Journal of Medical Case Reports and Reviews

Received 10 Mar 2021 | Revised 14 Mar 2021 | Accepted 12 May 2021 | Published Online 16 May 2021

JMCRR 04 (05), 858-871 (2021) ISSN (O) 2589-8655 | (P) 2589-8647

JMCRR

ALCOHOL CONSUMPTION AND CARDIOPROTECTION:MODERATION IS THE KEY

Shashi K. Agarwal, MD

Center for Contemporary and Complementary Cardiology

2227 US Highway 1, Suite 309, North Brunswick, NJ 08902, USA

Orcid # 0000-0003-0007-5582

Publons # E-4889-2016

Researchgate: https://www.researchgate.net/profile/Shashi_Agarwal

Article Info

***Corresponding Author:**

Shashi K. Agarwal, MD

Abstract

Cardiovascular diseases are the leading cause of global morbidity and mortality. Besides inflicting tremendous human suffering, they also result in huge direct and indirect financial costs on the worldwide society. With the ready availability of affordable therapeutics globally, and the relative lack of newer innovations, lifestyle interventions are gaining importance to further control this epidemic. Low to moderate alcohol intake is consistently and strongly related with lower risk of cardiovascular disease incidence and mortality. However, most studies indicate that heavy drinking has a detrimental effect. This paper reviews the effects of alcohol consumption on several cardiovascular diseases.

Keywords: Alcohol, Cardiovascular Diseases, Coronary Artery Disease, HTN, Stroke

Introduction:

Alcohol is a popular drink [1]. It is estimated that almost 2 billion people across the world consume alcoholic drinks [2]. In 2016, 32.5% of the world population were current drinkers with an intake of one or more alcoholic drinks in the past 12 months [3].

The effects of alcohol on health can vary depending on the amount (low-to-moderate versus heavy consumption) and pattern of intake [4]. Moderate alcohol intake is considered as two standard drinks a day for men and one standard drink a day for women [5]. Binge drinking is considered as 4 or more drinks for women and 5 or more drinks for men in one sitting or over 2 hours [6]. Compulsive alcohol intake leads to alcohol use disorder (AUD) [7]. Although low to moderate alcohol intake may have some beneficial effects on cardiovascular diseases (CVDs), alcohol consumption, in general, is associated with several negative health consequences]8-21]. Alcohol can cause several liver diseases, such as fatty liver, hepatitis, and cirrhosis, digestive problems such as pancreatitis. cancers of the breast, mouth, throat, esophagus, liver, and colon

and mental health disorders, such as depression and anxiety [8-10]. Alcoholics also experience learning and memory problems and are at a higher risk of becoming demented [11]. They are more prone to injuries, such as motor vehicle crashes, falls, drownings, and burns. and more likely to be involved in homicide, suicide, sexual assault, and intimate partner violence [12-13]. They also tend to participate in risky sexual behaviors (such as unprotected sex or sex with multiple partners), which can result in unintended pregnancy or sexually transmitted diseases, including HIV [14]. They often face social problems, family disturbances, and unemployment [15,16]. Drinking alcohol during pregnancy can increase the risk of miscarriage, stillbirth, or fetal alcohol spectrum disorders in the offspring [17,18]. Children of parents with alcohol or drug use disorders are more likely to be involved in drugs and often suffer from behavioral and mental problems [19]. Alcohol may also weaken the immune system, making alcoholics more prone to contracting infectious diseases like pneumonia and tuberculosis [20]. In 2012, alcohol was responsible for 139 million net DALYs (disability-adjusted life years), or 5.1% of the global burden of disease and injury [21]. Alcohol consumption also increases mortality from several diseases, including certain cancers [22]. During 2012, about 3.3 million deaths, or 5.9% of all global deaths, were attributed to alcohol consumption [23].

The health effects of alcohol on CVD appear to be J or U-shaped, with low to moderate doses being beneficial compared to no alcohol intake, while heavy intake being harmful [23,24]. It is estimated that 19% of all alcohol-related deaths are cardiovascular. [22]

Discussion:

CVDs include coronary artery disease/coronary heart disease (CAD/CHD), high blood pressure (HTN), stroke, heart failure (HF), cardiac arrhythmias (including atrial fibrillation (AF) and sudden cardiac death or SCD), peripheral arterial disease (PAD), venous thromboembolism (VTE), and vasculogenic erectile dysfunction (ED) [25]. CVDs impart enormous human suffering and are associated with a significant reduction in the quality of life [26]. CVDs are also a leading cause of mortality worldwide [27]. It is estimated that the number of global CVD deaths will rise to 20 million by 2030 [28]. Health-related direct and indirect costs of CVDs are enormous and continue to climb [29].

Alcohol intake has consistently shown a J- or U-shaped relationship with several cardiovascular diseases [23,24]. Light to moderate alcohol intake has been associated with a lower risk of coronary artery disease (CAD), heart failure, as well as CVD mortality [30]. On the other hand, heavy consumption has been associated with deleterious CVD outcomes, including increased mortality [31, Binge drinking and AUD are also harmful to the cardiovascular system [32,33].

Several mechanisms are involved in the noted benefit of low dose intake on CVDs [34]. Alcohol appears to enhance endothelial function by increasing the production of nitric oxide in healthy subjects [35] Alcohol intake also raises high-density lipoprotein cholesterol and apolipoprotein A-I, which are inversely associated with the risk of occlusive arterial disease [36]. Alcohol beneficially alters the atherosclerotic plaque composition and induce stabilization [37]. Alcohol also exerts several effects on factors involved in hemostasis, such as inhibition of platelet aggregation, lowering of fibrinogen and plasma viscosity as well as increasing the levels of tissue plasminogen activator [38-41]. Low to moderate consumption of alcohol also tends to reduce blood pressure (BP), improve insulin sensitivity, and reduce fasting insulin resistance,– both HTN and DM are major risk factors for occlusive arterial disease [42-44]. Inflammation, a major player in cardiovascular diseases, is lowered with moderate alcohol consumption, while higher intake induces oxidative stress and increases systemic inflammatory markers [45,46]. Although the major driver behind the beneficial CVD effects is ethanol, some alcoholic beverages, like red wine, are high in polyphenols which also provide antioxidant, anti-inflammatory, and antiplatelet effects [47.48].

Some questions have been raised regarding the beneficial effects of alcohol on CVD – most studies have not ruled out the contribution from healthy lifestyles and social behavior that may be present in these drinkers [49]. Secondly, non-drinkers may also have higher morbidity and mortality due to pre-existing CVD or other diseases, (and become ‘quitters’ or die prematurely) thereby confounding the benefits of alcohol intake [50,51]. Recent Mendelian randomization studies using genetic

polymorphisms have also questioned the beneficial association of low-moderate drinking with the cardiovascular system [52].

