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European Code against Cancer 4th Edition: Alcohol drinking and cancer☆

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ABSTRACT

Alcohol consumption is the third leading risk factor for disease and mortality in Europe. As evaluated by the International Agency for Research on Cancer (IARC) Monographs, a causal relationship is established for consumption of alcoholic beverages and cancers of the oral cavity, pharynx, larynx, oesophagus, liver, colorectum and female breast, even at low and moderate alcohol intakes. The higher the amount of alcohol consumed, the higher the risk of developing cancer. In Europe, an estimated 10% (95% CI: 7%–13%) of all cancer cases in men and 3% (95% CI: 1%–5%) of all cancer cases in women are attributable to alcohol consumption. Several biological mechanisms explain the carcinogenicity of alcohol; among them, ethanol and its genotoxic metabolite, acetaldehyde, play a major role. Taking all this evidence into account, a recommendation of the 4th edition of European Code against Cancer is: " If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention."
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Abbreviations: IARC, International Agency for Research on Cancer; EU, European Union; RR, Relative risk; UADT, Upper aero digestive tract; ADH, Alcohol dehydrogenase; ALDH, Acetaldehyde dehydrogenase; MTHFR, Methylenetetrahydrofolate reductase; ER, Estrogen receptor; PR, Progesterone receptor; WHO, World Health Organization.

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1. Introduction

Alcohol consumption is linked to a large number of health impairments, chronic diseases and deaths worldwide [1]. The 2012 Monograph of the International Agency for Research on Cancer (IARC) strengthens the evidence on the carcinogenicity of alcohol by tumour sites and by mechanisms of alcohol carcinogenesis even for low and moderate alcohol intakes [2,3]. The IARC Monographs reached the conclusion: "alcohol consumption is carcinogenic to humans (Group 1); ethanol in alcoholic beverages is carcinogenic to humans (Group 1); acetaldehyde associated with the consumption of alcoholic beverages is carcinogenic to humans (Group 1)" [2]. Overall, there is no consistent difference in cancer risk between different types of alcoholic beverages [4–6]. While the mechanisms of alcohol carcinogenesis are not fully understood, the direct carcinogenicity of ethanol and its metabolites, the interplay with folate metabolism and the oestrogen pathway have been suggested, all of which would be further modulated by use patterns and genetic and environmental factors [2,3].

Box 1. European Code Against Cancer.

EUROPEAN CODE AGAINST CANCER
12 ways to reduce your cancer risk

1. Do not smoke. Do not use any form of tobacco.
2. Make your home smoke free. Support smoke-free policies in your workplace.
3. Take action to be a healthy body weight.
4. Be physically active in everyday life. Limit the time you spend sitting.
5. Have a healthy diet:
   - Eat plenty of whole grains, pulses, vegetables and fruits.
   - Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks.
   - Avoid processed meat; limit red meat and foods high in salt.
6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention.
7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds.
8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.
9. Find out if you are exposed to radiation from naturally high radon levels in your home. Take action to reduce high radon levels.
10. For women:
    - Breastfeeding reduces the mother's cancer risk. If you can, breastfeed your baby.
    - Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT.
11. Ensure your children take part in vaccination programmes for:
    - Hepatitis B (for newborns)
    - Human papillomavirus (HPV) (for girls).
12. Take part in organized cancer screening programmes for:
    - Bowel cancer (men and women)
    - Breast cancer (women)
    - Cervical cancer (women).

The European Code Against Cancer focuses on actions that individual citizens can take to help prevent cancer. Successful cancer prevention requires these individual actions to be supported by governmental policies and actions.

Europe is the highest alcohol-consuming region in the world, with an average consumption of more than twice the global average, a high prevalence of hazardous drinkers and an average alcohol-attributable cancer burden which by far exceeds the global average as well [1]. Taken together, the 4th edition of the European Code Against Cancer (Box 1) [7] advocates action-oriented recommendations for the general public. The Code recommends decreasing or cutting alcohol consumption in order to both prevent several types of cancer and to improve overall health.

