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Estimates of the current and future burden of cancer attributable to alcohol consumption in Canada

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ABSTRACT

Alcohol consumption is associated with elevated risk of oropharyngeal, laryngeal, esophageal, colon, rectal, breast, liver, pancreatic and stomach cancers. The purpose of this analysis was to provide national and provincial estimates of the number and proportion of cancers attributable to alcohol consumption in Canada and to project the numbers of potentially avoidable cancers using possible intervention scenarios. We estimated the population attributable risk (PAR) for cancers associated with alcohol consumption levels (drinks/day) using: i) relative risks obtained from the World Cancer Research Fund/(WCRF) reports or meta-analyses, ii) alcohol consumption (prevalence) data from the 2003 Canadian Community Health Survey, and iii) cancer incidence data from the 2015 Canadian Cancer Registry. We used potential impact fractions (PIFs) to estimate the future avoidable cancer burden under four counterfactual scenarios: (1) lowering alcohol consumption to meet the WCRF low risk guidelines, (2) meeting the Canada's Low-Risk Drinking Guidelines, (3) reducing daily intake by one drink/day, and (4) decreasing consumption to 50% of the 2003 levels by 2032. We estimated that 3282 incident cancer cases (5.2% of alcohol-associated cancers and 1.8% of all cancers) diagnosed in Canada in 2015 were attributable to alcohol consumption. At the current consumption levels, alcohol-attributable cancers are expected to increase to 10,122 (8.8% of cases among alcohol-associated cancers) by 2042. Under the best case scenario, reducing alcohol consumption to 50% of 2003 levels by 2032, could prevent 70,261 cases by 2042. Strategies that effectively reduce alcohol consumption at a population level can have a meaningful impact on reducing the cancer burden in Canada.

1. Introduction

Alcohol has been classified as a human carcinogen by the International Agency for Research on Cancer (IARC) since 1988 (International Agency for Research on Cancer, 1988). The IARC working group has concluded that alcohol consumption is a causal risk factor for developing cancers of the oral cavity, pharynx, larynx, esophagus, liver, colorectum, and breast (in females) (International Agency for Research on Cancer, 2010). The World Cancer Research Fund/ American Institute of Cancer Research (WCRF/AICR), and the

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Continuous Update Project further concluded that consuming more than three alcoholic drinks per day increases the risks of stomach cancer (World Cancer Research Fund/American Institute for Cancer Research, 2015b, 2016b). Evidence on alcohol drinking and pancreatic cancer risk was determined as being limited by the WCRF in the 2012 Continuous Update Project Report (World Cancer Research Fund/American Institute for Cancer Research, 2012). However, subsequent pooled analyses and meta-analyses have provided additional evidence that high alcohol consumption (i.e. > 4 drinks per day) leads to increased risk of pancreatic cancer (Bagnardi et al., 2015; Lucenteforte et al., 2012; Wang et al., 2016).

The WCRF/AICR stated that no level of alcohol consumption was proven to be safe when considering cancer risks (World Cancer Research Fund/American Institute for Cancer Research, 2007). To provide guidance on reducing the risks of alcohol-related diseases and injuries, the Canadian Centre on Substance Abuse (CCSA) released the first pan-Canadian low-risk alcohol drinking guidelines in 2011 recommending no more than two drinks per day, or 10 per week, for women and no more than three drinks per day, or 15 per week, for men (Butt et al., 2011). The Canadian Cancer Society recommends that if an individual chooses to drink it should be limited to less than one drink a day for women and less than two drinks per day for men to reduce the risks of developing cancer (Canadian Cancer Society, 2018). One Canadian standard drink is equal to 13.5 g of alcohol, which is equivalent to one five ounce glass of wine with 12% of alcohol content or a 12 oz bottle of beer with 5% of alcohol content (Butt et al., 2011).

Previous studies have estimated the cancer incidence and mortality attributable to alcohol consumption in Canada (Ouellet et al., 1979; Rehm et al., 2006) and worldwide (GBD 2016 Alcohol Collaborators, 2018; Praud et al., 2016; Roswall and Weiderpass, 2015; Whiteman and Wilson, 2016). The Global Burden of Disease Study estimated that 3.8% of all deaths were attributable to alcohol consumption globally (Rehm et al., 2009), making it the seventh leading cause of death in 2016 (GBD 2016 Alcohol Collaborators, 2018). It was estimated that the proportion of alcohol-attributable cancer cases worldwide grew from 3.6% in 2002 to 5.5% in 2012 (Boffetta et al., 2006; Praud et al., 2016). The analysis of Canadian consumer trends showed that alcoholic drink sales grew steadily between 2006 and 2011 and the growing trends were projected to continue in Canada (Agriculture and Agri-Food Canada, 2013). A clear understanding of the magnitude of the current and future cancer burden associated with alcohol consumption in Canada will demonstrate the potential for cancer prevention by reducing alcohol consumption. This can then inform development of cancer prevention strategies by national and provincial stakeholders.

In this study, we estimated the number and proportion of cancer cases in 2015 that were attributable to alcohol consumption in Canada and projected the future burden of alcohol-associated cancers up to 2042. In addition, we estimated the proportions of avoidable cancer cases by 2042 in Canada if alcohol consumption was reduced under four evidence-based counterfactual scenarios.

2. Methods

This paper is part of a series of exposure-specific manuscripts estimating the number and proportion of current and future cancer cases attributable to modifiable risk factors involving lifestyle, environment, and infectious agents in Canada. The methods have been described in detail previously (Brenner et al., 2018) and are included in brief here. To estimate the attributable and avoidable burden of cancer in Canada, three types of data were used: i) relative risk estimates for the association of alcohol consumption with associated cancers, ii) the prevalence of alcohol consumption in Canada and Canadian provinces by age and sex, and iii) age- and sex-specific cancer incidence data at both the national and provincial levels.

