



ALCOHOL AND HEALTH

ALCOHOL AND CANCER RISK



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PREFACE

A recent Éduc'alcool survey on Quebecers and alcohol revealed that one in ten drinkers felt that drinking was affecting their physical health. More than a third of all respondents (37%) believe that health issues are the main problem related to alcohol abuse. It is therefore easy to understand why nearly two-thirds of Quebecers put health at the top of the list of topics of interest with regard to drinking.

This is no surprise. The media report regularly on the results of studies on the impact of alcohol on human health, because an ever-increasing amount of research is demonstrating the benefits and risks of different amounts of alcohol and approaches to drinking. Information is being disseminated primarily by the scientific community, but advocacy groups are joining the debate, making provocative statements that are often alarmist and terrifying. At the other end of the spectrum are those who minimize and even trivialize the risks associated with drinking.

Nevertheless, the subject of alcohol and cancer risk is particularly charged, because of the fear that the disease still evokes and the strong emotions it arouses. It's a fact that one in two Quebecers will be affected by cancer at some point during their lifetime, and that many myths about cancer are still widely believed.

It is therefore extremely important to provide comprehensive, serious and solidly founded information about the relationship between alcohol and cancer risk. Furthermore, the information must be presented calmly, it must distinguish relative risk from absolute risk, and it must neither trivialize nor terrorize.

Éduc'alcool intends to contribute to this process by clarifying the scientific data and making it available to the public, so that those who drink alcohol can make enlightened choices. And, as always, we hope to convince people that moderation is always in good taste.

INTRODUCTION

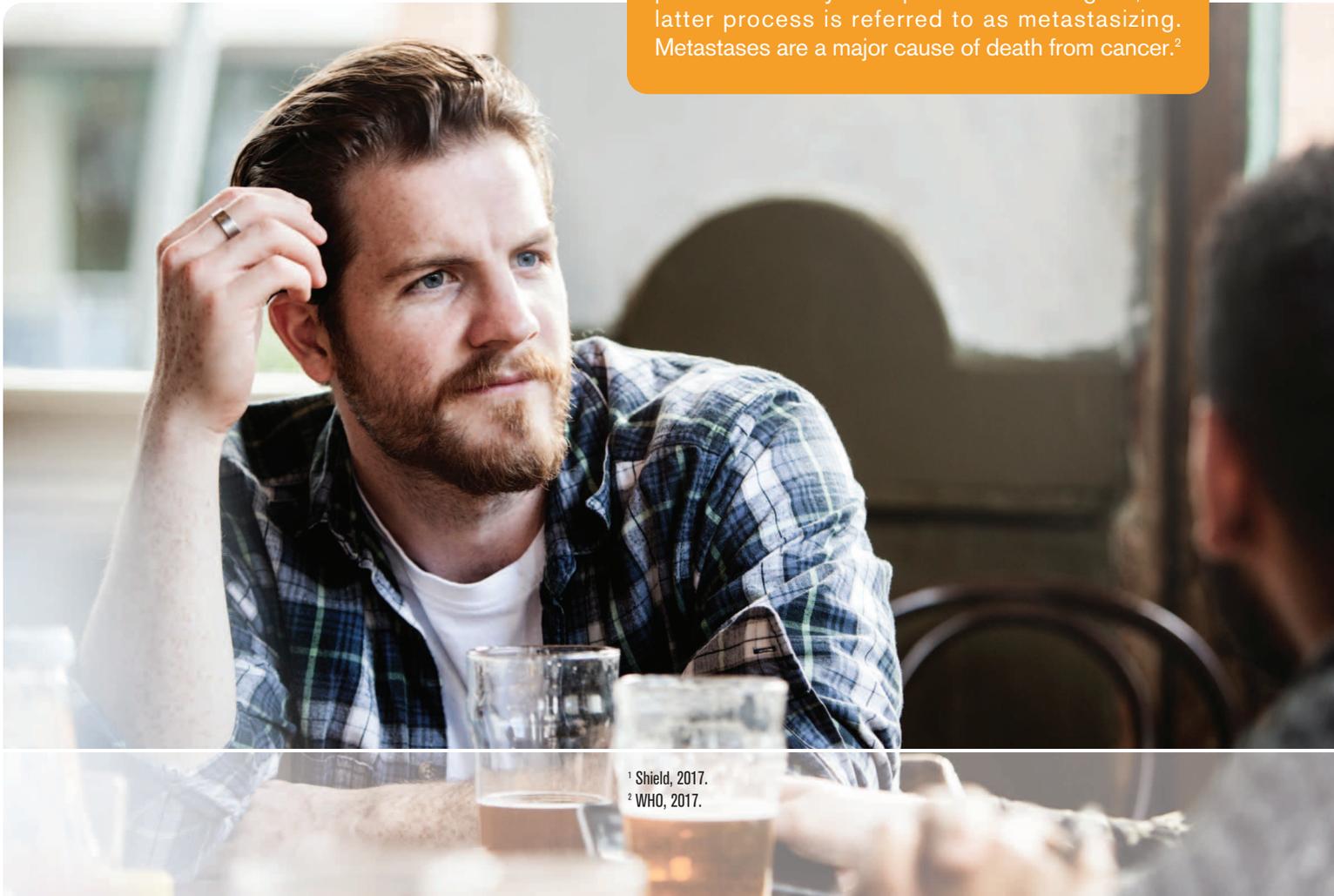
We have known for some time that moderate drinking can be beneficial for cardiovascular health.

