



Centre for Addiction and Mental Health
Centre de toxicomanie et de santé mentale

Alcohol and Cancer: Best Advice

Centre for Addiction & Mental Health

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Introduction

While many people have a sense of the risks of heavy drinking, and may be aware of problems such as drinking and driving, the link between drinking and cancer is less familiar to the general public (Giesbrecht et al. 2000; Anglin et al. 2005). Media coverage on the protective effects that alcohol can have on cardiovascular disease rarely mentions that alcohol consumption also increases the risk of cancer and other chronic diseases. Also, the benefits of moderate alcohol consumption for chronic heart disease may not be as strong as previously reported (see Jackson et al. 2005). Changes need to be made so that the public is more aware that alcohol consumption is associated with both risks and benefits. This paper focuses on alcohol-related cancers, showing alcohol as a risk factor for cancer of the mouth, larynx, oesophagus and liver (Aronson 2003), as well as breast cancer (World Cancer Research Fund 1997; Collaborative Group on Hormonal Factors in Breast Cancer 2002) and cancers of the colon and rectum (Boffetta et al. 2006; Boffetta & Hashibe 2006).

A World Health Organization (WHO) affiliated publication (Babor et al. 2003) noted that alcohol-related morbidity and mortality includes cancers, neuropsychiatric conditions, cardiovascular conditions, gastrointestinal conditions, and maternal and prenatal conditions. Alcohol consumption has been related to more than 60 diseases (Rehm et al. 2003). In developed countries such as Canada, alcohol (9.2%) is just below tobacco (12.2%) and blood pressure (10.9%) for contributing to disability adjusted life years (World Health Organization 2002).

The loss of life, along with the personal, physical and emotional costs associated with having cancer necessitate bringing together the latest research linking alcohol consumption and cancer so that effective prevention initiatives can be planned and implemented. This association is not well known to members of the general public, and it is a topic that needs to be included in policy, planning, and prevention and treatment initiatives.

This paper will add to the series of alcohol policy position papers produced by the Centre for Addiction and Mental Health (CAMH) in recent years, including "Reducing the Harms of Alcohol Related Collisions Position Statement" (2002) and "Retail Alcohol Monopolies and Regulation: Preserving the Public Interest Position Paper" (2004).

Background

Surprisingly, alcohol has been linked to cancer since the nineteenth and early twentieth centuries. Many people with oesophageal cancer at that time were heavy drinkers or worked in the alcohol service or alcohol production industries. There was an assumption that the employees were frequent or heavy drinkers. More recently, the relationship between alcohol and cancer has been examined primarily over the past 40 years.

In 1997, the World Health Organization, European Region, identified alcohol as a risk factor for cancers of the upper aerodigestive tract, liver and breast. In the same year, the World Cancer Research Fund noted that the risk of breast cancer increases with the consumption of just a few drinks a week. The American Cancer Society had already reported (World Cancer Research Found 1997) that alcohol increased the risk of cancers of the mouth, pharynx, larynx, and oesophagus with the risk rising at two standard drinks a day. The United States National Toxicology Program and the International Agency for Research on Cancer (Aronson 2003) have both listed alcohol as a human carcinogen. A Cancer Care Ontario report advises that alcohol should be less than 5% of total energy for men (no more than 2 drinks/day) and 2.5% total energy for women (<1 drink/day) to prevent the adverse effect of alcohol on the risks of cancer (Jenkins 2001).

A point worth noting is that heavy drinking is often accompanied by smoking. Tobacco contributes to about 30% of mortality and incidence of all cancers (Canadian Cancer Society 2005). When tobacco and alcohol are combined, the risk for certain cancers increases dramatically. For example, Bagnardi et al. (2001, p. 267) indicate that case control studies of exposure to both risk factors suggest that 75% of upper digestive and respiratory tract cancers that occur in developed countries are attributable to alcohol and tobacco use. The combined effect of these two substances needs to be considered when developing comprehensive prevention and treatment plans.

