metabolism.
- A food-induced increase in the rate of disposal of ethanol was also confirmed when subjects ate a meal 5 hours after drinking, that is, when the post-absorptive phase of ethanol metabolism was well established.
- The mean rate of disappearance of alcohol from blood was increased by between 36-50%.



Journal of Forensic Sciences 1994;39:1084-93.

Alcohol drinking patterns and liver cirrhosis risk

- At every level of alcohol consumption, cirrhosis incidence was lower in women who usually drank with meals compared with those who did not in the analysis of the prospective UK Million Women Study.

- After adjusting for the amount of alcohol consumed and 6 other potential confounding factors the RR for cirrhosis associated with usually drinking with meals compared with not drinking with meals was 0.69 (95% CI 0.62-0.77).

Lancet Public Health 2019;4:e41-48

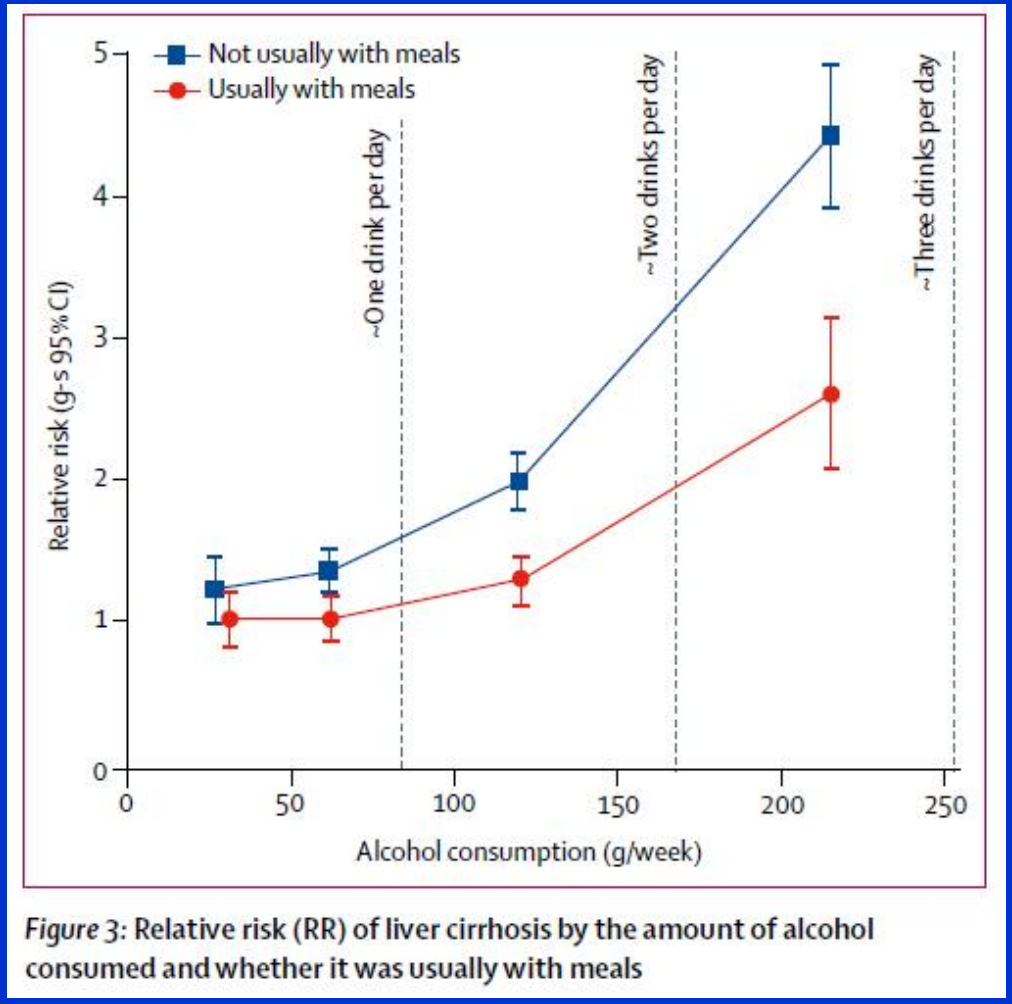


Figure 3: Relative risk (RR) of liver cirrhosis by the amount of alcohol consumed and whether it was usually with meals