1.1. European alcohol consumption among adult and young generations

Per capita alcohol consumption has been falling in the European Union (EU) as a whole over the past three decades, while remaining particularly high compared to the global average consumption. The most recent data from the Organisation for Economic Co-operation and Development show that individuals aged ≥15 years drink on average 9.4 L of pure alcohol per year [8]. Consumption tends to be higher in the Central-Eastern and Eastern countries as, for example, Estonia, Lithuania and Austria, all of which have an average consumption higher than 12 L per capita. At the other end of the spectrum, Mediterranean countries (e.g. Italy, Malta and Greece) and Nordic Countries (e.g. Norway, Sweden and Iceland) have relatively lower levels of consumption, in the region of 6–8 L of pure alcohol per adult person (Fig. 1). Gender, age and socio-economic status [9] are key factors in determining levels of alcohol consumption. Men are more likely to consume alcohol than women, and to drink more when they do [10], particularly in Central, Western and Northern EU countries. Compared to older adults, young and middle-aged people tend to drink higher volumes of alcohol [11]. Women with higher level of education tend to drink more alcohol while the opposite is generally true for men [10]. Hazardous drinking behaviours, such as binge drinking (i.e., the consumption of ≥60 g of pure alcohol on the same occasion and at least one day in the last month), have been increasing over the past 20 years [13], especially in Germany and Ireland and among younger generations [14–17]. The volume of alcohol consumed on a single occasion is important for many acute consequences of drinking such as alcohol poisoning, injury and violence. The prevalence of binge drinkers doubled in France and has increased by about 30% in Germany between 2002 and 2008 [13]. Repeated drunkenness among 15-years olds was reported by 36% of girls and 40% of boys in 2010 [8].

1.2. Effect of alcohol drinking on coronary heart disease

The evidence of a reduced risk of coronary heart disease at light to moderate alcohol consumption is important to consider. Several studies suggest a lower risk of both nonfatal myocardial infarction and fatal heart disease, likely confined to middle-aged or older individuals, when consuming one drink every second day compared to none [18–20]. However, controversy remains about whether this relationship is truly causal. Recent studies argue that alcohol consumption may increase the risk of heart disease even at low intakes and that the observed protective associations could be due to reverse causation and residual confounding [21,22].

2. Association with cancer

2.1. Cancer types associated with alcohol drinking

As evaluated by the IARC Monographs, alcohol consumption causes cancers of the oral cavity, pharynx, larynx, oesophagus,