Many organizations in the world have developed Low-Risk Drinking Guidelines (LRDG), and the recommendations of the Centre for Addiction and Mental Health fall in the middle of the range¹. According to new data, CAMH's Low-Risk Drinking Guidelines, as developed some years ago, actually overlap with modest risk for cancer. For example, a study by Ellison et al. (2001) showed that one standard drink per day (12 grams) is associated with a 10% increase in breast cancer risk (compared to non-drinkers). Thus, this increased risk occurs when consuming at a level even below that Guideline's recommended two standard drinks a day. However, it should be noted that these are "low risk" guidelines and not "no risk"

¹ In Canada a 'standard drink' is 13.6 grams of ethanol, or about one 12 oz bottle of beer (5% ethanol), a 5 oz glass of table wine (10-12% ethanol), a 3 oz glass of fortified wine (16-18% ethanol) or 1.5 oz shot of spirits (40% ethanol).

guidelines. Also, the current LRDG do indicate: "the Guidelines do not apply if you have a family history of cancer or other risk factors for cancer."

Cancer in Canada and the World

Cancer is one of the leading causes of death and the leading cause of premature death in Canada (Canadian Cancer Society, Canadian Cancer Statistics 2006). The Canadian Strategy for Cancer Control shows an increase in new cases accompanied by an aging population. Currently, more than two thirds of all new cases occur in those 60 and older and the age standardized incidence rates have remained relatively stable for most cancers. The Canadian Cancer Society (CCS) estimated that new cancer cases in 2006 affected 78,400 men and 74,700 women (Canadian Cancer Society 2006).

On a global basis, the results of a World Health Organization project indicated that of the total mortality attributed to alcohol in 2000, an estimated 20% was attributed to cancers, with the only higher general category being unintentional injuries at 32% (World Health Organization 2002; Rehm 2003).

Alcohol and Cancer

Alcohol has been labelled as a carcinogen by both the International Agency for Research on Cancer (IARC 1988) and the US National Toxicology Program (2005). As mentioned before, research has shown that this association includes the risk of breast cancer, liver cancer, head and neck cancer, and cancers of the rectum and colon (see Appendix A). Some studies have demonstrated increased risk with increased alcohol consumption on stomach, lung, ovary and prostate cancers but, on balance, the body of scientific evidence has been inconclusive (Appendix A). Cancers of the endometrium, pancreas and urinary tract have not shown any statistically significant correlation between risk and alcohol consumption. In general, these analyses indicate the 'net' impact from alcohol, that is, after controlling for the impact of smoking.

All cancers associated with alcohol consumption have a dose-response relationship that is typically linear in terms of relative risk and all are significant at low dose. Corrao and colleagues (2004) conducted a meta-analysis of 156 higher quality studies selected from 561 initially reviewed. They state: ""Direct trends in risk were observed for cancers of the oral cavity and pharynx, esophagus, and larynx. Direct relations were also observed for cancers of the colon, rectum, and liver, as well as breast cancer." (Corrao et al. 2004, p. 615).

Research still needs to be undertaken to provide further evidence of the impact of alcohol on cancer-specific morbidity and mortality. Nevertheless, the available and

extensive international research that focuses on specific cancers can be used as the basis for prevention initiatives. Cancer statistics vary between developed and developing countries. This needs to be taken into consideration when looking at the statistics and interventions.

Alcohol and Specific Types of Cancer

The causal associations between alcohol consumption and cancer have been determined by consistency across meta-analyses, reviews (Appendix A) and biological analyses (e.g. Purohit et al. 2005)². The following sections provide more detail on cancers that are specifically linked to alcohol consumption.

Breast Cancer: The risk of breast cancer increases with greater alcohol consumption. Research shows for every 12 grams/day (1 Canadian standard drink = 13.6g) of alcohol consumed, there is a 7 to 10% increased risk of breast cancer in women (varies by type of study) (Ellison et al. 2001; see also Collaborative Group on Hormonal Factors in Breast Cancer 2002). About 4% of new cases of breast cancer are linked to alcohol; using this conservative number, 700 cases of breast cancer/year in Canada could have been attributed to alcohol (Aronson 2003).

Head and Neck Cancer: Alcohol is a lifestyle factor that contributes to increasing the risk of oral cavity, larynx, pharynx and oesophageal cancers (Adami et al. 2001). It has been noted that 1.8 drinks/day (25 grams) over several years can increase the risk of: oesophageal cancer by 31-34%; 26% for cancer of the larynx; and 42-47% for oral cavity cancer (Bagnardi et al 2001).

