Toronto Cancer Prevention Coalition Alcohol Work Group

Report on the Links between Alcohol and Cancer

Norman Giesbrecht¹, Janet McAllister², Paula Neves³, Barbara Steep⁴ & Krista Koch⁵

Based on material prepared for:

From Policy to Action, Symposium of the Toronto Cancer Prevention Coalition March 7 & 8, 2000 Metro Hall, Toronto, Ontario

¹ Senior Scientist, Centre for Addiction and Mental Health

² Program Consultant, Centre for Addiction and Mental Health; Member, London-Middlesex Task Force on Cancer Prevention

³ Project Manager, Alcohol Policy Network, Ontario Public Health Association

⁴ Senior Program Consultant, Centre for Addiction and Mental Health

⁵ Research Associate, Centre for Addiction and Mental Health

Acknowledgements

The Alcohol Work Group would like to thank several individuals who made substantial contributions to this report. Susan Bondy, affiliated with the Institute for Clinical Evaluative Studies, Sunnybrook & Women's College Health Science Centre, and University of Toronto, provided permission to use material from a report entitled *Evidence regarding the level of alcohol consumption considered to be low-risk for men and women* (Single, et al., 1999a). She also provided comments on an earlier draft of this report. Juergen Rehm, affiliated with the Centre for Addiction and Mental Health and the World Health Organization, offered suggestions on an earlier draft and directed our attention to additional literature. John Garcia, Melody Roberts, Kinga David, and Gordon Fehniger, affiliated with Cancer Care Ontario, provided suggestions on an earlier draft and directed our attention to additional data and resources. Mazood Zangehan assembled and summarized research documents and organized material for a number of the tables.

We also wish to acknowledge in-kind support provided by the Centre for Addiction and Mental Health and the Alcohol Policy Network, Ontario Public Health Association. Their contributions included the use of resources such as library facilities, office space, and staff time of the team members who contributed to this report.

Disclaimer

The views and opinions expressed in this report are those of the authors and do not necessarily represent the perspectives of the individuals acknowledged above, or the policies of the institutions mentioned.

Executive Summary 1
Introduction 5
A. Alcohol and Health 7
 B. Links Between Alcohol and Cancer Oropharyngeal and esophageal cancer Cancers of the liver, stomach, and pancreas Cancers of the colon and rectum Cancer of the breast Summary of the evidence
 C. Cancer Prevention Research Levels of prevention Potential for prevention Approaches to prevention
 D. Recommendations 23 An environmental perspective Recommendations by Miller, Rootman et al. (1995) Work Group recommendations Promote healthy alcohol policies Support targeted education Expand cancer research
E. Conclusion 30
Bibliography 31
Appendix A: Summary of Relevant Cancer Statistics 40
Appendix B: Low-Risk Drinking Guidelines 46

Executive Summary

Alcohol is causally related to cancers of the mouth, pharynx, oesophagus, colon, rectum, and liver. It is also causally linked with breast cancer in women. Cancer is one of the few alcohol-related problems where the association is largely linear and dose-related—that is, the risk of cancer increases with the amount of alcohol consumed. The dose-response threshold is not consistent over all cancer sites. Breast cancer, in particular, appears to be significantly impacted by low levels of consumption.

In general, a dose-response relationship signals that any measures that control per capita alcohol consumption will reduce the risks of alcohol-related cancer in the population. Initiatives to curtail alcohol consumption may take place at the population or individual level, although their impact is greater when used in combination. Examples include: 1) laws, policies and regulations related to the distribution and sale of alcohol; 2) use of mass media and other population-level measures to promote health; and 3) targeted information and best advice campaigns, including efforts by health practitioners to inform their target populations about low-risk drinking or abstention.

Recommendations aimed at decreasing the harm of alcohol take an environmental perspective in this paper. This perspective, based on extensive research, recognizes that there are numerous factors that contribute to drinking-related problems. Chief among them is the availability of or access to alcohol. Price, number of alcohol outlets per capita, hours of sale, number of selling days per week and legal drinking age are all examples of environmental factors that influence alcohol availability and consumption. All are subject to government control.

The Miller Rootman Report on The Primary Prevention of Cancer published in 1995 supported the environmental perspective regarding the prevention of alcohol-related cancer. Among other things, the authors recommended that: 1) governments resist pressures to reduce the price of alcohol since the societal costs of increased alcohol consumption greatly outweigh its economic benefits to alcohol producers and the hospitality industry; 2) the provincial government keep its existing system of alcohol distribution and not move toward deregulation of alcohol sales; 3) prevention initiatives aimed at reducing excessive consumption be population-based; 4) publicly administered mandatory server training be introduced in Ontario and its efforts and impact be evaluated; 4) community mobilization to encourage support for alcohol controls be increased; and 5) guidelines for low risk consumption of alcoholic beverages be developed and promoted.

These recommendations are still valid today. Indeed, progress has been made on a few. The Low-Risk Drinking Guidelines (LRDGs), for example, were developed in 1997. Based on a review of the literature by international experts, they have been endorsed and promoted by the Centre for Addiction and Mental Health, the Ontario Public Health Association, the Association of Local Public Health Agencies, the College of Family Physicians, municipal public health departments and others. The LRDGs balance the risks and benefits of alcohol

consumption by advising healthy adults who choose to drink to have no more than 2 standard drinks on any single day – up to a weekly maximum of 14 standard drinks for men, and 9 standard drinks for women. They further outline instances when it is best to drink less or not at all.

Not all of the recommendations in the Miller-Rootman report (1995) have been implemented, however. Certainly, opportunities for more extensive promotion of the *Low-Risk Drinking Guidelines*, particularly in connection with policy initiatives and other prevention measures, abound.

Preventing alcohol-related cancer will not be an easy task. Only a sustained, long-term commitment to a healthy public policy, targeted public education and adequately funded research is likely to yield results. Below are recommendations for action in each of these areas.

Recommendations

The Alcohol and Cancer Working Group recommends that the Toronto Cancer Prevention Coalition work collaboratively with other agencies and institutions to:

1. Promote healthy alcohol policies by:

- a) Persuading the Ontario and Canadian governments to retain strong controls on alcohol availability and avoid policies or practices that lower the price of alcohol, increase outlet density, or expand access to alcohol.
- b) Persuading the Ontario government to make server intervention training mandatory for all licensees.
- c) Persuading Health Canada, the Ministry of Health, the Canadian Cancer Society, Dieticians of Canada and others to officially endorse the *Low-Risk Drinking Guidelines* and allocate resources to the development and dissemination of clinical practice guidelines and the provision of relevant professional development opportunities.
- d) Persuading the Ministry of Health to explicitly recognize alcohol as a risk factor for cancer (particularly cancer of the breast) in the *Mandatory Health Programs and Services Guidelines* and outline areas for public health activity in this area.
- e) Persuading the Ministry of Education and Training to officially renew its commitment to a comprehensive Drug Education Policy Framework, and all school boards to review their current policies and practices and take steps to ensure they meet the prescribed standards.

2. Support targeted education by:

- a) Working with Cancer Care Ontario, public health, health promotion and substance abuse prevention groups to educate the public and groups at risk about the links between alcohol and cancer, and promote adherence to the *Low-Risk Drinking Guidelines*.
- b) Working with medical schools and professional associations to educate health professionals about the links between alcohol and cancer and provide them with the tools and resources they need to screen for risk and intervene at an early stage.

3. Expand cancer research by:

- a) Encouraging Cancer Care Ontario, the Canadian Cancer Society and addictions research organizations to improve data collection related to alcohol-related cancers and ensure this information is publicly available in a timely manner.
- b) Encouraging Ontario-based research institutions to play a lead role in standardizing data collection on alcohol and cancer in order to facilitate the sharing and verification of research outcomes in different jurisdictions, both locally and internationally, and ensure researchers take into account both volume of drinking and drinking patterns in their studies.
- c) Encouraging funders of cancer research to support projects that address underdeveloped areas of knowledge or less understood cancers, and Canadian research institutes to increase funding for addictions research.

Introduction

In the fall of 1999, the Toronto Cancer Prevention Coalition (TCPC)⁶ invited the Ontario Public Health Association's Alcohol Policy Network to bring together a small group of researchers and health promoters active in the substance abuse field. Our task: to examine the links between alcohol and cancer and make recommendations for action building on the final report of the *Task Force on the Primary Prevention of Cancer* published in 1995.

This report is based on a summary of the epidemiological and prevention literature on alcohol and cancer. It draws on statistics provided by Cancer Care Ontario and the National Cancer Institute of Canada, research on the links between alcohol and cancer included in a comprehensive report on low-risk drinking by Single et al. (1999a), as well as other research documents.

The report is organized into five sections. Section A focuses on alcohol and health, including important differences between the chronic and acute complications of drinking. Section B looks at alcohol use and cancer. Based upon research reviewed and summarized by Dr. Susan Bondy (in Single et al. 1999a), this section provides an up-to-date analysis of what is known about the links between alcohol and cancer. It also includes relevant cancer statistics. Section C makes a case for an environmental perspective with regard to the prevention of alcohol-related cancers and summarizes recommendations from researchers, governments and health-related groups interested in this topic. Section D considers the evidence on the effectiveness of various prevention strategies and analyzes the status and relevance of recommendations pertaining to alcohol in the Miller, Rootman et al report (1995). It concludes with recommendations for action in three areas: policy, education and research.

A. Alcohol and Health

Drinking alcoholic beverages has been shown to be associated with a wide range of chronic and acute problems (Bruun et al., 1975; Edwards et al., 1994; Holder and Edwards, 1995). It also exacts a heavy financial toll on Canadian society (Single et al., 1996). Examples of acute problems include: drinking-related car, boat, bicycle, and snowmobile crashes; falls and associated traumas; various forms of violence and social disruptions in public venues or in domestic situations; unplanned and/or unprotected sex; work-related injuries; fires; alcohol poisonings; and complications from mixing alcohol with over-the-counter medications and prescription or illicit drugs.

_

⁶ The Toronto Cancer Prevention Coalition comprises groups and individuals with an interest in cancer prevention from across Metropolitan Toronto. Toronto Public Health has taken a lead role in convening and facilitating its development. Ten working groups form the basis of the coalition, focusing on the following topics: screening and early detection; environmental carcinogens; occupational carcinogens; ultraviolet radiation; diet; tobacco and alcohol. Each working group is preparing a report. It is proposed that the coalition produce a comprehensive, integrated, and sustainable agenda for cancer prevention across the GTA, with recommendations and priorities for policy and action, to be presented at a policy and planning conference March 7 and 8, 2000.

The range of chronic conditions associated with drinking is also long and includes cardiovascular and neurological conditions, liver cirrhosis, and cancer. Although the heaviest drinkers are at highest risk of experiencing both acute and chronic complications related to alcohol use, there are some noteworthy differences between these two types of problems. Drinking-related trauma is affected by three general conditions: 1) the environmental, temporal and social contexts; 2) the drinking pattern associated with the event, including the blood alcohol concentration of the drinker and victim; and 3) the mental condition and volition of those involved in the incident.

These conditions are likely of lesser importance for most chronic problems associated with drinking, including cancer. Here, the volume of alcohol ingested over a period of months or years is considered of particular relevance, as may be the patterns of drinking over time. Other factors such as environmental hazards, genetic predisposition, general health status, and lifestyle behaviours like diet, exercise and tobacco use also need to be considered.

Members of the general public have a growing appreciation for the risks associated with heavy drinking, both for the drinker and those with whom he or she comes in contact. A study of community alcohol concerns conducted in Sudbury, Ontario, for example, found that 70% of adult respondents had experienced disruptions or more serious problems in the past year due to drinking by others (Allen et al., 1999). Still, while the public may be aware of problems such as violence, drinking and driving, public intoxication, liver cirrhosis, and alcohol dependence, the link between alcohol and cancer is perhaps less well understood.

