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Alcohol and Your Ticker - Concurrent Workshop Repeated

Saturday, 11 June 2011	Start 11:00am	Duration: 55mins	Picasso
	Start 12:05pm	Duration: 55mins	Picasso

Alcohol & Your Ticker

Graham Gulbransen
FRNZCGP, FAChAM

- GP, Kingsland, Auckland
- Senior Medical Officer, CADS

[Community Alcohol & Drugs Services, Auckland]

Rotorua GPCME 11 June 2011

Drink to your health –

Is alcohol really cardioprotective?

NZ Family Physician, April 2007

http://www.rnzcgp.org.nz/assets/Uploads/NZFP/April2007/Gulbransen_April_07.pdf

Authors: Graham Gulbransen and
Ross McCormick

Medline search:

Alcohol and heart

1979 – 2009: 4409 English articles

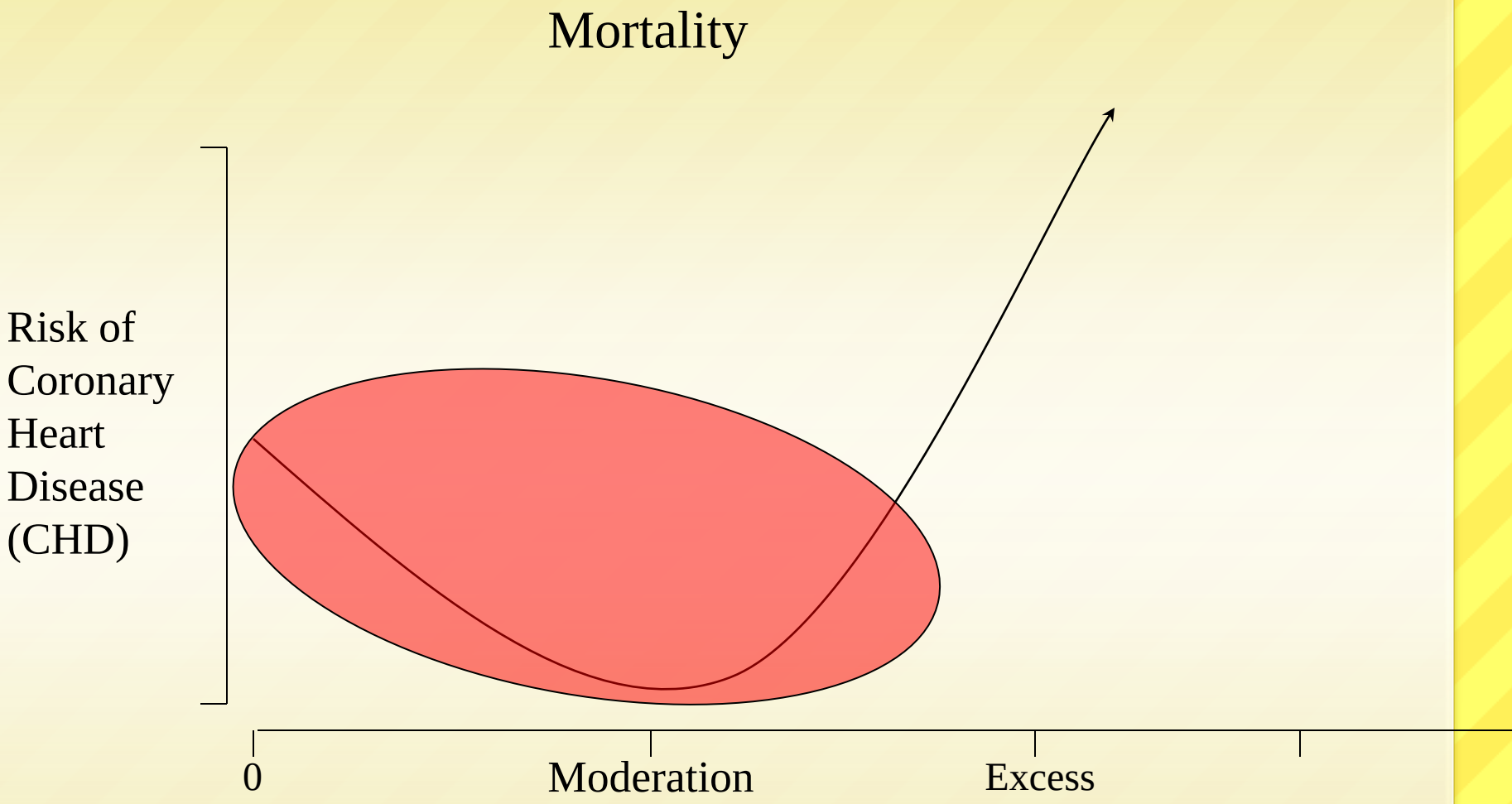
= 12 papers per month

Coronary Heart Disease – CHD

‘Few things are more complicated to study than the relationship between alcohol habits and health.