Alcohol and HTN:

The relationship between alcohol intake and hypertension is well studied [53-56]. Briasoulis et al, in their meta-analysis, found that consumption of <10g/day of alcohol in women appeared to have a protective effect on hypertension, while a consumption of 21 to 30 g/day significantly increased the risk of hypertension [53] MacMahon analyzed 29 cross-sectional studies and 6 prospective studies from populations from North America, Australia, Japan, Europe, and New Zealand and found a significant positive association between hypertension and alcohol consumption [54]. They estimated that intake of 3 to 4 drinks per day increased the prevalence of hypertension by 50% when compared with non-drinkers and an intake of 6 to 7 drinks per day, increased the prevalence by 100% [54]. This alcohol-related hypertension risk is J-shaped in women while it is linear in men [55,56]. Binge drinking (drinking more than 5 standard drinks in a single sitting) raises the systolic BP from 4 to 7 mmHg and the diastolic BP from 4 to 6 mmHg, in the short term [57]. These elevations are significant as even a 2-mmHg increase in BP increases mortality from coronary artery disease by 7 percent and from stroke by 10 percent [58,59]. Most professional associations including the American Society of Hypertension and the International Society of Hypertension recommend that men limit their alcohol consumption to no more than 2 drinks a day, and women to no more than 1 drink a day [60]

Alcohol consumption can cause HTN by causing endothelial dysfunction, vasoconstriction, sympathetic activation, and activation of the renin-angiotensin-aldosterone system [61,62]. Alcohol intake also contributes to obesity, chronic renal disease, obstructive sleep apnea, and high insulin resistance – all known risk factors for the development of hypertension [63-66]. Alcohol withdrawal, by triggering a severe sympathetic response, can dangerously elevate BP levels [67]. Reduction in alcohol intake to <2 alcoholic drinks per day reduces blood pressure in a dose-response manner [68].

Alcohol and CAD/CHD:

The relationship between alcohol consumption and CAD/CHD has been extensively investigated [69,70]. A meta-analysis done by Bagnardi and colleagues found that there is a lower risk of CHD in regular low-moderate drinkers [71]. Another study reported that alcohol consumption between <1 standard drink/day to ~5 drinks/day was cardioprotective for CHD mortality [72]. Mostofsky and colleagues conducted a systematic review and meta-analysis of 23 studies and found that within a week after moderate alcohol consumption, there was a lower risk of myocardial infarction [73]. The cardioprotective benefit of low to moderate alcohol use has also been noted in a Mendelian randomization study [74]. The relationship between CHD and alcohol is however harmful if alcohol consumption is high [71-74]. In a meta-analysis done by Bagnardi and colleagues, the risk of CHD is higher in binge and heavy drinkers, when compared with non-drinkers [71]. Mostofsky and colleagues found that within a week after heavy alcohol consumption, there is a higher risk of myocardial infarction [73]. A recent Mendelian randomization study documented that increased alcohol consumption was associated with an increased risk of subclinical coronary atherosclerosis [75]. The harmful effects on CAD/CHD with a higher intake of alcohol occur, despite there being a tendency for a 10% increase in HDL-C levels and a 14% reduction in fibrinogen levels with its consumption [76]. Overall, most studies find the relationship between alcohol intake and the risk of CAD/CHD is U or J shaped. [77-79]

The 'French Paradox' suggested that the polyphenols found in red wine may be responsible for the lower CAD seen in the Mediterranean red wine drinking population [80]. However, a systematic review of 25 studies did not find a consistent pattern of a CAD/CHD benefit with a specific beverage type [81]. It appears that the observed lower risk of CAD is mainly from the ethanol content of alcoholic drinks [47].

Alcohol and Stroke:

Alcohol has a J-shaped relationship with stroke. Reynolds and group in 2003, in a meta-analysis, found that although consumption of 24 g/day was associated with a reduction in ischemic stroke when compared with abstainers, consumption of

more than 60g/day resulted in an increased risk of ischemic stroke by 69% and hemorrhagic stroke by 118%.[82]. In a systematic review of 37 studies, Feigin and colleagues noted that drinking more than 150 g of ethanol a week doubled the risk of subarachnoid hemorrhage [83]. Ronksley and his group found that the risk of stroke was increased by 69% with consumption of >4 drinks per day [84]. In a systematic review of 37 studies, Zhang and colleagues reported that consumption of 0 to 20g/day of alcohol (<2 drinks per day) was associated with a reduced risk for all types of stroke and stroke-related mortality [85]. However, drinking more than 2 drinks a day resulted in an increased risk of stroke and all stroke-related outcomes [85]. In a more recent systemic review and meta-analysis of 27 prospective studies, Larsson et al. reported that light to moderate alcohol consumption (1-2 drinks/day) was associated with a lower risk of ischemic stroke, whereas high (>2-4 drinks/day) and heavy drinking (>4 drinks/day) was associated with an increased risk, especially of hemorrhagic stroke [86]. Genetic factors may also play a role. Holmes and colleagues in a Mendelian randomization study found that individuals with the A allele variant ADH1Brs1229984 consumed less alcohol and had a reduced risk of ischemic stroke compared with noncarriers [52]. Other, more recent studies have also implicated genetic influence and demonstrate that heavy alcohol consumption is associated with a greater risk of stroke [87,88]. Overall, it appears that although 1 to 2 drinks per day may have no effect on or a slight reduction in stroke events, greater daily alcohol consumption increases the risk for stroke

Alcohol and Heart Failure:

The effects of alcohol on heart failure are not clear. Larsen et al. in a meta-analysis determined that consumption of 7 drinks/week was associated with a 17 percent lower risk of developing heart failure [89]. Wannamethee and colleagues did not find any protective benefit on incident heart failure in an older population with light-moderate drinking. They also reported that heavier drinking (≥5 drinks/day or ≥35 drinks/week) significantly increased the risk for heart failure [90]. However, a recent Mendelian randomization study suggests that higher alcohol consumption in heart failure may not be as dangerous as previously presumed [91]. At this time, however, it can only be said that low levels of alcohol consumption are safe in patients with heart failure and may even be beneficial in heart failure due to CHD.

Alcohol and Arrhythmias:

The causal relationship between alcohol intake and atrial fibrillation has been known for a long time [92]. An alcohol binge causing AF (often referred to as the "holiday heart syndrome") in healthy people is well known [93] Alcohol not only may directly affect the heart but also is related to obesity, sleep-disordered breathing, and hypertension, all of which contribute to an increased risk of AF [94]. According to Koskinen and group, 5%-10% of all new episodes of atrial fibrillation are related to alcohol use [95]. Most cases of SCD are due to malignant ventricular arrhythmias [96]. Alcohol also plays a significant role in SCD [97,98]. In a study of the Finnish population, Perkiömäki and colleagues determined that 4 of 10 victims of unexpected SCD had evidence of alcohol intake before the fatal event [99].

