



Alcohol use and Alcohol Use Disorder

Stefano Gitto¹, Lucia Golfieri², Margherita Falcini¹, Fabio Caputo^{3,4}

¹Department of Experimental and Clinical Medicine, University of Florence, Italy

²S.S. Servizio di psicologia clinica ospedaliera, Direzione sanitaria, AOU di Bologna IRCCS.

³Centre for the Study and Treatment of Alcohol-Related Diseases, Department of Translational Medicine, University of Ferrara, Ferrara, Italy.

⁴Department of Internal Medicine, SS Annunziata Hospital, University of Ferrara, Cento (Ferrara), Italy.

Corresponding Author: Fabio Caputo, MD; e-mail: fabio.caputo@unife.it

ABSTRACT

Alcohol habit represents a major public health problem, being a chief cause of both morbidity and mortality. Binge drinking, a particularly dangerous alcohol intake pattern, has been growing in the last years, especially in younger people. Alcohol use disorder is defined by the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-V) as the spectrum of a maladaptive pattern of alcohol intake with a noteworthy clinical impact. It is important to underline that no amount of alcohol is risk-free. The present review analyzes and discusses the evolution of alcohol habit, the complex clinical burden and the future perspectives with an interdisciplinary approach.

KEYWORDS

ALCOHOL USE DISORDER

BINGE DRINKING

LIFESTYLE

INTRODUCTION

Disorders due to an unhealthy lifestyle represent a major public health challenge¹⁻³.

In 2012, 38 million people died of a noncommunicable disease (NCD), which accounted for 68% of deaths worldwide4,5. NCDs include cardiovascular diseases, cancer, chronic respiratory diseases and diabetes, and by 2030, NCDs will be the leading cause of death in the world5. Notably, the global NCD burden is mainly associated (almost half of the cases) with the following four behavioural risk factors: tobacco use, unhealthy diets, physical inactivity, and habitual alcohol consumption².

Habitual alcohol consumption certainly represents a noteworthy health problem and a main cause of death in Western countries⁶.

In Europe, alcohol is the third most common risk factor for morbidity (after smoking and hypertension) and, in 2016, its use accounted for 10% of deaths^{7,8}. Remarkably, alcohol is a risk factor for more than 200 disorders, such as cancer, liver disease, and neuropsychiatric diseases, and is also a major cause of disability and both domestic and road accidents⁹⁻¹².

In light of the significant clinical as well as social impact of alcohol use, the aim of the present non-systematic overview is to analyze and discuss the evolution of alcohol consumption patterns, the clinical burden, and future prospects from an interdisciplinary point of view.

NUTRIMENTUM ET CURAE

Nutrimentum et Curae is an Indicon S.r.l. project

1



PATTERNS OF ALCOHOL CONSUMPTION

As of today, studies concerning possible harmless levels of alcohol intake are inconclusive⁶.

Notably, the "International Statistical Classification of Diseases and Related Health Problems 10th Revision" defines alcohol consumption as "harmful" when it causes a health impairment, whether mental or physical¹³. The World Health Organization (WHO) defined it as "light-to-moderate" drinking less than 20 g of pure alcohol per day (that is equivalent to 1.5 litres of wine or less than 3.5 litres of beer or less than 450 millilitres of spirits per week). "Heavy" drinking can be defined in the following way: for women, 8 drinks or more per week; for men, 15 drinks or more per week¹⁴. Again, according to WHO, heavy episodic drinking is a specific type of alcohol intake defined as consumption of 60 g or more of pure alcohol on at least one occasion in the past 30 days¹⁴.

The definitions of alcohol use patterns, such as the type of drinks and the length of drinking, are critical in clinical practice to assess and evaluate alcohol-related damage^{15,16}. A recent study has supported a potential change in the global view of alcohol consumption¹⁷. Its authors conducted a large multi-center systematic review covering a long period of time (from 1990 to 2016). Alcohol was the seventh most significant risk factor for both deaths and disability-adjusted life years, accounting for 10% of mortality in young people (aged 15-49). The authors demonstrated unequivocally that the risk of all-cause mortality, and specifically of cancer, increases with rising levels of alcohol intake. They concluded that the level of intake that effectively minimizes health damage can only be zero.