Alcohol habits are interwoven with a large number of biological and psychosocial background factors, everything from genetics to national legislation.’

Addiction Research and Theory, February 2007, p1-46.



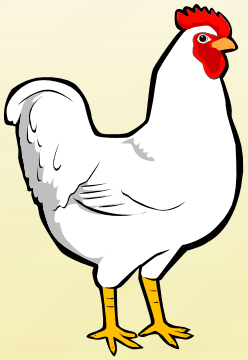
Is this Real?

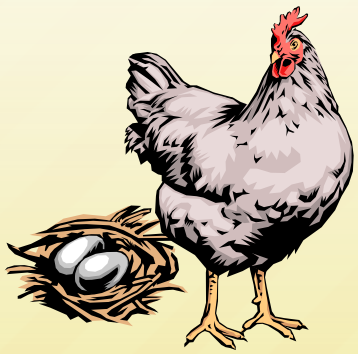
(Modified from Jonathan Powell, MRC Human Nutrition Research, Cambridge)

Raymond Pearl (1879 – 1940)

- American, founder of biometry

- 1926: *Alcohol and Longevity*
- J-shaped curve in alcoholised fowls!
- Followed by human studies





The case for and against….

FOR J-CURVE

- > 100 studies show J-curve
- Biological plausibility

AGAINST J-CURVE

- Confounding
- Misclassification
- Young people
- Patterns of drinking
- Changing patterns
- Study endpoints
- Non-cardiac diseases
- No RCTs

Evidence for cardioprotection

- >100 studies confirm J-shaped curve for CHD, even after adjusting for many risk factors
- High quality studies show less protective effect

A few of the studies

- Alcohol and mortality in British men: Explaining the U-shaped curve, Shaper et al, Lancet, 1988
- Alcohol and coronary heart disease: A meta-analysis, Corrao et al, Addiction, 2000
- Alcohol and mortality: A ten-year Kaiser-Permanente experiment, Klatsky et al, Ann Intern Med, 1981
- Prospective study of alcohol consumption and risk of coronary disease in men, Rimm et al, Lancet, 1991

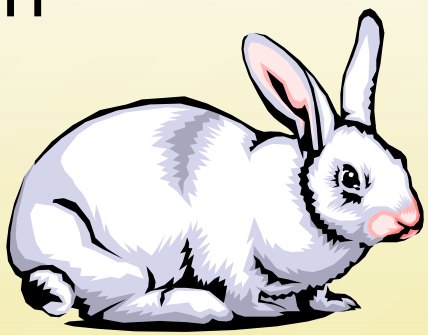
More examples

- Changes in alcohol intake and mortality: a longitudinal population-based study, Gronbaek et al, Epidemiology, 2004
- Alcohol consumption and mortality among women, Fuchs et al, NEJM, 1995
- Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors, Doll et al, BMJ, 1994
- Roles of drinking pattern and type of alcohol consumed in coronary heart disease in men, Mukamal et al, NEJM, 2003

Biological plausibility

Alcohol

- ↑HDL by 8-12% in moderate drinkers
- ↓platelet aggregation
- ↑fibrinolysis
- ↓tissue reperfusion injury
- ↑endothelial NO → vasodilatation

