

Drinking and Cancer

BACKGROUND

According to the World Health Organization, cancer is one of the main NCDs worldwide, and accounts for 21.7% of all NCD-related deaths [2].

- The prevalence of cancer is increasing around the globe, as lifestyles and exposure to various risk factors change, and as the world's population ages.

Cancers include over 100 distinct diseases, each with its own set of potential risk factors whose relationships with each other are complex.

- For some cancers, these risk factors also include ethanol in alcohol beverages and acetaldehyde, one of the products of ethanol metabolism.
- It is estimated that some 3.6% of all cancer cases globally are attributable to alcohol consumption [3].

However, the relationship between alcohol consumption and cancer is complex and increasingly a topic of discussion in the media and also within public health when it comes to offering information and guidance to consumers regarding potential health risks and outcomes. Understanding this relationship is essential for the crafting of prevention measures aimed at reducing harmful drinking and cancer risk.

DRINKING AND CANCER

Alcohol has been identified as a known human carcinogen by the International Agency for Research on Cancer (IARC), and as a risk factor implicated in several discrete types of cancer.

- The IARC list of potential carcinogens includes over 1,000 substances and agents that cover the range from various solvents and chemical compounds, certain drugs (including antibiotics and even medications used to prevent cancer), viral infection, to solar radiation from exposure to sunlight, and red and processed meats [4].
- It is important to note that not every potential carcinogen for a particular type of cancer is necessarily implicated in each cancer case.

In general, the degree of cancer risk is related to the dose of a carcinogen and to the length of exposure. The higher the dose and the longer the period of exposure, the higher the risk for developing cancer.

- This relationship also applies to the consumption of alcohol; the most clear association of cancer risk is with heavy drinking, particularly regular heavy drinking over extended periods of time.

Cancers, like other NCDs, have multiple risk factors.

- These include genetics and family history of cancer, environmental factors, and behavioral variables such as exercise, smoking, obesity, or the consumption of alcohol beverages.
- While some risk factors are independent of each other and are sufficient on their own to cause cancer, others act in synergy.

- The confluence of individual risk factors is different for each person and determines the likelihood of developing particular types of cancer.

Alcohol-associated cancers

While many cancers are not associated with alcohol consumption, certain site-specific cancers are, although they can also occur in the absence of drinking and may be related to a number of other potential risk factors.

- In general, alcohol-associated cancers have been linked with heavy drinking [5-9].
- Recent research suggests that light to moderate drinking is not significantly associated with an increased risk for total cancer in either men or women [10].
 - Among women, light drinking was found to increase the risk of all cancers by 2%, and moderate drinking by 4%, over the risk for non-drinkers.
 - Among men, light drinkers had a 3% increase in risk over non-drinkers, while the risk for moderate drinkers was 4%.
- However, according to this study, moderate drinking among women increased risk for developing an alcohol-related cancer by 13% [10]; the main driver of this risk was breast cancer.
- Among men, an increase was observed only among men who were also smokers. For them, the increase in risk was primarily due to colorectal cancer.

Alcohol-associated cancers include the following diseases, as laid out in the most recent IARC report that summarizes the body of available evidence [11].

Upper digestive tract cancers

A dose-response relationship has been reported for cancers of the upper digestive tract, specifically for those occurring in the oral cavity, larynx, pharynx, and esophagus.

- The highest levels of risk have been observed for heavy drinking [5, 6], but some studies have also found a weaker link with moderate consumption [12].
- Alcohol consumption and smoking are both independent risk factors for cancers of the oral cavity and pharynx, but together their effects are multiplicative [6, 13, 14].
- This association does not vary by beverage type and is the same for men and women [6, 11].

Reducing heavy drinking can change the level of risk for upper digestive cancers [15].

- According to one study, reducing consumption by 7 drinks a week (the equivalent of 63-91g ethanol/week) can significantly lower cancer risk at all levels of drinking [15].
- While cessation of alcohol consumption may lower risk for oral, pharyngeal, and esophageal cancers, research suggests that this decrease occurs gradually and may take place over decades [16-19].

While ethanol itself is a risk factor for head and neck cancers, so is its breakdown product acetaldehyde [8].

- As a result, individuals with a lesser ability to break down acetaldehyde, such as persons of East Asian descent with a genetic variant of the enzymes that metabolize ethanol, may be at heightened risk for esophageal, and head and neck cancers [20, 21].

Liver cancer

In 2012, liver cancers were estimated to account for 9% of all cancer deaths globally [22], although most cases of liver cancer do not involve alcohol consumption.