The associations between alcohol and cancer are important to consider for several reasons. First, drinking has been associated with a wide range of cancers and its health risks involve a diverse sector of the general population. Second, heavy drinking is associated with smoking and both alcohol and tobacco use have been associated with cancers and in some instances have been shown to have a synergistic effect in cancer development. Third, in some cases the volume of drinking required to increase the risks of cancer is not typically considered "heavy drinking" and considerably lower than that consumed by persons labeled alcohol dependent. Fourth, recent media coverage about the protective effects of modest amounts of alcohol for selected segments of the population has tended to overshadow the elevated risks associated with alcohol use for many conditions, including cancers. Fifth, public education campaigns have stressed acute and more dramatic complications, such as car crashes, while virtually ignoring chronic conditions, such as alcohol-related cancers. Finally, it is unlikely that the public is aware of the potential of alcohol control measures and policies for reducing alcohol-related cancers.

According to the 1999 *Canadian Profile*⁷, approximately 1,207 of the 6,503 men and women who died of alcohol-related causes in 1995 perished due to cancer of the breast, larynx, lip, oral cavity, pharynx, liver and esophagus. This is higher than the estimated number who died in impaired driving crashes that year.

_

⁷ See Single et al. (1996) for their study on the economic costs of substance abuse.

Among women, cancer was the leading cause of alcohol-related death in 1995, ahead of motor vehicle accidents and liver cirrhosis. For men, cancer was the second leading cause of alcohol-related death after suicide/self-inflicted injury, followed by motor vehicle accidents and liver cirrhosis.

Table 1. Deaths, potential years of life lost, and hospital separations attributed to alcohol by cause, Canada. 1995

Disease (ICD-9 Code)	Mortality	Potential Years of Life Lost	Hospital Separations
Breast Cancer (174, 233.0)	192	4,259	813
Laryngeal Cancer (161, 231.0)	190	3,093	624
Lip & Oropharangyeal Cancer (140-1, 143-6, 148-9, 230.0)	201	3,413	735
Liver Cancer (155, 230.8)	251	4,289	393
Esophageal Cancer (150, 230.1)	373	5,606	657
Total Cancer	1,207	20,660	3,222
All Alcohol-related Causes (cirrhosis, injuries, poisonings, suicide, birth defects, etc.)	6,503	172,126	82,003
Cancer as % of all causes	19%	12%	4%

Data Source: Canadian Profile: Alcohol, tobacco, and other drugs, 1999. Toronto: CAMH and CCSA.

B. Links Between Alcohol and Cancer⁸

The potential role of beverage alcohol intake in the development of human cancers has been the subject of several critical reviews over the last 15 years. Important examples include the pivotal 1988 International Agency for Research on Cancer Report on alcohol carcinogenesis (IARC, 1988), and the overview led by Sir Richard Doll (Doll et al., 1993). English et al. (1995) systematically examined evidence for cancers of the upper aerodigestive system, digestive organs, female breast, female reproductive system, bladder and kidneys. Several meta-analyses focusing on individual sites have also appeared (for example, Longnecker, 1994; Smith-Warner et al., 1998; Corrao et al., 1999). In addition, various governments routinely provide overviews and updates to this literature, even if these do not include a formal critical appraisal or quantitative summary (United States Department of Health and Human Services, 1997). The pages that follow provide a summary of the research literature on the links between alcohol and various cancer sites⁹, along with an overview of the Ontario data. 10

⁸ Excerpt, with some rewording and additional tables, from *Evidence regarding the level of alcohol consumption* considered to be low-risk for men and women (Single et al., 1999a) written by Dr. Susan Bondy, Research Scientist, Institute for Clinical and Evaluative Sciences. Permission given.

⁹ This overview updates earlier summary reports, but does not present meta-analytic summaries of the observed associations. Rather, new studies that present relative risk data have been identified where they have been located. Preferential attention was given to reports pertaining to moderate drinking.

¹⁰ For a detailed overview of cancer statistics, along with figures and table, please refer to Appendix A.

Oropharyngeal and esophageal cancer

Specific sites of the upper aerodigestive tract including the mouth, pharynx, larynx and esophagus are among those for which the evidence of a causal association with alcohol is most clear and long-standing. Both the 1988 IARC Report and Doll (1993) found a causal association. English et al. (1995) similarly concluded there was sufficient evidence for a casual role of alcohol in cancers of the oropharynx and esophagus. This evidence is strongly supported by research directed toward disentangling the role of potential confounders, notably tobacco use (La Vecchia and Negri, 1989; Doll et al., 1993). There is also supportive research investigating dose-response, both in terms of individual consumption and associations with alcoholic beverages of differing strengths (Doll et al., 1993). A recent report shows a positive association between dysplasia of the oral epithelium and beverage types of increasing alcohol concentration (Jaber et al., 1998).

Possible mechanisms for alcohol-related carcinogenesis in the upper digestive system pertain to direct contact of alcohol, or acetaldehyde, with local tissues (Doll et al., 1993; Garro and Lieber, 1992; Doll, 1998). Alcohol has been found to have an association with oral epithelial dysplasia that is both independent of and synergistic with tobacco use (Jaber et al., 1998). A recent report by Gronbaek et al. (1998) examines the effect of different beverages alone and in combination. They found an association between alcohol and cancers of the oropharynx and esophagus within ranges of 'moderate' drinking, but only for beer and spirits, not wine.

Ethanol is cytotoxic (IARC, 1988). Direct contact of cells in the mouth and esophagus to alcohol may lead to a process of cell death and proliferation that may increase the likelihood of carcinogenic mutations. As well, the production of acetaldehyde through alcohol dehydrogenase activity of bacteria in the mouth and upper digestive system may be important in carcinogenesis. Acetaldehyde is found in the mouth after ethanol is consumed (Homann et al., 1997a). Acetaldehyde applied to the epithelium of the upper digestive system in animals also causes hyperplasia and hyperproliferation (Homann et al., 1997b).

It has been suggested, although not directly demonstrated, that where alcoholic beverages are taken with food (most often noted for wine) the ethanol is prevented from remaining in the mouth and esophagus, so the ethanol does not interact with oral bacteria. This may explain the lower relative risks associated with wine (Gronbaek et al., 1998) and observed in studies conducted in primarily wine-drinking populations (Garidou et al., 1996).

Some 2,000 Ontarians, most of them men, are diagnosed with oropharyngeal and esophageal cancers and an estimated 960 die from these diseases each year. These numbers represent just over 4% of new cancer cases and cancer deaths annually in the province. According to Cancer Care Ontario, cancer rates in these sites are either stable or declining among the general population (Cancer Care Ontario, 1999).

Table 2. Incidence and Mortality: Oropharyngeal and Esophageal Cancers in Ontario, 1995

Cancer Site	New Cases			Deaths			
	М	F	Total	M	F	Total	
Lip & Oral Cavity (140-145)	523	270	793	145	83	228	
Pharynx (146-148)	220	91	311	79	31	110	
Larynx (161)	323	69	392	127	38	165	
Esophagus (150)	303	136	439	322	143	465	
Total	1,369	566	1,935	673	295	968	
As % of all cancers	6.0	2.6	4.4	6.0	2.9	4.5	

Source: Cancer Care Ontario, www.cancercare.on.ca

Cancers of the liver, stomach, and pancreas

Cancers of the liver, stomach, and pancreas are discussed together because for each of these organs, alcohol and heavy drinking are clearly associated with inflammatory changes. This inflammation may precipitate hyperplasia and neoplastic changes, particularly in the presence of co-carcinogens (Garro and Lieber, 1992; Doll et al., 1993). The intermediate link of inflammatory change is more generally accepted for cancer of the liver, but considered only plausible for cancers of the stomach and pancreas (Doll et al., 1993). The effect of alcohol on liver metabolism may also have an indirect effect on cancer risk of the digestive organs, as a result of reduced clearance of other carcinogens from the system (Anderson et al., 1996; Chhabra et al., 1996). The importance of hepatitis B infection as a possible confounder in the association between alcohol and liver cancer has been considered in some studies, with inconsistent results thus far (Thomas, 1995).

IARC (1988) concluded alcohol caused liver cancer based on the consistent, monotonic association and biologic plausibility. Cirrhosis is a well-documented consequence of chronic heavy drinking and is known to be associated with cancer (Columbo, 1998). English et al. (1995) claimed that there was limited evidence of a causal association and noted that alcohol is toxic to liver cells in the absence of cirrhosis, and that alcohol intake has a dose-response relationship with liver cancer in patients without cirrhosis.

A thorough review by Farber (1996) concluded there is no convincing evidence that alcohol has a direct causal role in liver cancer. It is more likely that it plays an indirect role, through cirrhosis, as a promoter of tumors, and through possible metabolic effects on clearance of other carcinogens. A 1999 meta-analysis by Corrao et al. (1999) found a significant positive association between liver cancer and alcohol consumption, with estimated relative risks of 1.2 for 25g/day, 1.4 for 50g/day, and 1.8 for 100g/day.

Case-control or cohort studies on primary liver cancer, which do not focus on patient cohorts with existing cancer of cirrhosis and published from 1995 forward, are rare. A cohort study from Nagasaki, Japan, found a slight positive association with total alcohol intake (Goodman et al., 1995).

The link between alcohol use and chronic gastritis is clearly shown, although progression from chronic gastritis to neoplasia is less well understood and probably involves other factors in addition to alcohol (Bode and Bode, 1997; Bode and Bode, 1992). The interaction between alcohol intake and smoking in the development of gastric cancers is unclear, but the possibility of a synergistic interaction of these risk factors (possibly with diet as well) cannot be dismissed.

A similar situation may exist for pancreatic cancer. Doll concluded that although alcohol intake is associated with calcifying pancreatitis, a direct role in pancreatic cancer was unlikely (Doll et al., 1993). In fact, the most up-to-date conclusions of researchers in this area are that prospective and case-control studies do not support a causal association between alcohol and either cancer of the stomach or pancreas (MacDonald, 1999).

According to statistics collected by Cancer Care Ontario, pancreatic cancer is the fifth leading cause of cancer mortality in the province, followed by stomach cancer. Liver cancer is relatively rare.¹¹

Table 3. Incidence and Mortality: Stomach and Pancreas Cancer in Ontario, 1995

Cancer Site	New Cases			Deaths		
(ICD-9 Code)	М	F	Total	М	F	Total
(ICD-9 Code)	IVI	Г	iotai	IVI	-	iotai
Stomach (151)	618	367	985	413	280	693
Pancreas (157)	469	487	956	470	503	973
Total	1087	854	1941	883	783	1666
As % of all cancers	4.8	3.9	4.4	7.8	7.8	7.8

Source: Cancer Care Ontario, www.cancercare.on.ca

Cancers of the colon and rectum

Authoritative reviews of studies of alcohol and colorectal cancer have found evidence of a weak but fairly consistent positive association, particularly for rectal cancer (Doll et al., 1993; Longnecker, 1992; Longnecker et al., 1990; Seitz and Poschl, 1997; Seitz et al., 1998a; Seitz et al., 1998b; Simanowski et al., 1995). These reviews tend to agree in their conclusion that a positive dose-response association exists between alcohol intake and colorectal cancer risk, but that there is inadequate evidence of a direct causal role (IARC, 1988; Doll et al., 1993; Longnecker, 1992; English et al., 1995). Corrao et al. (1999) found colorectal cancer to be associated significantly with alcohol consumption, with estimated relative risks of 1.4 for 25g/day, 1.9 for 50g/day, and 3.6 for 100g/day.

_

¹¹ Rates for primary liver cancer (ICD9 site 155) are not reliable because many liver cancers are metastases most commonly arising from the breast, lung and colon. The Canadian Centre on Substance abuse, however, estimates that some 251 Canadians died of alcohol-related liver cancer in 1995 (Canadian Profile, 1999), based on the etiologic fractions developed by Single et al. (1995).

The most recent reports are not entirely consistent in their findings. A recent cohort of Finnish men (Glynn et al., 1996) found a positive trend for alcohol intake within smokers, and an estimated increased risk of 17% with each additional drink. The American Nurses Health Study showed a positive association for colon cancer (Giovannucci et al., 1995). A cohort of Japanese-American men also reported a strong positive association for rectal cancer (Chyou et al., 1995). However, an Italian case-cohort study reporting on cancers of colon and rectum by tumor site, failed to show any dose-response relationships (Tavani et al., 1998).

