

Alcohol consumption and cancer risk: revisiting guidelines for sensible drinking

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Recommendations for what constitutes sensible drinking are not new and have varied across time and place. In 1981, concerned by the increase in admissions to hospital for alcohol-related diseases in the United Kingdom, health educators and clinicians developed the general concept of sensible drinking.¹ Drinking sensibly was defined as the opposite of alcohol misuse, which is “drinking to excess or drinking in situations which are not appropriate when the effect in either case is to put the drinker or others at risk of harm.”² In 1984, the British Health Education Council described sensible drinking as the amount to which people should limit their consumption of alcohol.¹ Proposed British limits were 18 standard drinks per week for men (i.e., with 8 g ethanol/drink, 144 g of ethanol weekly) and 9 standard drinks per week for women (72 g of ethanol weekly). In 1987, the British Health Education Council raised the limits to 21 units per week for men (168 g ethanol) and 14 units per week for women (112 g ethanol).¹ Those recommendations were based on studies that had focused on the short-term effects of different levels of alcohol consumption, such as social and psychological problems or admissions to hospital. Subsequently, these recommendations were endorsed by three medical colleges (general practitioners, psychiatrists and physicians) and finally adopted by the UK government in 1992. Other countries also adopted this approach. Some countries have adapted the limits to reflect the patterns of drinking in their jurisdictions, i.e., the limits for drinking range from less than one to as many as four drinks or units of alcohol per day, and the measure of a unit of alcohol varies between 8 and 15 g of ethanol (Table 1 and Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.110363/-/DC1).

In the meantime, the Alcohol Use Disorders Identification Test (AUDIT) international questionnaire was developed by a World Health Organization (WHO) collaborative group as a simple method for screening people who may have problems due to their drinking habits. A brief interven-

tion program was developed and proposed for use among general practitioners from the participating countries. The aim of the program was for primary-care physicians to help people reduce their consumption of alcohol before dependence developed. Experts leading the collaborative group proposed adopting the guidelines already in use in their countries (UK, Australia, Denmark, France, etc.): 21 units per week for men and 14 for women.⁴ However, the limits proposed by the WHO collaborative group were sometimes wrongly considered to be official WHO guidelines. The WHO has never issued official quantified recommendations for alcohol consumption. Moreover, in plans for reducing the consumption of alcohol in the WHO European region, the message “less is better,” launched at a WHO European Conference in 1995, is the only recommendation consistently promoted.⁵

Limitations of guidelines

Guidelines for sensible drinking have several limitations. First, previous studies have shown that there is a potential conflict of interest in defining “sensible drinking,” since representatives of alcohol producers have sometimes been involved in the process.^{1,6-8} For example, in France, the guidelines are directly promoted by the producers of alcoholic beverages.⁹ In summarizing this issue, Professor David Hawks, the former director of Australia’s National Drug Research Institute, wrote “what is good for the industry is not necessarily good for the public.”⁷ Second, guidelines developed to reduce the risk of social and psychological problems or

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KEY POINTS

- Guidelines for sensible drinking are based on the short-term effects of consuming alcohol, such as social and psychological problems or admissions to hospital, and disregard the dose-response relationship between alcohol consumption and cancer risk.
- The current guidelines for sensible drinking for the general population are not adequate for the prevention of cancer.
- Revised guidelines that are based on complete and up-to-date scientific evidence are needed.

admissions to hospital are inadequate for the prevention of certain risks, particularly chronic diseases. Third, guidelines are not suitable for some situations, such as during pregnancy or before driving a motor vehicle, or in specific subpopulations.¹⁰ Finally, until recently, the progress of scientific knowledge concerning alcohol-related harms, especially the relationship between the consumption of alcohol and the risk of cancer, has not been given adequate consideration.

Recent developments

The amount of evidence for the link between alcohol consumption and cancer has recently increased. In 1988, a working group from the WHO International Agency for Research on Cancer, using data on exposure and from studies of cancer in humans and animal models, as well as mechanistic studies, concluded that alcoholic beverages are carcinogenic to humans and are causally related to malignant tumours of the oral cavity, pharynx, larynx, esophagus and liver.¹¹ These conclusions were confirmed in 2007 and

2009 by two other working groups from the WHO International Agency for Research on Cancer.^{12,13} In addition, it was concluded that the ethanol in alcoholic beverages¹² and the acetaldehyde associated with alcoholic beverages are carcinogenic to humans.¹³