Healthy/prudent drinking patterns

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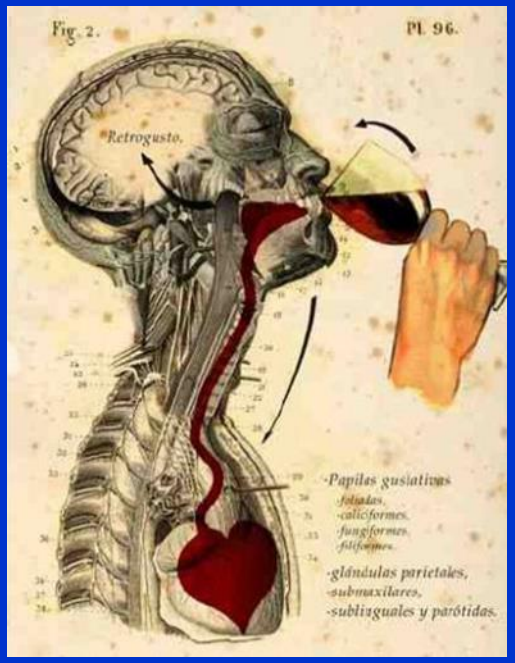

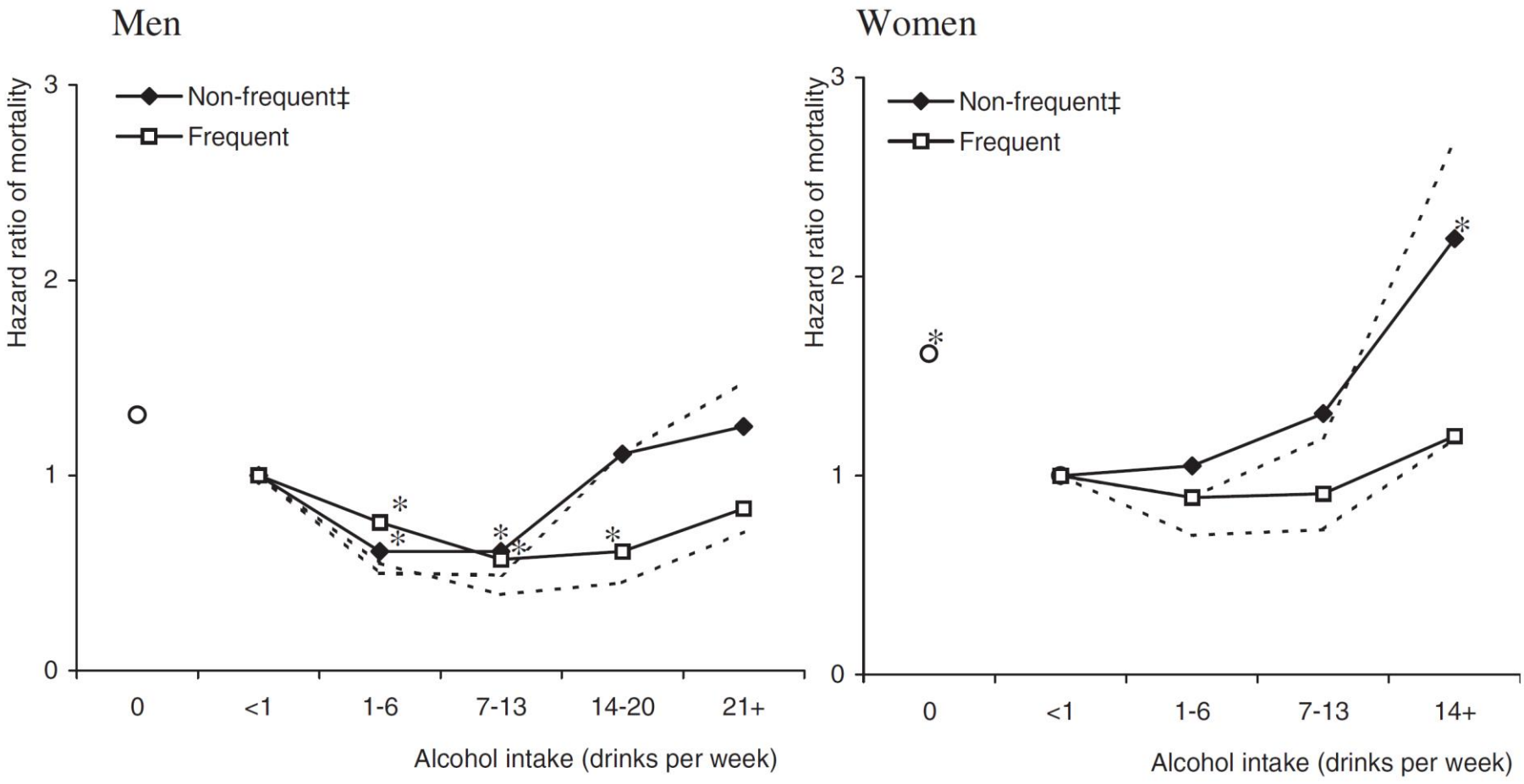

- In a population-based cohort study of 26 909 men and 29 626 women aged 55-65 years drinking pattern and not just the total amount of alcohol consumed was important for the association between alcohol intake and mortality. For the same average consumption of alcohol, a non-frequent intake implied a higher risk of death than a frequent one. *Addiction 2004;99:323–30*

Binge drinking

- NIAAA defines binge drinking as a pattern of drinking that brings a person's blood alcohol concentration to 0.08 grams percent or above. This typically happens when men consume 5 or more drinks, and when women consume 4 or more drinks, in about 2 hours (https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking)
- Several factors of importance for BAC after alcohol intake are not taken into account: the individuals weight, rate of drinking and drinking without food (fasting) or drinking with a meal.