- According to research findings, a positive association with alcohol has only been shown for heavy drinking [23, 24].
- Some studies also suggest that the association with alcohol may vary depending on the type of liver cancer [11].

In addition to alcohol consumption, other risk factors also play a key role in liver cancer.

- Alcohol and tobacco are independent risk factors for liver cancer [25].
- Liver cirrhosis, which is associated with chronic heavy drinking, has also been implicated as a risk factor for liver cancer [7].
- Hepatitis B and C infections are further risk factors that are independently associated with liver cancer; they do not appear to affect the relationship with alcohol consumption [11].

- It has also been shown that alcohol and obesity have a multiplicative effect on the risk of developing a particular type of liver cancer (hepatocellular carcinoma) [26].

Breast cancer

Breast cancer is the leading cancer among women, and is associated with a large number of individual risk factors [8].

- Research has shown that breast cancer risk is associated with family history and hormonal and reproductive factors [27].
- Increased risk has been reported with hormone replacement therapy, but varies by the type of breast cancer (ductal, lobal, or mixed) [28].
- Similarly, risk associated with other reproductive factors, such as age at menarche or breastfeeding, have been shown to differ by cancer subtypes [29].

According to IARC, cancer of the female breast is causally associated with the consumption of alcohol beverages [8].

- Recent studies indicate a dose-response relationship between alcohol consumption and breast cancer [8, 23], although this relationship was not evident in some past studies.
- According to a recent study, light to moderate drinking (between 5 and 14.9g / day) has been reported to increase the risk for breast cancer [10].
- Some evidence suggests that at moderate or high levels of alcohol consumption, adequate intake of the amino acid folate may attenuate the risk for breast cancer [30].
- Estrogen and progesterone receptor status has been shown to affect the association between alcohol consumption and breast cancer in some studies, however the role played by receptor status remains unclear [8].
- The association between alcohol and breast cancer does not differ by beverage type and is related to the ethanol in wine, beer, and spirits [8].

There is significant variation in the degree of risk associated with individual factors that have been linked with breast cancer.

- For example, for women with a genetic predisposition, the relative risk for developing breast cancer is 200-400% [27, 31-33].
- Among women who do not have children, the risk of developing breast cancer is 30% higher than for those who do [34].
- Breast cancer risk increases by a factor of 1.05 for every year that a young woman begins menarche before age 14 [35].

Recent research suggests a 13% increase in total relative risk for alcohol-related cancers among women who drink moderately compared to those who do not drink at all [10]. Much of this is due to breast cancer.

Evidence of an association of alcohol with cancer of the male breast is inconsistent [11].

Colorectal cancer

According to IARC, alcohol consumption is causally associated with colorectal cancer, notably at heavy drinking levels [8].

- While an increased risk of colorectal cancer has been established at heavy drinking levels, there is uncertainty around the risk at lower levels of consumption [8, 23, 36, 37].

Risk for precursor adenomas increases progressively for light, moderate, and heavy drinkers, compared to nondrinkers or occasional drinkers, but effects at lower levels of consumption are not significant [10, 38].

However, among long-term smokers consumption of alcohol has been shown to be protective against colorectal adenomas [39].

Some studies show gender differences in the association between drinking and risk of colorectal cancer [36], although other studies have failed to find differences between men and women [8].

Risk for colorectal cancer is similar for all beverage types [8].

Risk for colorectal cancer has also been shown to be independently influenced by dietary habits.

- An independent association has been shown between adherence to a Mediterranean diet and reduced odds of developing colorectal cancer [40].
- Colorectal cancer may be associated with a diet low in folate. However, research has produced inconsistent results on the influence of folate intake on the relationship between alcohol and colorectal cancer [11].

Ovarian and urinary bladder cancer

As reported by IARC, no association has been found between alcohol consumption and urinary bladder cancer [8].

Research on an association between alcohol consumption and ovarian cancer has produced inconsistent results. However, the majority of studies find no association [11, 23, 41, 42].

Brain cancer

While research on the relationship between alcohol consumption and brain cancer is limited, a meta-analysis failed to find a clear association, but indicated the need for further research examining the potential association with heavy drinking [43].

Renal cancer

There is evidence that alcohol consumption can be a protective factor against kidney cancer, and recent studies have shown a consistent inverse association between alcohol consumption and renal cancer [11, 44-47].