Alcohol and Cardiomyopathy:

Although heart failure is commonly due to hypertensive or ischemic cardiovascular disease, alcohol may also cause alcoholic cardiomyopathy - a progressive heart chamber dilatation leading to heart failure [100,101]. These patients are more likely to develop atrial fibrillation and malignant ventricular arrhythmias [102,103]. In long-term follow-up studies, a mortality rate of 10% of patients/year has been observed in the group of patients with persistent high-dose ethanol consumption due to progression of cardiomyopathy and occurrence of malignant arrhythmias [104,105].

Alcohol and Valvular Diseases/Aortic Aneurysm:

Some earlier studies have indicated that low to moderate levels of alcohol consumption is associated with a smaller abdominal aortic diameter and alcohol helps reduce mortality due to aortic disease [106,107]. However, later studies have documented a higher risk for the development of abdominal aortic aneurysm with alcohol consumption [108,108]. In a recent population-based study, alcohol-related diseases were associated with a nearly 2.4-fold increased incidence of abdominal aortic aneurysm, after

adjusting for age, gender, and comorbidities [110]. In another recent study, regular alcohol consumption was noted to increase the aortic root diameter [111].

Alcohol and Congenital Heart Disease:

Many child-bearing-age women consume alcohol during pregnancy, intentionally or unintentionally, thereby increasing the potential risk for congenital diseases in the offspring. In a meta-analysis of 23 studies, Wen and the group found no association between maternal alcohol intake during pregnancy and the risk of congenital heart disease in the offspring [112]. Another study also reached similar conclusions, with low-to-moderate alcohol consumption during pregnancy, having no significant adverse impact on congenital heart defects in the offspring [113]. However, some studies suggest that prenatal alcohol exposure may be teratogenic and cause several kinds of heart defects (aberrant great vessels, conotruncal anomalies, atrial septal defects, and ventricular septal defects) [114-116]. A recent meta-analysis of 55 studies concluded that maternal alcohol consumption may increase the risk of congenital heart disease in the offspring [117]. Off-springs born with congenital heart disease are living longer and these survivors appear to be drinking more alcohol than the general population [118,119].

Alcohol and Heart Transplant:

The data on the use of donor hearts from patients with a previous history of alcoholism is unclear. Freimark and his associates found that heart transplant patients experienced poor survival when compared to those who received donor hearts from non-alcoholics [120]. However, a later study found that donor hearts from chronic alcoholics were associated with a better survival rate in transplant patients compared to non-alcohol-related donor heart transplants [121. In a recent study of 370 heart transplant patients, Newman and colleagues reported that alcohol abuse did not appear to impact rejection, cardiac allograft vasculopathy, or intermediate-term survival [122]. The transplanted patients however did experience an increased incidence of post-transplantation atrial fibrillation and impaired cardiac allograft diastolic function [122].

Alcohol and PAD:

Several studies have noted an inverse relationship between moderate alcohol intake and PAD [123,124]. Evaluating results from the Cardiovascular Health Study, Mukamal and colleagues found that drinking 1 to 13 drinks/week resulted in a lower risk of hospitalization due to PAD [125] In 2011, Garcia-Diaz and colleagues reported in a study of 1073 patients from the FRENA registry, lower all-cause mortality, and lower cardiovascular mortality rates in alcohol drinkers with PAD compared to non-drinkers [126]. However, as with most other cardiovascular diseases, high levels of alcohol intake are associated with an increased risk of PAD. [127] This has been confirmed by a recent Mendelian study [128].

Alcohol and Erectile Dysfunction:

Wang et al, in a meta-analysis, determined that light to moderate alcohol intake (<21 drinks/week) resulted in a decreased risk of erectile dysfunction [129]. This benefit was also reported in diabetic male individuals [130,131]. It is believed that alcohol reduces ED by increasing the bioavailability of NO and thereby improves endothelial function in vasculogenic ED.

Alcohol and Venous Disease:

The data on the effects of alcohol intake on VTE is not clear. VTE benefits from alcohol intake were reported in men who drank between four to 14 drinks per week [132]. In a cohort of older women (The Iowa Women's Health Study), greater intake of alcohol was associated with a lower risk of incident VTE [133]. Patients with chronic liver disease, especially when due to excessive alcohol consumption, exhibit a low prevalence of VTE during hospitalization [134]. Similarly, a lower risk of DVT is noted in trauma patients with a history of chronic alcohol consumption [135,136]. Some data, however, suggests otherwise. Alcohol consumption of ≥ 3 units of liquor per week (One unit = approximately 14 grams of alcohol.) revealed a 53% increased risk of VTE compared to teetotalers in analysis, after adjusting for other potentially confounding factors [137]. In patients with AUD, an increase in the risk of VTE has also been noted [138]. Overall, the literature has studies reporting both benefits and harmful effects regarding VTE with alcohol intake. In a recent meta-analysis (10 prospective studies with a total of 441,128 individuals and 10,221 VTE

cases), Chen et al. found no relationship between alcohol intake and the risk of VTE [139].

Alcohol and other CVD risk factors:

Alcohol consumption in more than moderate amounts is also associated with many other CVD risk factors, such as sleep disorders, chronic kidney disease, weight gain, depression, and smoking [140-144].

Conclusion:

The effects of alcohol consumption on the cardiovascular system can be a double-edged sword. For low to moderate drinkers, alcohol consumption appears to be safe and often associated with a decreased risk of most CVDs. However, excess alcohol intake is associated with adverse cardiovascular outcomes. The Dietary Guidelines for Americans recommends that alcohol intake be limited to two standard drinks a day for men and one standard drink a day for women. Since it is extremely difficult to predict who may become an excessive drinker, it is recommended that non-drinking individuals not start drinking alcohol for potential cardiovascular benefits. Other healthy lifestyles, and the absence of other diseases that may induce 'quitting' or even premature death, may also play a role in the observed benefits of low to moderate alcohol intake on cardiovascular diseases. And finally, there appears to be no lower threshold for overall health harm, as even low-dose alcohol tends to increase morbidity and mortality from many other diseases.