- The variation of "standard" drinks from nation to nation, makes cross-national comparisons difficult. In the United States, one "standard" drink contains roughly 14 grams of pure alcohol. (https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/what-standard-drink).
- There is no consensus about what the cut off for binge drinking should be and no scientific basis for the various cut offs adopted. *J Epidemiol Community Health 2008;62:476-79.*

Binge drinking is associated with many health problems, including:

- Unintentional injuries (car crash, falls, burns, drowning).
- Intentional injuries (sexual assault, domestic violence).
- Alcohol poisoning.
- Sexually transmitted diseases.
- Unintended pregnancy.
- Children born with Fetal Alcohol Spectrum Disorders.
- High blood pressure, stroke, fatal myocardial infarction.
- Liver disease.
- Neurological damage.
- Sexual dysfunction.

Healthy/prudent drinking patterns

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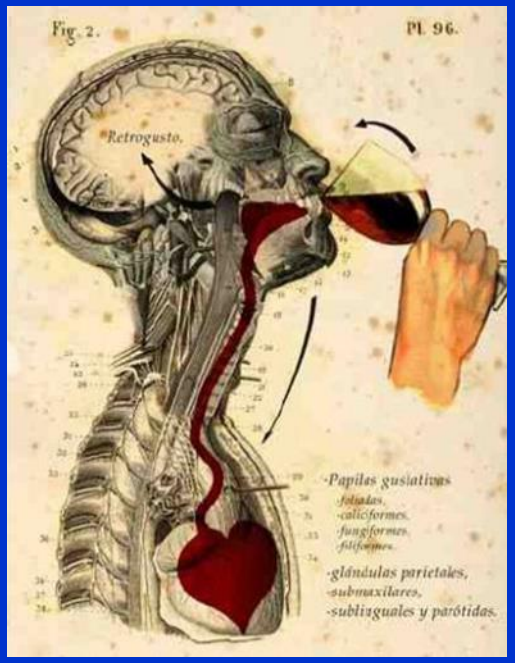


BAC after drinking 0.5 g of alcohol per kg body weight as vodka/tonic (20% v/v), white wine (12.5% v/v or beer (5.1% v/v) over 20 minutes after an overnight fast.