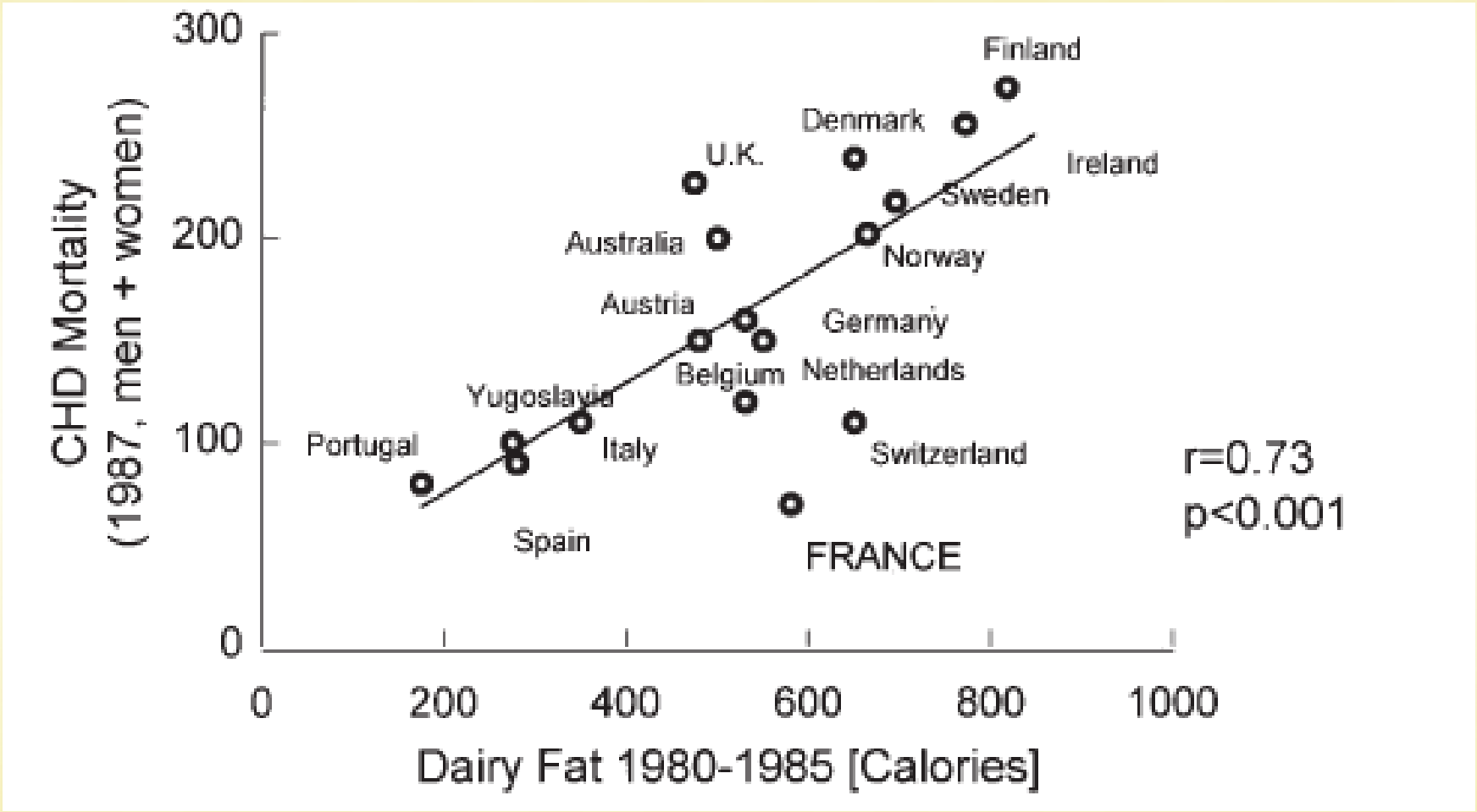


Alcoholic drinks & lipids

- Increased HDL, ↑ sub-fraction HDL3 possibly important
- ↓ of LDL susceptibility to oxidation & aggregation
- Alcohol may affect fibrinogen concentration, platelet aggregation, tissue plasminogen activator, plasminogen-activator inhibitor
- ↑ omega-3 polyunsaturated fatty acids assoc w wine, and less so w beer & spirits, 'a fish-like effect of moderate wine drinking'

Di Castelnuovo 2009

French paradox



- WHO stats show incidence of CVD in France may have been underestimated [Wikipedia]
- 'The French still have a relatively low CHD mortality' [Rod Jackson, May 2011]
- Wine consumption in France is lower than Luxembourg, Germany, Croatia where CVD rates are higher

Brie de Meaux

French diet

- Up to 80% of fat from dairy & vege sources
- Fish at least 3x a week
- Smaller portions eaten slowly
- Less added sugar
- Fewer snacks between meals
- Less deep fried food [???French fries]
- Mediterranean climate / vitamin D

Wikipedia

Alcohol dehydrogenase

The Physicians' Health Study found that moderate drinkers homozygous for the slow-oxidising alcohol dehydrogenase allele had higher HDL levels and reduced risk of myocardial infarction.

alcohol dehydrogenase

Alcohol ---------→ acetaldehyde → acetate

‘the protective effect of alcohol consumption disappears in very high drinkers, because the beneficial increase in high density lipoprotein cholesterol is offset by the increases in BP levels’

[Alcohol drinking and cardiovascular risk in a population with high mean alcohol consumption, M Foester et al, Am J Card, 17 Nov 2008]

Beer vs wine vs spirits

- Any alcohol = effective at ↓ CHD
- Red wine: richest source of bioavailable polyphenols including resveratrol
- Procyanidins [bioflavanoid polyphenols] present up to 1g/L, cardioprotective

‘Different groups of rats were gavaged with red wine, white wine, resveratrol, tyrosol, and hydroxytyrosol…The results of this study suggest that white wine can provide cardioprotection similar to red wine if it is rich in tyrosol and hydroxytyrosol.’

[Does white wine qualify for the French paradox? Comparison of the cardioprotective effects of red and white wines and their constituents, Dudley et al, J Ag & Food Chem, Oct 2008]

Red wine

- Polyphenols resveratrol & quercitin inhibit platelet aggregation & inhibit biosynthesis of thromboxane A_2

- And the perfect delivery vehicle has existed for thousands of years, namely red wine!