2.1. Current cancer burden - population attributable risk estimation

2.1.1. Latency period

A considerable latency period is presumed between alcohol consumption and cancer detection. As previously described (Brenner et al., 2018), we distinguish between a theoretical latency period (the time between initiation of exposure and cancer detection) and a measured latency period (the time between exposure measurement and cancer detection). Based on a review of large cohort studies, the average latency period is estimated to be approximately 12 years for breast, colorectal, oropharyngeal, and esophageal cancers and approximately nine years for larynx and liver cancers (Allen et al., 2009; Chen et al., 2011; Cho et al., 2012; Freedman et al., 2007; Ishiguro et al., 2009; Persson et al., 2013; Schutze et al., 2011; Weikert et al., 2009). Accordingly, we estimated the number of alcohol-attributable cancer cases in 2015 using alcohol consumption prevalence data from the 2003 Canadian Community Health Survey (CCHS) (cycle 2.1) (Statistics Canada, 2003). This time period corresponds to a latency period of 12 years for all associated cancer sites.

2.1.2. Relative risk estimate

We abstracted the relative risk (RR) estimates for alcohol consumption for pre-menopausal and post-menopausal breast, colon, rectal, liver, stomach, esophageal (squamous cell carcinoma only) and kidney cancers from the WCRF Continuous Update Project Reports (World Cancer Research Fund/American Institute for Cancer Research, 2012, 2015a, b, 2016a, b, 2017) (Table 1). RRs adjusted for age and site-specific confounders were selected for the analysis whenever available to partially control for confounding. All RRs were for consumption measured “in grams per day” to be consistent with alcohol consumption prevalence data which are reported in drinks per day. RRs were converted to the equivalent “drinks per day” based on the standard 13.5 g of alcohol per drink in Canada (Butt et al., 2011). The resulting values were then combined with the median alcohol consumption of the six exposure categories, which were 0, 0.2, 1.4, 2.4, 3.3, and 5.3 drinks per day. The RR of alcohol consumption for pre-menopausal breast cancer was applied for women age 50 and below, and the RR for post-menopausal breast was used for women above age 50 since the median age at natural menopause was reported to be age 51 among Canadian women (Costanian et al., 2018). For cancers of the oropharynx, larynx, and pancreas, we used RRs from a recent meta-analysis (Bagnardi et al., 2015).

2.1.3. Exposure prevalence estimates

The prevalence of alcohol consumption was obtained from national and provincial data in the 2003 CCHS. Details on the method used for the CCHS have been published (Beland, 2002). The average daily alcohol consumption was derived from participants' responses to a range of alcohol-related questions. Participants who responded “No” to questions on alcoholic beverage intake in the past 12 months and who had never consumed alcoholic drinks were defined as non-drinkers. Based on the reported average daily drinks or drinking status (i.e., current or past drinkers) and drinking frequency, survey respondents who were 20 years of age were grouped into five additional categories stratified by sex and age (Table 2). The five categories were: 0–≤1, > 1–≤2, > 2–≤3, > 3–≤4, > 4 drinks per day. The median number of drinks from each category was assigned to estimate risk exposure. For participants whose average daily drinks could not be directly estimated, the median daily drinks of the participants' categories were assigned. Details of respondents grouping procedure was previously published (Grundy et al., 2016).

2.1.4. Cancer incidence data

Cancer incidence data for adults aged 18 years and older were obtained from the population-based Canadian Cancer Registry (CCR) for the year 2015, as these were the most recent figures available at the

Table 1
Relative risks of cancers for alcohol consumption.

Cancer site	Level of exposure	Relative risk (95% confidence interval)	
		Men	Women
Colon[b]	10 g/day increase	1.1 (1.06–1.14)	1.03 (0.96–1.14)
Rectum[b]	10 g/day increase	1.10 (1.07–1.13)	1.09 (1.03–1.16)
Breast – Pre-menopause[a]	10 g/day increase	–	1.05 (1.02–1.08)
Breast – Post menopause[a]	10 g/day increase	–	1.09 (1.07–1.12)
Pancreas[f]	Light (≤12.5 g/day)	0.95 (0.89–1.01)	0.95 (0.89–1.01)
	Moderate (≤50 g/day)	1.03 (0.97–1.09)	1.03 (0.97–1.09)
	Heavy (> 50 g/day)	1.19 (1.11–1.28)	1.19 (1.11–1.28)
Oropharynx[f]	Light (≤12.5 g/day)	1.13 (1.00–1.26)	1.13 (1.00–1.26)
	Moderate (≤50 g/day)	1.83 (1.62–2.07)	1.83 (1.62–2.07)
	Heavy (> 50 g/day)	5.13 (4.31–6.10)	5.13 (4.31–6.10)
Stomach[d]	10 g/day increase	1.03 (1.01–1.05)	1.02 (0.90–1.15)
Liver[c]	10 g/day increase	1.03 (1.01–1.05)	1.19 (1.04–1.35)
Esophagus[e,h]	10 g/day increase	1.25 (1.12–1.41)	1.25 (1.12–1.41)
Larynx[f]	Light (≤12.5 g/day)	0.87 (0.68–1.11)	0.87 (0.68–1.11)
	Moderate (≤50 g/day)	1.44 (1.25–1.66)	1.44 (1.25–1.66)
	Heavy (> 50 g/day)	2.65 (2.19–3.19)	2.65 (2.19–3.19)
Kidney[g]	10 g/day increase	0.92 (0.89–0.97)	0.92 (0.89–0.97)

[a] Estimates from WCRF/IARC CUP: Breast Cancer 2017 Report (World Cancer Research Fund/American Institute for Cancer Research, 2017).
[b] Estimates from WCRF/IARC CUP: Colorectal Cancer 2011 Report (World Cancer Research Fund/American Institute for Cancer Research, 2011).
[c] Estimates from WCRF/IARC CUP: Liver Cancer 2015 Report (World Cancer Research Fund/American Institute for Cancer Research, 2015b).
[d] Estimates from WCRF/IARC CUP: Stomach Cancer 2016 Report (World Cancer Research Fund/American Institute for Cancer Research, 2016b).
[e] Estimates from WCRF/IARC CUP: Esophagus Cancer 2016 Report (World Cancer Research Fund/American Institute for Cancer Research, 2016a).
[f] Estimates from Bagnardi and colleagues (Bagnardi et al., 2015).
[g] Estimates from WCRF/IARC CUP: Kidney Cancer 2015 Report (World Cancer Research Fund/American Institute for Cancer Research, 2015a).
[h] Relative risk estimates for squamous cell carcinoma.