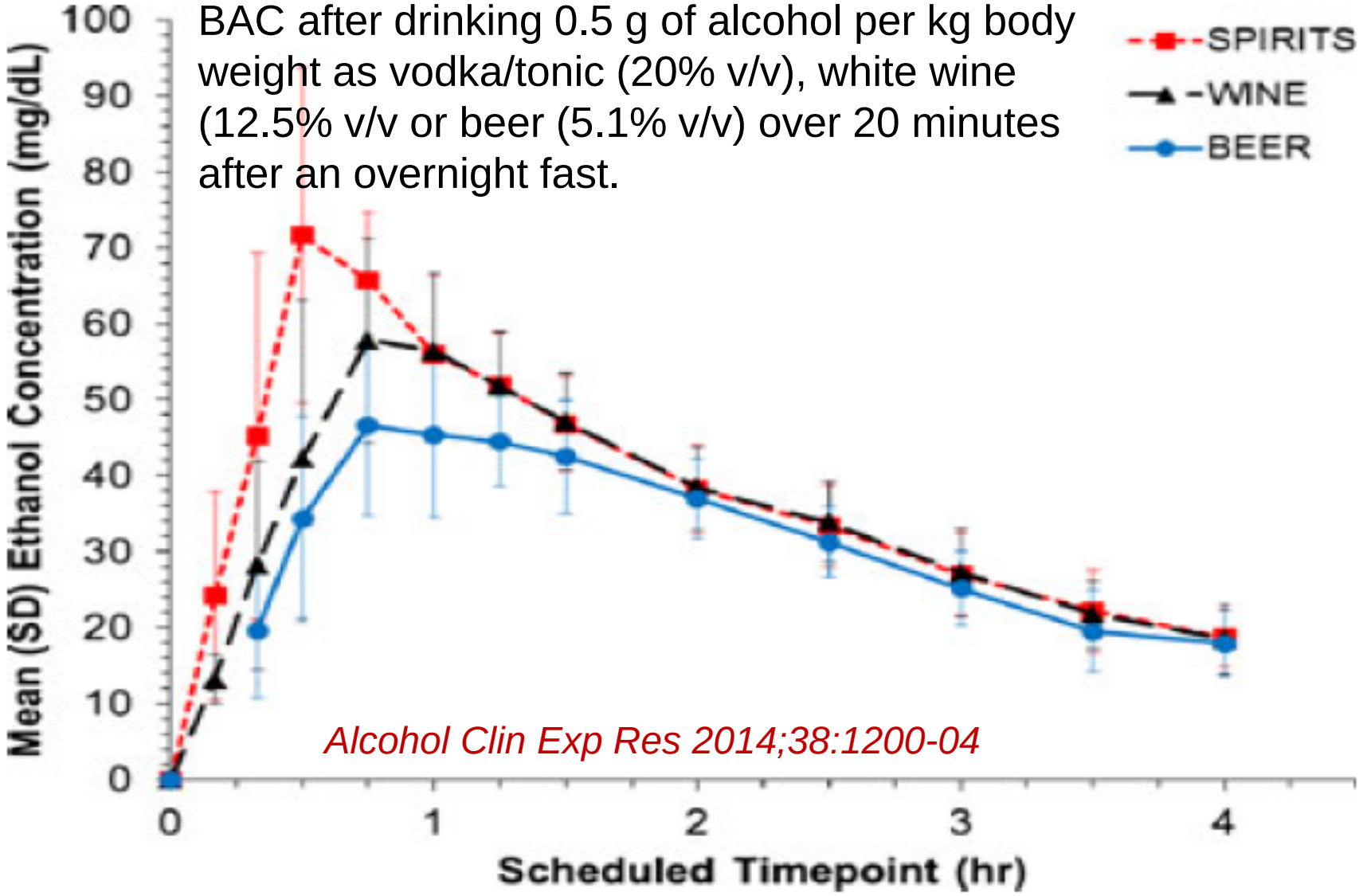


Fig. 1. Geometric mean values for blood alcohol concentrations following consumption of vodka/tonic (red squares), wine (black triangles), or beer (blue circles) are shown over time. Time zero represents initiation of consumption of beverages that was complete within 20 minutes.