And yet, alcohol can also have a harmful impact. It has been widely shown that alcohol can increase the mortality rates associated with certain diseases and increase the incidence of such diseases, including several cancers. The International Agency for Research on Cancer (IARC), the World Health Organization (WHO) agency specializing in cancer, reported for the first time in 1988 that drinking alcohol was a risk factor for many types of cancer.

According to the Canadian Cancer Society, there were 206,200 new cases of cancer and 80,800 deaths caused by the disease in Canada in 2017. It is estimated that alcohol was a factor in 10,310, or 5%, of the new cancer cases and 3,636, or 4.5%, of the cancer deaths.¹

This Educ'alcohol report begins by illustrating the risk of developing certain kinds of cancer, depending on the amount of alcohol consumed. It then explains the biological mechanisms triggered by alcohol and thereby influencing cancer risk. There follows a discussion of the various risk factors that can affect the link between alcohol and cancer, while the last part covers the different ways in which drinking profiles can influence cancer risk.

Cancer is a generic term for a large group of diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs; the latter process is referred to as metastasizing. Metastases are a major cause of death from cancer.²



¹ Shield, 2017.
² WHO, 2017.



ALCOHOL USE AND RELATIVE CANCER RISK

A number of epidemiological studies have shown an association between alcohol use and the risk of several kinds of cancer. A search of PubMed—the main search engine for bibliographical data in biology and medicine—using the keywords “alcohol,” “cancer” and “epidemiology” returned more than 200 articles published on the subject between 2012 and 2017.

When people drink moderately, the association between alcohol and various forms of cancer is low, and thus, when examined one at a time, the different studies do not always come to the same conclusions. Sometimes, low to moderate drinking is linked to cancer risk, sometimes the opposite is observed, and sometimes no link is established.³ This is why, for several years now, World Health Organization researchers

have been working to synthesize all the evidence, so as to determine whether there truly is a connection between drinking and different types of cancer. To that end, they have undertaken to combine the results of all the independent studies on the subject, in an attempt to identify trends. Based on these studies, it is now acknowledged that drinking alcohol increases the risk of cancers of the mouth, pharynx, larynx, esophagus, liver, pancreas, colon, rectum, prostate and breast. Studies have also shown that drinking had no effect, and occasionally even had a beneficial effect, on cancer of the kidneys (renal cell carcinoma), as well as on Hodgkin’s and non-Hodgkin’s lymphoma.⁴ Of course, this does not mean that people with kidney cancer are encouraged to drink alcohol.

IN SCIENCE, IT IS IMPORTANT TO DISTINGUISH ASSOCIATION FROM CAUSATION.

³ Rehm and Shield, 2014.

