Evidence paper

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ALCOHOL AND HEART HEALTH

This paper summarises the evidence which forms the basis of the Heart Foundation's position on alcohol and heart health

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SUMMARY

RECOMMENDATIONS

FOR THE GENERAL POPULATION

Drinking alcohol comes with risks to health, and not drinking alcohol is a healthy choice. The most damaging pattern of drinking is frequent heavy drinking episodes. The following recommendations are consistent with current guidelines from the Health Promotion Agency (formerly ALAC).

Reduce your long-term health risks by drinking no more than:

- 2 standard drinks a day for women and no more than 10 standard drinks a week
- 3 standard drinks a day for men and no more than 15 standard drinks a week
- AND at least two alcohol-free days every week.

Reduce your risk on a single drinking occasion by drinking no more than:

- 4 standard drinks for women
- 5 standard drinks for men

Advice for pregnant women or those planning to get pregnant: No alcohol. There is no known safe level of alcohol use at any stage of pregnancy.

Advice for parents of children and young people under 18 years: Not drinking alcohol is the safest option, and any drinking should be supervised. Under 15 years alcohol should be avoided completely. Delaying the onset of drinking alcohol as long as possible is the healthiest option.

FOR PEOPLE AT HIGH RISK

Conditions for which abstinence is recommended:

- Pregnancy, planning pregnancy, or breastfeeding
- Chronic active liver disease
- Uncontrolled hypertension
- Congestive heart failure
- Previous haemorrhagic stroke
- Depression
- Medications that interact with alcohol

Apart from these, the advice for the general population is appropriate.

Advice for drinkers is to reduce consumption to within the low risk drinking guidelines or abstain, in order to reduce risks to the health and welfare of themselves and others. Screening of consumption should be undertaken as routine. Advice and assistance with reducing consumption should be offered.

Advice for non-drinkers or infrequent drinkers is that their consumption is low risk and that they should not start drinking more for health reasons despite "common wisdom". There is no evidence that increased alcohol consumption will improve heart health for any individual.

Drinkers should be made aware that alcohol contributes excess energy (calories) to their diet and may contribute to unwanted weight gain.

Evidence-based guidelines for reduction of cardiovascular risk should be followed.

KEY POINTS

Review of the recent scientific literature suggests that although some cardio-protective effects of alcohol are possible, there is no uniform benefit even at low levels of consumption.

The "J-shaped" curve that describes the observed association of average alcohol consumption with ischaemic heart disease (IHD) in much research is contested on methodological grounds, and any benefit varies in subgroups of the population in a complex manner. There is uncertainty about which specific groups might benefit, and at what dose and pattern of drinking.

Heavy drinking episodes increase IHD risk even in non-heavy drinkers.

Alcohol is an unsuitable therapeutic agent as it is addictive, intoxicating, toxic and carcinogenic. There is no safe drinking threshold for many harmful impacts of alcohol, and therefore no potential "window of benefit" where benefits can accrue without risk of harm.

The New Zealand drinking pattern and level of harm from alcohol is such that any promotion of alcohol as therapeutic would be irresponsible. There are evidence-based guidelines and safe effective treatments for reduction in cardiovascular risk.

EVIDENCE

INTRODUCTION

Alcohol consumption contributes to a wide range of social and physical health harms. In New Zealand it is estimated to have been responsible for 802 deaths (5.4% of all deaths) and 13,769 years of life lost (YLLs) under 80 years of age in 2007. Much of the harm (43%) was due to injury (unintentional, violence and self-harm) but alcohol also contributed to a range of chronic non-communicable diseases, including cancers, liver disease and cardiovascular diseases.[1]

There is a common belief that drinking also brings health benefits, particularly for the heart (cardio-protection). A beneficial association with ischaemic heart disease, ischaemic stroke, and possibly diabetes has been observed when average alcohol consumption is not heavy,[2] but serious concerns have been raised in the scientific literature about reliability of the evidence for this.