- The relationship between alcohol consumption and kidney cancer appears to hold for all three beverage types (beer, spirits, and wine), and for both men and women [45, 47].
- Recent research suggests that the protective effect of alcohol consumption for renal cancer may differ by smoking status, but studies have found conflicting results [44, 45].

Lymphatic cancer and cancers of the hematopoietic system

IARC reports a weak protective relationship between drinking and non-Hodgkin's lymphoma [8, 48], as well as some cases of Hodgkin's lymphoma [8, 23, 49, 50].

Alcohol consumption may provide modest protection against multiple myeloma, although individual studies have produced inconsistent results [51, 52].

No clear association has been observed for leukemia [11].

Lung cancer

According to IARC, there is insufficient evidence to establish a causal association between alcohol consumption and lung cancer [8].

- Smoking has a significant confounding effect, making it difficult to draw firm conclusions regarding the association.
- There is also some evidence that the association between consumption and lung cancer may vary across different beverage types [11].

Pancreatic cancer

Heavy drinking has been identified as a risk factor for pancreatic diseases, including chronic pancreatitis [9].

- Evidence suggests that chronic pancreatitis may also result in an increased risk for pancreatic cancer [53].
- However, research findings on the association between alcohol consumption and pancreatic cancer are mixed, although there is some evidence that high levels of alcohol consumption may increase risk [8, 23].

Prostate cancer

Evidence of an association between alcohol consumption and risk of prostate cancer is mixed, although IARC reports that most studies have found no association [8, 54, 55].

Endometrial cancer

Findings on the association between alcohol consumption and endometrial cancer have been inconsistent [8, 23].

- According to IARC, this may be due, in part, to the potential confounding effects of smoking and body size [11].

Stomach cancer

Evidence on the association between alcohol and stomach cancer is mixed, based on IARC's assessment of the evidence [11].

- However, results may be confounded by dietary and lifestyle factors, socioeconomic status, and infection with *Helicobacter pylori* [8].

METHODOLOGICAL CONSIDERATIONS

Various factors can influence or obscure observed relationships in health outcomes and should be taken into consideration when interpreting results.

While epidemiological studies attempt to control for additional variables that may obscure the real nature of relationships between individual risk factors and outcomes, it is not always possible to control for all potential confounding variables.

- For example, smoking plays an important role in the development of many types of cancer, especially lung cancer, and may influence the relationship with alcohol consumption, so needs to be controlled for and addressed in a study's design or data analysis.
- Socioeconomic status, body size, and nutrition also play an important role in the association between alcohol consumption and cancer risk, but can be more difficult to adequately control.

An important concern in alcohol-related research, particularly where surveys are involved, is the underreporting of alcohol consumption by respondents, which may influence the results and the resulting interpretation of the relationship between different levels of alcohol consumption and outcomes.

Studies also suggest that the underreporting of alcohol consumption can result in the misclassification of drinkers, especially of those who are in the low and moderate consumption categories. This misclassification can make it difficult to establish a clear relationship between low or moderate alcohol intake and cancer, making it difficult, in turn, to identify a threshold at which alcohol consumption increases cancer risk [56].

TERMS AND CONCEPTS

A **carcinogen** is any substance or agent that causes cancer. The International Agency for Research on Cancer (IARC) classifies carcinogens into different groups: Group 1 (carcinogenic to humans); Group 2A (probable carcinogens); Group 2B (possibly carcinogenic to humans); Group 3 (not classifiable as to their carcinogenicity to humans); and Group 4 (probably not carcinogenic to humans).

To be classified as a Group 1 carcinogen, a substance or agent must meet particular criteria, including:

- sufficient evidence of carcinogenicity in humans;
- or
- less than sufficient evidence of carcinogenicity in humans, but sufficient evidence in experimental animals and strong evidence in exposed humans of action through a relevant mechanism of carcinogenicity.

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Reviews

IARD Health & Policy Reviews cover the effects of alcohol consumption on health. They offer an overview of the relationship between drinking patterns and health outcomes, compile the key literature, and provide the reader with an extensive bibliography that refers to original research on each topic. The *Reviews* attempt to present the balance of the available evidence. They do not necessarily reflect the views of IARD or its sponsoring companies.

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The International Alliance for
Responsible Drinking (IARD)
The Jefferson Building
1225 19th Street NW, Suite 500
Washington, DC 20036

IARD
INTERNATIONAL ALLIANCE FOR
RESPONSIBLE DRINKING
action on alcohol and global health

Phone: 1.202.986.1159
Fax: 1.202.986.2080
Email: info@iard.org
Web: www.iard.org