⁴ INCa, 2007; INRC, 2012; Rehm and Shield, 2014.

People sometimes joke that “when you’re sick, you’d better not go to the hospital, because you’re more likely to die in a hospital bed than at home.” While it’s true that there are seriously ill people in hospitals (association), being in a hospital does not cause death (causation). This is why, in epidemiology, criteria have been developed to determine what constitutes adequate proof of a causal relationship between two events⁵—in this case, between drinking and cancer.

It can be said that drinking alcohol causes a certain type of cancer when:

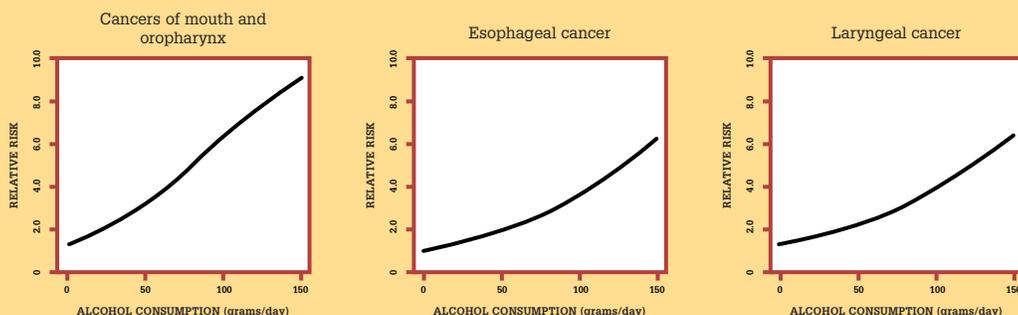
- ① there is a dose-effect relationship, that is, the more alcohol people drink, the greater the likelihood of a certain cancer;
- ② a variety of evidence has been collected; and
- ③ the mechanism by which alcohol causes a particular cancer can be explained.

Based on these criteria, the various cancer agencies and research institutes currently recognize that alcohol causes seven different types of cancer. Drinking alcohol leads to a significant increase in the risk of cancers of the mouth (including the oral cavity and pharynx), the esophagus and the larynx, and there is a moderate increase in the risk of cancers of the liver, colon, rectum and female breast. While it is possible that the link between drinking and these cancers might differ, depending on whether we are talking about the risk of developing (morbidity) or dying from (mortality) one of these cancers, science does not have enough information at this point to make that distinction.

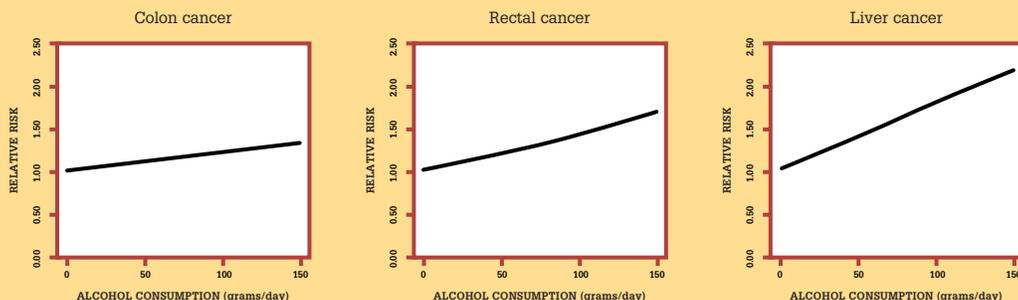
The graphs shown below illustrate these causal relationships and indicate the relative risks of developing these seven cancers (morbidity and mortality combined), based on average amount of alcohol, in grams consumed per day.

Figure 1 Combined illustration of the relative risks of cancer of the mouth and oropharynx, the esophagus, the larynx, the colon, the rectum, the liver and the female breast, depending on alcohol use (based on the meta-analyses by Rehm and Shield [2014]).