Alcohol may be important as a cofactor in tumors associated with smoking (Yamada et al., 1997) and poor diet, including low folate intake (Boutron-Ruault et al., 1996; Kato et al., 1999). Alcohol has been associated with the formation of adenomatous polyps, a precancerous lesion (Kearney et al., 1995), and may play a role in later stages of tumor growth (Boutron-Ruault et al., 1995). One recent line of work in this area regarding biological mechanisms is focused on the role of acetaldehyde (a first metabolite of ethanol) and its production in the gut by intestinal bacteria (Seitz et al., 1998a).

According to Cancer Care Ontario, colorectal cancer is the third most commonly diagnosed type of cancer among women and men across the province. While rates of colorectal cancer continue to decline they remain high in most industrialized countries, with Ontario having among the highest in the world.

Table 4. Incidence and Mortality: Colorectal Cancer in Ontario, 1995

Cancer Site	New Cases				Deaths	
(ICD-9 Code)	М	F	Total	М	F	Total
Colorectum (153-54)	3,054	2,797	5,851	1,268	1,096	2,364
As % of all sites	13.5	12.9	13.2	11.2	11	11.1

Source: Cancer Care Ontario, www.cancercare.on.ca

In Toronto,¹² colorectal cancer was the eighth leading cause of death out of all possible causes for both females (280) and males (298) in 1995. It was tied as the fifth leading specific cause of potential years of life lost (PYLL) for female Torontonians in 1995, accounting for 4% of total PYLL (Toronto Profile III, 1999).

12 We have included selected Toronto statistics for colorectal and breast cancers in order to give a sense of their health impact relative to all causes of death.

11

Cancer of the breast

A rapid expansion of research on the association between alcohol intake and breast cancer in women has taken place in recent years. An association between alcohol and breast cancer has been suspected for two decades (Rosenberg et al., 1993; Henderson et al., 1989). Many of the earlier overviews, particularly those prior to 1995, concluded that there was insufficient evidence of a causal relationship (IARC, 1988; McPherson et al., 1993; Rosenberg et al., 1993; Schatzkin and Longnecker, 1994).

A series of meta-analyses and other overviews have appeared in recent years. Most have found a modest, but inconsistent and linear association with risk (Longnecker, 1992; Longnecker, 1994) although one such synthesis found a greater association with heavy drinking (Howe et al., 1991). The 1994 meta-analysis by Longnecker indicated a RR (relative risk) of 1.38 associated with 3 drinks per day. English and colleagues reviewed 7 cohort studies and 22 case-control studies and identified a moderately strong and consistent dose-response association between alcohol intake and breast cancer risk (English et al., 1995). In their overview, Hunter and Willett (1996) describe the evidence as showing alcohol to be probably the best-established dietary risk factor for breast cancer (p. 63).

A critical review and meta-analysis conducted by Single et al. (1999) concluded that there is sufficient evidence to consider alcohol a cause of breast cancer. Another recent meta-analysis (Smith-Warner et al., 1998) examined seven prospective studies and included a closer examination of the dose-response curve. In the analysis presented, which used alcohol intake as a continuous regression term, the risk of breast cancer increased nearly 10% with each additional $10g^{13}$ of alcohol per day. In a categorical analysis, consumption of 30g to 60g per day was associated with a relative risk of 1.41 (CI: 1.18-1.69) relative to non-drinkers, with limited evidence of a similar relative risk for intakes of 60g per day or more. The meta-analysis by Corrao et al. (1999) found breast cancer to be associated significantly with alcohol consumption, with estimated relative risks of 1.2 for 25g/day, 1.5 for 50g/day, and 2.2 for 100g/day (RRs were significantly higher for women living in Mediterranean areas).

Not many recent publications have presented RR (relative risk) data. Enger and colleagues presented data from two American case-control studies and reported a significant relative risk of 1.7 for drinkers consuming greater than or equal to 27g/day versus those drinking under 27g/day (Enger et al., 1999). Ferraroni and colleagues reported data on an Italian case-control study in women described by the authors as relatively light drinkers. They found a significant positive trend with increasing levels of intake (Ferraroni et al., 1998). Zhang and colleagues reported contrasting data in women in the Framingham study, in which the highest category of alcohol quartile of alcohol intake reported on was greater than or equal to 15g/day (Zhang et al., 1999). These authors found no association between alcohol intake and breast cancer incidence.

A number of possible causal mechanisms have been discussed linking ethanol to carcinogenesis in breast tissue (Longnecker, 1995; Longnecker and Enger, 1996; Ringborg,

_

¹³ In Canada, one standard drink contains 13.5g of alcohol.

1998; Seitz et al., 1998b; Singletary, 1997; Thomas, 1995; Wright et al., 1999). For none of these, however, is there definitive evidence from animal or human data (Singletary, 1997). Nor is there any consensus as to the most important mechanisms.

One proposition of a causal mechanism for alcohol in breast cancer is through hormonal influences (Longnecker, 1995). Alcohol has been reported to increase estrogen levels and bioavailability of estrogen (Reichman et al., 1993). The hormonal effects of alcohol remain unclear, as is the question of whether alcohol is more closely associated with premenopausal breast cancer (Schatzkin and Longnecker, 1994). Some studies have found no difference in the association between alcohol intake and cancer risk when comparing pre-menopausal and post-menopausal disease. A very recent publication by Enger found alcohol to be most closely associated with estrogen-receptor and progesterone-receptor positive primary tumors in post-menopausal women, and not associated with cancer risk in pre-menopausal women (Enger et al., 1999).

Other evidence corroborating a possible role of alcohol in mediating hormonal effects includes the observation that breast cancer risk associated with postmenopausal estrogen use (hormone replacement therapy) may be increased among alcohol users (Zumoff, 1997; Zumoff, 1998). Such an association was observed in the Womens Health Study (Colditz et al., 1990b) and one other cohort of women (Gapstur et al., 1992), but not in a third (Friedenreich, 1994). Experimental administration of alcohol along with estrogen treatment results in markedly increased estrogen levels (Ginsberg et al., 1996).

Another possible mechanism, not exclusively relevant to breast cancer, pertains to circulating levels of acetaldehyde and the formation of reactive oxygen species chemicals. These chemicals could plausibly be associated with the nature of cellular changes seen in breast cancer (Wright et al., 1999).

Epidemiological studies have also focused on the timing of exposure, as this is related to the role of alcohol as an initiator or promoter. Two very recent case-control studies found intensity of drinking to be associated with breast cancer more strongly than duration of exposure (Bowlin et al., 1997; Levi et al., 1996). Alcohol use in later years, closer to the age of diagnosis, is often found to have the closest association. It has been suggested that alcohol may act as a late-stage promoter of breast tumors (Swanson et al., 1997), although method effects (for example, more recent drinking is recalled with less random error) and other possible biases have not been ruled out. Alcohol may also have a complex effect in potentiating various other risk factors (Singletary, 1996; Singletary, 1997).

While breast cancer is uncommon in men, it is the most frequently diagnosed form of cancer in women. According to Cancer Care Ontario, over 1 in four women in the province are diagnosed with this disease each year and about 2,000 will die from it annually. While incidence and mortality rates have fallen slightly in recent years they are relatively high, with Ontario having some of the highest rates in the world.

Table 5. Incidence and Mortality: Breast Cancer in Ontario, 1995

iii Olitalio, 1773								
	New Cases			Deaths				
Cancer Site								
(ICD-9 Code)	M	F	Total	M	F	Total		
Breast (174-5))	48	6,167	6,215	7	1,948	1,955		
As % of all	0.2	28.5	14		19.5	9.2		
cancers								

Source: Cancer Care Ontario, www.cancercare.on.ca

In Toronto, breast cancer was the cause of death for 433 Toronto women, making it the 4th leading cause of death out of all possible causes for women in 1995. It was also the leading specific cause of potential years of life lost, accounting for 10% of total PYLL for women in 1995 (Toronto Profile III, 1999; see footnote 10).

Summary of the evidence

Even in 1995 sufficient evidence existed to conclude that alcohol consumption is associated with an increased risk of cancer overall (IARC, 1988). Pre-existing authoritative overviews have demonstrated that alcohol has a causal role in cancer, at a minimum for the mouth, pharynx, and esophagus, and that consistently positive associations are observed for other important cancer sites, including colorectal and breast cancer. An analysis of the research on the links between alcohol and cancer reproduced from a study published by Longnecker and Enger in 1996 is provided in Table 6.

More recently, a stringent 1999 meta-analysis by Corrao and colleagues found high alcohol-related risks for cancers of the oral cavity, larynx, and esophagus. Significant, although weaker, associations were indeed found for colorectum, liver and breast cancers. Moreover, well-conducted studies on these diseases tended to report higher alcohol-related risks. For all these conditions, low intakes, corresponding to daily consumption of two drinks or two glasses of wine (25 g/day), have shown significant risks (Corrao et al., 1999).

In terms of the shape of the association, a monotonic positive association is observed in most instances of alcohol and cancer. Because of the high incidence of colorectal and breast cancers in most developed countries, evidence of a positive association between alcohol and cancers of the colon and rectum and breast is of major public importance. The significance of this effect is not diminished by the possibility that alcohol may play a role primarily as a co-carcinogen. In light of these conclusions, and because no cancer preventive effect is indicated for ethanol, it can be concluded that total cancer risk is positively associated with total alcohol intake.

⁻

¹⁴ For discussions of methodological issues concerning potential *under-* or *over-*estimations of the correlation between alcohol intake and cancer, see Jain et al., 1991; Friedenreich et al., 1993; Francesci & La Vacchi, 1994; Schatzkin & Longnecker, 1994; Marshal & Boyle, 1996; Potter, 1996; Bradley et al., 1998; Graubard & Korn, 1999.

Table 6. Summary of Epidemiological Data on Alcoholic Beverage Consumption and Risk of Cancer

Cancer Site	No of Studies ¹⁵	Evidence of Causality	% Increase in Risk per daily drink ¹⁶	Synergy with Tobacco
Breast	60	<u>+</u>	10	0
Colon	45	<u>+</u>	5	0
Esophagus	30	+	30	+
Larynx	20	+	30	+
Liver	25	+	20	0
Mouth	30	+	30	+
Pancreas	30	0	0	0
Pharynx	25	+	30	+
Rectum	45	<u>+</u>	5	0
Stomach	45	0	0	0
Bladder	20	0	0	0
Lung	15	0	0	0
Melanoma	5	0	0	0
Ovary	10	0	0	0
Prostate	5	0	0	0
Uterus	5	0	0	0

Source: Longnecker & Enger (1996), p.133. Permission to reprint.

The vast majority of individual studies along with formal and critical overviews have focused exclusively on measures of total dose of exposure. The observation of a monotonic positive association is in fact somewhat tautological, in that such a dose-response relationship is heavily used as a criterion for a causal association (Weed and Gorelic, 1996). In the setting of research on alcohol-related cancers, evidence of a differential effect attributed to different drinking patterns might serve to reject the null hypothesis of a simple linear dose-response relationship. Zhao et al. (1996) offer what appears to be a rare assessment of models other than a strictly linear association in defining the dose-response relationship between alcohol intake and colon cancer.

Most reviews of alcohol and cancer make no mention of patterns of drinking. In Corrao et al. (1999), however, the authors suggest that, given equal doses, use of daily constant amounts of alcohol may be riskier than weekend 'binge' consumption for cancers of the upper aeorodigestive tract, and possibly breast cancer. One discussion on breast cancer (Kohlmeier and Mendez, 1997) argues that the differences between binge versus regular drinking are likely important but that these have not been adequately explored. One might speculate that research on drinking patterns and breast cancer will increase in light of the attention being paid to breast cancer risk.

15 Approximate, rounded to multiples of 5. Includes only studies using self-reported alcohol intake.

¹⁶ Rough estimates based on authors' impression after reviewing available data. The estimated risk of drinking 3 drinks daily would be 1.9 (3 x30% = 90% increase). Whether moderate alcohol intake in the order of one drink daily increases cancer risk is not known.