Acknowledgments: None

Funding: None

Conflict of Interest: None

References:

1. https://www.who.int/substance_abuse/facts/alcohol/en/ - accessed March 3, 2021.
2. https://www.greenfacts.org/en/alcohol/ - accessed April 3, 2021.
3. Griswold M.G., Fullman N., Hawley C., et al. Alcohol use and burden for 195 countries and territories, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2018;392:1015–1035. doi: 10.1016/S0140-6736(18)31310-2.
4. O'Keefe E.L., DiNicolantonio J.J., O'Keefe J.H., Lavie C.J. Alcohol and CV Health: Jekyll and Hyde J-Curves. Prog. Cardiovasc. Dis. 2018;61:68–75. doi: 10.1016/j.pcad.2018.02.001.
5. https://www.cdc.gov/alcohol/fact-sheets/moderate-drinking.htm - accessed April 4, 2021.
6. Kuntsche E., Kuntsche S., Thrul J., Gmel G. Binge drinking: Health impact, prevalence, correlates and interventions. Psychol. Health. 2017;32:976–1017. doi: 10.1080/08870446.2017.1325889.
7. Esser MB, Hedden SL, Kanny D, Brewer RD, Gfroerer JC, Naimi TS. Prevalence of Alcohol Dependence Among US Adult Drinkers, 2009–2011. Prev Chronic Dis 2014;11:140329.
8. World Health Organization. Global status report on alcohol and health—2018external icon. Geneva, Switzerland: World Health Organization; 2018.; Rehm J, Baliunas D, Borges GL, Graham K, Irving H, Kehoe T, et al. The relation between different dimensions of alcohol consumption and burden of disease: an overviewexternal icon. Addiction. 2010;105(5):817-43.
9. World Health Organization. Global status report on alcohol and health—2018external icon. Geneva, Switzerland: World Health Organization; 2018.; International Agency for Research on Cancer. Personal Habits and Indoor Combustions: A Review of Human Carcinogens, Volume 100E 2012.
10. Castaneda R, Sussman N, Westreich L, Levy R, O'Malley M. A review of the effects of moderate alcohol intake on the treatment of anxiety and mood disorders. J Clin Psychiatry 1996;57(5):207–212.
11. Gutwinski S, Schreiter S, Priller J, Henssler J, Wiers CE, Heinz A. Drink and Think: Impact of Alcohol on Cognitive Functions and Dementia - Evidence of Dose-Related Effects. Pharmacopsychiatry. 2018 Jul;51(4):136-143. doi: 10.1055/s-0043-118664.
12. Smith GS, Branas CC, Miller TR. Fatal nontraffic injuries involving alcohol: A metaanalysis. Ann Emerg Med. 1999 Jun;33(6):659-68.
13. Abbey A. Alcohol-related sexual assault: a common problem among college students. J Stud Alcohol Suppl. 2002 Mar;(14):118-28. doi: 10.15288/jsas.2002.s14.118.

14. Naimi TS, Lipscomb LE, Brewer RD, Colley BG. Binge drinking in the preconception period and the risk of unintended pregnancy: Implications for women and their children. Pediatrics 2003;11(5):1136–1141.
15. Leonard KE, Rothbard JC. Alcohol and the marriage effect. J Stud Alcohol Suppl 1999;13:139–146.
16. Booth BM, Feng W. The impact of drinking and drinking consequences on short-term employment outcomes in at-risk drinkers in six southern states. J Behavioral Health Services and Research 2002;29(2):157–166.
17. Kesmodel U, Wisborg K, Olsen SF, Henriksen TB, Sechler NJ. Moderate alcohol intake in pregnancy and the risk of spontaneous abortion. Alcohol & Alcoholism 2002;37(1):87–92.
18. American Academy of Pediatrics, Committee on Substance Abuse and Committee on Children with Disabilities. 2000. Fetal alcohol syndrome and alcohol-related neurodevelopmental disorders. Pediatrics 2000;106:358–361.
19. Solis JM, Shadur JM, Burns AR, Hussong AM. Understanding the diverse needs of children whose parents abuse substances. Curr Drug Abuse Rev. 2012;5(2): 135–147.
20. Rehm J, Baliunas D, Borges GL, Graham K, Irving H, Kehoe T, et al. The relation between different dimensions of alcohol consumption and burden of disease: an overview. Addiction. 2010;105(5):817-43.
21. https://www.who.int/substance_abuse/facts/alcohol/en/ - accessed April 3, 2021.
22. Hartz SM, Oehlert M, Horton AC, et al. Daily Drinking Is Associated with Increased Mortality. Alcohol Clin Exp Res. 2018 Nov;42(11):2246-2255. doi: 10.1111/acer.13886.
23. Roerecke M, Rehm J. Alcohol consumption, drinking patterns, and ischemic heart disease: a narrative review of meta-analyses and a systematic review and meta-analysis of the impact of heavy drinking occasions on risk for moderate drinkers. BMC Med. 2014 Oct 21;12:182. doi: 10.1186/s12916-014-0182-6.
24. Veenstra J. Moderate alcohol use and coronary heart disease: a U-shaped curve? World Rev Nutr Diet. 1991;65:38-71. doi: 10.1159/000419467.
25. Mendis S, Puska P, Norrving B. Global Atlas on Cardiovascular Disease Prevention and Control. World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization. 2011:pp. 3–18. ISBN 978-92-4-156437-3.
26. Djärv T, Wikman A, Lagergren P. Number and burden of cardiovascular diseases in relation to health-related quality of life in a cross-sectional population-based cohort study. BMJ Open 2012;2:e001554.
27. Roth GA, Nguyen G, Forouzanfar MH, Mokdad AH, Naghavi M, Murray CJ. Estimates of global and regional premature cardiovascular mortality in 2025. Circulation. 2015 Sep 29;132(13):1270-82. doi: 10.1161/CIRCULATIONAHA.115.016021.
28. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3:e442. 10.1371/journal.pmed.0030442.
29. Brouwer ED, Watkins D, Olson Z, Goett J, Nugent R, Levin C. Provider costs for prevention and treatment of cardiovascular and related conditions in low- and middle-income countries: a systematic review. BMC Public Health. 2015;15:1183. Published 2015 Nov 26. doi:10.1186/s12889-015-2538-z.
30. Suliga E, Kozieł D, Ciesla E, Rebak D, Głuszek-Osuch M, Naszydłowska E, Głuszek S. The Consumption of Alcoholic Beverages and the Prevalence of Cardiovascular Diseases in Men and Women: A Cross-Sectional Study. Nutrients. 2019 Jun 12;11(6):1318. doi: 10.3390/nu11061318.
31. Goel S, Sharma A, Garg A. Effect of Alcohol Consumption on Cardiovascular Health. Curr Cardiol Rep. 2018 Mar 8;20(4):19. doi: 10.1007/s11886-018-0962-
32. Ogunmoroti O, Osibogun O, McClelland RL, Burke GL, Nasir K, Michos ED. Alcohol and ideal cardiovascular health: The Multi-Ethnic Study of Atherosclerosis. Clin Cardiol. 2019 Jan;42(1):151-158. doi: 10.1002/clc.23125. Epub 2018 Dec 17.
33. Kozela M, Doryńska A, Bobak M, Pająk A. Alcohol use disorder increases the risk of

nonfatal and fatal cardiovascular disease: an 11-year follow-up of a Polish population-based cohort. The HAPIEE study. Pol Arch Intern Med. 2020 Nov 30;130(11):960-966. doi: 10.20452/pamw.15616.