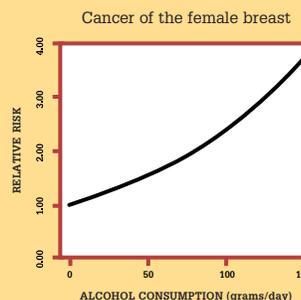
Neoplasms of the upper digestive tract



Neoplasms of the lower digestive tract



Other neoplasms



⁵ Hill, 1965.

As these graphs show, whether the increase is linear (such as with oral, colon, rectal and liver cancer) or exponential, i.e. rapid and continuous (such as with esophageal, laryngeal and breast cancer), any amount of alcohol increases the risk of cancer.

Nevertheless, before becoming alarmed, we have to examine the absolute risks for such cancers. In other words, we must go through the process of quantifying and assessing statements claiming that alcohol is carcinogenic. (See Figure 2 below.)

For example, risk increases most dramatically as alcohol use goes up when it comes to cancers of the oral cavity and pharynx. Studies done for Canada’s National Alcohol Strategy Advisory Committee have shown that drinking an average of one glass of alcohol a day increases the risk of death from these cancers by 42%, and having two drinks a day is associated with a 96% increase in risk.⁶ However, it should

be noted that the risk of death from oral or pharyngeal cancer among men and women under the age of 70 is between 0.2% and 0.5%.⁷ These relative increases of 42% and 96% mean the risk for men of actually dying from this type of cancer increases from 0.5% (1 in 200) to 0.71% (1 in 141) if they have one drink a day, and to 0.98% (1 in 102) if they have two drinks a day.

As Figure 2 shows, the smallest risk increase is for colon cancer. Risk increases from 3% to 26% as average alcohol use goes from one to six drinks a day. However, compared to other types of cancer, the incidence of colon cancer is high (2.5%, or 1 in 40).⁸ Consequently, the increased risk related to increased drinking could be of greater concern for some people, particularly those with a genetic risk for colon cancer.

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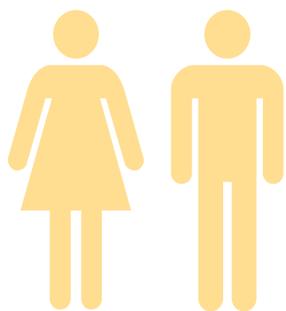
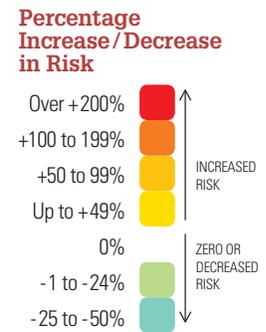


Figure 2 Variation in percentage risk for men and women of premature death from the 7 cancers caused by alcohol



Type of Illness or Disease	Proportion of All Deaths, 2002-2005	1 DRINK	2 DRINKS	3-4 DRINKS	5-6 DRINKS	+6 DRINKS
Oral cavity & pharyngeal cancer	1 in 200	+42	+96	+197	+368	+697
Oral esophageal cancer	1 in 150	+20	+43	+87	+164	+367
Colon cancer	1 in 40	+3	+5	+9	+15	+26
Rectal cancer	1 in 200	+5	+10	+18	+30	+53
Liver cancer	1 in 200	+10	+21	+38	+60	+99
Laryngeal cancer	1 in 500	+21	+47	+95	+181	+399
Breast cancer	1 in 45	+13	+27	+52	+93	+193

⁶ Butt *et al.*, 2011.

⁷ According to the most recent report from the Canadian Cancer Society Advisory Committee on Cancer Statistics (2017), the risk of dying from oral and pharyngeal cancer is 0.5% for men and 0.2% for women.

⁸ According to the most recent report from the Canadian Cancer Society Advisory Committee on Cancer Statistics (2017), the risk of dying from colorectal cancer is 3.5% for men and 2.9% for women.

HOW ALCOHOL ACTS ON THE BODY TO AFFECT CANCER RISK

The notion that drinking causes a certain type of cancer is acknowledged in the scientific community when the biological mechanisms by which alcohol increases cancer risk can be explained plausibly. To date, researchers have identified some mechanisms common to all cancers, and other mechanisms specific to certain types of cancers, such as those of the upper aerodigestive tract (mouth, esophagus and larynx), the liver and the breast.