Interactions of wine drinking with omega-3 fatty acids in patients with coronary heart disease: A fish-like effect of moderate wine drinking

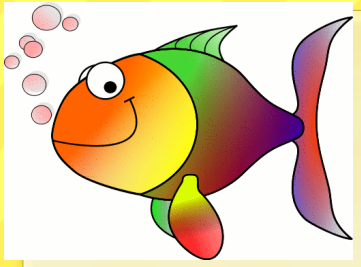
De Lorgeril et al, Am Heart J 2008;155:175-81

CHD patients

- Group 1: Mediterranean diet rich in α-linolenic acid [ALA]
- Group 2: Western-type diet poor in ALA

- Followed for 27 months

- In both groups ‘a progressive increase in marine omega-3 levels with increased alcohol intake’ both EPA and DHA
- This may explain some of the CHD protective effect of wine.



‘This means that the fish-like effect resulting from the combination of an increased ALA intake and moderate wine ethanol drinking may represent a useful alternative to fish consumption in areas with low fish availability or in populations (or patients) that cannot consume fatty fish for any reason.’ [!!!]

The case against the J-curve –
Is there really cardioprotection from consuming moderate amounts of alcohol?

Confounding 1

Moderate people do moderate things

Moderate drinkers

- ate more f & v,
- smoked less than abstainers & heavy drinkers

Confounding 2

Abstainers

had more ‘poor health and serious illness’, tended to be older,

non-White,

less educated,

unemployed

Confounding 3

Unmeasured confounders

such as mental health,

social networks,

socioeconomic status in early life

may be CHD risk factors

Relation of Alcohol Consumption and Coronary Heart Disease in Hypertensive Male Physicians (from the Physicians' Health Study), Britton et al, Am J Cardiol 2009; 104:932-935

From the Physicians' Health Study

Compared to subjects consuming <1 drink per week,

MI risk decreased as drinks per week increased

'adjusted for age, body mass index, smoking, exercise, diabetes, multivitamin use, vegetable intake, breakfast cereal intake, and cholesterol.'

My underlining

Eliminating confounders

- Known confounders: age, smoking, social status, ‘dietary factors’ reduced the maximum protection afforded by alcohol from 19 → 16%

- ‘even in the pessimistic hypothesis that residual (possibly unknown) confounding factors would have a similar strength as the known one in lowering the protection, one can assume that the ‘real’ (maximum) protection against total mortality associated with low consumption of alcohol would be largely higher than 10%.’

Di Castelnuovo 2009

‘regular light drinking may be a marker for good health among middle-aged and older people, not the cause of it.’ Fillmore et al, 2006

Misclassification 1

- Sick quitters counted as abstainers

- Fillmore et al, 2006:

  In the ‘abstainer group’, just 2 of 54 studies separated

  never, rare & former drinkers.

  Combined they lacked statistical power to show if association was linear or J-shaped

Misclassification 2

- Self-reported consumption may be inaccurate
- Board consumption categories may obscure or reduce effects at low levels of drinking

Warning

‘alcohol intake reported in face-to-face interviews is lower than for anonymous surveys’

Young people

- Before middle-age: linear mortality from alcohol
- Younger people more likely than older to die from accidents or suicides, increased by any level of alcohol consumption
- In 2000 in NZ [Jennie Connor et al, NZMJ, April 2005]
- 1037 alcohol related deaths
- 981 deaths prevented
- = net loss of 56 lives, or 12,000 years of life lost as most deaths are in the young.

Changing drinking patterns over time

- Older people tend to drink less
- Difficult to classify

Example:
Alcohol Consumption and Risk of Heart Failure in the Physicians' Health Study I, Djoussé et al, Circulation, 2007; 115: 34-39

‘A total of 21 601 participants of the Physicians’ Health Study I who were free of HF and provided data on alcohol intake at baseline were prospectively followed up from 1982 to 2005.’

Djoussé et al

‘Information about usual alcohol consumption was self-reported on a standard questionnaire. Participants were asked, “How often do you usually consume alcoholic beverages?”

Possible response categories included “rarely/never,” “1 to 3/mo,” “1/wk,” “2 to 4/wk,” “5 to 6/wk,” “daily,” “and “2+/d.”

The response was interpreted as number of alcoholic drinks consumed during the specified period.’

Djoussé et al

Study limitations acknowledged: data did not allow separation of former drinkers from lifetime abstainers

However when they reanalysed data excluding cases of HF occurring in the first 2 years, that 'did not alter our results suggests that we did not have a substantial number of presymptomatic HF cases who reduced or stopped alcohol consumption to be wrongfully classified with lifetime abstainers'

Djoussé et al

Study limitations cont.

‘there is a possibility of under-reporting of alcohol consumption, especially among heavy drinkers, because these data were self-reported’

‘because only 3% of our participants reported consumption of ≥ 2 drinks per day, we did not have enough data to examine the effects of heavy drinking on HF.

