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Alcohol & Heart Health



Summary of Evidence

This Summary of Evidence presents the contemporary evidence relating to alcohol and cardiovascular health and underpins the Heart Foundation's Position Statement: *Alcohol and Heart Health*. The Heart Foundation sought contemporary evidence regarding secondary prevention and consumption of alcohol to provide specific recommendations for those with cardiovascular risk factors, and those at high risk of cardiovascular disease and related chronic conditions. This review includes evidence from the National Health and Medical Research Council (NHMRC)'s *Australian Guidelines to Reduce Health Risks from Drinking Alcohol*, published in 2020.



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Summary

The relationship between alcohol and cardiovascular disease is complex. However, the contemporary evidence portrays a clear picture of the harms of alcohol consumption. Alcohol is not a necessary or recommended part of a heart healthy eating pattern.

The mechanisms by which alcohol affects cardiovascular disease risk have been extensively researched but are varied and not completely understood. These mechanisms include, but are not limited to, an effect on heart rhythm, blood pressure, lipid regulation, insulin resistance, inflammation, endothelial function, platelet aggregation and coagulation.

Previous evidence has shown a small positive effect of low to moderate consumption of alcohol on cardiovascular outcomes (often referred to as the cardioprotective effect), including coronary heart disease, stroke, heart failure, hypertension, type 2 diabetes, and acute cardiovascular events. This research influenced previous recommendations. More recently, Mendelian randomisation studies, a robust analytical method used to examine the causal effects of modifiable risk factors on disease, have called into question this positive effect, and there is now less confidence in its existence. Previous research findings of the so called cardioprotective effect may have been biased by confounders or reverse causality bias.

In alcohol research, alcohol is expressed in grams, and the Heart Foundation recommendations are expressed as standard drinks. An Australian standard drink contains 10g of alcohol (12.5ml of pure alcohol), regardless of container size or alcohol type (for example, beer, wine or spirits).

Background

Alcohol is a drug, a depressant and a carcinogen and is the intoxicating constituent of wine, beer, and spirits. When consumed, it can affect the way a person feels and behaves.¹ Alcohol consumption in Australia is high compared to other countries in the world.²

Studies of the relationship between alcohol and heart health are mainly observational in nature, with a limited number of randomised controlled trials. Observational studies are a type of research design in which the exposure is not controlled by the researchers. These studies are common in alcohol research as they are not constrained by ethical considerations. Observational studies can only show significant associations and cannot identify causes and effects. These types of studies may be limited by confounding factors and biases, and often reverse causality bias cannot be excluded when interpreting the study results.

Confounders refer to variables that can affect the cause and supposed effect identified in research studies (for example, a study investigating an association between cardiovascular disease and obesity should ideally control for confounders that might affect the results, such as age and diet). Reverse causality bias occurs when a cause and effect relationship is reversed; occurring when a risk factor is also a known effect of the disease (for example, physical inactivity is a risk factor for cardiovascular disease, but people with cardiovascular disease may also be less physically active). Randomised controlled trials are a more robust type of study design that can more clearly delineate the impact of an intervention on an outcome (that is, they can more clearly identify a true cause and effect relationship). However, in some fields of study, such as alcohol and health outcomes, it is unethical to conduct this type of study.

Evidence for the association between alcohol and health outcomes is characterised by a U- or J-shaped curve rather than a linear dose-response relationship. This U- or J-shaped curve indicates a small positive relationship, or a cardioprotective effect, of small amounts of alcohol and cardiovascular outcomes, compared with not drinking at all and with more heavy drinking. There is the potential that this cardioprotective effect is due to reverse causation. This could occur due to the classification of both 'current abstainers' and 'never drinkers' into the reference group (that is, no alcohol consumption). These two groups that share one characteristic – not currently drinking – are likely to be different with respect to other health characteristics.

For current abstainers, there is the possibility of having previously consumed alcohol at risky levels or having other health conditions that lead them to abstain, and they may have a higher risk of death or disability compared to individuals who have never consumed alcohol. This summary of evidence explains some of the limitations of the perceived cardioprotective effect, and its implications for making recommendations, later in the document.