34. Day E, Rudd JHF. Alcohol use disorders and the heart. Addiction. 2019 Sep;114(9):1670-1678. doi: 10.1111/add.14703. Epub 2019 Jul 15.
35. Matsuo S, Nakamura Y, Takahashi M, Ouchi Y, Hosoda K, Nozawa M, Kinoshita M. Effect of red wine and ethanol on production of nitric oxide in healthy subjects. Am J Cardiol. 2001 Apr 15;87(8):1029-31: A6. doi: 10.1016/s0002-9149(01)01446-1.
36. Gaziano JM, Buring JE, Breslow JL, Goldhaber SZ, Rosner B, VanDenburgh M, Willett W, Hennekens CH. Moderate alcohol intake, increased levels of high-density lipoprotein and its subfractions, and decreased risk of myocardial infarction. New Engl J Med 1993;329:1829–1834.
37. Gisbertz SS, Derksen WJ, de Kleijn DP, Vink A, Bots ML, de Vries JP, Moll FL, Pasterkamp G. The effect of alcohol on atherosclerotic plaque composition and cardiovascular events in patients with arterial occlusive disease. J Vasc Surg 2011;54:123–131.
38. Pace-Asciak CR, Hahn S, Diamandis EP, Soleas G, Goldberg DM. The red wine phenolics trans-resveratrol and quercetin block human platelet aggregation and eicosanoid synthesis: implications for protection against coronary heart disease. Clin Chim Acta, (2):207-219 19957.
39. Dimmitt SB, Rakic V, Puddey IB, et al. The effects of alcohol on coagulation and fibrinolytic factors: a controlled trial.. Blood Coagul Fibrinolysis, (1):39-45 19988-10.
40. Mukamal KJ, Jadhav PP, D'Agostino RB, et al. Alcohol consumption and hemostatic factors: analysis of the Framingham Offspring cohort. Circulation, (12):1367-1373 200110.
41. Yarnell JW, Sweetnam PM, Rumley A, Lowe GD. Lifestyle and hemostatic risk factors for ischemic heart disease : the Caerphilly Study. Arterioscler Thromb Vasc Biol, (1):271-279 2000.MED: 10634829.
42. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360(9349):1903–1913.
43. Mori TA, Burke V, Beilin LJ, Puddey IB. Randomized controlled intervention of the effects of alcohol on blood pressure in premenopausal women. Hypertension. 2015;66(3):517–523.
44. Koppes LL, Dekker JM, Hendriks HF, Bouter LM, Heine RJ. Meta-analysis of the relationship between alcohol consumption and coronary heart disease and mortality in type 2 diabetic patients. Diabetologia 2006;49:648–652.
45. Piano MR, Phillips SA. Alcoholic cardiomyopathy: pathophysiologic insights. Cardiovasc Toxicol. 2014 Dec;14(4):291-308. doi: 10.1007/s12012-014-9252-4.
46. Barr T, Helms C, Grant K, Messaoudi I. Opposing effects of alcohol on the immune system. Prog Neuropsychopharmacol Biol Psychiatry. 2016 Feb 4;65:242-51. doi: 10.1016/j.pnpbp.2015.09.001.
47. Spaggiari G, Cignarelli A, Sansone A, Baldi M, Santi D. To beer or not to beer: A meta-analysis of the effects of beer consumption on cardiovascular health. PLoS One. 2020 Jun 3;15(6):e0233619. doi: 10.1371/journal.pone.0233619.
48. Freedman JE, Parker C, 3rd, Li L. et al. Select flavonoids and whole juice from purple grapes inhibit platelet function and enhance nitric oxide release. Circulation. 2001:103(23), 2792–2798.
49. Tsai MC, Lee CC, Liu SC, Tseng PJ, Chien KL. Combined healthy lifestyle factors are more beneficial in reducing cardiovascular disease in younger adults: a meta-analysis of prospective cohort studies. Sci Rep. 2020 Oct 23;10(1):18165. doi: 10.1038/s41598-020-75314-z.
50. Stockwell T, et al. Do "moderate" drinkers have reduced mortality risk? a systematic review and meta-analysis of alcohol consumption and all-cause mortality. J. Stud. Alcohol Drugs. 2016;77:185–198. doi: 10.15288/jsad.2016.77.185.
51. Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men:

explaining the U-shaped curve. Lancet. 1988;2(8623):1267-73.

52. Holmes MV, Dale CE, Zuccolo L, et al. Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. BMJ. 2014;349:g4164.
53. Briasoulis A, Agarwal V, Messerli FH. Alcohol consumption and the risk of hypertension in men and women: A systematic review and meta-analysis. Journal of Clinical Hypertension (Greenwich) 2012;14(11):792–798.
54. MacMahon S. Alcohol consumption and hypertension. Hypertension. 1987;9:111–121.
55. Okojie OM, Javed F, Chiwome L, Hamid P. Hypertension and Alcohol: A Mechanistic Approach. Cureus. 2020;12(8):e10086. Published 2020 Aug 27. doi:10.7759/cureus.10086.
56. Taylor B, Irving HM, Baliunas D, Roerecke M, Patra J, Mohapatra S, Rehm J. Alcohol and hypertension: gender differences in dose-response relationships determined through systematic review and meta-analysis. Addiction. 2009;104:1981–90. doi: 10.1111/j.1360-0443.2009.02694.x.
57. Seppä K, Sillanaukee P. Binge drinking and ambulatory blood pressure. Hypertension. 1999;33(1):79–82.
58. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360(9349):1903–1913.
59. Mori TA, Burke V, Beilin LJ, Puddey IB. Randomized controlled intervention of the effects of alcohol on blood pressure in premenopausal women. Hypertension. 2015;66(3):517–523.
60. Weber MA, Schiffrin EL, White WB, et al. Clinical practice guidelines for the management of hypertension in the community: A statement by the American Society of Hypertension and the International Society of Hypertension. Journal of Clinical Hypertension (Greenwich) 2014;16(1):14–26.
61. Husain K, Ansari RA, Ferder L. Alcohol-induced hypertension: Mechanism and prevention. World J Cardiol. 2014 May 26;6(5):245-52. doi: 10.4330/wjc.v6.i5.245.
62. Kleinhenz DJ, Sutliff RL, Polikandriotis JA, et al. Chronic ethanol ingestion increases aortic endothelial nitric oxide synthase expression and nitric oxide production in the rat. Alcoholism: Clinical and Experimental Research. 2008;32(1):148–154.
63. Suter PM. Is alcohol consumption a risk factor for weight gain and obesity? Crit Rev Clin Lab Sci. 2005;42(3):197-227. doi: 10.1080/10408360590913542.
64. Fan Z, Yun J, Yu S, Yang Q, Song L. Alcohol consumption can be a "double-edged sword" for chronic kidney disease patients. Med Sci Monit. 2019;25:7059–7072.
65. Scanlan MF, Roebuck T, Little PJ, Redman JR, Naughton MT. Effect of moderate alcohol upon obstructive sleep apnoea. Eur Respir J. 2000 Nov;16(5):909-13. doi: 10.1183/09031936.00.16590900.
66. Effects of ethanol on nervous system and vascular system especially in connection with the pathogenesis of hypertension [article in Japanese] Wakabayashi I, Hatake K. Jpn J Hyg. 2001;55:607–617.
67. Linnoila M, Mefford I, Nutt D, Adinoff B. NIH conference. Alcohol withdrawal and noradrenergic function. Ann Intern Med. 1987 Dec;107(6):875-89. doi: 10.7326/0003-4819-107-6-875.
68. Roerecke M, Kaczorowski J, Tobe SW, Gmel G, Hasan OSM, Rehm J. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. Lancet Public Health. 2017;2:e108–e120. doi: 10.1016/S2468-2667(17)30003-8.
69. Schnohr P, Jensen JS, Scharling H, Nordestgaard BG. Coronary heart disease risk factors ranked by importance for the individual and community: A 21 year follow-up of 12,000 men and women from the Copenhagen City Heart Study. European Heart Journal. 2002;23:620–626.
70. Leong DP, Smyth A, Teo KK, et al. Patterns of alcohol consumption and myocardial infarction risk: Observations from 52 countries in the INTERHEART case-control study. Circulation. 2014;130(5):390–398.

