Alcohol and Health – **fundaments for a common** approach

Introduction

Drinking alcoholic beverages is a part of the habits and cultural background of the European Union. It is often associated with family and social gatherings and celebrations even if, in many countries, risky single-occasion drinking is frequent in leisure contexts, especially for young people. In fact, there are differences between countries in the drinking patterns and volumes, as well as in the types of alcoholic beverages and the amounts of pure alcohol these contain.

The yearly average consumption of pure alcohol per capita (15 years old and above) estimated for the period 2008-2010, ranged from 6,7 litres in Italy to 15,4 litres in Lithuania.¹ These estimates include a component of unrecorded alcohol consumption, which also varies across Member States.

In 2010, the standardized mortality rate due to alcohol-attributable cancer, liver cirrhosis and injuries in the EU was 35,95 per 100.000 inhabitants (1). Globally, alcohol use was the leading risk factor in DALYs between the ages 15-49 years in 2016 (2), and the global seventh-leading risk factor, accounting for over 2.800.000 net estimated deaths world-wide, of which ca. 400.000 in the EU².

The evidence

Consuming alcoholic beverages is a **risk factor** for several **illnesses** and overall premature **mortality**. Alcohol consumption contributes to a wide range of disease and injury conditions (3). A recent systematic review of reviews and meta-analyses of the risk relationships between alcohol and health outcomes identified more than 40 disease categories³ as *fully* attributable to alcohol. Moreover, alcohol has been found to be a component cause contributing to the development of more than 200 disease and injury conditions (4).

Ethanol is the main alcohol found in alcoholic beverages. Chemically, ethanol is an organic solvent. It is a psychoactive substance (i.e. it affects mental processes). Ethanol is classified as a sedative/hypnotic and has **toxic and dependence-producing** properties (5). Alcoholic beverages are classified as **carcinogenic** to humans, which means their consumption increases the risk of developing cancer (group I in IARC monographs classification; (6–8).

Acute, short-term harm includes injuries such as those from vehicle accidents or violence, interaction with medication, or (lethal) intoxication. Chronic harm includes cancer at seven sites⁴, liver cirrhosis, cardiovascular diseases, alcohol dependency, depressive disorders and suicide, among others. Importantly, even low levels of alcohol consumption are linked to increases in risk of certain cancers (oral cavity and pharynx, oesophagus and female breast; (8,9). In the long term, alcohol can interact with other substance use or mental health conditions. In particular, the interaction of drinking alcoholic beverages and smoking tobacco

¹ Global Health Observatory Data Repository -European Region GISAH, accessed 22/02/2017

² <u>Global Burden of Disease Study 2016 (GBD 2016) Results. Seattle, United States; Institute for Health Metrics and Evaluation (IHME), 2017</u>. Available from http://ghdx.healthdata.org/gbd-results-tool. <u>Accessed 06/10/2017</u>

³ International Classification of Diseases 10 three-digit categories.

⁴ Oral cavity, pharynx, larynx, oesophagus, colorectum, liver and breast.

products increases the risk of certain cancers, and this interaction is multiplicative rather than additive (e.g. see (10)).

Risk of alcohol-related harm depends on the volume of alcohol drunk, on the drinking pattern (with heavy drinking occasions as the most harming pattern), and in some cases on the quality of the product (3). The characteristics of the person drinking (age group, sex, pregnancy, etc.) also play a role in shaping the risk curves. Generally, the higher the consumption, the higher the risk, with different risk curves linking the amount (**dose-response**) and pattern of drinking to specific diseases, injuries or causes of death. For several types of cancer, there is no safe threshold of exposure. According to the Global Burden of Disease 2016 Study, ca 24.400 deaths by self-harm (suicide) in the EU were attributed to alcohol use.