Moderate smoking or moderate drinking, independently, may have little effect on risk of head or neck cancer, but used simultaneously, in moderate amounts, there is a 12-19 times increase in the risk of oesophageal cancer in men and women (Pera and Pera 2001). Some research shows that oral cancer and alcohol consumption is associated with drinking as little as one drink/day with the risk increasing the longer the period of consumption (Castellsague et al. 2004).

Liver Cancer: Researchers have found that consuming alcohol increases the risk of liver cancer. The more one drinks, the higher the risk of liver cirrhosis and liver cancer. Two analyses reported an increase in relative risk for liver cancer beginning at just less than 2 standard drinks a day (25 grams) (Corrao et al. 1999; Bagnardi et al. 2001).

Colon and Rectum Cancer: Earlier research indicated that the evidence was inconclusive with regard to a causal link between alcohol consumption and cancers

² See also recent synopsis in Beneditti et al. (2006).

of the colon and rectum (see IARC 1988; Longnecker et al. 1990; English et al. 1995). However, recent research has pointed to a causal link (Boffetta & Hashibe 2006; Boffetta et al. 2006). It was recently estimated that relative risk of cancer was moderately elevated for both men and women among those who drank 2-4 drinks/day (40-59 grams)³, and higher for those who were drinking 4 or more drinks/day (60 or more grams) (Boffetta et al. 2006, see Table II).

Lung Cancer: A recent Canadian study by Beneditti and colleagues (2006) found that lung cancer risk increased with average number of beers consumed per week and this was particularly evident among study subjects whose fruit and vegetable consumption was low. The same study also noted that moderate wine drinkers had a *decreased* risk for lung cancer. The relationship between beer consumption and risk of lung cancer did not disappear when the investigators controlled for smoking. It should be noted that the study protocol did not facilitate controlling for second hand smoke, a known risk factor for lung cancer. What we believe to be the best review to date, Bandera et al. (2001), indicates inconclusive results with regard to alcohol consumption as a contributor to lung cancer.

Alcohol-related Cancers in Canada

A recent CAMH research project has estimated the alcohol attribution for a number of conditions (Rehm et al. 2005, 2006a). The findings specific to selected cancers are presented in Table 1 (below), indicating the proportion of deaths attributable to alcohol, the estimated number of cancer deaths that are alcohol-related, and relevant hospital days for Canada in 2002.

Generally, the alcohol attribution for mortality is higher for men than women, as is the case for alcohol-related hospital days associated with cancers. Overall, 657 women and 1,172 men were estimated to have died from cancer caused by alcohol in 2002 in Canada, compared to 608 deaths due to unintentional injuries for women and 1,710 such deaths among men. Alcohol-related cancer deaths and disability represent a substantial share of overall alcohol-related harm in Canada (Rehm et al. 2005, 2006a; Giesbrecht et al. 2005; Rehm et al. in press).

Furthermore, a conservative estimate indicates that in 2002 there were 37,295 alcohol-attributable acute care hospital days due to cancer, with estimated cost of \$41.4 million for 2002. This estimate is modest and likely low, given that not all types of hospitals are included in this calculation and indirect costs attributable to mortality have not been calculated.⁴

³ A "standard drink" is 13.6 grams of ethanol (pure alcohol).

⁴ For an overview of costs attributable to alcohol consumption in Canada, see Rehm et al. 2006b.

Table 1: Population attributable fractions (PAF) for mortality, number of deaths, and number of hospital days for selected cancers, Canada, 2002
(Source: Rehm et al. 2005)

Malignant neoplasms	PAF* mortality (%)		Mortality* (n)		Hospital days* (n)	
	Men	Women	Men	Women	Men	Women
Oropharyngeal cancer	32.7	18.6	247	61	12,407	3,818
Laryngeal cancer	42.5	31.0	172	27	8,099	1,556
Oesophageal cancer	37.6	24.1	407	95	12,030	3,241
Liver cancer	31.7	22.0	285	117	8,164	3,399
Breast cancer	-	6.4	-	318	-	8,237

*All ages

Discussion

Seventy-eight percent of adult Canadians drink alcohol, indicating that alcohol is a part of most people's social experience. The majority of drinkers in Canada drink at lower levels. While it may appear that there is no safe level of alcohol consumption with regard to cancer risks⁵, there are complications in looking at low doses, such as residual confounding, measurement error and other factors that make it difficult to identify lower thresholds with any confidence. Although the relative risk is likely to be small at low levels of alcohol consumption, a substantial proportion of the population may be at risk (Bagnardi et al. 2001), which has important public health implications.