time of our study (except for the province of Quebec, for which we extrapolated to 2015 from 2010 data (Brenner et al., 2018)). For esophageal cancer, alcohol consumption was reported to increase the risk of squamous cell carcinoma (World Cancer Research Fund/American Institute for Cancer Research, 2016a); however, CCR cancer incidence data do not provide further details on morphological subtypes. We estimated the squamous cell carcinoma incidence rates to be 30% for men and 60% for women among all esophageal cancers that occurred in 2015. This estimate was based on a previous report of Canadian incidence trend projections of esophageal cancer by morphological subtypes (Otterstatter et al., 2012).

2.1.5. Population attributable risk estimation

The population attributable risk (PAR) was estimated for each cancer site stratified by sex and age with:

$$PAR = \frac{\sum_x (P_x \times ERR_x)}{1 + \sum_x (P_{ex} \times ERR_x)}$$

where P_x is the proportion of the population in alcohol consumption category x (Table 2), ERR_x is the excess relative risk ($RRx - 1$) in each consumption category. ERR_x is estimated using the following equation:

$$ERR_x = \exp(R_x \times G_x) - 1$$

where R_x is the excess risk per gram of alcohol consumption and G_x is the median consumption of alcohol in grams for category x.

Monte Carlo approaches used to estimate the 95% confidence intervals for these PAR estimates, as described elsewhere (Brenner et al., 2018).

To estimate the attributable cases (ACs) for each cancer site of interest, we multiplied the PARs by the 2015 CCR cancer incidence rates. AC estimates for individual sex, age groups and province/territory were

Table 2
Prevalence of alcohol consumption in Canada[a], 2003.

Age (years)	Prevalence (95% confidence interval)					
	Non-drinker	0–≤1 drink/day	> 1–≤2 drinks/day	> 2–≤3 drinks/day	> 3–≤4 drinks/day	> 4 drinks/day
Men						
20–34	4.4 (3.7–5.0)	65.2 (63.8–66.5)	16.5 (15.4–17.6)	6.1 (5.4–6.7)	2.5 (2.1–2.9)	3.1 (2.6–3.6)
35–44	4.3 (3.6–4.9)	70.3 (68.9–71.6)	14.7 (13.7–15.7)	4.7 (4.0–5.4)	1.6 (1.3–2.0)	1.9 (1.5–2.4)
45–64	3.1 (2.6–3.6)	67.4 (66.3–68.5)	19.3 (18.4–20.2)	4.1 (3.7–4.6)	1.9 (1.6–2.2)	1.6 (1.3–1.9)
≥65	4.9 (4.2–5.5)	69.6 (68.3–70.9)	17.2 (16.1–18.3)	2.9 (2.4–3.3)	1.3 (0.9–1.6)	0.9 (0.6–1.1)
Women						
20–34	7.3 (6.6–8.1)	80.6 (79.5–81.6)	7.1 (6.5–7.8)	1.7 (1.4–2.0)	0.5 (0.3–0.7)	0.4 (0.3–0.6)
35–44	7.0 (6.1–7.9)	81.9 (80.7–83.2)	7.0 (6.3–7.7)	1.2 (0.8–1.5)	0.2 (0.1–0.4)	0.2 (0.1–0.3)
45–64	7.5 (6.8–8.1)	81.2 (80.3–82.1)	7.5 (6.9–8.0)	1.2 (0.9–1.4)	0.3 (0.2–0.4)	0.1 (0.0–0.2)
≥65	14.2 (13.3–15.2)	77.9 (76.8–78.9)	4.1 (3.6–4.5)	0.4 (0.3–0.5)	0.1 (0.0–0.1)	0.0 (0.0–0.1)
Total						
20–34	5.8 (5.3–6.3)	72.8 (71.9–73.7)	11.8 (11.2–12.4)	3.9 (3.5–4.2)	1.5 (1.3–1.8)	1.8 (1.5–2.0)
35–44	5.6 (5.1–6.2)	76.1 (75.1–77.0)	10.9 (10.3–11.5)	3.0 (2.6–3.3)	0.9 (0.8–1.1)	1.1 (0.8–1.3)
45–64	5.3 (4.9–5.7)	74.4 (73.7–75.1)	13.3 (12.8–13.8)	2.7 (2.4–2.9)	1.1 (0.9–1.2)	0.8 (0.7–1.0)
≥65	10.1 (9.5–10.7)	74.2 (73.4–75.1)	9.8 (9.3–10.4)	1.5 (1.3–1.7)	0.6 (0.5–0.8)	0.4 (0.3–0.5)

[a] Data from cycle 2.1 of the Canadian Community Health Survey (2003).

also calculated whenever possible. The total proportion of attributable cancer cases associated with alcohol consumption for each cancer site was estimated as the total number of ACs for a given cancer, across all sex and age groups, divided by the total number of observed cancers for that particular site. Kidney cancer is the only cancer site reported to have reduced risk with consumption of two drinks per day or less (World Cancer Research Fund/American Institute for Cancer Research, 2015a). We presented the estimations on kidney cancers separately rather than a reduction from the total.

2.2. Future cancer burden – potential impact fraction (PIF) estimation

2.2.1. Prevalence of exposure projections

To project the future prevalence of alcohol consumption in Canada, we used the alcohol consumption prevalence data from the 1994, 1996, and 1998 National Population Health Surveys and the 2000, 2003, and 2005 CCHS. These six survey cycles used identical questions on alcohol consumption, and thus the prevalence estimated for these years are comparable. The 2007 and 2011 CCHS cycles were not included in the projection model because the questions related to alcohol was changed in these two cycles, making their prevalence non-comparable to the other survey cycles. For prevalence projection, historical data between 1994 and 2005 were modelled with multinomial logistic regression. We projected the probability of each drinking category to the year 2032 at the national and provincial levels and applied 10 year latency to estimate potential avoidable cancers in 2042. The projections of exposure prevalence were made under three main assumptions: i) the historical trends of alcohol consumption are predictive of the future trend; ii) no events occur during the projected period that drastically change the alcohol consumption pattern; iii) the probability of being in each drinking category relative to the probability of the reference non-drinker category is a logistic function of time.