71. Bagnardi V, Zatonski W, Scotti L, La Vecchia C, Corrao G. Does drinking pattern modify the effect of alcohol on the risk of coronary heart disease? Evidence from a meta-analysis. J Epidemiol Community Health 2008;62:615-9. 10.1136/jech.2007.065607.
72. Ronksley PE, Brien SE, Turner BJ, et al. Association of alcohol consumption with selected cardiovascular disease outcomes: A systematic review and meta-analysis. BMJ. 2011;342:d671.
73. Mostofsky E, Chahal HS, Mukamal KJ, et al. Alcohol and immediate risk of cardiovascular events: A systematic review and dose-response meta-analysis. Circulation. 2016;133(10):979–987.
74. Au Yeung SL, Jiang C, Cheng KK, et al. Moderate alcohol use and cardiovascular disease from Mendelian randomization. PLoS One. 2013;8(7):e68054. Published 2013 Jul 16. doi:10.1371/journal.pone.0068054.
75. Yun KE, Chang Y, Yun SC, Davey Smith G, Ryu S, Cho SI, Chung EC, Shin H, Khang YH. Alcohol and coronary artery calcification: an investigation using alcohol flushing as an instrumental variable. Int J Epidemiol. 2017 Jun 1;46(3):950-962. doi: 10.1093/ije/dyw237.
76. Mori TA, Burke V, Beilin LJ, Puddey IB. Randomized controlled intervention of the effects of alcohol on blood pressure in premenopausal women. Hypertension. 2015;66(3):517–523.
77. Corrao G, Bagnardi V, Zambon A, La Vecchia C. A meta-analysis of alcohol consumption and the risk of 15 diseases. Prev Med 2004;38:613-9. 10.1016/j.ypmed.2003.11.027.
78. O'Keefe JH, Bhatti SK, Bajwa A, et al. Alcohol and cardiovascular health: the dose makes the poison...or the remedy. Mayo Clin Proc 2014; 89: 382–393.
79. O'Keefe EL, DiNicolantonio JJ, O'Keefe JH, et al. Alcohol and CV health: Jekyll and Hyde J-curves. Prog Cardiovasc Dis 2018; 61: 68–75.
80. Renaud S, de Lorgeril M. Wine, alcohol, platelets, and the French paradox for coronary heart disease. Lancet 1992;339:1523–1526.
81. Rimm EB, Klatsky A, Grobbee D, Stampfer MJ. Review of moderate alcohol consumption and reduced risk of coronary heart disease: is the effect due to beer, wine, or spirits. BMJ 1996;312:731–736.
82. Reynolds K, Lewis B, Nolen JD, Kinney GL, Sathya B, He J. Alcohol consumption and risk of stroke: a meta-analysis. JAMA. 2003;289:579–588.
83. Feigin VL, Rinkel GJ, Lawes CM, et al. Risk factors for subarachnoid hemorrhage: An updated systematic review of epidemiological studies. Stroke. 2005;36(12):2773–2780.
84. Ronksley PE, Brien SE, Turner BJ, et al. Association of alcohol consumption with selected cardiovascular disease outcomes: A systematic review and meta-analysis. BMJ. 2011;342:d671.
85. Zhang C, Qin YY, Chen Q, et al. Alcohol intake and risk of stroke: A dose-response meta-analysis of prospective studies. Internal Journal of Cardiology. 2014;174(3):669–677.
86. Larsson SC, Wallin A, Wolk A, Markus HS. Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. BMC Med. 2016;14(1):178. Published 2016 Nov 24. doi:10.1186/s12916-016-0721-4.
87. Millwood IY, Walters RG, Mei XW, et al. China Kadoorie Biobank Collaborative Group. Conventional and genetic evidence on alcohol and vascular disease aetiology: a prospective study of 500 000 men and women in China. Lancet. 2019;393:1831–1842. doi: 10.1016/S0140-6736(18)31772-0.
88. Larsson SC, Burgess S, Mason AM, Michaëlsson K. Alcohol Consumption and Cardiovascular Disease: A Mendelian Randomization Study. Circ Genom Precis Med. 2020 Jun;13(3):e002814. doi: 10.1161/CIRCGEN.119.002814.
89. Larsson SC, Orsini N, Wolk A. Alcohol consumption and risk of heart failure: A dose-response meta-analysis of prospective studies. European Journal of Heart Failure. 2015;17(4):367–373.
90. Wannamethee SG, Whincup PH, Lennon L, et al. Alcohol consumption and risk of incident heart failure in older men: A

prospective cohort study. Open Heart. 2015;2(1):e000266.