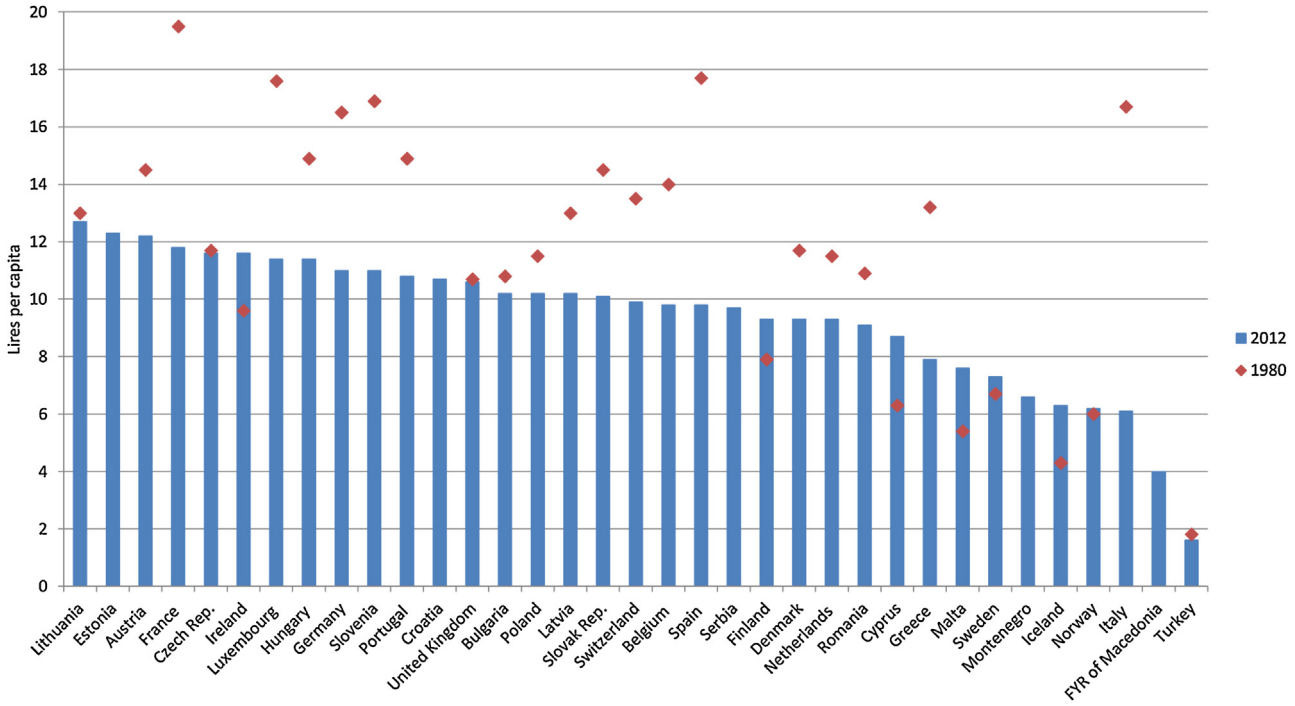


Fig. 1. Average European alcohol consumption in adults.
Average alcohol consumption in litres/capita/year among populations aged 15 years and over (years 2012 and 1980).
Source: Calculations provided by the OECD based on "Health at a glance: Europe 2014. OECD Publishing, 2014" [8].

colorectum, liver (hepatocellular carcinoma), colorectum, and female breast [2]. The level of evidence from main meta-analyses at both light and heavy drinking is indicated in Table 1. The relationship between alcohol consumption and the risk of cancer is shown in Fig. 2. More research is needed to determine if and to what extent these relative risk functions differ by cancer incidence and mortality. For the majority of the above cited cancer sites the associations are linear, except for those cancers more strongly related to alcohol consumption such as the upper digestive tract cancers.

Also an association has been observed between alcohol consumption and cancer of the pancreas [2]. For cancer of the kidney, Hodgkin and non-Hodgkin lymphomas there is evidence suggesting lack of carcinogenicity [2]. It is not possible to draw any conclusions for cancers of the prostate, bladder, lung, stomach, endometrium, ovary, cervix, vulva and vagina, testis, brain, thyroid, skin, leukaemia and multiple myelomia [23].

Overall, the risk of cancer in men who consume less than two alcoholic drinks per day and in women who consume less than one alcoholic drink per day is 6% lower than that in people with higher alcohol consumptions. In Europe, it has been estimated that about 10% (95% CI: 7%–13%) of all cancer cases in men and 3% (95% CI: 1%–5%) of all cancer cases in women are attributable to alcohol consumption [24]. In both genders, the alcohol-attributable fraction is high for upper aero-digestive tract (25%–44%), liver (18%–33%), and colorectal (4%–17%) cancers, and in women for breast cancer (about 5%), with variation across EU countries related to different levels of exposure to alcohol [24]. Drinking patterns play an important role in modulating the relationship between alcohol and cancer risk, as the strongest associations are observed for heavy drinking, in particular

Table 1
Risk of cancer at light or heavy alcohol drinking.

Cancer	ICD-10 code	Reference	RR (95% CI)[a] Light drinkers[b]	RR (95% CI)[a] Heavy drinkers[b]
Oral cavity	C00-C06	Turati 2010 [88]	1.17 (1.01–1.35)	4.64 (3.78–5.70)
Pharynx	C09-C14		1.23 (0.87–1.73)	6.62 (4.72–9.29)
Oral cavity and Pharynx	C00-C14	Turati 2013[c] [30]	1.36 (1.20–1.54)	5.40 (4.49–6.50)
Larynx	C32	Islami 2010[c] [28]	0.88 (0.71–1.08)	2.62 (2.13–3.23)
Oesophagus and gastric cardia	C15-C16	Tramacere 2012 [89]	0.86 (0.75–0.99)	1.16 (0.92–1.46)
Oesophagus	C15	Islami 2011 [29]	1.32 (0.90–1.60)	3.35 (2.35–4.78)
Colorectal	C18-C21	Fedirko 2011 [40]	1.00 (0.95–1.05)	1.52 (1.27–1.81)
Liver	C22	Corrao 2004[c] [41]	1.19 (1.12–1.27)	1.40 (1.25–1.56)
Female breast	C50	Bagnardi 2013 [44]	1.05 (1.02–1.08)	
		Corrao 2004[c] [41]	1.25 (1.20–1.29)	1.55 (1.44–1.67)