2.2.2. Cancer incidence projections

Using 1983 to 2012 historical cancer incidence data and projected population data from Statistics Canada, we projected Canadian cancer incidence up to year 2042 (Poirier et al., 2019). The detailed methods and results for estimating cancer incidence in the future have been described elsewhere (Poirier et al., 2019). A summary of the method is also included in the method overview in this issue (Brenner et al., 2019).

2.2.3. Counterfactual scenarios

We examined a range of evidence-based counterfactual scenarios of future projected levels of alcohol consumption. These scenarios were selected as they either represent the recommendations made by national or international agencies, or they were possible aspirational objectives for alcohol consumption at population level. Counterfactual scenario one was based on successful instantaneous reduction in consumption to the level of the WCRF/AICR recommendation (≤2 drinks/day for men; ≤1 drink/day for women) (World Cancer Research Fund/American Institute for Cancer Research, 2007) in year 2018, whereas the second scenario was based on reduction to the Canadian low-risk alcohol drinking guidelines (≤3 drinks/day for men; ≤2 drink/day for women) (Butt et al., 2011). In a third scenario, we projected the potential future impact of everyone who reported drinking more than one drink per day reducing consumption by one drink per day from 2018. Lastly, we included the scenario that between 2018 and 2032 alcohol consumption would gradually decrease to 50% of the 2003 estimated prevalence levels.

2.2.4. PIF estimation

PIF uses the relative risk, the projected prevalence and the projected cancer incidence estimates to examine the potential impact of an exposure prevalence change or a population distribution shift (counterfactual). We used the RR shift method, which keeps the prevalence in each category constant while changing the RR of the category (Barendregt and Veerman, 2010), to estimate the counterfactual effects on scenarios that involve some reduction by the number of drinks:

$$PIF_i = \frac{\sum_j P_{ij}RR_{ij} - \sum_j P_{ij}RR^*_{ij}}{\sum_j P_{ij}RR_{ij}}$$

where P_{ij} is the projected prevalence for sex i (male or female) in category j of alcohol consumption, RR_{ij} is the RR for category j of sex i, and RR_{ij}^* is the RR for that category after a counterfactual scenario was applied.

We used the proportional shift method to estimate the counterfactual effects for scenarios that involve the reduction of prevalence among the drinkers, including the 0–≤1, > 1–≤2, > 2–≤3, > 3–≤4, and > 4 drinks/day categories:

$$PIF_i = \frac{\sum_j P_{ij}RR_{ij} - \sum_j P^*_{ij}RR_{ij}}{\sum_j P_{ij}RR_{ij}}$$

where P_{ij} is the prevalence for sex i in alcohol consumption category i, P^*_{ij} is the counterfactual prevalence in that category after a counterfactual scenario was applied, and RR_{ij} is the relative risk for that category.

Ethics approval was granted for this project by the Health Research Ethics Board of Alberta - Cancer Committee (HREBA.CC-14-0220_REN4).

3. Results

3.1. Prevalence of alcohol consumption

Based on data collected in the 2003 CCHS, we estimated that < 10% of the Canadian population over age 20 were non-drinkers. The majority of the population (> 80%) across all age groups reported daily consumption of less than two drinks (Table 2). The highest prevalence of heavy drinking (> 4 drinks/day) was reported among the 20–34 age group (1.8%), especially among men (3.1%), and the prevalence decreased with age. Based on the 2003 CCHS survey, we estimated that between 5.1%–11.7% of men and between 4.6%–9.7% of women exceeded the recommended limit for reduced cancer risks (no more than two drinks per day for men and no more than one per day for women) across different age groups. The prevalence estimates of alcohol consumption by sex and Canadian province/territory are shown in Supplementary Table 1.

3.2. Current cancer burden - population attributable risk

Overall, 3282 cancer cases in 2015 were estimated to be attributable to alcohol consumption, which represented 1.8% of cases among all cancers (n = 187,070) and 5.2% of cases among all alcohol-associated cancer sites (n = 63,535) (Table 4). Among the cancer sites associated with alcohol consumption, PARs were higher for upper aerodigestive tract cancers including cancer of the oropharynx (17.9%), esophagus (squamous cell carcinoma, 16.3%) and larynx (11.1%) (Tables 3 and 4). The highest numbers of attributable cases were associated with cancers of the breast (n = 791), colon (n = 745) and rectum (n = 503) given their higher incidence. The number of attributable cases in men (n = 2089) nearly doubled the number estimated for women (n = 1193). Across all sites with the exception of the liver, the PARs were higher in men than in women (Tables 3 and 4). The PARs and ACs attributable to alcohol consumption for Canadian provinces and territories are summarized in Supplementary Table 2. Results with confidence intervals are presented in Supplementary Table 3.

Consuming up to 30 g of alcohol (approximately two drinks) per day is associated with a reduction in the risk of kidney cancer (World Cancer Research Fund/American Institute for Cancer Research, 2015a). We estimated that 840 kidney cancers (n = 245 in women and n = 595

Table 3
Cancer cases and proportions attributable to alcohol consumption in Canada (2015)[b].

