Drink to your health
– is alcohol really cardioprotective?

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ABSTRACT

A convenient and widely held belief is that a few drinks are good for the heart. This view is based largely on epidemiological studies similar to those that mistakenly showed that menopausal hormone replacement therapy (HRT) was cardioprotective. Because of confounding and misclassification, non-randomised uncontrolled studies can never confirm such beliefs.[1,2]

This article reviews the medical literature on alcohol and coronary heart disease (CHD), looking at evidence for and against cardioprotection.

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Key words

Alcohol, coronary heart disease, cardiovascular disease

Introduction

In 1926 Raymond Pearl[3] first described the J-shaped alcohol-mortality curve: moderately alcoholised fowls had the lowest mortality, followed by those not exposed, with heavily alcoholised fowls having the highest mortality!

In the past 30 years more than 100 epidemiological studies have suggested that moderate alcohol consumption (in humans!) is cardioprotective (Figure 1).[4] In New Zealand we follow the Alcohol Advisory Council of New Zealand guidelines that define safer or moderate drinking as up to 20 grams of alcohol daily for women and 30 grams for men.[5]

However, a 1987 *Lancet* editorial, *'Dying for a Drink'* urged caution, *'The higher mortality among abstainers has not been fully explained but may well be a spurious finding in a group of men who may be at higher risk for other reasons... The U- [J-] shaped curve has been interpreted uncritically... The message we should be delivering unequivocally is that alcohol is bad for health.'*[6]

Others have supported this view,[7,8] and some recent critical literature has found never-drinkers to be at no greater risk than light drinkers.[9,10,11]

Alcohol may *not* be cardioprotective

Critical appraisal of the literature uncovers weaknesses in key areas, casting doubt on the veracity of papers finding alcohol to be cardioprotective:

Confounding

Many large studies have found that moderate people do things moderately, and *'regular light drinking may be a marker for good health among middle-aged and older people, not a cause of it.'*[10]

A telephone survey of 250 496 Americans found that those who had not drunk in the past month were more likely to be older, non-white, have less education and income, more diabetes and hypertension and poorer physical and mental health. In contrast, moderate drinkers had many social and lifestyle characteristics favouring their survival. (Heavy drinkers were less likely to respond to such a study.) *'These results suggest that residual confounding or unmeasured effect modification would bias observational studies in favour of moderate drinkers.'*[12]

In their analysis of The National Health and Nutrition Examination Survey in the USA (N=9533), Fillmore, Kerr and Bostrom[9] found that *'many*

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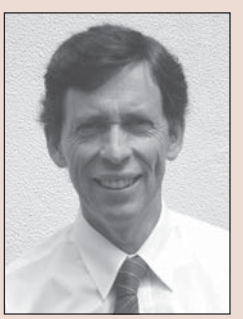

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confounding variables are unevenly distributed across the drinking categories'. For instance, they found that abstainers had more *'poor health and serious illness'* than drinkers, and were more likely to be older, non-white, less well educated and unemployed.

Fuchs et al.[8] analysed the *Atherosclerosis Risk in Communities Study* where 15 792 participants were controlled for physical activity, smoking, blood lipid levels, blood pressure, income, education and nutrition. The more white males drank, the lower their risk of cardiovascular disease (CVD). In black males the opposite was found: the more they drank, the greater the risk. They suggested that unmeasured confounders such as mental health, social networks, and socioeconomic position in early life might be the real causes of CVD risk, rather than alcohol consumption.

Peele and Brodsky verified psychological benefits associated with moderate use of alcohol but found difficulty in attributing causality because of multiple social and cultural variables.[13] Connor notes *'that alcohol consumption is very strongly socially determined and so it is likely that there is substantial residual confounding'.*[14]

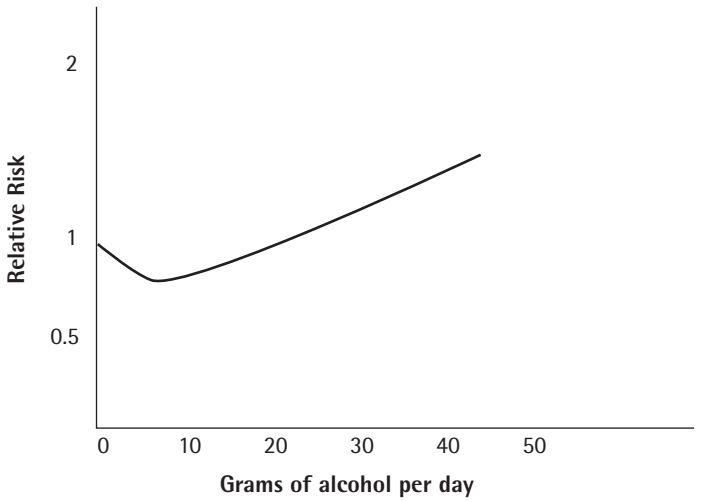
A Danish study with 53 000 respondents found that *'smoking and low intake of fruit and vegetables were common at both extremes of drinking frequency'.*[15]