Drinking has effects beyond the person who drinks. Harm to others is an important facet of its impact and includes deaths and injuries from traffic accidents (ca. 10.800 estimated deaths attributable to alcohol use in 2016 in the EU)², and victims of domestic and other violence (ca 1.400 estimated deaths in the EU in 2016)². A recent cross-national survey⁵ delivered in 15 European countries shows that approximately two thirds of respondents had experienced negative effects due to others' drinking in the previous year (ranging from 40 % in Catalonia, Spain, to 85 % in Bulgaria; (11)). The prevalence of those who lived with a fairly heavy drinker or with someone who drank a lot during childhood varied from 7 - 8 % in Italy to ca. 40 % in Estonia. Other studies have found that most of the negative consequences caused by other people's drinking are experienced by women and young people (12,13). Parental drinking is associated with negative outcomes in children, such as adolescent drinking (14,15), poorer school performance (16), self-damage, harm to others and adverse life experiences (17). Drinking alcoholic beverages during pregnancy can cause foetal alcohol spectrum disorders, which include permanent physical, cognitive and behavioural problems (18-20). The global prevalence of FASD among children 0-16 years old in the general population has recently been estimated to be 7,7 per 1.000 population (95% CI 4,9 - 11,7 per 1.000 population), being the highest prevalence that of the WHO European Region at 19,8 per 1.000 population (95%Cl 14,1 - 28,0 per 1.000 population;(21)).

Alcohol and cancer

Alcoholic beverages, as well as the ethanol in such beverages and the acetaldehyde associated with the metabolism of alcoholic beverages, have all been classified as **carcinogenic to humans (Group 1)** by the International Agency for Research on Cancer (6–8). **Group 1 is the category with the strongest level of evidence; smoking** tobacco products or being exposed to **asbestos, plutonium, or ionizing radiation** are also classified by IARC as Group 1 agents.

There is a dose-dependent increased risk of developing cancer in the following sites: mouth, pharynx, larynx; oesophagus (oesophageal squamous cell carcinoma); colon-rectum (men); breast (both pre- and post-menopause); for all these cancer sites, **no lower safe threshold exists**. There is increased risk of developing cancer of the liver for consumption of 45 g of pure alcohol per day or more.

Alcoholic beverages are probably carcinogenic to humans regarding stomach cancer and pancreas cancer (8,22). There is accumulating evidence that alcohol drinking is associated with other cancers such as prostate cancer and melanoma (23).

⁵ Standardised European Alcohol Survey; RARHA SEAS.

Preventive effects

Reports have attributed beneficial or protective health effects (and potential biological mechanisms) to low-to-moderate drinking, in particular regarding ischemic diseases and diabetes, based on J-shaped mortality curves seen in observational studies (for a recent example see (24). However, at least in industrialized countries, low-to-moderate drinking is often an indicator of well-being, a potential major confounding factor, and there is no demonstrated causal relation between low-to-moderate drinking and protective health effects. The studies that report such effects have also been challenged by robust analyses with higher quality records of the exposure, including drinking patterns, and that account for confounding and selection bias (4,25,26). The most recent Global Burden of Disease Study, with data from 2016 (2) shows either minor or non-significant preventive effect for causes previously estimated to have large preventive effects (diabetes mellitus and ischemic stroke), while confirming a much larger risk of cancer than previously reported (with the exception of ischemic heart disease). Recent evidence suggests that even light to moderate drinkers may benefit in terms of cardiovascular health from reducing their alcohol consumption (27) and overall, the potential health benefits attributed to low-to-moderate alcohol drinking are not sufficient to outweigh the risks (1,28,29).

There is no scientific evidence that drinking alcoholic beverages can replace conventional measures for heart health such as lowering cholesterol, lowering high blood pressure, weight control, being sufficiently physically active or following a healthy diet⁶.

Alcohol and calorie intake

Alcoholic beverages are highly caloric, the energy conversion factor for ethanol being 29 kJ/g or 7 kcal/g (30). In addition, alcohol consumption interferes with the metabolism and has been shown to stimulate spontaneous food intake in experimental conditions (31).