Age at exposure	Age at Dx	Colon			Rectum			Breast			Pancreas			Oropharynx		
		Obs.	PAR	AC	Obs.	PAR	AC	Obs.	PAR	AC	Obs.	PAR	AC	Obs.	PAR	AC
Men																
20–34	30–44	230	9.8	22	165	9.8	16				60	2.4	1	145	25.1	36
35–44	45–54	655	8.7	57	600	8.6	52				195	2.2	4	480	22.1	106
45–64	55–74	4130	8.9	367	2705	8.9	241				1315	2.3	30	1835	22.3	409
≥65	≥75	2930	7.6	222	1260	7.6	95				750	2.0	15	585	19.1	112
Total		7945	8.4	668	4730	8.5	404				2320	2.2	51	3045	21.8	663
Women																
20–34	30–44	245	1.3	3	180	3.8	7	2245	2.1	48	40	1.2	0	70	11.3	8
35–44	45–54	595	1.2	7	475	3.7	17	4920	3.0	147	150	1.1	2	215	9.9	21
45–64	55–74	3105	1.2	38	1425	3.7	52	12,685	3.7	466	1025	1.1	11	730	9.9	72
≥65	≥75	3120	0.9	29	825	2.7	23	4705	2.8	130	870	0.8	7	365	7.2	26
Total		7065	1.1	78	2905	3.4	99	24,555	3.2	791	2085	1.0	20	1380	9.3	128
Total																
20–34	30–44	475	5.4	26	345	6.7	23	2245	2.1	48	100	1.9	2	215	20.6	44
35–44	45–54	1250	5.1	64	1075	6.4	69	4920	3.0	147	345	1.7	6	695	18.3	127
45–64	55–74	7235	5.6	405	4130	7.1	293	12,685	3.7	466	2340	1.8	41	2565	18.8	481
≥65	≥75	6050	4.1	250	2085	5.7	118	4705	2.8	130	1620	1.3	22	950	14.5	138
Total		15,010	5.0	745	7635	6.6	503	24,555	3.2	791	4405	1.6	71	4425	17.9	791

Age at exposure	Age at Dx	Stomach			Liver			Esophagus[a]			Larynx		
		Obs.	PAR	AC	Obs.	PAR	AC	Obs.	PAR	AC	Obs.	PAR	AC
Men													
20–34	30–44	65	2.8	2	35	2.9	1	6	21.9	1	5	12.3	1
35–44	45–54	195	2.6	5	160	2.6	4	36	22.3	8	65	12.7	8
45–64	55–74	1100	2.7	29	1085	2.7	29	251	22.3	56	625	12.8	80
≥65	≥75	865	2.3	19	410	2.3	9	120	18.8	23	250	11.0	28
Total		2225	2.5	56	1690	2.6	44	413	21.3	88	945	12.3	116
Women													
20–34	30–44	40	0.9	0	10	7.7	1	0	12.0	0	10	5.4	1
35–44	45–54	120	0.8	1	45	7.5	3	14	9.8	1	20	5.7	1
45–64	55–74	530	0.8	4	250	7.5	19	124	10.0	12	115	5.8	7
≥65	≥75	560	0.6	3	210	5.7	12	129	7.3	9	55	4.3	2
Total		1250	0.7	9	515	6.8	35	267	8.6	23	200	5.4	11
Total													
20–34	30–44	105	2.1	2	45	4.0	2	6	21.9	1	15	7.7	1
35–44	45–54	315	1.9	6	205	3.7	8	50	18.9	9	85	11.0	9
45–64	55–74	1630	2.1	34	1335	3.6	48	374	18.2	68	740	11.7	87
≥65	≥75	1425	1.6	23	620	3.4	21	250	12.8	32	305	9.8	30
Total		3475	1.9	65	2205	3.6	79	680	16.3	111	1145	11.1	127

Abbreviations: AC = Attributable cases due to exposure, Dx = Diagnosis, Obs. = Total number of observed cases per age-sex group, PAR = Population attributable risk.

[a] Squamous cell esophageal carcinoma.

[b] Confidence intervals for these results are available in Supplementary Table 3.

in men) were prevented by alcohol consumption, which was equivalent to 14.2% of kidney cancers diagnosed in 2015. These results are presented in Supplementary Table 6.

3.3. Future cancer burden – potential impact fraction

Our projection for alcohol consumption prevalence suggests a decreasing trend for non-drinkers and light drinkers and an increasing trend for moderate drinkers. The number of heavy drinkers is projected to remain the same (Supplementary Fig. 1).

The projection of future cancer burden associated with alcohol consumption shows that both the PAR and the number of incident cases for all associated cancer sites will continue to increase steadily up to 2042 for both men and women across Canada if no interventions are implemented to change the consumption prevalence trend (Table 5). PARs are estimated to increase nearly two-fold by 2042 for all associated cancer sites. With higher predicted numbers of cancers, the ACs are projected to triple the current levels for colon, rectum, breast, pancreas, stomach, and liver cancers by the year 2042. Esophageal cancer is the only associated cancer projected to have a decline in incident cases, reducing from 680 cases in 2015 to 615 cases in 2042; however, the ACs are estimated to increase because of the higher attributable risk estimate due to increased consumption. The future burden of cancer attributable to alcohol consumption in the Canadian provinces is presented in Supplementary Table 4.

The proportions and numbers of avoidable cancer cases in 2042 and the cumulative preventable cancer cases are presented in Table 5. Between 18,365 and 70,261 alcohol-attributable cancers could be prevented by 2042 if one of the four counterfactual scenarios was in place in 2018. The scenario of a 50% reduction in alcohol consumption prevalence by 2032 showed the greatest potential in reducing alcohol-attributable cancers. It could prevent 5061 associated cancers in 2042 and 70,261 cumulative cases by 2042 if the scenario was applied in 2018 (Fig. 1). Reducing the number of drinks by one for everyone who reported drinking more than one drink per day could prevent 4799 associated cancers in 2042 and it could all together prevent 68,954 cancer cases between 2018 and 2042. Meeting the WCRF guidelines for reduced cancer risks could avoid 36,536 incident cancer cases attributable to alcohol consumption by 2042. This scenario is the only scenario that could reduce greater numbers of cumulative attributable

Table 4
Summary of cases and proportions of cancer in Canada in 2015 attributable to alcohol consumption[a].