AIMS AND OBJECTIVES

The aim of this paper is to assess the evidence linking alcohol and cardiovascular disease, and place it in the wider context of alcohol use, as the basis for advice on low risk alcohol consumption.

LITERATURE OVERVIEW

ALCOHOL AND ISCHAEMIC HEART DISEASE

There is a large body of epidemiological literature describing associations between alcohol consumption and ischaemic heart disease, and it is one of the most investigated dietary risk factors.[3] There have been several meta-analyses, including two major publications in 2011-12.[4] [5] All of the component studies of the meta-analyses have had case-control and cohort designs, and there is currently no prospect of long term randomised trials of this question, for ethical and logistical reasons.

Most, but not all, epidemiological studies suggest a protective association of low to moderate average alcohol consumption with ischaemic heart disease. A pattern of risk described as a "J shaped curve" is usually seen, where low volume drinkers have a reduced risk of IHD compared with non-drinkers, and the risk remains below baseline up to 60-70 grams of alcohol per day (6-7 standard drinks), after which the effect is detrimental.[6-8] However, there is considerable heterogeneity between studies and several major challenges to causal inference. That is, the reduction in risk of IHD that is observed may not be due to the level of alcohol consumption but to other factors.

The two recently published high quality meta-analyses both found protective associations between alcohol consumption and IHD using differing methods, but came to different overall conclusions.

The Ronskley et al study was essentially concerned with any alcohol consumption (active drinkers) vs none (current non-drinkers), and included only prospective cohort studies. It concluded that the findings were very consistent, with overall reductions in cardiovascular mortality, IHD mortality, and IHD morbidity of about 25%, and a maximum benefit at a dose of 1-2 drinks per day.[5] The authors felt confident that no further studies were now needed and that the focus should move to the integration of the findings into clinical and public health practice. This included promotion of alcohol consumption in selected patients as a therapy, and the adoption of public health messages that promote drinking.

In the Roercke study,[4] both case-control and cohort designs were included, and stratified continuous meta-analyses were conducted for IHD morbidity, IHD mortality and men and women separately. Differences were seen in the risk curves by sex and by endpoint. Categorical meta-analysis was undertaken for low levels of drinking because of the overestimation of precision by the continuous models. Evidence of a cardioprotective association in both sexes was borderline (not clearly statistically significant) for 1-3 drinks a day compared with lifetime abstainers. The authors reported substantial heterogeneity across component studies that remained unexplained, and wide confidence intervals especially at low levels of consumption. Their conclusion was that a benefit cannot be assumed for all drinkers even at low levels of average intake and that more evidence is required before advice can be formulated about safe drinking levels.

BIOLOGICAL PLAUSIBILITY

Short-term experimental evidence of alcohol's effects on surrogate biomarkers, such as increasing HDL cholesterol, reducing fibrinogen level and inhibiting platelet activation, supports the biological plausibility of a protective association.[9 10] Roercke et al[4] consider this to be stronger evidence of a preventive effect than the epidemiological studies of drinking and CVD events, due to fewer methodological limitations.

A systematic review and meta-analysis of intervention studies of the effects of alcohol consumption on 21 biological markers associated with the risk of coronary heart disease was published in the British Medical Journal in 2011, as a companion paper to the first meta-analysis described above.[11]

The findings of this meta-analysis were consistent with the previous major review conducted more than 10 years earlier by Rimm et al[9] with respect to alcohol increasing HDL cholesterol, and apolipoprotein A1, but also found

that alcohol significantly decreased fibrinogen concentrations. Triglycerides were unchanged by alcohol apart from in two studies of heavy alcohol consumption, which demonstrated an increase in triglycerides.