Drinking patterns may be germane in determining the role of alcohol in the development of those cancers for which the most likely causal pathways involve direct tissue injury and metaplasia, or with bacterial production of acetaldehyde, such as may be relevant for cancers of the mouth, esophagus, stomach, and rectum. The timing of alcohol use in relation to meals, and opportunities for ethanol to remain in contact with oral mucosa have not been explored in detail. The consumption of wine with food has been suggested as possibly dampening the effect of alcohol intake and cancers of the oropharynx and esophagus. The consumption of ethanol with meals also reduces the amount of ethanol passing into the gut (Kalant and Khanna, 1989; Eckardt et al., 1998), and this may reduce the risk of cancers of the lower gastrointestinal system. This supposition, however, does not appear to have been tested directly. Overall, differences in the degree of association by beverage type have not been consistently found.

In summary, average alcohol intake can be expected to have a positive and generally monotonic association with total risk of cancer. Evidence of an association between alcohol consumption and cancer, and observed levels of associated risk, tend to be greatest at the highest levels of alcohol intake, including levels associated with alcohol dependence. Importantly, however, there are scarcely any data to indicate a lower limit associated with risk, with no level of alcohol intake serving a protective action against cancer. Similarly, little evidence is available to indicate that any specific patterns of drinking pose less risk of cancer relative to others.

C. Cancer Prevention Research

The research literature on the links between alcohol and cancer is extensive, numbering over 110 research reviews published in the past decade alone. The predominant focus of this research is on etiology and epidemiology. ¹⁷ In contrast, publications focusing specifically on the *prevention* of alcohol-related cancer are rare, possibly a reflection of the expertise and orientation of those typically involved in cancer issues, or the criteria for research funding. Where studies of the etiology and epidemiology of alcohol-related cancers do point toward prevention, they are suggestive but incomplete. Reduction of alcohol intake by heavy drinkers, and even by moderate drinkers, has the potential to reduce the population risk of several types of cancer. What the etiologic research on its own does not demonstrate is how to accomplish this goal.

Levels of prevention

Prevention initiatives may target the population-at-large and the socio-cultural environment where alcohol is purchased and consumed. It can also focus on individuals, or selected drinking populations or groups at a high risk for cancer. Prevention measures at the broadest level such as the population, group or community, might be oriented to lowering the overall level of alcohol use, reducing the number of consumers practicing high-risk drinking or

17 Much of the discussion about alcohol and cancer tends to be folded into analyses of the role of diet. Alcoholic beverages are part of diet but their unique risks, benefits, and status should not be overlooked.

16

reducing the frequency of high risk drinking practices in the population-at-large. For individuals at risk of cancer who are regular drinkers, a complementary goal might be to lower their daily and weekly alcohol intake. Enhanced screening and early intervention and treatment for problem drinkers also constitute primary prevention of cancer if such measures lead to lower alcohol consumption.

The range of distinctive strategies with regard to preventing drinking-related cancers is not large but, in combination, their potential is substantial. These strategies arise out of a body of literature devoted to the prevention of a broad range of alcohol problems. Typically, they focus on: 1) laws, policies and regulations related to the distribution and sale of alcohol; 2) mass media and other population-level health promotion measures; and, 3) targeted information and best advice campaigns, including efforts by health practitioners to inform users of service or target populations about low-risk drinking and abstention. When used in combination, these measures can be assumed to reduce the risks of alcohol-related cancers by reducing the overall rate of alcohol consumption and preventing an increase in heavy drinking and directly encouraging heavy drinkers to reduce their intake of alcohol.

Potential for prevention

A large percentage of cancers are preventable through changes in lifestyle, drinking patterns, and diet. Such lifestyle changes are conceivably open to influence from public policy and other interventions. Doll (1996) notes that both nature and nurture play major roles in the development of cancers, and devotes much of his writings to the latter. In his words:

The practical aspects of nurture...have been demonstrated by the discovery of many avoidable causes and by the fact that the incidence of nearly all the common cancers varies greatly on migration from one country to another and, in stable populations, over time. If the causes responsible for this variation could be identified and controlled we could reduce the age-specific incidence of the disease by some 80-90%. Half of this could be achieved by the application of existing knowledge (Doll, 1996, p.178).

Others have voiced a similar perspective. Oliveria et al (1997), for instance, observe that cancer is largely an avoidable disease and that more than two-thirds of cancers might be prevented through lifestyle modification. Specifically, diet, including alcohol-intake, is thought to be related to roughly one-third of all cancer cases in North America (American Cancer Society, 1999; Canadian Cancer Society, 1999).

Some researchers have suggested that trends in certain cancers are associated with population trends in alcohol consumption. Writing on the increased incidence in head and neck cancers in European males, Sankaranarayanan et al., (1998) postulate that the rising rates are related to the rising consumption of alcohol and cigarettes in Central and Eastern Europe. The authors conclude that:

The increase in incidence is most marked in young and middle-aged males and the changes are found to be related to birth-cohort, with rates increasing in successive birth cohorts after 1910 (Plesko et al., 1994). Per capita consumption of alcohol has declined in France in the last three decades and the recent decline in incidence and mortality from oropharyngeal and laryngeal cancers are consistent with the trends in alcohol use...(Sankaranarayanan et al., 1998, p. 4785).

In general, there is a substantial body of research that points to a strong association between per capita consumption and extent of heavy drinking (Edwards et al., 1994, Holder & Edwards, 1995). Risk of alcohol-related cancers tends to increase with amount consumed and the proportion of heavy consumers tends to be higher in those countries with higher per capita rates of consumption.

In Canada, there are no recent studies based on the relationship between alcohol consumption trends and cancer rates (see Anglin et al., 1995 for data from 1963-1983). While carcinogenesis develops over many years, it is interesting to note that both cancer rates and drinking levels have followed a similar stable or downward trend over the past decade. The prevalence of current drinkers in Ontario in 1998 was the lowest in a decade, with 82% of men and almost 73% of women reporting having consumed alcohol within the past year. Rates of daily drinking have also dropped from earlier years for both men and women, with 10% of male drinkers and 5% of female drinkers consuming alcohol on a daily basis in 1998 (see Table 7). Per capita alcohol sales have also declined. According to Statistics Canada, Ontarians aged 15 and up, bought 97.2 litres of alcohol in 1997-98, down from 134 litres in 1976 and 121.7 litres in 1988 (Statistics Canada, June 24, 1999). This downward trend appears to be reversing, however. Also, sales data generally underestimate per capita consumption, as the latter would also include homemade products and alcohol from illegal sources.

In contrast, there are emerging and potentially worrisome drinking trends. The proportion of men who reported consuming five or more drinks in a single sitting on a weekly basis rose to one in four in 1998, up from 16% in 1987 and 1977. During the same period, the rate of heavy drinking among women rose incrementally, from 4% in 1977 to 5% in 1987 to 6% in 1998 (see Table 7).

Table 7. Percentage of Current Drinkers, Daily Drinkers and Binge Drinkers, Ontario, 1977, 1987, 1998

	Adult Women (aged 18+)			Adult Men (aged 18+)		
	1977	1987	1998	1977	1987	1998
% Drinking in past year	73.4	78.8	72.5	85.9	87.6	82.0
% Drinking Daily	5.7	6.7	5.0	19.5	16.6	9.8
% Drinking 5+ drinks ¹⁸ at a sitting	4.1	4.9	6.3	16.3	15.9	24.6

Source: Ontario Drug Monitor 1998: Alcohol, Tobacco and Illicit Drug Use, 1977-1998.

According to Cancer Care Ontario, cancer incidence and mortality rates have been falling for most of the past decade. In men, the decline is most pronounced for lung colorectal and stomach cancer. In women, falling rates in breast and colorectal cancer have been partially offset by rising rates of lung cancer. Nevertheless, the number of cancer cases and cancer deaths is expected to increase in coming decades concurrently with population growth, longer life spans and the aging of the boomer generation (Cancer Care Ontario, March 1999). Therefore, any advancement in prevention, however small, has the potential to substantially reduce cancer-related costs, both human and economic.

In summary, over the past decade or so declines in overall cancer rates, and specifically alcohol-related cancers have mirrored declines in per capita alcohol sales, percentage of current drinkers and percentage of daily drinkers in the population. However, per capita sales rates appear to be on the upswing, as are the rates of heavy or high-risk drinking among vulnerable populations including women.¹⁹

As life expectancy lengthens and the Ontario population grows, cancer cases and deaths will rise, as will health-related costs. While data from several years ago indicate that 2.1% of all cancers are directly attributable to alcohol (Single et al., 1995), its role in potentiating the impact of tobacco, by far the biggest risk factor for cancer, has yet to be calculated. It can thus be argued that, at minimum, maintaining or reducing per capita consumption and lowering the incidence of risky drinking patterns among selected groups will make a positive contribution to the prevention of cancer in Ontario.

⁻

¹⁸ In Canada, a standard drink contains 13.5 g of alcohol, the equivalent of a 5 oz glass of wine, a 12 oz serving of regular strength beer, or a 1.5 oz serving of distilled spirits

¹⁹ Interestingly, while Aboriginal Peoples have higher rates of problem drinking and alcohol addiction than the general population, their overall incidence of cancer of all sites is lower. Specifically, native men had lower-than-average rates of cancer of the colon, lung and prostate as well as of lymphoma and leukemia but a higher rate of kidney cancer. Native women had a significantly higher-than-average incidence of cancer of the gallbladder, cervix and kidney but lower rates of cancer of the colon, breast, uterus and lymph nodes (MacMillan et al, 1996). http://www.cma.ca/cmaj/vol-155/issue-11/1569.htm

Approaches to Prevention

Much of the popular literature addressing the prevention of alcohol-related cancer deals less with developing strategies *per se* and more with setting reasonable drinking targets defined variously as:

- "No more than 1 drink a day," (Harvard Center for Cancer Prevention, 1999).
- "Alcohol consumption should be limited or avoided" (International Union Against Cancer, 1999).
- "If you don't drink alcohol, don't start. If you do drink...limit yourself to no more than 2 drinks per day for men and one for women" (American Institute for Cancer Research, 1999).
- "If you drink alcohol, whether beer, wine or spirits, moderate your consumption... limits should not exceed between 20 to 30 grams of ethanol per day (i.e. about two to three drinks of beer, wine or spirits each day) and may be lower than this for women." (European Code Against Cancer).

Most recommendations are presented within the general context of dietary guidelines and healthy lifestyle choices. For example, the American Cancer Society (ASC) recommends that individuals: 1) choose most of the foods they eat from plant sources; 2) limit their intake of high-fat foods, particularly from animal sources; 3) be physically active: achieve and maintain a healthy weight; and 4) limit consumption of alcoholic beverages, if they drink at all. The latter point is clarified in ACS's 1999 Nutrition and Prevention Recommendations as follows:

Public health officials [should] advise people who already drink alcoholic beverages to limit their intake to two drinks per day for men and one drink per day for women. Women generally tolerate alcohol less well than men as a result of smaller body size and greater ability to absorb alcohol. Women with an unusually high risk for breast cancer might reasonably consider abstaining from alcohol. Children and adolescents, pregnant women, people taking medications affected by alcohol, and those who are driving, operating machinery, or unable to limit themselves to moderate drinking should abstain from alcohol consumption (American Cancer Society, 1999).20

The Canadian Cancer Society's guidelines are very similar, with the second of its *Seven Steps of Health*, encouraging Canadians to "choose a variety of lower fat, high fibre foods, maintain a healthy body weight and limit... alcohol intake" (Canadian Cancer Society, 1999).²¹ Moreover, the Canadian Cancer Society endorses *Canada's Food Guide for Healthy Canadians* which states that "for most adults, moderate drinking means no more than 1 drink a day and

20

²⁰ See http://www2.cancer.org/prevention/index.cfm?prevention=recommendations.

²¹ See http://www.cancer.ca/info/pubs/sevene1.htm for more information.

no more than 7 drinks a week. ²² Having more than 4 drinks on any one occasion, or more than 14 drinks a week are a risk to health and safety. Women who are pregnant or breast-feeding are advised to avoid alcohol."