91. van Oort S, Beulens JWJ, van Ballegooijen AJ, Handoko ML, Larsson SC. Modifiable lifestyle factors and heart failure: A Mendelian randomization study. Am Heart J. 2020 Sep;227:64-73. doi: 10.1016/j.ahj.2020.06.007.)\
92. Lowenstein SR, Gabow PA, Cramer J, Oliva PB, Ratner K. The role of alcohol in new-onset atrial fibrillation. Arch Intern Med. 1983 Oct;143(10):1882-5.
93. Tonelo D, Providência R, Gonçalves L. Holiday heart syndrome revisited after 34 years. Arq Bras Cardiol. 2013 Aug;101(2):183-9. doi: 10.5935/abc.20130153.
94. Voskoboinik A, Prabhu S, Ling LH, Kalman JM, Kistler PM. Alcohol and Atrial Fibrillation: A Sobering Review. J Am Coll Cardiol. 2016 Dec 13;68(23):2567-2576. doi: 10.1016/j.jacc.2016.08.074.
95. Koskinen P, Kupari M, Leinonen H, Luomanmäki K. Alcohol and new onset atrial fibrillation: a case-control study of a current series. Br Heart J. 1987 May;57(5):468-73.
96. Mehra R. Global public health problem of sudden cardiac death. J. Electrocardiol. 2007;40:118–122. doi: 10.1016/j.jelectrocard.2007.06.023.
97. Hietanen S, Herajärvi J, Junttila J, Pakanen L, Huikuri HV, Liisanantti J. Characteristics of subjects with alcoholic cardiomyopathy and sudden cardiac death. Heart. 2020 May;106(9):686-690. doi: 10.1136/heartjnl-2019-315534.
98. Kauppila JP, Pakanen L, Porvari K, Vähätalo J, Holmström L, Perkiömäki JS, Huikuri HV, Junttila MJ. Blood alcohol levels in Finnish victims of non-ischaemic sudden cardiac death. Ann Med. 2021 Dec;53(1):413-419. doi: 10.1080/07853890.2021.1890204.
99. Perkiömäki J, Hookana E, Kaikkonen K, Junttila J, Kortelainen ML, Huikuri H. Blood alcohol in victims of sudden cardiac death in northern Finland. Europace. 2016 Jul;18(7):1006-9. doi: 10.1093/europace/euv341.
100. George A, Figueredo VM. Alcoholic cardiomyopathy: a review. J Card Fail. 2011 Oct;17(10):844-9. doi: 10.1016/j.cardfail.2011.05.008.
101. Day E., Rudd J.H.F. Alcohol use disorders and the heart. Addiction. 2019;114:1670–1678. doi: 10.1111/add.14703.
102. Sulaiman S, Yousef N, Benjamin MM, Sundararajan S, Wingert R, Wingert M, Mohammed A, Jahangir A. Burden of arrhythmia and electrophysiologic procedures in alcoholic cardiomyopathy hospitalizations. Int J Cardiol. 2020 Apr 1;304:61-68. doi: 10.1016/j.ijcard.2020.01.068.
103. Guzzo-Merello G., Dominguez F., González-López E., Cobo-Marcos M., Gómez-Bueno M., Fernández-Lozano I., Millán I., Segovia J., Alonso-Pulpon L., Garcia-Pavia P. Malignant ventricular arrhythmias in alcoholic cardiomyopathy. Int. J. Cardiol. 2015;199:99–105. doi: 10.1016/j.ijcard.2015.07.029.
104. Fernández-Solà J. Cardiovascular risks and benefits of moderate and heavy alcohol consumption. Nat. Rev. Cardiol. 2015;12:576–587. doi: 10.1038/nrcardio.2015.91.
105. Manthey J., Rehm J. Mortality from Alcoholic Cardiomyopathy: Exploring the Gap between Estimated and Civil Registry Data. J. Clin Med. 2019;8:1137. doi: 10.3390/jcm8081137.
106. Stackelberg O, Wolk A, Eliasson K, et al. Lifestyle and risk of screening-detected abdominal aortic aneurysm in men. J Am Heart Assoc 2017;6:e004725.
107. Shirakawa T, Yamagishi K, Yatsuya H, et al. Alcohol consumption and mortality from aortic disease among Japanese men: the Japan Collaborative Cohort study. Atherosclerosis 2017;266:64–8.
108. Spencer SM, Trower AJ, Jia X, et al. Meta-analysis of the association between alcohol consumption and abdominal aortic aneurysm. Br J Surg 2017;104:1756–64. ; Han SA, Joh JH, Park HC. Risk factors for abdominal aortic aneurysm in the Korean population. Ann Vasc Surg 2017;41:135–40.
109. Wood AM, Kaptoge S, Butterworth AS, et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current

drinkers in 83 prospective studies. Lancet 2018;391:1513–23 4–6.

110. Li LY, Chien WC, Wang JC, Tzeng NS, Chung CH, Lin CY, Tsai SH. Association between abdominal aortic aneurysms and alcohol-related diseases. Medicine (Baltimore). 2020 Oct 30;99(44):e22968. doi: 10.1097/MD.0000000000022968.
111. Oikonomou E, Lazaros G, Tsalamandris S, et al. Alcohol Consumption and Aortic Root Dilatation: Insights from the Corinthia Study. Angiology. 2019 Nov;70(10):969-977. doi: 10.1177/0003319719848172.
112. Wen Z, Yu D, Zhang W, Fan C, Hu L, Feng Y, Yang L, Wu Z, Chen R, Yin KJ, Mo X. Association between alcohol consumption during pregnancy and risks of congenital heart defects in offspring: meta-analysis of epidemiological observational studies. Ital J Pediatr. 2016 Feb 3;42:12. doi: 10.1186/s13052-016-0222-2.
113. Kurita H, Motoki N, Inaba Y, Misawa Y, Ohira S, Kanai M, Tsukahara T, Nomiyama T; Japan Environment and Children's Study (JECS) Group. Maternal alcohol consumption and risk of offspring with congenital malformation: the Japan Environment and Children's Study. Pediatr Res. 2020 Nov 23. doi: 10.1038/s41390-020-01274-9.
114. Chen Z, Li S, Guo L, Peng X, Liu Y. Prenatal alcohol exposure induced congenital heart diseases: From bench to bedside. Birth Defects Res. 2020 Jun 24. doi: 10.1002/bdr2.1743.
115. Caputo C, Wood E, Jabbour L. Impact of fetal alcohol exposure on body systems: A systematic review. Birth Defects Res C Embryo Today. 2016 Jun;108(2):174-80. doi: 10.1002/bdrc.21129.
116. Denny L, Coles S, Blitz R. Fetal Alcohol Syndrome and Fetal Alcohol Spectrum Disorders. Am Fam Physician. 2017 Oct 15;96(8):515-522.
117. Li Q, Yao H, Gu GJ, Ma ZH, Wu DK, Wu G, Chen YM, Luo TN. [Association between maternal alcohol consumption and risk of congenital heart disease in offspring: a Meta analysis]. Zhongguo Dang Dai Er Ke Za Zhi. 2020 Jun;22(6):643-650. Chinese. doi: 10.7499/j.issn.1008-8830.1912083.
118. Baumgartner H, Bonhoeffer P, De Groot NM, et al; Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC); Association for European Paediatric Cardiology (AEPC); ESC Committee for Practice Guidelines (CPG). ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). Eur Heart J. 2010 Dec;31(23):2915-57. doi: 10.1093/eurheartj/ehq249.
119. Caruana M, Grech V. Lifestyle Habits among Adult Congenital Heart Disease Patients in Malta. Congenit Heart Dis. 2016 Jul;11(4):332-40. doi: 10.1111/chd.12366.
120. Freimark D, Aleksic I, Trento A, Takkenberg JJ, Valenza M, Admon D, Blanche C, Queral CA, Azen CG, Czer LS. Hearts from donors with chronic alcohol use: a possible risk factor for death after heart transplantation. J Heart Lung Transplant. 1996 Feb;15(2):150-9.
121. De La Zerda DJ, Cohen O, Beygui RE, Kobashigawa J, Hekmat D, Laks H. Alcohol use in donors is a protective factor on recipients' outcome after heart transplantation. Transplantation. 2007 May 15;83(9):1214-8. doi: 10.1097/01.tp.0000261713.24244.ea.
122. Newman J, Liebo M, Lowes BD, Ilias Basha H, Peled Y, Cendrowski E, Zolty R, Douglas D, Um JY, McGee E Jr, Heroux A, Raichlin E. The effect of donor alcohol abuse on outcomes following heart transplantation. Clin Transplant. 2019 Feb;33(2):e13461. doi: 10.1111/ctr.13461.
123. Fabsitz RR, Sidawy AN, Go O, et al. Prevalence of peripheral arterial disease and associated risk factors in American Indians: The Strong Heart Study. American Journal of Epidemiology. 1999;149(4):330–338.
124. Vliegenthart R, Geleijnse JM, Hofman A, et al. Alcohol consumption and risk of peripheral arterial disease: The Rotterdam Study. American Journal of Epidemiology. 2002;155(4):332–338.
125. Mukamal KJ, Kennedy M, Cushman M, et al. Alcohol consumption and lower extremity arterial disease among older adults: The Cardiovascular Health Study. American