CO_2 bubbles & blood alcohol levels

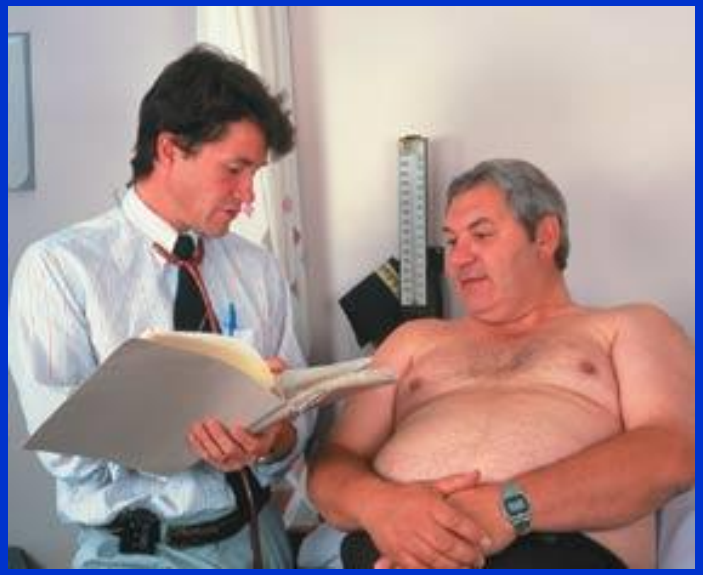
- Champagne doses were poured from freshly opened bottles of non-vintage brut champagne. The degassed champagne condition consisted of the same champagne, from which the carbon dioxide (CO_2) had been removed by whisking with an electric blender. All subjects (6♂ + 6♀) received a dose of 0.6 g alcohol/kg body weight with 20 min to consume the drinks.

- Champagne produced significantly greater BACs (52 mg/100 ml / 0.52 ‰) and significantly increased reaction times in a divided attention task than degassed champagne (40 mg/100 ml / 0,40 ‰).
- The CO_2 in champagne may accelerate absorption of alcohol, leading to more rapid or severe intoxication.

Alcohol Alcoholism 2003;38:381-5

How do you find the heavy drinkers in need of advice?

- A RCT (brief counselling intervention vs no intervention) involving 39 Danish general practitioners showed little effect: At one-year follow-up, average weekly consumption had increased by 0.7 drinks in both comparison groups.



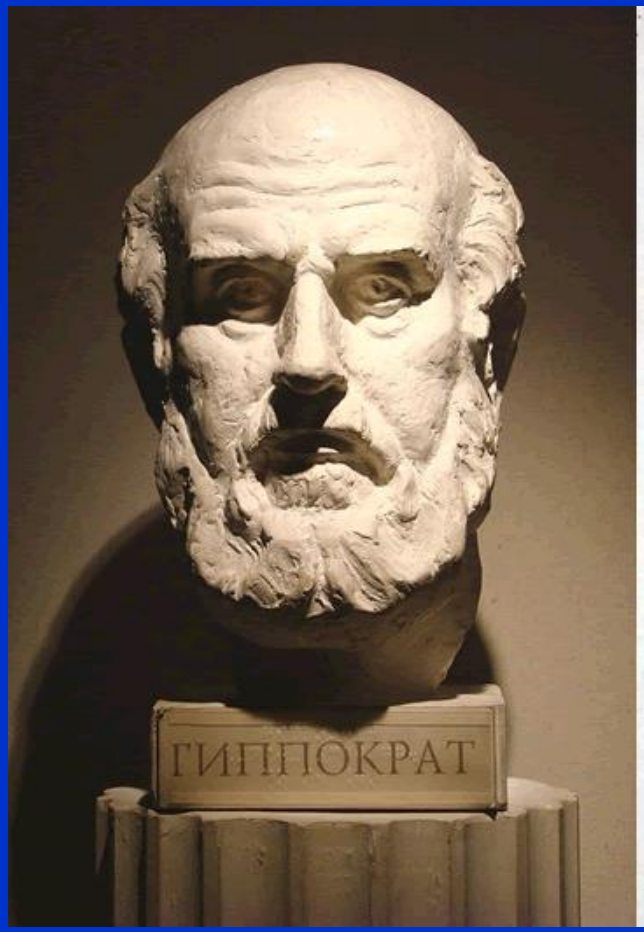
- Some of the unselected patients identified by systematic screening were defensive and more than four out of five declined further consultations on the alcohol issue.
- If the GP seizes the right moment for addressing the issue, and does so in a manner that allows the patients to see advice as an integral part of the GP's care activities, drinking assessment and advice giving may be likely to help a larger fraction of drinkers and to provoke less dissonance and resistance. *Alcohol & Alcoholism 2007;42:593-603*