Similar conclusions were reached by expert groups from the World Cancer Research Fund and the American Institute for Cancer Research, as stated in reports they issued jointly in 1997 and 2007.^{14,15} The 2007 report presented the strength of evidence from scientific literature published up to 2006 that had been evaluated by a panel of international experts, notably the results of systematic reviews and meta-analyses of epidemiologic studies on alcohol and 20 anatomic cancer sites and the results of mechanistic studies.¹⁵ It concluded that “the evidence that alcoholic drinks are a cause of cancers of the mouth, pharynx, larynx, the oesophagus, the colorectum (men), and the breast is convincing” and that “alcoholic drinks are probably a cause of colorectal cancer in women and of liver cancer.”¹⁵ It is important to note that the meta-analyses of cohort and case-control studies pre-

Table 1: Current limits set by guidelines for sensible drinking in some countries

Country	Alcohol content of a standard drink, g	Recommended limit for adult men	Recommended limit for adult women	Institutional source	Average annual consumption of alcohol per capita (2003–2005), ³ L
Australia	10	2 drinks/d (20 g/d)	2 drinks/d, (20 g/d)	National Health and Medical Research Council	10.0
Austria	8	24 g/d	16 g/d	Ministry of Health	13.2
Bulgaria	15	< 20 mL or 16 g/d	< 10 mL or 8 g/d	National Center of Public Health Protection	12.4
Canada	13.6	2 drinks/d (27.2 g/d), up to 14 drinks/w (190.4 g/w)	2 drinks/d (27.2 g/d) up to 9 drinks/w (122.4 g/w)	Center for Addiction and Mental Health	9.8
Denmark	12	21 drinks/w (252 g/w)	14 drinks/w (168 g/w)	Ministry of Health and Prevention, National Board of Health	13.4
France	10	3 units/d (30 g/d)	2 units/d (20 g/d)	French Institute for Prevention and Health Education	13.7
Great Britain	8	3–4 units/d (24–32 g/d)	2–3 units/d (16–24 g/d)	National Health Service	13.4
Ireland	10	21 drinks/w (210 g/w)	14 drinks/w (140 g/w)	Health Service Executive	14.4
Italy	12	20–40 g/d (2–3 units/d), ≥ 65 yr, 12 g/d	10–20 g/d (1–2 units/d), ≥ 65 yr, 12 g/d	Ministry of Health	10.7
Spain	10	17 units/w (170 g/w)	11 units/w (110 g/w)	Ministry of Health	11.6
United States	13.7	2 drinks/d (27.4 g/d)	1 drink/d (13.7 g/d)	Centers for Disease Control and Prevention; US Department of Health and Human Services	9.4

sented in the 2007 report showed dose–response relationships with statistically significant increases in risk per drink per week for cancers of the upper aerodigestive tract (mouth, pharynx, larynx, esophagus) and liver, as well as significantly increased risk of colorectal, breast and liver cancer per 10 g ethanol per day. No threshold for risk-free consumption was identified.

Since 2007, several cohort studies have been published that support the conclusions made by the World Cancer Research Fund and the American Institute for Cancer Research regarding cancer sites for which the level of evidence is convincing or probable (Appendix 2, available at www.cmaaj.ca/lookup/suppl/doi:10.1503/cmaj.110363/-/DC1). Most of these recent studies show a significant increase in the risk of cancer with alcohol consumption. The studies that investigated the positive association between risk and increments of 10 g of ethanol per day found it to be significant.

Several biologic mechanisms support the results of observational epidemiologic studies on alcohol and cancer. In animals, ethanol and its metabolite, acetaldehyde, have been shown to be carcinogenic.¹⁶ A critical step in the metabolism of ethanol is the production of acetaldehyde and reactive oxygen species. These compounds are genotoxic, since they induce the formation of DNA adducts.¹⁶ The amount of acetaldehyde produced after alcohol has been consumed is determined by the activities of alcohol dehydrogenase, the enzyme that converts ethanol to acetaldehyde, and aldehyde dehydrogenase, which converts acetaldehyde to the less-toxic compound acetate. In humans, current data suggest that polymorphisms of the genes encoding alcohol dehydrogenase (*ADH*) and aldehyde dehydrogenase (*ALDH*), in combination with alcohol consumption, play a role in the development of cancers of the upper aerodigestive tract. People with the *ADH1B*1* allele (common in most populations) or *ALDH2*2* allele (common in the Asian population) who consume alcohol are at a higher risk for cancer than carriers of other alleles.^{13,17} Not only is acetaldehyde a metabolite of ethanol, it can also be found in alcoholic beverages.¹⁸ It can therefore exert a local carcinogenic effect, particularly in the upper aerodigestive tract.¹⁸ Other site-specific mechanisms that have been identified include irritation of the mucosa and an increase in its permeability to carcinogens (such as tobacco) involved in cancers of the upper aerodigestive tract, inflammatory reactions such as hepatitis and cirrhosis leading to liver cancer, interference with the metabolism of folates leading to colorectal cancer and modification of the plasma levels of sex hormones leading to breast cancer.^{16,19}

On the whole, alcohol is considered an avoid-

able risk factor for cancer incidence and, more generally, for the global burden of disease.^{3,20}

Recommendations

Although drinking guidelines used in the context of a brief intervention have proven effective,²¹ in many countries, their application to the general population should be revisited.