ICD-10: International Classification of Diseases, 10th Revision [87].
[a] Summary relative risk and 95% confidence interval.
[b] Light drinker: ≤ 1drink (or 12.5 g) per day; Heavy drinker: ≥4 drinks (or 50 g) per day.
[c] Light drinker: 1–2 drinks (or ≤ 25 g) per day; Heavy drinker: ≥4 drinks (or 50 g) per day.

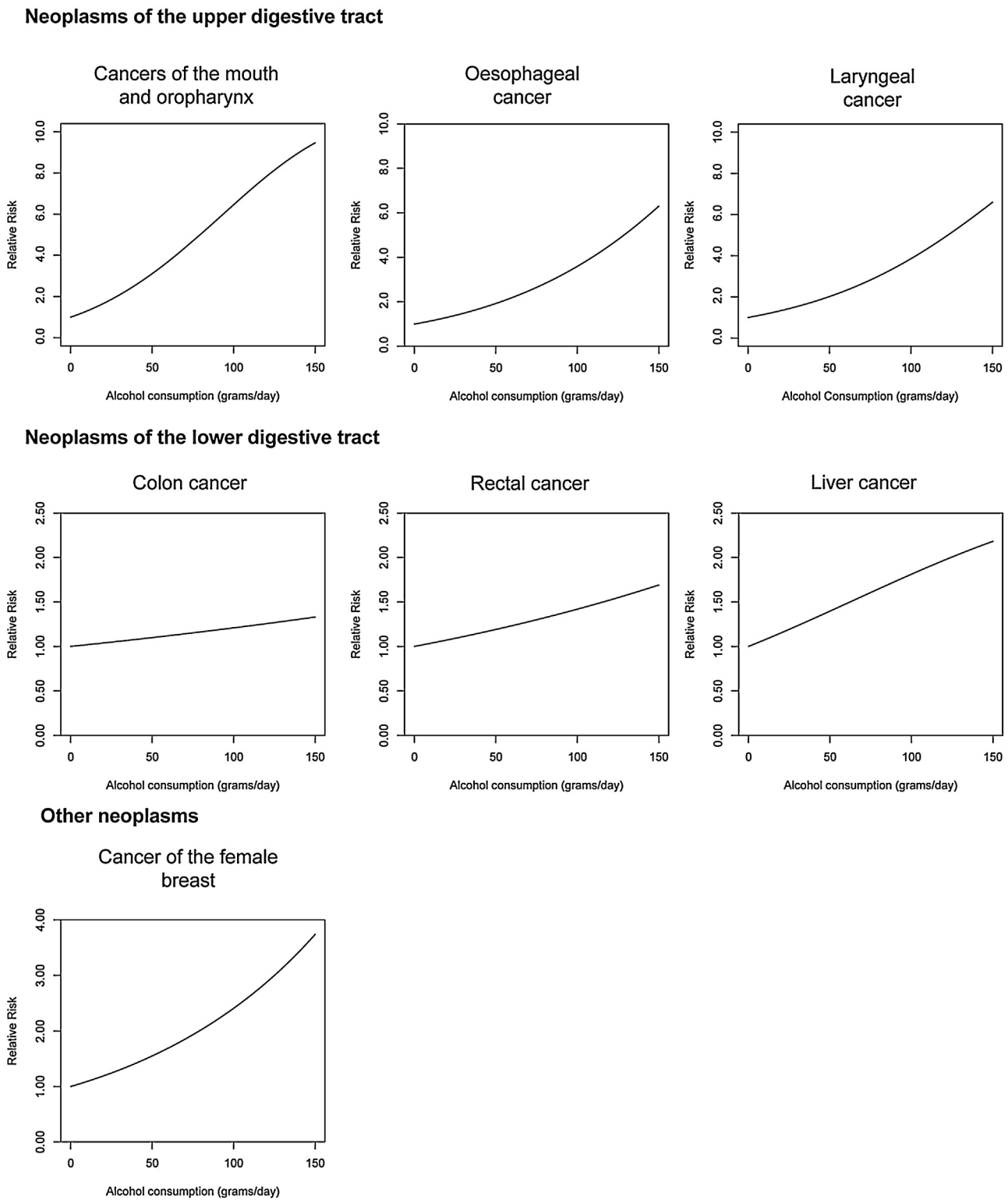


Fig. 2. Relationship between average daily alcohol consumption and relative risk of cancer.
Plots of the relative risk functions for all cancers causally associated with alcohol consumption. Relative risks of cancer are strongest for the upper digestive tract (scale 0.0-10.0), followed by female breast (scale 0.0-4.0) and lower digestive tract (scale 0.0-2.5).
Source: G. Corrao, V. Bagnardi, A. Zambon, C. La Vecchia A meta-analysis of alcohol consumption and the risk of 15 diseases. Prev. Med. 2004, 38:613–619. http://dx.doi.org/10.1016/j.ypmed.2003.11.027 PMID:15066364 [41].

regular heavy drinking. Any reduction in alcohol consumption has a beneficial effect on reducing the risk of cancer.

2.1.1. Neoplasms of the upper digestive tract

Results from cohort studies and recent meta-analyses provide convincing evidence that the consumption of alcoholic beverages increases the risk of neoplasms of the upper digestive and respiratory tract (UADT: oral cavity, pharynx, larynx and squamous cell carcinoma of the oesophagus) even in the absence of smoking. Significant dose-response relationships are found with different metrics of exposure to alcohol, such as level, frequency [25] and duration [26] of consumption and for moderate intake in women [4,27,28]. Among non-smokers, reported RRs for oesophageal squamous cell carcinoma and laryngeal cancer range from 0.74 (95% CI: 0.47–1.16) for light intakes, to 3.09 (95% CI: 1.75–5.46) for high intakes [27–29]. Risks for oropharyngeal cancer are as high as 5.40 (95% CI: 4.49–6.50) [30]. The combined exposure to alcohol consumption and tobacco smoking results in a supra-multiplicative synergistic effect which enhances the risk of these neoplasms up to 14-fold, among heavy-smokers and heavy drinkers (4 or more drinks/day) [31,32] (Fig. 3).