Common mechanisms

Alcoholic beverages contain a number of carcinogenic compounds, such as ethanol, acetaldehyde, aflatoxins and ethyl carbamate,⁹ all of which can contribute to increasing the risk of alcohol-related cancer. For example, the acetaldehyde contained in alcoholic beverages is also produced by the human body.¹⁰ When ethanol is ingested, it is metabolized in the liver and oxidized into acetaldehyde, and subsequently into acetic acid. Exposure to the acetaldehyde associated with drinking is considered carcinogenic for humans.¹¹ Thus, exposure to acetaldehyde is particularly bad when it comes to the risk of liver cancer, since the liver is the main organ responsible for metabolizing alcohol.

Another biological mechanism proposed as an explanation for the link between drinking and cancer risk has to do with changes in the metabolism of folate.¹² It is now known that drinking alcohol causes specific nutritional deficiencies, particularly in folates and other vitamins that normally play a role in protecting against cancer. Such deficiencies could thus lead to an increased cancer risk.

⁹ Lachenmeier, Przybylski and Rehm, 2012.

¹⁰ National Toxicology Program, 2016.

¹¹ IARC, 2012.

¹² Rehm and Shield, 2014.



Specific mechanisms

Cancer of the upper aerodigestive tract

Various studies using animals have shown that chronic exposure to alcohol leads to a thinning of the mucous membranes of the upper aerodigestive tract, and that ethanol makes the mucous membranes more permeable by carcinogens.¹³ In other words, following exposure to alcoholic beverages, the carcinogens mentioned above (ethanol, acetaldehyde, aflatoxins and ethyl carbamate) find their way more easily into the oral cavity, the pharynx, the larynx and the esophagus. If the permeability of these organs is also a function of the alcohol content of the beverages consumed, then it is possible that beverages with a high alcohol content could be more harmful than those with a low alcohol content.¹⁴ However, this hypothesis remains unconfirmed.

Another possible mechanism, albeit an indirect one, is that drinking alcohol leads to reduced saliva flow, which, in turn, impairs the drainage of impurities from the mouth and thus promotes exposure to carcinogens.¹⁵

Liver cancer

A number of biological mechanisms have been suggested to explain how alcohol increases the risk of liver cancer.¹⁷ Aside from explanations above, regarding acetaldehyde and nutritional deficiencies, the main hypothesis is that heavy alcohol use over a long period of time promotes the development of cirrhosis of the liver,¹⁷ a condition known to contribute to the risk of liver cancer.¹⁸



Breast cancer

Specifically with regard to breast cancer, studies have shown that alcohol is linked to cancer risk because drinking promotes an increase in sex hormones, which are known to contribute to the appearance and growth of breast tumours.

Another explanation, advanced and supported by the results of a recent study, is that alcohol contributes to the risk of breast cancer because of its impact on breast tissue density.¹⁹ This could be particularly concerning for very young women, since breast tissue is more malleable between the onset of menstruation and first pregnancy.²⁰ Unfortunately, these are also the years during which women tend to drink excessively. By drinking a lot at a time when their breast tissue is most fragile, young women expose themselves to a greater risk of breast cancer.

¹³ INCa, 2007.

¹⁴ E.g. Freedman *et al.*, 2007.

¹⁵ INCa, 2007.

¹⁶ For a summary, see INCa, 2007.

¹⁷ Cirrhosis is a disease characterized by the progressive replacement of healthy liver tissue by nodules and scar tissue, which gradually impairs liver function. It is a serious and progressive disease.

¹⁸ Canadian Cancer Society, 2017.

¹⁹ Ziembicki *et al.*, 2017.

²⁰ Liu *et al.*, 2015.

RISK FACTORS AFFECTING THE ASSOCIATION BETWEEN ALCOHOL AND CANCER

Cancer arises from the transformation of normal cells into tumour cells in a multistage process that generally progresses from a pre-cancerous lesion to a malignant tumour. These changes are the result of the interaction between a person's genetic factors and external agents, such as alcohol.²¹

Genetic factors

Since the early 2000s, it has been understood that the risk of cancer among people who drink alcohol varies according to their genetic profile. The body of evidence to date shows that the risk of cancers of the upper aerodigestive tract, in particular the esophagus, is higher among people of a certain genotype particularly prevalent among Asian populations.²² The blood, and occasionally the saliva, of these individuals has been found to contain a higher amount of acetaldehyde, which, as we know, is considered carcinogenic to humans.