Lighter, frequent alcohol consumption does not seem to be associated with weight gain, whereas more frequent heavier alcohol consumption is (individuals who drink lightly and regularly may have other *moderation* characteristics protecting them from weight gain). Alcohol intake, and in particular heavy drinking, may be a risk factor for weight gain and obesity in some individuals (32).

Health inequalities

The so called "**alcohol harm paradox**" arises from the observation that, in high income countries, mortality and morbidity traced down to alcohol use are much more frequent in people from low socioeconomic status (SES), while these typically report similar or lower average alcohol consumption and higher rates of abstaining than high SES groups (33). It has been postulated that small groups of individuals in low SES groups are more likely to report extreme drinking levels, partially explaining this alcohol harm paradox (34). Another hypothesis proposes that individuals in low SES groups who drink alcohol also present more frequently a combination of risks (e.g. smoking, obesity) increasing alcohol harm (35). A significant proportion of social inequality in premature mortality can be attributed to SES differences in alcohol-related mortality in many European countries (36–38).

Research

For several decades, epidemiological and economic studies have provided evidence and estimates of the harm that consuming alcoholic beverages can cause to the individual's health, to others, and of the societal costs derived thereof. Research on the link between alcohol and

⁶ American Heart Association. <u>Alcohol and Heart Health</u> Updated Jan 12, 2015. (Accessed 25/10/2017)

health outcomes most frequently consist of prospective observational studies, as well as animal models and some clinical research.

The use of randomized controlled trials to confirm causal relationships is not used as it would be unethical, since there is no reason to allocate abstainers or former drinkers to a drinking group⁷. Mendelian randomization, which uses naturally occurring genotypes as instrumental variables, partly overcomes this limitation (27).

The Commission, with the aim of informing people about actions they can take for themselves or their families to reduce their risk of cancer, has built on these decades-worth of evidence to produce the **European Code against Cancer**.⁸

Public health

Given the evidence on the magnitude of the health impact of alcohol, action is required. This means acting to minimise harmful consumption of alcohol –directly related to overall consumption– and in no circumstance recommending abstainers to start drinking since, according to the scientific evidence, there are no safe thresholds for alcohol consumption. Key public health messages are:

- Promoting alcohol consumption is contrary to public health.
- Reducing population average consumption prevents alcohol-related harm in that population.
- There are several groups in the population who should not drink alcohol, including children and adolescents, women planning to become pregnant, women who are pregnant or who are breast-feeding, people under treatment for alcohol use disorder when advised by a physician, and people with alcohol-induced organ damage.
- Targeting heavier drinkers with specific interventions to reduce harm is important. This may also have an impact in reducing related health inequalities.

Alcohol-related policies must focus on evidence-based interventions with the potential to protect as many people as possible from alcohol related harm (39,40).

Reductions in population average consumption are most effectively and cost-effectively achieved by policies regulating price, availability and marketing of alcoholic beverages since they have an impact on the consumption of the entire population and specifically on heavier drinkers (3,33,41,42).

Accurate information and guidance, including the degree of risk associated with alcohol consumption, must be provided for citizens to make informed choices. Even if information campaigns targeting the general population have not been shown to be effective in isolation to reduce consumption or alcohol-related harm (43), they can have a modest effect when combined with other interventions and can be effective in preparing the public for other measures. In any case, citizens are entitled to accurate information on consumer protection rights and ethical grounds.

⁷ Without randomization, it is more difficult to separate if the attributed beneficial effects of light drinking are due to the alcohol itself, or rather to a set of other characteristics or circumstances that frequently co-occur with light to moderate drinking, at least in high income countries. These other variables include a better general health status (frequently, abstainers have worse health status and that is a reason for their not drinking; other times, former drinkers, who have worse health conditions because of their past drinking, are included in this "abstainers" category). Mendelian randomization, which uses naturally occurring genotypes as instrumental variables, partly overcomes this limitation, and this approach suggests, as mentioned before, that even light to moderate drinkers may benefit in terms of cardiovascular health from reducing their alcohol consumption.