There is evidence that risk of UADT cancer decreases with time since drinking cessation, without however ever falling to that of lifetime abstainers. A recent meta-analysis reports an average 2% decreased risk of pharyngeal and laryngeal cancers per year of cessation [33]. A trend for decreased risk is suggested for laryngeal, oropharyngeal and oesophageal cancers, among former drinkers. After at least 6 years of drinking cessation, odds ratios decreased to 1.24 (95% CI: 0.68–2.47) [34], 1.74 (95% CI: 0.77–3.92) [35], and 0.85 (95% CI: 0.78–0.92) [36,37], for laryngeal, oropharyngeal and oesophageal cancers, respectively.

2.1.2. Neoplasms of the lower digestive tract

Results from cohort studies and recent meta-analyses provide overall evidence of a linear dose-response relationship between average alcohol consumption and colorectal and liver cancers. Summary effect estimates for colorectal cancer are about 11% (RR = 1.11; 95% CI: 0.90–1.38) at one drink/day (corresponding to 10-12 g of ethanol) and 40% (RR = 1.41; 95% CI: 1.16–1.72) at more than 4–5 drinks/day [38]. Risk is higher for drinkers with a family history of colorectal cancer (RR = 2.80; 95% CI: 2.00–3.91, at ≥30 g/d compared with non-drinkers with no family history) [39]. Overall, the estimated RRs at 2–3 drinks per day compared with non-drinkers are 1.23 (95% CI: 1.13–1.35) and 1.15, (95% CI: 1.06–1.24), respectively for rectal and colon cancer, and slightly higher in men (RR = 1.24; 95% CI: 1.13–1.37) than in women (RR = 1.08; 95% CI: 1.03–1.13) [40]. In both genders combined, dose-response analyses show RRs of 1.07 (95% CI: 1.04–1.10), 1.38 (95% CI: 1.28–1.50) and 1.82 (95% CI: 1.41–2.35) at 10, 50 and 100 g/day of alcohol consumption, respectively [40].