The new meta-analysis also examined several other biomarkers that had not been previously reviewed. Of these adiponectin, an abundant adipocyte hormone that has been associated with lower risk of diabetes and IHD, was found to be significantly increased by alcohol. Markers unaffected by alcohol included LDL cholesterol, Lp(a) lipoprotein, C reactive protein, Interleukin 6, TNF-alpha, plasminogen activator inhibitor 1, and tissue plasminogen activator. The findings were similar for alcohol consumed as beer, wine or spirits.

CRITIQUE OF THE EPIDEMIOLOGICAL STUDIES

A number of substantial limitations of the observational studies of alcohol and IHD have been widely discussed (eg.[12-15]) and have been the subject of additional research. The first consideration is that the meta-analyses of case-control and cohort studies, no matter how well conducted, cannot overcome biases in the component studies, and could simply produce biased effect estimates measured with more precision. There are a number of sources of bias that are likely to affect all studies to some degree. In brief these are:

- Misclassification of exposure measurement: Some misclassification may result from underestimation of consumption by self–report. As well as this, consumption changes over time and is seldom re-measured adequately.[16-18]
- The definition and verification of the comparison (non-drinker group): Former drinkers have been demonstrated to have higher cardiovascular risk than lifetime abstainers, and therefore if they are included in the comparison group they will bias the risk estimates.[14] [19-21] While lifetime abstainers are the most appropriate comparison group, self-report of lifetime abstention has also been demonstrated to be unreliable.[22]
- Over adjustment for intermediate CVD risk factors.[2 4]
- Residual confounding: Studies control for a variety of potential confounding variables, ranging from age alone, to an array of CVD risk factors, but it is likely that substantial confounding remains.[2 12 15] [23] This is supported by evidence from Naimi et al who conducted a survey of 200,000 US adults and found moderate drinkers to be healthier than abstainers on 27 risk factors for heart disease.[24]

Scepticism about the adequacy of the evidence to establish a causal association between alcohol and reduced cardiovascular disease risk[25] has recently been dismissed by Ronskley et al as "an extreme methodological

position"[26] in an attempt to marginalise the critics. However, there is a clear analogy between this body of evidence and the observational studies of the effect of HRT and IHD. The accepted findings from reputable cohort and case-control studies that HRT conferred a benefit (even larger than that associated with non-heavy drinking) were overturned by the publication of randomised trials showing HRT to have no effect on IHD and to increase the risk of stroke.[15 27] Importantly one of the lessons from the HRT story was "do not be seduced by mechanism" as there was a vast literature on the favourable effects of HRT on lipids and other CVD biomarkers.[28]

Even when IHD epidemiology is accepted at face value it seems likely that there is little overall benefit from alcohol, and it accrues in very specific groups in population. Roerecke and Rehm (2012) sound a number of warnings with regard to protective effects:

1. Any cardioprotective effects vary by sex and by end-point (mortality vs morbidity);
2. The levels of drinking associated with the largest protective effect for men (33-69 g/day) are associated with detrimental effects from disease and injury;
3. Low average volume drinking (1-2 drinks per day) may not be beneficial for all groups. The attenuation of the effect with age found by Rehm et al means the expected large benefit for older people due to their high incidence of IHD may not eventuate;
4. The unexplained heterogeneity may be due to the impact of heavy drinking occasions, which have been shown to increase risk even in drinkers with low average consumption.

Overall, a cardio-protective effect cannot be uniformly assumed at any specific level of consumption.[4]

WIDER PUBLIC HEALTH ISSUES

If the evidence was conclusive that alcohol consumption reduced the risk of IHD, alcohol would still not be a suitable therapeutic agent. The intoxicating and addictive properties of alcohol mean that some individuals are at risk of progression to problem drinking, and individual susceptibility to this is known to vary. The toxic and carcinogenic properties of alcohol result in a range of harms even when average consumption is not heavy, for example, fetal alcohol spectrum disorder, haemorrhagic stroke, large bowel cancer, and female breast cancer. Alcoholic drinks are also high in kilojoules and low in nutritional value. The alcohol itself contains 29kJ/g or 290 kJ per standard drink,[29] but it is also commonly added to sweet mixers. When drinking is additional to normal dietary intake, drinkers are liable to gain weight. The World Health Organization concluded in 2007 that "from both the public

health and clinical viewpoints, there is no merit in promoting alcohol consumption as a preventive strategy."[23]