The 2004 Canadian Addictions Survey estimates that about 23% of drinkers consume amounts of alcohol that are above the low risk drinking guidelines (Adlaf et al. 2005; Centre for Addiction & Mental Health 2000). Furthermore, about 17% of past-year drinkers were considered to drink hazardously – as indicated by the Alcohol Use Disorders Identification Test (AUDIT) (Adlaf et al. 2005; Canadian Centre on Substance Abuse 2004). Given the limitations of self-reported data, and

⁵ Bagnardi et al. (2001, p. 263) stated: "The analysis did not identify a threshold level of alcohol consumption below which no increased risk of cancer was evident."

under-reporting of alcohol consumption, the problem of high risk, hazardous drinking and the risks of alcohol-related cancer may be greater than indicated.

In addition, in recent years the overall rate of alcohol consumption has been increasing in Canada (Statistics Canada 2002, 2005a). National surveys indicate that the percentage of high-risk drinkers was on the increase between 1994 and 2003 (Haydon et al 2006, p. 78; Statistics Canada 1997, 1999, 2004, 2005b).

These developments indicate that a multi-faceted approach is needed to prevent an increase in drinking-related risks, including those involving risk of cancer. A World Health Organization report by Thomas Babor and colleagues (2003) identified 10 policies that have success in either reducing consumption, modifying drinking patterns, encouraging lower risk drinking, and/or reducing harm associated with alcohol consumption. These include: raising alcohol taxes and 'real prices' of alcohol beverages; brief interventions for hazardous drinkers; restriction on hours or days of sale; outlet density restrictions; promoting government monopolies of retail sales with a strong control and prevention agenda; ; and enforcing the minimum legal purchase age (Babor et al, 2003: chapter 16). This research makes a strong case for promoting provincial and federal interventions that have demonstrated an impact in reducing harm from alcohol.

Prevention of harms related to alcohol needs to become a priority at the provincial and community level, and should include cancer prevention as a central focus. Suggested initiatives include those mentioned above, along with enhancing server intervention and challenge and refusal interventions, and promoting interventions related to consumption in the home and other private venues (where most of the alcohol in Ontario is consumed). Last but not least, brief interventions delivered by doctors, nurses, or other health care providers have been shown to reduce high risk drinking and are thus a useful strategy in reducing cancer risks and other harms associated with heavy drinking. The lessons from these experiences provide a rich resource that needs to be assessed and adapted in planning interventions for reducing alcohol-related cancers in Ontario.

Recommendations⁶

1. *Put alcohol on the agenda of chronic disease and cancer prevention.*

Given the relationship between alcohol and the risk of some cancers, alcohol needs to be part of provincial and federal chronic disease prevention planning

⁶ While this report was in preparation, the Report on Cancer 2020 was released (Canadian Cancer Society and Cancer Care Ontario, 2006). The recommendations below are congruent with those appearing in the Report on Cancer 2020, pages 38-41, particularly those pertaining to alcohol and cancer.

priorities. There have been some promising developments in this area. For example, the Provincial Cancer Prevention and Screening Council and the Ontario Chronic Disease Prevention Alliance recognize alcohol as a risk factor by including CAMH representation on their committees. The Toronto Cancer Prevention Coalition has included alcohol as a risk factor for cancer from the outset, that is, since 2000. Health Canada has recently sponsored a report on alcohol and chronic disease. The National Framework has advocated “developing and promoting policies to reduce chronic disease, including FASD” (Fetal Alcohol Spectrum Disorder) as one of many identified approaches to reducing alcohol-related harms (National Framework 2005, p. 17).

As other organizations such as the Public Health Agency of Canada make alcohol-related cancer a priority, progress will be made in reducing those cancers where alcohol is a risk factor. The work of these organizations could include alcohol specific harm reduction campaigns, as well as other initiatives that are part of chronic disease prevention campaigns focusing on multiple risk factors.