These guidelines, released a decade ago, were consistent with the definition of moderate drinking offered by *Canada's Drug Strategy* at the time. Interestingly, they differ slightly from the recommendations in the technical background report upon which the Food Guide nutrition recommendations were based. The latter states, among other things, that a healthy diet should "include no more than 5% of total energy as alcohol, or 2 drinks daily, whichever is less" (*Canadian Dietary Guidelines*, *Recommendations and Standards*).²³

Since the publication of both these documents, there has been much research on the "health benefits" of alcohol. A group of internationally respected researchers from the University of Toronto and the Addiction Research Foundation (now the Centre for Addiction and Mental Health) reviewed the literature and, in 1997, released the Low Risk Drinking Guidelines ²⁴ (LRDGs). Intended for use in health promotion initiatives targeting healthy adults, the LRDGs seek to balance the benefits of alcohol to heart health with the increased risks of myriad health and social problems including injury, violence and chronic disease, including cancer. They recommend that alcohol consumption be limited to no more than 2 standard drinks on any single day – up to a weekly maximum of 14 standard drinks for men, and 9 standard drinks for women. Consuming alcohol at or below these levels, together with other recommendations such as drinking slowly, waiting at least one hour between drinks, and eating while drinking can minimize the risks alcohol poses to health by limiting overall exposure to ethanol, and eliminating heavy drinking episodes.

The LRDGs also advise that no one start drinking alcohol for its protective effect against heart disease as less risky alternatives such as exercise, better nutrition and quitting smoking are recommended. Those who choose to drink can achieve benefits with as little as one drink every other day. Those seeking help for a drinking problem are encouraged to follow the advice of their counsellor or health professional. Pregnant or breastfeeding women, individuals engaged in potentially dangerous activities or responsible for the safety of others, and persons on certain types of medication or at risk of health problems such as liver disease are advised to drink less or not at all.

While setting and disseminating information about low-risk drinking levels is considered an important component in prevention, to date the efficacy of these messages and guidelines in influencing drinking behaviour has not been determined (Walsh et al., 1998). Some even posit that the mere existence of guidelines, or publicized changes in recommended daily or weekly limits, encourages those who abstain from alcohol to start drinking, and drinkers, particularly those who already drink at high levels, to increase their alcohol consumption.

-

¹⁸ One drink equals 1 bottle (or about 350 mL) of beer, 150 mL (or about 5 oz) of wine or 50 mL (or about 1 $\frac{1}{2}$ oz) of liquor.

²³ See http://www.sfu.ca/~ifremont/lesson1.html

²⁴ See Appendix 2 for a more comprehensive discussion of the Low Risk Drinking Guidelines.

Nevertheless, the LRDGs provide health practitioners and the general public with clear, practical and research-based advice on drinking levels and practices. These guidelines are meant to maximize the benefits of alcohol for certain segments of the population while minimizing the overall risks to health and safety for drinkers and non-drinkers alike. All other things being equal, the LRDGs can be expected to have as much impact as guidelines related to diet or exercise. Their influence will be maximized, however, if they are part of a comprehensive approach that also includes environmental supports in the form of controls on alcohol availability, effective enforcement of existing liquor laws and guidelines and community-based prevention and alcohol policy initiatives.

A comprehensive approach to the prevention of alcohol-related cancer is consistent with the landmark *Harvard Report on Cancer Prevention*. The authors recommend that "alcohol control programs ...go beyond awareness and education to bring about basic change at the institutional, community and public policy level to create an environment that discourages underage drinking and excessive alcohol consumption" (Colditz et al., 1997, p. S49). They advocate reducing the availability of alcohol, increasing excise taxes to fund community-based prevention campaigns, requiring responsible beverage service programs, and eliminating irresponsible advertising.²⁵

The potential role of alcohol policies in preventing cancer is of growing interest to both cancer and alcohol researchers. Austoker (1994), for example, points out that a large portion of the total morbidity and mortality attributable to alcohol occurs among moderate drinkers, even though individually they are at a lower risk of problems (see also Edwards et al., 1994). He suggests that the best way to reduce the risks associated with alcohol consumption is to combine national and local population-based alcohol policies with brief interventions by general practitioners aimed at high-risk individuals (Austoker, 1994). Doll (1996) likewise suggests that education, taxation, and medical interventions have the possibility of reducing the prevalence of heavy drinking and thus reducing cirrhosis of the liver and certain cancers.

In general, research evidence on the impact of control and regulatory measures is stronger, more consistent, and more broadly supported internationally than is the case for research evidence on education and information dissemination (e.g., Moskowitz, 1989; Edwards et al., 1994; Holder & Edwards, 1995; Munro, 1997).

_

²⁵ In a study on the effects of alcohol advertising on consumption, Saffer (1996) concludes "although limited, economic studies to date suggest that either new restrictions on advertising or more counter-advertising could help reduce levels of alcohol use" (p.271).

D. Recommendations

An environmental perspective

In developing the recommendations below, the Alcohol Work Group has adopted what in the alcohol prevention literature is known as the environmental perspective. The term as applied to alcohol problems is finding renewed popularity, although the older epidemiological paradigm focusing on the host, agent and the environment is not out of step with this perspective and continues to hold sway with many health professionals and policymakers. The environmental perspective claims that there are numerous factors that contribute to drinking-related problems. Among them, the conditions related to alcohol distribution, promotion, sale and consumption are particularly critical.

Access to alcohol is an important aspect of the environment of alcohol sales and consumption and can be broken down into several categories: *price* (e.g., price of alcohol compared to other goods and services); *geography* (e.g., number of outlets per capita); *time* (e.g., hours of sale and number of selling days of the week); *psychosocial factors* (e.g., advertising practices and social views of drinking); and *demography* (e.g., low legal drinking age).

Alcohol is a consumer product and, in the marketplace, behaves much like other consumer products (Bruun et al., 1975). On balance, if it is relatively inexpensive, extensively promoted and sold widely, available at most hours of the day and with few restrictions on the age or condition of the purchaser, one might expect high rates of drinking and drinking-related problems. Research examining price and taxation, legal age of consumption, density of alcohol retail outlets, and serving practices, for example, has found associations between the degree of public access to alcohol and various alcohol-related problems (Holder & Edwards, 1995).

Prevention of alcohol-related cancers will require consideration of structural and environmental conditions related to alcohol distribution and sale. This is particularly important for the following three reasons: 1) environmental conditions can be modified by broad social policy; 2) a change in policy can reduce risk for many people and therefore is cost effective; and 3) previous research has shown that policies bearing on drinking environments are particularly effective in reducing drinking-related risks. A number of other factors, including behaviors of current or future consumers of alcohol, interventions by professionals, societal attitudes to alcohol, and awareness of risks associated with certain drinking patterns and levels are also important to address within a comprehensive prevention strategy.

The challenge is less that of finding new strategies than that of determining which strategies, or combination of strategies, are most effective at a given time and place. At the same time, political, logistic, and resource/economic constraints must be negotiated so that these strategies, in synergistic combination, are implemented. Health-oriented policies and interventions do not just happen. They require strong support from populations and

decision-makers. Unfortunately, the views of the public may not always be consistent with what research points to as the most effective strategies (e.g., Giesbrecht & Greenfield, 1999).

Recommendations of Miller, Rootman et al. (1995)

An environmental perspective on cancer prevention, and the prevention of alcohol-related cancer in particular, underlined the recommendations of the *Report of the Task Force on the Primary Prevention of Cancer* (Miller, Rootman, et al., 1995). The authors noted that cancers attributable to alcohol were largely preventable. In keeping with a broad environmental perspective, they recommended that: a) guidelines for low risk consumption of alcoholic beverages be developed and promoted; b) governments resist pressures to reduce prices of alcohol since the societal costs of increased consumption greatly outweigh the economic benefits to the alcohol and hospitality industries; c) prevention interventions aimed at reducing excessive consumption be population-based; d) the provincial government keep its existing system of alcohol distribution and not move toward deregulation of alcohol sales; e) a publicly administered mandatory server training be introduced in Ontario and its efforts and impact evaluated; and f) community mobilization to encourage support for alcohol control measures be increased.

These recommendations are still relevant today. Indeed, progress has been made on some fronts. The Low-risk Drinking Guidelines have been widely distributed and plans are underway for a more comprehensive campaign. And the relative price of alcohol beverages has not declined in recent years in Ontario. However, there is also cause for concern: recent efforts to deregulate alcohol sales; a growing emphasis on alcohol sponsorship and marketing; a far from optimum server-training program. Population-based strategies and community mobilization related to alcohol policy could also be strengthened.

Toronto Cancer Prevention Coalition Alcohol Work Group Recommendations Cancer is one of the few alcohol-related problems where the association between consumption and risk is largely linear. That is, the higher the consumption, the greater the risk. Measures that stabilize or reduce per capita consumption have the potential for reducing the risk of cancer and should be supported.

The focus of the recommendations in the pages that follow, then, is on strategies that reduce drinking-related harm by influencing high-risk and overall alcohol consumption in Ontario. These strategies fall in the domains of policy, education and research, and call for sustained commitment and involvement from governments, specific professions and interest groups, and individuals.

The Alcohol and Cancer Working Group recommends that the Toronto Cancer Prevention Coalition work collaboratively with other agencies and institutions to:

1. Promote healthy alcohol policies by:

a) Persuading the Ontario and Canadian governments to retain strong controls on alcohol availability and avoid policies or practices that lower prices of alcohol, increase outlet density, or expand access to alcohol.

Controls on sales and service

Currently, the province regulates the sale of alcohol through the Liquor Control Board of Ontario (LCBO) and Alcohol and Gaming Commission of Ontario (AGCO). Among the benefits of the system are responsible sale and service training and practices such as challenge and refusal programs to prevent the sale of alcohol to underage purchasers and intoxicated patrons. These controls operate in both licensed establishments and retail outlets like liquor stores, beer stores and Ontario wine outlets. Alcohol control measures exercised by the AGCO include the regulation of days and hours of operation of licensed establishments, granting of liquor licenses and enforcement of compliance with licensing regulations and alcohol advertising guidelines. In recent years there have been a number of changes to the regulatory system governing alcohol in Ontario — many of them emphasizing deregulation and increased availability. As noted earlier, alcohol policy research shows that when restrictions are lifted, the well-being of communities is compromised. The Alcohol Work Group strongly urges that existing alcohol control systems remain in place, existing laws and regulations be better enforced and further efforts to privatize be resisted.

Controls on prices and taxes

Pricing, including taxation of beverage alcohol, can be an effective and scientifically established means of limiting alcohol availability, and thus reducing consumption. Drinkers are price sensitive; heavy and dependent drinkers at least as much as moderate drinkers. Reducing the cost of alcohol through price reductions and/or changes in tax structure can result in greater buying power for the consumer, leading to increased consumption and increased exposure to alcohol-related harms. The LCBO standardizes prices for its products and provides lower prices for some lower alcohol products. These practices help to promote moderate consumption and should be maintained. The Alcohol Work Group encourages the Toronto Cancer Prevention Coalition to recognize the role of taxes and price controls in limiting alcohol availability, promoting public health and preventing alcohol-related problems, including cancer.

Controls on advertising and promotion practices

Alcohol availability is also influenced by advertising and promotional strategies. Arms-length regulatory agencies such as the AGCO and the CRTC have a role to play in monitoring alcohol product marketing. Guidelines and/or restrictions on advertising and sponsorship should be strictly enforced, especially where certain groups (e.g., women) are targeted without concomitant public education on the potential risks of even low-level consumption. Liquor control boards also have a role to play in ensuring that their marketing practices continue to serve the public interest and uphold their broad social responsibility mandate.

b) Persuading the Ontario government to make server intervention training mandatory for all licensees.

Drinking rates and patterns can be affected by responsible service practices in places where alcohol is sold or served. Server training generally covers practices that prevent patrons from becoming intoxicated. Training typically covers ways to avoid overservice and intoxication. Sample topics include: serving standard drinks, pacing drinks, serving food, understanding how alcohol is metabolized and the factors that influence metabolization (e.g., tolerance for alcohol, gender, body weight, fatigue, food in stomach, presence of other drugs, etc.), legal responsibilities regarding service to minors and the intoxicated, and ways to deal with intoxicated patrons.

