







## REVIEW ARTICLE

## Red Wine and Alcoholic Beverages: Evolution of Our Knowledge Focusing on All-Cause Morbidity and Mortality

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Pages: 105 - 109 / Published online: 18 December 2024

Cite this article: Ostojic M, Kovacevic-Preradovic T, Stanetic B, Vulic D, Djajic V, Bojic M. Red Wine and Alcoholic Beverages: Evolution of Our Knowledge Focusing on All-Cause Morbidity and Mortality. Sar Med J. 2024; 1(2): Online ahead of print.  10.70119/0018-24

**Original submission:** 23 October 2024; **Revised submission:** 27 October 2024; **Accepted:** 15 November 2024

### Abstract

Medical professionals have a responsibility to inform the public about contemporary research on alcohol consumption. Earlier health recommendations focused primarily on the link between alcohol and cardiovascular diseases. Over time, these guidelines have expanded to consider the broader impact of alcohol on all-cause morbidity and mortality. Unlike the tobacco industry, which remains profitable but faces strict regulations on marketing and lobbying, the alcohol industry benefits from fewer regulations. This allows alcohol manufacturers to freely promote their products and influence both federal and state policies. Clear emphasis on the importance of ceasing alcohol consumption is crucial, particularly in primary and secondary prevention efforts.

**Keywords:** cardiovascular diseases, alcoholics, prevention.

### INTRODUCTION

Even though the population in general, as well as medical professionals all over the world, have positive associations with red wine, imagining parties, celebrations, good times, and, of course, its health benefits for the cardiovascular system, partially due to resveratrol, the time has come to suppress the conditional reflex (1,2). Medical professionals must advise the population on contemporary research related to alcoholic beverages. That understanding has evolved (3, 4). Some time ago, on 17 September 2008, the author of this text gave an interview to "Politika", the oldest daily newspaper in the Balkans, about

the global epidemic of cardiovascular diseases, with a particular focus on Serbia. The interview, prominently featured on the front page, recommended that consuming 150 ml of red wine three to seven times a week could potentially reduce the incidence of cardiovascular diseases. This suggestion was made with the caveat that such consumption posed only a small health risk, as outlined in the recommendations. In the same interview, the author also recommended including fish, fruits, vegetables, nuts, and dark chocolate in one's diet, all of which, in combination with red wine, were calculated to lower the risk of

cardiovascular diseases by up to 75%. Soon after, an anonymous reader commented, "It was inappropriate for Professor Ostojic to promote alcohol consumption at all" (the original interview can be accessed upon request from Miodrag Ostojic's file). This thoughtful comment proved to be prescient, as it accurately anticipated future developments.

## OVERVIEW OF CLINICAL PRACTICE GUIDELINES

Guidelines for the prevention of cardiovascular diseases concerning alcohol use, especially red wine, were backed up by research, also saying that an increase in non-cardiovascular morbidity and mortality was not registered (4). However, new research contradicted the previous one. In retrospect, one may suspect that influences by different authorities have been involved in publishing guidelines relating to alcoholic beverages (6). In Table 1, Guidelines on alcoholic beverages from different sources in males and females regarding the amount of alcohol expressed in grams are presented in the time coordinate (7-13).

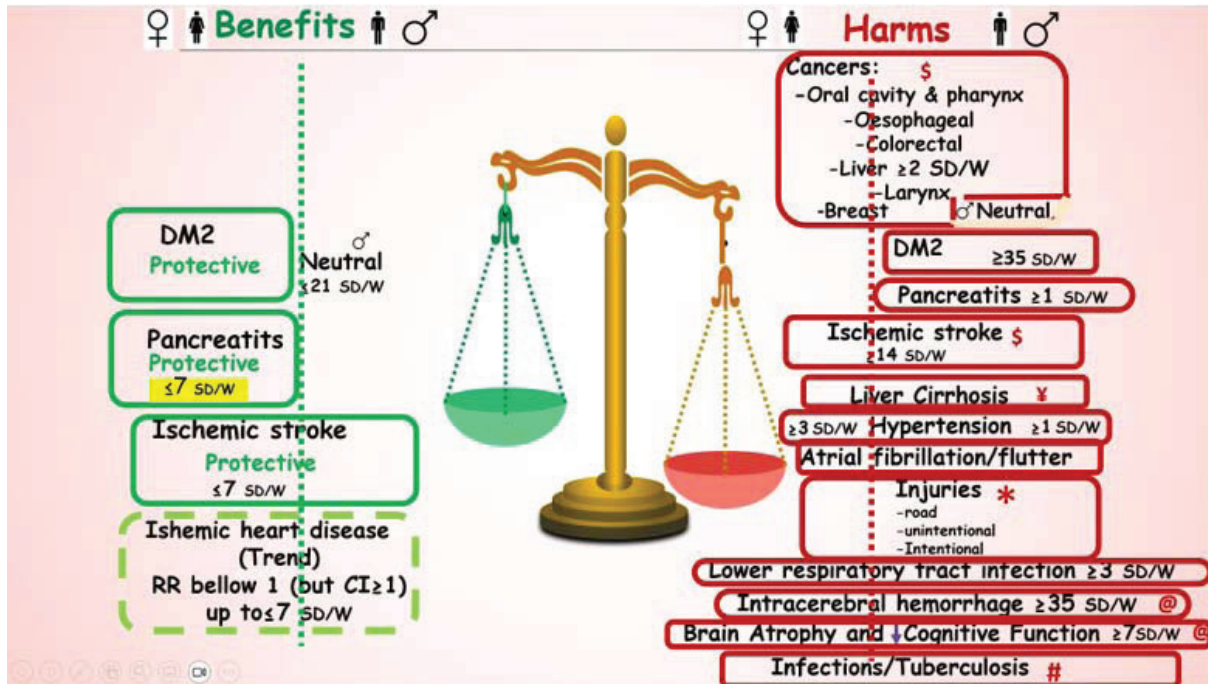
It could be appreciated that earlier recommendations were related to cardiovascular diseases, while later on all-cause morbidity and mortality were taken into account. The dose of alcohol was gradually decreased over time to come to zero dose considered to be safe. World Health Organization, as well