BINGE DRINKING

Binge drinking (BD) is a specific type of alcohol intake defined as a pattern of drinking leading to a blood alcohol concentration of 0.08 grams per deciliter (0.08%) or higher. It occurs after a woman consumes 4 drinks or a man 5 drinks in a 2-hour time frame¹⁴. BD is a growing public health problem, specifically, in most cases, for young people¹⁴.

Rapid and huge alcohol intake can lead to a blood/ethanol concentration over 80 mg/dL, particularly in very young people (<18 years)¹⁸. A recent cross-sectional study of Italian adolescents19 demonstrated a significant association between BD and Alcohol Use Disorder (AUD). Indeed, BD can morph into AUD with potentially severe clinical effects, an increased burden of disease and relevant socioeconomic costs²⁰.

Furthermore, compared to chronic alcohol consu-

mption, BD may involve a higher risk of acute and/ or chronic liver damage²¹, an increase in gut permeability and bacterial translocation²², fat accumulation, a pro-inflammatory state and, simultaneously, immunosuppression²³, in addition to precocious brain dysfunction and a higher incidence of both cardiovascular and gastrointestinal disorders²⁴.

Current public programs and, more in general, initiatives aimed at preventing alcohol consumption among youngsters have filed to overcome or significantly address the problem²⁵.

ALCOHOL USE DISORDER

AUD is defined by the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-V) as the spectrum of a maladaptive pattern of alcohol intake with a significant clinical impact²⁶. The definition of AUD includes a collection of DSM-IV abuse and dependence criteria with "craving" as a new parameter. AUD is diagnosed when at least two diagnostic criteria are present during observation for 12 months²⁶. AUD can be classified according to levels of severity and criteria (mild, 2-3 criteria; moderate, 4-5 criteria; and severe, ≥ 6)²⁶. This definition of AUD should help to improve the previous dichotomous differentiation between "alcoholic" and "non-alcoholic" which ultimately favoured the social stigma historically associated with alcohol abuse²⁷.

Another instrument describing AUD is the International Classification of Disease (ICD), with the 11th review available since January 1, 2022^{28.}

Chapter 6 of the ICD-11, "Mental, behavioral and neurodevelopmental disorders" (MBND), includes in the 12th section a new grouping of conditions called "Disorders due to Substance Use and Addictive Behaviors" which are described as follows: "Disorders due to substance use and addictive behaviors are mental and behavioral disorders that develop as a result of the use of predominantly psychoactive substances, including medications, or specific repetitive rewarding and reinforcing behaviors"²⁸.

The main innovations of ICD-11, compared to ICD-10, are the larger groups of psychoactive substances, the introduction of single episodes of substance use, the introduction of harmful patterns of substance use and severity qualifiers for substance intoxication, as well as the new category "Disorders due to addictive behaviours"^{28,29}.

The introduction of single episodes of substance use and harmful patterns of substance use are important steps. ICD-10 used only "Substance dependence" and "Harmful substance use" classifications while in the



ICD-11 the primary diagnosis classes are "Substance dependence", "Harmful Pattern of Psychoactive Substance Use" and "Episode of Harmful Psychoactive Substance Use"^{28,29}. The new categories are hierarchical and mutually exclusive, so only one can diagnosed for one substance group, eliminating overlapping and ambiguity^{28,29}.

The new definitions adopted by ICD-11 call for a renewed public health response and policies fostering the multi-professional and multidisciplinary management of alcohol and substance abuse therapy, giving these forms of addiction new chances of reaching the United Nations 2030 Agenda Sustainable Development Goals^{28,29}.

However, interestingly, Rehm et al³⁰ underlined that although the ICD-11 can help clinicians define the most severe forms of AUD, it should be complemented with other tools to enhance both prevention and public health actions.

MODERATE DRINKING: FROM CANCER RISK TO THE REDUCTION OF MORTALITY. ARE WE AT THE END OF THE LINE OF THIS CONTROVERSIAL ISSUE?

In the past three decades, several studies have demonstrated the existence of so called "J shaped": subjects with moderate drinking (1-2 drinks per day, almost 10-20 g of alcohol) who have a reduced risk of mortality (irrespective of the quality of drinking) compared to people who do not drink alcohol^{31,32}.