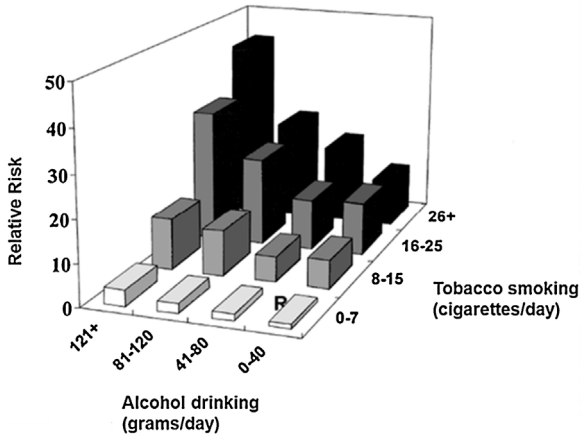


Fig. 3. Estimated RR for the interaction between tobacco smoking and alcohol drinking on cancers of the upper digestive and respiratory tract (reference category, risk = 1).
Combined exposure to alcohol drinking and tobacco smoking increases the risk of upper digestive and respiratory tract neoplasms in a supra-multiplicative manner. Source: P. Boyle, P. Autier, H. Bartelink, et al. European Code Against Cancer and scientific justification: third version (2003) Annals of Oncology 2003, 14: 973–1005, by permission of Oxford University Press [7,86].

Chronic liver cirrhosis, associated with prolonged heavy (≥60–80 g/day) alcohol consumption, usually develops well ahead of hepatocellular carcinoma. Thus, associations of alcohol consumption with hepatocellular carcinoma are generally found at high intakes with significant increased risks of about 30–40% at consumption levels greater than 40 g/day [41–43]. However, increased risks at low to moderate alcohol consumption are also reported [4,44,45] and overall the dose-response relationship between alcohol consumption and the risk of liver cancer is linear.

2.1.3. Neoplasms of the female breast

A positive association between alcoholic beverages consumption and breast cancer risk is supported by more than 100 epidemiological studies [2]. The risk per 10 g/day of ethanol is increased by 8% for post-menopausal breast cancer, 9% for pre-menopausal breast cancer, and 10% for all-age breast cancer [46]. While studies on binge drinking and cancer risk are still sparse and a standardized measure of exposure is lacking, the available evidence shows that risk is increased between 33% (95% CI: 1.11–1.59, for monthly binge drinking) [47] and 55% (95%: CI 1.07–2.26, for weekly binge drinking) [48].

Women may be more susceptible to alcohol carcinogenesis when exposed at young age, since alcohol may act early in the carcinogenic process upon the expression of oestrogen receptors which regulate the development of the mammary gland. This susceptibility window of exposure to alcohol consumption may be further defined by hormonal status or first full-term pregnancy [49]. However, at present few studies have investigated whether and to what extent the age at exposure increases cancer risk and the evidence is generally limited. In the Nurses' Health Study (NHS) II, alcohol consumption before first pregnancy was consistently associated with an increased risk of proliferative benign breast disease, which may lead to invasive breast cancer later in life [50]. In a recent analysis of the EPIC study, breast cancer risk was stronger among women who started drinking alcohol prior to first full-time pregnancy suggesting that timing of exposure to alcohol drinking may affect the risk [51]. Alcohol consumption in both early and late adulthood appears to increase the risk of breast cancer. A NHS prospective analysis also reported similar breast cancer risks for categories of age at alcohol exposure of 18–40 years and >40 years (RRs = 1.21, 95% CI: 0.88–1.67 and 1.18, 95% CI: 1.03–1.34, respectively, for a daily intake ≥20 g compared to none) [47]. Similar results were also observed in a large Danish cohort of post-menopausal women, suggesting that lifetime alcohol consumption is an important factor for breast cancer risk [52].