Cancer site	Total			Men			Women		
	Observed cases[b]	Attributable cases[c]	% attributable[d]	Observed cases	Attributable cases	% attributable	Observed cases	Attributable cases	% attributable
Colon	15,010	745	5.0	7945	668	8.4	7065	78	1.1
Rectum	7635	503	6.6	4730	404	8.5	2905	99	3.4
Breast	24,555	791	3.2				24,555	791	3.2
Pancreas	4405	71	1.6	2320	51	2.2	2085	20	1.0
Oropharynx	4425	791	17.9	3045	663	21.8	1380	128	9.3
Stomach	3475	65	1.9	2225	56	2.5	1250	9	0.7
Liver	2205	79	3.6	1690	44	2.6	515	35	6.8
Esophagus[g]	680	111	16.3	413	88	21.3	267	23	8.6
Larynx	1145	127	11.1	945	116	12.3	200	11	5.4
All associated cancers[e]	63,535	3282	5.2	23,313	2089	9.0	40,222	1193	3.0
All cancers[f]	187,070	3282	1.8	94,910	2089	2.2	92,160	1193	1.3

[a] Data on prevalence of alcohol exposure from the Canadian Community Health Survey (2003).
[b] Number of observed cancer cases in Canada in 2015 at individual cancer sites from the Canadian Cancer Registry.
[c] Number of cancer cases at individual cancer sites that can be attributed to alcohol exposure.
[d] Proportion of cancers at individual cancer sites attributable to alcohol exposure.
[e] All associated cancers includes all cancers known to be associated with alcohol exposure (as listed in the current table).
[f] All cancers includes all incident cancer cases in Canada for all ages in 2015.
[g] Squamous cell esophageal carcinoma.

cancer cases in women than in men. Compliance with Canadian low-risk alcohol drinking guidelines had the lowest PIF across all associated cancer sites; nonetheless, it was projected to prevent 1246 cancers in 2042 and 18,365 cancers cumulatively by 2042. Sex-specific projections are presented in Supplementary Fig. 2. Projections for Canadian provinces are presented in Supplementary Table 5.

4. Discussion

We estimated that, in Canada, over 3200 newly diagnosed cancer cases in 2015 could be attributed to alcohol consumption, which represented 5.2% of cases among alcohol-associated cancers, including colorectal, breast, pancreas, oropharyngeal, laryngeal, esophageal, stomach, and liver cancers, and 1.8% of all cancers diagnosed in that year. PARs were highest for oropharyngeal, squamous cell esophageal carcinoma, and laryngeal cancers. For ACs, cancers of the colon, breast and oropharynx had the highest number of cases. The PAR and the number of cases attributable to alcohol consumption were much higher in men than in women. We project that, with no intervention, in excess of 10,000 cancer cases would be attributable to alcohol consumption per year and the PAR could rise to 8.8% by 2042. A gradual reduction in alcohol consumption prevalence to 50% of the 2003 levels by 2032 was estimated to prevent over 5000 cancers in 2042 and > 70,000 cases cumulatively between 2018 and 2042.

Our results are comparable to previous studies conducted in other countries where alcohol-attributable cancer burden has been estimated, but our PAR estimates are lower than the estimates reported in these studies. Pandeya and colleagues estimated that 2.8% of all cancers diagnosed among Australian adults in 2010 could be attributed to alcohol consumption; they also noted a sex difference (3.0% for men and 2.5% for women) (Pandeya et al., 2015). The study identified oropharynx, squamous cell carcinoma of the esophagus, and larynx to have the highest PARs and colon and breast to have the largest number of alcohol-attributable cancer cases (Pandeya et al., 2015). A study conducted in the United Kingdom (UK) estimated that 4.0% of all cancers (4.6% for men and 3.3% for women) could be attributed to alcohol consumption in 2010 (Parkin, 2011). Our estimation of 1.8% of all cancers (2.2% in men and 1.3% in women) attributable to alcohol consumption is lower than the Australian and UK estimates. This difference could be largely explained by the lower alcohol consumption in Canada compared to the UK and Australia. Data from the WHO's Global Information System on Alcohol and Health show that the Canadian three-year averages (2003–2005 and 2008–2010) of alcohol consumption (per capita) and 2010 average daily intake (g/day) are both lower than those in the UK and Australia (World Health Organization, 2014). In addition, the WHO data on consumption patterns showed that in 2010 Canada had a lower prevalence of alcohol consumption in the past 12 months (77.1%) compared to the UK (83.9%) and Australia (84%).

To our knowledge, this analysis provides the most recent national and provincial estimates of current and future cancer burden attributable to alcohol consumption in Canada. Krueger and colleagues estimated the proportion of cancers in Canada attributable to several modifiable risk factors including alcohol consumption at the national and provincial levels in 2000 and 2013 (Krueger et al., 2016). They estimated that the proportions of cancer attributable to alcohol consumption were 3.5% (95% CI: 2.1%–4.8%) in 2000 and 3.9% (95% CI: 2.4%–5.3%) in 2013. Krueger et al. included a wider age range (15 years and above) and additional cancer sites, which included prostate (a very high incidence site) and ovary. Thus, their PIF estimates were higher than our results. We did not include ovarian and prostate cancers in our analysis, as WCRF/AICR does not conclude alcohol as a probable cause for these cancers (World Cancer Research Fund/American Institute for Cancer Research, 2018). Previous efforts were also made to estimate PARs and ACs at the provincial levels, such as in Ontario and Alberta (Cancer Care Ontario, 2014; Grundy et al., 2016). Our provincial estimates are comparable to previous results.

In an effort to provide the most current assessment on cancer burden, our estimates incorporated the latest cancer incidence data currently available in Canada and alcohol consumption prevalence estimates from the CCHS which is a nationally representative survey with population weights. In addition, we included cancer sites associated with alcohol consumption in order to reflect the latest evidence published by WCRF/AICR and meta-analyses. We included pancreatic and stomach cancers as recent evidence suggests that alcohol consumption is associated with an increased risk of these cancers (Bagnardi et al., 2015; World Cancer Research Fund/American Institute for Cancer Research, 2016b). These sites were not included in large-scale studies that estimated the PARs of alcohol consumption published prior to 2016. To be comprehensive, we included kidney cancer in our analysis and presented the results separately. We would like to emphasize that, although there is evidence that consuming up to two alcoholic drinks per day decreases kidney cancer risks (World Cancer Research Fund/

Table 5
Projections of alcohol attributable risks (%) and cases in 2042 in Canada with no interventions and projections of potential impact fraction (%) and preventable cases in 2042 under four counterfactual scenarios.