Djoussé et al

Study limitations cont.

‘our sample consists of highly educated male physicians who may have different behaviors than the general population. It is thus possible that residual confounding in this cohort by unmeasured factors such as diet may partially explain our findings.’

Djoussé et al

Results of Djoussé et al study

With the stated list of limitations, should we even bother to read the conclusion?

'Although heavy drinking should be discouraged, our data indicate that moderate drinking may lower the risk of HF.'

Pattern of drinking

- Most studies do not separate regular heavy drinking from binging
- Coronary calcification more common in binge drinkers
- Binge drinkers more likely to die from their myocardial infarctions

- Some studies have shown that drinking wine w meals provides maximum benefit

- Others have found ‘the highest protective effect among men who consumed alcohol 3 or more days a week...’

- ‘Moderate regular drinking, possibly during meals, appears as the ideal behavior while binge drinking is to be absolutely avoided.’

Di Castelnuovo 2009

French Paradox

Study endpoints

- Most studies looked at fatal CHD: a very definite endpoint!
- But not necessarily a true reflection on incidence of CHD
- Most new cases of CHD are non-fatal with up to 20% undiagnosed

Non-cardiac diseases

- CHD and ischaemic strokes stand alone with J-curve

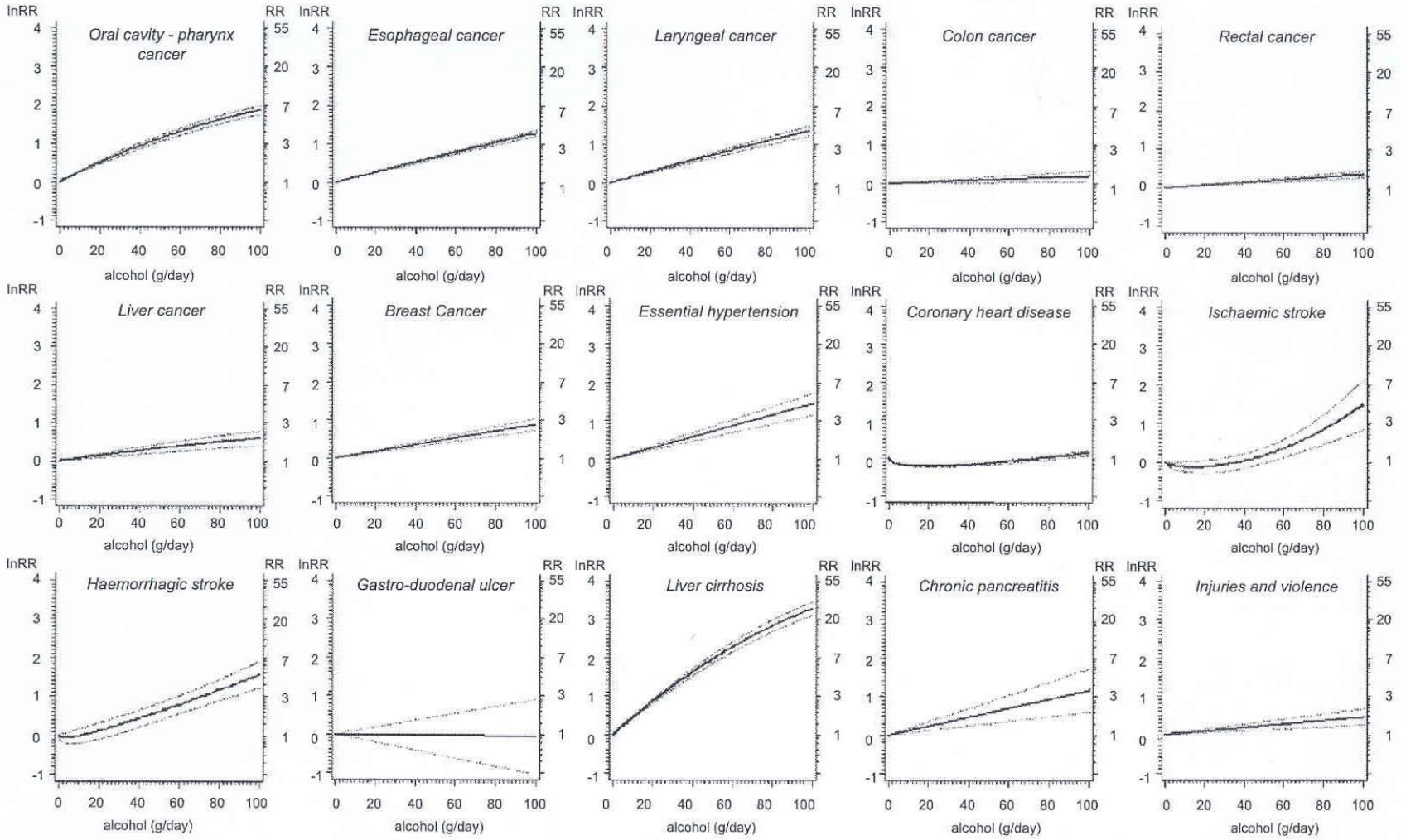


Fig. 1. Relative risk functions and corresponding 95% confidence intervals describing the dose-response relationship between alcohol consumption and the risk of 15 alcohol-related conditions obtained by fitting meta-regression models.