2.2. Possible biological mechanisms

Alcoholic beverages mainly comprise ethanol and water and, in minor percentage, other volatile and non-volatile compounds. Ethanol is the most important carcinogen, moreover, ethanol's metabolism activates various pro-carcinogens present, as well as inhaled or ingested, in alcoholic beverages. Regarding breast cancer, ethanol most likely acts as both a weak cumulative carcinogen and a tumour promoter of pre-existing breast cancer cells [53]. For cancers of the oral cavity, pharynx, larynx and

oesophagus, the higher than multiplicative risk observed among drinkers and smokers is explained by the synergistic effect of carcinogens contained in tobacco smoke and in alcoholic beverages which leads to mucosal hyperproliferation [54–61].

The risk of digestive tract cancers is modulated by variants of the ethanol metabolising enzymes, the alcohol and acetaldehyde dehydrogenases (ADH and ALDH). The *ADH1B* 47Arg allele is strongly associated with increased UADT cancer risk (RR = 3.47; 95% CI: 2.76–4.36 for the Arg/Arg genotype compared to the His/His genotype) [58]. The fast metabolising *ADH1C*1* variant, which is more frequent in Caucasians [59], may increase risk of head and neck cancer [60,61]. The *ALDH2* Lys487 allele promotes acetaldehyde accumulation and is associated with higher risk of oesophageal cancer [2].

Ethanol also disrupts folate metabolism regulated by methylenetetrahydrofolate reductase (MTHFR) [62]; an individual's genotype for the C677T *MTHFR* variant modulates the effect of alcohol consumption on cancer risk. The CC or CT variants may increase colorectal cancer risk among alcohol drinkers (RR = 1.87; 95% CI: 1.29–2.71) [63]. The TT variant decreases MTHFR activity by 70% and appears to modulate risks of breast cancer, in association with low folate intake [64,65], and of oral cancer [66], at daily consumption of $\geq$2 drinks.

An important mechanism for breast cancer development might be an alcohol-related increase in androgen and oestrogen levels [67]. Most studies observe an overall stronger association with the most common oestrogen receptor positive (ER+) and/or progesterone receptor positive (PR+) compared with ER- and/or PR- breast tumours, for the highest versus the lowest alcohol consumption group [67–70]. However, a recent meta-analysis showed that for each additional drink, breast cancer risk increases by 12% among ER+, by 11% among ER+ PR+, by 15% among ER+ PR−, and by 7% for all ER- tumours, and no association was apparent with ER-/PR- or ER−/PR+ tumours when considered separately, thus suggesting that the impact of ethanol can only be explained by the oestrogen-dependent pathway [71]. In the EPIC study, increased breast cancer risk was observed for ER+/PR+, ER-/PR- and ER-/PR-HER- supporting the concept that non-hormonal pathways such as DNA damage might be involved in the incidence of receptor negative tumours [51].

Other ethanol-mediated toxic effects associated with cancer development are cirrhosis of the liver and gastro-oesophageal reflux disease, which leads to hyperproliferation of the oesophageal mucosa. Also, ethanol-associated immune suppression may facilitate tumour cell spread [62].

3. Justification for recommendation

The consumption of alcoholic beverages is causally associated with cancers of the oral cavity, pharynx, larynx, oesophagus, liver, colorectum and female breast. For these organ sites, risk estimates of alcohol-related cancer incidence and mortality emphasize a dose-dependent relationship that does not vary by beverage type and does not show a threshold of intake, with an adverse effect observed even at consumption of less than 1 alcoholic drink per day [12,72]. Ethanol carcinogenesis may not uniformly target tissues and may depend on drinking patterns and timing of exposure, as based on observed differences in cancer risk across all organ sites.

3.1. Alcohol-attributable burden of disease

In Europe, alcohol is the third leading risk factor for disease and mortality after tobacco and high blood pressure [73]. In addition to cancer, alcohol consumption is causally associated with about 60 types of diseases, including heart disease, stroke and vascular diseases, as well as liver cirrhosis, birth defects and intellectual impairments. Alcohol also contributes to death and disability through accidents and injuries, assault, violence, homicide and suicide. Alcohol is a psychoactive substance with dependence-producing properties. Disease burden is mostly related with alcohol's capacity to produce dependence and with acute intoxication, which together represent 44.5% of the alcohol-related morbidity in men [1].