In Ontario, server training is only mandatory under certain conditions. For example, when a new liquor license is issued or when a license is under disciplinary action. Some municipalities have set policies that make server training mandatory for anyone involved in the service of alcohol at a special occasion permit event on their property. However, this is not the case throughout the province. Given the research evidence that server training programs can both reduce heavy drinking and promote responsible serving practices, the Alcohol Work Group recommends that recognized server intervention programs be made mandatory for all managers and staff involved in alcohol service. We also recommend that these programs be periodically evaluated, and updated and improved based on the findings.

Currently, Smart Serve is the only server intervention program recognized by the AGCO. However, there are gaps in groups receiving training, retraining requirements, enforcement of responsible service practices and research on the impact of the program. The Alcohol Work Group believes that addressing these gaps would improve the program and have a beneficial impact on service practices and drinking norms in licensed establishments.

c) Persuading Health Canada, the Ministry of Health, the Canadian Cancer Society, Dieticians of Canada and others to officially endorse the Low-Risk Drinking Guidelines and allocate resources to the development and dissemination of clinical practice guidelines and relevant professional development opportunities.

The Low-Risk Drinking Guidelines were developed from a population-based perspective. They strike a balance between the harms and benefits associated with alcohol consumption based on the latest research. As noted earlier, the LRDGs set a daily upper limit of two standard drinks for both men and women, with a weekly maximum of 9 drinks for women given their greater vulnerability to alcohol's effects due to smaller body size and other differences. The Guidelines discourage "bingeing" or periodic heavy drinking. They acknowledge the benefits to some people of low amounts of alcohol but also indicate that there are other ways to attain to improve heart health, including a better diet, not smoking and getting more exercise. Finally, the Guidelines recognize a number of groups and situations where less alcohol is better and no alcohol may be best.

There is research to indicate that the risk of cancer increases as alcohol consumption levels

rise. If we were to look at alcohol consumption strictly from a cancer prevention perspective, no drinking would be preferable. However, alcohol also has some health benefits for some groups. The Low-Risk Drinking Guidelines effectively balance these two sides, particularly in cases where population-level messages are required.

There are slight inconsistencies between the LRDGs and drinking limits recommended by *Canada's Food Guide*. As noted earlier, it appears that the alcohol recommendations were nuanced so as to support the CCSA/ARF moderate drinking guidelines in existence at the time the Food Guide was released. Since the latter have been updated based on the latest research, it is expected that inconsistencies related to drinking limits and days off from drinking, for example, will be eliminated in upcoming revisions to *Canada's Food Guide*.

Physicians, dentists, nutritionists, nurse practitioners, and other medical personnel have an opportunity to educate patients, and screen for and manage health problems. Yet few are trained in how to address alcohol and other drug issues in their practice, particularly in the context of prevention. Like other groups, health professionals are exposed to persistent messages about the benefits of alcohol and may be providing inaccurate or outdated information to their patients. Developing evidence-based tools, resources and training opportunities based on the latest research on alcohol and health would improve the consistency of messages to the public and, in particular, to groups in contact with the health system. Clinical practice guidelines would also facilitate screening for and early identification of drinking problems and alcohol-related cancers.

Dissemination and uptake of clinical tools and resources would be facilitated if they were developed and endorsed by key organizations and opinion leaders in the health sector. The Alcohol Work Group therefore recommends that Health Canada, the Ministry of Health, the Canadian Cancer Society, Dieticians of Canada and others officially endorse the *Low-Risk Drinking Guidelines* and allocate resources to the development and dissemination of clinical practice guidelines and tools, as well as relevant professional development opportunities.

d) Persuading the Ministry of Health to explicitly recognize alcohol as a risk factor for cancer, particularly cancer of the breast, in the Mandatory Program Standards for Public Health and outline areas for public health activity in this area.

The Mandatory Program Standards for Public Health guide the work of municipal public health departments across the province in the areas of health protection and promotion. The current standards have been in place since December 1997. The section on early detection of cancer focuses primarily on increasing awareness of screening for breast and cervical cancers. The section on chronic disease prevention discusses healthy weights, physical activity, nutrition, tobacco-free living and sun protection but not alcohol explicitly. The section on Injury Prevention, including Substance Abuse Prevention, requires boards of health to, among other things: 1) support policies and educate the public and targeted groups about low-risk drinking, 2) work with workplaces and school and college and university communities to address alcohol and other drug issues, and 3) work with health professionals

to enhance their knowledge and skills about substance abuse prevention. Explicit recognition of alcohol as a risk factor for cancer, as well as a requirement to increase the proportion of Ontarians who consistently follow the Low-Risk Drinking Guidelines, would promote awareness of health practitioners active in or in contact with public health settings and enhance the work of the LRDG Campaign Committee.

d) Persuading the Ministry of Education and Training to officially renew its commitment to a comprehensive Drug Education Policy Framework and require all school boards to review their current practices and take steps to ensure they meet the prescribed standards.

School-based education programs can complement initiatives directly aimed at reducing alcohol-related problems such as cancer. They can play a role in delaying the onset of drinking and educating young people about low risk consumption practices, both of which can reduce overall lifetime exposure to alcohol.

School settings offer opportunities to reach a large number of youth and help them to develop skills and knowledge that will contribute to positive health practices in later years. The ability to influence health choices spans JK to OAC.

In order for school-based programs to be effective, however, their delivery must be focused, intensive, repeated, tailored to the specific audience, and offered in combination with other interventions. When combined with alcohol control policies and community-based efforts rooted in the family, workplace, government and media, school-based education programs can play a role in increasing awareness and may contribute to changing values and behaviours of students. The Best Advice paper *Alcohol and Drug Prevention Programs for Youth: What Works* by the Centre for Addiction and Mental Health (CAMH) identifies some of the components of effective programs school systems might wish to put in place.

A Drug Education Policy Framework requiring schools to develop a comprehensive approach to alcohol and other drug issues would provide clarity and guidance to educators, parents and students regarding prevention and early intervention programming, peer education, community supports and policies and procedures for dealing with student drinking.

2. Support targeted education by:

a) Working with Cancer Care Ontario, public health, health promotion and substance abuse prevention groups to educate the public and groups at risk about the links between alcohol and cancer and encourage them to follow the Low-Risk Drinking Guidelines.

Wider dissemination and awareness of the Low Risk Drinking Guidelines may contribute to changing norms about appropriate levels of consumption. A population-based strategy to disseminate the Low Risk Drinking Guidelines to the citizens of Toronto would target the media, health professionals, schools, social/recreational facilities, libraries, licensed establishments and workplaces. Effective strategies for dissemination would take into consideration the age, gender, literacy level, and culture of the intended audience.

At the college and university level, effective social marketing campaigns are needed to discourage immoderate consumption. University and colleges must also adopt alcohol policies that support a low-risk drinking environment in student residences and on campus.

Social marketing campaigns can be useful communication and education tools. Mass media is most likely to be effective when it is used to set the agenda for public discussion. Currently there is diverse and potentially conflicting information regarding the impact of alcohol on health. A social marketing campaign could help to clarify the messages and offer research-based guidelines. Such a campaign would also need to include specific messages for populations who drink heavily and are therefore at higher risk for alcohol-related cancers.

b) Working with medical schools and professional associations to educate human service professionals about the links between alcohol and cancer and provide them with the tools and resources they need to screen for risk and intervene at an early stage.

There is research to show that a portion of the public responds favourably to changing their behaviour around alcohol and tobacco use when they receive a health message or a brief intervention from their physician.

Health professionals continue to be the first contact for health information about alcohol and tobacco for a significant proportion of the population. Enabling human service practitioners such as physicians, nurses, social workers, addictions workers, counselors and others to discuss the links between alcohol and cancer and ways to lower risk may facilitate early screening and intervention for both cancer and alcohol problems. It may also contribute to changing drinking practices among some groups of patients and clients.

Enhanced screening for, and treatment of, problem drinking behaviour, while secondary prevention of addiction, constitute primary prevention of alcohol-related cancer and should be supported.

3. Expand cancer research by:

a) Encouraging Cancer Care Ontario, the Canadian Cancer Society and addictions research organizations to improve data collection related to alcohol-related cancers and ensure this information is publicly available in a timely manner.

Background research conducted in the preparation of this paper revealed a paucity of Canadian data on alcohol and cancer. If collected over a period of time, such data can uncover trends in types of cancers, patterns of drinking, geographic regions and connections with other lifestyle factors that may prove useful for planning prevention and treatment programs.

Periodic reports on the status of alcohol consumption, problems and policy developments, and links to cancer trends and patterns are needed. It is also important to monitor and evaluate the impact of prevention and treatment initiatives and keep the public abreast of the findings. Cancer Care Ontario, the Canadian Cancer Society, the Centre for Addiction and Mental Health and the Canadian Institutes for Health Research have an important role to play in these areas.

b) Encouraging Canadian research institutions to play a lead role in standardizing data collection on alcohol and cancer in order to facilitate sharing and verification of research outcomes in different jurisdictions, both locally and internationally, and ensure researchers take into account both volume of drinking and drinking patterns in their studies.

There is a lack of consistency in the way information about cancer and its association to alcohol is collected and recorded. For example, there are differing definitions of light, moderate and heavy drinking, binge drinking, standard drink size, pattern of drinking, and years of drinking. There is also inconsistency in the recording of primary and secondary sites of cancer cause of death, and lifestyle factors and diseases that may have preceded the cancer and may have played a role in its development (i.e. liver cirrhosis preceding liver cancer).

Much of the research involving alcohol and cancer uses self-report information on the *volume* of alcohol consumed by the participants. Research in other domains indicates that drinking *patterns* may be related to a wide variety of health issues. A greater understanding of the effects of alcohol consumption in the development of cancer could be achieved if, in addition to volume, drinking patterns were also measured. The risks involved with different patterns of drinking should also be explored in relation to other lifestyle factors such as smoking, nutrition, and physical activity, as well as contextual factors such as the social and physical environments.

c) Encouraging funders of cancer research to support projects that address underdeveloped areas of knowledge or less understood cancers, and Canadian research institutes to increase funding for addictions research.

Current statistics from the Canadian Cancer Society do not record liver cancer in their morbidity and mortality data. There is a strong link to alcohol consumption and cirrhosis of the liver. Cirrhosis of the liver is a pre-existing condition for liver cancer. In order to understand the impact of alcohol on liver cirrhosis and cancer, this data is required.

Studies focusing on specific geographic areas provide an opportunity for researchers to discover more about potential causes and prevention of cancer. It is recommended that there be more research conducted in locations and among populations where numbers of alcohol-related cancers are expected to be high.

Local information, especially for a municipality the size of Toronto, is important for fine-tuning the approach for prevention of alcohol-related cancers. This fine-tuning may be according to geographic area, culture, age or gender. However, in light of the methodological constraints of relatively infrequent events such as mortality from certain cancers, these studies may need to be long-term in order to allow for collapsing of data over several years. It is recommended that more studies be conducted on the role of alcohol and the development of particular cancers and that the focus of this research be on the population of Toronto and Ontario.

Some sectors of the population may be more (or less) vulnerable to developing alcohol-related cancer. Causal factors are inevitably interconnected. However, relatively little is known about the interaction of various causal factors such as alcohol use, environmental hazards, lifestyle conditions, and/or genetic predisposition. It is recommended that population-based research be conducted to further elucidate these relationships, including studies that look at populations with exceptional vulnerabilities, such as heavy drinkers and smokers living in hazardous ecological environments.

Toronto received 80,000 immigrants from 169 countries in 1997. Over 80 languages are spoken in the city. By 2001, foreign-born residents will comprise more than 50 per cent of the population. Research into the relationship of alcohol, cancer and culture is needed to study causal effects and interventions. It is recommended that more research be devoted to the studying the drinking patterns in different ethno-racial groups, the role alcohol plays in the development of particular cancers, and effective strategies for prevention among these groups.

Given the societal costs related to alcohol use and to alcohol-related cancers, it is recommended that Canadian research institutes increase funding for addictions research in general, and research into effective prevention and intervention strategies in particular.