A meta-analysis of alcohol consumption and risk of 15 diseases, Corrao et al, Preventive Medicine, 2004, 38, 613-619

Possible publication bias

Hormone Replacement Treatment Trials

Epidemiological studies: cardioprotection

40 – 60% reduction in Coronary Heart Disease (CHD)

? 'healthy user effect'

RCTs: WHI HRT trial ↑CHD

Confounding & misclassification

in observational studies limit their usefulness

- ‘In our meta-analysis of studies that enrolled only men, the protection offered by wine was found to be surprisingly small (13%) and not significant, in contrast to studies enrolling both sexes (47%)....

- ‘Thus, a posssible sex difference in the protective effect of alcohol might exist and explain apparently controversial results in different epidemiological studies’

Di Castelnuovo 2009

No RCTs

‘it is hard to imagine – at least in Italy or other Mediterranean countries – a controlled trial in which half of a large group of randomized wine-drinking persons would give their informed consent to avoid wine for five years to assess whether the other half of the group continuing to drink would have a reduced chance of developing myocardial infarction[!].’ de Gaetano et al, 2002

RCTs for alcohol consumption pose various problems:

- Selection
- Blinding
- Compliance
- Ethics
- Expence

The magic to make the ‘preventive effect’ of alcohol disappear and reappear, Kari Poikolainen, Addiction, 2008

The effects of magic in medical epidemiology, Fillmore et al, Addiction, 2008

Alcohol consumption and cardiovascular mortality accounting for possible misclassification of intake: 11-year follow-up of the Melbourne Collaborative Cohort Study

[paper title]

Harriss et al, Addiction, vol 102, 2007

- Prospective study of 38,200 volunteers
- Self-reported alcohol intake at the start of the study – no other record of pattern of drinking
- Monitor death certs
- Found that women averaging 2 drinks per day had slightly less CVD than abstainers or heavier drinkers (mainly wine drinkers)
- Is this from increased oestrogen levels induced by alcohol ?

- In men, only the more frequent drinkers [>2 days per week] appeared cardioprotected
- However, this was a self-selected healthy group with few CVD deaths [59% less than average for Victoria]
- 13% of men and 38% of women: life-time abstainers
- ‘no material relationship between alcohol and CV mortality in this study’

Commentary by Poikolainen, Addiction, 2007

Summary – can you decide?

FOR J-CURVE

- > 100 studies show J-curve
- Biological plausibility

KNOWN HARMS

- Trauma
- Dependence
- High doses → many diseases

AGAINST J-CURVE

- Confounding
- Misclassification
- Young people
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- Study endpoints
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- No RCTs

The Harms & Benefits of Moderate Drinking: Findings of an International Symposium [Ann Epidemiol, 17, 2007]

'debate at the symposium regarding the apparent protective effects for alcohol on coronary heart disease and…opinion regarding the matter was highly polarised.'

[letter by Kaye Fillmore et al, Am J Med, 2008]