It is important to note that even if there is a cardioprotective effect of alcohol, it is not clear for whom this effect exists (that is, what age groups) and at what level of consumption it occurs. The link between alcohol and other serious health conditions, including several types of cancer, is strong enough that individuals should not drink alcohol to protect themselves from cardiovascular disease.³

Given the relationship between alcohol and heart health and the development and advances in the research, and our understanding of the potential harms of alcohol, the Heart Foundation sought to update our recommendations for key groups. This Summary of Evidence summarises the available evidence and informs the Heart Foundation's position on alcohol and heart health.

Methodology

The Heart Foundation reviewed the NHMRC's Australian Guidelines to *Reduce Health Risks from Drinking Alcohol*, published in 2020. Based on the methods and quality of the review, including use of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework, the Heart Foundation has adopted the recommendations for healthy men and women, children and young people, and pregnant and breastfeeding women.

The evidence compiled by the NHMRC relates to reducing alcohol-related harm but it does not rule out all risk from drinking alcohol.⁴ Alcohol affects people differently and due to this variability, there is no alcohol consumption limit that is safe for any group of people.

The Heart Foundation sought contemporary evidence regarding secondary prevention and consumption of alcohol to provide specific recommendations for people with, or at high risk, of cardiovascular disease and related chronic conditions, and people with cardiovascular disease risk factors. This involved a review of the evidence utilising PubMed, including meta-analyses, systematic reviews and Cochrane Reviews using keywords 'alcohol' 'ethanol' 'secondary prevention' 'heart disease' 'cardiovascular disease' and 'patients'. This was then supplemented with hand searching reference lists and key reports to identify reviews, significant trials and meta-analyses published from 2001 until 2017 (the cut-off search date of the NHMRC review).



Summary of Evidence

NHMRC Guidelines

Alcohol consumption and cardiovascular disease risk factors and outcomes

Short term health risks

There is a consistent U-shaped association between alcohol consumption and acute cardiovascular events. This systematic review of case-control and case-crossover studies (n=17,966) found that there may be a lower risk of acute events for low levels of alcohol consumption compared to no alcohol consumption, but a higher risk for higher levels of alcohol consumption.⁵

Long term health risks

The systematic review and meta-analysis of 16 prospective cohorts, (men n=33,904 and women n=193,752) reported a small decreased risk of hypertension for alcohol consumption of < 10g/day in women. Also for women, no difference was reported at 11-20g/day while an increased risk of hypertension was seen at 31-40g/day; risk was not reported for >40g a day. In men, similar results were seen, with an increased risk of hypertension seen at 31-40g/day and >50g/day. This indicates that people who drink more heavily (both men and women) are at higher risk of developing hypertension.⁶

Another review investigated the relationship between type 2 diabetes and alcohol consumption.⁷ It included one nested case-control study and 27 cohort studies (n=1,902,605). The review reported a dose-response decreased risk of type 2 diabetes up to 63g/day, compared to current and lifetime abstainers, with considerable heterogeneity. Above this level of consumption, the risk of developing type 2 diabetes increases.

Evidence from 18 prospective cohort studies (n=7756) showed a J- shaped association between chronic alcohol consumption and coronary heart disease when compared to abstainers. This association indicates that low levels of alcohol consumption offer a small decreased risk, however there was no difference in risk of coronary heart disease at higher consumption levels.⁸

A meta-analysis of eight prospective cohort studies (n=6,211) indicated that at low levels of alcohol consumption there is a small decreased risk of heart failure (incidence, hospitalisation and/or mortality) however there is no difference with higher levels of consumption.⁹

Seven prospective cohort studies (n=11,419) reported by Larsson et al (2014) found a dose-response relationship between chronic alcohol consumption and atrial fibrillation, when compared to lifetime abstainers.¹⁰ For every 12g per day of ethanol consumption, the relative risk increased by 1.08 (95% CI: 1.06 to 1.10). This indicates that the risk of atrial fibrillation increases with the amount of alcohol consumed.