Ira Goldberg *'wonders if the alcohol-consuming groups also drank more tea, ate more nuts, or consumed more fish – all lifestyle factors associated with reduced cardiovascular risk...'*[16]

Systematic error: Misclassification: Non-drinkers include never, rare and former drinkers

Many studies have counted former drinkers and occasional drinkers as abstainers. Some of these may have stopped drinking because of illness or medication use (sick quitters[7]), contaminating and elevating the 'abstainer' CVD mortality.[14]

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



A recent meta-analysis of 54 studies found just two CVD studies where never, rare and former drinkers were classified separately. Combined they lacked statistical power to show whether the association was linear or J-shaped.[10]

'Self-reported consumption [including lifetime abstinence] may be inaccurate' and broad consumption categories *'could obscure or reduce effects at low levels of drinking'.*[14]

Young people: Linear relationship (not J-shaped curve)

Cardioprotection cannot be demonstrated in young people. Several studies suggest that before middle-age there is a linear dose-response mortality from alcohol.[17–19]

Younger men are more likely to die from accidents or suicides, increased at any level of alcohol consumption.[18]

Older people – changing drinking habits over time

As people age they generally reduce alcohol consumption because of changes in body chemistry, *'health reasons, disability, frailty and/or medication use'.*[10] Some are consistent in their drinking pattern throughout life, and others vary, making them difficult to classify.[14]

Coronary artery calcification

The more you drink, the more likely you are to have coronary calcification, a strong predictor of CHD events.

The Coronary Artery Risk Development in Young Adults (CARDIA) Study followed 3037 participants for 15 years, reaching an age range of 33–45 years. Coronary calcification occurred in 8% of non-drinkers, 9% for 13–80g per week, 13% for 95–176g per week and 19% for more than 176g per week ($p<0.001$ for trend). In black men this was found to be a linear relationship and in other groups *'there was a faint suggestion of J-shaped relation'.* They found calcification to be more common among binge drinkers, and proposed *'dysregulation of inflammatory cytokines associated with the "hangover"'* as a potential explanation.[20]

Pattern of drinking

Binge drinkers appear to be at greatest risk of CVD. In the CARDIA study the greater the degree of bingeing, the higher the risk of coronary calcification.[20] A study of 1641 Finnish men found no difference in CVD rates between those who drank 36g and those drinking 72g or alcohol per session, but heavier (binge) drinkers were much more likely to die if they suffered a myocardial infarction.[21]

Northern Europe and the United States populations tend to drink heavily on weekends. Mediterraneans tend to drink moderate amounts daily.

Most studies do not separate regular heavy drinking from bingeing, limiting the conclusions we can draw.[14,22]

Non–cardiac diseases (and possible publication bias)

CVD stands alone with its J-shaped curve. Corrao et al. are suspicious of this and suggest there may be a publication bias whereby contradicting studies have not been published.[22,23] Their meta-analysis involving 50 000 patients demonstrated strong linear associations with alcohol and cancers of the oral cavity, oesophagus and larynx, hypertension, liver cirrhosis, chronic pancreatitis, and injuries and violence. *'Less strong direct relations were observed for cancers of the colon, rectum, liver and breast.'* In contrast, other research suggests health benefits from moderate alcohol use in diabetes, obesity, cognitive disorders and osteoporosis.[24,25]

No randomised trials

There have been no randomised trials of alcohol consumption with any mortality endpoint.[12]

Large scale randomised trials are unlikely to be done[14] because of the huge cost, (potentially USD50m),[4] and *'it is hard to imagine – at least in Italy or other Mediterranean countries – a controlled trial in which half of a large group of randomised 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[!].'*[26]

Alcohol appears to be cardioprotective

What is the evidence supporting cardioprotection from alcohol?

Biphasic nature of alcohol: the J–shaped curve

Most recent epidemiological studies confirm the J-shaped curve (Figure 1)[17,18,27,28] though some reviews have found a U-shaped curve with similar mortality rates for non-drinkers and heavy drinkers.[18,26] Emberson, Shaper et al. found this even when they adjusted for levels of drinking over time: at five, 13, 17 and 20 years in 3706 men in the British Regional Heart Study.[29]

Even after adjusting for many physical risk factors, *'reported studies have been remarkably consistent in showing that moderate alcohol intake is strongly associated with lower risk of CVD and reduced total mortality.'*[30]

In their meta-analysis, Corrao et al. found that high quality studies show less protective effect from drinking, but still found a J rather than U shaped correlation. Studies in the Mediterranean region tended to report a higher protective effect.[22]

Biological plausibility

Alcohol raises HDL by about eight to 12% in moderate drinkers, accounting for half its possible benefit.[31,32] The Physicians' Health study found that moderate drinkers homozygous for the slow-oxidizing alcohol dehydrogenase[3] allele had higher HDL levels and reduced risk of myocardial infarction.[33]

Overall, case-control, cohort and animal studies do not show any protective advantage for one alcoholic beverage over another