However, a paper recently appeared in the Lancet analyses all previously published studies and shows a decrease in the protective amount of alcohol, down to 5 g per day (almost $\frac{1}{2}$ unit of alcohol per day) drastically redefining the protective quantity of alcohol intake³³.

In addition, another recent study has clearly shown that the methodology of studies published from the beginning of the 90s was inaccurate because only the quantity of alcohol consumed was recorded, while the lifestyle of subjects was not considered in the analysis of the data³⁴. Indeed, in this cohort study of 371 463 individuals adjusted for coincident, favourable lifestyle factors attenuated the observational benefits of modest alcohol intake: moderate drinking is not directly responsible for the reduction in mortality risk, but a good lifestyle (exercise, a Mediterranean diet with plenty of fruit and vegetables, as well as an active social life) is the real factor in the reduction of this risk³⁴. Prior meta-analysis confirms the following conclusion: mortality risk from alcohol is significantly altered by study design and characteristics, and adjusting for these factors shows that low-volume alcohol consumption has no net mortality benefit compared to lifelong abstention or occasional drinking³⁵.

Another recent systematic review and meta-analysis³⁶ of 107 cohort studies involving more than 4.8 million participants found no significant reduction in the risk of all-cause mortality for drinkers who consumed less than 25 g of ethanol per day compared with lifelong non-drinkers after adjustment for key study characteristics such as median age and the gender of study cohorts: low-volume alcohol drinking was not associated with protection against death from all causes definitively ruling out so-called J shaped subjects.

Furthermore, two recent narrative reviews^{32,37} have focused attention on wine, in particular red wine, as differing from other beverages: the intake of low amounts of wine is protective due to the increased quantity of flavonoids or other elements; however, this review cites papers that adopted the uncorrected method of analysis mentioned above so its conclusions are open to question. Moreover, it is worth noting that, in the Mediterranean Diet (rich in fruit and vegetables), alcohol is optional, indicating that alcohol intake does not necessarily have a positive effect over and above those of the diet itself³⁸.

In the past two decades, the International Agency for Research on Cancer, supported by the WHO, has classified alcohol as a Group 1 carcinogen, causally associated with the development of cancers of the upper digestive tract and liver, with sufficient evidence of a positive association with colorectal and breast cancer, irrespective of the type of alcoholic drink and even with moderate drinking^{39,40}. This is the result of several studies which have shown that even moderate alcohol consumption (1 drink per day) and not only excessive alcohol intake is responsible for the increased risk of some forms of cancer, in particular breast cancer in females⁴¹. Until now, this association cannot be disproved⁴². Therefore, at present, it cannot be asserted assert that moderate drinking is safe or protects health. No amount of alcohol is safe. The WHO definition requires greater care: a moderate intake of alcohol is low risk but not safe; the more we drink the greater the risk of numerous diseases⁴³.

The general population should be informed clearly of this. No amount of alcohol is safe, irrespective of the quantity and quality of drinking. Properly informed, people may of course decide to take the risk.



REMARKS AND CONCLUSIONS

Alcohol consumption is one of the main risk factors for countless pathological conditions and social problems, drastically impacting on public health.

Over the past years, consumption patterns have changed and those with a high risk of organ damage, such as binge drinking, have grown gradually, especially in the younger generations.

Recent evidence shows that a safe consumption threshold cannot be established. Therefore, full awareness of the risks is necessary to reduce the harm to public health. Public and private institutions should provide more information, training and knowledge and future social, psychological, and clinical studies should investigate the mechanisms connecting various addictions to prevent switching from one addiction to another and to limit the damage to public health of the addictions themselves.

In conclusion, habitual alcohol consumption should be considered part of a lifestyle deserving a multidisciplinary approach. Proper nutrition and exercise should be vigorously promoted starting with the younger generation.

Conflict of interest statement

Authors have no conflicts to declare.

References

1. Allen L. Are we facing a noncommunicable disease pandemic? J Epidemiol Glob Health. 2017; 7(1): 5-9.

2. Toebes B, Hesselman M, van Dijk JP, Herman J. Curbing the lifestyle disease pandemic: making progress on an interdisciplinary research agenda for law and policy interventions. BMC Int Health Hum Rights. 2017; 17(1): 25.