Conclusion

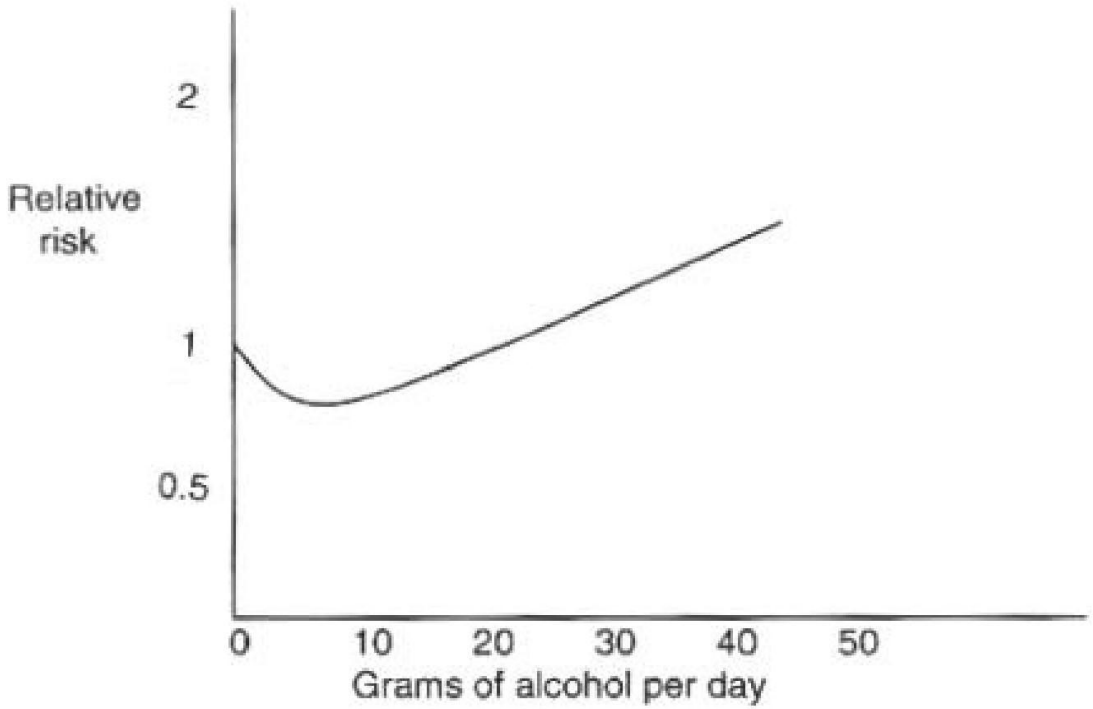


Figure 1. J-shaped curve: alcohol-related relative risk of cardiovascular disease

Bottom line….

- 'If alcohol were a newly discovered drug (instead of a drink dating back to the dawn of human history), we can be sure that no pharmaceutical company would develop it to prevent cardiovascular disease.' Goldberg, 2003
- **Preventive measures such as exercise and smoking cessation, reducing lipids and hypertension have been shown useful without the potential harms of alcohol.**
- The protective effect of wine is comparable to that of eating fish!

NZMJ 25 Sept 2009

If alcohol was a new drug, it would be Class B, high risk to public health:

- Safety ratio = 10, similar to heroin, and greater than LSD or cannabis = 1000+
- Kills 1000+ pa
- Most are injury related deaths
- Half of all physical & sexual assaults committed by intoxicated perpetrators [Doug Sellman]

Alcohol cardio-protection has been talked up.

Doug Sellman, Jennie Connor, Geoffrey Robinson, Rod Jackson

- Alcohol intake increases circulating levels of estrone
- A 50 yo woman consuming 10g alcohol per day has a 0.1% increase in 5-year risk of breast cancer
- Osteoporotic fractures have a J-shaped relation to alcohol consumption: higher bone density w light drinking & more falls w heavier drinking.

Mukamal, JAMA, 26 May 2010

Studies of 320,000 women showed that having 2 or more drinks a day increased the lifetime risk of developing breast cancer from 13 per 100 women to 18 per 100 women.

Folate from food or tablets appears to cancel out this risk, as alcohol blocks the absorption of folic acid.

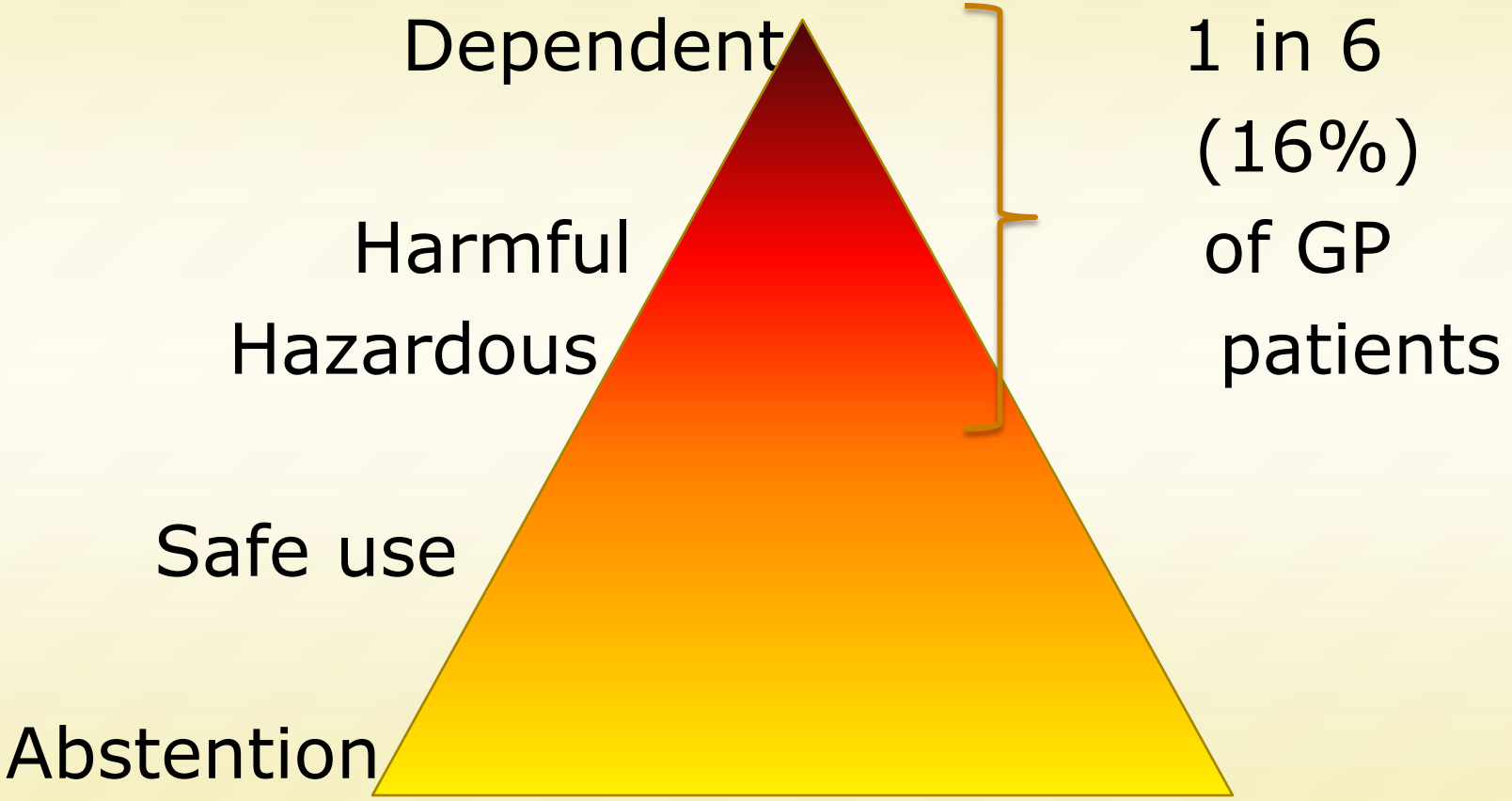
Alcohol and the preventive paradox: serious harms and drinking patterns