Evidence from 25 prospective cohort studies (n=19,302) and reported a J- shaped curve between chronic alcohol consumption and ischaemic stroke when compared with the reference group.¹¹ This J- shaped curve indicates a small decrease in risk of ischaemic stroke with low levels of alcohol consumption. Evidence from 11 prospective cohort studies (n=2,359) reported an association between chronic alcohol consumption and intracerebral haemorrhage. There was no reported difference in risk for four or less drinks per day but an increased risk when drinking more than four drinks per day compared to the reference group¹¹.

One systematic review with 11 prospective cohorts (n=1,164) reported no difference in risk of subarachnoid haemorrhage with four or less drinks a day but an increased risk when drinking more than this.

In summary, the evidence for an association between alcohol consumption and heart health consistently demonstrates a U- or J- shaped curve, although confounding is likely to be a key factor. A dose-response relationship with alcohol is evident in atrial fibrillation. Higher intake/heavier drinking confers consistently poorer outcomes; therefore a maximum is recommended as per the NHMRC guidelines. However, there is not enough robust evidence to define a 'healthy' or protective level of alcohol consumption, beyond the recommendation to drink less than the maximum.

Heart Foundation review: Alcohol and secondary prevention

Data indicating a lower risk of cardiovascular events with low to moderate alcohol consumption in healthy people (the J-shaped curve) has been consistent (albeit of low quality), whereas the impact of alcohol consumption among people with established cardiovascular disease is less clear. When compared to primary prevention, there are far fewer reviews and original research studies within those reviews, reflecting the need for more research on this topic.

A meta-analysis of eight prospective studies investigated alcohol consumption and mortality in people with pre-existing cardiovascular disease. In this pooled analysis, among people who had cardiovascular disease, a J-shaped curve was found, with low to moderate alcohol consumption of 5 to 25g/day significantly associated with a lower incidence of cardiovascular and all-cause mortality.¹² The major limitation of this meta-analysis was that only a small number of studies were included. It is important to note that another limitation was the inability of the analyses to separate former drinkers from lifetime abstainers in all cases due to the lack of information from original studies. This phenomenon of classifying former drinkers from lifetime abstainers together in alcohol studies is problematic in studies and limits the quality of the evidence and our understanding of the causal pathways of alcohol consumption.

Another meta-analysis examined alcohol consumption and vascular and total mortality in patients with type 2 diabetes, hypertension or history of cardiovascular disease.¹³ For people with hypertension, moderate drinking is associated with a lower risk of vascular and all-cause mortality.

In the analysis examining people at high cardiovascular disease risk, moderate alcohol consumption (5-10g/day) was significantly associated with a lower incidence of all-cause mortality.

In 2011, the American Heart Association and American College of Cardiology Foundation developed a guideline on secondary prevention and risk reduction therapy for people with coronary and other atherosclerotic vascular disease. To maintain blood pressure <140/90mmHg, the guideline recommends moderate alcohol consumption based upon strong, Level B evidence.¹⁴

A systematic review and analysis examined the effect of various lifestyle and dietary changes on all-cause mortality in people with coronary heart disease.¹⁵ Five cohort studies were included in the alcohol consumption analysis, and four studies demonstrated a statistically significant effect of a 15-25% reduction in all-cause mortality for moderate drinking.

Another study investigated alcohol consumption in people with peripheral arterial disease revealing that moderate alcohol consumption was associated with a lower risk of mortality, when adjusted for confounders.¹⁶



Another study investigated the effects of long-term moderate alcohol consumption on all-cause mortality and cardiovascular disease mortality among survivors of myocardial infarction.¹⁷ A U-shaped association was found in this cohort of men, indicating an inverse relationship between moderate alcohol consumption and all-cause mortality in those who had survived a myocardial infarction. It should be noted that the association was strongest in the cohort with less impaired cardiac function after myocardial infarction or those who had had a less severe heart attack.