E. Conclusion

This paper has provided an overview of the links between alcohol and cancer and suggested several areas for preventive action. Underlining our recommendations are three core messages: 1) that the cancer community continue to recognize and pay attention to alcohol as a risk factor for cancer; 2) that the public health and addictions fields more explicitly address cancer as a risk factor for alcohol consumption in their educational, prevention and screening activities; and 3) that all devote more attention and resources to population-based approaches to cancer prevention, including the development, maintenance and enforcement of health-promoting policies regarding the distribution, promotion, sale, service and consumption of alcohol.

Bibliography

Adlaf, E.M., Paglia, A. & Ialomiteanu, A. (1998). Ontario Drug Monitor 1998: Alcohol, tobacco, and illicit drug use, 1977. Toronto: Centre for Addiction and Mental Health Research Document, Series #4.

Allen, B., Anglin, L., & Giesbrecht, N. (1999). Effects of others' drinking as perceived by community members. *Canadian Journal of Public Health*, 89 (5), 337-341.

American Cancer Society (1999). The importance of nutrition in cancer prevention. [WWW document] URL http://www2.cancer.org/prevention/index.cfm?prevention=recommendations.

Anderson, L.M., Souliotis, V.L., Chhabra, S.K., Moskal, T.J., Harbaugh, S.D., & Kyrtopoulos, S.A. (1996). N-nitrosodimethylamine-derived O(6) methylguanine in DNA of monkey gastrointestinal and urogenital organs and enhancement of ethanol. *International Journal of Cancer*, 66, 130-134.

Anglin, L., Mann, R. E., & Smart, R. G. (1995). Changes in cancer mortality rates and per capita alcohol consumption in Ontario, 1963-1983. *International Journal of the Addictions*, 30 (4), 489-95.

Austoker, J. (1994). Reducing alcohol intake. BMJ, 308 (6943), 1549-1552.

Bode, J.C., & Bode, C. (1992). Alcohol malnutrition and the gastrointestinal tract. In R. Watson & B. Watzl (Eds.), *Nutrition and alcohol* (pp. 403-428). Boca Raton, FL: CTC Press.

Bode, C., & Bode, J.C. (1997). Alcohol's role in gastrointestinal tract disorders. *Alcohol Health & Research World*, 21, 76-83.

Bondy, S., Rehm, J., Ashley, M.J., Walsh, G., Single, E., & Room, R. (1999). Low-risk drinking guidelines: The scientific evidence. *Canadian Journal of Public Health*, *90*, 264-271.

Boutron-Ruault, M.C., Faivre, J., Dop, M.C., Quipourt, V., & Senesse, P. (1995). Tobacco, alcohol, and colorectal tumors: A multistep process. *American Journal of Epidemiology*, 141, 1038-1046.

Boutron-Ruault, M.C., Senesse, P., Faivre, J., Couillault, C., & Belghiti, C. (1996). Folate and alcohol intake: Related or independent roles in the adenoma-carcinoma sequence? *Nutrition & Cancer*, 26, 337-346.

Bowlin, S.J., Leske, M.C., Varma, A., Nasca, P., Weinstein, A., & Caplan, L. (1997). Breast cancer risk and alcohol consumption: Results from a large case-control study. *International Journal of Epidemiology*, 26 (5), 915-23.

Boyle, P., Macfarlane, G.J., Blot, W.J., Chiesa, F., Lefebvre, J.L., Azul, A.M., deVries, N., & Scully, C. (1995). European School of Oncology Advisory report to the European Commission for the Europe Against Cancer Programme: oral carcinogenesis in Europe. *European Journal of Cancer. Part B, Oral Oncology, 31B* (2), 75-85.

Bradley, K. A., Badrinath, S., Bush, K., Boyd-Wickizer, J., & Anawalt, B. (1998). Medical risks for women who drink alcohol. *Journal of General Internal Medicine*, 13(9), 627-39.

Bruun, K., Edwards, G., Lumio, M., Makela, M., Pan, L. Popham, et al. (1975). *Alcohol control policies in public health perspective*, Vol. 25. Helsinki: The Finnish Foundation for Alcohol Studies.

Canadian Cancer Society (1999). Canadian Cancer Statistics.

Canadian Cancer Society (n.d./2000). Eating for the good of your health: tips to help reduce your risk of cancer. [WWW document]. URL http://www.cancer.ca/info/pubs/eatinge1.htm

Cattaruzza, M.S., Maisonneuve, P., & Boyle, P. (1996). Epidemiology of laryngeal cancer. European Journal of Cancer. Part B, Oral Oncology, 32B (5), 293-305.

Chhabra, S.K., Souliotis, V.L., Kyrtopoulos, S.A., & Anderson, L.M. (1996). Nitrosamines, alcohol, and gastrointestinal tract cancer: Recent epidemiology and experimentation. *In Vivo*, 10, 265-284.

Chyou, P.H., Nomura, A.M., & Stemmermann, G.N. (1995). Diet, alcohol, smoking and cancer of the upper aerodigestive tract: A prospective study among Hawain Japanese men. *International Journal of Cancer*, 60, 616-621.

Colditz, G.A., Dejong, W., Emmons, K., Hunter, D.J., Mueller, N., & Sorensen, G. (1997). Harvard Report on cancer prevention. Volume 2: Prevention of human cancer. *Cancer Causes & Control*, 8 (Suppl 1), S1-S50.

Colditz, G.A., Stampfer, M., Willett, W., Hennekens, C., Rosner, B., & Speizer, F. (1990b). Prospective study of estrogen replacement therapy and risk of breast cancer in postmenopasual women. *Journal of the American Medical Association*, 264, 2648-2653.

Colombo, M. (1998). The role of hepatitis C virus in hepatocellular carcinoma. Recent Results in Cancer Research, 154, 337-344.

Corrao, G., Bagnardi, A., Zambon, A., & Arico, S. (1999). Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis. *Addiction*, 94 (10), 1551-1573.

Doll, R. (1996). Nature and nurture: possibilities for cancer control. Carrinogenesis, 17 (2), 177-184.

Doll, R., Forman, D., La Vecchia, C., & Verschuren, P.M. (1993). Alcoholic beverages and cancers of the digestive tract and larynx. In P.M. Verschuren (Ed.) *Health issues related to alcohol consumption*, pp. 125-166. Brussels: ILSI Europe.

Doll, R., Peto, R., Hall, E., Wheatley, K., & Gray, R. (1994). Mortality in relation to consumption of alcohol: 13 years' observation on male British doctors. *British Medical Journal*, 309, 911-918.

Eckardt, M.J., File, S.E., Gessa, G.L., Grant, K.A., Guerri, C., Hoffman, P.L., Kalant, H., Koop, G.F., Li, T.K., & Tabakoff, B. (1998). Effects of moderate alcohol consumption on the central nervous system. *Alcoholism, Clinical & Experimental Research*, 22, 998-1040.

Edwards, G., Anderson, P., Babor, T.F., Casswell, S., Ferrence, R., Giesbrescht, N. et al. (1994). *Alcohol policy and the public good.* Oxford: Oxford University Press.

Enger, S.M., Ross, R.K., Paganini-Hill, A., Longnecker, M.P., & Bernstein, L. (1999). Alcohol consumption and breast cancer oestrogen and progesterone receptor status. *British Journal of Cancer*, 79, 1308-1314.

English, D.R., Holman, C.D., Milne, E., Winter, M.J., Hulse, G.K., Codde, G., Bower, C.I., Cortu, B., de Klerk, N., Lewin, G.F., Knuiman, M., Kurinczuk, J.J., & Ryan, G.A. (1995). *The quantification of drug caused morbidity and mortality in Australia, 1992.* Canberra: Commonwealth Department of Human Services and Health.

Erickson, P.G. (1997). Reducing the harm of adolescent substance use. *Canadian Medical Association*, 156. [+ WWW document] URL http://www.drugtext.org/articles/ericks8.html.

European Code Against Cancer (n.d./2000). Preventing cancer, what I can do: I drink less alcohol. [WWW document]. URL http://telescan.nki.n1/code/leaflet2.html

Farber, E. (1996). Alcohol and other chemicals in the development of hepatocellular carcinoma. *Clinics in Laboratory Medicine*, 16, 377-394.

Ferraroni, M., Decarli, A., Franceschi, S., & La, V.C. (1998). Alcohol consumption and risk of breast cancer: a multicentre Italian case-control study. *European Journal of Cancer*, 34, 1403-1409.

Francesci, S., & La Vacchia, C. (1994). Alcohol and the risk of cancers of the stomach and colon-rectum. *Digestive Disease*, 12(5), 276-89.

Friedenreich, C. (1994). Increased risk of breast cancer with alcohol consumption in postmenopausal women (letter). *American Journal of Epidemiology*, 139, 541-542.

Friedenreich, C. M., Howe, G. R., Miller, A. B., & Jain, M. G. (1993). A cohort study of alcohol consumption and risk of breast cancer. *American Journal of Epidemiology*, 137 (5), 512-20.

Gapstur, S., Potter, J., Sellers, T., & Folsom, A. (1992). Increased risk of breast cancer with alcohol consumption in postmenopausal women. *American Journal of Epidemiology*, 136, 1221-1231.

Garidou, A.T.A.L.L., Signorello, L.B., Kalapothaki, V., & Trichopoulos, D. (1996). Life-style factors and medical conditions in relation to esophageal cancer by histologic type in a low-risk population. *International Journal of Cancer*, 68, 295-299.

Garro, A., & Lieber, C. (1992). Alcohol and cancer. Annual Review of Pharmacology and Toxicology, 30, 219-249.

Giesbrecht, N., & Greenfield, T.K. (1999). Public opinions on alcohol policy issues: a comparison of American & Canadian surveys. *Addiction*, 94 (4), 521-531.

Ginsberg, E.S., Mello, N.K., & Mendelson, J.H. (1996). Effects of alcohol ingestion on estrogens in postmenopausal women. *Journal of the American Medical Association*, 276, 1747-1751.

Giovannucci, E., Rimm, E.B., Acherio, A., & Stampfer, M. (1995). Alcohol, low-methionine, low folate diets, and risk of colon cancer in men. ?????, 87 (4), 223.

Glynn, S.A., Albanes, D., Pietinen, P., Brown, C.C., Rautalahti, M., Tangrea, J.A., Taylor, P.R., & Virtamo, J. (1996). Alcohol consumption and risk of colorectal cancer in a cohort of Finnish men. *Cancer Causes & Control*, 7, 214-223.

Goodman, M.T., Moriwaki, H., Vaeth, M., Akiba, S., Hayabuchi, H., & Mabuchi, K. (1995). Prospective cohort study of risk factors for primary liver cancer in Hiroshima and Nagasaki, Japan. *Epidemiology*, *6*, 36-41.

Graubard, B. I., & Korn, E. L (1999). Analyzing health surveys for cancer-related objectives. *Journal of the National Cancer Institute*, 91(12), 1005-16.

Gronbaek, D.A., Becker, U., Johansen, D., Tonnesen, H., Jensen, G., & Sorensen, H. (1998). Population based cohort study of the association between alcohol intake and cancer of the upper digestive tract. *British Medical Journal*, 317, 844-847.

Hammink, J. (1999). Nutrition education in the Netherlands: A joint enterprise. Paper presented at the 2nd UICC Cancer Management Meeting, Antwerp, Belgium, April 14-18, 1999. [WWW document]. URL http://www3.uicc.org/publ/antwerp/nutrition4.htm

Harnack, L.J., Anderson, K.E., Zheng, W., Folsom, A.R., Sellers, T.A. and Kushi, L.H. (1997). Smoking, alcohol, coffee, and tea intake and incidence of the exocrine pancreas: The Iowa Women's Health Study. *Cancer Epidemiology, Biomarkers & Prevention*, 6, 1081-1086.

Harvard Center for Cancer Prevention (n.d). Cancer prevention guidelines. [WWW document]. URL http://www.hsph.harvard.edu/Organizations/Canprevent/7ways.htm

Henderson, I., Harris, J., Kinne, D., DeVita Jr.V., Hellman, S., & Rosenberg, S. (1989). Cancer of the breast. In *Cancer: Principles & Practices of Oncology*, pp. 1197-1268. Philadelphia: JB Lippincott Company.