⁸ <u>https://cancer-code-europe.iarc.fr/index.php/en/ecac-12-ways/alcohol-recommendation</u>

Guidelines

Several Member States have published **lower risk** drinking guidelines. These suggest what average daily (or weekly) alcohol intake should not to be exceeded in order to keep the long-term risk of mortality as low as acceptable in the given society (no level can be considered safe regarding certain conditions like developing a range of cancers). They also warn against heavy single occasion (or binge) drinking (44) and against drinking of certain population groups.

Typically, single risky occasion drinking is discouraged to reduce acute harms, whereas a reduction in consumption is recommended especially (but not exclusively) among heavier drinkers to avoid long term, chronic harms. National recommendations for lower risk consumption vary between average daily consumptions not exceeding 8 to 20 g of pure alcohol for women and 10 to 40 g for men.

If the standard acceptable lifetime risk threshold of 1 in 1,000 (commonly used for voluntary risks) were applied for alcohol-attributable mortality⁹, the current recommended maximum daily consumption levels would largely exceed the risk threshold in several EU countries (29,44).

BIBLIOGRAPHY

- 1. Shield K, Rylett M, Gmel G, Rehm J, Brummer J, Møller L. Status Report on Alcohol and Health in 35 European Countries 2013. Copenhagen, Denmark: World Health Organization; 2013.
- 2. GBD 2016 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks,. Lancet Lond Engl. 2017 Sep 16;390(10100):1345–422.
- 3. World Health Organization. Global status report on alcohol and health 2014. Geneva: World Health Organization; 2014.
- 4. Rehm J, Gmel GE, Gmel G, Hasan OSM, Imtiaz S, Popova S, et al. The relationship between different dimensions of alcohol use and the burden of disease—an update. Addiction [Internet]. 2017; Available from: http://dx.doi.org/10.1111/add.13757
- 5. WHO. Lexicon of alcohol and drug terms [Internet]. World Health Organization; 1994. Available from: http://apps.who.int/iris/bitstream/10665/39461/1/9241544686_eng.pdf
- 6. IARC. IARC Monographs on the evaluation of the carcinogenic risks to humans. Alcohol Drinking. Volume 44 [Internet]. Lyon, France: International Agency for Research on Cancer (IARC); 1988. Report No.: Volume 44. Available from: https://monographs.iarc.fr/ENG/Monographs/vol44/mono44.pdf
- 7. IARC. IARC Monographs on the evaluation of the carcinogenic risks to humans. Alcohol Consumption and Ethyl Carbamate. Volume 96 [Internet]. Lyon, France: International Agency for Research on Cancer (IARC); 2010. Report No.: Volume 96. Available from: http://monographs.iarc.fr/ENG/Monographs/vol96/mono96.pdf
- IARC. IARC Monographs on the evaluation of the carcinogenic risks to humans. Personal habits and indoor combustions. Volume 100E. A review of human carcinogens [Internet]. Lyon, France: International Agency for Research on Cancer (IARC); 2012. Report No.: Volume 100E. Available from: http://monographs.iarc.fr/ENG/Monographs/vol100E/mono100E.pdf
- 9. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Light alcohol drinking and cancer: a metaanalysis. Ann Oncol Off J Eur Soc Med Oncol ESMO. 2013 Feb;24(2):301–8.
- 10. Prabhu A, Obi KO, Rubenstein JH. The Synergistic Effects of Alcohol and Tobacco Consumption on the Risk of Esophageal Squamous Cell Carcinoma: A Meta-Analysis. Am J Gastroenterol. 2014 Jun;109(6):822–7.
- 11. Moskalewicz J, Room R, Thom B. Comparative monitoring of alcohol epidemiology across the EU. Baseline assessment and suggestions for future action. Synthesis report. [Internet]. JA RARHA, PARPA The State Agency for Prevention of Alcohol Related Problems. Warsaw, Poland; 2016 Dec [cited 2017 Apr 21]. Available from: http://www.rarha.eu/Resources/Deliverables/Lists/Work%20Package%204/Attachments/7/Comparative%20monitori ng%20%20of%20alcohol%20epidemiology%20%20across%20the%20EU.pdf
- 12. Huhtanen P, Tigerstedt C. Women and young adults suffer most from other people's drinking. Drug Alcohol Rev. 2012 Nov;31(7):841–6.