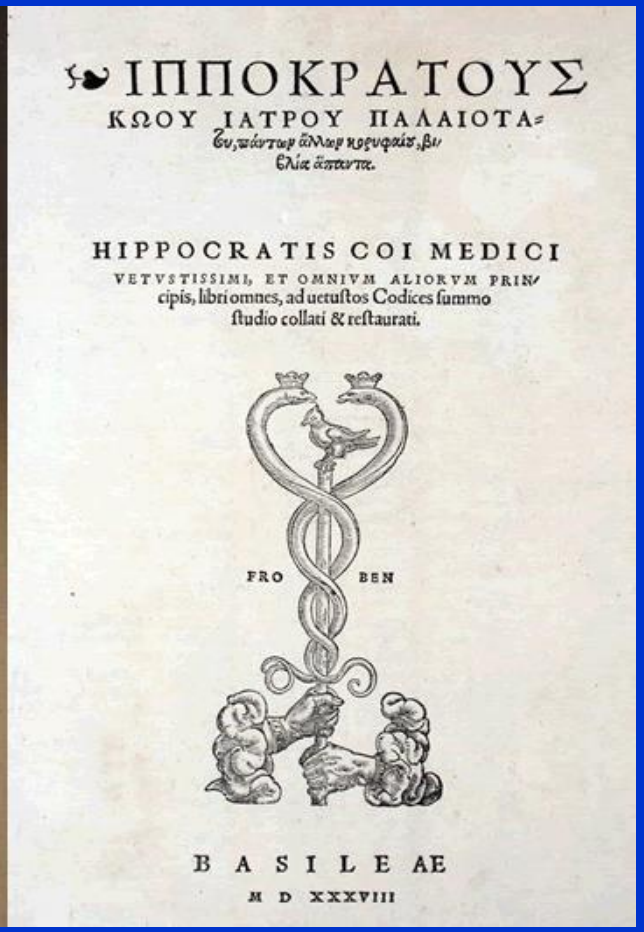
- GPs should have the skills necessary for raising sensitive lifestyle issues like drinking, smoking, diet, and exercise, whenever appropriate like patients with vague physical symptoms, appetite loss, non-specific abdominal discomfort or fatigue without key physical findings.
- Men falling asleep in front of the TV.
- Mild to moderate uncomplicated hypertension.
- Patients with gout flares.
- Patients with fatty liver disease.
- Transaminasemia: the presence of elevated transaminases.
- Men with erectile dysfunction.
- Sleep problems: insomnia and/or daytime sleepiness.
- Anxiety and/or depression.
- Stress

Classification af evidence-level

Publikationtype	Evidence	Strength
Meta-analysis of RCT	Ia	A
RCT = randomised, controlled trial	Ib	
Controlleret, non-randomised trial	IIa	B
Cohort studies	IIb	
Case-control studies	III	C
Cross-sectional studies		
Case reports / Expert opinions	IV	D

Expert opinions have low evidence level, however, they may provide deep insight.




ΙΠΠΟΚΡΑΤΟΥΣ
ΚΩΟΥ ΙΑΤΡΟΥ ΠΑΛΑΙΟΤΑ=

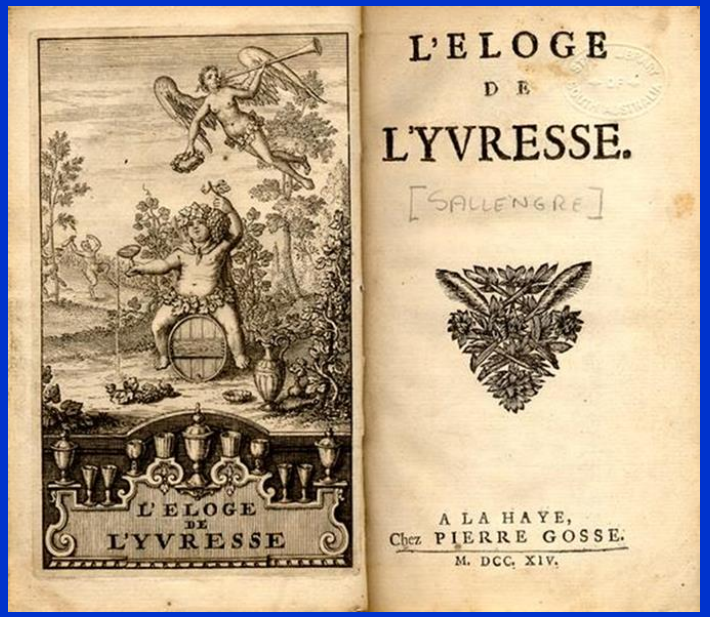
HIPPOCRATIS COI MEDICI
VETVSTISSIMI, ET OMNIVM ALIORVM PRIN/
cipis, libri omnes, ad uetuſtos Codices ſummo
ſtudio collati & reſtaurati.