CTF[a]	Gender	Statistics	Colon	Rectum	Breast	Pancreas	Oropharynx	Stomach	Liver	Esophagus	Larynx	All
Base	Men	Projected cases	15,949	11,109		3967	3364	4139	3342	420	1230	43,520
	Men	PAR(%)	13.2	13.2		3.5	31.1	4.1	4.1	31.2	18.7	12.5
	Men	AC	2112	1471		140	1047	169	136	131	230	5436
	Women	Projected cases	14,683	6416	40,712	3501	1913	2573	909	195	186	71,086
	Women	PAR(%)	2.7	8	7.4	2.3	21.4	1.8	16.5	21.5	12.6	6.6
	Women	AC	396	513	3024	82	410	46	150	42	23	4686
	All	Projected cases	30,631	17,524	40,712	7467	5278	6712	4251	615	1415	114,606
	All	PAR(%)	8.2	11.3	7.4	3	27.6	3.2	6.7	28.2	17.9	8.8
	All	AC	2508	1984	3024	221	1457	215	287	173	253	10,122
1	Men	Projected cases	15,511	10,804		3942	3068	4110	3318	383	1177	42,315
	Men	PIF(%)	2.7	2.7		0.6	8.8	0.7	0.7	8.8	4.3	2.8
	Men	Prevented cases	437	305		24	296	30	24	37	52	1205
	Men	Cumulative cases	6739	4694		386	5448	424	387	806	849	19,733
	Women	Projected cases	14,535	6211	39,511	3471	1721	2556	842	175	176	69,198
	Women	PIF(%)	1	3.2	2.9	0.9	10.1	0.7	7.3	10.1	5.3	2.7
	Women	Prevented cases	147	204	1200	30	192	17	67	20	10	1888
	Women	Cumulative cases	1813	2507	15,552	404	2729	194	862	351	140	24,551
	All	Projected cases	30,047	17,015	39,511	7413	4790	6666	4160	558	1353	111,513
	All	PIF(%)	1.9	2.9	2.9	0.7	9.2	0.7	2.1	9.2	4.4	2.7
	All	Prevented cases	584	509	1200	54	488	47	91	57	62	3093
	All	Cumulative cases	8552	7201	15,552	790	8177	617	1249	1156	989	44,284
2	Men	Projected cases	15,751	10,971		3956	3210	4127	3332	401	1205	42,953
	Men	PIF(%)	1.2	1.2		0.3	4.6	0.3	0.3	4.6	2	1.3
	Men	Prevented cases	198	138		10	155	12	10	19	25	567
	Men	Cumulative cases	3189	2221		169	2964	186	170	439	420	9758
	Women	Projected cases	14,634	6343	40,288	3491	1832	2568	882	186	182	70,407
	Women	PIF(%)	0.3	1.1	1	0.3	4.2	0.2	2.9	4.3	2	1
	Women	Prevented cases	48	72	423	10	81	6	26	8	4	679
	Women	Cumulative cases	577	863	5323	128	1125	61	334	145	51	8607
	All	Projected cases	30,385	17,314	40,288	7447	5042	6695	4214	587	1387	113,359
	All	PIF(%)	0.8	1.2	1	0.3	4.5	0.3	0.9	4.5	2	1.1
	All	Prevented cases	246	210	423	20	236	18	36	28	29	1246
	All	Cumulative cases	3767	3084	5323	297	4089	247	504	584	472	18,365
3	Men	Projected cases	14,938	10,405		3902	2832	4061	3279	353	1118	40,888
	Men	PIF(%)	6.3	6.3		1.6	15.8	1.9	1.9	15.9	9.1	6
	Men	Prevented cases	1010	704		65	532	78	63	67	112	2631
	Men	Cumulative cases	14,674	10,224		976	9085	1063	969	1335	1699	40,023
	Women	Projected cases	14,506	6179	39,322	3465	1709	2553	836	174	174	68,918
	Women	PIF(%)	1.2	3.7	3.4	1	10.7	0.8	8	10.7	6	3
	Women	Prevented cases	176	236	1390	36	204	21	73	21	11	2168
	Women	Cumulative cases	2237	2975	18,518	500	2955	240	964	380	162	28,931
	All	Projected cases	29,445	16,585	39,322	7366	4541	6614	4115	527	1292	109,806
	All	PIF(%)	3.9	5.4	3.4	1.4	14	1.5	3.2	14.3	8.7	4.2
	All	Prevented cases	1187	940	1390	101	737	99	136	88	123	4799
	All	Cumulative cases	16,911	13,199	18,518	1476	12,040	1303	1933	1714	1860	68,954
4	Men	Projected cases	14,893	10,373		3897	2841	4055	3274	355	1115	40,802
	Men	PIF(%)	6.6	6.6		1.8	15.6	2	2	15.6	9.3	6.2
	Men	Prevented cases	1056	736		70	523	84	68	66	115	2718
	Men	Cumulative cases	14,703	10,246		1014	8415	1107	1005	1229	1660	39,377
	Women	Projected cases	14,485	6159	39,199	3460	1708	2550	833	174	174	68,743
	Women	PIF(%)	1.3	4	3.7	1.2	10.7	0.9	8.3	10.8	6.3	3.3
	Women	Prevented cases	198	256	1512	41	205	23	75	21	12	2343
	Women	Cumulative cases	2501	3202	19,946	559	2891	271	977	369	168	30,884
	All	Projected cases	29,377	16,533	39,199	7357	4549	6605	4108	528	1288	109,545
	All	PIF(%)	4.1	5.7	3.7	1.5	13.8	1.6	3.4	14.1	8.9	4.4
	All	Prevented cases	1254	992	1512	111	728	108	143	87	127	5061
	All	Cumulative cases	17,203	13,448	19,946	1574	11,306	1378	1982	1597	1828	70,261

Abbreviations: AC = Attributable cases due to exposure, CTF = counterfactual scenario, PAR = Population attributable risk, PIF = Potential impact fraction.