⁹ Calculations in seven European countries on the lifetime risk of alcohol-related mortality indicate that these consumption levels are close or exceed those for which mortality would be 1 in 100 (17-31 grams of per day for men and 11-15 grams for women).

- Ramstedt M, Sundin E, Moan IS, Storvoll EE, Lund IO, Bloomfield K, et al. Harm Experienced from the Heavy Drinking of Family and Friends in the General Population: A Comparative Study of Six Northern European Countries. Subst Abuse Res Treat. 2015;9(Suppl 2):107–18.
- 14. Rossow I, Keating P, Felix L, McCambridge J. Does parental drinking influence children's drinking? A systematic review of prospective cohort studies. Addiction. 2016;111(2):204–17.
- Rossow I, Felix L, Keating P, McCambridge J. Parental drinking and adverse outcomes in children: A scoping review of cohort studies. Drug Alcohol Rev. 2016 Jul;35(4):397–405.
- Berg L, Back K, Vinnerljung B, Hjern A. Parental alcohol-related disorders and school performance in 16-year-olds-a Swedish national cohort study. Addict Abingdon Engl. 2016 Oct;111(10):1795–803.
- 17. Christoffersen MN, Soothill K. The long-term consequences of parental alcohol abuse: a cohort study of children in Denmark. J Subst Abuse Treat. 2003 Sep;25(2):107–16.
- 18. Jones KL, Smith DW, Ulleland CN, Streissguth P. Pattern of malformation in offspring of chronic alcoholic mothers. Lancet Lond Engl. 1973 Jun 9;1(7815):1267–71.
- Popova S, Lange S, Probst C, Gmel G, Rehm J. Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis. Lancet Glob Health [Internet]. [cited 2017 Jan 16]; Available from: http://dx.doi.org/10.1016/S2214-109X(17)30021-9
- Warren KR, Bast RJ. Alcohol-related birth defects: an update. Public Health Rep Wash DC 1974. 1988 Dec;103(6):638–42.
- Lange S, Probst C, Gmel G, Rehm J, Burd L, Popova S. Global Prevalence of Fetal Alcohol Spectrum Disorder Among Children and Youth: A Systematic Review and Meta-analysis. JAMA Pediatr. 2017 Oct 1;171(10):948–56.
- 22. World Cancer Research Fund International/ American Institute for Cancer Research. Continuous Update Project Report: Diet, Nutrition, Physical Activity and Stomach Cancer. [Internet]. 2016 [cited 2017 Oct 29]. Available from: www.wcrf.org/stomach-cancer-2016
- 23. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer. 2015 Feb 3;112(3):580–93.
- 24. Bell S, Daskalopoulou M, Rapsomaniki E, George J, Britton A, Bobak M, et al. Association between clinically recorded alcohol consumption and initial presentation of 12 cardiovascular diseases: population based cohort study using linked health records. BMJ. 2017 Mar 22;356:j909.
- Fillmore KM, Stockwell T, Chikritzhs T, Bostrom A, Kerr W. Moderate alcohol use and reduced mortality risk: systematic error in prospective studies and new hypotheses. Ann Epidemiol. 2007 May;17(5 Suppl):S16-23.
- 26. 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 Mar;77(2):185–98.
- 27. Holmes MV, Dale CE, Zuccolo L, Silverwood RJ, Guo Y, Ye Z, et al. Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. BMJ. 2014;349:g4164.
- 28. Knott CS, Coombs N, Stamatakis E, Biddulph JP. All cause mortality and the case for age specific alcohol consumption guidelines: pooled analyses of up to 10 population based cohorts. BMJ. 2015;350:h384.
- 29. Rehm J, Gmel G, Probst C, Shield KD. Lifetime-risk of alcohol attributable mortality based on different levels of alcohol consumption in seven European countries. Implications for low-risk drinking guidelines. [Internet]. Toronto, On, Canada: Centre for Addiction and Mental Health.; 2015. Available from: https://www.camh.ca/en/research/news_and_publications/reports_and_books/Documents/Lifetime%20Risk%20of% 20Alcohol-Attributable%20Mortality.pdf
- 30. EFSA Panel on Dietetic Products N and A (NDA). Scientific Opinion on Dietary Reference Values for energy. EFSA J. 2013 Jan 1;11(1):3005–n/a.
- 31. Chapman CD, Benedict C, Brooks SJ, Schioth HB. Lifestyle determinants of the drive to eat: a meta-analysis. Am J Clin Nutr. 2012 Sep;96(3):492–7.
- 32. Traversy G, Chaput J-P. Alcohol Consumption and Obesity: An Update. Curr Obes Rep. 2015 Mar;4(1):122–30.
- 33. Organisation for Economic Co-operation and Development. OECD Statistics [Internet]. OECD Statistics. 2015 [cited 2015 Apr 7]. Available from: http://stats.oecd.org/ (Archived by WebCite® at http://www.webcitation.org/6Xbn2dYWW)
- 34. Lewer D, Meier P, Beard E, Boniface S, Kaner E. Unravelling the alcohol harm paradox: a population-based study of social gradients across very heavy drinking thresholds. BMC Public Health. 2016 Jul 19;16:599.