In summary, while the cardioprotective effect is also apparent in secondary prevention, the evidence is limited. Overall, there is insufficient evidence to recommend a 'healthy' or protective level of alcohol consumption for people with established cardiovascular disease. It is likely that it is less than the maximum amount set by the NHMRC and it is likely there is no cardioprotective effect at all.

Cardioprotective effect

Stroke, heart failure, hypertension, diabetes, coronary heart disease and acute cardiovascular events traditionally have a U- or J- shaped association with alcohol consumption. This relationship indicates that there is a small positive effect or cardioprotective effect of small amounts of alcohol consumption, or that low levels of consumption confer a small decreased risk compared with people who do not drink at all. However, at higher consumption levels this protective effect does not exist.

The limitations of alcohol research methodology mean the cardioprotective effect of alcohol is in question. Mendelian randomisation provides a novel approach to overcome the biases and possibility of reverse causation, whereby genetic variants that are associated with drinking alcohol are utilised as a proxy for self-reported alcohol consumption.

A Mendelian randomisation study looked at the association between alcohol and cardiovascular disease and concluded that a reduction in alcohol consumption, even for light to moderate drinkers, is beneficial for cardiovascular health.¹⁸ Individuals with the genetic variant associated with non-drinking (alcohol dehydrogenase), and therefore lower alcohol consumption, had a more favourable cardiovascular profile and reduced risk of coronary heart disease than those without the genetic variant. This further suggests that the J- shaped relationship observed between alcohol and cardiovascular disease is likely driven by confounding and/or reverse causality.

Findings from Mendelian randomisation studies which are not subject to confounding or reverse causality provide more confidence than those from observational research.^{19, 20, 21, 22} The NHMRC concluded that there is less confidence in the evidence that small or moderate amounts of alcohol truly reflect a positive effect on cardiovascular outcomes, and that if it does exist, it is at much smaller doses than once thought.

Mechanisms of action: How alcohol affects cardiovascular health

The mechanisms by which alcohol affects cardiovascular disease risk have been extensively researched but are varied and not always fully understood. These mechanisms include, but are not limited to, an effect on heart rhythm, blood pressure, lipid regulation, insulin resistance, inflammation, endothelial function, platelet aggregation and coagulation. Some of the main mechanisms are described below.

Many epidemiological and clinical studies have indicated the relationship between alcohol consumption and raised blood pressure.⁶ The mechanisms through which alcohol increases blood pressure are not clear. Several mechanisms have been proposed, including blood pressure changes related to vascular endothelial dysfunction or altered vascular responsiveness. Low to moderate levels of alcohol consumption may improve endothelial function and higher amounts impair it. Endothelial dysfunction is an early indicator of blood vessel damage and atherosclerosis.¹

Chronic alcohol consumption over time can cause oxidative stress and the production of inflammatory markers, while lower doses are associated with reduced inflammation as indicated by markers of C-reactive protein and certain interleukins.¹ Chronic alcohol consumption causes dysbiosis (alteration of the balance of bacteria in the gut), which affects the immune system and can lead to an overgrowth of harmful bacteria and endotoxins.²³

Alcohol can also weaken the intestinal barrier and its permeability, causing it to become 'leaky', allowing these harmful endotoxins to enter the bloodstream and spread to other organs, which can further promote inflammation. The liver plays a key role in the breakdown of alcohol and also in the detoxification of circulating toxins; chronic alcohol use impairs the gut and the liver, leading to systemic inflammation and to organ damage.^{24, 25}

Alcohol intake also affects coagulation and platelet aggregation in the blood; it can either promote a favourable haemostatic profile or an adverse one. Several studies have indicated that alcohol intake decreases fibrinogen concentrations, which is a cardiovascular disease risk marker at elevated levels.²⁶ Alcohol has varying and often complex effects on platelet function, which in turn alters platelet activation or aggregation, potentially increasing the risk of cardiovascular disease.¹ Low to moderate alcohol consumption decreases platelet aggregation and significant daily alcohol consumption increases platelet aggregation and reactivity.²⁷ Chronic alcohol consumption can also predispose people to bleeding and result in a longer time to clot formation.²⁷