Finnish study of alcohol-related hospital admissions & alcohol related deaths.

See next slides:

[Poikolainen et al, Addiction, vol 102, p571-578, 2007]

Spectrum of Alcohol Use



continued

'The paradox arises because although the high-risk group of alcoholics and other heavy drinkers are at highest risk of alcohol problems, most problems still accrue to the lesser-drinking majority of the population simply because the latter group is much larger.'

cf in NZ there are more trisomy 21 babies conceived to women <35 than >35 yo

Standard Drink

- NZ: 10g alcohol [12.7ml ethanol]
- 330ml beer
- 100ml wine
- 30ml spirits

- 1 can RTD (ready to drink, alcopops) = 1.5 SD

- http://alac.org.nz/WhatsInAStandardDrink.aspx

Safe Alcohol Limits

WOMEN	MEN
• No more than 4 drinks per day	• No more than 6 drinks per day
• No more than 14 drinks per week	• No more than 21 drinks per week
• And have some alcohol-free days each week	• And have some alcohol-free days each week

Single screening question

Q: ‘How many drinks do you have in the average 7-day week?’

A: If women say 4 or less => safe drinker

If men say 6 or less => safe drinker

More than 4 or 6 requires more questions to establish amounts & patterns etc

Australian Alcohol Guidelines 2009

- For healthy adults, drinking no more than **2 standard drinks on any day** reduces the lifetime risk of harm from alcohol-related disease or injury
- For healthy adults, drinking no more than **4 standard drinks on a single occasion** (period of drinking where blood alcohol level does not drop to zero) reduces the risk of alcohol-related injury on that occasion

Alcohol Guidelines cont

- Young people under 18 are advised not to drink, especially children under 15
- Pregnant and breast feeding women are advised not to drink.
- Gender differences have gone from these guidelines: although women have greater physiological vulnerability, men tend to be greater risk-takers after drinking alcohol.

Harvard Heart Letter, January 2011

'5 white knights to protect your heart, your arteries, and the rest of you.'

1. Avoid tobacco
2. Be active
3. Aim for healthy weight
4. Enliven your diet
5. Drink alcohol in moderation (if at all) – one to two drinks a day for men, no more than one a day for women.

Brief References

- Drink to your health - is alcohol really cardioprotective? Gulbransen & McCormick, *NZ Family Physician*, April 2007, p122-126 (Contact gg@woosh.co.nz)
- *Addiction Research and Theory*, February 2007, p1-46
- See papers by

Kaye Fillmore, Tanya Chikritzhs, etc.

Waitemata District Health Board
Te Wai Awhina

The 5+ Solution to the Alcohol Crisis

1. Raise alcohol prices.
2. Raise the purchase age.
3. Reduce alcohol accessibility.
4. Reduce marketing and advertising.
5. Increase drink-driving counter-measures.

PLUS: Increase treatment opportunities for heavy drinkers.

Thank you