In the EU in 2004, almost 95,000 men and more than 25,000 women, aged 15–64, died prematurely of alcohol-attributable causes. This means that 1 in 7 male and 1 in 13 female premature deaths in this age category were caused by alcohol [73]. In men in 2004, approximately two-fifths of deaths were due to liver cirrhosis, one third to injuries, compared to one in five (15.9%) for cancer. In women, approximately more than two thirds of alcohol-attributable deaths arose from liver cirrhosis and from cancer (30.7%; the largest proportion of which, 21%, concerns breast cancer), with cardiovascular disease other than ischaemic heart disease as a distant third cause.

Almost 90% of the burden of disease attributable to alcohol is caused by heavy drinking, both regular and irregular. This has important implications for prevention and alcohol policy: any measure which wants to successfully reduce alcohol-attributable harm has to cut down regular and irregular heavy drinking occasions.

3.2. Public policies on alcohol taxation as measures of prevention

Negative health effects and social harm caused by detrimental alcohol consumption can be reduced though effective prevention strategies. In 1979, the World Health Assembly called upon World Health Organization (WHO) member states to develop and adopt appropriate legislation and measures to tackle alcohol misuse [74]. In 2010, a global strategy on the harmful use of alcohol was endorsed, to support target areas for national actions including health sector response, drink-driving policies, limitation of the availability of alcohol, and action on marketing and pricing policies [75]. Based on four key criteria (namely effectiveness, affordability, efficiency and acceptability/feasibility), WHO has more recently identified restricted access to retailed alcohol, limitation of alcohol advertising and taxes on alcohol as the best performing interventions to tackle harmful alcohol use [76].

Alcohol prices, and consequently affordability, are a strong determinant of alcohol consumption and can be altered by using taxes or direct price controls, including minimum price policies [77]. Overall, and despite inhomogeneous public policies on alcohol taxation across the EU, countries with more strict alcohol policies and decreased affordability generally report lower levels of alcohol consumption [75]. On average, a 10% increase in the price of alcohol is correlated to a 4.4% decrease in consumption, with some variability depending on the type of alcoholic beverage [78]. Time-series analyses in Canada (British Columbia) showed that a 10% increase in the minimum price for alcohol reduces consumption of spirits by 6.8%, of wine by 8.9%, of alcopops (flavoured, often sweet, alcoholic beverages) by 13.9% and of beer by 1.5% [79]. In spite of the above evidence, the real price of alcoholic beverages is decreasing and an approximate 50% increase in affordability was recorded between 1996 and 2004 in several European countries [80].

The most common approach in the EU is based on a combination of excise duty and value added taxes, which should account for potential effects of the type of beverage consumed. As an example, the introduction of a tax on alcopops in Germany simply shifted consumption from spirit-based to beer-based

beverages [81]. Observational studies suggest that the effects of taxation would be larger for moderate than heavy drinkers [82], women [83] and young consumers [84].

Taking all these issues into account, the European Code Against Cancer has developed the following recommendation:

"If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention."

4. Conclusion

Worldwide, alcohol use is the second leading risk factor in terms of morbidity, and it accounts for a significant number of deaths, particularly in high-income countries. In Europe, it has been estimated that about 3%-10% of all cancer cases are attributable to alcohol consumption [24]. There is strong evidence that people can reduce their risk of cancer by limiting or cutting their consumption of alcoholic drinks. Overall, in European populations the risk of cancer in men who consume less than two alcoholic drinks (less than 20 g of pure alcohol) per day and in women who consume less than one alcoholic drink (less than 10 g of pure alcohol) per day is 6% lower (hazard ratio = 0.94; 95% CI: 0.90–0.96) than that in people with higher alcohol intakes [85]. On average, reducing the consumption from four-or-more to one-or-less alcoholic drinks per day may reduce the risk of liver cancer by 21% [41], the risk of colorectal cancer by 31% [40], and the risk of female breast cancer by 30% [41]. WHO have stated clearly that increasing price, reducing availability and banning advertising are the most effective policy measures that should be implemented at the European level in order to decrease the alcohol-related burden of disease.

The resulting recommendation of the 4th edition of the European Code Against Cancer targeted to individuals is to limit or cut the consumption of alcoholic beverages.

Conflict of interest

The authors declare no conflict of interest.

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