A common modifiable risk factor for cardiovascular disease is a person's lipid profile. Hepatic lipid metabolism and homeostasis in the body is tightly controlled, however ethanol affects all aspects of this process.¹ Alcohol consumption affects circulating lipids, including triglycerides and high-density lipoprotein cholesterol (HDL-c). Many researchers have found that following alcohol consumption, there is a rise in HDL-c circulating in the blood.²⁸

Previously, it was thought that all alcohol consumption also increased circulating triglycerides. However in recently conducted Mendelian randomisation studies, low to moderate alcohol consumption reduced triglycerides and low-density lipoprotein (LDL-c) and increased HDL-c.²⁹ This finding supports the notion that alcohol-induced changes in HDL-c do not fully account for the lower risk of coronary heart disease with low to moderate alcohol consumption, and that there are other mechanisms involved to explain the J-shaped curve.

There is an undeniable link between alcohol and atrial fibrillation, and it is widely known that even moderate drinking can trigger atrial fibrillation symptoms.³⁰ Any cardiovascular benefit that is seen with low to moderate drinking does not extend to people living with atrial fibrillation. Acute alcohol consumption has a direct impact at a cellular level, causing oxidative stress, inflammation, damage to gap junction intercellular channels and direct myocyte injury, influencing autonomic functioning, in turn leading to the electrophysiological onset of atrial fibrillation.³⁰ Whereas chronic alcohol consumption predisposes to atrial fibrillation via direct effects on left atrial structure and via other atrial fibrillation risk factors, including hypertension. Chronic drinking and binge drinking are both associated with the onset of atrial fibrillation, with an increase in recurrence in those who continue to drink.³⁰

Alcohol is also related to the risk of overweight and obesity, a major modifiable risk factor for cardiovascular disease. Alcohol is high in energy and therefore a source of excess kilojoules. The body metabolises alcohol in preference to carbohydrates and fat, with alcohol taking priority due to the by-products of its metabolism being toxic to the body, therefore fat and carbohydrate oxidation are inhibited.^{31, 32} The consumption of alcohol can also initiate feelings of hunger and less satiety due to inhibiting some key hormones, including leptin and glucagon-like peptide -1 (GLP-1). The reduced inhibition and impaired judgement associated with alcohol consumption can also lead to poor food choices.³³ Alcohol consumed before or with a meal can increase food intake, however in some studies only heavy drinking or binge drinking is associated with weight gain, with those drinking low to moderate amounts gaining less weight than those that abstain from alcohol.³⁴ Surprisingly, low to moderate consumption of alcohol seems to be protective of weight gain, especially in women.³³ Overall, alcohol consumption can contribute to intake of excess kilojoules, however in some studies this does not always result in weight gain and the relationship between alcohol and weight is still not well understood. The evidence may be plagued by issues of reverse causality whereby those who are overweight change their behaviours.

In summary, alcohol and its mechanisms of action are varied and have not been fully elucidated. Alcohol has varied short and long term impacts on many body systems, including the cardiovascular system.

Commentary on characteristics of the evidence base

GRADE is a framework used to grade the quality of evidence. The quality of the evidence based on the GRADE framework, across the primary studies included in the reviews, was most often low quality, except for a systematic review exploring atrial fibrillation which was graded as moderate. Low quality as assessed by GRADE indicates there is more risk of bias in the primary studies included in the systematic review and some caution needs to be applied when interpreting the evidence.

As with other areas of nutrition research, the evidence evaluating the relationship between alcohol and health has its limitations. Much of the evidence regarding alcohol and health outcomes is observational, often seen as a lower standard of research, as observational studies are more prone to bias and confounding than experimental studies. Observational studies, although the most appropriate study design for these types of research questions, are not able to determine causation and, although most observational studies adjust for confounders, this may not occur consistently.³⁵

Alcohol intake, like other dietary intake exposures, is assessed via self-report, which has limitations. Self-report measures are prone to recall and social desirability bias, that is, individuals may not always remember their true intake or may not want to report their true intake, which is known to be the case particularly in people who drink heavily. Furthermore, alcohol consumption, like other dietary behaviours, may change frequently over time. Therefore, studies which assess a single point in time may not be as accurate as those which include more than one time point.