From the latest evaluations by the WHO International Agency for Research on Cancer and joint evaluations by the World Cancer Research Fund and the American Institute for Cancer Research, it can be concluded that there is no level of alcohol consumption for which cancer risk is null.^{12,13,15} Thus, for cancer prevention, the consumption of alcoholic beverages should not be recommended. As has recently been done in France with the aim of improving the prevention of cancer,²² health professionals can be advised not to suggest starting consumption of alcohol for their patients who do not drink, even at moderate levels; to encourage their patients who do drink to reduce the amount they consume and the frequency of their consumption; and to recommend that children and pregnant women not consume any alcoholic beverages.

This advice might be weakened or counteracted by the widely disseminated message that attributes a beneficial effect to the moderate consumption of alcohol with respect to cardiovascular diseases.²³ However, several recent publications underline the methodological bias of most studies mentioning an apparent reduction of risk, such as nutritional, lifestyle or social confounders^{24,25} or the inclusion of people who used to consume alcohol, but no longer do, in the reference group.²⁶ Taking these important limitations into consideration, the 2007 WHO international expert committee on the prevention of cardiovascular disease concluded that “there is no merit in promoting alcohol consumption as a preventive strategy.”²³

Guidelines for the low-risk consumption of alcohol may be perceived by the general population as a “safe” baseline from which to range upward in setting personal limits,²⁷ which is why WHO Europe still promotes the message “less is better”²⁷ and considers that “region-wide specific drinking guidelines are not advisable.”²⁷ For this reason, the 1997 Canadian guidelines for low-risk consumption start at zero drinks for the lowest level of risk for an alcohol-related problem; levels above zero (up to 2 drinks per day, totalling 9 drinks per week for women and 14 drinks per week for men) are considered to be guidelines for “low-risk” and not “no-risk” consumption.²⁸ It should be noted that these guide-

lines do not apply to certain subpopulations, such as people with a family history of, or other risk factors for, cancer.

In 2011, the Canadian Centre on Substance Abuse, in partnership with Health Canada, provincial and territorial medical officers of health and other stakeholders, is expected to release Canada's first national drinking guidelines.

To circumvent the difficulties linked to such guidelines, Australia has adopted an alternative strategy.²⁹ Its 2010 guidelines (not more than two drinks per day [20 g of ethanol per day]) were chosen for their lifetime alcohol-attributable risk for chronic disease mortality of less than 1%, which is considered an acceptable level of risk at the population level.³⁰

Knowledge gaps

As shown in Table 1, some countries with a higher consumption of alcohol per capita (as estimated by the WHO)³ also tend to have higher limits in their drinking guidelines. This observation needs to be confirmed with information from more countries.

There is also a lack of data on the impact drinking guidelines have on the consumption of alcohol at the population level or in subgroups. Unfortunately, such investigations are difficult to conduct for several reasons. First, introducing guidelines is not the only factor affecting trends in alcohol consumption in a country. Secular trends, variation in the availability, pricing and advertising of alcohol, economics and increased work-related stress may all have an impact on consumption. Second, a country's population may not be aware of the guidelines, understand what constitutes a standard drink, know how to follow the guidelines or agree with the guidelines. Different subgroups could also react differently to the guidelines, which may not be noticed at the population level.

The amount of data available is limited. In the province of Ontario, surveys on alcohol consumption have been conducted every year since 1992. Between 1994, the year in which guidelines for low-risk drinking were introduced, and 2007, alcohol consumption by adults remained stable: no significant change was seen in the percentage of people who consumed alcohol, who consumed alcohol daily or who consumed five or more drinks in one sitting on a weekly basis, nor did the number of drinks consumed show any significant change.³¹ In the United States, the proportion of adults reporting a level of consumption that exceeded the recommended limits was estimated between 1991–1992 and 2001–2002, the period during which low-risk guidelines were introduced, and a significant decrease in consumption was reported.³²

Future research should estimate the level of alcohol consumption in the population before guidelines are introduced, and the association between subsequent awareness of the guidelines and any change in alcohol consumption at the individual level.

The way forward

Although guidelines are currently practical for health professionals and health authorities, the time has come to reconsider them using a scientific basis independent of any cultural and economic considerations and to discuss the eventuality of abandoning them. Considering our current knowledge of the relationship between alcohol consumption and cancer risk, national health authorities should be aware of the possible legal consequences of promoting drinking guidelines that allow consumers to believe that drinking at low or moderate levels is without risk.

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