as the Canadian Guidance on Alcohol and Health, state that the risk of alcoholic beverages starts with the first drop. Recently, the German Nutrition Society issued the same statement. Is that a brand-new position? In 2015, the Netherlands guidelines recommended zero alcohol as the only safe (14). However, prominent regional societies like ESC, AHA/ACC, etc., did not consider so. In the context of the risk of alcohol consumption on carcinogenesis, which was announced approximately 30 years ago by WHO (15), the late-breaking news is the fight to put into effect Ireland's parliamentary act of 2018 which will impose labeling alcoholic beverage containers with a range of health information as of 2026, including a warning of the direct link between alcohol and fatal cancers. Twelve countries exporting alcohol within the World Trade Organization oppose this, with the justification that it will put barriers on trading between countries (16). A similar cancer warning on alcoholic beverage packages existed in the Yukon province of Canada from 2017 until 2018. However, due to threats of legal action by the alcohol industry, it was withdrawn. The empire (industry) strikes back (16). Compiling eight scientific reports (4) and the new progress report (17), some of which reported Disability-Adjusted Life Years (DALYs – taking into account morbidity as well as mortality) and years of life lost (YLLs), the author presented the scale with benefits versus harms of consuming alcoholic beverages in Figure 1.

**Table 1. Guidelines on alcoholic beverages from different sources in males and females regarding the amount of alcohol expressed in grams are presented in the time coordinate**

Year of publication	Title	Safe dose	
		Females G per day or week	Males G per day or week
2024 (Aug 16)	The German Nutrition Society (DGE) (position statement)	0 (Zero) Daily	
2023 (Jan 23)	Canada's Guidance on Alcohol and Health	0 (Zero) Daily	28g Weekly Low Risk
2023 (Jan 4)	World Health Organization	0 (Zero) Daily	
2021	New Australian Treatment Guidelines for the treatment of alcohol problems: an overview of recommendations	11 Daily 80 Weekly Not >40g daily	
2021	ESC Guidelines on Cardiovascular Disease Prevention in Clinical practice	14 Daily 100 Weekly	
2020	Dietary Guidelines for Americas	14 Daily	28 Daily
2019	2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease	14 Daily	28 Daily

ESC- European Society of Cardiology; ACC/AHA - American College of Cardiology/American Heart Association



CI - Confidence Intervals; RR - Relative Risk; SD/W - Standard Alcoholic Drink per Week, 1 SD = 13.45 grams of Alcohol (Canada)

**Figure 1. Alcohol effects sorted by the number of standard drinks are estimated by relative risk and confidence intervals and diagnostic criteria for different diseases. If a dashed line crosses the rectangle, it refers to both genders; if the rectangle is left or right of a dashed line, it refers to females and males, respectively. In males, alcohol consumption is neutral for breast cancer. If the number of standard alcoholic drinks per week (SD/W) is not filled in, it is  $\geq 1$ . 1 SD equals 13.45 g of Alcohol (Canada).**

The highest relative proportions of Disability-Adjusted Life Years (DALYs) for causes associated with harmful alcohol consumption were reported by Global Burden of Diseases researchers by super-region, age group, and sex in 2020 (§ Cancers: high-income countries in age group 40–64 years; ¥ liver cirrhosis: Central Europe, Eastern Europe, and Central Asia, Latin America and Caribbean, South Asia and Sub-Saharan Africa, especially males; \* injuries: 15–39 years in all regions; @ intra cerebral hemorrhage and brain atrophy and decrease in cognitive function: high-income countries in age group  $\geq 65$  years, hypertension, high body mass index and low educational level are predisposing risk factors; # tuberculosis: low-income countries in the age group 15–40 years ).