However, it is important to note that the data on polymorphism—the occurrence of different forms of the same gene within a given population—with regard to drinking and cancer risk is currently insufficient and sometimes contradictory. For example, it is not yet possible to identify with certainty which people with which genotypes are most at risk for colorectal, liver and breast cancer.²³ In the field of genetic vulnerability or predisposition, many theories have yet to be confirmed.



²¹ WHO, 2017.

²² IARC, 2012.

²³ INCa, 2007.



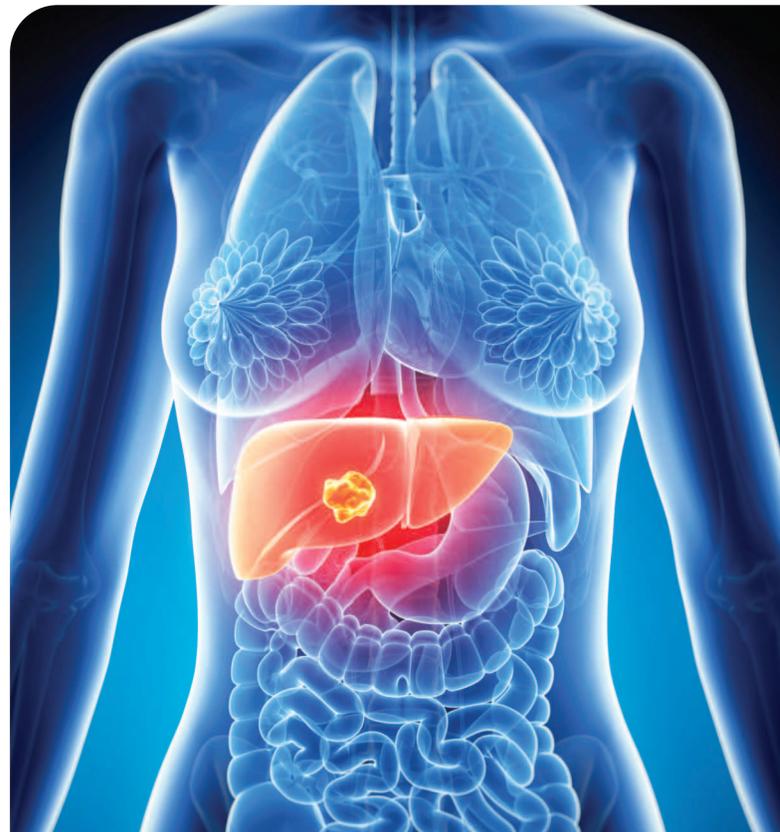
External carcinogens

Alcohol appears to interact with various other risk factors, tobacco in particular. Because alcohol alters mucous membranes, drinkers who smoke are more at risk for cancers of the upper aerodigestive tract: alcohol leads to greater permeability of the mucous membranes, which promotes the absorption of carcinogens in tobacco products. It is also believed that alcohol acts as a kind of solvent, helping tobacco carcinogens pass through the mucous membranes.²⁴

A few epidemiological studies also suggest that combining alcohol and tobacco increases the risk of colorectal and liver cancer. Similar results have been seen in the interaction between alcohol and obesity, with an increased risk of colorectal cancer noted in case-control studies.²⁵ However, these results have not been confirmed and further research is necessary to ascertain these interactions.

²⁴ INCa, 2007.

²⁵ E.g. Zhao *et al.*, 2012.



EFFECTS OF ALCOHOL ACCORDING TO DRINKING PROFILE

Amount consumed

When it comes to alcohol and health, drinking profile is important. How much people drink, what they drink and how they drink are all factors that can affect their health.²⁶ So how does drinking profile affect cancer risk?