The Mediterranean diet and alcohol

The Mediterranean diet is high in minimally processed plant-based foods such as vegetables, legumes, fruits, nuts and wholegrains, olive oil and fish and low in saturated fat, meats, and dairy products. The Mediterranean diet has shown promise with regard to reducing cardiovascular disease risk factors and improving health. This well-researched eating pattern has strong evidence and underpins Heart Foundation recommendations about heart healthy eating. Traditionally, the Mediterranean diet includes alcohol in the form of red wine.³⁶

The Mediterranean diet is one of the only dietary patterns that has been extensively studied and consistently includes alcohol, although it is important to note that the evidence is for the total dietary pattern, so the effects of alcohol cannot be separated from the health benefits of the overall diet. Alcohol is not a defining feature of healthy eating patterns nor of heart healthy eating, despite its inclusion in the Mediterranean diet. Therefore, the Heart Foundation does not recommend people drink alcohol for heart health, despite the inclusion of alcohol in the Mediterranean diet.



Conclusions

The relationship between alcohol and health is clear. Alcohol is a Group 1 carcinogen and there is strong evidence that consuming alcohol increases the risk of various cancers including mouth, pharynx, larynx, some oesophageal, breast, colorectal, stomach and liver cancers.³

Modern statistical and analytical methods have raised serious uncertainty about the evidence for the cardioprotective effect of alcohol consumption, while evidence for the association between high alcohol intake and adverse cardiovascular outcomes has strengthened over the last 20 years. Alcohol consumption increases the risk of atrial fibrillation, which can lead to devastating stroke. Therefore, the Heart Foundation does not recommend that people drink alcohol for heart health.³

The Heart Foundation supports the NHMRC recommendations to reduce the health risks associated with alcohol consumption. For people at higher risk of cardiovascular disease, or who have cardiovascular disease, the Heart Foundation recommends the NHMRC guidelines also apply, acknowledging that drinking below these limits, or not drinking at all, is likely the safest option.