Cardioprotection from alcoholic drinks *'has been attributed to the direct effects of ethanol/polyphenols on increasing high-density lipoproteins, decreasing platelet aggregation, enhancing fibrinolytic activity by the upregulation of tissue plasminogen activator, decreasing fibrinogen and decreasing ischaemia-reperfusion injury'*.[34]

In vitro animal studies have shown that low doses of alcohol release nitric oxide, relaxing endothelium and causing vasodilatation, but higher doses inhibit this relaxation and are associated with hypertension.[35]

Beer vs wine vs spirits

Overall, case-control, cohort and animal studies do not show any protective advantage for one alcoholic beverage over another.[36,37]

Red wine is popularly thought to offer most protection. The presence of skin and seeds during the fermentation gives red wine about 200mg of phenolics per glass compared with 40mg from white wine.[38] There is a wide variation depending on grape variety and method of processing.[39–41] In a study of 13 adults,[42] red wine increased HDL more than white wine as well as decreasing total cholesterol and LDL more effectively.

Beer is as rich as red wine in polyphenols and contains more protein and B vitamins.[43] A German study[44] of 12 young adults found dealcoholised beer, beer and ethanol equally effective at inhibiting thrombogenesis.

In a meta-analysis of 12 cohort and two case-control studies, Cleophas[45] found any alcohol to be equally beneficial in reducing myocardial infarction and ischaemic heart disease deaths. The Health Professionals Follow-up Study[46] found similar cardioprotection from all forms of alcohol regardless of whether it was consumed with food or not.

Alcohol–related years of life lost (NZ)

Connor et al.[19] calculated alcohol-related conditions for the NZ population. Average alcohol consumption and patterns of drinking in NZ were taken from eight published reports. Alcohol–disease relationships were established from NZ and international data. They found that Maori and non-Maori had similar average daily alcohol consumption. However Maori drank more in a typical session and suffered a higher burden of disease.

They estimate that 3.9% (1037) of NZ deaths in 2000 were alcohol-related, mainly from car accidents and other injuries in younger people and men. The benefits of drinking were thought to be mainly from reduced CVD in elderly people, preventing 981 deaths, leaving a net loss of 56 lives. Most deaths involved younger people, resulting in a net loss of 12 000 years of life.

Other harms

(In New Zealand 10g of alcohol is called a standard drink although some other countries use higher or lower definitions.[5,13,37]) One or two standard drinks a day may retard fetal growth, and four or more standard drinks a day runs the risk of fetal alcohol syndrome. The occasional drink during pregnancy may be safe, but this is not certain.[37]

About 20% of NZ men and 10% of women report risky or dangerous drinking.[47] Alcohol dependence is associated with hypertension, increased risk of stroke, pancreatitis, fatty liver, alcoholic hepatitis and eventually cirrhosis and their sequelae.[48] Two standard drinks daily increase the risk of upper aerodigestive cancers.[37]

An analysis of 53 studies involving 58 515 women with breast cancer[49] found a 20% increase in breast cancer for 30g of alcohol consumed per day, but uncertainty on the risk of 10–20g per day. A Danish study of 473 women with breast cancer[50] found that two standard drinks or less per day appeared safe. A higher intake increased breast cancer. McDonald et al.[51] studied 4575 women with breast cancer and found that less than seven standard drinks per week was safe. These studies looked at average consumption and acknowledge difficulty assessing patterns of drinking. Controversy persists about relative risks pre- and post-menopausal, if alcohol is a breast cancer promoter rather than initiator, and if wine confers a greater risk than other drinks.[37,50,51]

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Conclusion

Epidemiological studies cannot eliminate confounding differences between groups,[1] and for reasons outlined earlier a controlled clinical trial is unlikely to be done.[4]

Recent experience with HRT shows that observational data are not always confirmed by clinical trials. In an editorial on this topic, Ira Goldberg stated, *'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'*.[16] Preventive measures such as exercise and smoking cessation, reducing lipids and hypertension have been shown useful without the potential harms of alcohol.[2,16]

Naimi et al. conclude that *'the strength of the association between moderate drinking and CVD outcomes is modest relative to other risk factors.'*[12] And Jackson et al. noted *'the potential for confounding'* accounting *'for much of the protective association in lighter drinkers'*.[1]

Connor et al.[19] concluded that currently there are no health benefits in consuming alcohol before middle age because of injuries that result to younger people.

Of course some groups should not drink: those with a personal or strong family history of alcohol dependence, uncontrolled hypertension, high triglyceride levels, heart failure, liver disease, pancreatitis, pregnancy and the use of medications that interact with alcohol.[4]

Advice to patients? Up to 20g of alcohol daily for women and 30g for men are unlikely to be harmful and might have some health benefits, including cardioprotection. But should you encourage a non-drinker to start drinking moderately? We think the evidence isn't strong enough. In the end it's the patient's choice. Cheers!

Competing interests

Graham Gulbransen declares he has no competing interests.

Ross McCormick is a past member of the Medical Advisory Group of the now defunct Beer Wine and Spirits Council of New Zealand.

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