With regard to drinking and cancer, there is no dose without effect. Whether the causal relationship is linear (as in oral, colon, rectal and liver cancer) or exponential (as in esophageal, laryngeal and breast cancer), the risk of developing or dying from one of these cancers increases with the average amount of alcohol consumed.



Type of alcoholic beverage

It was noted above that beverages with a high alcohol content may be more harmful to the mucous membranes of the upper aerodigestive tract, specifically the larynx. However, further research is necessary before this can be confirmed. At this stage, researchers generally agree that, when it comes to cancer, the only thing that matters is the amount of alcohol consumed, regardless of the type. All alcoholic beverages—beer, wine, fortified wine, spirits and cider— have the same effect and are associated with cancer risk.²⁷

It would appear that the risk of developing a chronic disease could be reduced when alcohol is consumed with a meal, rather than without food.²⁸ As regards cancer specifically, this theory has not been confirmed and requires further study.²⁹

Duration of use

With regard to cancers of the upper aerodigestive tract only, a combined analysis of the epidemiological research suggests that cancer risk declines after 10 years of alcohol abstinence and that, after 20 years, the risk is equivalent to that for people who have never drunk alcohol.³⁰



²⁷ Allen *et al.*, 2009; IARC, 2012; WCRF, 2007.

²⁸ Éduc'alcool, 2016.

²⁹ INCa, 2007.

³⁰ Rehm *et al.*, 2007.



CONCLUSION

Drinking alcohol is associated with the risk of several cancers, with the data confirming that alcohol may cause, or at least be involved in causing, seven specific types of cancer. Alcohol is carcinogenic and is one of the avoidable risk factors. Because Éduc'alcool's mission is to improve Quebecers' relationship to alcohol, we believe it is necessary to make drinkers aware of the risks of drinking, while ensuring that this is done rigorously and carefully, without trivializing or dramatizing the data.

People rarely drink because of some pact with the devil. Rather, drinking is generally associated with seeking pleasurable sensations and is often seen as an occasional treat. Any statements about cancer risk must therefore be understood within that context.³¹ More precisely, the association between alcohol and the risk of developing cancer must be recognized while also considering the absolute risk for various cancers. The dose-effect relationship is stronger for less common cancers, such as oropharyngeal or laryngeal cancer, and weaker for more common cancers, such as colorectal cancer.³²

Cancer may also appear as a result of an interaction between personal genetic factors and a variety of external carcinogenic agents. These agents may be biological (infections caused by viruses, bacteria or parasites), physical (ultraviolet radiation and ionizing radiation) or chemical, including alcohol.³³ The association between alcohol and cancer risk should be recognized while keeping in mind that cancer is not a disease with a single cause.

Finally, any recommendations with regard to drinking and health must be made in light of epidemiological data and evidence for all diseases known to be caused, in part, by alcohol. This obviously includes cancer, but also includes other diseases, such as diabetes, pancreatitis and cardiovascular diseases. With regard to the latter, significant data has shown that, compared to those who do not drink alcohol, people who drink excessively increase their risk of coronary disease, but people who drink moderately reduce that risk.

Health is a complex matter that cannot be reduced to a single concern about whether or not one is likely to develop cancer. For those who are concerned solely about cancer prevention, given what is currently known, it is recommended that drinking be reduced as much as possible. For everyone else, following the low-risk drinking guidelines remains a very reasonable choice. As we have been saying for years, moderation is always in good taste.

Éduc'alcool would like to thank Dr. Philippe Sauthier, Chief of Oncological Gynecology at CHUM, medical associate at the Centre intégré de cancérologie du CHUM, associate professor in the Faculty of Medicine at the Université de Montréal, and director of the Quebec Cancer Foundation, for his valuable contribution in revising the final version of this publication.



³¹ Holmes and Sumnall, 2017.

³² Butt *et al.*, 2012.

³³ WHO, 2017.

IN THE SAME COLLECTION



THE EFFECTS OF MODERATE AND REGULAR ALCOHOL CONSUMPTION

A review of the research on how moderate, regular alcohol consumption affects human health.



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