Holder, H., & Edwards, G. (Eds.) (1995). Alcohol and public policy: evidence and issues. Oxford: Oxford University Press.

Homann, N., Jousimies-Somer, H.J.K., Heine, R., & Salaspuro, M. (1997a). High acetaldehyde levels in saliva after ethanol consumption: Methodological aspects and pathogenetic implications. *Carcinogenesis*, 18, 1739-1743.

Homann, N., Karkkainen, P., Koivisto, T., Jokelainen, K., & Salaspuro, M. (1997b). Effects of acetaldehyde on cell regeneration and differentiation of the upper gastrointestinal tract mucosa. *Journal of the National Cancer Institute*, 89, 1692-1697.

Howe, G.R., Decarli, A., Kaldor, J.K., Marubini, E.M.A., Riboli, E., & Toniolo, P. (1991). The association between alcohol and breast cancer risk: Evidence from the combined analysis of six dietary case-control studies. *International Journal of Cancer*, 47, 707-710.

Hunter, D. J., & Willett, W. C (1996). Nutrition and breast cancer. Cancer Causes & Control, 7(1), 56-68.

International Agency for Research on Cancer (IARC) (Ed.) (1988). Alcohol drinking. Lyon: IARC.

International Union Against Cancer (UICC). (n.d.). WWW site. URL http://www.uicc.org

Jaber, M.A., Porter, S.R., Scully, C., Gilthorpe, M.S., & Bedi, R. (1998). The role of alcohol in non-smokers and tobacco in non-drinkers in the aetiology of oral epithelial dysplasia. *International Journal of Cancer*, 77, 333-336.

Jain, M., Howe, G. R., St Louise, P., & Miller, A. B. (1991). Coffee and alcohol as determinants of risk of pancreas cancer: a case-control study from Toronto. *International Journal of Cancer*, 47(3), 384-9

Kalant, H., & Khanna, J. (1989). The alcohols. In H. Kalant & W. Roschlau (Eds.), *Principles of medical pharmacology*, pp. 244-254. Toronto: Decker, Inc.

Kato, I., Dnistrian, A.M., Schwartz, M., Toniolo, P., Koenig, K., Shore, R.E., Akhmedkhanov, A., Zeleniuch-Jacquotte, A., & Riboli, E. (1999). Serum folate, homocysteine and colorectal cancer risk in women: A nested case-control study. *British Journal of Cancer*, 79, 1917-1922.

Kearney, J., Giovannucci, E., Rimm, E.B., Stampfer, M., Colditz, G.A., Ascherid, B., & Willett, W. (1995). Diet, alcohol, and smoking and the occurrence of hyperplastic polyps of the colon and rectum (United States). *Cancer Causes & Control*, 6, 45-56.

Kohlmeier, L., & Mendez, M. (1997). Controversies surrounding diet and breast cancer. *Proceedings of the Nutrition Society*, 56, 369-382.

La Vecchia, C., & Negri, E. (1989). The role of alcohol in esophageal cancer in non-smokers, and of tobacco in non-drinkers. *International Journal of Cancer*, 43, 784-785.

Levi, F., Pasche, C., Lucchine, F., & La Vecchia, C. (1996). Alcohol and breast cancer in the Swiss Canton of Vaud. *European Journal of Cancer*, 32A, 2108-2113.

Longnecker, M.P. (1992). Alcohol consumption in relation to risk of cancers of the breast and large bowel. *Alcohol Health & Research World*, 16, 223-229.

Longnecker, M.P. (1994). Alcoholic beverage consumption in relation to risk of breast cancer: Meta-analysis and review. *Cancer Causes & Control*, 5, 73-82.

Longnecker, M.P. (1995). Alcohol consumption and risk of cancer in humans: An overview. *Alcohol*, 12, 87-96.

Longnecker, M.P., & Enger, S.M. (1996). Epidemiologic data on alcoholic beverage consumption and risk of cancer. *Clinica Chimica Acta*, 246, 121-141.

Longnecker, M.P., Orza, M.J., Adams, M.E., Vioque, J., & Chalmers, T.C. (1990). A meta-analysis of alcoholic beverage consumption in relation to risk of colorectal cancer. *Cancer Causes & Control*, 1, 59-68.

MacDonald, __. (Ed.) (1999). Health issues related to alcohol consumption, 2nd Edition. Brussels: ILSI

Press.

Marshal, J. R., & Boyle, P. (1996). Nutrition and oral cancer. Cancer Cause & Control, 7(1), 101-11.

McPherson, K., Engelsman, E., & Conning, D. (1993). Breast cancer. In P.M. Verschuren (Ed.) *Health issues related to alcohol consumption*, pp. 221-244. Brussels: ILSI Europe.

Miller, A.B., Rootman, I., et al. (1995). Recommendations for the primary prevention of cancer. Report of the Ontario Task Force on the Primary Prevention of Cancer, March 1995.

Munro, G. (1997). School-based drug education: realistic aims or certain failure? Paper presented at the 8th International Conference on the Reduction of Drug Related Harm, Paris 26 March 1997. [+ WWW document] URL http://www.adf.org.au/cyds/papers/sded.htm.

National Cancer Institute of Canada (1999). Canadian Cancer Statistics 1999. Toronto, Canada

Oliveria, S.A., Christos, P.J., & Berwick, M. (1997). The role of epidemiology in cancer prevention. *Proceedings of the Society for Experimental Biology & Medicine, 216* (2), 142-150.

Plesko, I., Macfarlane, G.J., Evstifeeva, T.V., Obsitnikova, A. & Kramarova, E. (1994). Oral and pharyngeal cancer incidence in Slovakia 1968-1989. *International Journal of Cancer*, 56, 481-486.

Potter, J.D. (1996). Nutrition and colorectal cancer. Cancer Causes & Control, 7(1), 127-46.

Reichman, M., Judd, J., Longcope, C., Schatzkin, A., Clevidence, B., Nair, P., Campbell, W., & Taylor, P. (1993). Effects of alcohol consumption on plasma and urinary hormone concentrations in premenopausal women. *Journal of the National Cancer Institute*, 85, 722-727.

Ringborg, U. (1998). Alcohol and risk of cancer. Alcoholism, Clinical & Experimental Research, 22, 323S-328S.

Rosenberg, L., Metzger, L.S., & Palmer, J.R. (1993). Alcohol consumption and risk of breast cancer: A review of the epidemiologic evidence. *Epidemiological Reviews*, 144, 598-609.

Saffer, H. (1996). Studying the effects of alcohol advertising on consumption. *Alcohol Health & Research World*, 20 (4), 266-271.

Sankaranarayanan, R., Masuyer, E., Swaminathan, R. Ferlay, J., & Whelan, S. (1998). Head and neck cancer: a global perspective on etiology and prognosis. *Anticancer Research*, 18 (6B), 4779-86.

Schatzkin, A., & Longnecker, M. P. (1994). Alcohol and breast cancer. Where are we now? And where do we go from here? *Cancer*, 74 (Supplement), 1101-10.

Seitz, H.K. and Poschl, G. (1997) Alcohol and gastrointestinal cancer: Pathogenic mechanisms. *Addiction Biology* **2**, 19-33.

Seitz, H.K., Poschl, G. and Simanowski, U.A. (1998a) Alcohol and cancer. Recent Developments in Alcoholism 14, 67-95.

Seitz, H.K., Simanowski, U.A., Homann, N. and Waldherr, R. (1998b) Cell proliferation and its evaluation in the colorectal mucosa: Effect of ethanol. Zeitschrift fur Gastroenterologie 36, 645-655.

Simanowski, U.A., Stickel, F., Maier, H., Gartner, U. and Seitz, H.K. (1995) Effect of alcohol on gastrointestinal cell regeneration as a possible mechanism in alcohol-associated carcinogenesis. *Alcohol* 12, 111-115.

Single, E., Ashley, M. J., Bondy, S., Rankin, J, and Rehm, J. (1999a). Evidence regarding the level of alcohol consumption considered to be low-risk for men and women. Prepared for the Australian commonwealth department and aged care.

Single, E., Robson, L., Rehm, J., & Xi, X. (1999b). Morbidity and mortality attributable to alcohol, tobacco, and illicit drug use in Canada. *American Journal of Public Health*, 89 (3), 385-390.

Single, E., Robson, L., Xie, X., & Rehm, J. (1998). The economic costs of alcohol, tobacco and illicit drugs in Canada, 1992. *Addiction*, *93*, 991-1006.

Singletary, K.W. (1996). Alcohol and breast cancer: Interactions between alcohol and other risk factors. *Alcoholism, Clinical & Experimental Research*, 20, 57A-61A.

Singletary, K.W. (1997). Ethanol and experimental breast cancer: A review. *Alcoholism, Clinical & Experimental Research, 21, 334-339*.

Smith-Warner, S.A., Spiegelman, D., Yaun, S.S., van den Brandt PA, Folsom, A.R., Goldbohm, R.A., Graham, S., Holmberg, L., Howe, G.R., Marshall, J.R., Miller, A.B., Potter, J.D., Speizer, F.E., Willett, W.C., Wolk, A., & Hunter, D.J. (1998). Alcohol and breast cancer in women: A pooled analysis of cohort studies. *Journal of the American Medical Association*, 278, 535-540.

Swanson, C.A., Coates, R.J., Malone, K.E., Gammon, M.D., Schoenberg, J.B., Brogan, D.J., McAdams, M., Potischman, N., Hoover, R.N., & Brinton, L.A. (1997). Alcohol consumption and breast cancer risk among women under age 45 years. *Epidemiology*, 8, 231-237.

Thomas, D.B. (1995). Alcohol as a cause of cancer. Environmental Health Perspectives, 103, 153-160.

Torontoprofile III- Part I: Facts on the health of residents of Toronto. (June 1999). Toronto: Toronto District Health Council, Epidemiology Unit.

United States Department of Health and Human Services (1997). *Ninth special report to the U.S. Congress on alcohol and health from the secretary of health and human services.* Washington, DC.: U.S. Department of Health and Human Services, Public Health Service, National Institute of Health, National Institute on Alcohol Abuse and Alcoholism.

Walsh, G.W., Bondy, S.J., & Rehm, J. (1998). Review of Canadian low-risk drinking guidelines and their effectiveness. *Canadian Journal of Public Health*, 89(4), 241-247.

Weed, D.L., & Gorelic, L.S. (1996). The practice of causal inference in cancer epidemiology. *Cancer Epidemiology, Biomarkers & Prevention*, 5, 303-311.

World Health Organization: Programme on Cancer Control. (n.d). [WWW site].

URL http://who-pcc.iarc.fr

Wright, R.M., McManaman, J.L., & Repine, J.E. (1999). Alcohol-induced breast cancer: A proposed mechanism. Free Radical Biology & Medicine, 26, 348-354.

Yamada, K., Araki, S., Tamura, M., Sakai, I., Takahashi, Y., Sashihara, H., & Kono, S. (1997). Case-control study of colorectal carcinoma in situ and cancer in relation to cigarette smoking and alcohol use. *Cancer Causes & Control*, 8, 780-785.

Zhang, Y., Kreger, B.E., Dorgan, J.F., Splansky, G.L., Cupples, L.A., & Ellison, R.C. (1999). Alcohol consumption and risk of breast cancer: the Framingham Study revisited. *American Journal of Epidemiology*, 149, 93-101.

Zhao, L.P., Kristal, A.R., & White, E. (1996). Estimating relative risk functions in case-control studies using a nonparametric logistic regression. *American Journal of Epidemiology*, 144, 598-609.

Zumoff, B. (1997). Alcohol, estrogens, and breast cancer. *Journal of Clinical Endocrinology & Metabolism*, 82, 2378

Zumoff, B. (1998). Does postmenopausal estrogen administration increase the risk of breast cancer? Contributions of animal, biochemical, and clinical investigative studies to a resolution of the controversy. *Proceeding of the Society for Experimental Biology & Medicine, 217, 30-37.*