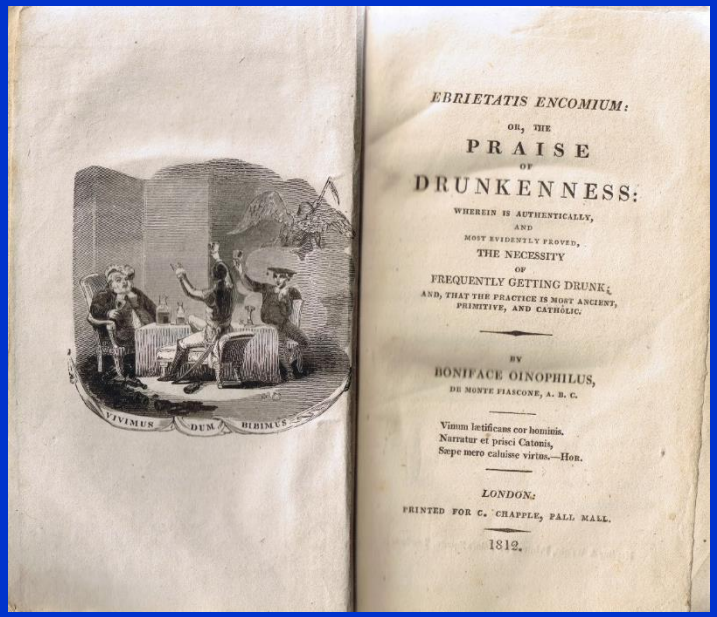
FRO BEN

BASILEAE
M D XXXVIII

”Wine is a thing marvellously suited to man, in health as in sickness, if it is administered appropriately, and in just measure in accordance with the individual constitution.” *Hippocrates (460–377 BC)*

- Rules to be followed in getting drunk:
- Not forcing a person to drink
- Not too often
- In good compagny
- With good wine
- In the right time
- Knowing your limits

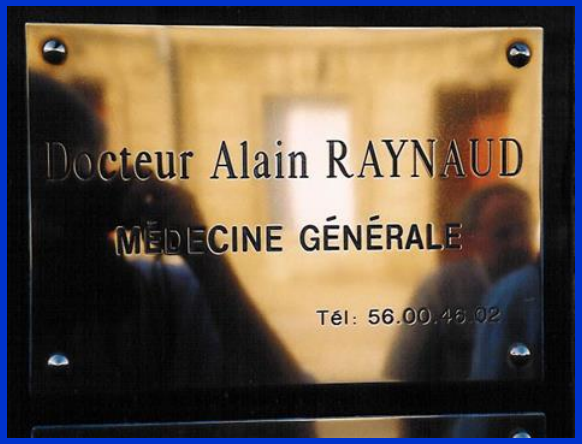




Praise of Drunkenness was published (London 1723) as a translation of *L'Eloge De L'Yvresse (Paris 1714)*

Gerald Asher quote from a talk after dinner at the Wine, Health & Society Symposium 1981 in San Fransisco.

- “Since this is a seminar dedicated to a scientific understanding of wine and medicine, let me confess right away that I do not drink wine for subversive purposes like improving my ratio of high density lipoproteins or helping my digestive system extract more nutrients from food. I drink wine because I like it, it makes me happy, and it encourages me to like my fellow men. I think it is great that wine does wonders for our kidneys, our cardiovascular system, our digestion. But its blessing lies beyond that. “Bronze is the mirror of form” said Aeschylus, the Greek poet, “wine, of the heart.””



"A little bit of what you fancy does you good"