3. Sharma M, Majumdar PK. Occupational lifestyle diseases: An emerging issue. Indian J Occup Environ Med. 2009; 13(3): 109-112.

4. https://www.who.int/news-room/fact-sheets/detail/ noncommunicable diseases#:~:text=The%20main%20 types%20of%20NCD,disease%20and%20asthma)%20and%20diabetes.. Accessed Nov 14, 2023.

5.https://www.who.int/publications-detail-redirect/9789241564854. Accessed 6 Mar 2017.

6. Addolorato G, Abenavoli L, Dallio M, Federico A, Germani G, Gitto S, Leandro G, Loguercio C, Marra F, Stasi E. Alcohol associated liver disease 2020: A clinical practice guideline by the Italian Association for the Study of the Liver (AISF). Dig Liver Dis. 2020 Apr; 52(4): 374-391. Doi: 10.1016/j.dld.2019.12.008.

7. World Health Organization, Geneva. Switzerland Global status report on alcohol and health, 2014.

8. World Health Organization, Geneva. Switzerland

Global status report on alcohol and health, 2018.

9. GBD 2013 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015; 386: 2287-2323.

10. Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, Altieri A, Cogliano V; WHO International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of alcoholic beverages. Lancet Oncol. 2007; 8: 292-293.

11. Shield KD, Parry C, Rehm J. Chronic diseases and conditions related to alcohol use. Alcohol Res. 2013; 35: 155-173.

12. Stewart BW, Wild CP. International Agency for Research on Cancer. World Cancer Report; 2014.

13. World Health Organization. International Statistical Classification of Diseases and Related Health Problems 10th Revision [Internet]. Geneva (CH): WHO, c2011 [cited 2020 Mar 5]. Available from: https://www.who. int/ classifications/icd/ICD10Volume2_en_2010.pdf.

14.https://www.who.int/data/gho/indicator-metadata-registry/imr-details/459.

 European Association for the Study of the Liver.
EASL clinical practice guidelines: management of alcohol related liver disease. J Hepatol. 2018; 69: 154-181.
Gitto S, Aspite S, Golfieri L, Caputo F, Vizzutti F, Grandi S, Patussi V, Marra F. Alcohol use disorder and liver transplant: new perspectives and critical issues.
Korean J Intern Med. 2020 Jul;35(4):797-810. Doi: 10.3904/kjim.2019.409.

17. GBD 2016 Alcohol Collaborators. 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.

18. Fillmore MT, Jude R. Defining "binge" drinking as five drinks per occasion or drinking to a.08% BAC: which is more sensitive to risk? Am J Addict. 2011; 20: 468-475.

19. Addolorato G, Vassallo GA, Antonelli G, Antonelli M, Tarli C, Mirijello A, Agyei-Nkansah A, Mentella MC, Ferrarese D, Mora V, Barbàra M, Maida M, Cammà C, Gasbarrini A; Alcohol Related Disease Consortium. Binge Drinking among adolescents is related to the development of alcohol use disorders: results from a cross-sectional study. Sci Rep. 2018; 8: 12624.

20. Cederbaum AI. Alcohol metabolism. Clin Liver Dis 2012; 16: 667-685.

21. Åberg F, Helenius-Hietala J, Puukka P, Jula A. Binge drinking and the risk of liver events: a population-based cohort study. Liver Int 2017; 37: 1373-1381.



22. Bala S, Marcos M, Gattu A, Catalano D, Szabo G. Acute binge drinking increases serum endotoxin and bacterial DNA levels in healthy individuals. PLoS One. 2014; 9: e96864.

23. Afshar M, Richards S, Mann D, Cross A, Smith GB, Netzer G, Kovacs E, Hasday J. Acute immunomodulatory effects of binge alcohol ingestion. Acute immunomodulatory effects of binge alcohol ingestion. Alcohol. 2015; 49: 57-64.

24. Sundell L, Salomaa V, Vartiainen E, Poikolainen K, Laatikainen T. Increased stroke risk is related to a binge drinking habit. Stroke. 2008; 39: 3179-3184.