2. Build more effective links with mainstream cancer organizations.

In order to make this an even greater priority, CAMH proposes to work with a number of organizations or groups. These include, for example, Cancer Care Ontario, the Canadian Cancer Society, the Ontario Provincial Cancer Prevention and Screening Council, the Toronto Cancer Prevention Coalition, the Ontario Chronic Disease Prevention Alliance, the Ontario Public Health Association, and provincial and federal partners. In order to raise the profile of alcohol-related cancers, CAMH and the other partners noted above are encouraged to seek opportunities to raise awareness about alcohol issues and prevention initiatives, and to work collaboratively on policy and prevention initiatives bearing on reducing alcohol-related cancers.

Use and misuse of alcohol is commonly interrelated with other determinants of health such as tobacco use and other addictions, as well as mental illness. Integrated planning with regards to prevention and treatment of these health issues can potentially also decrease problems with alcohol use. Recent initiatives by the Ontario Chronic Disease Prevention Alliance point to a strategic planning approach that considers multiple risk factors for cancer and other chronic diseases.

3. Promote Effective Interventions

There is an emerging literature about which interventions and policies have demonstrated effectiveness and wide scope of impact with regard to reducing

high-risk drinking and damage from alcohol (Babor et al. 2003, chapter 16). A number of these also have the potential in reducing alcohol-related chronic diseases, including cancers. Some operate at the population and community level, such as controls on availability to alcohol, and others at the more personal level, such as brief interventions directed at high-risk drinkers.

All organizations with an interest in reducing alcohol-related cancers are encouraged to work in a coordinated and collaborative manner to promote a systemic and strategic response, involving those interventions which have proven to be most effective. This would involve a combination of interventions delivered in a coordinated way, and include interventions ranging from controls on access to alcohol and of promotion and marketing to brief interventions offered by health care providers. Intervention strategies should also be aimed at high-risk drinkers, including young adults who drink heavily and other populations where heavy drinking is a common phenomenon.

4. Develop effective information dissemination strategies

Effective information dissemination strategies are needed in order to enhance the awareness among professionals, policy makers and the general public of links between alcohol consumption and cancer. It is proposed that partnerships be developed between CAMH and the mainstream cancer and chronic disease prevention organisations (listed in recommendation #2) to develop a plan for dissemination

5. Promote monitoring, research and prevention planning

There is substantial information on cancer-related morbidity and mortality in Ontario and Canada; however, statistics related to alcohol need to be enhanced. Periodic estimates of mortality and morbidity related to alcohol should be undertaken in order to monitor developments and provide guidance for planning policies and other interventions. Furthermore, consideration should be given to developing bi-annual or tri-annual reports that included a regional breakdown of information on several dimensions, such as level of alcohol consumption and drinking patterns, rates of alcohol-related cancers, developments in alcohol policy and recent prevention initiatives, and prevention initiatives that need to be promoted and supported in order to reduce alcohol-related cancer.

Conclusion

It is expected that the implementation of these recommendations will lead to reduced mortality and morbidity from cancer as well as other harms resulting

from alcohol use.

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Appendix A: Alcohol & Cancer – Overview of Meta-analyses & Reviews⁷

Table 2 (below) gives an overview of cancers that are not wholly attributable to alcohol, but where at least one meta-analysis has found significant relations to alcohol. Light yellow shaded rows indicate cancers for which the recent literature has been consistent in concluding sufficient evidence in support of a causal relationship. Sufficient evidence of causality is defined as: (1) that there is evidence of an association between alcohol consumption and the type of cancer; (2) that chance, confounding variables and other bias can be ruled out with reasonable confidence as factors in this association; and (3) that there is evidence of a plausible mediating process (English et al. 1995). This judgement was made using the usual criteria for establishing causality in epidemiology (Hill 1965; see Rothman & Greenland 1998), with the most weight placed on the following four criteria:

- Consistency across several studies
- Established experimental biological evidence of mediating processes or at least physiological plausibility (biological mechanisms)
- Strength of the association (effect size)
- Temporality (i.e. cause before effect).