As far as ischemic heart disease is concerned, up to seven standard drinks (1 SD/W 13.45 g alcohol) per week, there was a trend toward decrease. Still, as CI is  $\geq 1$ , it was not significant, but it was significant for ischemic stroke, Diabetes Mellitus type 2 in both genders. Interestingly, there was only a protective value of up to 7 SD/W for pancreatitis in women. However, the harms presented on the right side of the scale were more numerous. All cancers were more frequent (except breast in males). Alcoholic cardiomyopathy is not presented in the graph, as it was assumed that it is encompassed with atrial fibrillation and hypertension. However, new findings in the small series of patients have pointed in the direction that alcoholic cardiomyopathy may be a distinct disease with a genetic predisposition (18).

Although Figure 1 is self-explanatory, it accentuates brain changes and a decline in cognitive function (19, 20). As previously sta-

ted, most of our scientific knowledge in these recommendations is based on observational studies, which point out a link between alcohol consumption and different illnesses but no direct cause-consequence relation. Our calculations are usually considered correct until proven wrong. Everyone knows at least someone who has spent their life drinking alcohol daily and yet lived a very long life. To be clear, in this text we do not discuss or refer to alcoholism as an addiction but rather to the effects of consuming small or moderate doses of alcohol. In nutritional medicine, randomized controlled trials are very scarce. That is therefore the argument of the alcohol industry, to strike back. In contrast with the tobacco industry, which is still profitable, and whose manufacturers are strictly regulated in the ways they market their products or influence federal and state institutions to promote their interests, the food and alcohol manufacturing industry enjoys the lack

of regulations, which enables the alcohol manufacturing industry to promote its interests vigorously and freely by marketing their products and influencing and lobbying the federal and state governing and regulatory bodies (21-23). Very recently, in September 2024, the American Association on Cancer Research published that alcohol consumption is the third reversible cause of cancer after smoking cigarettes and obesity, appealing for the cancer warning label on alcoholic beverage packages (17). Concerning warning labeling, a similar war against the tobacco industry was won back in 1965 in the USA Senate and adopted by WHO in 2003. Genetic links and markers regarding susceptibility towards carcinogenesis elucidated by alcohol are still incomplete. However, as discovered in pharmacogenetics, hereditary factors may be crucial in substance-individual reaction response. Being aware of the fact, the industry of alcoholic beverages opted for one of the exclusion criteria to be a family history of cancer in the randomized controlled "Moderate Alcohol and Cardiovascular Health Clinical Trials (MACH)", which was prematurely terminated only after recruiting 104 of 7800 planned healthy individuals due to unclear reasons (supported by \$ 100 million, but two-thirds coming from alcohol industry) (24). Of particular note is that the proportion of drinkers worldwide has remained the same since 1990; due to population growth, absolute numbers increased from 983 million to 1.34 billion in 2020. An especially worrisome fact is that 59.1% belong to the 15-to-39-year age group (25). The current controversy, with conflicting guidelines for alcoholic beverage consumption, may stimulate more fundamental investigations up to genetic ones and find the cause-effect relations in the era of next-generation evidence-based medicine (26), i.e., precision medicine. Hopefully, we may come closer to discovering

the causes (etiopathogenesis) of cancers and many other diseases, enabling us to predict reactions to alcoholic beverages by each person, not just in the population. "Canada has a right to know" (8). "The risk starts with the first drop" (9). The planet should not ignore these dramatic warnings.

## CONCLUSION

Alcohol consumption is linearly associated with an increased risk of all-cause morbidity and mortality. Non-pharmacological measures, particularly the reduction of alcohol consumption (similar to the approaches established for smoking cigarettes) should be integral components of primary and secondary prevention strategies that take a holistic approach. Even optimized pharmacological and other lifestyle interventions may be insufficient and ineffective without addressing these factors.

**Acknowledgment:** None.

**Authors' Contributions:** Conceptualization: Miodrag Ostojic. Formal analysis: Miodrag Ostojic, Tamara Kovacevic-Preradovic, Bojan Stanetic, Dusko Vulic, Vlado Djajic, Milovan Bojic. Project administration: Miodrag Ostojic, Milovan Bojic. Software: Miodrag Ostojic, Tamara Kovacevic-Preradovic, Bojan Stanetic, Dusko Vulic, Vlado Djajic, Milovan Bojic. Visualization: Miodrag Ostojic, Tamara Kovacevic-Preradovic, Milovan Bojic. Writing – original draft: Miodrag Ostojic, Tamara Kovacevic-Preradovic, Bojan Stanetic, Dusko Vulic, Vlado Djajic, Milovan Bojic. Writing – review & editing: Miodrag Ostojic, Tamara Kovacevic-Preradovic, Bojan Stanetic, Dusko Vulic, Vlado Djajic, Milovan Bojic.

**Financial support and sponsorship:** There was no funding.

**Conflict of interest:** The authors have nothing to disclose.

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