References

1. M. R. Piano, "Alcohol's Effects on the Cardiovascular System," *Alcohol Research*, vol. 38, no. 2, pp. 219-41, 2017.
2. World Health Organization, "Global Status Report on Alcohol and Health," WHO Library Cataloguing, Switzerland, 2018.
3. World Cancer Research Fund/American Institute for Cancer Research, "Alcoholic drinks and the risk of cancer," Available at <https://www.wcrf.org/sites/default/files/Alcoholic-Drinks.pdf>, 2018.
4. National Health and Medical Research Council, "Australian Guidelines to reduce health risks from drinking Alcohol," NHMRC, Canberra, 2020.
5. E. Mostofsky, H. Chehal and K. Mukamal, "Alcohol and Immediate Risk of Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis.," *Circulation*, vol. 133, no. 10, pp. 979-987, 2016.
6. A. Briasoulis, V. Agarwal and F. Messerli, "Alcohol consumption and the risk of hypertension in men and women: a systematic review and meta-analysis.," *Journal of Clinical Hypertension*, vol. 14, no. 11, pp. 792-798, 2012.
7. C. Knott, S. Bell and A. Britton, "Alcohol Consumption and the Risk of Type 2 Diabetes: A Systematic Review and Dose-Response Meta-analysis of More Than 1.9 Million Individuals From 38 Observational Studies.," *Diabetes Care*, vol. 38, no. 9, pp. 1804-1812, 2015.
8. Y. Yang, D. C. Liu and Q. Wang, "Alcohol consumption and risk of coronary artery disease: A dose-response meta-analysis of prospective studies.," *Nutrition*, vol. 32, no. 6, pp. 637-644, 2016.
9. S. Larsson, N. Orsini and A. Wolk, "Alcohol Consumption and Risk of Heart Failure: A Dose-Response Meta-Analysis of Prospective Studies," *European Journal of Heart Failure*, vol. 4, pp. 367-73, 2015.
10. S. Larsson, N. Drca and A. Wolk, "Alcohol consumption and risk of atrial fibrillation: a prospective study and dose-response meta-analysis.," *Am Coll Cardio*, vol. 64, no. 3, pp. 281-89, 2014.
11. S. Larsson, A. Wallin, A. Wolk and et al, "Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis," *BMC Medicine*, vol. 14, no. 178, 2016.
12. S. Costanzo, A. Di Castelnuovo, M. Donati, L. Iacoviello and G. de Gaetano, "Alcohol consumption and mortality in patients with cardiovascular disease: a meta-analysis.," *Journal of the American College of Cardiology*, vol. 55, no. 13, pp. 1339-1347, 2010.
13. S. Costanzo, A. Di Castelnuovo, M. Donati, L. Iacoviello and G. de Gaetano, "Alcohol consumption in relation to vascular and total mortality in patients with diabetes, hypertension or history of cardiovascular disease: A meta-analysis.," *Journal of wine research*, vol. 22, no. 2, pp. 119-122, 2011.
14. S. Smith Jr, E. Benjamin, R. Bonow, L. Braun, M. Creager, B. Franklin, R. Gibbons, S. Grundy, L. Hitatzka, D. Jones and D. Lloyd-Jones, "AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation.," *Circulation*, vol. 124, no. 22, pp. 2458-2473, 2011.
15. J. Iestra, D. Kromhout, Y. Van der Schouw, D. Grobbee, H. Boshuizen and W. Van Staveren, "Effect size estimates of lifestyle and dietary changes on all-cause mortality in coronary artery disease patients: a systematic review.," *Circulation*, vol. 112, no. 6, pp. 924-934, 2005.
16. A. Garcia-Diaz, P. Marchena, J. Toril, G. Arnedo, J. Munoz-Torrero, M. Yeste, E. Aguilier and M. Monreal, "Alcohol consumption and outcome in stable outpatients with peripheral artery disease.," *Journal of vascular surgery*, vol. 54, no. 4, pp. 1081-1087, 2011.
17. J. Pai, K. Mukamal and E. Rimm, "Long-term alcohol consumption in relation to all-cause and cardiovascular mortality among survivors of myocardial infarction: the Health Professionals Follow-up Study.," *European Heart Journal*, vol. 33, no. 13, pp. 1598-1605, 2012.
18. J. Holmes, C. Angus, P. Buykx, A. Ally, T. Stone, P. Meier and A. Brennan, "Mortality and morbidity risks from alcohol consumption in the UK: analyses using the Sheffield Alcohol Policy Model (v. 2.7) to inform the UK Chief Medical Officers' review of the UK lower risk drinking guidelines.," University of Sheffield, Sheffield, 2016.

19. S. Yeung , C. Jiang, K. Cheng, B. Cowling , B. Liu, w. Zhang, T. Lam , G. Leung and C. Schooling , "Moderate alcohol use and cardiovascular disease from Mendelian randomization.," *PloS one*, vol. 8, no. 7, p. e68054, 2013.

20. A. Taylor , F. Lu , D. Carslake , Z. Hu , Y. Qian , S. Liu, J. Chen , H. Shen and G. Smith , "Exploring causal associations of alcohol with cardiovascular and metabolic risk factors in a Chinese population using Mendelian randomization analysis.," *Scientific reports.*, vol. 15, no. 6, pp. 1-6, 2015.

21. I. Milwood , R. Walters, X. Mei , Y. Guo , L. Yang , Z. Bian , d. Bennett, Y. Chen , C. Dong , R. Hu and G. Zhou , "Conventional and genetic evidence on alcohol and vascular disease aetiology: a prospective study of 500 000 men and women in China," *The Lancet*, vol. 393, no. 10183, pp. 1831-42., 2019.