25. Georgie JM, Sean H, Deborah MC, Matthew H, Rona C. Peer-led interventions to prevent tobacco, alcohol and/or drug use among young people aged 11-21 years: a systematic review and meta-analysis. Addiction. 2016; 111: 391-407.

26. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders DSM-5TM. 5th ed. Arlington (VA): American Psychiatric Publishing, 2013.

27. Rehm J, Anderson P, Manthey J, et al. Alcohol use disorders in primary health care: what do we know and where do we go? Alcohol Alcohol 2016; 51: 422-427. 28. Available from: https://icd.who.int/en.

29. Saunders JB, Degenhardt L, Reed GM, Poznyak V. Alcohol Use Disorders in ICD-11: Past, Present, and Future. 2019. Alcoholism 2019; 43(11)2296-2300.

30. Rehm J, Heilig M, Gual A. ICD-11 for Alcohol Use Disorders: Not a Convincing Answer to the Challenges. Alcohol Clin Exp Res. 2019 Nov;43(11):2296-2300. Doi: 10.1111/acer.14182.

31. Thun MJ, Peto R, Lopez AD, Monaco JH, Henley SJ, Heath CW Jr, Doll R. Alcohol consumption and mortality among middle-aged and elderly U.S. adults. N Engl J Med. 1997 Dec 11;337(24):1705-14. Doi: 10.1056/NEJM199712113372401.

32. Hrelia S, Di Renzo L, Bavaresco L, Bernardi E, Malaguti M, Giacosa A. Nutrients. Moderate Wine Consumption and Health: A Narrative Review. 2022; 15(1): 175. Doi: 10.3390/nu15010175.

33. GBD 2020 Alcohol Collaborators. Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020. Lancet. 2022; 400(10347): 185-235. Doi: 10.1016/S0140-6736(22)00847-9. 34. Biddinger KJ, Emdin CA, Haas ME, Wang M, Hindy G, Ellinor PT, Kathiresan S, Khera AV, Aragam KG Association of Habitual Alcohol Intake With Risk of Cardiovascular Disease..JAMA Netw Open. 2022; 5(3): e223849. Doi: 10.1001/jamanetworkopen.2022.384.

35. Stockwell T, Zhao J, Panwar S, Roemer A, Naimi T, Chikritzhs T. 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(2): 185-198. Doi: 10.15288/jsad.2016.77.185).

36. Zhao J, Stockwell T, Naimi T, Churchill S, Clay J, Sherk A. Association Between Daily Alcohol Intake and Risk of All-Cause Mortality: A Systematic Review and Meta-analyses. JAMA Netw Open. 2023; 6(3): e236185. Doi: 10.1001/jamanetworkopen.2023.6185.

37. Serio F, Imbriani G, Acito M, Moretti M, Fanizzi FP, De Donno A, Valacchi G. Moderate red wine intake and cardiovascular health protection: a literature review. Food Funct. 2023; 14(14): 6346-6362. Doi: 10.1039/d3fo01004j.

38. Santos-Buelga C, González-Manzano S, González-Paramás AM. Wine, Polyphenols, and Mediterranean Diets. What Else Is There to Say? Molecules. 2021; 26(18): 5537. Doi: 10.3390/molecules26185537.

39. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 2012; Volume 96.

40. Alcohol Consumption and Ethyl Carbamate; International Agency for Research on Cancer: Lyon, France, 2010.

41. GBD 2019 Cancer Risk Factors Collaborators. The global burden of cancer attributable to risk factors, 2010-19: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022; 400(10352): 563-591. Doi: 10.1016/S0140-6736(22)01438-6.

42. Testino G, Scafato E, Patussi V, Balbinot P, Ghiselli A, Caputo F. Alcohol and cancer: a denied association the statement of the Italian society on alcohol (Società Italiana di Alcologia – SIA). Alcohol Alcohol. 2023: agad064. Doi: 10.1093/alcalc/agad064.

43. Anderson BO, Berdzuli N, Ilbawi A, Kestel D, Kluge HP, Krech R, Mikkelsen B, Neufeld M, Poznyak V, Rekve D, Slama S, Tello J, Ferreira-Borges C. Health and cancer risks associated with low levels of alcohol consumption. Lancet Public Health. 2023; 8(1): e6-e7. Doi: 10.1016/S2468-2667(22)00317-6.