- Bellis MA, Hughes K, Nicholls J, Sheron N, Gilmore I, Jones L. The alcohol harm paradox: using a national survey to explore how alcohol may disproportionately impact health in deprived individuals. BMC Public Health. 2016 Feb 18;16:111.
- Mackenbach JP, Kulhánová I, Bopp M, Borrell C, Deboosere P, Kovács K, et al. Inequalities in Alcohol-Related Mortality in 17 European Countries: A Retrospective Analysis of Mortality Registers. PLoS Med. 2015 Dec;12(12):e1001909.
- 37. Hemstrom O. Alcohol-related deaths contribute to socioeconomic differentials in mortality in Sweden. EurJPublic Health. 2002 Diciembre;12(4):254–62.
- Makela P, Valkonen T, Martelin T. Contribution of deaths related to alcohol use to socioeconomic variation in mortality: register based follow up study. BMJ. 1997 Jul 26;315(7102):211–6.
- WHO. Global strategy to reduce the harmful use of alcohol [Internet]. Geneva, Switzerland: World Health Organization; 2010 [cited 2016 Jun 4]. Available from: http://apps.who.int/iris/handle/10665/44395
- 40. WHO. European action plan to reduce the harmful use of alcohol 2012-2020. Copenhagen, Denmark: WHO Regional Office for Europe; 2012.
- 41. Anderson P, Chisholm D, Fuhr DC. Effectiveness and cost-effectiveness of policies and programmes to reduce the harm caused by alcohol. Lancet. 2009 Jun 27;373(9682):2234–46.
- 42. Babor TF, Caetano R, Casswell S, Edwards G, Giesbrecht N, Graham K, et al. Alcohol: No Ordinary Commodity: Research and Public Policy. New York: Oxford University Press; 2010. 378 p.
- Martineau F, Tyner E, Lorenc T, Petticrew M, Lock K. Population-level interventions to reduce alcohol-related harm: an overview of systematic reviews. Prev Med. 2013 Oct;57(4):278–96.
- 44. Broholm K, Galluzzo L, Gandin C, Ghirini S, Ghiselli A, et al. Good practice principles for low risk drinking guidelines [Internet]. JA RARHA, National Institute for Health and Welfare (THL), FInland; 2016 Oct. Available from: https://user-ucadpix.cld.bz/Good-practice-principles-for-low-risk-drinking-guidelines/1

[December 2017]