Journal of Epidemiology. 2008;167(1):34–41.

126. Garcia-Diaz AM, Marchena PJ, Toril J, Arnedo G, Muñoz-Torrero JF, Yeste M, Aguilar E, Monreal M; FRENA Investigators. Alcohol consumption and outcome in stable outpatients with peripheral artery disease. J Vasc Surg. 2011 Oct;54(4):1081-7. doi: 10.1016/j.jvs.2011.03.285. PMID: 21684714.
127. Huang JY, Chen WK, Lin CL, Lai CY, Kao CH, Yang TY. Increased risk of peripheral arterial disease in patients with alcohol intoxication: A population-based retrospective cohort study. Alcohol. 2017 Dec;65:25-30. doi: 10.1016/j.alcohol.2017.06.003.
128. Larsson SC, Burgess S, Mason AM, Michaëlsson K. Alcohol Consumption and Cardiovascular Disease: A Mendelian Randomization Study. Circ Genom Precis Med. 2020 Jun;13(3):e002814. doi: 10.1161/CIRCGEN.119.002814.
129. Wang XM, Bai YJ, Yang YB, Li JH, Tang Y, Han P. Alcohol intake and risk of erectile dysfunction: a dose-response meta-analysis of observational studies. Int J Impot Res. 2018 Nov;30(6):342-351. doi: 10.1038/s41443-018-0022-x.
130. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, et al. Sexual function in men older than 50 years of age: results from the health professionals follow-up study. Ann Intern Med. 2003;139:161–8.
131. Kalter-Leibovici O, Wainstein J, Ziv A, Harman-Bohem I, Murad H, et al. Clinical, socioeconomic, and lifestyle parameters associated with erectile dysfunction among diabetic men. Diabetes Care. 2005;28:1739–44.
132. Gaborit FS, Overvad K, Nørgaard M, et al. Alcohol intake and risk of Venous Thromboembolism: A Danish Follow-up Study. Thromb Haemost 2013; 110: 39-45. dx.doi.org/10.1160/TH12-10-0790.
133. Lutsey PL, Steffen LM, Virnig BA, Folsom AR. Diet and incident venous thromboembolism: the Iowa Women's Health Study. Am Heart J. (2009) 157:1081–7. doi: 10.1016/j.ahj.2009.04.003.
134. Saleh T, Matta F, Alali F, Stein PD. Venous thromboembolism with chronic liver disease. Am J Med. 2011 Jan;124(1):64-8. doi: 10.1016/j.amjmed.2010.08.014.
135. Hanna K, Khalid A, Hamidi M, Gries L, Haddadin Z, Kulvatunyou N, Zeeshan M, Joseph B. Chronic Alcohol Consumption and Risk of Deep Venous Thrombosis: A Propensity-Matched Analysis. J Surg Res. 2019 Dec;244:251-256. doi: 10.1016/j.jss.2019.06.067.
136. Grigorian A, Gambhir S, Al-Khouja L, Gabriel V, Schubl SD, Nastanski F, Lekawa M, Joe V, Nahmias J. Decreased incidence of venous thromboembolism found in trauma patients with positive blood alcohol concentration on admission. Am J Drug Alcohol Abuse. 2019;45(1):77-83. doi: 10.1080/00952990.2018.1504951.
137. Hansen-Krone IJ, Brækkan SK, Enga KF, Wilsgaard T, Hansen JB. Alcohol consumption, types of alcoholic beverages and risk of venous thromboembolism - the Tromsø Study. Thromb Haemost. 2011 Aug;106(2):272-8. doi: 10.1160/TH11-01-0043.
138. Zöller B, Ji J, Sundquist J, Sundquist K. Alcohol use disorders are associated with venous thromboembolism. J Thromb Thrombolysis. 2015 Aug;40(2):167-73. doi: 10.1007/s11239-015-1168-8.
139. Mengyan Chen, Mingxia Ji, Tiejiang Chen, Xiaofei Hong and Yian Jia. Alcohol Consumption and Risk for Venous Thromboembolism: A Meta-Analysis of Prospective Studies. Front. Nutr., 02 April 2020.
140. Chakravorty S, Chaudhary NS, Brower KJ. Alcohol Dependence and Its Relationship With Insomnia and Other Sleep Disorders. Alcohol Clin Exp Res. 2016 Nov;40(11):2271-2282. doi: 10.1111/acer.13217.
141. Pan CS, Ju TR, Lee CC, Chen YP, Hsu CY, Hung DZ, Chen WK, Wang IK. Alcohol use disorder tied to development of chronic kidney disease: A nationwide database analysis. PLoS One. 2018 Sep 6;13(9):e0203410. doi: 10.1371/journal.pone.0203410.
142. Sayon-Orea C, Martinez-Gonzalez MA, Bes-Rastrollo M. Alcohol consumption and body

weight: a systematic review. Nutr Rev. 2011 Aug;69(8):419-31. doi: 10.1111/j.1753-4887.2011.00403.x.

143. Boden JM, Fergusson DM. Alcohol and depression. Addiction. 2011 May;106(5):906-14. doi: 10.1111/j.1360-0443.2010.03351.x.

144. Stamler J, Caggiula AW, Grandits GA. Relation of body mass and alcohol, nutrient, fiber, and caffeine intakes to blood pressure in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr 1997;65: 1 suppl: 338s–65s.