NEW ZEALAND CONTEXT

Alcohol use is a major public health concern in New Zealand, with impacts on health and welfare of drinkers,[1 30] and of others.[31-33] The level of harm results from both the average level of consumption and the predominant pattern of intermittent heavy drinking occasions.[34 35]

The impacts of alcohol use fall disproportionately on Māori and add to overall health disparities. The age-standardised alcohol-attributable death rate for Māori overall in 2007 was 2.5 times the rate for non-Māori.[1]

CONCLUSION

Review of the recent scientific literature suggests that although some cardioprotective effects of alcohol are possible, there is no uniform benefit even at low average consumption. There is uncertainty about which specific groups might benefit and at what dose and pattern of drinking. Heavy drinking episodes increase IHD risk even in non-heavy drinkers. Alcohol is an unsuitable therapeutic agent as it is addictive, intoxicating, toxic and carcinogenic. As there is no safe drinking threshold for many harms, there is no potential "window of benefit". The New Zealand drinking pattern and level of harm from alcohol is such that any promotion of alcohol would be irresponsible. There are evidence-based guidelines and safe effective treatments for reduction in cardiovascular risk.

RECOMMENDATIONS

FOR THE GENERAL POPULATION

Drinking alcohol comes with risks to health, and not drinking alcohol is a healthy choice. The most damaging pattern of drinking is frequent heavy drinking episodes. These recommendations are consistent with current guidelines from the Health Promotion Agency (formerly ALAC).

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Advice for parents of children and young people under 18 years: Not drinking alcohol is the safest option, and any drinking should be supervised. Under 15 years alcohol should be avoided completely. Delaying the onset of drinking alcohol as long as possible is the healthiest option.

FOR THOSE WITH OR AT HIGH RISK OF HEART DISEASE

Conditions for which abstinence is recommended:

- Pregnancy, planning pregnancy, or breastfeeding
- Chronic active liver disease
- Uncontrolled hypertension
- Congestive heart failure
- Previous haemorrhagic stroke
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- Medications that interact with alcohol

Apart from these the advice for the general population is appropriate.

FOR HEALTH PROFESSIONALS

Advice for drinkers is to reduce consumption to within the low risk drinking guidelines or abstain, to reduce risks to the health and welfare of themselves and others. Screening of consumption should be undertaken as routine. Advice and assistance with reducing consumption should be offered.

Advice for non-drinkers or infrequent drinkers is that their consumption is low risk and that they should not start drinking more for health reasons despite "common wisdom". There is no evidence that increased alcohol consumption will improve heart health for any individual.

Drinkers should be made aware that alcohol contributes excess energy (calories) to their diet and may contribute to unwanted weight gain.

Evidence-based guidelines for reduction of cardiovascular risk should be followed.

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APPENDICES

KEY EVIDENCE TABLES

LEVEL OF EVIDENCE

The New Zealand Guidelines Group evidence grading system has been used to give guidance on the level of evidence for key papers included in this paper.