[a] Base = maintaining current alcohol consumption status. 1 = WCRF guideline of ≤2 drinks/day for men, and ≤ 1 drink/day for women. Scenario 2 = Canadian guideline of ≤3 drinks/day for men, and ≤ 2 drinks/day for women. Scenario 3 = everyone who drinks > 1 drink/day reduces # of drinks by 1. Scenario 4 = alcohol drinking prevalence decreases by 50% by 2032.

American Institute for Cancer Research, 2018), alcohol consumption at this level increases the risk of several other cancers which are included in our analysis.

This study has a number of limitations that could have affected our estimates. First, the prevalence of alcohol consumption was based on data collected from self-reported population surveys, which tend to underestimate the true intake levels by 30–70% (Shield et al., 2012) due to exclusion of certain populations (i.e. persons living on reserves, people who are institutionalized, and full-time members of the Canadian Forces), self-selection bias (i.e. non-response to survey by heavy drinkers), response bias (i.e. under-reporting of true consumption level). This underestimation of the alcohol consumption level could subsequently result in an underestimation of the attributable cancer burden. To address this limitation, we conducted a sensitivity analysis by using sales of alcoholic beverage data from Statistics Canada. In addition, consumption of unrecorded alcohol, including home-brewing

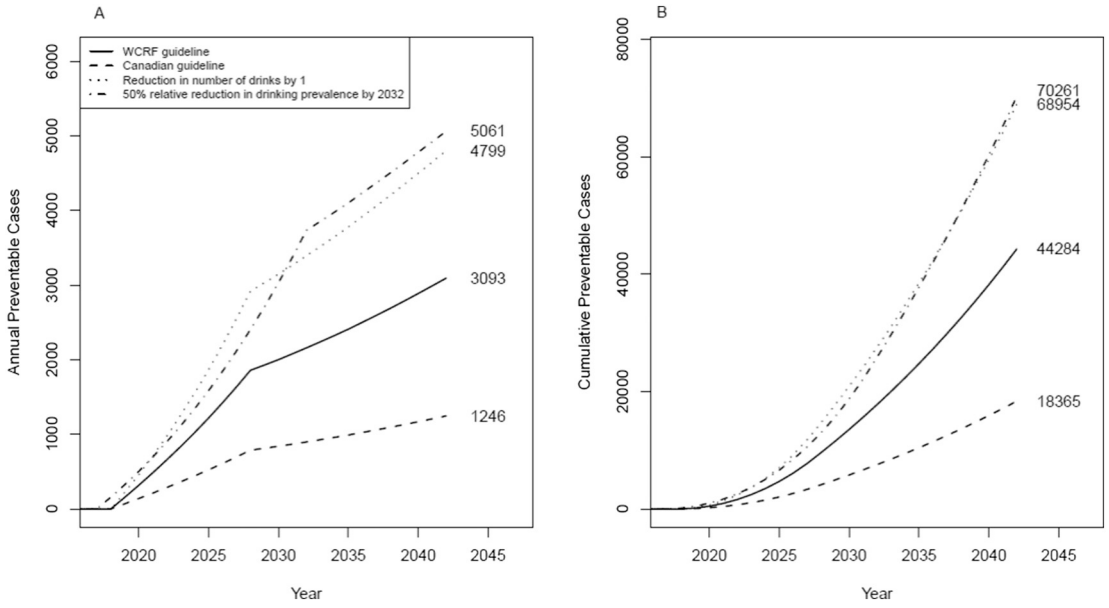

Fig. 1. A) Projected annual preventable cases attributable to alcohol consumption by applying four counterfactual scenarios; B) Projected cumulative preventable cases attributable to alcohol consumption by applying four counterfactual scenarios.

or illegal imports, was also taken into account when adjusting for under-reporting of alcohol consumption (Cancer Care Ontario, 2014; Macdonald and Giesbrecht, 1999). We used Ontario data to adjust for unrecorded alcohol consumption across all of Canada as these data do not exist elsewhere in the country. After these adjustments, the proportion of alcohol-associated cancers increased from 5.2% to 14.4%. It is important to note that the accuracy of the sensitivity analysis results is limited by an assumption that all alcohol sold was consumed, and that the national unrecorded alcohol consumption is similar to the Ontario estimates. Another limitation is that there will be some residual confounding of relative risk estimates. To reduce confounding, we included RRs adjusted for age and site-specific confounders in the analysis, when available. Residual confounding is likely to have biased the risk estimates to some extent and thus affected our PAR and PIF estimates. For example, Bagnardi et al. suggested that small yet significant residual confounding by smoking may contribute to the positive association between alcohol consumption, especially heavy consumption, and stomach cancer (Bagnardi et al., 2015).

4.1. Conclusion

In this study, we estimated the current and the future avoidable cancer burden attributable to alcohol consumption. Our analyses highlight the importance of developing public health strategies to reduce alcohol consumption and, thus, reduce the cancer burden attributable to alcohol consumption. Our PAR and PIF estimates can be instrumental in helping provincial and national policymakers and stakeholders understand the extent of current and future cancer burden caused by alcohol consumption. Although no level of alcohol consumption is considered completely safe with respect to cancer risk, a shift to total abstinence from alcohol consumption is unrealistic in countries like Canada. Our projections of the four counterfactual scenarios suggest that between 18,000 and 70,000 cancers could be avoided by 2042 if actions are taken now. These projections can guide policymakers in the development and evaluation of policies aimed at lowering alcohol consumption to reduce the future cancer burden. Future studies assessing the economic impact of cancer burden attributable to alcohol consumption would be useful to provide evidence of the economic impact of alcohol consumption on the Canadian healthcare system.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2019.03.020.

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