22. Y. Cho , S.-Y. Shin , S. Won , C. Relton , G. Davey Smith and M.-J. Shin , "Alcohol intake and cardiovascular risk factors: a Mendelian randomisation study," *Scientific Reports*, vol. 5, p. 18422, 2015.

23. H. Wang , S. Zakhari and M. Jung , "Alcohol, inflammation, and gut-liver-brain interactions in tissue damage and disease development.," *World Journal of gastroenterology*, vol. 16, no. 11, p. 1304, 2010.

24. S. Patel , R. Behara , G. Swanson, C. Forsyth, R. Voight and A. Keshavarzian , "Alcohol and the Intestine.," *Biomolecules*, vol. 5, no. 4, pp. 2573-2588, 2015.

25. F. Bishehsari , E. Magno, G. Swanson, V. Desai, R. Voigt, C. Forsyth and A. Keshavarzian , "Alcohol and gut-derived inflammation.," *Alcohol research: current reviews*, vol. 38, no. 2, p. 163, 2017.

26. T. Mori , V. Burke, L. Beilin and I. Puddey , "Randomized controlled intervention of the effects of alcohol on blood pressure in premenopausal women.," *Hypertension*, vol. 66, no. 3, pp. 517-523, 2015.

27. R. O. Salem and M. M. Laposata , "Effects of Alcohol on Hemostasis," *Pathology Patterns Reviews*, vol. 123, no. 1, pp. 96-105, 2005.

28. N. Muth, G. Laughlin , D. von Muhlen, S. Smith and E. Barrett-Conner, "High-density lipoprotein subclasses are a potential intermediary between alcohol intake and reduced risk of cardiovascular disease: the Rancho Bernardo Study.," *British Journal of Nutrition*, vol. 104, no. 7, pp. 1034-1042, 2010.

29. K. Vu, C. Ballantyne, R. Hoogeveen, V. Nambi, K. Valcik, E. Boerwinkle and A. Morrison, "Causal role of alcohol consumption in an improved lipid profile: the Atherosclerosis Risk in Communities (ARIC) study.," *PloS one*, vol. 11, no. 2, p. p.e01487, 2016.

30. A. Voskoboinik, S. Prabhu, L. Lin , Kalman JM and P. Kistler , "Alcohol and atrial fibrillation: a sobering review.," *Journal of the American College of Cardiology.*, vol. 68, no. 23, pp. 2567-2576, 2016.

31. D. Forman, "The effect of ethanol and its metabolites on carbohydrate, protein, and lipid metabolism," *Annals of Clinical & Laboratory Science*, vol. 18, no. 3, pp. 181-189, 1988.

32. Y. Schutz, "Role of substrate utilization and thermogenesis on body-weight control with particular reference to alcohol.," *Proceedings of the Nutrition Society*, vol. 59, no. 4, pp. 511-517, 2000.

33. M. Yeomans , "Alcohol, appetite and energy balance: is alcohol intake a risk factor for obesity?.,," *Physiology and behavior*, vol. 100, no. 1, pp. 82-29, 2010.

34. L. Wang , I. Lee , J. Manson , J. Buring and H. Sasso , "Alcohol consumption, weight gain, and risk of becoming overweight in middle-aged and older women.," *Archives of Internal Medicine*, vol. 170, no. 5, pp. 453-461, 2010.

35. K. Wingrove , M. Lawrence and S. McNaughton , "Dietary patterns, foods and nutrients: a descriptive analysis of the systematic reviews conducted to inform the Australian Dietary Guidelines. pp.1-8.," *Nutrition Research Reviews*, pp. 1-8, 2020.

36. V. Rosato, N. Temple, C. La Vecchia , G. Castellan , A. Tavani and V. Guercio, "Mediterranean diet and cardiovascular disease: a systematic review and meta-analysis of observational studies," *European Journal of Nutrition*, vol. 58, no. 1, pp. pp.173-191., 2019.



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The Heart Foundation acknowledges the Traditional Owners and custodians of Country throughout Australia and their continuing connection to land, waters and community. We pay our respect to them and their cultures, and Elders past, present and future.