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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. The International Agency for Research on Cancer (IARC) Monographs provide strengthened evidence that the consumption of alcoholic beverages is causally associated with cancers of the oral cavity, pharynx, larynx, oesophagus, liver, colorectum and female breast, even for low and moderate alcohol intakes. The risk of cancer increases in a dose-dependent manner, and the higher the amount of alcohol consumed, the higher the risk of developing cancer. 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 the European Code against Cancer (ECAC) is: "If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention."

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) provides stronger 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 beverage [4–6]. Europe is the region of highest alcohol consumption in the world, with an average consumption of more than twice the global average; it has

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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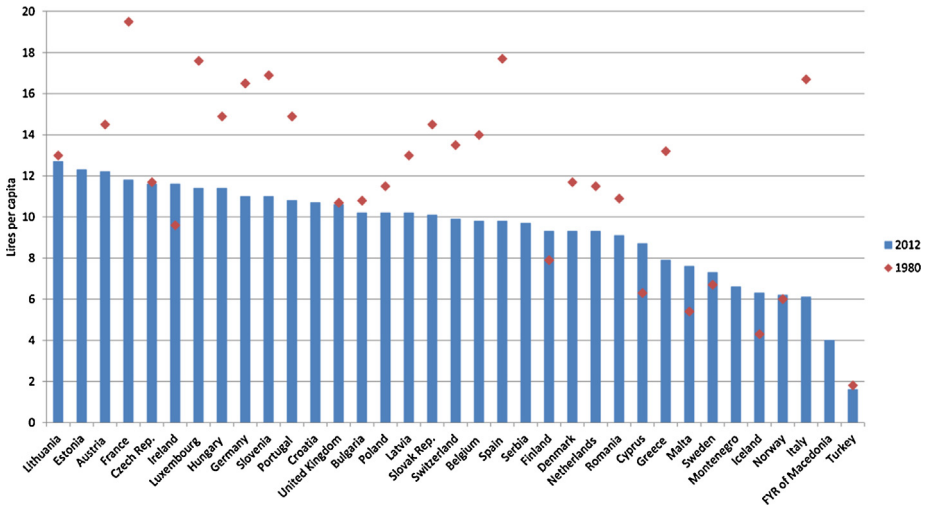

Fig. 1. Average European adult alcohol consumption in litres/capita/year among populations aged ≥15 years (years 2010 and 1980). From calculations provided by the OECD based on "Health at a glance: Europe 2012. OECD Publishing, 2012" [8].

a high prevalence of hazardous drinkers and an average alcohol-attributable cancer burden which also exceeds by far the global average [1]. Taken together, the 4th edition of the European Code Against Cancer (ECAC) [7] advocates action-oriented recommendations for the general public. The ECAC recommends decreasing or cutting alcohol consumption in order to 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. The most recent sales data show that individuals aged ≥15 years drink on average 10.7 l of pure alcohol per year [8]. Consumption tends to be higher in the Central-Eastern and Eastern countries such as, for example, Latvia, Romania, Lithuania and Austria, all of which have an average consumption >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 7–8 l of pure alcohol per adult person (Fig. 1). Gender, age and socio-economic status are key factors in determining levels of alcohol consumption [9]. 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 occasional 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 prevalence of binge drinkers doubled in France and has increased by about 30% in Germany between 2002 and 2008 [13]; binge drinking was reported by 36% of girls and 40% of boys in 2010 [8].

1.2. Effect of alcohol drinking on coronary heart disease

Light to moderate alcohol consumption might be associated with a reduced risk of coronary heart disease. A small reduction in risk has been suggested for the consumption of one drink every second day (not including as 'abstainers' those who reduced or stopped drinking [18]), and is probably confined to middle-aged or older individuals [18–20]. Similarly, a recent systematic review suggests that light to moderate alcohol consumption might be associated with a reduced risk of cardiovascular outcome, in particular coronary heart disease mortality compared to stroke [21], but again reverse causation and residual confounding cannot be excluded. While there is some evidence that low doses of alcohol may raise blood levels of high-density lipoprotein and improve reduction in coagulation [22,23], high doses may precipitate cardiac arrhythmias, myocardial ischaemia or infarction, and coronary death [24–26].

2. Association with cancer

2.1. Cancer types associated with alcohol drinking

As established by the IARC Monographs, consumption of alcoholic beverages is causally associated with cancers of the oral cavity, pharynx, larynx, oesophagus, colorectum, liver (hepatocellular carcinoma), and female breast in a dose-dependent manner [2]. Summary relative risks (RR) supporting these associations both for light and heavy drinking are indicated in Table 1. The relationship between alcohol consumption and cancer risk is monotonic and without a threshold (Fig. 2). Alcohol consumption accounts for about 3% and 10% of total cancers diagnosed in women and men, respectively [27]. 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 [27]. Drinking patterns play an important role in modulating the relationship between alcohol and cancer risk. The strongest associations are observed for heavy drinking, in particular 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: oral cavity, pharynx, larynx and squamous-cell carcinoma of the oesophagus

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 tracts (UADT) even in the absence of smoking. Significant dose–response relationships are found with different