Level of evidence 1++: High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Level of evidence 1+: Well-conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Level of evidence 2++: High quality systematic reviews of case control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

Level of evidence 2+: Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

Level of evidence 1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

Level of evidence 2-: Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

Level of evidence 3: Non-analytic studies eg. case reports, case series

Level of evidence 4: Expert opinion

Level of evidence: 2-	**Roerecke M, Rehm J. The cardioprotective association of average alcohol consumption and ischaemic heart disease: a systematic review and meta-analysis. Addiction 2012;107(7):1246-60.**
Study type	*Systematic review and meta-analysis of observational (cohort, case control) studies*
Population	Published studies of adults, most from US, UK or Japan
Intervention	Average alcohol consumption
Comparator	Lifetime abstention from alcohol
Outcomes	The analyses used 38 627 IHD events (mortality or morbidity) among 957 684 participants. Different risk curves were found by sex and end-point. Although some form of a cardioprotective association was confirmed in all strata, substantial heterogeneity across studies remained unexplained and confidence intervals were relatively wide, in particular for average consumption of one to two drinks/day.
Limitations	Misclassification of exposure; residual confounding; sparse data for heavy average drinking
Reviewer's conclusion	A cardioprotective association between alcohol use and ischaemic heart disease cannot be assumed for all drinkers, even at low levels of intake.

Level of evidence: 2-	**Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ 2011;342:d671.**
Study type	Systematic review and meta-analysis of prospective cohort studies
Population	
Intervention	Alcohol consumption
Comparator	No alcohol consumption

Outcomes	Overall mortality from CVD, incidence and mortality from coronary heart disease; incidence and mortality from stroke.
	The pooled adjusted relative risks for alcohol drinkers relative to non-drinkers in random effects models for the outcomes of interest were
	    0.75 (95% confidence interval 0.70 to 0.80) for cardiovascular disease mortality (21 studies),
	    0.71 (0.66 to 0.77) for incident coronary heart disease (29 studies),
	    0.75 (0.68 to 0.81) for coronary heart disease mortality (31 studies),
	    0.98 (0.91 to 1.06) for incident stroke (17 studies), and
	    1.06 (0.91 to 1.23) for stroke mortality (10 studies).
	Dose-response analysis revealed that the lowest risk of coronary heart disease mortality occurred with 1–2 drinks a day, but for stroke mortality it occurred with ≤1 drink per day. Secondary analysis of mortality from all causes

	showed lower risk for drinkers compared with non-drinkers (relative risk 0.87 (0.83 to 0.92)).
Limitations	Misclassification of exposure; definition of non-drinker comparison group (inclusion of former drinkers); residual confounding; lack of stratification by sex and by stroke subtype. Publication bias is unlikely
Reviewer's conclusion	This meta-analysis draws similar conclusions to previous reviews, but the risk reduction for coronary heart disease associated with light to moderate drinking is also present for heavier drinking. The association with stroke (combined types) is close to the null. Major sources of bias still remain.

Level of evidence: 1-	**Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA. Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies. BMJ 2011;342:d636.**
Study type	Systematic review and meta-analysis of intervention studies
Population	Adults without known cardiovascular disease
Intervention	Alcohol (beer, wine, spirits) consumption for at least a week
Comparator	No alcohol consumption
Outcomes	Biomarkers associated with cardiovascular disease. Of 63 eligible studies, 44 on 13 biomarkers were meta-analysed in fixed or random effects models. Analyses were stratified by type of beverage (wine, beer, spirits). Alcohol significantly increased levels of high density lipoprotein cholesterol (pooled mean difference 0.094 mmol/L, 95% confidence interval 0.064 to 0.123), apolipoprotein A1 (0.101 g/L, 0.073 to 0.129), and adiponectin (0.56 mg/L, 0.39 to 0.72). Alcohol showed a dose-response relation with high density lipoprotein cholesterol (test for trend P=0.013). Alcohol decreased fibrinogen levels (−0.20 g/L, −0.29 to −0.11) but did not affect triglyceride levels. Results were similar for crossover and before and after studies, and across beverage types.
Limitations	Unblinded intervention studies, with variation in design, dosing and duration
Reviewer's conclusion	Consumption of up to 15g alcohol a day for women and 30 g a day for men significantly increased circulating levels of HDL cholesterol, apolipoprotein A1, and adiponectin and significantly decreased fibrinogen levels, all changes reported to be cardioprotective.