Two examples of judgements regarding somewhat controversial outcomes may illustrate this process. For lung cancer, after adjusting for smoking, one meta-analysis showed a consistent effect with a relatively large effect size (English et al. 1995). However, since evidence for the possible biological mechanism was not conclusive and residual confounding from smoking could not be excluded, English et al. (1995) decided to exclude lung cancer from the list of diseases influenced by alcohol. A more recent meta-analyses showed only borderline significant effects (Bagnardi et al. 2001) and the most recent review again concluded that the evidence for a causal relation was not sufficient (Bandera et al. 2001). Thus, the evidence for alcohol causing lung cancer at this point in time could not be judged sufficient to establish causality according to the criteria listed above, and on this basis, lung cancer was excluded from the list of alcohol-related disease outcomes.

⁷ This appendix is adapted from a report for Health Canada by Rehm, Giesbrecht, Popova, Petra & Adlaf (2005).

On the other hand, although English et al. (1995) concluded there was not sufficient evidence linking alcohol consumption and breast cancer, recent advances both in biological and epidemiological research (Ellison et al. 2001; Smith-Warner et al. 1998) have changed this evaluation, so that breast cancer was included in the present analysis as an alcohol-related outcome.

Table 2: Alcohol-related cancers identified by various analyses

Cancers	ICD-9 ⁸	Reference to analyses
Lip & oropharyngeal cancer	140, 141, 143-146, 148, 149, 230.0	English et al. 1995; Single et al. 1996, Single et al 1999; Sjören et al. 2000; Gutjahr et al. 2001; Ridolfo & Stevenson 2001; Rehm et al. 2004 <i>Enough data to calculate relative risk for subcategories of disease, e.g. Corrao et al. 1999; Bagnardi et al. 2001</i>
Oesophageal cancer	150, 230.1	English et al. 1995; Single et al. 1996; Single et al. 1999; Sjören et al. 2000; Gutjahr et al. 2001; Ridolfo & Stevenson 2001; Rehm et al. 2004
Stomach cancer	151	Bagnardi et al. 2001 <i>English et al. (1995) concluded inadequate evidence that alcohol causes stomach cancer because of the inconsistency of the research evidence.</i>
Colon cancer	153	Bagnardi et al. 2001 <i>English et al. (1995), consistent with Longnecker et al. (1990) and IARC (1988), concluded inadequate evidence that alcohol causes colorectal cancer. However, IARC is currently reconsidering this classification and recent reports by Boffetta & Hashibe (2006) and Boffetta et al. (2006) point to causal link.</i>
Rectal cancer	154	Bagnardi et al. 2001 <i>English et al. (1995), consistent with Longnecker et al. (1990) and IARC (1988) concluded inadequate evidence that alcohol causes colorectal cancer. However, recent reports by Boffetta & Hashibe (2006) and Boffetta et al. (2006) point to a causal link.</i>
Liver cancer	155, 230.8	English et al. 1995; Single et al. 1996, Single et al. 1999; Sjören et al. 2000; Gutjahr et al. 2001; Ridolfo & Stevenson 2001; Rehm et al. 2004
Laryngeal cancer	161, 231.0	English et al. 1995; Single et al. 1996, Single et al 1999; Sjören et al. 2000; Gutjahr et al. 2001; Ridolfo & Stevenson, 2001; Rehm et al. 2004
Lung cancer	162	<i>Was excluded from the list of outcomes causally related to alcohol by English et al. (1995). This decision has not been revised by any further meta-analyses. The most recent meta-analysis on alcohol and lung cancer found only a borderline significant result (Bagnardi et al. 2001) and the last substantive review found no sufficient support for a causal relation (Bandera et al. 2001).</i>
Female breast cancer	174, 233.0	Single et al. 1996; Single et al. 1999; Sjören et al. 2000; Gutjahr et al. 2001; Ridolfo & Stevenson 2001; Rehm et al. 2004 <i>English et al. (1995) concluded there was only limited evidence for causality, although they found a consistent relationship. Subsequent studies using the same criteria concluded that there was sufficient evidence of a relationship.</i>
Ovarian cancer	183	Bagnardi et al. 2001 <i>English et al. (1995), consistent with IARC (1988) concluded inadequate evidence that alcohol causes ovarian cancer.</i>
Prostate cancer	185	Bagnardi et al. 2001 <i>Causality of relationship is not yet clear.</i>

Light yellow shaded rows indicate conditions for which the recent literature has been consistent in concluding sufficient evidence for a causal relationship.

⁸ International Classification of Diseases – 9th edition.